Turkish Journal of GERIATRICS

Volume: 23 • Issue: 4 • Year: 2020

The Official Scientific Journal of Turkish Geriatrics Society

e-ISSN: 1307-9948
www.turkgeriatri.org

www.turkgeriatri.org

e-ISSN: 1307-9948

The official scientific journal of Turkish Geriatrics Society

Member of IAGG

OWNER
On Behalf of Turkish Geriatrics Society
Yeşim **GÖKÇE KUTSAL**

EDITORIAL MANAGER
Orhan **YILMAZ**

TECHNICAL ASSISTANCE
Erkam EVLİCE

Turkish Journal of Geriatrics is indexed in: Thomson Reuters Science Citation Index Expanded (SCI-Exp) and Social Sciences Citation Index (SSCI) since 2008. And also in Scientific and Technological Research Council of Turkey (TÜBİTAK), Turkish Academic Network and Information Center (ULAKBİM) regional TR index (TR dizin) since 1998.

Published four times (March, June, September, December) a year

CORRESPONDANCE
Turkish Geriatrics Society
www.turkgeriatri.org
info@geriatri.org
www.geriatri.dergisi.org
editor@geriatri.dergisi.org

Date of Publication: 01 December 2020

Turkish Journal of
GERIATRICS
Volume: 23 • Issue: 4 • Year: 2020

INFORMATION TO AUTHORS

http://www.geriatri.dergisi.org/static.php?id=7

TURKISH JOURNAL OF GERIATRICS

PUBLICATION POLICY

Turkish Journal of Geriatrics is a peer-reviewed journal and is devoted to high standards of scientific rules and publication ethics. The Editors of the Journal accept to follow 'Editorial Policy' of the 'Council of Science Editors' (www.councilscienceeditors.org/).

Any article published in the journal is also published in electronic format and is shown at http://www.turkgeriatri.org or http://www.geriatri.dergisi.org/

Instructions for authors are based on the report of International Committee of Medical Journal Editors (Last Version)- (Uniform Requirements for manuscripts Submitted to Biomedical Journals, www.icmje.org).

Editor in Chief: Prof. Yesim GOKCE-KUTSAL, MD

Owner: Turkish Geriatrics Society www.turkgeriatri.org

INSTRUCTIONS FOR AUTHORS

Turkish Journal of Geriatrics is the official publication of Turkish Geriatrics Society and is published four times a year. Articles published in the journal are shown at http://www.turkgeriatri.org & http://www.geriatri.dergisi.org

Turkish Journal of Geriatrics is a peer-reviewed journal and is devoted to high standards of scientific rules and publication ethics. The Editorial Board Members of the Journal accept to follow 'Editorial Policy' of the 'Council of Science Editors' (www.councilscienceeditors.org/) and the guidelines provided by the Committee on Publication Ethics (COPE), the World Association of Medical Editors (WAME), the International Committee of Medical Journal Editors (ICMJE) for dealing with scientific misconduct, such as falsification of data, plagiarism, improprieties of authorship, violation of generally accepted research practices and redundant publication and duplicate publication.

Instructions for authors are based on the report of International Committee of Medical Journal Editors (Uniform Requirements for manuscripts Submitted to Biomedical Journals, www.icmje.org).

Manuscripts must be original and not under consideration by another publication at the time of submission. The authors must ensure that they have read and understood the details noted in the publication policy of our journal. Failure to comply can lead to delays in the processing of the manuscript, or even rejection.

INSTRUCTIONS FOR AUTHORS

Official language of the journal is **English.** Turkish Journal of Geriatrics invites submission of Original Articles based on clinical and laboratory studies. Review Articles are published only after the invitation from the Editorial Board.

Manuscripts and the necessary documents should be submitted online at: Online Manuscript Submission.

Authors are advised to keep a copy of their papers for reference. It is the responsibility of **all authors** to agree on the content of their paper before submission.

As recommended by TUBİTAK ULAKBIM, the authors should get their **ORCID** (Open Researcher and

Contributor ID) numbers from the web address free of charge: **http://orcid.org**

Preparation of Manuscript

Papers must be written in English. Authors should have their papers checked for linguistic accuracy by a native English speaker. For the language editing of the article and to get the **"Formal Certificate of Language Control and Correction"**, contact to the below addresses:

EDITAGE https://www.editage.com, **WILEY** https://www.wiley.com/en-tr, **SCRIBENDI** https://www.scribendi.com, **AMERICAN JOURNAL EXPERTS** http://www.journalexperts.com

The corrected manuscript should be sent to the journal after it has received the **"formal certificate of language control and correction"** – this certificate should be uploaded to journal on line system with the manuscript.

Articles published in the Turkish Journal of Geriatrics should be prepared in ethical rules. The ethical responsibilities of the articles belong to the authors. For all the studies both conducted on human beings and animals as well as drug research, ethical committee approval should be taken and a signed copy of **"Ethical Committee Approval"** should be uploaded to the journal system.

The manuscripts will not be published without a copy of the "ethical committee approval" document. For all the studies conducted on human beings **"Informed Consent"** of all the participants of the study should be taken.

Authors should obey the rules in **"Helsinki Declaration", "Good Medical Practice Guidelines"**, and **"Good Laboratories Practice Guidelines".**

Names of the patients, protocol numbers, etc which identify participants' identities should not be used in the manuscript. If the editorial board finds necessary, the admitted articles will be reviewed not only by the scientific advisors, but by the ethical advisors of the journal as well. Authors submitting an article must accept this situation.

All of the articles submitted to the Turkish Journal of Geriatrics should fit to the **"Information of authors"** details. The assessment process will not start until this step is completed.

Via online submission 1) English Title, 2) Names, Surnames and Titles of the authors, 3) Institutions, 4) Present communication details should be loaded to the system. Original articles and Invited Reviews should be between 1500-3500 words (excluding Abstract). When a manuscript is submitted, authors must provide a word count for both the abstract and the text. Editors can request that authors shorten their papers further.

The text of observational and experimental articles should be divided into sections with the headings Introduction, Materials and Method, Results, and Discussion. Long articles may need subheadings within some sections (especially the Results and Discussion sections) to clarify their content. Invited reviews and editorials are likely to take their own relevant main headings.

Abstract. A structured abstract of not more than 250 words in English should be structured, including Introduction, Materials and Method, Results, and Conclusion. New and important observations or aspects of the study should be emphasized. Abstracts of the review articles should be a brief overview of the main points from the review. Abstracts should reflect the whole manuscript and the consistency between the text. No abbreviations should be used in this section.

Keywords. Up to six keywords should be provided that might be used by researchers searching bibliographic databases for the paper. The authors have to use terms from the Medical Subjects Headings list from Index Medicus.(www.nlm.nih.gov/mesh/MBrowser.html)

Introduction. Acquaint the readers with the problem and with the findings of others. Quote the most pertinent papers and state clearly the nature and purpose of the work.

Materials and Method. Your clinical, technical or experimental procedures should be clearly explained. Previously published papers related to methods should be cited. Ethical approval of the study should be mentioned here.

Results. Findings must be described without comment. A concise textual description of the data presented in tables, chats and figures should also be included.

Discussion. Comment on your findings and relate them to those from other authors. You should define their relevance to experimental research or clinical practice.

References. The author is responsible for the accuracy of the references. Citations in the text should be identified by numbers in standart brackets. The list of the references at the end of the paper should be given according to their first appearance in the text. Journal abbreviations should be used as listed in Index Medicus.

1-Articles from journals (with PMID numbers):

Cruz Jentoft AJ, Sayer AA. Sarcopenia. Lancet 2019;393 (10191): 2636-46. (PMID: 31171417)

2-Articles from journals (without PMID numbers):

Piers R, Albers G, Gilissen J, et al. Advance care planning in dementia: recommendations for healthcare professionals. BMC Palliative Care 2018;17(88):1-17.(DOI:10.1186/s12904-018-0332-2).

3-Articles in Turkish:

Ozturk S. Clinical and Nuropathological Classification of Dementia. Turkish Journal of Geriatrics 2010; 13 (Suppl 3):15-19. (in Turkish)

Give PMID or DOI numbers if possible.

4-More than 6 authors will be mentioned with the three authors' names:

Groessl EJ, Kaplan RM, Rejeski WJ et al. Physical Activity and Performance Impact Long-term Quality of Life in Older Adults at Risk for Major Mobility Disability. Am J Prev Med 2019; 56 (1): 141-146. (PMID: 30573142).

5-Books:

BG Katzung. Special Aspects of Geriatric Pharmacology, In:Bertram G. Katzung,Susan B. Masters, Anthony J. Trevor (Eds). Basic and Clinical Pharmacology. 10th edition, Lange, Mc Graw Hill, USA 2007, pp 983-90.

6-Articles or documents from electronic publications:

World Health Organization. Global Health and Aging [e-book] NIH Publication; 2011. [Internet]. Available from: http://www.who.int/ageing/publications/ global_health.pdf. Accessed: 09.09.2019.

Access date, DOI or ID numbers of the articles should be mentioned. The UPDATED reference should be available in the referred web address.

Tables. Tables should be supplement not duplicate the text. Each table should be typed (double spaced) on a separate sheet and numbered consecutively with arabic numerals. Place explanatory matters in footnotes. Footnotes to tables should be indicated by lower-case superscript letters. Each table must be cited in text in consecutive order.

Illustrations. Illustrations should be limited to those essential for the text. The same results should be presented as either graphs or tables not as both. All figures, whether photographs, graphs, or diagrams, should be numbered consecutively and shown in the text. The publisher reserves the right to reduce or enlarge illustrations. Arrows, letters, and numbers should be inserted professionally.

Graphs, figures, and illustrations should be placed in the main text. And also separate files should be prepared for graphs, figures, and illustrations (each one on a separate file),

The authors should supply the electronic files for all figures and illustrations including photographs as gif or jpeg images with a minimum resolution of 600 dpi.

Micrographs should have an internal magnification marker; the magnification should also be stated in the caption. Legends must be brief, self-sufficient explanations of the illustrations in no more than four or five lines. Remarks such as "For explanation, see text" should be avoided. The legends should also be typed at the end of the text.

Screening resolution. The image should be at least 600 dpi resolution. For the web site resolution, 300 dpi is acceptable.

Measurements. Metric system should be used for all types of measurements.

Abbreviations and Symbols. Only standard abbreviations should be used in the main text. In the first use, long version of the abbreviation should be written. Abbreviations and Symbols should not be used in abstract and title sections.

Acknowledgement. Authors can thank to the persons, institutions, etc in this section.

Conflict of Interest. The authors should state whether there is a conflict of interest or not.

Review Articles. The journal is open only for "Invited Reviews".

Besides their article, there are 5 important documents that the authors should send:

I- For all the articles **Application Fee Receipt**

II- For all the studies signed copy of **"Ethical Committee Approval Document"** (including all the names of the authors) (For all the studies conducted on human beings, "informed consent" of the participants should be taken).

III- **"Copyright Transfer Form"** with all of the authors' signatures,

IV- **"Author Contribution Form"** with all of the authors' signatures,

V- Copy of **"Certificate of Language Control and Correction".**

The manuscript cannot be sent out for review if the submissions are received without these 5 documents. These documents should be uploaded in related sections of the online system.

Attention ! Last Control Before Submission (Checklist for Submitted Articles)

All of the articles submitted to the Turkish Journal of Geriatrics should fit to the "information of authors' details in the below address:

http://geriatri.dergisi.org/static.php?id=7

The review process will not start until all the below steps are completed.

1-Letter of submission written for the chief editor.

2-E-mail address as well as postal address, official telephone number of the corresponding author.

3-Affiliations (in English) and ORCID numbers (http://orcid.org) of all the authors.

4-For the language editing of your article and to get the "Certificate of Language Control and Correction", you can contact to:

EDITAGE https://www.editage.com, **WILEY** https://www.wiley.com/en-tr, **SCRIBENDI** https://www.scribendi.com, **AMERICAN JOURNAL EXPERTS** http://www.journalexperts.com

5-English heading.

6-English "structured" abstract (250 words at maximum).

7-Keywords in accordance with Medical Subjects Headings-MeSH List (up to 6 words) (https://meshb.nlm.nih.gov/search)

8-Article divided into appropriate sections.

9-All figures (with subtitles) and tables (with titles) cited (should be 5 at maximum)

10-Complete and accurate references (references should be 25 at maximum with the PMID numbers) written according to the rules and of the journal (http://geriatri.dergisi.org/static.php?id=7).

11-Original articles should not exceed 3500 words (excluding abstract).

In order to start the evaluation process, the below 5 documents should be sent through the online system for all the articles:

I- For all the articles **Application Fee Receipt**

II- For all the studies signed copy of **"Ethical Committee Approval Document"** (including all the names of the authors) (For all the studies conducted on human beings, "informed consent" of the participants should be taken).

III- **"Copyright Transfer Form"** with all of the authors' signatures,

IV- **"Author Contribution Form"** with all of the authors' signatures,

V- Copy of **"Certificate of Language Control and Correction".**

Turkish Journal of
GERIATRICS
Volume: 23 • Issue: 4 • Year: 2020

Contents

www.turkgeriatri.org

From The Editor In Chief

For many years, the courses organized by the Scientific Boards of the Turkish Geriatrics Society and the Turkish Journal of Geriatrics were organized with care and were also conducted successfully this year, in spite of the Covid-19 pandemic.

Organized with the support of International Institute on Aging-INIA as a joint event with Hacettepe University Geriatric Sciences Application and Research Center-GEBAM "7 th Geriatrics and Gerontology course" was held on March 2-6, 2020.

The main theme of the "12th Basic Geriatrics Update Course" was looking through the pandemic window at the multiple problems of the seniors. Starting on October first- "International Seniors Day", was held online October 1-3, 2020.

The 5th "Sscientific Research Course in the Field of Geriatrics" was again held online on November 26-28, 2020.

In line with the positive feedback received regarding all courses organized in 2020, the Society's and the Journal's Scientific Board will carry out studies on the continuation of the courses and a multidisciplinary online congress even if there is still the shadow of the Covid-19 pandemic affecting the whole world.

I wish you a healthy, happy, peaceful and prosperous New Year.

Yeşim Gökçe Kutsal

REVIEW

IMPACT OF COVID-19 AMONG THE ELDERLY POPULATION

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2020.179
2020; 23(4): 419-423

Önder İLGİLİ[1]
Yeşim GÖKÇE KUTSAL[2]

Abstract

Humanity worldwide experienced an unprecedented, tremendous change since the end of 2019 and some scholars use the term "new normal" for our current state. A coronavirus disease outbreak occurred in December 2019, which was originated from Wuhan city of Hubei province in the People's Republic of China and erupted into an international public health emergency in a month. It is clear that the elderly population is at a significantly higher risk of the severe outcome of COVID-19 and has the greatest risk of mortality. Since the early stages of the pandemic several measures adopted including social distancing, promoting staying home, cancellation of mass gatherings, and school closures, larger containment processes (such as entire towns or cities) to control the spread of the disease, and mitigate the negative consequences. At the same time, these measures have significant effects on the health of the elderly. An action in solidarity is needed to prevent the further community spread of the virus, protecting older people living alone in the community, as well as supporting all health and social care workers. In these difficult times, the elder people should not neglect or underestimate their own health problems and cling to life. They should keep in mind that; they are very valuable to their loved ones. Additionally, during the post-pandemic period, permanent problems may arise in adults in the older age group, which differ greatly from adults. It is necessary to be ready to deal with this, which depends on solving foreseeable problems.

Keywords: Covıd-19; Pandemics; Aged; Nursing Homes; Frailty

CORRESPONDANCE

[1]Önder İLGİLİ

Hacettepe University, Faculty of Medicine, History of Medicine and Medical Ethics, Ankara, Turkey

Phone: +905325481322
e-mail: ilgili@hacettepe.edu.tr

Received: Oct 14, 2020
Accepted: Oct 18, 2020

[1] Hacettepe University, Faculty of Medicine, History of Medicine and Medical Ethics, Ankara, Turkey

[2] Hacettepe University, Faculty of Medicine, Physical Medicine and Rehabilitation, Ankara, Turkey

Humanity worldwide experienced an unprecedented, tremendous change since the end of 2019 and some scholars use the term "new normal" for our current state. A coronavirus disease outbreak occurred in December 2019, which was originated from Wuhan city of Hubei province in the People's Republic of China and erupted into an international public health emergency in a month (1). Turkey reported its first COVID-19 case on March 10, 2020 (2) The unfortunate spread was rapid and World Health Organization shared assessments on the situation that COVID 19 shows characteristics of a pandemic on the 11th of March (3).

COVID 19 is a contagious disease, that uses the transfer of respiratory droplets as the mode of transmission, primarily targets the respiratory system and causes symptoms as fatigue, cough, and fever (4). However, various gastrointestinal, cardiovascular, and neurological symptoms are also been recognized (5). The disease can be categorized in asymptomatic, mild, moderate, severe, and critical forms according to severity (4).

In the light of available data from many countries it is clear that the elderly population is at a significantly higher risk of the severe outcome of COVID-19 and has the greatest risk of mortality (4,6,7). Referencing an age-wise comparative study, it's reported that patients of COVID 19 who are over 55 had increased mortality (three times), hospitalization, pulmonary involvement, delayed clinical recovery, increased need for mechanical ventilation, and oxygen therapy. These statements strengthen the central position of health services for the elderly during the pandemic but we should be vigilant against a negative perception of these statements as an additional burden on the society during the pandemic which may lead to an escalation in ageism, marginalization, segregation, abuse, and increased institutionalization of the elderly. Additionally, under-reporting of symptoms of the aged population due to the interpretation of symptoms as reflections of the frailty of the elderly also emerges as a serious risk. This may pave the way to under-detection of the disease, faulty treatment, and an increase in asymptomatic carriers (7).

Since the early stages of the pandemic several measures adopted including social distancing, promoting staying home, cancellation of mass gatherings, and school closures, larger containment processes (such as entire towns or cities) to control the spread of the disease, and mitigate the negative consequences (8). At the same time, these measures have significant effects on the health of the elderly. These have dimensions bringing isolation and pandemics are not merely biological phenomena; they also affect society at a large. In many societies, also depending on the culture and common lifestyle, the elderly people are living alone, and loneliness is identified as a potential risk factor for cognitive disorders and depression (7). A comprehensive review article aiming to present the psychological impact of quarantine by Brooks et al., presented post-traumatic stress symptoms, confusion, and anger as most reported negative psychological effects of quarantine. They also identified the stressors during quarantine including duration of quarantine, fears of infection, frustration and boredom, inadequate supplies and information, and post quarantine stressors like finances and stigma. According to literature, psychiatric history, consist of disaster-related trauma or preexisting mental health problems, also necessitates close attention, and extra support during the pandemic (8).

The fear of the pandemic is also suspected to have an increased psychological effect on the aged concerning their pre-existed awareness of their vulnerability. The fear of death and the existential fear of losing the loved ones also reported. The psychological impact of quarantine is accepted to be wideranging, substantial, and can be long-lasting. Avoidance attitude from people with symptoms, crowded places, public spaces, vigilant handwashing were expressed considering long-lasting effects (8).

Social relationships, access to social networks, engagement in social activities, and access to social support are of particular interest in improving factors on positive health outcomes (9). Social support is much more related to functional aspects of social relationships and it signifies a person's perception of the availability of support and help from the other individuals connected to their social network. Social support can be examined under subgroups emotional, instrumental, and informational support. In this context contemporary advanced information infrastructure and culture seem to have a double effect in control of the psychosocial effects of the pandemic and lack of social support. Mobile phones, Wi-Fi networks, social media provide an opportunity to relieve the isolation feelings, to keep in touch with loved ones, however, many aged individuals might not be practical with technology. On the other hand, if the information overload couldn't be coped with properly as in the situation of the elderly, they may become easy targets of inadequate and misinformation due to their generation limitations and sensory-cognitive deficits. The establishment of phone lines and online services to reach public health authorities and health professionals to provide information, guidance, and necessary instructions are considered to be effective in alleviating negative psychological effects (7,8).

In COVID 19 times, organization and attendance of group physical activities were decreased which were also creating and strengthening social ties and provides encouragement (1). Older adults should adhere to isolation cautions since they have a higher risk of COVID 19 disease but they also need to prevent themselves from the negative consequences of a sedentary lifestyle. Physical inactivity among older adults is a risk factor for mortality and a major contributor to disability. Physical activity is also proved to be critical for older adults, to protect from frailty, sarcopenia, risk of falls and to maintain their level of independence, mental health, and well-being (1,10). Online videos, booklets of physical activity advice, and exercises were offered as alternative solutions. Ultimately, the receptiveness of older adults seems to be an important determiner of the success of nationwide efforts to promote safe and simple ways to physical activities in limited spaces (1).

Having inadequate basic supplies (eg, food, water, clothes, or accommodation) during quarantine was another source of frustration, and for many older persons to get regular medical care and prescriptions was also appeared to be a problem (8). Self-medication and misinformation leading to it can be fatal (especially with drugs like hydroxychloroquine) and should be strictly avoided. The advice of a health professional is a prerequisite before any prescription and repeat (7). Hence, medical treatments should be meticulously assessed, arranged, and updated; realization of deprescribing aims is also at stake during the pandemic. As a result of COVID-19, deprescribing procedures, which are directed to maintain or improve the quality of life of patients, reduce harm from medications in patients, and reduce healthcare expenditures, have been on hold because of the restrictions on direct interactions. The alternative presented to secure these benefits is virtual care however it also has difficulties regarding the elderly. Infrastructure including technological equipment and private rooms to facilitate the access to health services electronically from home and nursing homes expressed as a necessity (4).

COVID-19 disease may be more problematic for the institutionalized elderly. The conditions of nursing homes (retirement homes) ease the acquisition and spread of the infection. Air, food, water, health care is all shared among susceptible residents in these institutions. In addition, routine movement of visitors, and staff involves the risk of forming transmission ways with the outside community. Despite accepting the limitations of scientific knowledge on this issue; the urgent need for focusing on nursing homes by public health authorities is strongly em-

phasized (6,7). Efforts directed to a more home-like, person-centric facility design, providing sufficient medical staff and gear, training for the staff, arrange isolation rooms, daily screening for early detection, implementation of new information technologies were suggested (6,11).

Shielding the most susceptible aged population seems to be a priority to reduce the mortality, morbidity, and the overburden to the health system (6). On the other hand, restricting the length of preventive measures as required according to scientific evidence and avoidance from the exorbitant approach would limit the negative effects on the elder population. Transparently sharing of the rationale behind these measures with the community and refraining from unnecessary extensions are also suggested. At the same time, education of the public in general about the disease may be beneficial in reducing fear, ageism, and stigmatization (8). Tele-facilities for health care, social relations, and ensuring delivery of basic amenities including medications are offered as a proper step to reduce fear and stress (7,8).

This situation needs an action in solidarity to prevent the further community spread of the virus, protecting older people living alone in the community, as well as supporting all health and social care workers. In these difficult times, the elder people should not neglect or underestimate their own health problems and cling to life. They should keep in mind that; they are very valuable to their loved ones. The motivation of the elderly in the home environment is important (12).

There are spesific models that are developed for the prevention of frailty in the elderly during the pandemic. As an example SAVE model includes: a-Socialization: Encouraging the elderly to use social media, establishing telephone and video connections, and thus preventing social isolation and providing cognitive stimulation, b-Adequate nutrition: Providing versatile and adequate nutrition, taking necessary protein for the protection of muscle mass and physical functions, c-Vitamin D: Going outdoors by maintaining social distance and providing vitamin D synthesis, taking it with diet and support if necessary, d-Exercise: Ensuring multi-dimensional exercises using body weight, reducing sedentary periods and increasing physical activity (13).

During the post-pandemic period, permanent problems may arise in adults in the older age group, which differ greatly from adults. It is necessary to be ready to deal with this, which depends on solving foreseeable problems. That is the way to include the seniors in this struggle against an unprecedented epidemic. Thus, rational and realistic preparation plans can be made after the pandemic by making use of their wisdom, knowledge and future suggestions.

REFERENCES

1. Goethals L, Barth N, Guyot J, Hupin D, Celarier T, Bongue B. Impact of Home Quarantine on Physical Activity Among Older Adults Living at Home During the COVID-19 Pandemic: Qualitative Interview Study. JMIR Aging. 2020 May 7;3(1):e19007. (PMID: 32356777)
2. Cakir B. COVID-19 in Turkey: Lessons Learned. J Epidemiol Glob Health. 2020;10(2):115–7. (DOI: https://doi.org/10.2991/jegh.k.200520.001)
3. World Health Organization. Archived: WHO Timeline - COVID-19 [Internet]. Available from: https://www.who.int/news-room/detail/27-04-2020-who-timeline---covid-19 Accessed: 03.07.2020.
4. Elbeddini A, Prabaharan T, Almasalkhi S, Tran C, Zhou Y. Barriers to conducting deprescribing in the elderly population amid the COVID-19 pandemic. Res Soc Adm Pharm. 2020 May;S1551741120306021. (PMID: 32499161)
5. Neumann-Podczaska A, Al-Saad SR, Karbowski LM, Chojnicki M, Tobis S, Wieczorowska-Tobis K. COVID 19 - Clinical Picture in the Elderly Population: A Qualitative Systematic Review. Aging Dis. 2020;11(4):988. (PMID: 32765959)
6. Kemenesi G, Kornya L, Tóth GE, Kurucz K, Zeghbib S, Somogyi BA, et al. Nursing homes and the elderly regarding the COVID-19 pandemic: situation report from Hungary. GeroScience. 2020; 42(4):1-7. (PMID: 32426693)
7. Banerjee D. 'Age and ageism in COVID-19': Elderly mental health-care vulnerabilities and needs. Asian J Psychiatry. 2020 Jun;51:102154. (PMID: 32403024)
8. Brooks SK, Webster RK, Smith LE, Woodland L, Wessely S, Greenberg N, et al. The psychological impact of quarantine and how to reduce it: rapid review of the evidence. Lancet. 2020;395:912–20. (PMID: 32112714)
9. Kelly ME, Duff H, Kelly S, McHugh Power JE, Brennan S, Lawlor BA, et al. The impact of social activities, social networks, social support and social relationships on the cognitive functioning of healthy older adults: a systematic review. Syst Rev. 2017 Dec;6(1):259. (PMID: 29258596)
10. Jiménez-Pavón D, Carbonell-Baeza A, Lavie CJ. Physical exercise as therapy to fight against the mental and physical consequences of COVID-19 quarantine: Special focus in older people. Prog Cardiovasc Dis. 2020 May;63(3):386–8. (PMID: 32220590)
11. Wee SL, Yap PKL. Timely lessons from a pandemic on the benefits of person centric care in long term care facilities. J Frailty Aging. 2020;9(3):132–3. (PMID: 32588025)
12. Kutsal YG. From the editör in chief. Turk J Geriatr 2020;23(2) [Internet]. Available from: http://www.geriatri.dergisi.org/abstract.php?id=1193 Accessed: 10.07.2020.
13. Boreskie KF, Hay JL, Duhamel TA, Preventing Frailty Progression During the Covid-19 Pandemic. J Frailty Aging. 2020 Jun 6: 1–3. (PMID: 32588024)

RESEARCH

INVESTIGATION OF THE RELATIONSHIP BETWEEN MORTALITY AND RED CELL DISTRIBUTION WIDTH, MEAN PLATELET VOLUME, PLATELET-TO-LYMPHOCYTE RATIO, AND NEUTROPHIL-TO-LYMPHOCYTE RATIO IN GERIATRIC PATIENTS

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2020.180
2020; 23(4): 424-433

Remzive Nur EKE[1]
Mehmet ÖZEN[1]
Yasin ALTUN[2]
Hamit Yaşar ELLİDAĞ[3]

CORRESPONDANCE
Remzive Nur Eke
University of Health Sciences, Antalya Training and Research Hospital, Family Medicine Department, Antalya, Turkey

Phone: +05055018155
e-mail: drnureke@gmail.com

Received: May 12, 2020
Accepted: Nov 10, 2020

[1] University of Health Sciences, Antalya Training and Research Hospital, Family Medicine Department, Antalya, Turkey

[2] Serik Family Health Center No. 3, Family Medicine Unit, Antalya, Turkey

[3] University of Health Sciences, Antalya Training and Research Hospital, Biochemistry Department, Antalya, Turkey

Abstract

Introduction: This study aimed to investigate the relationship between all-cause mortality and the values of red-cell distribution width, mean platelet volume, platelet-to-lymphocyte ratio, and neutrophil-to-lymphocyte ratio in geriatric patients who had become bedridden.

Materials and Method: The retrospective study reviewed 1981 patients aged 65–104 years who were bedridden and followed at University of Health Sciences, Antalya Training and Research Hospital Family Medicine Clinic from 2016 to 2018. Due to the effects on studied test parameters, patients with anemia were excluded from the study, and 898 patients included. The baseline variables red cell distribution width, mean platelet volume, platelet-to-lymphocyte ratio, and neutrophil-to-lymphocyte ratio were compared between survivors and non-survivors.

Results: Of the 898 patients, 141 (15.7%) died during follow-up. Mean red cell distribution width (15.7%), platelet-to-lymphocyte ratio (140.5), and neutrophil-to-lymphocyte ratio (3.14) levels in non-survivors were statistically significantly higher than those of survivors (14.9%, $p<0.001$; 125, $p=0.030$; and 2.38, $p<0.001$, respectively). The retrospective follow-up revealed that red cell distribution width, platelet-to-lymphocyte ratio and neutrophil-to-lymphocyte ratio levels (17.6%, 205.82, and 4.99, respectively) had increased during the last three months before death, but this was not statistically significant. The results of univariate logistic regression analyses showed that mortality was positively associated with red cell distribution width and neutrophil-to-lymphocyte ratio. In a multivariate model, red cell distribution width was identified as an independent predictive factor associated with mortality.

Conclusion: Red cell distribution width, platelet-to-lymphocyte ratio, and neutrophil-to-lymphocyte ratio may be strong predictors of mortality in patients who have become bedridden, and alarms to take action for measures.

Keywords: Erythrocytes; Neutrophils; Lymphocytes; Blood Platelets; Mortality; Aged

INTRODUCTION

Red blood cell distribution width (RDW), mean platelet volume (MPV), and neutrophil, lymphocyte, and platelet (PLT) counts are inexpensive and rapid tests routinely used in clinical practice as part of a complete blood count (CBC), which have great potential as prognostic markers. RDW is a quantitative measure of variability in the size of circulating erythrocytes. Higher values reflect greater heterogeneity in cell sizes and indicate anisocytosis (1). Although the mechanism explaining the relationship between RDW and survival is not fully understood, it is believed that systemic factors affecting erythrocyte homeostasis such as inflammation and oxidative stress may be responsible (2). Like RDW, others such as MPV, platelet-to-lymphocyte ratio (PLR), and neutrophil-to-lymphocyte ratio (NLR) are novel inflammatory markers that are indicative of systemic inflammation (3-5). MPV reflects mean platelet size and larger platelets are more active than functionally, metabolically, and enzymatically smaller ones. Platelets with a larger volume contain more prothrombotic material, and increased MPV indicates increased platelet production and activation. Platelet activation is associated with adverse clinical outcomes of vascular diseases such as coronary artery disease, stroke, and venous thromboembolism (6). In the setting of cancer, NLR, PLR, and RDW are biomarkers indicating systemic inflammation and are considered as early diagnostic and prognostic factors (7, 8). Inflammatory cells, chemokines, cytokines, and proinflammatory mediators that play a role in inflammation in cancer-related mortality contribute to tumor cell formation, proliferation and metastasis (9). Similarly, inflammation accounts for the atherosclerotic process and mortality associated with cardiovascular diseases. Atherosclerotic plaques are thought to develop as an inflammatory response to vascular injury (10, 11). As a result, inflammation is the most prominent mechanism behind all-cause mortality, particularly in vascular diseases such as cardiovascular diseases, stroke, and venous thromboembolism as well as cancer-related mortality and this process can be assessed by tests such as RDW, MPV, PLR, and NLR, which are very simple.

Several studies have reported that RDW, MPV, PLR, and NLR are strong predictors of mortality. For example, high RDW was associated with increased mortality in patients with acute heart failure in a study by Van Kimmenade (12), in patients with community-acquired intra-abdominal sepsis followed up in the intensive care unit in a study by Özdogan (13), and in patients older than 65 years presenting to the emergency department in a study by Soo Hyun Kim (14). On the other hand, in their meta-analysis of 11 cohort studies Tajarernmuang et al. reported MPV as the predictor of all-cause mortality for non-cardiac critically ill patients (6), while Bozkurt et al. reported MPV and NLR as the predictor of all-cause mortality in geriatric patients followed up in the intensive care unit, and Wang et al. reported NLR as the predictor of all-cause mortality in a meta-analysis of 10 cohort studies (3, 15).

Despite all these studies, large scale and follow-up studies are still needed to fully understand the effect of RDW, MPV, PLR, and NLR on mortality. To this end, this study aimed to investigate the relationship of RDW, MPV, PLR, and NLR with mortality in geriatric patients who had become bedridden due to various diseases.

MATERIALS AND METHOD

Study population

The retrospective study reviewed a population of 1981 patients aged 65–104 years who were bedridden and followed at the University of Health Sciences, Antalya Training and Research Hospital (TRH) Family Medicine Clinic between January 1, 2016 and December 31, 2018. The patients' laboratory test results were obtained from the hospital's information management system. Patients with anemia (The World Health Organization defined

Table 1. Comparison of study parameters and laboratory data between groups

Variables		Total (n=898)	Survivors (n=757)	Non-survivors (n=141)	p
Age		79 (19-104)	78 (19-104)	83 (24-103)	<0.001
Gender	Female	599 (66.7)	505 (66.7)	94 (66.7)	0.992
	Male	299 (33.3)	252 (33.3)	47 (33.3)	
Diagnoses	Cancer	55 (6.1)	35 (4.6)	20 (14.2)	<0.001
	DM	100 (11.1)	90 (11.9)	10 (7.1)	0.096
	Alzheimer	167 (18.6)	133 (17.6)	34 (24.1)	0.067
	CVD	218 (24.3)	187 (24.7)	31 (22)	0.490
	CVS diseases	285 (31.7)	247 (32.6)	38 (27)	0.183
	Lung diseases	37 (4.1)	36 (4.8)	1 (0.7)	0.026
Mean values of study parameters	HGB (g/dL)	13.5 ± 1.11 (10-18.6)	13.6 ± 1.1 (10-18.6)	13.25 ± 1 (12-16.7)	0.004
	HCT (%)	41 (31.7-58.5)	41 (31.7-58.5)	41.2 (36.6-51.8)	0.417
	WBC (103/mm3)	7.5 (2.1-22.5)	7.4 (2.1-22)	8.2 (3.2-22.5)	0.002
	PLT (103/mm3)	232 (37-1071)	232 (52-1071)	227 (37-542)	0.965
	RDW (%)	15.1 (12.1-28.9)	14.9 (12.1-28.9)	15.7 (12.6-26)	<0.001
	MPV (µm3)	8.99 ± 1.25 (6-13.6)	8.98 ± 1.24 (6-13.6)	9.04 ± 1.3 (6.3-12.8)	0.584
	PLR	127.74 (29.3-1750)	125 (29.3-1750)	140.5 (35.43-805)	0.030
	NLR	2.5 (0.11-70.5)	2.38 (0.11-47.4)	3.14 (0.64-70.5)	<0.001
Study parameters above the upper limits	RDW>16,5 (%)	185 (20.6)	139 (18.4)	46 (32.6)	<0.001
	MPV>10,5 (µm3)	118 (13.1)	99 (13.1)	19 (13.5)	0.898
	PLR>132.5	418 (46.5)	338 (44.6)	80 (56.7)	0.008
	NLR>1.77	660 (73.5)	546 (72.1)	114 (80.9)	0.031

Data are presented as n (%), mean ± SD (min-max) and median (min-max). Mann-Whitney U test, Student t test, Pearson Chi-Square test. DM: Diabetes mellitus, CVD: Cerebrovascular diseases, CVS: Cardiovascular system, HGB: Hemoglobin, HCT: Hematocrit, WBC: White blood cells, PLT: Platelet, RDW: Red cell distribution width, MPV: Mean platelet volume, PLR: Platelet-to-lymphocyte ratio, NLR: Neutrophil-to-lymphocyte ratio.

anemia as serum hemoglobin levels of < 13 g/dL in men over 15 years of age, < 12 g/dL in women over 15 years of age and in non-pregnant women, and < 11 g/dL in pregnant women), were excluded, as anemia may affect the study parameters. The clinical data of 898 patients were examined from patients' files. The Antalya TRH Clinical Research Ethics Committee approved the study prior to its implementation (approval no; 8/20, date; 07 March 2019), and the study was performed in compliance with the Declaration of Helsinki.

Data collection and laboratory measurements

The demographic data, diagnoses, mortality, and CBC parameters of the patients were recorded on previously developed forms.

CBC parameters (hemogram) were analyzed using a Beckman Coulter LH 780 Hematology Analyzer (Beckman Coulter Inc., Miami, Florida). The NLR was calculated by dividing the number of neutrophils with the number of lymphocytes, and the PLR by dividing the number of platelets with the number of lymphocytes.

The normal distribution ranges for RDW, MPV, PLR, and NLR vary, but have been reported as approximately 12–16%; 9.5–11.5 µm3; 125–135, and 1.50–2.0, respectively, in a variety of studies (2, 16-19).

Table 2. Comparison of patients according to RDW and MPV values

Variables		RDW≤16,5 (n=713)	RDW>16,5 (n=185)	p	MPV≤10,4 (n=780)	MPV>10,5 (n=118)	p
Age		78 (19-104)	81 (22-104)	0.005	79 (19-104)	78 (20-96)	0.077
Gender	Female	460 (64.5)	139 (75.1)	0.006	517 (66.3)	82 (69.5)	0.491
	Male	253 (35.5)	46 (24.9)		263 (33.7)	36 (30.5)	
Diagnoses	Cancer	40 (5.6)	15 (8.1)	0.207	49 (6.3)	6 (5.1)	
	DM	78 (10.9)	22 (11.9)	0.714	86 (11)	14 (11.9)	0.613
	Alzheimer	138 (19.4)	29 (15.7)	0.252	145 (18.6)	22 (18.6)	0.787
	CVD	174 (24.4)	44 (23.8)	0.861	189 (24.2)	29 (24.6)	0.989
	CVS diseases	225 (31.6)	60 (32.4)	0.820	253 (32.4)	32 (27.1)	0.935
	Lung diseases	28 (3.9)	9 (4.9)	0.567	26 (3.3)	11 (9.3)	0.247
HGB (g/dL)		13.57 ± 1.13 (10-18.6)	13.22 ± 0.94 (12-16.7)	<0.001	13.45 ± 1.06 (12-18.6)	13.86 ± 1.32 (10-18.5)	0.001
HCT (%)		41 (31.7-58.5)	40.9 (35-51.4)	0.868	40.8 (35-58.5)	42 (31.7-56.4)	<0.001
WBC (103/mm3)		7.4 (2.1-22.5)	7.9 (3.8-22.4)	0.008	7.4 (2.1-22.5)	8.19 (3.3-22)	0.018
PLT (103/mm3)		228 (65-598)	245 (37-1071)	0.011	237.5 (65-1071)	183 (37-747)	<0.001
RDW (%)		14.7 (12.1-16.5)	17.6 (16.6-28.9)	<0.001	15.1 (12.1-26)	14.8 (12.4-28.9)	0.886
MPV (µm3)		8.95 ± 1.24 (6.2-13.4)	9.12 ± 1.31 (6-13.6)	0.110	8.64 ± 0.91 (6-10.4)	11.26 ± 0.7 (10.5-13.6)	<0.001
PLR		124.3 (29.3-805)	140 (33.7-1750)	0.016	132.4 (29.3-1750)	93.8 (30.7-315.5)	<0.001
NLR		2.4 (0.11-70.5)	2.67 (0.5-47.43)	0.013	2.46 (0.11-70.5)	2.68 (0.6-15.7)	0.408
Mortality status	Survivors	618 (86.7)	139 (75.1)	<0.001	658 (84.4)	99 (83.9)	0.898
	Non-survivors	95 (13.3)	46 (24.9)		122 (15.6)	19 (16.1)	

Data are presented as n (%), mean ± SD (min-max) and median (min-max). Mann-Whitney U test, Student t test, Pearson Chi-Square test, Fisher's Exact test. DM: Diabetes mellitus, CVD: Cerebrovascular diseases, CVS: Cardiovascular system, HGB: Hemoglobin, HCT: Hematocrit, WBC: White blood cells, RDW: Red cell distribution width, MPV: Mean platelet volume, PLR: Platelet-to-lymphocyte ratio, NLR: Neutrophil-to-lymphocyte ratio.

Similar to those in the literature, the normal intervals were identified in this study by our hospital laboratory as 11.5–16.5%; 7.4–10.4 µm3; 107.77–132.5, and 1.5–1.77 for RDW, MPV, PLR, and NLR, respectively.

Statistical Analysis

Statistical analyses were made using IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY, USA). Pearson chi-square and Fisher's exact tests were performed for categorical variables. Conformity of the data to normal distribution was assessed with the Shapiro-Wilk test. Mann–Whitney U tests and Student's t tests were used for analysis of non-normally and normally distributed numerical data, respectively. For nonparametric variables Kruskal-Wallis tests were used to compare between groups and Bonferroni-Dunn tests were used as a post-hoc test for significant cases, while for parametric variables one-way ANOVA with post-hoc Tukey HSD tests were used. To compare previous measurements with those in the last three months, paired t-tests were used for the parametric data, and Wilcoxon signed-ranks tests were used for nonparametric data. Spearman and Pearson correlations were applied to investigate the correlation between continuous variables. Univariate and multivariate logistic regression

Table 3. Comparison of patients according to PLR and NLR values

Variables		PLR≤132,5 (n=480)	PLR>132,5 (n=418)	p	NLR≤1,77 (n=238)	NLR>1,77 (n=660)	p
Age		78 (19-104)	80 (19-99)	0.002	76 (20-104)	79 (19-102)	0.002
Gender	Female	307 (64)	292 (69.9)	0.061	169 (71)	430 (65.2)	0.100
	Male	173 (36)	126 (30.1)		69 (29)	230 (34.8)	
Diagnoses	Cancer	29 (6)	26 (6.2)	0.911	14 (5.9)	41 (6.2)	0.856
	DM	44 (9.2)	56 (13.4)	0.044	22 (9.2)	78 (11.8)	0.279
	Alzheimer	101 (21)	66 (15.8)	0.044	49 (20.6)	118 (17.9)	0.357
	CVD	113 (23.5)	105 (25.1)	0.582	63 (26.5)	155 (23.5)	0.357
	CVS diseases	148 (30.8)	137 (32.8)	0.533	72 (30.3)	213 (32.3)	0.566
	Lung diseases	23 (4.8)	14 (3.3)	0.278	16 (6.7)	21 (3.2)	0.018
HGB (g/dL)		13.62 ± 1.13 (12-18.6)	13.36 ± 1.06 (10-16.9)	0.001	13.52 ± 1.03 (12-18.3)	13.49 ± 1.13 (10-18.6)	0.786
HCT (%)		41.2 (35.4-58.5)	40.7 (31.7-51.8)	0.005	41.15 (35-52.9)	41 (31.7-58.5)	0.640
WBC (103/mm3)		7.7 (3.2-22.4)	7.4 (2.1-22.5)	0.158	6.5 (3.2-15.7)	7.9 (2.1-22.5)	<0.001
PLT (103/mm3)		209 (37-471)	264 (101-1071)	<0.001	224 (98-1071)	234 (37-947)	0.022
RDW (%)		14.8 (12.1-24.4)	15.3 (12.3-28.9)	<0.001	14.8 (12.3-24.4)	15.1 (12.1-28.9)	0.004
MPV (µm3)		9.31 ± 1.25 (6.3-13.4)	8.62 ± 1.15 (6-13.6)	<0.001	9.01 ± 1.21 (6.3-13.1)	8.98 ± 1.27 (6-13.6)	0.778
PLR		97.8 (29.3-132.5)	171 (132.6-1750)	<0.001	93.8 (29.3-428.4)	142.2 (30.7-1750)	<0.001
NLR		1.96 (0.5-14.9)	3.4 (0.1-70.5)	<0.001	1.42 (0.11-1.77)	3.06 (1.78-70.5)	<0.001
Mortality status	Survivors	419 (87.3)	338 (80.9)	0.008	211 (88.7)	546 (82.7)	0.031
	Non-survivors	61 (12.7)	80 (19.1)		27 (11.3)	114 (17.3)	

Data are presented as n (%), mean ± SD (min-max) and median (min-max). Mann-Whitney U test, Student t test, Pearson Chi-Square test, Fisher's Exact test. DM: Diabetes mellitus, CVD: Cerebrovascular diseases, CVS: Cardiovascular system, HGB: Hemoglobin, HCT: Hematocrit, WBC: White blood cells, PLT: Platelet, RDW: Red cell distribution width, MPV: Mean platelet volume, PLR: Platelet-to-lymphocyte ratio, NLR: Neutrophil-to-lymphocyte ratio.

analysis was used to determine independent risk factors associated with mortality. The variables which showed significant association with mortality in the univariate analyses were further tested in the multivariate model. Data are expressed as n (%), mean±standard deviation or median (min–max), as appropriate. P values <0.05 were considered statistically significant.

RESULTS

The study included 898 patients, 299 of whom were male (33.3%) and 599 of whom were female (66.7%). The mean age of the patients was 79 (65–104) years. Of the patients, 757 were survivor and 141 were non-survivor. The mean follow-up period of the patients was calculated as 19±10,5 (3-52) months. Of the patients, 285 (31.7%) had cardiovascular system (CVS) disease, 218 (24.3%) had cerebrovascular disease (CVD), and 167 (18.6%) had Alzheimer's disease. The rate of non-survival was significantly higher in patients with cancer ($p < 0.001$). The mean levels of RDW (15.7%), PLR (140.5), and NLR (3.14) in non-survivors were statistically significantly higher than those in survivors (14.9%, $p < 0.001$; 125, $p = 0.030$, and 2.38 $p < 0.001$), respectively (Table 1).

Based on the guidance of our hospital laboratory, the upper normal limits for RDW, MPV, PLR, and

Table 4. Correlation between RDW and MPV levels and other factors in survivor and non-survivor patients

Study parameters	RDW				MPV			
	Survivor (n=757)		Non-Survivor (n=141)		Survivor (n=757)		Non-Survivor (n=141)	
	r	p	r	p	r	p	r	p
Age	0.222	< 0.001	0.070	0.408	-0.030	0.417	0.065	0.442
HGB (g/dL)	-0.245	< 0.001	-0.090	0.290	0.087	0.016	0.116	0.171
HCT (%)	-0.097	0.007	0.094	0.268	0.108	0.003	0.098	0.249
WBC (103/mm3)	0.068	0.061	0.255	0.002	0.143	< 0.001	-0.031	0.715
PLT (103/mm3)	0.046	0.211	0.204	0.015	-0.355	< 0.001	-0.330	< 0.001
MPV (µm3)	0.013	0.725	0.021	0.808	-	-	-	-
RDW (%)	-	-	-	-	0.013	0.725	0.021	0.808
PLR	0.108	0.003	0.086	0.309	-0.353	< 0.001	-0.275	0.001
NLR	0.127	< 0.001	0.162	0.054	-0.028	0.440	-0.01	0.907

Spearman correlation test. HGB: Hemoglobin, HCT: Hematocrit, RDW: Red cell distribution width, WBC: White blood cells, PLT: Platelet, MPV: Mean platelet volume, PLR: Platelet-to-lymphocyte ratio, NLR: Neutrophil-to-lymphocyte ratio.

NLR were established as 16.5%, 10.4 µm3, 132.5, and 1.77, respectively. Of the 141 non-survivors, 46 (32.6%) had RDW>16.5%, 80 (56.7%) had PLR>132.5, and 114 (80.9%) had NLR>1.77, which were all significantly higher than the survivor patients (Table 1).

On comparing the patients according to RDW, MPV, PLR, and NLR values in terms of demographic and laboratory characteristics, the ratio of survivor patients (86.7%) with RDW≤16.5 was found to be statistically significantly higher than those who died (13.3%) (p<0.001). Similarly, the rates of PLR≤132.5 (87.3%, p=0.008) and NLR≤1.77 (82.7%, (p=0.031) were found to be statistically significantly higher in survivors than those who died (Table 2, 3).

Although the mean RDW (16%), MPV (9.39±1.69 µm3), PLR (154.2), and NLR (4.45) levels of the 141 patients who died in the retrospective evaluation were not statistically significant, the highest rates were found in the patients who were tested in the last month before death. On comparing the relationship of the study parameters of 36 patients who had CBC in the last three months and more than three months before death (16.5%, 156.67, and 3.7, respectively), the mean RDW, PLR, and NLR levels (17.6%, 205.82, and 4.99, respectively) were found to have increased in the last three months before death, but this was not statistically significant.

A positive but weak correlation was observed between RDW levels and age (r=0.222, p<0.001), PLR (r=0.108, p=0.003), and NLR (r=0.127, p<0.001) in survivors. RDW levels also negatively correlated with HGB (r=–0.245, p<0.001) and hematocrit (HCT) (r=–0.097, p=0.007) in survivors. In non-survivors, RDW levels positively correlated with white blood cell (WBC) count (r=0.255, p=0.002) and PLT (r=0.204, p=0.015) (Table 4).

In survivors, MPV levels positively correlated with HGB (r=0.087, p=0.016), HCT (r=0.108, p=0.003), and WBC (r=0.143, p<0.001), and also negatively correlated with PLT (r=–0.355, p<0.001) and PLR (r=–0.353, p<0.001). A negative but weak correlation was observed between MPV and PLT (r=–0.330, p<0.001) and PLR (r=–0.275, p=0.001) in non-survivors (Table 4).

The results of univariate logistic regression analyses showed that mortality was positively associated with age (odds ratio, [OR]: 1.03; 95% confidence interval [CI]: 1.016–1.043; p<0.001), cancer (OR: 3.41; 95% CI: 1.905–6.103; p<0.001),

Table 5. Logistic regression analysis of the mortality predictors

Variables		Univariate logistic regression		Multiple logistic regression	
		OR (95%CI)	p value	OR (95%CI)	p
Age		1.03 (1.016-1.043)	<0.001	1.027 (1.012-1.041)	<0.001
Gender (Ref= female)		1.002 (0.684-1.467)	0.992	-	-
Diagnoses	Cancer	3.41 (1.905-6.103)	<0.001	3.189 (1.716-5.926)	<0.001
	Diabetes mellitus	0.566 (0.287-1.116)	0.100	-	-
	Alzheimer	1.491 (0.971-2.289)	0.068	-	-
	CVD	0.859 (0.558-1.322)	0.490	-	-
	CVS diseases	0.762 (0.51-1.139)	0.184	-	-
	Lung diseases	0.143 (0.019-1.052)	0.056	-	-
HGB (g/dL)		0.765 (0.638-0.917)	0.004	0.882 (0.726-1.071)	0.206
HCT (%)		1.009 (0.956-1.065)	0.734	-	-
WBC (103/mm3)		1.152 (1.083-1.226)	<0.001	1.102 (1.027-1.182)	0.007
PLT (103/mm3)		1 (0.998-1.002)	0.711	-	-
RDW (%)		1.209 (1.114-1.312)	<0.001	1.132 (1.033-1.239)	0.008
MPV (µm3)		1.04 (0.903-1.199)	0.584	-	-
PLR		1.002 (1-1.003)	0.074	-	-
NLR		1.142 (1.066-1.223)	<0.001	1.053 (0.997-1.113)	0.064

CVD: Cerebrovascular diseases, CVS: Cardiovascular system, HGB: Hemoglobin, HCT: Hematocrit, WBC: White blood cells, PLT: Platelet, RDW: Red cell distribution width, MPV: Mean platelet volume, PLR: Platelet-to-lymphocyte ratio, NLR: Neutrophil-to-lymphocyte ratio.

WBC (OR: 1.152; 95% CI: 1.083–1.226; p<0.001), RDW (OR: 1.209; 95% CI: 1.114–1.312; p<0.001), and NLR (OR: 1.142; 95% CI: 1.066–1.223; p<0.001), while it was negatively associated with HGB (OR: 0.765; 95% CI: 0.638–0.917; p=0.004) (Table 5).

In a multivariate model, age (OR: 1.027; 95% CI: 1.012–1.041; p<0.001), cancer (OR: 3.189; 95% CI: 1.716–5.926; p<0.001), WBC (OR: 1.102; 95% CI: 1.027–1.182; p=0.007), and RDW (OR: 1.132; 95% CI: 1.033–1.239; p=0.008) were identified as independent predictive factors associated with mortality (Table 5).

DISCUSSION

In this study, we found that in patients who had become bedridden, higher RDW, PLR, and NLR levels were significantly associated with higher mortality risk. We did not find any correlation between MPV levels and mortality. In addition, we found that mortality positively correlated with age, cancer, WBC, RDW, and NLR, while it negatively correlated with HGB, and that RDW was an independent predictive factor related to mortality. In this retrospective follow-up, we also found that RDW, MPV, PLR, and NLR were highest in the last month before death, and that RDW, PLR, and NLR values increased in the last three months in patients who had undergone multiple examinations.

The effects of diseases such as cancer, cardiovascular diseases, and cerebrovascular diseases on the study parameters have not been determined definitely. It is thought that the most accepted common mechanism may be inflammation. In this study, it was aimed to determine the relationship between study parameters and mortality due to all causes (cancer, cardiovascular diseases, cerebrovascular diseases, etc.). For this

reason, cancer patients as well as patients with cardiovascular and cerebrovascular diseases in particular, were included in the study.

The relationship between elevated RDW, MPV, PLR, and NLR levels and increased risk of mortality has been previously reported in various patient groups (such as middle-aged and elderly patients, critically ill patients, patients presenting to the emergency department, or special diagnostic groups such as patients with coronary artery stenos, acute myocardial infarction, or chronic kidney disease) (2, 6, 13-15, 17, 20). However, to our knowledge there has been no study in which these four inflammatory markers were evaluated in patients who had become bedridden.

Many studies have investigated the relationship of high RDW to increased risk of mortality. For instance, Kushang et al. analyzed seven population-based studies and demonstrated that high RDW values were associated with increased mortality risk. This study found that every 1% increase in RDW increased the total mortality risk by 14%. Moreover, RDW was found to be strongly associated with CVD, cancers, and other disease-related deaths as well as total mortality even in patients without age-related disease (1). In a study conducted by Patel et al. with 8175 adults aged 45 and over showed that each 1% increase in RDW increased the risk of mortality by 22% and that RDW is strongly associated with mortality even in non-anemic participants (2). Only non-anemic patients were evaluated in our study, in which mean RDW levels of non-survivors were found to be significantly higher than those of the survivors, and univariate logistic regression analysis showed a strong relationship between RDW and mortality, whereas multivariate logistic regression analysis showed that RDW was an independent risk factor of mortality.

Wang et al. studied 134 patients with adenosquamous carcinoma of the lung and reported that high PLR levels were independently associated with low survival rate (21). Likewise, Oylumlu et al. found that PLR values greater than 142 predicted in-hospital deaths in patients with acute coronary syndrome (20). In our study, mean PLR levels of non-survivors were found to be significantly higher (140.5) than those of the survivors (125).

Tamhane et al. studied 2833 patients presenting with acute coronary syndrome and stated that the level of NLR measured at admission was an independent predictor of in-hospital and six-month mortality (22). Liu et al. reported that 80% of 333 patients with sepsis died within 28 days, and NLR was found to be significantly higher in patients who died (23). A similar study in patients with sepsis and septic shock reported that high NLR was predictive of 28 day mortality (24). Similarly, in our study, the highest levels of NLR were found in the last month before death in non-survivors, and NLR levels increased in the last three months prior to death in non-survivor patients with multiple examinations.

In a study by Yoldas, in which PLR and NLR were evaluated together as a marker of mortality, NLR and PLR levels of non-survivors were found to be significantly higher than those of survivors (25). In our study, in addition to RDW and MPV, PLR and NLR were evaluated as markers of all-cause mortality in patients who had become bedridden, and mean PLR, and NLR levels were found to be significantly higher in non-survivor patients compared to survivors.

Iron, ferritin, vitamin B12 and folic acid deficiencies can affect RDW levels. The fact that these data of all patients were not available and that patients with these deficiencies were not excluded from the study can be shown as a limitation of our study. Being followed patients from a single-center and cross-sectional may be the other limitations of our study.

Strengths of our study are; the population was quite large, and patients with anemia were excluded from the study due to the effects on studied test parameters -especially RDW-, and some patients' test results of the last three months before death included to study.

In conclusion, we found significant statistical associations of RDW, PLR, and NLR with mortality in patients with comorbidities who had become bedridden for various reasons. These tests, which are very simple, quick, and cheap, can predict deteriorating prognosis in both elderly and bedridden patients, and the necessary measures (such as hospitalization) can be life-saving for the patient. For this purpose, further research is necessary to establish RDW, PLR, and NLR as prognostic markers.

CONFLICT OF INTEREST

None.

FUNDING

None.

REFERENCES

1. Patel KV, Semba RD, Ferrucci L, et al. Red cell distribution width and mortality in older adults: a meta-analysis. J Gerontol A Biol Sci Med Sci 2009;65(3):258-65. (PMID:19880817).
2. Patel KV, Ferrucci L, Ershler WB, Longo DL, Guralnik JM. Red cell distribution width and the risk of death in middle-aged and older adults. Arch Intern Med 2009;169(5):515-23. (PMID:19273783).
3. Wang X, Zhang G, Jiang X, Zhu H, Lu Z, Xu L. Neutrophil to lymphocyte ratio in relation to risk of all-cause mortality and cardiovascular events among patients undergoing angiography or cardiac revascularization: a meta-analysis of observational studies. Atherosclerosis 2014;234(1):206-13. (PMID:24681815).
4. Yilmaz G, Sevinc C, Ustundag S, et al. The relationship between mean platelet volume and neutrophil/lymphocyte ratio with inflammation and proteinuria in chronic kidney disease. Saudi J Kidney Dis Transpl 2017;28(1):90-4. (PMID:28098108).
5. Cataudella E, Giraffa CM, Di Marca S, et al. Neutrophil-to-lymphocyte ratio: an emerging marker predicting prognosis in elderly adults with community-acquired pneumonia. J Am Geriatr Soc 2017;65(8):1796-801. (PMID:28407209).
6. Tajarernmuang P, Phrommintikul A, Limsukon A, Pothirat C, Chittawatanarat K. The role of mean platelet volume as a predictor of mortality in critically ill patients: A systematic review and meta-analysis. Crit Care Res Pract 2016; Article ID:4370834:1-8. (PMID:26966574).
7. Yildirim MA, Seckin KD, Togrul C, et al. Roles of neutrophil/lymphocyte and platelet/lymphocyte ratios in the early diagnosis of malignant ovarian masses. Asian Pac J Cancer Prev 2014;15(16):6881-5. (PMID:25169540).
8. Cakmak E, Soylu S, Yonem O, Yilmaz A. Neutrophil-to-lymphocyte ratio, platelet-to- lymphocyte ratio, and red blood cell distribution width as new biomarkers in patients with colorectal cancer. Erciyes Med J 2017;39(3):131-6. (DOI:10.5152/etd.2017.0051).
9. Janakiram NB, Rao CV. The Role of Inflammation in Colon Cancer, In: Aggarwal B, Sung B, Gupta S (Eds). Inflammation and Cancer. Advances in Experimental Medicine and Biology Series. Springer, Basel 2014;816, pp 25-52. (PMID:24818718).
10. Libby P, Ridker PM. Novel inflammatory markers of coronary risk: theory versus practice. Circulation 1999;100(11):1148-50. (PMID:10484532).
11. Plutzky J. Inflammatory pathways in atherosclerosis and acute coronary syndromes. Am J Cardiol 2001;88(8A):10K-15K. (PMID:11694213).
12. van Kimmenade RR, Mohammed AA, Uthamalingam S, van der Meer P, Felker GM, Januzzi Jr JL. Red blood cell distribution width and 1-year mortality in acute heart failure. Eur J Heart Fail 2010;12(2):129-36. (PMID:20026456).
13. Ozdogan HK, Karateke F, Ozyazıcı S, et al. The predictive value of red cell distribution width levels on mortality in intensive care patients with community-acquired intra-abdominal sepsis. Ulus Travma Acil Cerrahi Derg 2015;21(5):352-7. (PMID:26388271).
14. Kim SH, Yeon JH, Park KN, et al. The association of red cell distribution width and in-hospital mortality in older adults admitted to the emergency department.

Scand J Trauma Resusc Emerg Med 2016;24, Article number: 81. (PMID:27267984).

15. Bozkurt D, Kilavuz A, Caferov N, Kose T, Akcicek F. Non-traditional mortality predictors for geriatric intensive care unit patients. Turkish Journal of Geriatrics, 2018;21(3):323-32. (DOI:10.31086/tjgeri.2018344046).
16. Al-Kindi SG, Refaat M, Jayyousi A, Asaad N, Suwaidi JA, Khalil CA. Red cell distribution width is associated with all-cause and cardiovascular mortality in patients with diabetes. BioMed Res Int 2017; Article ID: 5843702. (PMID:29359154).
17. Skjelbakken T, Lappegard J, Ellingsen TS, et al. Red cell distribution width is associated with incident myocardial infarction in a general population: The Tromso Study. J Am Heart Assoc 2014;3(4):e001109. (PMID:25134681).
18. Alexander NI. Reference values of neutrophil-lymphocyte ratio, platelet- lymphocyte ratio and mean platelet volume in healthy adults in North Central Nigeria. J Blood Lymph 2016;6(1):1000143. (DOI:10.4172/2165-7831.1000143).
19. Lee JS, Kim NY, Na SH, Youn YH, Shin CS. Reference values of neutrophil- lymphocyte ratio, lymphocyte-monocyte ratio, platelet-lymphocyte ratio, and mean platelet volume in healthy adults in South Korea. Medicine 2018;97(26):e11138. (PMID:29952958).
20. Oylumlu M, Yildiz A, Oylumlu M, et al. Platelet-to-lymphocyte ratio is a predictor of in-hospital mortality patients with acute coronary syndrome. Anatol J Cardiol 2015;15(4):277-83. (PMID:25413224).
21. Wang YQ, Zhi QJ, Wang XY, Yue DS, Li K, Jiang RC. Prognostic value of combined platelet, fibrinogen, neutrophil to lymphocyte ratio and platelet to lymphocyte ratio in patients with lung adenosquamous cancer. Oncol Lett 2017;14(4):4331-8. (PMID:28943947).
22. Tamhane UU, Aneja S, Montgomery D, Rogers EK, Eagle KA, Gurm HS. Association between admission neutrophil to lymphocyte ratio and outcomes in patients with acute coronary syndrome. Am J Cardiol 2008;102(6):653-7. (PMID:18773982).
23. Liu X, Shen Y, Wang H, Ge Q, Fei A, Pan S. Prognostic significance of neutrophil-to- lymphocyte ratio in patients with sepsis: A prospective observational study. Mediators Inflamm 2016; Article ID:8191254. (PMID:27110067).
24. Hwang SY, Shin TG, Jo IJ, et al. Neutrophil-to-lymphocyte ratio as a prognostic marker in critically-ill septic patients. Am J Emerg Med 2017;35(2):234-9. (PMID:27806894).
25. Yoldas H, Karagoz I, Ogun MN, et al. Novel mortality markers for critically ill patients. J Intensive Care Med 2020;35(4):383-5. (PMID:29334832).

RESEARCH

HOW DID COVID-19 PANDEMIC AFFECT THE OLDER PATIENTS? COMPARISON OF CLINICAL FEATURES IN OLDER VERSUS YOUNGER PATIENTS.

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2020.181
2020; 23(4): 434-445

Nesrin ÖCAL[1]
Betül Gülsüm YAVUZ VEİZİ[2]
Ferhat CÜCE[3]
Gülden YILMAZ[4]
Gürhan TAŞKIN[5]
Yahya Ayhan ACAR[6]
Ervin GJONİ[3]
Esra ŞAFAK YILMAZ[7]
Serkan ŞENKAL[8]
Yakup ARSLAN[1]
Deniz DOĞAN[1]
Gonca FİDAN[4]
Cantürk TAŞÇI[1]
Mehmet İlkin NAHARCI[2]

CORRESPONDANCE
[1]Nesrin ÖCAL

University of Health Sciences, Gulhane Medical Faculty, Chest Diseases, Ankara, Turkey

Phone: +905055044715
e-mail: nesrinbaygin@yahoo.com

Received: Aug 19, 2020
Accepted: Nov 12, 2020

[1] University of Health Sciences, Gulhane Medical Faculty, Chest Diseases, Ankara, Turkey
[2] University of Health Sciences, Gulhane Medical Faculty, Geriatric Medicine, Ankara, Turkey
[3] University of Health Sciences, Gulhane Medical Faculty, Radiology, Ankara, Turkey
[4] University of Health Sciences, Gulhane Medical Faculty, Infectious Diseases and Clinical Microbiology, Ankara, Turkey
[5] University of Health Sciences, Gulhane Medical Faculty, Intensive Care Medicine, Ankara, Turkey
[6] University of Health Sciences, Gulhane Medical Faculty, Emergency Medicine, Ankara, Turkey
[7] University of Health Sciences, Gulhane Medical Faculty, Medical Informatics, Ankara, Turkey
[8] University of Health Sciences, Gulhane Medical Faculty, Anesthesiology and Reanimation, Ankara, Turkey

Abstract

İntroduction: COVID-19 infection may be atypically presented in the older adults with a poor prognosis. In this study, we aimed to investigate the clinical and laboratory differences of COVID-19 course in older patients.

Materials and Method: The demographic, clinical, laboratory and radiological data of the patients hospitalized with COVID-19 infection were compiled retrospectively. A randomized control group was created from younger patients. Chest tomography of the patients were examined and scored.

Results: Data of 100 older and 127 younger patients with COVID-19 infection, and 80 non-COVID older patients were evaluated retrospectively. While the mean CRP, fibrinogen, procalcitonin, urea, LDH, INR, PT, Troponin-I, CK-MB and total radiological lung score were significantly higher in older patients; the mean hemoglobin, hematocrit and d-dimer were significantly higher in younger patients. Lymphopenia was more common and the mortality rate was higher in the older adults. Lymphopenia, presence of comorbidity, being over the age of 75, and radiological lung involvement were identified as mortality risk factors in older patients. The cut-off values for mortality were as follows; age≥77 years, lymphocyte#≤ 700x103 cells/μL, CRP≥108.71 mg/L, d-dimer≥2.25 mg/L, fibrinogen≥383 mg/L, INR≥1.05, PT ≥12.5 seconds, aPTT≥31 seconds, Troponin-I≥19.1 pg/mL, total lung score≥6 points. COVID-19 did not increase mortality much more than other hospital-requiring clinical events in older adults (17% vs 26.25%).

Conclusion: The older adults require special attention in COVID-19 pandemic. Those with comorbidities, lymphopenia, high d-dimer levels, and extensive lung involvement in the initial tomography should be followed-up closely.

Keywords: Covıd-19; Aged; Geriatrics; Mortality; Radiology

INTRODUCTION

World Health Organization (WHO) indicated that the incidence of COVID-19 is higher in young and middle-aged adults, but mortality rates increase with age (1, 2). This fact is even more important in the European region, where the older population is highest (3). The population aged over 65 years constitutes about 8.7% of the entire population and has reached over 7 million in Turkey (4). Despite the similar proportion of older adults, the number of deaths observed in Turkey is lower than in many European countries (1, 2). From this point of view, sharing the clinical conditions determining mortality will be beneficial for developing global strategies to struggle with COVID-19.

The mortality - age relationship of COVID-19 has multifactorial mechanisms (3, 5). The infectious diseases may have atypical presentations and poorer progress in older people due to the decline in the immune, anatomical and physiological defense systems. Available data suggest that COVID-19 infection can begin with atypical presentations in a significant proportion of the older adults (2, 5, 6).

This fact may contribute to late diagnosis and even a fatal course in the older patients.

Laboratory and radiological findings may also evolve with advancing age. Conditions such as underlying chronic diseases, polypharmacy, and suppression in the aging bone marrow create a need for a different perspective in the examination of laboratory data in older patients (7, 8). Lung radiology may change late due to dehydration. In addition, the declined respiratory reserve, may be inadequate in the patient with lung involvement (2, 5, 7). Considering that the current COVID-19 screening strategies are based on the typical findings of the disease, a need for a specialized clinical perspective for older adults arises (3, 6). Limited data are available in the literature on the course of COVID-19 in older patients. In this study, we aimed to reveal what clinical and laboratory differences are observed in older people diagnosed with COVID-19 in comparison with younger people. To the best of our knowledge, this is the first study comparing the older patients with confirmed COVID-19 infection and the patients hospitalized with a pre-diagnosis of COVID-19 but excluded from COVID-19 by clinical findings and real-time reverse-transcriptase polymerase chain reaction (PCR) tests.

METHODS

We obtained approval from the local ethic committee. A retrospective review was carried out between the dates of May 15th and March 11th, the date of the first COVID-19 case in Turkey.

Study population:

All of the patients aged 65 and over who were hospitalized with a pre-diagnosis of COVID-19 were searched. Cases with missing clinical, laboratory or radiological data were excluded from the study. Patients with confirmed COVID-19 infection were assessed as PCR (+) older patients. Patients excluded from the diagnosis of COVID-19 due to clinical findings and at least twice PCR negativity were assessed as PCR (-) older patients. A randomized control group consisting of 127 younger patients (young and middle-aged adults) with positive PCR results was composed by sorting younger patients according to age and randomly selection by skipping at regular intervals.

Clinical and laboratory findings

Demographic and clinical features were scanned. Laboratory data were obtained from the blood tests on the first day of admission. The pre-hospitalization residencies were grouped as “home residents” and “health care center/nursing home residents”.

Radiological assessment

Chest computed tomography (CT) images were examined by two radiologists. Disputes in the radiologists were resolved by consensus. If there is a lung involvement, the infiltration pattern was determined and grouped as “sub-pleural” (mainly containing peripheral third of the lung), “random”

(without dominance in the sub-pleural or central regions) or "diffuse" (continuous involvement). To measure the degree of lung involvement, a CT scoring system, a semi-quantitative evaluation method, was applied. Two lungs were evaluated in a total of 5 lobes. First, the extent of the lesion in each lobe was visually estimated, and a point between 1 and 5 was given due to the extent of the involvement (0 point: no involvement, 1 point: 1-25%, 2 points: 26-50%, 3 points: 51-75%, 4 points: 76-100%). Secondly, the total lung score ranged from 0 to 20 was obtained by summing the points of the five lobes.

Statistical analysis

The mean and standard deviation (± SD) were calculated for continuous variables and proportions were calculated for categorical variables. Chi-square and Fisher exact tests were used in univariate analysis of categorical variables; and Student-T and Wilcoxon rank-sum tests were used in univariate analysis of continuous variables. Tests were selected according to their usefulness to meet assumptions for binary comparisons. Survival analysis was made to investigate mortality as a time-to event outcome. Kaplan–Meier analysis for estimating the proportional surviving by time, bilateral log rank test for the comparison of the curves, and multivariate logistic regression analysis for determining the risk factors were used. In calculations, type I error rate alpha: 0.05 was accepted. P-value less than 0.05 was considered as statistically significant.

RESULTS

A total of 192 patients aged 65 and over were hospitalized in the COVID-19 clinic during the study period. The data of 180 were properly accessible.

Evaluation of all older patients hospitalized in the COVID-19 clinic

Demographic findings such as age, gender, body mass index (BMI) did not differ significantly between groups. While the mean hospital-stay length and the frequency of residence in a nursing home/health care center were higher in PCR (+) older patients; the mean body temperature, and the frequency of comorbidities and smoking history were significantly higher in PCR (-) older patients. Comorbidity was present in 74% of PCR (+) older patients, 37% of whom had multiple comorbidities. However, 95% of PCR (-) older patients had co-morbidities (multiple comorbidities in 71.25%). The major comorbidities and their frequencies observed in PCR (+) cases were hypertension (56%), diabetes mellitus (DM) (20%), coronary artery disease (15%), cerebrovascular events (10%), atrial fibrillation (AF) (9%), chronic obstructive pulmonary disease (COPD) (9%), Parkinson's disease (4%) and cancer (3%). Those of PCR (-) older adults were as follows; hypertension (66.25%), coronary artery disease (41.25%), DM (38.75%), COPD (16.25%), chronic kidney disease (12.5%), cancer (11.25%), AF (6.25%), congestive heart failure (5%), cerebrovascular accident (5%) and asthma (3.75%). It can be concluded that the high number of these comorbidities plays an important role in hospitalization indications and mortality frequencies of the PCR (-) older adults. The most notable laboratory data differences between the two groups are the significant elevation of the mean white blood cell count (Wbc), d-dimer, urea, creatinine and troponin-I in PCR (-) older patients. These differences were emerged due to bacterial infections and comorbid conditions, especially cardiac events. The mortality rate was higher in PCR (-) older patients (26.25% vs 17%). This was interpreted as COVID-19 does not increase mortality much more than other hospital-requiring clinical events in older adults (Table 1).

Evaluation of PCR (+) older adults and PCR (+) young and middle-aged control group

The demographic, clinical, laboratory and radiological data of the patients were compared between the groups (Table 2).

- Demographic and clinical findings: The younger patients had a mean body temperature of 0.7 degrees higher than the older adults. While the duration of hospitalization, residency in a nursing

Table 1. Comparison of clinical and laboratory data of PCR positive and negative older adults. Case numbers and % values of non-variable parameters, mean values and standard deviations (SD) of variable parameters are listed. PCR: polymerase chain reaction, BMI: body mass index, Wbc: white blood cell, Hgb: hemoglobin, Hct: hematocrit, Plt: platelet, Neut#: absolute neutrophil number, Lymph#: absolute lymphocyte number, Eos#: absolute eosinophil number, CRP: C-reactive protein, LDH: lactate dehydrogenase, INR: international normalized ratio, PT: prothrombin time, aPTT: activated partial thromboplastin time, Trop-I: Troponin-I CK-MB: creatine kinase-MB, ICU: intensive care unit, IMV: invasive mechanical ventilation, ARDS: acute respiratory distress syndrome.

		PCR (+) older adults (n: 100)	PCR (-) older adults (n: 80)	p
Age (years) (SD)		73.68 (8.06)	75.34 (7.29)	0. 061
Gender	Female (n, %)	57 (57%)	35 (43.75%)	0.099
	Male (n, %)	43 (43%)	45 (56.25%)	
BMI (SD)		26.08 (2.88)	25.96 (2.69)	0.764
Fever (°C)		36.70 (0.5)	37.40 (0.6)	0.065
Hospital stay, days (SD)		11.85 (4.87)	6.69 (3.78)	<0.001
Nursing home/health care center (n, %)		12 (12%)	1 (1.25%)	0.007
Comorbidity (n, %)		74 (74%)	76 (95%)	0.001
Dementia / Alzheimer's disease (n, %)		8 (8%)	6 (7.5%)	>0.999
Smoking history (n, %)		13 (13%)	23 (28.75%)	0.033
Wbc, $x10^3$ cells/μL (SD)		5551.00 (2079.36)	9117.50 (4217.53)	<0.001
Hgb, g/dL (SD)		13.07 (1.61)	12.47 (1.91)	0.028
Hct, % (SD)		38.87 (4.69)	37.79 (5.68)	0.210
Plt, $x10^3$ cells/μL (SD)		207950.00 (78560.45)	235150.00 (92022.30)	0.029
Neut#, $x10^3$ cells/μL (SD)		3659.00 (1815.82)	6945.00 (4009.23)	<0.001
Lymph#, $x10^3$ cells/μL (SD)		1333.70 (616.76)	1448.75 (1101.21)	0.992
Eos#, $x10^3$ cells/μL (SD)		50.10 (75.82)	125.00 (138.25)	<0.001
CRP, mg/L (SD)		42.71 (60.08)	76.87 (86.63)	0.003
D-dimer, mg/L (SD)		2.19 (8.14)	4.02 (10.12)	<0.001
Fibrinogen, mg/dL (SD)		388.32 (126.56)	461.82 (173.46)	0.036
Ferritin, ng/mL (SD)		253.86 (295.61)	342.47 (406.52)	0.699
Procalcitonin, ng/mL (SD)		0.37 (1.44)	1.01 (3.33)	0.003
Urea, mg/dl (SD)		44.34 (26.83)	62.60 (34.63)	<0.001
Creatinine, mg/dL (SD)		0.98 (0.38)	1.42 (1.07)	<0.001
LDH, U/L (SD)		293.23 (245.26)	324.48 (147.35)	0.006
INR (SD)		1.12 (0.46)	1.26 (0.89)	0.223
PT, seconds (SD)		12.83 (4.03)	14.82 (10.02)	0.127
aPTT, seconds (SD)		29.65 (7.22)	35.58 (40.55)	0.782
Trop-I, pg/mL (SD)		47.88 (180.69)	227.65 (1358.40)	<0.001
CK-MB, ng/mL (SD)		3.17 (4.61)	7.80 (27.31)	0.003
Transfer to ICU (n, %)		23 (23.00%)	28 (35.00%)	0.096
IMV (n, %)		16 (16.00%)	15 (18.75%)	0.693
Acute cardiac events (n, %)		10 (10.00%)	15 (18.75%)	0.128
ARDS (n, %)		11 (11.00%)	4 (5.00%)	0. 181
Acute renal failure (n, %)		22 (22.00%)	25 (31.25%)	0.175
Sepsis (n, %)		13 (13.00%)	14 (17.50%)	0.410
Mortality (n, %)		17 (17.00%)	21 (26.25%)	0.145

home/health care center, presence of comorbidity, and dementia/Alzheimer's disease were observed more frequently in older patients, the frequency of smoking was significantly higher in younger patients (Table 2). Comorbidities were rarer in younger patients with a frequency of 29% (multiple comorbidities in 10%). The major comorbidities observed in younger cases were hypertension (13.38%), diabetes mellitus (DM) (6.29%), COPD (3.93%), coronary artery disease (3.15%), asthma (2.36%).

- Laboratory findings: While the mean C-reactive protein (CRP), fibrinogen, procalcitonin, urea, lactate dehydrogenase (LDH), international normalized ratio (INR), prothrombin time (PT), Troponin-I and creatine kinase-MB (CK-MB) values were significantly higher in older patients; the mean hemoglobin, hematocrit and d-dimer values were significantly higher in younger patients (Table 2). Lymphopenia (lymphocyte#<1000x103 cells/μL) was present in 40% of older adults, and 26.7% of younger patients.

- Radiological findings: Lung involvement was observed significantly more frequently in the older adults. The most common radiological pattern was peripheral infiltration and the greatest amount of involvement was in the lower lobes, especially right lower lobe, in the both age groups. The total lung score was significantly higher in the older adults (Table 2).

- Survival analysis: Considering older patients and the control group together, a total of 227 cases were divided to "survival" and "mortality" groups. The mean age, body temperature, length of hospital-stay, Wbc, platelet, neutrophil#, lymphocyte#, CRP, d-dimer, fibrinogen, procalcitonin, urea, creatinine, LDH, INR, PT, activated partial thromboplastin time (aPTT), troponin-I, CK-MB; the presence of comorbidity and dementia/Alzheimer's disease; the frequency of radiological involvement and the mean total lung scores had significant differences between groups (Table 3). A separate mortality assessment was performed only in older patients (Table 4). The mean body temperatures did not have significant difference between survival groups among older patients. While gender was not statistically significant in the overall mortality assessment, male gender mortality was significant in older adults.

- Analysis of mortality risk factors: When regression analysis is performed for data with Akaike's information criterion (AIC) review, the age (HR:1.11, CI:1.04-1.20) (p=0.006), length of hospital-stay (HR:0.83, CI:0.69-0.98) (p=0.038), and uremia (HR:1.05, CI:1.02-1.08) (p=0.004) were determined as statistically significant risk factors for all PCR (+) patients. When we apply the AIC modeling to the data of PCR (+) older adults separately, only uremia was found to be statistically significant risk factor (HR:1.04, CI:1.01-1.08) (p=0.024). In terms of mortality analysis, Kaplan-Meier analysis was also performed. When older and younger PCR (+) cases were examined together, older age, male gender, and presence of comorbidities were determined as mortality risk factors. When only older patients were examined, lymphopenia, presence of comorbidities, age of 75, and radiological lung involvement were identified as mortality risk factors. Although mortality was observed more frequently in smokers, smoking was not found as a significant risk factor for mortality (Figure 1). As known, "older adults" has been defined as a chronological age of 65 years old or older. On the other hand, according to what is generally accepted, those whose age are between 65-74 are considered to be "early elderly", while those over 75 years old as "late elderly". In this regard, we considered it appropriate to look at the effect of being early and late elderly on mortality. Indeed, being late elderly was found as a mortality risk factor. Lymphopenia was also a mortality risk factor in older ages (Figure 1). The cut-off values for mortality were as follows; age≥77 years, lymphocyte#≤700x103 cells/μL, CRP≥108.71 mg/L, d dimer≥2.25 mg/L, fibrinogen≥383 mg/L, INR≥1.05, PT≥12.5 seconds, aPTT≥31 seconds, Troponin I≥ 19.1 pg/mL, total lung score≥6 points. It was observed that mortality increased significantly above these values in PCR (+) older patients.

Table 2. Comparison of demographic, clinical, laboratory and radiological data of PCR positive older and younger adults. Case numbers and % values of non-variable parameters, mean values and standard deviations (SD) of variable parameters are listed. PCR: polymerase chain reaction, BMI: body mass index, ICU: intensive care unit, IMV: invasive mechanical ventilation, ARDS: acute respiratory distress syndrome, Wbc: white blood cell, Hgb: hemoglobin, Hct: hematocrit, Plt: platelet, Neut#: absolute neutrophil number, Lymph#: absolute lymphocyte number, Eos#: absolute eosinophil number, CRP: C-reactive protein, LDH: lactate dehydrogenase, INR: international normalized ratio, PT: prothrombin time, aPTT: activated partial thromboplastin time, Trop-I: Troponin-I CK-MB: creatine kinase-MB.

		PCR (+) older adults (n: 100)	PCR (+) young and middle-aged adults (n: 127)	p
Age (years) (SD)		73.68 (8.06)	42.74 (12.83)	<0.001
Gender	Female (n, %)	57 (57.00%)	67 (52.76%)	0.592
	Male (n, %)	43 (43.00%)	60 (47.24%)	
BMI (SD)		26.08 (2.88)	25.89 (3.16)	0.420
Fever (°C)		36.70 (0.5)	37.50	0.045
Hospital stay, days (SD)		11.85 (4.87)	10.77 (3.91)	0.049
Nursing home/health care center (n, %)		12 (12.24%)	0 (0.00%)	<0.001
Comorbidity (n, %)		74 (74.00%)	29 (22.83%)	<0.001
Dementia / Alzheimer's disease (n, %)		8 (8.00%)	0 (0.00%)	0.001
Smoking history (n, %)		11 (13.25%)	38 (39.18%)	<0.001
Wbc, x10^3 cells/µL (SD)		5551.00 (2079.36)	5360.47 (2266.31)	0.405
Hgb, g/dL (SD)		13.07 (1.61)	13.75 (1.72)	<0.001
Hct,% (SD)		38.87 (4.69)	40.38 (5.58)	0.001
Plt, x10^3 cells/µL (SD)		207950.00 (78560.45)	205748.03 (61159.69)	0.594
Neut#, x10^3 cells/µL (SD)		3659.00 (1815.82)	3392.91 (1981.83)	0.227
Lymph#, x10^3 cells/µL (SD)		1333.70 (616.76)	1405.51 (544.86)	0.182
Eos#, x10^3 cells/µL (SD)		50.10 (75.82)	59.06 (86.70)	0.490
CRP, mg/L (SD)		42.71 (60.08)	21.64 (44.85)	<0.001
D-dimer, mg/L (SD)		2.19 (8.14)	2.99 (25.94)	<0.001
Fibrinogen, mg/dL (SD)		388.32 (126.56)	318.71 (110.93)	0.006
Ferritin, ng/mL (SD)		253.86 (295.61)	245.55 (288.93)	0.875
Procalcitonin, ng/mL (SD)		0.37 (1.44)	0.16 (0.56)	0.022
Urea, mg/dl (SD)		44.34 (26.83)	28.23 (16.79)	<0.001
Creatinine, mg/dL (SD)		0.98 (0.38)	0.89 (0.20)	0.251
LDH, U/L (SD)		293.23 (245.26)	248.43 (165.67)	0.020
INR (SD)		1.12 (0.46)	0.99 (0.07)	0.026
PT, seconds (SD)		12.83 (4.03)	11.74 (0.80)	0.045
aPTT, seconds (SD)		29.65 (7.22)	28.13 (5.08)	0.716
Trop-I, pg/mL (SD)		47.88 (180.69)	5.41 (11.43)	<0.001
CK-MB, ng/mL (SD)		3.17 (4.61)	1.24 (1.26)	<0.001
Transfer to ICU (n, %)		23 (23.00%)	4 (3.15%)	<0.001
IMV (n, %)		16 (16.00%)	3 (2.36%)	<0.001
Acute cardiac events (n, %)		10 (10.00%)	2 (1.57%)	0.006
ARDS (n, %)		11 (11.00%)	3 (2.36%)	0.010
Acute renal failure (n, %)		22 (22.00%)	9 (7.09%)	0.002
Sepsis (n, %)		13 (13.00%)	3 (2.36%)	0.003
Mortality (n, %)		17 (17.00%)	2 (1.57%)	<0.001
Radiological lung infiltration	No infiltration (n, %)	19 (20.88%)	36 (32.43%)	0.027
	Peripheral infiltration (n, %)	40 (43.96%)	46 (41.44%)	
	Randomized infiltration (n, %)	28 (30.77%)	18 (16.22%)	
	Diffuse infiltration (n, %)	4 (4.40%)	11 (9.91%)	
Radiological infiltration score	Right upper lobe (SD)	0.67 (0.75)	0.52 (0.77)	0.075
	Right middle lobe (SD)	0.65 (0.94)	0.50 (0.88)	0.109
	Right lower lobe (SD)	1.00 (0.93)	0.81 (0.95)	0.067
	Left upper lobe (SD)	0.60 (0.73)	0.53 (0.78)	0.244
	Left lower lobe (SD)	0.87 (0.93)	0.80 (0.97)	0.423
Total lung score (SD)		3.78 (3.70)	3.13 (3.88)	0.050

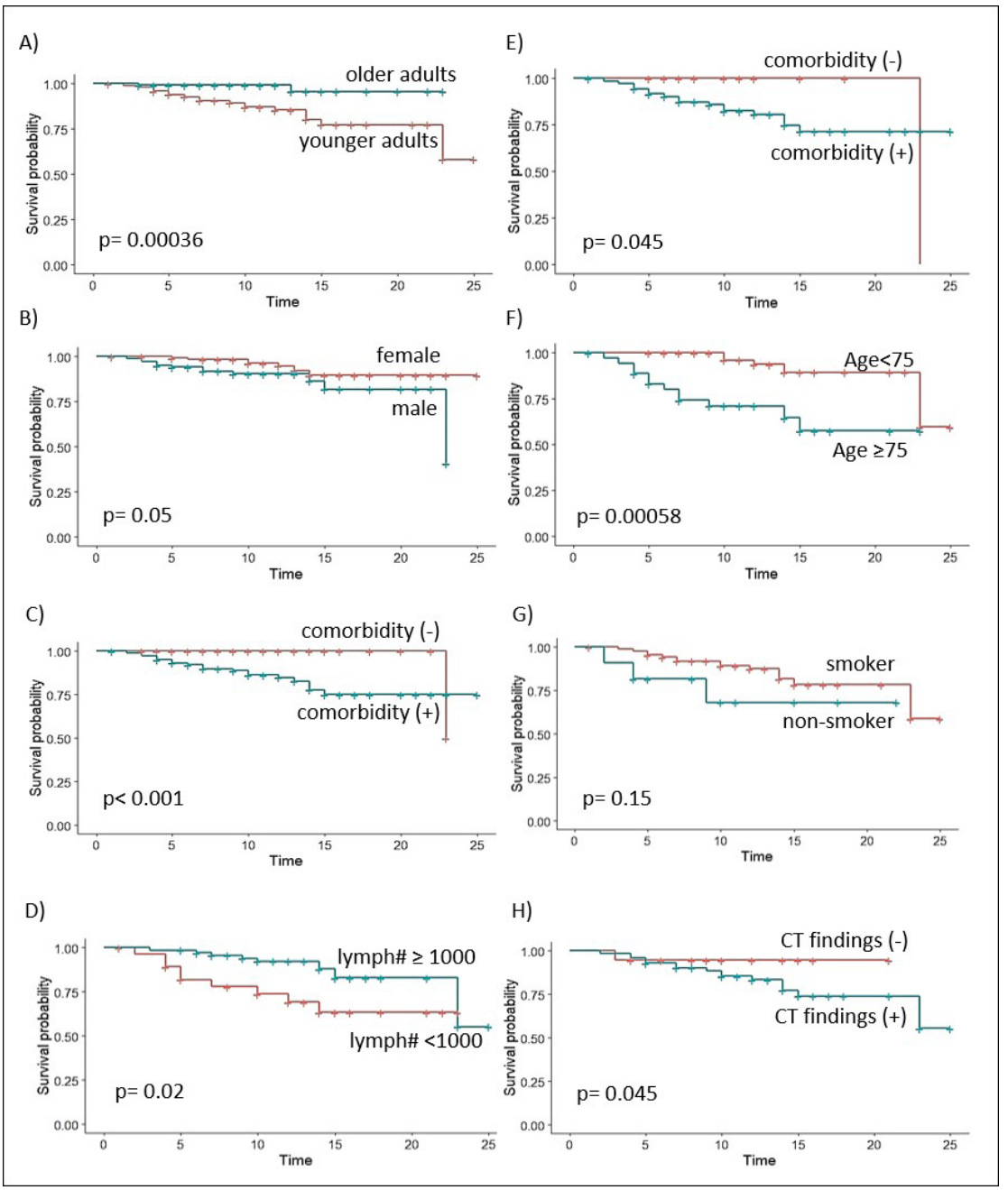
Table 3. Comparison of PCR positive cases according to their survival and mortality status regardless of age (older and younger adults together). Case numbers and % values of non-variable parameters, mean values and standard deviations (SD) of variable parameters are listed. PCR: polymerase chain reaction, BMI: body mass index, Wbc: white blood cell, Hgb: hemoglobin, Hct: hematocrit, Plt: platelet, Neut#: absolute neutrophil number, Lymph#: absolute lymphocyte number, Eos#: absolute eosinophil number, CRP: C-reactive protein, LDH: lactate dehydrogenase, INR: international normalized ratio, PT: prothrombin time, aPTT: activated partial thromboplastin time, Trop-I: Troponin-I CK-MB: creatine kinase-MB, ICU: intensive care unit, IMV: invasive mechanical ventilation, ARDS: acute respiratory distress syndrome.

		Survival group (n: 208)	Mortality group (n: 19)	p
Age (years) (SD)		54.62 (18.53)	75.53 (10.67)	<0.001
Gender	Female (n, %)	117 (56.25%)	7 (36.84%)	0.148
	Male (n, %)	91 (43.75%)	12 (63.16%)	
BMI (SD)		25.97 (2.89)	26.10 (4.31)	0.580
Fever ($^{\circ}$C)		37.10 (0.5)	37.66 (0.8)	0.043
Hospital stay, days (SD)		11.48 (4.22)	8.74 (5.41)	0.011
Nursing home/health care center (n, %)		11 (5.37%)	1 (5.26%)	>0.999
Comorbidity (n, %)		85 (40.87%)	18 (94.74%)	<0.001
Dementia / Alzheimer's disease (n, %)		5 (2.40%)	3 (15.79%)	0.021
Smoking history (n, %)		45 (27.27%)	4 (26.67%)	>0.999
Wbc, x10^3 cells/µL (SD)		5265.29 (1775.60)	7405.26 (4377.27)	0.019
Hgb, g/dL (SD)		13.49 (1.71)	13.01 (1.62)	0.077
Hct,% (SD)		39.80 (5.28)	38.81 (4.88)	0.093
Plt, x10^3 cells/µL (SD)		209451.92 (69177.48)	176789.47 (63857.98)	0.012
Neut#, x10^3 cells/µL (SD)		3310.58 (1458.83)	5694.74 (3984.48)	<0.001
Lymph#, x10^3 cells/µL (SD)		1397.93 (567.21)	1110.53 (637.61)	0.018
Eos#, x10^3 cells/µL (SD)		56.30 (81.38)	42.11 (90.16)	0.169
CRP, mg/L (SD)		23.43 (38.84)	111.94 (101.18)	<0.001
D-dimer, mg/L (SD)		2.31 (19.90)	5.94 (17.31)	0.003
Fibrinogen, mg/dL (SD)		340.64 (110.28)	453.23 (171.94)	0.011
Ferritin, ng/mL (SD)		221.23 (232.39)	420.28 (498.88)	0.136
Procalcitonin, ng/mL (SD)		0.13 (0.45)	1.43 (2.96)	<0.001
Urea, mg/dl (SD)		32.04 (16.78)	71.32 (44.81)	<0.001
Creatinine, mg/dL (SD)		0.89 (0.21)	1.35 (0.59)	<0.001
LDH, U/L (SD)		248.32 (158.54)	483.05 (429.27)	<0.001
INR (SD)		1.05 (0.36)	1.15 (0.19)	<0.001
PT, seconds (SD)		12.13 (3.11)	13.63 (2.17)	<0.001
aPTT, seconds (SD)		27.97 (5.44)	33.85 (7.99)	0.003
Trop-I, pg/mL (SD)		11.40 (47.98)	148.19 (353.28)	<0.001
CK-MB, ng/mL (SD)		1.85 (2.97)	4.41 (5.39)	<0.001
Transfer to ICU (n, %)		9 (4.33%)	18 (94.74%)	<0.001
IMV (n, %)		3 (1.44%)	16 (84.21%)	<0.001
Acute cardiac events (n, %)		4 (1.92%)	8 (42.11%)	<0.001
ARDS (n, %)		1 (0.48%)	13 (68.42%)	<0.001
Acute renal failure (n, %)		15 (7.21%)	16 (84.21%)	<0.001
Sepsis (n, %)		2 (0.96%)	14 (73.68%)	<0.001
Radiological lung infiltration	No infiltration (n, %)	54 (29.19%)	17 (8.42%)	0.026
	Peripheral infiltration (n, %)	80 (43.24%)	1 (5.88%)	
	Randomized infiltration (n, %)	38 (20.54%)	6 (35.29%)	
	Diffuse infiltration (n, %)	13 (7.03%)	2 (11.76%)	
Radiological infiltration score	Right upper lobe (SD)	0.54 (0.71)	1.12 (1.11)	0.015
	Right middle lobe (SD)	0.48 (0.83)	1.47 (1.23)	<0.001
	Right lower lobe (SD)	0.81 (0.88)	1.82 (1.13)	<0.001
	Left upper lobe (SD)	0.51 (0.73)	1.12 (0.86)	<0.001
	Left lower lobe (SD)	0.77 (0.91)	1.53 (1.12)	0.001
Total lung score (SD)		3.09 (3.50)	7.06 (5.07)	<0.001

Table 4. Comparison of death and survival groups of PCR (+) older adults. Case numbers and % values of non-variable parameters, mean values and standard deviations (SD) of variable parameters are listed. PCR: polymerase chain reaction, BMI: body mass index, Wbc: white blood cell, Hgb: hemoglobin, Hct: hematocrit, Plt: platelet, Neut#: absolute neutrophil number, Lymph#: absolute lymphocyte number, Eos#: absolute eosinophil number, CRP: C-reactive protein, LDH: lactate dehydrogenase, INR: international normalized ratio, PT: prothrombin *time*, aPTT: activated partial thromboplastin time, Trop-I: Troponin-I CK-MB: *creatine kinase-MB*, ICU: intensive care unit, IMV: *invasive mechanical ventilation*, ARDS: acute respiratory distress syndrome.

		Survival group (n: 83)	Mortality group (n: 17)	p
Age (years) (SD)		72.73 (7.97)	78.29 (7.05)	0.004
Gender	Female (n, %)	51 (61.45%)	6 (35.29%)	0.050
	Male (n, %)	32 (38.55%)	11 (64.71%)	
BMI (SD)		26.15 (2.83)	25.72 (3.22)	0.424
Fever (°C)		36.62 (0.4)	37.09 (0.7)	0.065
Hospital stay, days (SD)		12.47 (4.53)	8.82 (5.46)	0.004
Nursing home/health care center (n, %)		11 (13.58%)	1 (5.88%)	0.686
Comorbidity (n, %)		58 (69.88%)	16 (94.12%)	0.046
Dementia / Alzheimer's disease (n, %)		5 (6.02%)	3 (17.65%)	0.043
Smoking history (n, %)		8 (9.64%)	3 (17.65%)	0.392
Wbc, x10^3 cells/µL (SD)		5403.61 (2035.92)	6270.59 (2201.64)	0.167
Hgb, g/dL (SD)		13.04 (1.62)	13.18 (1.62)	0.894
Hct,% (SD)		38.79 (4.66)	39.27 (4.94)	0.901
Plt, x10^3 cells/µL (SD)		216987.95 (81023.86)	163823.53 (45278.63)	0.002
Neut#, x10^3 cells/µL (SD)		3442.17 (1667.71)	4717.65 (2170.90)	0.017
Lymph#, x10^3 cells/µL (SD)		1404.46 (609.25)	988.24 (546.45)	0.004
Eos#, x10^3 cells/µL (SD)		50.72 (72.12)	47.06 (94.32)	0.368
CRP, mg/L (SD)		30.31 (40.00)	102.50 (97.08)	<0.001
D-dimer, mg/L (SD)		1.40 (3.84)	6.09 (17.87)	0.050
Fibrinogen, mg/dL (SD)		368.05 (102.95)	462.67 (176.03)	0.050
Ferritin, ng/mL (SD)		228.38 (255.80)	330.30 (395.84)	0.289
Procalcitonin, ng/mL (SD)		0.11 (0.27)	1.48 (3.12)	<0.001
Urea, mg/dl (SD)		39.82 (21.84)	66.41 (37.24)	<0.001
Creatinine, mg/dL (SD)		0.91 (0.26)	1.33 (0.61)	<0.001
LDH, U/L (SD)		272.06 (225.07)	395.35 (314.02)	0.005
INR (SD)		1.12 (0.51)	1.15 (0.20)	0.005
PT, seconds (SD)		12.60 (4.38)	13.68 (2.28)	0.002
aPTT, seconds (SD)		27.86 (6.04)	34.37 (8.13)	0.002
Trop-I, pg/mL (SD)		21.65 (74.10)	158.96 (372.82)	<0.001
CK-MB, ng/mL (SD)		2.81 (4.28)	4.63 (5.67)	0.111
Transfer to ICU (n, %)		7 (8.43%)	16 (94.12%)	<0.001
IMV (n, %)		2 (2.41%)	14 (82.35%)	<0.001
Acute cardiac events (n, %)		3 (3.61%)	7 (41.18%)	<0.001
ARDS (n, %)		0 (0.00%)	11 (64.71%)	<0.001
Acute renal failure (n, %)		8 (9.64%)	14 (82.35%)	<0.001
Sepsis (n, %)		1 (1.20%)	12 (70.59%)	<0.001
Radiological lung infiltration	No infiltration (n, %)	18 (24.00%)	1 (6.25%)	0.160
	Peripheral infiltration (n, %)	34 (45.33%)	6 (37.50%)	
	Randomized infiltration (n, %)	20 (26.67%)	8 (50.00%)	
	Diffuse infiltration (n, %)	3 (4.00%)	1 (6.25%)	
Radiological infiltration score	Right upper lobe (SD)	0.61 (0.71)	0.94 (0.85)	0.136
	Right middle lobe (SD)	0.51 (0.84)	1.31 (1.08)	<0.001
	Right lower lobe (SD)	0.85 (0.85)	1.69 (1.01)	0.002
	Left upper lobe (SD)	0.52 (0.70)	1.00 (0.73)	0.007
	Left lower lobe (SD)	0.76 (0.90)	1.38 (0.96)	0.007
Total lung score (SD)		3.24 (3.38)	6.31 (4.16)	0.001

Figure 1. Kaplan-Meier survival curves for demographic variables. A) effect of age on mortality in all patients, B) effect of gender on mortality regardless of age, C) effect of presence of comorbidity on mortality regardless of age, D) effect of lymphopenia on mortality in elderly, E) effect of presence of comorbidity on mortality in elderly, F) effect of being over 75 years old on mortality in elderly, G) effect of smoking on mortality in elderly, H) effect of presence of radiological lung infiltration on mortality in elderly. lymph#: absolute lymphocyte number



DISCUSSION

This study was carried out to reveal the course and the mortality risk factors of COVID-19 in older patients. Although our results support the previous knowledge that COVID-19 is worse in the elderly, it can be concluded that COVID-19 does not have a higher mortality rate than other diseases among older patients. To our knowledge, this is the first study to compare the prognosis of COVID-19 with other clinical conditions requiring hospitalization in older patients.

While COVID-19 is more common in young and middle-aged adults, mortality is higher in the older patients (9, 10). Among all deaths the percentage of older patients was found as 96.5% in Italy, 80.8% in China, 80% in USA (11-13). Age-related immune system changes, comorbidities and atypical clinical presentations may lead to increased mortality by complicating the diagnosis and the treatment of COVID-19 in older adults. The body temperature tends to be lower in elderly up to -1°C, even in patients with infection, than younger ones (2, 14, 15). Non-specific symptoms such as general condition disorders, confusion, urinary/stool incontinence may be the primary symptoms of pneumonia in older people (5, 16, 17). In accordance with previous reports, we observed that younger patients had a mean body temperature of 0.7 degrees higher than the older ones at the time of hospital admission. In other words, low fever should not exclude COVID-19 in the older adults.

Comorbidities are also one of the worsening factors of COVID-19 prognosis (10, 18, 19). Cardiovascular diseases have been reported as the most common comorbidities associated with mortality (17, 19, 20). Diabetes Mellitus and coronary artery diseases follow them (21). In the present study, the incidence of comorbidities increased significantly with age, and the mortality was correlated with the frequency of comorbidities. It can be clearly stated that the older adults with cardiovascular diseases and DM constitute the riskiest population for COVID-19 infection.

Increase in LDH, ferritin and CRP are common laboratory changes in patients with COVID-19 (18, 19). Lymphopenia was detected in 90% of the patients in New York and has been associated with mortality (21). High d-dimer and procalcitonin levels, and coagulopathy were also found to be related to severe disease (13, 18, 21). Despite the fact that the basal values and laboratory responses of older people to infection may differ from younger people, we still have limited data on laboratory changes in the older patients with COVID-19 infection. In the study of Liu et al., the mean Wbc, neutrophil# and CRP were significantly higher and the lymphopenia was more common in the older patients (22). They interpreted this situation as the older patients with COVID-19 infection are also prone to bacterial infections. In this study, the mean CRP, fibrinogen, procalcitonin, urea, LDH, INR, PT, Troponin-I and CK-MB levels were higher in older patients; and there were significant differences between survival groups in terms of Wbc, platelet, neutrophil#, lymphocyte#, CRP, d-dimer, fibrinogen, procalcitonin, urea, creatinine, LDH levels, cardiac enzymes and coagulation markers. Lymphopenia was a mortality risk factor especially for older adults. We took the results of previous studies a step further and examined the cut-off values for mortality. The mortality rate was increasing with cut-off values of lymphocyte# above $700x10^3$ cells/μL, CRP over 108.71 mg/L, d-dimer over 2.25 mg/L, fibrinogen over 383 mg/L. Older patients who exceed these cut-off values should be followed much more closely.

Thorax CT has a big role in the diagnosis of COVID-19 infection and predicting its prognosis (10, 23-25). However, data about the radiological findings of older patients is still limited. Right lower lobe of the lung was identified as the most frequently involved area (23). Using a scoring system similar to ours, Chung et al. associated the mean total lung score with mortality (23). Similarly, we observed the right lower lobe as the most common area involved, and the radiological involvement in "initial CT" was a mortality risk factor among all age

groups. The total lung score was lower than that of Chung et al. with a mean of 3.78 points in the older and 3.13 points in the younger patients. Li et al.'s study focused on the association of "initial CT" findings with mortality in patients aged 60 years and older (24). They reported that high CT score was a mortality risk factor in older patients. Liu et al. stated that the incidence of multiple lobe infiltration is significantly common in older patients (22). Similar to the previous results, we observed multiple lobe lung involvement more frequently in the older adults, with a peripheral pattern in lower lobes. The mean total lung scores had significant differences between older adults and younger patients, and also between survival groups. The radiological lung involvement was identified as a mortality risk factor for patients with total lung score above 6 points.

In conclusion, we emphasize that older adults, especially aged over 75 years, are worse affected by COVID-19 pandemic. While COVID-19 infection may show atypical presentations in older adults, a favorable course on prognosis can be achieved with a specialized clinical perspective. Older patients with lymphopenia, high d-dimer and fibrinogen levels, multiple comorbidities and significant pulmonary involvement in the initial CT should be considered as at high risk for mortality and be followed-up closely. Being single-centered and retrospective are the limitations of our study. Because we are a 3rd level health institution and critical patients are more frequently referred to our hospital, the mortality rates determined in this study should not be reflected in the general population in Turkey.

Acknowledgments: We would like to thank all the healthcare professionals working devotedly in the COVID-19 clinics and intensive care units. This study has emerged thanks to them.

Disclosure statement: The authors declare no conflict of interest.

REFERENCES

1. World Health Organization. [Internet]. Available from: https://covid19.who.int. Accessed: 19.06.2020.
2. Naharci MI, Katipoglu B, Tasci I. Coronavirus 2019 (COVID-19) outbreak and geropsychiatric care for older adults: A view from Turkey. International Psychogeriatrics. 2020;Jun(11):1-5. (DOI: 10.1017/S1041610220001167).
3. World Health Organization Regional Office for Europe. [Internet]. Available from: http://www.euro.who.int/en/health-topics/health-emergencies/coronavirus-covid-19/statements/statement-older-people-are-at-highest-risk-from-covid-19,-but-all-must-act-to-prevent-community-spread. Accessed:19.06.2020.
4. Turkish Statistical Institute. [Internet]. Available from: http://www.tuik.gov.tr/PreHaberBultenleri.do?id=30567. Accessed: 19.06.2020.
5. World Health Organization. [Internet]. Available from: https://www.who.int/news-room/q-a-detail/q-a-on-on-covid-19-for-older-people. Accessed: 19.06.2020.
6. Shahid Z, Kalayanamitra R, McClafferty B, et al. COVID-19 and Older Adults: What We Know. J Am Geriatr Soc. 2020;68(5):926-929. (PMID: 32255507).
7. Ocal N, Dogan D, Taskin G, Yildiz B, Ozturk S, Yamanel HL. Continual assessment of mortality risk factors in geriatric patients hospitalized in intensive care due to pneumonia. Turkish Journal of Geriatrics. 2016;19(1):1-8.
8. Ocal R, Arslan Y. Prognostic value of hematological parameters in geriatric patients hospitalized in intensive care units. Turkish Journal of Geriatrics. 2019;22(1):2-8. (DOI: 10.31086/tjgeri.2019150566)
9. Covino M, De Matteis G, Santoro M, et al. Clinical characteristics and prognostic factors in COVID-19 patients aged ≥80 years. Geriatr Gerontol Int. 2020;Jun(9): 10.1111/ggi.13960 (Epub ahead of print). (DOI: 10.1111/ggi.13960).
10. Lim WS, Liang CK, Assantachai P, et al. COVID ?19 and older people in Asia: Asian Working Group for Sarcopenia calls to actions. Geriatr Gerontol Int. 2020;20(6):547-58. (PMID: 32365259).

11. Guan W, Ni Z, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in china. N Engl J Med. 2020;382:1708-20. (DOI: 10.1056/NEJMoa2002032).

12. Wu Z, McGoogan JM. Characteristics of and Important Lessons from the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases from the Chinese Center for Disease Control and Prevention. JAMA. 2020; Feb 24 (Online ahead of print). (PMID: 32091533).

13. Onder G, Rezza G, Brusaferro S. Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy. JAMA. 2020; Mar 23 (Online ahead of print). (PMID: 32203977).

14. CDC COVID-19 Response Team. Severe outcomes among patients with Coronavirus Disease 2019 (COVID-19) - United States, February 12-March 16, 2020. MMWR Morb Mortal Wkly Rep. 2020;69(12):343-6. (PMID: 32214079).

15. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395(10229):1054-62. (PMID: 32171076).

16. Nikolich-Zugich J, Knox KS, Rios CT, Natt B, Bhattacharya D, Fain MJ. SARS-CoV-2 and COVID-19 in older adults: what we may expect regarding pathogenesis, immune responses, and outcomes. GeroScience. 2020;42(2):505-14. (PMID: 32274617).

17. Solana R, Pawelec G, Tarazona R. Aging and innate immunity. Immunity. 2006;24(5):491-4. (DOI: 10.1016/j.immuni.2006.05.003)

18. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. JAMA. 2020;323(11):1061-9. (PMID: 32031570).

19. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506. (PMID: 31986264).

20. Guan W-jie, Liang W-hua, Zhao Y, et al. Comorbidity and its impact on 1590 patients with Covid-19 in China: A Nationwide Analysis. Eur Respir J. 2020;55(5):2000547. (PMID: 32217650).

21. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City Area. JAMA. 2020;323(20):2052-9. (PMID: 32320003).

22. Liu K, Chen Y, Lin R, Han K. Clinical features of COVID-19 in elderly patients: A comparison with young and middle-aged patients. Journal of Infection. 2020;80(6):e14-e18. (PMID: 32171866).

23. Chung, M, Berheim A, Mei X, et al. CT Imaging Features of 2019 Novel Coronavirus (2019-nCoV). Radiology. 2020;295(1):202-7. (PMID: 32017661).

24. Li Y , Yang Z, Ai T , Wu S, Xia L. Association of "initial CT" findings with mortality in older patients with coronavirus disease 2019 (COVID-19). Eur Radiol. 2020; Jun 10:1-8 (Online ahead of print). (PMID: 32524220).

25. Prokop M, van Everdingen W, van Rees Vellinga T, et al. CO-RADS – A categorical CT assessment scheme for patients with suspected COVID-19: definition and evaluation. Radiology. 2020; Apr 27;201473 (Online ahead of print). (PMID: 32339082).

RESEARCH

FACTORS AFFECTING FRAILTY SYNDROME IN ELDERLY CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS AND ITS RELATIONSHIP WITH SYSTEMIC INFLAMMATION

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2020.182
2020; 23(4): 446-454

Burcu TALAY MUSTAFAOĞLU[1]
Şule TAŞ GÜLEN[1]
Fatih BİRTEKOCAK[2]
Aslıhan KARUL[2]
Fisun KARADAĞ[1]

CORRESPONDANCE
[1]Şule TAŞ GÜLEN

Adnan Menderes University, Faculty of Medicine, Department of Chest Diseases, Aydin, Turkey

Phone: +905309943091
e-mail: sule.tas@adu.edu.tr

Received: Oct 09, 2020
Accepted: Nov 19, 2020

[1] Adnan Menderes University, Faculty of Medicine, Department of Chest Diseases, Aydin, Turkey
[2] Adnan Menderes University, Faculty of Medicine, Department of Biochemistry, Aydin, Turkey

Abstract

Introduction: The aim was to identify the factors affecting the frailty syndrome in elderly chronic obstructive lung disease patients and to investigate its relationship with systemic inflammation.

Materials and Method: 61 stable patients (ages of 65-84) were included. Demographic data, body mass index, comorbidities, annual number of exacerbations were recorded. Pulmonary function test, six-minute walk test and Tilburg Frailty Test were performed in all cases. Patients were classified into groups A,B,C&D according to GOLD chronic obstructive lung disease guideline by annual exacerbation rate and dyspnea score. Neutrophil lymphocyte ratio, high sensitive C-reactive protein, IL-6, 8OH-dG, IL-18 levels were studied in serum.

Results: According to Tilburg test, 63.9% of the patients were evaluated as frail. There was a relationship between body mass index and Tilburg frailty score (p:0.035); body mass index was lower in the frail group. The number of comorbidities was higher in the frail group (p:0.007). There was a positive correlation between frailty and the number of drugs used. The frailty score was significantly higher in GOLD group B&C than in groups A&D (p: 0.006).

The neutrophil lymphocyte ratio was significantly higher in the frail group (p:0.007).

Conclusion: Frailty is more frequent in chronic obstructive lung disease patients, especially in those with malnutrition and comorbidities and it is associated with a systemic inflammation marker, neutrophil lymphocyte ratio. Routine assessment of frailty in chronic obstructive lung disease outpatients may allow early interventions, including referral to physical and respiratory rehabilitation, geriatric and nutritional specialists to improve physical performance and quality of life of these patients.

Keywords: Frailty; Pulmonary Disease, Chronic Obstructive; Inflammation

INTRODUCTION

Aging is described as a perpetual and universal process seen in every living being, leading to a reduction in all bodily functions. This process involves irreversible alterations in structural, functional, mental, and biopsychosocial functions of the organism at the level of molecules, cells, tissues, organs, and systems, manifesting in time (1). Frailty is defined as a geriatric syndrome manifesting with aging, characterized by fatigue and reduction of physiological reserves, and it is affected by various stressful situations. Considering the gradually increasing lifespan, this syndrome has been gaining more importance. Although numerous methods have been implemented for diagnostic assessment, the most commonly used methods are the Fried Scale (frailty phenotype) and the Frailty Index. The Fried Scale involves the parameters of fatigue, reduction in gait speed, reduction in physical activity, weakness, and weight loss, and describes frailty as a clinical syndrome involving three or more of these parameters. The Frailty Index involves a comprehensive geriatric evaluation consisting of cumulative clinical deficits. As these two scales comprise different parametes, there is no consensus on the validity of one over the other (2,3). Another method used for diagnostic assessment is the Tilburg Frailty Scale (TFS). TFS is a brief, simple, and global test that is suitable for use in both daily clinical practice and research; it measures the physical, psychological, and social function losses which are three essential components of frailty. TFS consists of 25 questions, and the validity and reliability of the Turkish form has been proven in the country (4).

Chronic obstructive pulmonary disease (COPD) is a systemic inflammatory disorder with high morbidity and mortality and is characterized by partially irreversible airway constriction (5,6). It is well known that COPD is not just a disease confined to the lung, but also has a clinical course with extrapulmonary manifestations and associated comorbidities related to systemic inflammation (7,8). Frailty syndrome is one of the comorbidities seen in COPD, with prevalence varying between 10-57%. Frailty has common risk factors with COPD, such as age, smoking, and endocrine dysfunction. Hypoxemia and dysfunction of skeletal muscles leading to reduction in cognitive and functional performance, and other phenotypic changes similar to those seen in frailty syndrome, such as fatigue, loss of appetite, weight loss, and decreased physical activity, are observed in patients with COPD. Additionally, recent studies have shown that frailty and related reduction of physical performance are among the significant determinative factors contributing to exacerbations and recurrent hospitalizations in COPD (9-11). In our study, we aimed to investigate factors such as the severity of COPD, frequency of exacerbations, functional assessment, and comorbidities, which may affect frailty syndrome in older patients with COPD, along with the association of frailty syndrome with systemic inflammation and oxidative stress.

MATERIALS and METHODS

The study was conducted in Adnan Menderes University Hospital, Department of Chest Diseases between June 2018 and October 2019, following the approval of the local ethics committee (protocol # 53043469-050.04.04). Sixty-one patients aged between 65-84 years, who were diagnosed with COPD and were stable according to the Global initiative for chronic obstructive lung disease (GOLD) 2019 criteria were included in the study, after obtaining their written informed consent (12). Those patients who did not have any acute worsening of symptoms, requiring additional treatment were considered "stable." Patients with a systemic inflammatory disease or malignancy, those within the COPD exacerbation period, and those who did not consent to participate were excluded from the study.

Study Protocol

Demographic data of all cases consisting of age, gender, occupation, smoking history, body

mass index (BMI), medical history, and physical examination were recorded. Patients were classified into groups A,B,C&D according to GOLD COPD guideline by annual exacerbation rate and dyspnea score (12). The additional details included associated comorbidities, names and doses of medications used, number of hospitalizations, exacerbation frequency, six-minute walking test (6MWT) result, COPD assessment test (CAT) result, and the results of Modified Medical Research Council (mMRC) dyspnea scale, and body-mass index, airflow obstruction, dyspnea, and exercise (BODE) Index used for determining the severity of dyspnea. BMI ≤ 21 kg/m^2 was considered low and BMI > 21 kg/m2 was considered normal. Pulmonary function tests (PFTs) and the TFS tests were performed in all cases. Serum samples were obtained for neutrophil-lymphocyte ratio (NLR), high-sensitivity C-reactive protein (hsCRP), interleukin-6 (IL-6), and interleukin-18 (IL-18) (as indicators of systemic inflammation), and for 8-hydroxy 2-deoxyguanosine (8OH-dG) levels (as an indicator of oxidative stress).

Pulmonary Function Test

Pulmonary function tests were performed in accordance with the American Thoracic Society (ATS) / European Respiratory Society (ERS) standards using the Jaeger Master Scope Spirometer (13). The diagnosis and staging of COPD were performed in accordance with the GOLD 2019 criteria (12).

Functional Assessment

The levels of dyspnea in participants were graded between 0 and 4 using the mMRC criteria. Exercise capacity was evaluated using the 6MWT in a 30-m long hospital corridor. The maximal distance that the patient could walk for 6 min at normal gait speed was recorded in meters. The BODE index was scored according to BMI, forced expiratory volume in 1st second (FEV1), mMRC dyspnea score, and 6MWT result.

Tilburg Frailty Test

Tilburg Frailty Score, which consisted of two sections and 25 questions, was applied to the cases. Section A involved potential determinants of frailty, such as sociodemographic characteristics, lifestyle, diseases, experienced events, and living environment. Section B involved 15 questions evaluating frailty components (physical, psychological, and social). Eleven items of TFS had the dual-answer form as "yes" and "no, whereas four items had the triple-answer form as "yes," "sometimes," and "no." The "yes" and "sometimes" answers were graded as one point, and the "no" answers as zero points. The results were scored between 0 to 15 points. Cases with scores ≥ 5 points were considered frail (4,14).

Biochemical Investigation

In all cases participating in the study, approximately 5 mL of blood was obtained and placed in a plain biochemistry tube, and then centrifuged at 3000 rpm for 15 min. The sera were separated and stored at -80°C until the day of the study. The hsCRP, IL-6, IL-18, and 8OH-dG tests were quantitatively studied using commercial ELISA kits. The test results were calculated using the Bioelisa Reader Elx800. The complete blood count parameters were studied using a BC 6800 Mindray device. For the calculation of NLR, the neutrophil count was divided by the lymphocyte count.

Statistical Analysis

Statistical evaluation was performed using SPSS (Statistical Package for Social Sciences v.21, IBM Corp., Armonk, NY, USA) statistical analysis software. Categorical measurements, such as sex and frailty groups, were expressed as numbers and percentages. Continuous measurements, such as age, height, and body weight, were expressed as mean ± standard deviation. Regarding the investigation of the difference between the two groups, the "in-

dependent samples t-test" was used for variables that were in conformity with a normal distribution, and the "Mann-Whitney U" test was used for variables that were not in conformity with a normal distribution. The "Chi-square" test was used for the analysis of relationships between categorical variables, and the results are presented in tables. The results were evaluated at a 95% confidence interval and a significance level of $p < 0.01$. The "Pearson correlation test" and "two-tailed test" were used for correlations. They were evaluated at significance levels of $p < 0.01$ and $p < 0.05$, respectively.

RESULTS

A total of 61 cases, consisting of 43 (70.5%) patients in the 65-74 years age group and 18 (29.5%) patients in the 75-84 years age group, were included in the study. 96.9% of the cases were males, whereas 3.1% were females. Among all cases, those with an educational level below high school consisted of 87.1%, whereas those with an educational level of high school or above consisted of 12.9%. While 71.9% of the cases had quit smoking, 18.1% were active smokers. A smoking history of over 40 pack-years was present in 62.5% of the cases. 31% of the cases had a history of hospitalization once or more in the last year due to exacerbations, with 12.5% of the cases having two or more exacerbations. In 57.8% of all cases, two or more comorbidities were present.

The cases were grouped as Group 1 (non-frail group [TFS < 5]) (36.1%) and Group 2 (frail group (TFS ≥ 5)] (63.9%). There was no statistically significant relationship between the two groups with regards to age, gender, marital status, education level, monthly income level, smoking history, exacerbation per year, and the number of exacerbations requiring hospitalization. There were statistically significant differences in BMI and the number of comorbidities between the two groups ($p = 0.035$ and $p = 0.007$, respectively). In Group 2, BMI was lower, and the number of comorbidities was higher (Table 1).

No statistically significant differences were determined between Groups 1 and 2 regarding the values of FEV1 (% predicted), forced vital capacity (FVC) (% predicted), and post-bronchodilator FEV1/FVC. The evaluation of GOLD staging showed that patients classified with GOLD group A, group B, group C and group D were 20 (32.8%), 21 (34.4%), 5 (8.2%), and 15 (24.5%) patients, respectively. Statistically significant differences were seen among GOLD stages regarding frailty status. The frailty scores of GOLD groups B and C were significantly higher than those of GOLD groups A and D ($p = 0.006$) (Table 2).

Analysis of mMRC dyspnea scores showed that 4.7% of the cases were mMRC-0, 35.0% were mMRC-1, 34.4% were mMRC-2, 18.18% were mMRC-3, and 4.3% were mMRC-4. While the CAT score was equal to or below 10 in 36.5% of the cases, it was above 10 in 63.5%. The BODE index score was 0-2 points in 60%, 3-4 points in 25%, 5-6 points in 5.1%, and 7-10 points in 5.5% cases. The comparison of Group 1 and Group 2 showed that, the CAT score was significantly higher in Group 2 than in Group 1 ($p = 0.027$), and the 6MWT distance percentage was significantly lower in Group 2 than in Group 1 ($p = 0.044$). However, no statistically significant difference was found between the two groups regarding the BODE index (Table 3).

When Groups 1 and 2 were compared regarding the indicators of systemic inflammation and oxidative stress, it was found that a significant difference was present for NLR ($p = 0.007$) which was higher in Group 2. However, no statistically significant differences were found regarding hsCRP, IL-6, IL-8, and 8OH-dG levels ($p > 0.01$) (Table 4).

The correlation analyses among frailty index, demographic data, functional parameters, and the indicators of systemic inflammation and oxidative stress revealed a negative correlation between frailty and body weight ($p = 0.017$, $r = -0.304$). The frailty index was positively correlated with the number of comorbidities and the number of drugs used by COPD patients ($p = 0.002$, $r = 0.383$; and $p = 0.002$, r

Table 1. Comparison of Demographic Data of Groups 1 and 2

		The frailty group according to the Tilburg score				P
	Group 1 (<5) (n=22)		Group 2 (≥5) (n=39)			
	N	%	N	%		
Age (years)	65-74	16	72.7	27	69.2	0.774
	75-84	6	27.3	12	30.8	
Gender	Male	22	100.0	37	94.9	0.405
	Female	0	0.0	2	5.1	
Marital status	Married	20	90.9	31	79.5	0.216
	Single/Widow	2	9.1	8	20.5	
Educational level	Less than high-school	20	90.9	34	87.2	0.505
	High-school and over	2	9.1	5	12.8	
Monthly income (TL)	≤ 1500	9	40.9	17	43.6	0.528
	>1500	13	59.1	22	56.4	
BMI (kg/m^2)	≤ 21	0	0.0	7	17.9	0.035
	>21	22	100.0	32	82.1	
Number of exacerbations -year	≥2	3	13.6	5	12.8	0.608
	<2	19	86.4	34	87.2	
Exacerbation requiring hospitalization	<1	18	81.8	24	61.5	0.101
	≥1	4	18.2	15	38.5	
Number of comorbidities	≥2	8	36.4	28	71.8	0.007
	<2	14	63.6	11	28.2	
Smoking status (pack-year)	≤ 40	7	31.8	17	43.6	0.366
	>40	15	68.2	22	56.4	

Abbreviations: BMI: body mass index

= 0.390, respectively). Regarding functional parameters, a positive correlation was present between the CAT score and TFS, and a negative correlation was found between the 6MWT percentage and the TFS (p = 0.005, r = 0.360; and p = 0.019, r = -0.319, respectively). No correlations were found between the frailty score and the indicators of systemic inflammation and oxidative stress.

DISCUSSION

In our study, according to the results of the TFS test, 63.9% of the cases were determined to be frail. Regarding the GOLD staging of COPD, frailty scores of Groups B and D were higher than those of Groups A and D. The frailty score was found to have significant relationships with BMI, the number of comorbidities, the CAT score, 6MWT distance percentage, and NLR, which is one of the indicators of inflammation. Frailty score had a negative correlation with body weight and 6MWT distance percentage, and positive correlations with the CAT score, the number of comorbidities, and the number of drugs used.

Frailty is a geriatric syndrome caused by age-re-

Table 2. Tilburg Frailty Score According to GOLD staging in COPD

Variable	A (n=20)	B (n=21)	C (n=5)	D (n=15)	P
Frailty score	3.95±2.13	7.33±3.45	7.00±2.65	6.13±3.05	0.006
Physical Component Score	2.10±1.79	4.10±2.23	4.00±1.73	3.13±2.36	0.023
Psychological Component Score	0.95±0.92	2.05±1.32	1.33±1.53	1.75±1.34	0.045
Social Component Score	1.00±0.45	1.19±0.60	1.67±0.58	1.25±2.00	0.138

Abbreviations: GOLD: Global initiative for chronic obstructive lung disease; COPD: Chronic obstructive pulmonary disease

lated reduction of reserves and functions, leading to decreased ability to cope with daily or acute stress factors. The prevalence of frailty increases with age. Studies have revealed an age related prevalence of 10.7% in over 65 years, 15.7% in 80-84 years, and 26.1% in over 85 years. Frailty is more commonly detected in females than in males (15). COPD patients who were followed up in our out-patient clinic were mostly males (96.9%), since COPD is a smoking burden-related disorder; as a result of which an inter-gender comparison could not be made.

Frailty is common in patients with chronic diseases. The prevalence of frailty in COPD patients was reported to be between 6.6-75% (15). The number of cases and age group that the study was conducted with, differences in methods used, and discrepancies between scales used for identification might be among the causes for such a wide range. In a study conducted by Ierodiakonou et al. on COPD patients using the Frail Non-disabled (FIND) survey, frailty was determined with a ratio of 82% (16). In our study, the prevalence of frailty determined by the TFS test was 63.9%; with the likely causes of such a high prevalence rate, being the screening tool, the number of patients, the study group involving patients over 65 years of age only, and COPD as a disorder with systemic inflammatory effects (15,17).

Most questionnaires used for frailty screening have not been developed to be self-applicable (18). The TFS test is a questionnaire used to determine the frailty status of the patients in our study; it is an understandable and straightforward test that can be used for early diagnosis of health-related problems in the elderly, and its validity and reliability has been proven in Turkey (4).

Chronic diseases are among the critical factors in determining frailty. According to the frailty phenomenon defined by Fried et al., chronic diseases play a significant role in the initiation of frailty (19). The Frailty Index, suggested by Rockwood et al., involves chronic disorders as a criterion of priority (20). Chronic diseases are common risk factors and symptoms associated with frailty. In addition, drugs used in chronic diseases may lead to frailty. In the TFS used in our study, chronic diseases were found to be determinants of frailty. In our study, statistically significant relationships and positive correlations between the number of comorbidities, the number of drugs used, and the TFS were determined, supporting the studies mentioned above.

In a study conducted by Ierodiakonou et al., in COPD patients, statistically significant differences were reported between the frail and non-frail

Table 3. Comparison of CAT, BODE Index, and 6MWT Results of Group 1 and 2

	Group 1 (n=22)	Group 2 (n=39)	P
CAT score	8.64±5.93	13.39±7.89	0.027
BODE index	2±1.75	2.82±2.08	0.232
6MWT (m)	348.57±126.59	322.45±80.68	0.277
6MWT (%)	64.81±16.45	56.55±12.87	0.044

Abbreviations: 6MWT: Six-minute walking test, CAT score: COPD evaluation questionnaire

groups with respect to age, GOLD stage, presence of uncontrolled disease, high CAT and mMRC scores, number of exacerbations, smoking cessation status, and accompanying comorbidities. Similarly, in our study, statistically significant differences were seen between the frail and non-frail patients with respect to the GOLD stage, the CAT score, the number of comorbidities, and the number of drugs used in COPD patients. The frailty score was significantly increased in patients with GOLD stages B and C compared to those in GOLD stages A and D. In a study conducted by Ierodiakonou et al., the frailty scores of patients in GOLD groups A and C were reported to be significantly higher than those in GOLD groups B and D (16). The reason for such a difference might be the differences in using the mMRC and CAT scores while determining the groups. In our study, no significant relationship was found between the prevalence of frailty and smoking cessation status, the number of exacerbations, and the mMRC score.

In a study conducted by Kusunose et al., the Kihon checklist score of frailty was found to correlate with the CAT score. In our study, a positive correlation was determined between the TFS and the CAT score, supporting the results of Kusunose's study. In the study by Kusunose et al., no correlation was determined between the total Kihon checklist score and the parameters of the PFTs (9). Similarly, in our study, no correlation was determined between the TFS and the parameters of the PFT.

COPD and frailty have common risk factors such as age and smoking. Besides, they involve common pathophysiological mechanisms such as chronic inflammation, dysregulation of the immune system, and impaired neuroendocrine regulation. Serum levels of inflammatory indicators such as hsCRP, IL-6, and TNF-α increase in systemic inflammation (21). In a study conducted by Dogrul et al., investigating the presence of inflammation in patients aged over 65 years, the CRP levels were similar whereas significant differences were reported to be present between frail and non-frail groups with respect to

Table 4. Comparison of Groups 1 and 2 Regarding NLR, and the Indicators of Systemic Inflammation and Oxidative Stress Parameters

Variable (mean ± SD)	Group 1 (n=22)	Group 2 (n=39)	P
NLR	2.27±1.23	3.05±1.46	0.007
HsCRP	1.49±0.27	1.79±1.18	0.859
IL-6	25.10±4.77	31.53±20.82	0.467
IL-18	5.26±3.33	6.24±4.67	0.912
8OH-dG	33.90±9.91	34.19±6.53	0.554

Abbreviations: NLR: neutrophil lymphocyte ratio, HsCRP: high sensitive C-reactive protein, IL-6: Interleukin-6, IL-18: Interleukin-18, 8OH-dG: 8-Hydroxy 2-deoxyguanosine

sedimentation, NLR, and CRP/albumin ratio (22). Similar to the study of Dogrul et al., a significant difference was determined between the groups with respect to NLR in the present study. However, no significant differences were found between the hs-CRP, IL-6, IL-18, and 8OH-dG values of the study groups. Besides, no significant correlations between the Tilburg score and the indicators of inflammation and oxidative stress were present in our study. The result that no difference was found between the two groups regarding the indicators of inflammation, except for NLO, might have originated from the fact that most of the patients in both groups were diagnosed as having severe COPD accompanied by systemic inflammation.

In COPD patients, dyspnea leads to immobility, and physical activity decreases with increasing age. Walking distance, which is an important determinant of frailty and showing exercise capacity, is an essential parameter reflecting the multi-systemic effects of disease severity in COPD. Walking distance can be evaluated using the 6MWT (23). Few studies investigating frailty and walking tests are available in the literature. In a study conducted by Gale et al., the 6MWT result of the frail group was reported to be significantly lower than that of the non-frail group. In addition, a negative correlation was reported between the 6MWT and frailty (24).

Similarly, a negative correlation was found between the 6MWT distance percentage and frailty score in our study.

In COPD patients, findings such as anorexia or weight loss, related to both systemic inflammation and aging, are frequently identified. In a meta-analysis study conducted by Verlaan et al., analyzing a total of 28 studies and 5447 malnourished elderly patients, it was reported that two out of three malnourished elderly individuals were physically frail (25). In our study, a negative correlation was found between body weight and frailty, and the BMI of the frail group was less than that of the non-frail group. Conducting further nutrition-related studies on frail COPD patients might help prevent the progression of frailty in these patients.

The TFS is in conformity with parameters such as the GOLD staging that is used to assess COPD patients, BMI, the number of comorbidities and the drugs used, the CAT score, and the 6MWT percentage. Conventional evaluation of frailty alongside other tests for COPD assessment might hamper the progress of frailty, offer physicians supplementary information regarding COPD follow-up, and enable intervention at an early period, such as forwarding to physical and pulmonary rehabilitation, geriatric and nutritional experts to increase physical performance and quality of life of such patients.

There are many studies about frailty in elderly, or in chronic diseases. However, frailty syndrome was not studied extensively in chronic obstructive pulmonary disease, which is quite common among elderly male smokers. Moreover, the Turkish validation study of Tilburg frailty scale is published recently (4) and as far as we know, the present study is the first and only one using it to evaluate frailty in COPD patients.

Besides, there is no comprehensive study in the current literature investigating factors effective for frailty syndrome in COPD and its relationship with systemic inflammation, and the TFS test is a practical test that can be performed in a short period at the out-patient clinic. For these reasons, we believe that our study would contribute to both the medical literature and the follow-up of COPD patients.

Conflicts of interest

The authors of this article state that they have no conflict of interest.

REFERENCES

1. Lunenfeld B, Stratton P. The clinical consequences of an ageing world and preventive strategies. Best Pract Res Clin Obstet Gynaecol 2013;27(5):643-59. (PMID:23541823).
2. Chen X., Mao G., Leng S.X. Frailty syndrome: an overview. Clin Interv Aging 2014;9:433-41. (PMID:24672230).
3. Tudorache E., Fildan A.P., Frandes M., Dantes E., Tofolean D.E. Aging and extrapulmonary effects of chronic obstructive pulmonary disease. Clin Interv Aging 2017;12:1281-87. (PMID:28860729).
4. Arslan M, Meltem K.E, Sözmen M et al. The Turkish adaptation of the Tilburg frailty indicator: a validity and reliability study. Turkish Journal of Geriatrics 2018;21(2):173-83.
5. Vestbo J, Hurd S.S, Agusti A.G et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med 2013;187(4):347-65. (PMID:22878278).
6. Fabbri L.M, Luppi F, Beghe B, Rabe K.F. Complex chronic comorbidities of COPD. Eur Respir J 2008;31(1):204-12. (PMID:18166598).
7. Barnes P.J, Celli B.R. Systemic manifestations and comorbidities of COPD. Eur Respir J 2009; 33(5):1165-85. (PMID:19407051).
8. Yazici O, Tas Gulen S, Eryilmaz U, Omurlu I.K. The evaluation of cardiac functions according to chronic obstructive pulmonary disease groups. Aging Male 2020;23(2):106-11. (PMID:31037993).

9. Kusunose M, Oga T, Nakamura S, Hasegawa Y, Nishimura K. Frailty and patient-reported outcomes in subjects with chronic obstructive pulmonary disease: are they independent entities? BMJ Open Respir Res 2017; 4(1): e000196. Published 2017 Jul 3. (doi:10.1136/bmjresp-2017-000196.) (PMID:28883929).

10. Limpawattana P, Putraveephong S, Inthasuwan P, Boonsawat W, Theerakulpisut D, Chindaprasirt J. Frailty syndrome in ambulatory patients with COPD. Int J Chron Obstruct Pulmon Dis 2017;12:1193-98. (PMID:28458530).

11. Bousquet J, Dinh-Xuan A.T, Similowski T. et al. Should we use gait speed in COPD, FEV1 in frailty and dyspnoea in both? Eur Respir J 2016;48(2):315-19. (PMID:27478189).

12. Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2019 Report. [Internet]. Available from: https://goldcopd.org/wp-content/uploads/2018/11/GOLD-2019-v1.7-FINAL-14Nov2018-WMS.pdf. Accessed:05.10.2020.

13. Miller M.R, Crapo R, Hankinson J. et al. General considerations for lung function testing. Eur Respir J 2005;26(1):153-61. (PMID:15994402).

14. Turner G, Clegg A. British Geriatrics Society; Age U.K., Royal College of General P. Best practice guidelines for the management of frailty: a British Geriatrics Society, Age UK and Royal College of General Practitioners report. Age Ageing 2014;43(6):744-7. (PMID:25336440).

15. Guan C, Niu H. Frailty assessment in older adults with chronic obstructive respiratory diseases. Clin Interv Aging 2018;13:1513-24. (PMID:30214171).

16. Ierodiakonou D, Kampouraki M, Poulonirakis I et al. Determinants of frailty in primary care patients with COPD: the Greek UNLOCK study. BMC Pulm Med 2019;19(1):63. (PMID:30876423).

17. Karadag F, Karul A.B, Cildag O, Yilmaz M, Ozcan H. Biomarkers of systemic inflammation in stable and exacerbation phases of COPD. Lung 2008;186(6):403-9. (PMID:18807087).

18. Walston J, Buta B, Xue Q.L. Frailty Screening and Interventions: Considerations for Clinical Practice. Clin Geriatr Med 2018;34(1):25-38. (PMID:29129215).

19. Fried L.P, Tangen C.M, Walston J et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001;56(3):M146-56. (PMID:11253156).

20. Rockwood K, Song X, MacKnight C et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173(5):489-95. (PMID:16129869).

21. Ershler W.B, Keller E.T. Age-associated increased interleukin-6 gene expression, late-life diseases, and frailty. Annu Rev Med 2000;51:245-70. (PMID:10774463).

22. Dogrul R.T, Varan H.C, Kizilarslanoglu M.C et al. Relationship between frailty and inflammation. Eur J Geriatr Gerontol 2019;1:17-23.

23. DePew Z.S, Karpman C, Novotny P.J, Benzo R.P. Correlations between gait speed, 6-minute walk distance, physical activity, and self-efficacy in patients with severe chronic lung disease. Respir Care 2013;58(12):2113-19. (PMID:23696689).

24. Gale N.S, Albarrati A.M, Munnery M.M et al. Frailty: A global measure of the multisystem impact of COPD. Chron Respir Dis 2018;15(4):347-55. (PMID:29334783).

25. Verlaan S, Ligthart-Melis G.C, Wijers S.L.J, Cederholm T, Maier A.B, de van der Schueren M.A.E. High Prevalence of Physical Frailty Among Community-Dwelling Malnourished Older Adults-A Systematic Review and Meta-Analysis. J Am Med Dir Assoc 2017;18(5):374-82. (PMID:28238676).

RESEARCH

THE EFFECT OF SURGICAL TREATMENT ON SURVIVAL IN GERIATRIC PATIENTS WITH STAGE I SMALL-CELL LUNG CANCER

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2020.183
2020; 23(4): 455-462

Gülay İlkhan DAŞDEMİR[1]
Hakan ÇELİKHISAR[2]
Aslı KILAVUZ[3]

CORRESPONDANCE

[3]Aslı KILAVUZ

Ege University Faculty of Medicine, Division of Geriatric Medicine, Department of Internal Medicine, Izmir, Turkey

Phone: +905323536570
e-mail: asli.kilavuz@gmail.com

Received: Sep 30, 2020
Accepted: Nov 24, 2020

[1] Tire Public Hospital, Chest Diseases Clinic, Izmir, Turkey
[2] Izmir Metropolitan Municipality Hospital, Chest Diseases Clinic, Izmir, Turkey
[3] Ege University Faculty of Medicine, Division of Geriatric Medicine, Department of Internal Medicine, Izmir, Turkey

Abstract

Introduction: The aim of our study is to investigate the effects of early stage surgical treatment on the survival of the geriatric patient group in small cell lung cancer.

Materials and Method: Patients over 65 years of age with a diagnosis of stage I small cell lung cancer were included. The patients included in the study were divided into three groups. 1. The surgical group 2. Non-surgical group 3. Untreated group. Overall survival and lung cancer-specific survival were evaluated among these 3 groups.

Results: A total of 1248 patients were included in the study. 28.9% of the patients did not receive any treatments, 47.2% of the patients received non-surgical treatment and 23.9% of the patients received surgical treatment. The 5-year overall survival rates of the untreated group, non-surgical group and surgical group were 7%, 10% and 32%, respectively ($p < 0.0001$). According to the results of multivariable analysis, surgical treatment was an important factor in increasing overall survival when compared to the non-surgical treatment.

Conclusion: In patients aged 65-84 with stage I small-cell lung cancer, surgical treatment increased overall survival at a statistically significant level.

Keywords: Geriatrics; Small Cell Lung Cancer; General Surgery; Survival

INTRODUCTION

Today, lung cancer is the most commonly observed type of cancer in the world (1), responsible for 12.8% of all cases. Lung cancer is also ranked first in cancer-related deaths, accounting for 17.8% of all cases (2). When 5-year survival rates are analyzed, the percentage is around 15% for all lung cancer patients (3). A further 15% of lung cancer patients are diagnosed with small-cell lung cancer (SCLC). At the time of diagnosis, the disease is generally at an extensive stage and, among untreated patients, the average survival time is limited to mere months (4). The prognostic significance of some parameters of SCLC patients were checked prior to treatment and analyzed with retrospective studies. It was shown that one of the most significant markers of survival is the stage of the tumor (5). Sex, age, and weight loss are also factors that affect prognoses (6). As humans' average lifespan has increased, so has the average age of patients diagnosed with SCLC. A study supporting this view found that the percentage of SCLC patients over the age of 70 increased from 23% to 44% over a period of 35 years, and that almost half of the limited-stage SCLC patients were diagnosed once past the age of 70 (7). Radiotherapy and chemotherapy are regarded as the basic treatments for patients with SCLC. Lately, however, several retrospective studies have shown that, in limited numbers of patients with SCLC who have undergone surgery, the overall survival duration increased and the 5-year survival rate was around 50% (8). Additionally, National Comprehensive Cancer Network (NCCN) guidelines state that surgical treatment should primarily be considered for Stage I (T1–2, N0) SCLC patients (9). However, in clinical practice, it is believed that younger patients may be more suitable candidates for surgical treatment, due to co-morbidities, post-operative complications, and patient performance (10).

Chronological age is often a poor predictor of treatment response and toxicity. An ECOG or Karnofsky Performance Status assessment, which are frequently used in patients to be treated with cancer, may also be insufficient (11). When planning cancer treatments in geriatric patients, their level of functionality and physiological capacity should be well evaluated before any other measures are undertaken. The International Society of Geriatric Oncology and the NCCN recommend a comprehensive geriatric assessment for patients over 65 years of age (12).

Nonetheless, in several studies, it is suggested that age is not a contraindication for surgery, so carefully selected Stage I SCLC patients aged 80 or above may benefit from surgical resection (13).

MATERIALS AND METHOD

Our study has a retrospective design. Patients over the age of 65 who were diagnosed with Stage I SCLC between January 1996 and December 2014 were analyzed using the data obtained from the records of two hospitals. A total of 1248 patients were included in the study. Stage I was defined clinically or pathologically in accordance with the American Joint Committee on Cancer (AJCC) Staging systems. Additionally, patients without sufficient survival data (whose survival duration in months is unknown, or whose survival duration is absent or not calculated) and patients whose pulmonary surgery details are not clear were excluded from the study. Patients whose pathological staging and surgery data are not present were also excluded. For each case, the patient's demographic data, the year and age at time of diagnosis, sex, location of the tumor, pathology, AJCC staging details, treatments (surgery, chemotherapy, or radiation), surgical procedures performed for reasons other than cancer, vital status, cause of death, and survival duration were recorded.

Ethical approval was obtained from the local ethics committee (approval number: 54022451-050.05.04-1786).

Statistical Analysis

In this study, SCLC patients were classified into surgical, non-surgical, and untreated groups. The clinicopathological characteristics among the three groups were analyzed with Pearson's Chi-squared test. The log-rank test and Kaplan-Meier analysis were used to estimate the patients' overall survival and lung cancer-specific survival (LCSS). Multivariate Cox models were realized to determine the predictors of survival. All statistical analyses were performed with IBM SPSS 22. The p-values are bilateral, and $p < 0.05$ was regarded as significant.

RESULTS

In total, 1248 patients were deemed to fulfil the study criteria and were assessed. The characteristics of the patients enrolled are provided in Table 1. Among all patients, 51.7% were male and 48.3% were female. The primary tumor location was most commonly the upper lobe (52.1%), followed by the lower lobe (32.1%), lingula (9.6%), and the middle lobe (6.2%) ($p < 0.0001$).

Distribution of patients based on the treatment administered was as follows: 365 patients were untreated (29.3% of total), 582 patients received non-surgical treatment (46.6%), and 301 patients received surgical treatment (24.1%) ($p < 0.001$). The percentage of untreated patients for patients ages 65–69 was 2.1%, 5.2% for patients aged 70–74, 11.9% for patients aged 75–79, 31.7% for patients aged 80–84, and 49.1% for patients older than 85 years.

Concerning the reasons for not performing surgery on 947 Stage I SCLC patients who received non-surgical treatment, we observed that, for 781 patients (82%), surgery was not recommended; in 65 patients (7%), there were surgical contraindications; a further 18 patients (2%) refused the operation; and 83 patients (9%) were not operated on for unknown reasons.

In general, the overall survival duration and the LCSS duration of patients receiving surgical treatment were observed to be longer. In terms of overall survival, the group receiving non-surgical treatment was second, following the surgical group. The median survival in the surgical group was 26 months (95% confidence interval [CI] 18.4–31.6 months), in the non-surgical group it was 14 months (95% CI 11.6–14.4 months), and in the untreated group, the duration was 6 months (95% CI 4.6–7.4 months). The 5-year survival percentages of the surgical group, non-surgical group, and untreated group were 34%, 13%, and 6%, respectively ($p < 0.0001$). The 5-year LCSS percentages of the surgical group, non-surgical group, and untreated group were 62%, 36%, and 21%, respectively ($p < 0.0001$). The multivariate Cox analysis of factors affecting the outcomes among the study population are presented in Table 2.

In multivariate analyses, surgical treatment was associated with longer overall survival duration (Hazard Ratio [HR] 0.506; 95% CI 0.391–0.655[$p < 0.0001$]) and LCSS duration (HR 0.449; 95% CI 0.309–0.653 [$p < 0.0001$]), as compared to the non-surgical treatments, as shown in Table 3. The adjusted HRs for the effect of surgery, non-surgical treatment, and no treatment on overall survival and LCSS in each age sub-group are provided in Table 3.

Similar results were observed in the patient group aged 80–84. The median survival in the surgical group was 23 months (95% CI 17.2–28.8 months); in the non-surgical group, it was 12 months (95% CI 11.4–14.6 months); and in the untreated group, this duration was 6 months (95% CI 4.2–7.8 months). The 5-year survival percentages of the surgical group, non-surgical group, and untreated group were 32%, 11%, and 5%, respectively ($p < 0.0001$). Lung cancer-specific survival percentages of the surgical group, non-surgical group, and untreated group were 55%, 27%, and 31%, respectively ($p < 0.0001$). In multivariate analyses, when compared to non-surgical treatment, surgical treatment remained an independent significant predictor of improved overall survival (HR 0.539; 95% CI 0.391–0.763 [$p < 0.0001$]) and LCSS (HR 0.449; 95% CI 0.281–0.729 [$p = 0.001$]).

In the patient group aged over 85, the median survival in the surgical group was 19 months (95%

Table 1. Characteristics of patients

Characteristics	Total n (%)		Untreated n (%)		Non-surgical n (%)		Surgical n (%)		p
Sex									0.198
Female	603	(48.3)	188	(51.5)	262	(45.1)	153	(50.8)	
Male	645	(51.7)	177	(48.5)	320	(54.9)	148	(49.2)	
Age									<0.0001
65-69	135	(10.8)	8	(2.1)	57	(9.8)	157	(52.1)	
70-74	188	(15.1)	19	(5.2)	72	(12.3)	72	(23.9)	
75-79	347	(27.8)	43	(11.9)	107	(18.4)	34	(11.3)	
80-84	414	(33.2)	116	(31.7)	146	(25.2)	21	(7.1)	
≥85	164	(13.1)	179	(49.1)	200	(34.3)	17	(5.6	
Tumour location									<0.0001
Upper lobe	650	(52.1)	149	(40.1)	312	(53.6)	178	(59.1)	
Lower lobe	401	(32.1)	116	(31.7)	187	(32.1)	98	(32.5)	
Middle lobe	77	(6.2)	63	(17.2)	48	(8.2)	22	(7.3)	
Lingula	120	(9.6)	37	(10.1)	35	(6.1)	3	(1.1)	
Grade									<0.0001
Grade I-II	217	(11.8)	41	(11.2)	7	(1.2)	178	(59.1)	
Grade III	421	(33.7)	98	(26.8)	228	(39.2)	87	(28.9)	
Grade IV	583	(46.7)	217	(59.4)	337	(57.9)	28	(9.3)	
Unknown	27	(2.2)	9	(2.4)	10	(1.7)	8	(2.7)	
Patients receiving adjuvant therapy	-		-		-		137	(45.5)	>0.05
Patients receiving no adjuvant therapy	-		-		-		164	(54.5)	>0.05

CI 16.0–22.0 months); in the non-surgical group, it was 13 months (95% CI 8.4–17.6 months); and in the untreated group, this duration was 6 months (95% CI 3.4–8.6 months). The 5-year overall survival percentages of the surgical group, non-surgical group, and untreated group were 18%, 14%, and 4%, respectively (p = 0.002). The 5-year LCSS percentages of the surgical group, non-surgical group, and untreated group were 55%, 40%, and 20%, respectively (p = 0.012). In multivariate analyses, surgical treatment was associated with higher overall survival (HR 0.913; 95% CI 0.511–1.649; [p = 0.771]) and LCSS rates (HR 0.661; 95% CI 0.271–1.617; [p = 0,361]), compared to the non-surgical group.

The 301 patients in the surgical group were assessed for the analysis performed for the assessment of patients receiving adjuvant therapy. Among this group, 137 (45.5%) patients received post-operative adjuvant therapy, while 164 (54.5%) received only surgical treatment. The median overall survival duration of patients who only received surgical treatment was 18 months (95% CI 11.8–24.2 months), while it was 38 months for those patients receiving post-operative adjuvant therapy (95% CI 24.2–51.8 months). The 5-year overall survival rate in patients receiving post-operative adjuvant therapy was 36%; the rate was 32% in patients who only received surgical treatment (p = 0.031). The 5-year LCSS rate in patients receiving post-operative adjuvant therapy was 65%, and it was 55% in patients who only received surgical treatment (p = 0.036).

Table 2. Multivariate analysis of clinicopathological factors affecting outcomes in elderly and geriatric patients

Clinical parameters	Overall survival			Lung cancer-specific survival		
	HR	95% CI	p	HR	95% CI	p
Sex						
Female	0.920	0.726-0.929	0.004	0.913	0.754-1.105	0.404
Male						
Age (years)						
65-69	1.110	1.065-1.345	0.011	1.186	0.934-1.442	0.189
70-74	1.170	1.048-1.362	0.013	1.174	0.910-1.476	0.217
75-79	1.185	1.035-1.374	0.017	1.161	0.755-1.480	0.329
80-84	1.205	1.029-1.386	0.014	1.158	0.949-1.423	0.128
≥85	1.255	1.016-1.540	0.035	1.106	0.816-1.516	0.465
Tumour location						
Upper lobe	0.834	0.831-1.119	0.039	0.896	0.746-1.124	0.029
Lower lobe	0.959	0.899-1.301	0.612	1.031	0.829-1.271	0.802
Middle lobe	1.399	1.071-1.839	0.021	1.539	1.049-2.259	0.031
Lingula	1.159	0.925-1.486	0.216	1.399	1.019-1.939	0.041
Grade						
Grade I-II	1.676	0.878-2.986	0.379	1.394	0.624-3.216	0.479
Grade III	1.669	0.899-3.089	0.099	1.369	0.589-3.181	0.459
Grade IV	1.611	0.869-2.949	0.131	1.541	0.681-3.499	0.299
Unknown	1.689	0.919-3.099	0.089	1.341	0.591-3.051	0.489
Treatment			<0.0001			<0.0001
Untreated	0.631	0.541-0.736	<0.0001[x]	0.619	0.501-0.771	<0.0001[x]
Surgical	0.549	0.279-0.431	<0.0001[y]	0.469	0.361-0.619	<0.0001[y]
Non-surgical	0.351	0.461-0.669	<0.0001[z]	0.289	0.221-0.389	<0.0001[z]

x: p to compare the untreated group with the non-surgical group,
y: p to compare the non-surgical group with the surgical group,
z: p to compare untreated group with the surgical group.

DISCUSSION

Although lung cancer is more common in elderly patients than young patients, studies specific to the elderly are very few. In studies conducted to determine the optimal treatment of lung cancers, patients under the age of 65 were often included in the patient group (14). In the last 10–15 years, studies have begun among geriatric patient groups; however, in these studies, patients in their seventh decade constitute the majority of subjects, and the number of patients over age 80 remains small (15).

Today, for early stage SCLC, the standard treatment is concomitant radiochemotheraphy; for advanced stage SCLC, the standard of care for first-line systemic therapy is platinum-based systematic chemotherapy (16). Some recent studies have reported positive outcomes for the surgical treatment of early stage SCLC patients (17). Additionally, NCCN guidelines state that surgical treatment should be considered for Stage I (T1–2, N0) SCLC patients (18). However, the median age of the patients included in the retrospective studies on which these guidelines are based was 60–75 years (19,20). To the best of our knowledge, there are no studies in the literature that specifically assesses the survival-related outcomes of surgical treatment in SCLC

Table 3. Adjusted hazard ratios for the effect of surgery, non-surgical treatment and no treatment on overall survival and lung cancer-specific survival in each age sub-group

Sub-group	Overall survival			Lung cancer-specific survival		
	HR	95% CI	p	HR	95% CI	p
Age ≥65 years			<0.0001			<0.0001
Untreated	0.935	0.615-0.904	<0.0001[x]	0.801	0.342-0.494	<0.0001[x]
Surgical	0.395	0.214-0.684	<0.0001[y]	0.234	0.225-0.433	<0.0001[y]
Non-surgical	0.265	0.274-0.856	<0.0001[z]	0.196	0.141-0.304	<0.0001[z]
Age ≥70 years			<0.0001			<0.0001
Untreated	0.786	0.584-0.836	<0.0001[x]	0.702	0.389-0.671	<0.0001[x]
Surgical	0.436	0.314-0.565	<0.0001[y]	0.364	0.274-0.514	<0.0001[y]
Non-surgical	0.296	0.286-0.915	<0.0001[z]	0.214	0.166-0.296	<0.0001[z]
Age ≥75 years			<0.0001			<0.0001
Untreated	0.610	0.479-0.769	<0.0001[x]	0.601	0.429-0.821	<0.0001[x]
Surgical	0.498	0.389-0.649	<0.0001[y]	0.451	0.310-0.649	<0.0001[y]
Non-surgical	0.299	0.231-0.409	<0.0001[z]	0.271	0.181-0.399	<0.0001[z]
Age ≥80 years			<0.0001			<0.0001
Untreated	0.659	0.509-0.861	0.002[x]	0.721	0.499-1.019	0.071[x]
Surgical	0.539	0.391-0.759	<0.0001[y]	0.449	0.281-0.729	0.001[y]
Non-surgical	0.359	0.249-0.521	<0.0001[z]	0.319	0.189-0.539	<0.0001[z]
Age ≥85 years			0.001			0.003
Untreated	0.449	0.291-0.719	0.001[x]	0.401	0.211-0.789	0.008[x]
Surgical	0.909	0.499-1.649	0.759[y]	0.661	0.271-1.621	0.361[y]
Non-surgical	0.421	0.229-0.749	0.004[z]	0.259	0.111-0.641	0.003[z]

x: p to compare the untreated group with the non-surgical group,
y: p to compare the non-surgical group with the surgical group,
z: p to compare untreated group with the surgical group.

patients over the age of 75. Due to this situation, our study was particularly focused on patients over the age of 75, in hopes of clarifying the clinical value of surgery in the treatment of elderly and geriatric patients with SCLC. In clinical practice, considering the association of old age with increased comorbidity, reduced functionality, more post-operative complications, and relatively higher mortality, surgery is rarely performed on geriatric patients. However, contradictorily, some studies show that age is not an independent prognostic factor affecting survival and that the performance status and treatments appear to be valid prognostic factors (21,22). Satisfactory long-term results were obtained when surgical resection was applied to carefully selected Stage I SCLC patients over the age of 80 (23,24). In our study, the median overall survival duration of the surgical group was found to be significantly higher than the non-surgical group.

Using subgroup analyses, we found that there was a clinical benefit and survival contribution of surgery observed in patients aged 65–69, 70–74, 75–79, and even in the population aged 80–84, who have traditionally been assumed to derive fewer benefits from lung resection. In the group of patients aged 85 and above, patients receiving surgical or non-surgical treatment had longer overall and LCSS durations, when compared to the untreated patients. No significant differences were observed between the surgical and non-surgical treatment

groups. According to our study, surgery may be an acceptable element of multimodal treatment in patients aged 75–84. Additionally, when the role of post-operative adjuvant therapy was compared with only surgical treatment in geriatric patients, it was observed that post-operative adjuvant therapy contributed to their survival.

This study had some restrictions. First, as this is a retrospective study, inherent selection bias was unavoidable. It is also possible that patients in the surgical group were healthier than the patients in the non-surgical and untreated groups. Another restriction was the lack of specific details regarding the performance status, chemotherapy and radiotherapy regimen, comorbidities, etc. in the patient records we consulted.

CONCLUSION

We have concluded that Stage I SCLC patients aged 65–84 benefit from surgical resection with a 5-year overall survival rate of 32% and a 5-year LCSS rate of 55%. Surgical resection treatment could be considered as a promising first-line treatment in suitable geriatric Stage I SCLC patients in the future.

REFERENCES

1. Low M, Ben-Or S. Thoracic surgery in early-stage small cell lung cancer. Thorac Surg Clin 2018;28(1):9-14. (PMID: 29150041).
2. Huang C-Y, Au K-K, Chen S-L, Wang S-C, Liao C-Y, Hsu H-H, Sung W-W, Wang Y-C. Unfavorable Mortality-To-Incidence Ratio of Lung Cancer Is Associated with Health Care Disparity. International Journal of Environmental Research and Public Health. 2018; 15(12):2889.
3. Garon EB, Hellmann MD, Rizvi NA, Carcereny E, Leighl NB, Ahn MJ, Eder JP, Balmanoukian AS, Aggarwal C, Horn L, Patnaik A, Gubens M, Ramalingam SS, Felip E, Goldman JW, Scalzo C, Jensen E, Kush DA, Hui R. Five-Year Overall Survival for Patients with Advanced Non‐Small-Cell Lung Cancer Treated with Pembrolizumab: Results From the Phase I KEYNOTE-001 Study. J Clin Oncol. 2019 Oct 1;37(28):2518-2527. doi: 10.1200/JCO.19.00934. Epub 2019 Jun 2. PMID: 31154919; PMCID: PMC6768611.
4. Du X, Tian D, Liu L, et al. Surgery in patients with small cell lung cancer: A period propensity score matching analysis of the Seer database, 2010-2015. Oncol Lett 2019;18(5):4865-81. (PMID: 31611997).
5. Shepherd FA, Ginsberg R, Patterson GA, et al. Is there ever a role for salvage operations in limited small-cell lung cancer? J Thorac Cardiovasc Surg 1991;101(2):196-200. (PMID: 1846927).
6. Matsumoto Y, Ohara S, Furukawa R, Usui K. The Prognosis of Small Cell Lung Cancer in Patients with Pulmonary Fibrosis. Anticancer Res. 2017 Oct;37(10):5791-5795. doi: 10.21873/anticanres.12021. PMID: 28982903.
7. Govindan R, Page N, Morgensztern D, et al. Changing epidemiology of small-cell lung cancer in the United States over the last 30 years: analysis of the surveillance, epidemiologic, and end results database. J Clin Oncol 2006;24(28):4539-44. (PMID: 17008692).
8. Wang Z, Pang L, Tang J, et al. Video-assisted thoracoscopic surgery versus muscle-sparing thoracotomy for non-small cell lung cancer: a systematic review and meta-analysis. BMC Surg 2019;19(1):144. (PMID: 31615490).
9. Zhong L, Suo J, Wang Y, et al. Prognosis of limited-stage small cell lung cancer with comprehensive treatment including radical resection. World J Surg Oncol 2020;18(1):27. (PMID: 32013993).
10. Tjong MC, Mak DY, Shahi J, Li GJ, Chen H, Louie AV. Current management and progress in radiotherapy for small cell lung cancer. Front Oncol 2020; 10:1146. (PMID: 32760673).
11. Repetto L, Fratino L, Audisio RA, et al. Comprehensive geriatric assessment adds information to Eastern Cooperative Oncology Group performance status in elderly cancer patients: An Italian Group for Geriatric Oncology Study. J Clin Oncol 2002;20(2):494-502. (PMID: 11786579).
12. Extermann M, Aapro M, Bernabei R, et al. Use of comprehensive geriatric assessment in older cancer patients: recommendations from the task force on CGA of the International Society of Geriatric Oncology (SIOG). Crit Rev Oncol Hematol 2005;55(3):241-52. (PMID: 16084735).
13. National Comprehensive Cancer Network (NCCN) guidelines. Non-small cell lung cancer. Version

2.2018. [Internet]. Avaliable from: http://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed: 20.06.2020.

14. Engelhardt KE, Coughlin JM, DeCamp MM, et al. Survival after adjuvant radiation therapy in localized small cell lung cancer treated with complete resection. J Thorac Cardiovasc Surg 2019;158(6):1665-77.e2. (PMID: 31627955).
15. Hutchins LF, Unger JM, Crowley JJ, Coltman CA, Albain KS. Underrepresentation of patients 65 years of age or older in cancer-treatment trials. N Engl J Med 1999;341(27):2061-7. (PMID: 10615079).
16. Duma N, Santana-Davila R, Molina JR. Non-Small Cell Lung Cancer: Epidemiology, Screening, Diagnosis, and Treatment. Mayo Clin Proc. 2019 Aug;94(8):1623-1640. doi: 10.1016/j.mayocp.2019.01.013. PMID: 31378236.
17. Blandin Knight S, Crosbie PA, Balata H, Chudziak J, Hussell T, Dive C. Progress and prospects of early detection in lung cancer. Open Biol. 2017 Sep;7(9):170070. doi: 10.1098/rsob.170070. PMID: 28878044; PMCID: PMC5627048.
18. Kalemkerian GP, Loo BW, Akerley W, Attia A, Bassetti M, Boumber Y, Decker R, Dobelbower MC, Dowlati A, Downey RJ, Florsheim C, Ganti AKP, Grecula JC, Gubens MA, Hann CL, Hayman JA, Heist RS, Koczywas M, Merritt RE, Mohindra N, Molina J, Moran CA, Morgensztern D, Pokharel S, Portnoy DC, Rhodes D, Rusthoven C, Sands J, Santana-Davila R, Williams CC, Hoffmann KG, Hughes M. NCCN Guidelines Insights: Small Cell Lung Cancer, Version 2.2018. J Natl Compr Canc Netw. 2018 Oct;16(10):1171-1182. doi: 10.6004/jnccn.2018.0079. PMID: 30323087.
19. Liu T, Chen Z, Dang J, Li G. The role of surgery in stage I to III small cell lung cancer: A systematic review and meta-analysis. PLoS One 2018;13(12):e0210001. (PMID: 30596754).
20. Wakeam E, Acuna SA, Leighl NB, et al. Surgery versus chemotherapy and radiotherapy for early and locally advanced small cell lung cancer: A propensity-matched analysis of survival. Lung Cancer 2017; 109:78-88. (PMID: 28577955).
21. Antonia SJ, Villegas A, Daniel D, et al. Durvalumab after chemoradiotherapy in stage iii non–small-cell lung cancer. N Engl J Med 2017; 377:1919-29. (PMID: 28885881).
22. Horn L, Mansfield AS, Szczęsna A, et al. First-line Atezolizumab plus chemotherapy in extensive-stage small-cell lung cancer. N Engl J Med 2018;379:2220-9. (PMID: 30280641).
23. Salazar MC, Rosen JE, Wang Z, et al. Association of delayed adjuvant chemotherapy with survival after lung cancer surgery. JAMA Oncol 2017;3(5):610-9. (PMID: 28056112).
24. Yang H, Xu J, Yao F, Liang S, Zhao H. Analysis of unexpected small cell lung cancer following surgery as the primary treatment. J Cancer Res Clin Oncol 2018;144(12):2441-7. (PMID: 30341687).

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2020.184
2020; 23(4): 463-472

Nergiz HÜSEYİNOĞLU[1]
Hatice KÖSE ÖZLECE[2]
Sadık ARDIÇ[3]

RESEARCH

COMPARISON OF SLEEP MACRO- AND MICROSTRUCTURES IN ELDERLY AND MIDDLE-AGED MALE PATIENTS WITH SEVERE OBSTRUCTIVE SLEEP APNEA: DOES THE DISEASE ERASE DIFFERENCES?

Abstract

Introduction: Age-related changes in sleep attract increased attention from researchers and are studied in the context of micro- and macrostructures. Macrostructures include sleep onset, total sleep time, sleep efficiency, wake time after sleep onset, and non-rapid eye movement and rapid eye movement sleep percentages, latencies and durations. Sleep microstructures refer to a cyclic alternating pattern.The present study aims to investigate how sleep structures in older and middle-aged patients are affected by the widespread disease of obstructive sleep apnea. The authors believe that it provide additional information about sleep disorder pathogenesis.

Materials and Method: Patients who received a diagnosis of severe sleep apnea were divided into two groups: age ≥ 65 years old and 35-45 years old. Macro-and microstructural data from polysomnographic investigations were collected and compared.

Results: There were no statistically significant differences for total sleep time, sleep efficiency, wake time after sleep onset, rapid eye movement sleep latency and separate percentages of non-rapid eye movement sleep stages N1, N2 and N3. Regarding sleep microstructures, there were no differences between arousal index, cyclic alternating pattern rates, or percentage ratio of phase subtype.

Conclusion: The parameters of the macro- and microstructures in the older group are similar to those of the middle-aged group and are also basically similar to the parameters of previous studies; however, the percentages from phases A1, A2 and A3 are different from most previous works. These considerations indicate the need for future investigation of geriatric sleep in different health and environmental conditions.

Keywords: Sleep; Sleep Stages; Sleep Apnea Syndromes; Aging; Polysomnography

CORRESPONDANCE

[1]Nergiz Hüseyinoğlu

Acıbadem University, Acıbadem Kayseri Hospital Department of Neurology and Sleep Diseases, Kayseri, Turkey

Phone: +905058119172
e-mail: nergizabbas@gmail.com

Received: Jul 24, 2020
Accepted: Nov 24, 2020

[1] 1Acıbadem University, Acıbadem Kayseri Hospital Department of Neurology and Sleep Diseases, Kayseri, Turkey

[2] Acıbadem Kayseri Hospital, Depatment of Neurology and Sleep Diseases, Kayseri, Turkey

[3] Koru Ankara Hospital, Department of Chest and Sleep diseases, Ankara, Turkey

INTRODUCTION

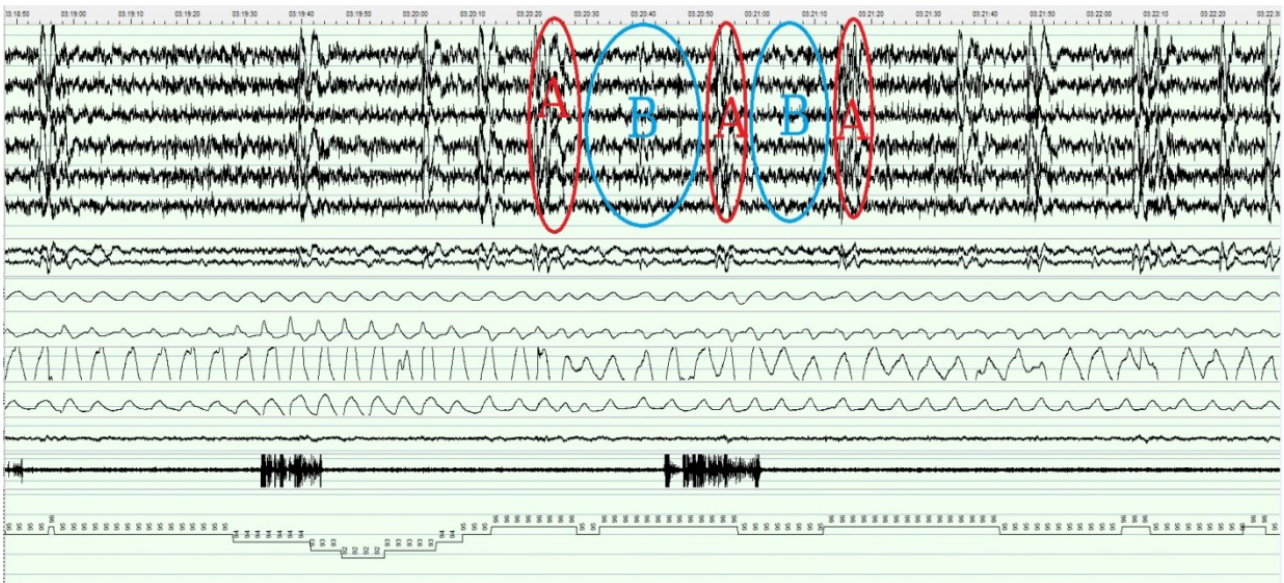
Sleep is an integral part of human life and is one of the main factors determining vitality, consciousness, mental functions, homeostasis and other physiological and psychosocial aspects of being human. Sleep is not a stable state, and its architecture dynamics change with age. Generally speaking, sleep in humans consists of cyclic turnover between rapid eye movement (REM) and non-REM (NREM) sleep. NREM sleep consists of light (N1 and N2) and deep (N3 or slow wave) sleep stages. REM sleep represents with a decrease in voluntary muscle tone and rapid eye movement. Aging per se is not the single reason for sleep disruption. The deterioration of architecture and quality of elderly people's sleep are caused by altered homeostatic sleep regulation, lifestyle changes, physical activity and diet properties, comorbidities, chronic pain, medications and senile brain changes.

The sleep structures are evaluated by EEG, divided into 30-second epochs to observe sleep macro- and microstructures. Macrostructures include NREM and REM sleep percentages, latencies and durations.

The definition of sleep microstructure includes waves which do not belong to the conventional 30-s scoring epoch (1,2). One of the microstructural phenomenon is the cyclic alternating pattern (CAP), which is defined as aperiodic activity during NREM sleep and reflects the brain's efforts in regulating the physiological structure of sleep (1,3). CAP is defined as repetitive spontaneous EEG patterns (arousal period/Phase A) lasting 10–60 s and subsequent return to background activity (quiet period/Phase B) (Figure 1) (1). The amount of CAP increases during sleep disruption, such as acoustic stimulation, insomnia, pain, sleep apnea, periodic limb movement or depression. Conversely, drug administration, narcolepsy or degenerative diseases reduce the CAP rate (4). CAP provides additional information about NREM sleep and may shed light on sleep disorder pathogenesis (3).

According to many studies, slow wave sleep (SWS), REM sleep, SE and TST decrease, but per-

Figure 1. Cyclic alternating pattern: arousal period (phase A), background period (phase B)



centage of lighter sleep, daytime sleepiness, daytime napping and the number of nocturnal awakenings increase with age, regardless of medication and comorbidities (5-8). However, some researchers argue that the effect of aging on REM sleep is unclear (9). Studies have examined the effect of age on CAP structure and have found that CAP rates and the ratio of CAP phases change depending on age and comorbidities (10).

Along with general deterioration in health among the elderly, there is an increased frequency of sleep disordered breathing, especially obstructive sleep apnea (OSA) (11). OSA is characterized by repetitive interruption of airflow during sleep, sleep fragmentation, snoring and day time sleepiness. The prevalence of OSA varies between 9%–38% in the general population and increases with age (12). A previous community-dwelling study reported a prevalence of sleep apnea1.7 times higher than average in subjects older than 60(13). Prevalence rates of severe OSA were 24% in the 65–95-year-old population (14).

Sleep apnea in the elderly worsens quality of life, existing diseases and such functions, as memory and learning, attention, motor and balance control. Sleep fragmentation, periodic nocturnal oxygen desaturation and increased sympathetic activation during sleep are major factors that change sleep structures, leading to daytime sleepiness and increasing the risk of cardio- and cerebrovascular events (15).

The diagnosis and severity of sleep apnea requires polysomnographic (PSG) investigation, including EEG, electro-oculography (EOG) and electromyography (EMG) as well as body position, cardiac, respiratory, audio and video monitoring during sleep. In addition to the usual scoring, this study employed a more advanced CAP scoring. Studies have shown that upper airway obstruction due to sleep apnea occurs in temporal connection with CAP. As a sensitive assessment, CAP involves EEG activity, muscle tone and autonomic responses even in the absence of apnea. Researchers believe that CAP analysis is a sensitive marker for detecting undercover sleep alterations that are not determinable by conventional scoring (9,16,17).

So far, a lot of research on sleep architecture has been done in populations with sleep apnea and mainly focused on young and middle-aged adults. We were attracted to this topic to try to understand the potential relationship between aging and sleep breathing disorders by exploring such a valuable dimension as the CAP. The authors suggest that differences in sleep macro- and micropatterns that normally exist between elderly and middle-aged adults would persist even in the presence of severe apnea.

MATERIAL AND METHODS

This retrospective study was approved by the Ethical Committee of the Local University Faculty of Medicine (2020/01) and performed at our sleep center between May 2016 and January 2020. This study was conducted according to the principles expressed in the Declaration of Helsinki.

The inclusion criteria were male gender and diagnosis of severe obstructive sleep apnea. The exclusion criteria were previous diagnosis or treatment of sleep disorders, such as central sleep apnea, obesity-hypoventilation syndrome, restless leg syndrome, periodic limb movement disorders, insomnia or parasomnia and serious systemic disorders such as heart, kidney or liver failure, uncontrolled hypertension and diabetes mellitus. Patients using certain medications within the previous month, such as antihistamines, antidepressants, sedative-hypnotics and neuroleptics were excluded from the study.

Of the 680 patients who underwent PSG, 47 patients who met our criteria were included in the study. These 47 patients were divided into two groups according to their ages: 23 patients aged 65 and over were in the first group, and 24 patients between 35-45 years were in the second group. The age, body mass index (BMI) and Epworth sleepiness

scale (ESS) scores of both groups were recorded (18).

Polysomnography

PSG was performed for both groups with video monitoring. No hypnotic drugs were allowed before recording. The recordings were carried out using a computerized recording workstation (Embla® RemLogic™).EEGs were recorded using bipolar montages(F3-M2, F4-M1, C3-M2, C4-M1, O1-M2 and O2-M1).The following parameters were recorded: body position, electrooculogram (EOG), electrocardiogram (ECG), electromyogram (EMG) of the submental space and both tibialis anterior muscles, oxygen saturation, nasal cannula, thermistor, snoring recorded by a microphone and respiratory efforts detected by inductance plethysmography.

EEG signals were subdivided into 30-s epochs and manually scored according to the American Academy of Sleep Medicine (AASM) Manual (19). Sleep scoring included stage W (wakefulness), NREM (stages N1, N2 andN3), REM, arousals, leg movements and respiratory measurements (apneas/hypopneas and desaturation indexes). AHI was calculated as the count of apneasor hypopneas per hour of sleep. The oxygen desaturation index (ODI) was calculated as the number of desaturations (decrease of SpO2≥3%) per hour of sleep.

From asleep macrostructure viewpoint, we calculated TST, SE, WASO, SL, REM sleep latency, arousal index and percentages of N1, N2, N3 and REM sleep.

These definitions are below:

Total sleep time: the time from sleep onset to the end of the final sleep epoch without time awake.

Sleep efficiency: the percentage ratio between total sleep time and time in bed.

Wake after sleep onset: the time spent awake in total sleep time.

Sleep latency: the interval between lights-off and the first appearance of a sleep stage.

REM sleep latency: the interval between lights-off and the first REM sleep stage.

Arousal index: number of arousals per hour.

Figure 2. Cyclic alternating pattern A1, A2 and A3 subtypes.

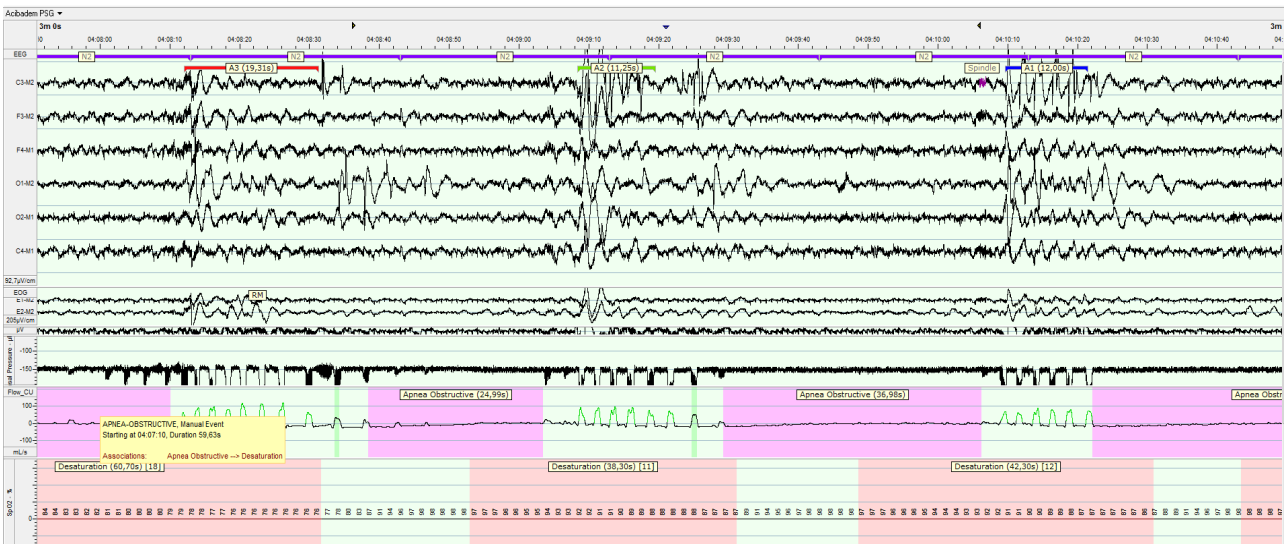


Figure 3. Cyclic alternating pattern A1 and A3 subtypes.

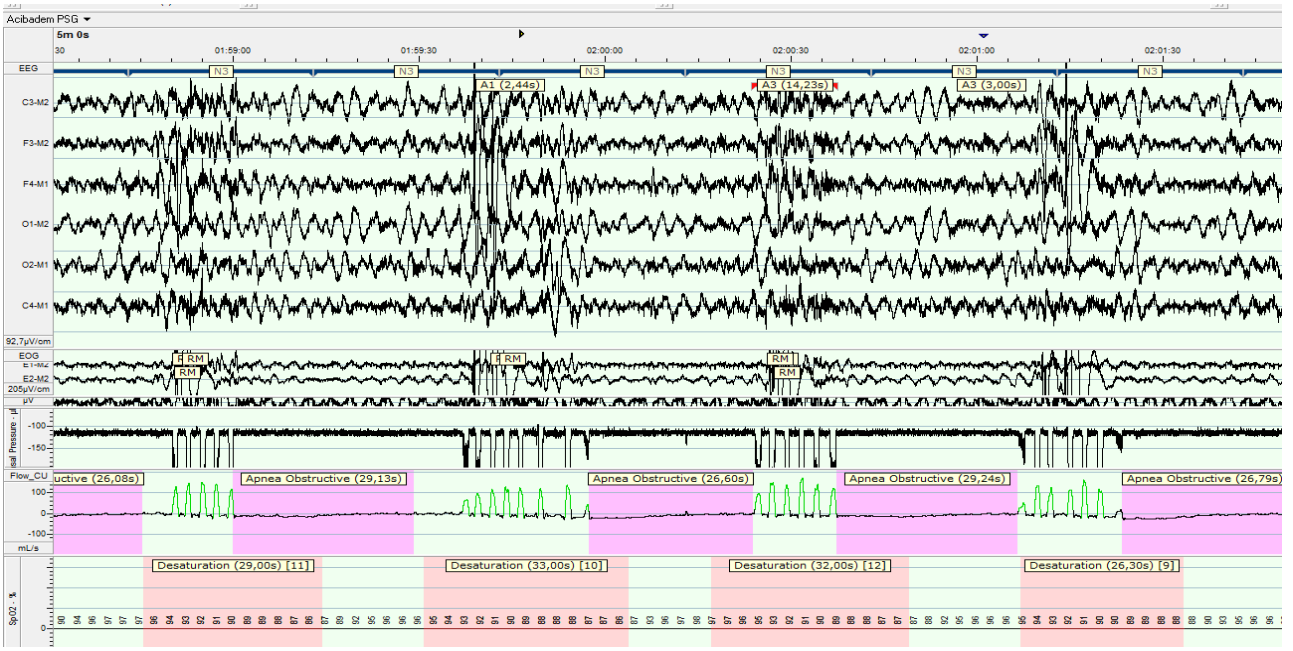
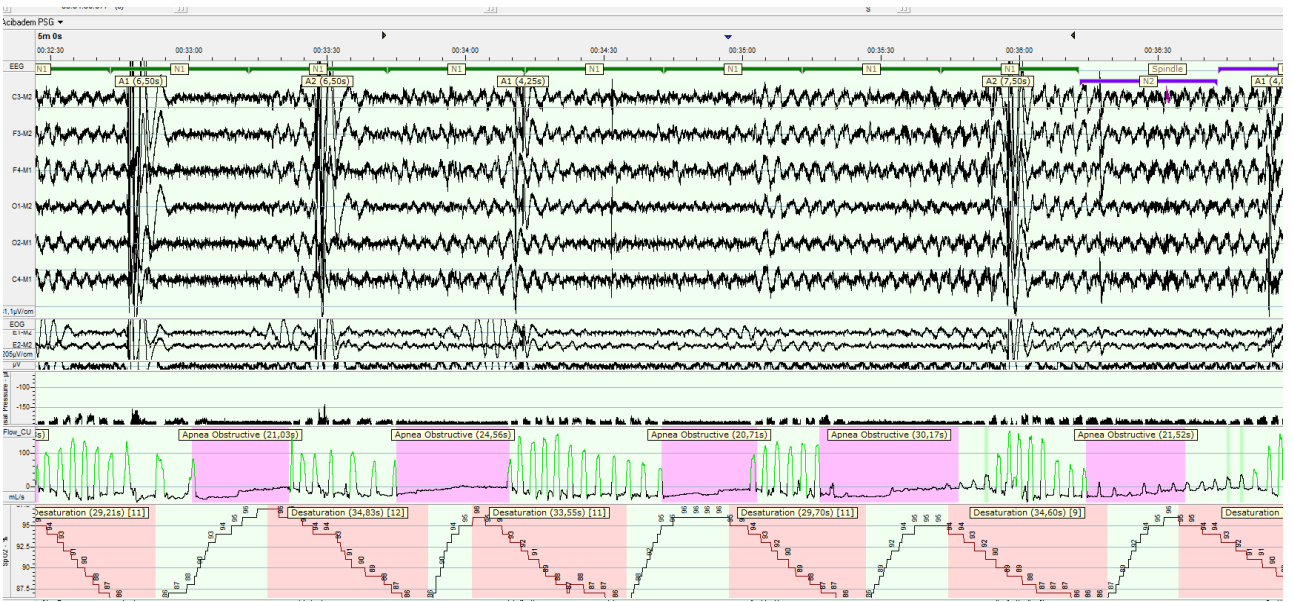


Figure 4. Cyclic alternating pattern A1 and A2 subtypes.



Percentage of N1, N2 N3 or REM sleep: percentage ratio of each sleep stage to total sleep time.

CAP scoring was annotated according to the conventional criteria (20). These are defined as follows:

A CAP sequence is composed of a succession of CAP cycles. Of the CAP cycles, ≥2 were compound CAP sequences.

A CAP cycle is composed of a phase A (activation period) and phase B (subsequent background period) (Figure 1).

Phase A is divided into three subtypes: A1, A2 and A3.

Subtype A1is composed of low-frequency activity, such as K-complexes and slow waves (Figures 2-4).

Subtype A2 is a transitional type between A1 and A3 and is composed of mixture of slow and fast EEG activities (Figure 4).

Subtype A3is represented by>50%of high-frequency activities, such as EEG arousals and polyphasic bursts (Figure 2-3).

The following CAP parameters were calculated: CAP rate (percentage of CAP time to total NREM sleep time) and, separately, percentages of phase A1, A2 and A3 time to total NREM sleep time.

All recordings were carried out by automatic scoring with the subsequent control and manual corrections. They were then calculated for statistical analysis.

Statistical Analysis

SPSS (Statistical Package for Social Sciences) 15.0 for Windows was used for statistical analysis. A Chi-square test was used to compare qualitative data. The Kolmogorov-Smirnov test was used to determine whether the data were normally distributed. The nonparametric Mann-Whitney U test was used for non-normal data, while the parametric Student t-test was used for normally distributed data. Normally distributed variables were expressed as mean±SD, while skewed variables were expressed as median (interquartile range). Pearson and Spearman's correlation analyses were used to assess correlation between ESS and BMI scores and various sleep structure parameters. Values of $p<0.05$ were accepted as significant.

RESULTS

The average age of 23 male patients with severe OSA in the first group was 67.9±6.91 years, while the group 2 was 41.0±4.40 years. BMI was found to be significantly higher in group 1 patients (group 1 BMI = 36.01; group 2 BMI = 31.5; p = 0.011). There was also a statistically significant difference between the groups in terms of ESS (group 1 mean ESS = 13.6, group 2 mean ESS = 8.7, p = 0.001). On the other hand, the groups showed no significant difference in ODI, which were 48.5±17.5 and 52.8±20.3 in the elderly and middle-aged groups, respectively. There were no statistically significant differences for all macro- and microstructural parameters (Table 1). Also, there was no significant correlation between BMI and ESS scores and sleep macro- and microparameters.

DISCUSSION

Based on this research, we have encountered unexpected results: data on the macrostructure of sleep in middle-aged apneic subjects statistically approached the data of elderly patients with the same disease, and these are also basically similar to the parameters of previous studies. In terms of microstructure, there were also no statistically significant differences between the two groups. Although the CAP rates in both groups from our study do not differ from each other or, on the whole, from the results of similar studies, our CAP subparameters were different from most previous works.

The authors did not find the literature a comparative study of sleep structure in severe apnea in different age categories. Many studies exploring the

Table 1. Comparison of parameters of sleep macro- and microstructure in Group 1 and Group 2. values of p<0.05 were accepted as significant.

	Group 1	Group 2	p
TST (min)	342.3 ± 31.8	335.1 ± 31.0	0.44
SE (%)	90.2 ± 7.7	88.1 ± 9.2	0.39
WASO (min)	25.1 ± 26.0	28.9 ± 33.2	0.66
SL (min)	10.3 ± 7.3	14.1 ± 8.5	0.11
REM sleep latency (min)	119.7(99.7)	124.4 (90.4)	0.65
NREM N1 stage latency (min)	15.4 ± 8.7	12.4 ± 7.9	0.23
NREM N2 stage latency (min)	40.8 ± 13.0	40.7 ± 15.0	0.96
NREM N3 stage latency (min)	33.8 ± 20.2	31.6 ± 13.4	0.66
N3 stage percentage (%)	11.42±9.91	13.58±7.45	0.39
REM sleep percentage (%)	12.4± 11.6	14.1 ± 8.9	0.56
Arousal index	23.0 ± 24.6	14.7 ± 14.4	0.17
CAP rate (%)	35.5 (18.1)	38.2 (20.9)	0.58
Phase A1 percentage (%)	25.8 (17.0)	26.7 (16.8)	0.92
Phase A2 percentage (%)	5.6 (6.0)	5.6 (3.9)	0.96
Phase A3 percentage (%)	4.1 (4.5)	5.9 (5.7)	0.27
AHI	48.2 ± 17.0	52.6 ± 17.9	0.39

Data are presented as mean±SD or median (interquartile range)
Abbreviations: TST: total sleep time; SE: sleep efficiency; WASO: wake after sleep onset; SL: sleep latency, CAP: cyclic alternating pattern; REM: rapid eye movement sleep; NREM: non-rapid eye movement sleep; AHI: apnea-hypopnea index

effect of age on sleep architecture have been carried out among healthy and in mixed groups consisting of healthy subjects and those suffering from various diseases, including sleep apnea.

Age-related sleep structural changes were confirmed by two different meta-analyses (5,21). Based on these and other previous investigations, TST and SE were significantly reduced in elderly subjects. On the other hand, there are contradictory reports of whether SL varies with age. Most studies have shown a positive association between SL and increasing age, particularly in studies that compared very young and elderly subjects. Our results showed statistically similar TST, SE and SL values in both groups, regardless of age.

Studies included participants with OSA have shown no significant correlation between age and percentage of N1 and N2 sleep (5,21). Similarly, in the present study, N1 and N2 percentage did not change between the different age groups.

In contrast, the percentage of SWS and REM sleep decreases with age in adults (5,6). The exclusion or inclusion of participants with OSA did not change the outcomes in all cases. Other authors have reported a small increase in the proportion of REM between ages 75 and 85 (21). The percentage and latency of REM sleep are close to values of a previous study whose participants were patients with severe OSA and an average age of 38.58 years (22). However, the percentage of slow sleep in our patients is significantly higher than in patients in that study.

Difficulty of sleep maintenance, which presents

as a longer duration of WASO and increased arousal index, tends to decrease up to the age of sixty and remains mostly unchanged after this age, regardless of the presence of sleep apnea (6). Arousal index values are similar to the data of previous studies, but WASO values are significantly different (17,22). This variability can be explained by the duration of polysomnographic monitoring and the patient's time leaving the device.

Usually, the CAP rate is correlated with age in healthy persons. Since the CAP rate is the measure of arousability, higher CAP rates are associated with poorer quality of sleep, the CAP rate shows a bimodal distribution along the normal lifespan with two peaks during adolescence and senescence, respectively. It reflects the development and subsequent decline of physiological processes (10).

Many previous studies have confirmed that untreated patients with OSA present an exaggerated increase of CAP rates. For example, a recent study that examined CAP rates in participants aged between 40 and 70 suggested a significant increase in CAP rates among OSA patients (50.01±10.6) versus control subjects (19.3±7.9) (15). Another study reported that untreated middle-aged patients with OSA presented extremely increased CAP rates(3). The clinical review of Parrino et al. indicated that CAP rates in healthy middle-aged and elderly subjects were approximately 37.5% and 55.3%, respectively (4). In our study, these rates were 35.3% in middle-aged participants and 39.1% in elderly OSA patients. CAP rates from the literature review and the present study are similar in middle age, although these compare healthy (in review) and OSA (in our study) patients. On the other hand, our elderly patients with OSA had lower CAP rates than elderly populations in the review. This can be explained by the fact that there were data used from a mixed population (healthy and with various comorbidities) in the review, while the present study chose only patients with severe OSA.

In the present study, both groups showed statistically similar phase A1, A2 and A3 percentages, but different counts of phase A subtypes (more A1 phases than A2 and A3). As known, phase A1 is associated with restorative processes in healthies; and decreased arousability in some disorders (4). Our data were different from previous studies, in which the percentage of A1 phases was significantly lower than those of phases A2 and A3 (4,22). Full parallelism between our study and previous studies is impossible due to the different ages, comorbidities, activity levels, medications and cognitive profiles, which could determine the difference in phase A subtypes.

The authors would like to note that this work was carried out in high altitude conditions (1100 m above sea level) and most patients were from nearby settlements located at a high altitude. The effect of high altitude on the microstructure of sleep is still unexplored.

There may also be other methodological reasons that led to the above results. The different EEG frequencies, particularly components of CAP, are not equally distributed over the scalp. The phase A1 components show a clear prevalence and are best recorded over the anterior frontal regions for the 0.25–2.5 Hz band; phase A3 components register best over the parietooccipital areas for the 7–12 Hz band (4). In our study, the CAP scoring was made from all recording electrodes. These EEG montages were mostly located in the frontocentral region. Since the A3 subtype mostly occurs in the parietooccipital region, the existing O1-M2 and O2-M1 montages may not be sufficient for detecting A3 subtype. Another explanation could be that slow rhythms (the main part of phase A1) and autonomic functions may have a reciprocal interaction in senescence. Autonomic reactions become softer and slower with advanced age. OSA patients have also observed termination of respiratory events with a predominant increase of delta power, which is a part of phase A1(4). Finally, the increase of slow oscillations and reduction of phases A2 and A3 can be explained by deterioration of the arousal system in elderly populations.

One major limitation of the present study is the absence of a healthy control age-matched group and the lack in the literature of normative data on structures of sleep for elderly healthy people. These make it impossible to compare healthy and OSA patients. Other limitations of the present study were the small number of participants and inclusion of only male patients. We chose to work only with male participants because elderly men experience much greater impairment in NREM sleep than age-matched women (7).

All these considerations indicate the need for future investigation of geriatric sleep in different health conditions. External and internal arousal-related conditions must be taken into account, such as homeostatic, neuropsychiatric and autonomic system status, diurnal vigilance, presence of any pain, comorbidities, drug application, relative inconvenience of sleep in a laboratory, ambient temperature and noise. It is obvious that all data need careful analysis in light of internal and environmental factors. We believe that a future abundance of studies on this topic will answer these questions about daily clinical applications of microstructural analyses on the diagnosis of diseases and effect of treatment.

Conflicts of interest: The authors declare that they have no conflict of interest.

REFERENCES

1. Terzano MG, Mancia D, Salati MR, Costani G, Decembrino A, Parrino L. The cyclic alternating pattern as a physiologic component of normal NREM sleep. Sleep1985;8(2):137-45. (PMID:4012156)
2. Muzet A. Alteration of sleep microstructure in psychiatric disorders.Dialogues Clin Neurosci. 2005;7(4):315-21. (PMID:16416707)
3. Parrino L, Smerieri A, Boselli M, Spaggiari MC, Terzano MG. Sleep reactivity during acute nasal CPAP in obstructive sleep apnea syndrome. Neurology 2000;54(8):1633-40. (PMID:10762505)
4. Parrino L, Ferri R, Bruni O, Terzano MG. Cyclic alternating pattern (CAP): the marker of sleep instability. Sleep Med Rev 2012;16(1):27-45. (PMID:21616693)
5. Ohayon MM, Carskadon MA, Guilleminault C, Vitiello MV. Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: developing normative sleep values across the human lifespan.Sleep2004;27(7):1255-73. (PMID:15586779)
6. Li J, Vitiello MV, Gooneratne NS. Sleep in normal aging. Sleep Med Clin 2018;13(1):1-11 (PMID:29412976)
7. Mander BA, Winer JR, Walker MP. Sleep and human aging. Neuron 2017;94(1):19-36.(PMID:28384471)
8. Crowley K. Sleep and sleep disorders in older adults. Neuropsychol Rev2011;21(1):41-53.(PMID:21225347)
9. Schwarz JFA, Åkerstedt T, Lindberg E, Gruber G, Fischer H, Theorell-Haglöw J. Age affects sleep microstructure more than sleep macro structure. J Sleep Res 2017;26(3):277-287. (PMID:28093830)
10. Parrino L, Boselli M, Spaggiari MC, Smerieri A, Terzano MG. Cyclic alternating pattern (CAP) in normal sleep: polysomnographic parameters in different age groups. Electroencephalogr Clin Neurophysiol. 1998;107(6):439-50. (PMID:9922091)
11. Young T, Peppard E, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a population health perspective. Am J RespirCritCareMed2002;165(9):1217-39. (PMID:11991871)
12. Senaratna CV, Perret JL, Lodge CJ et al. Prevalence of obstructive sleep apnea in the general population: A systematic review. Sleep Med Rev 2017;34:70-81. (PMID:27568340)
13. Young T, Shahar E, Nieto J et al. Predictors of sleep-disordered breathing in community-dwelling adults: the Sleep Heart Health Study. Arch Intern Med 2002;162(8):893-900. (PMID:11966340)
14. Ancoli-Israel S Kripke DF, Klauber MR, Mason WJ, Fell R, Kaplan O. Sleep-disordered breathing in community-dwelling elderly. Sleep 1991;14(6):486-495. (PMID:1798880)
15. Karimzadeh F, Nami M, Boostani R. Sleep microstructure dynamics and neurocognitive performance in obstructive sleep apnea syndrome patients. J Integr Neurosci 2017;16(2):127-142. (PMID:28891505)

16. Parrino L, Grassi A, Milioli G. Cyclic alternating pattern in polysomnography: what is it and what does it mean? Curr Opin Pulm Med. 2014;20(6):533-541. (PMID:25188718)

17. Priano L, Bigoni M, Albani G, et al. Sleep microstructure in Parkinson's disease: cycling alternating pattern (CAP) as a sensitive marker of early NREM sleep instability. Sleep Med 2019; 61:57-62. (PMID:31307885)

18. Izci B, Ardic S, Firat H, Sahin A, Altinors M, Karacan I. Reliability and validity studies of the Turkish version of the Epworth Sleepiness Scale. Sleep Breath 2008; 12:161–168. (PMID:17922157)

19. Iber C, Ancoli-Israel S, Chesson AL, Jr., Quan SF. The AASM manual for the scoring of sleep and associated events: rules, terminology and technical specifications. In: Iber C et al (Eds). American Academy of Sleep Medicine.1st edition, Westchester, IL USA 2007, pp 3-47.

20. Terzano MG, Parrino L, Smerieri A, et al. Atlas, rules, and recording techniques for the scoring of cyclic alternating pattern (CAP) in human sleep. SleepMed 2002;3(2):187-199. (PMID:14592244)

21. Floyd JA, Medler SM, Ager JW, Janisse JJ. Age-related changes in initiation and maintenance of sleep: a meta-analysis. Res Nurs Health 2000;23(2):106-117. (PMID:10782869)

22. Li N, Wang J, Wang D, et al. Correlation of sleep microstructure with daytime sleepiness and cognitive function in young and middle-aged adults with obstructive sleep apnea syndrome. Eur Arch Otorhinolaryngol 2019;276(12):3525-3532. (PMID:31263979)

RESEARCH

EFFECTIVENESS OF ORAL DIRECT ACTING ANTIVIRALS IN ELDERLY CHRONIC HEPATITIS C PATIENTS: REAL-WORLD DATA

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2020.185
2020; 23(4): 473-481

Mehmet ÇABALAK[1]
Tayibe BAL[1]

Abstract

Introduction: Objectives: Elderly cases have not been adequately represented in clinical trials with respect to chronic hepatitis C treatment. Extremely limited real-world data is available on new direct-acting antivirals in elderly patients. Herein, we aim to evaluate real-world data on new direct-acting antivirals used in the treatment of chronic hepatitis C virus.

Materials and Method: Medical records of 122 patients who started treatment with new direct-acting antivirals between January 2018 and December 2019 owing to chronic hepatitis C virus infection were analyzed retrospectively. Patients were divided into two age groups: those younger than 65 years and those aged 65 and older. Sustained virological response at 12 week rates were compared between the two groups. Sustained virological response at 12 week treatment efficacy analyses were performed with both modified intention to tract and per protocol.

Results: Sustained virological response in the 12th week post treatment was similar in both elderly patients and younger patients. Per protocol analysis was 97.6% (42/43) vs. 100% (56/56) and modified intention to tract analysis was 91.3% (43/45) vs. 91.8% (56/61), respectively. The most common genotype of patients aged 65 years and older were 1b 80%, and the most common genotype of patients younger than 65 years was 1b 57%.

Conclusion: In the present study, Sustained virological response rates were similar in elderly patients compared to younger patients; however, very limited information is available on the effectiveness and safety of new, recently approved direct-acting antivirals in the elderly population.

Key words: Hepatitis C, Chronic; Antiviral Agents; Sustained Virologic Response; Turkey

CORRESPONDANCE
[1]Mehmet ÇABALAK

Hatay Mustafa Kemal Üniversty, Infectious Disease and Clinical Microbiology, HATAY, Turkey

Phone: +905369685243
e-mail: mehcab@yahoo.com

Received: Aug 10, 2020
Accepted: Nov 17, 2020

[1] Hatay Mustafa Kemal Üniversty, Infectious Disease and Clinical Microbiology, HATAY, Turkey

INTRODUCTION

Hepatitis C infection (HCV) is a major global outbreak, and an estimated 71 million people worldwide are considered to be chronically infected with HCV. Approximately 399,000 people die annually because of HCV-related hepatic insufficiency and cancer (1,2). The estimated prevalence of HCV is 0.2%–0.5% in the United States of America (USA) and Western Europe and 1%–3% in Japan (3,4). The prevalence of HCV in the normal population of Turkey is 1% (5). In some European countries and in countries such as Japan and Taiwan, the prevalence of HCV is high in the elderly population (6). In Europe and Japan, the prevalence of HCV can reach up to 12% in people aged between 61 and 70 years. A study conducted in Egypt found that the prevalence of HCV significantly increased with age; it was 60% between 50 and 60 years of age, and about 40% cases occurred over 60 years of age (7).

Efficacy and safety data are very limited in the treatment of HCV in elderly patients, primarily in clinical trials, owing to incomplete reporting and exclusion (8,9). Historically, there have been significant age restrictions in interferon-based antiviral treatments. This is because compliance with treatment is low in elderly patients, side effects are more common, and the response to treatment is low (10).

Very limited information is available in the literature on the effectiveness of newly used direct-acting antiviral (DAA) drugs in Turkey. This study aims to compare the effectiveness of chronic hepatitis C treatment DAAs in patients aged 65 years and older as well as in patients aged younger than 65 years

MATERIALS AND METHOD

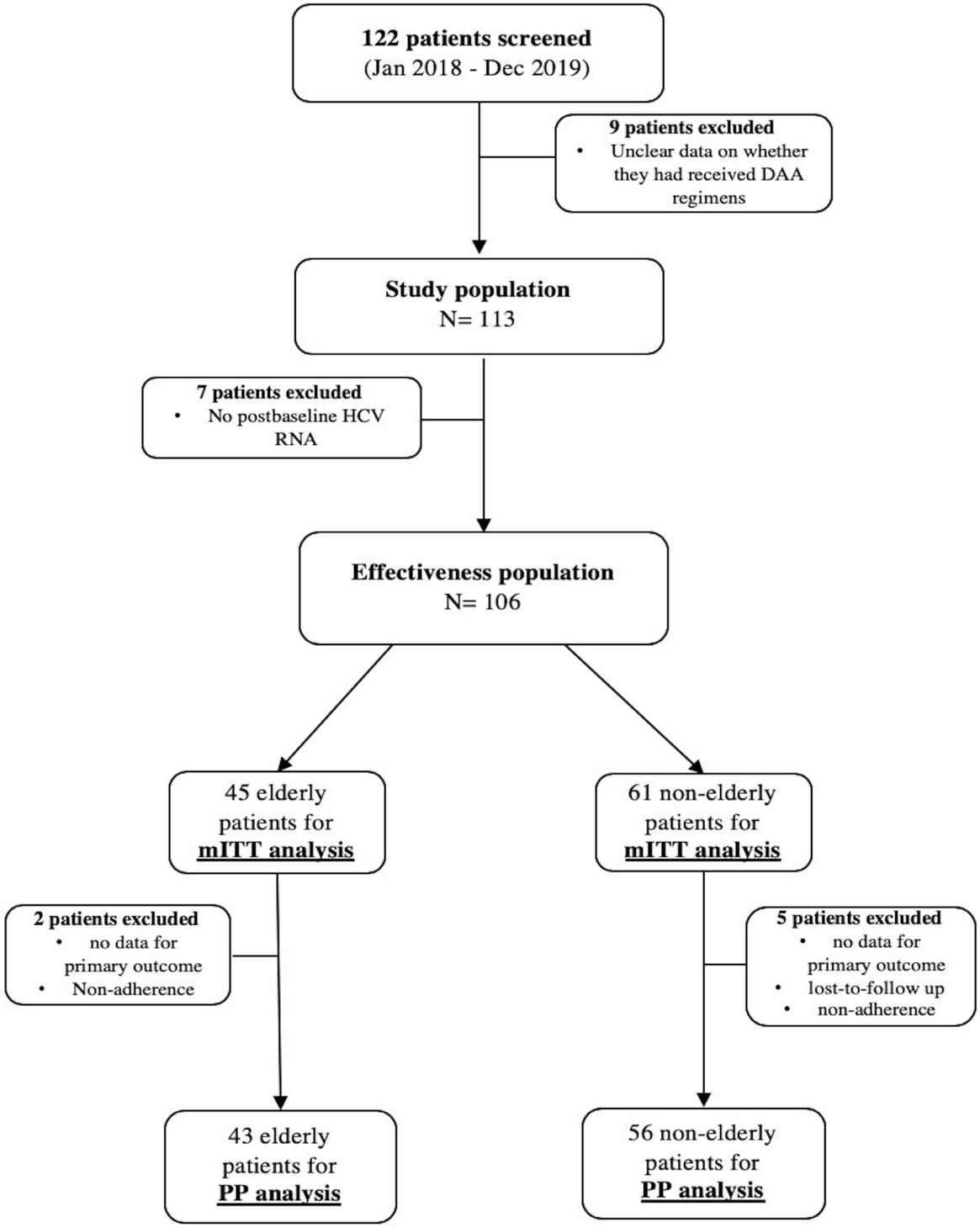
Medical records of 122 patients who started treatment with new DAAs between January 2018 and December 2019 because of chronic HCV infection were retrospectively analyzed. Sixteen cases were removed from the study for various reasons (Figure 1).

DAA drug selection and treatment decisions were made according to current guideline recommendations and according to the decision of the treating physician. The drugs used in the treatment were sofosbuvir (SOF) ± ledipasvir (LED) ± ribavirin (RBV), ombitasvir (OBV) + paritaprevir/ritonavir (PTV/r) ± dasabuvir (DSV) ± ribavirin (RBV), and glecapravir (GLE) + pibrentasvir (PIB). The RBV dose was started according to the weight of the patients. The duration of treatment was set as 8, 12, or 24 weeks based on previous treatment experience and the patients' cirrhosis status. In some cases, liver fibrosis was evaluated via invasive liver biopsy or clinically, radiologically, or through laboratory findings in others.

For viral load determination, HCV–RNA levels were studied via real-time PCR (COBAS AmpliPrep/COBAS Tagman, Roche Diagnostics, Germany) and HCV genotypes were studied using real-time HCV Genotype II (Anatolia geneworks, Turkey) system.

Sustained virological response (SVR-12) was described as the inability to detect HCV viral load 12 weeks after treatment completion. Efficiency assessments other than SVR-12 were defined as follows. Early virological response (EVR): absence of serum HCV RNA after 4 weeks of treatment. Virological breakthrough: detection of previously undetected HCV RNA during treatment. Relapse: detection of HCV RNA, which was not detected at the end of treatment or during the follow-up after treatment. EVR and SVR-12 treatment efficacy analyses were performed between both groups with modified intention to tract (mITT) and per protocol (PP). Patients who completed the treatment period and who had HCV RNA test results at the 12th week after end of treatment were included in the PP analysis. Patients with at least one HCV RNA test result in addition to pretreatment HCV RNA levels were included mITT analysis. All cases with unknown sustained viral responses (SVR-12) were considered as unresponsive in mITT analysis.

Figure 1. Study population flowchart



Statistical Analysis

IBM SPSS version 23.0 statistical package program (SPSS Inc, Chicago, IL, USA) was used for statistical analysis. The suitability of variables to normal distribution was tested using the Shapiro–Wilk test and histogram. Mean and standard deviation was used for variables that were normally distributed, median (median) and interquartile range was used for variables that were not normally distributed. The Chi-square test was used to compare categorical variables between groups. Biochemical and hematological parameters before and 12 weeks after treatment were compared between groups through the Wilcoxon test. P values below 0.05 were evaluated as statistically significant.

This study was performed with the approval of Mustafa Kemal University Faculty of Medicine Retrospective Ethics Board (reference number: 04.06.2020-01).

RESULTS

During the study period, DAA regiment was administered to 122 cases. 106 cases meeting the criteria for inclusion were included in the study. Of the 106 cases, patients in 45 cases (42.5%) were 65 years old and patients in over 61 cases (57.7%) were younger than 65 years of age. Of the cases having patients aged 65 years and older, 24 patients were female and 21 patients were male. Of the patients who were younger than 65 years of age, 23 were female and 38 were male. Table 1 shows the demographic, primary clinical characteristics, and biochemical as well as hematological parameters of patients according to age groups. Four cases had previous treatment experience: in one of these cases, the patient was over 65 years old, and in three cases, the patients were younger than 65 years of age. All experienced patients had previously used the combination of IFN and RBV.

The most common genotype was 1b in patients aged 65 years and older (80%; n = 36) as well as in patients younger than 65 years (57%; n = 35) of age. However, the difference was statistically significant (p = 0.022). Figure 2 shows the genotype distributions of cases by age.

SOF ± LED ± RBV treatment was started in 11.1%, OBV + PTV/r ± DSV ± RBV treatment was started in 73.3%, and GLE + PIB treatment was started in 15.6% patients aged 65 years and older. SOF ± LED ± RBV treatment was started in 8.2%, OBV +PTV/r ± DSV ± RBV treatment was started in 73.8%, GLE +

Figure 2. The genotype distribution by age groups

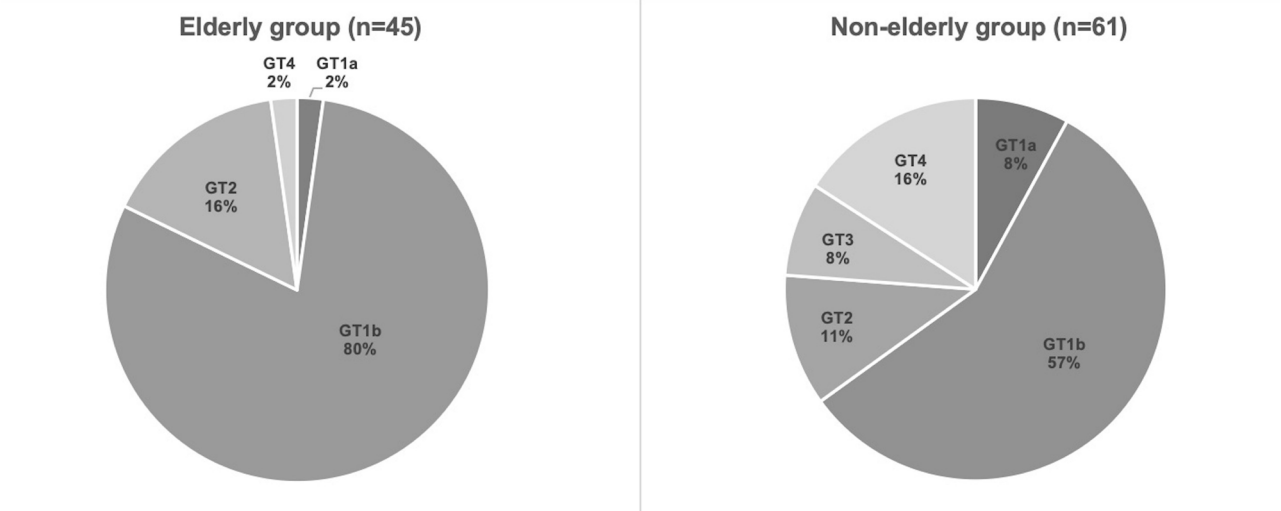


Table 1. Patients demographics and clinical characteristics at baseline by age groups in mITT population.

	Elderly (n=45)	Non-elderly (n=61)	p value
Age	73.6 ± 6.8	47.5 ± 14.32	<0.001
Gender, male	21 (46.6)	38 (62.2)	0.109
Cirrhosis	4 (8.9)	4 (6.6)	0.720
Treatment-experienced	1 (2.2)	3 (4.9)	0.635
Genotype 1	37 (82.2)	39 (63.9)	0.022
HCV RNA level	246000 (77600-14076712)	407300 (135547-1334478)	0.426
Biochemical parameters			
ALT	37 (19-56)	37 (18-58)	0.718
AST	35 (22-50)	35 (22-51)	0.898
BIL	0.70 (0.60-1.10)	0.70 (0.50-1.00)	0.162
ALB	4.30 (3.8-4.2)	4.26 ± 0.37	0.003
Crea	0.70 (0.60-0.90)	0.70 (0.60-0.90)	0.750
Hematological parameters			
HGB	12.73 ± 1.72	14.05 ± 2.31	0.001
PLT	239733 ± 86729	216213 ± 61696	0.232
INR	1.04 ± 0.11	1.02 ± 0.10	0.267

Data expressed as n (%), median (IQR) or mean ± SD. Bold font indicates statistical significance.
HCV RNA: hepatitis C virus ribonucleic acid, ALT: alanine aminotransferase, AST: aspartate aminotransferase, BIL: bilirubin, ALB: albumin, Crea: creatinine, HGB: hemoglobin, PLT: platelet, INR: international normalized ratio.

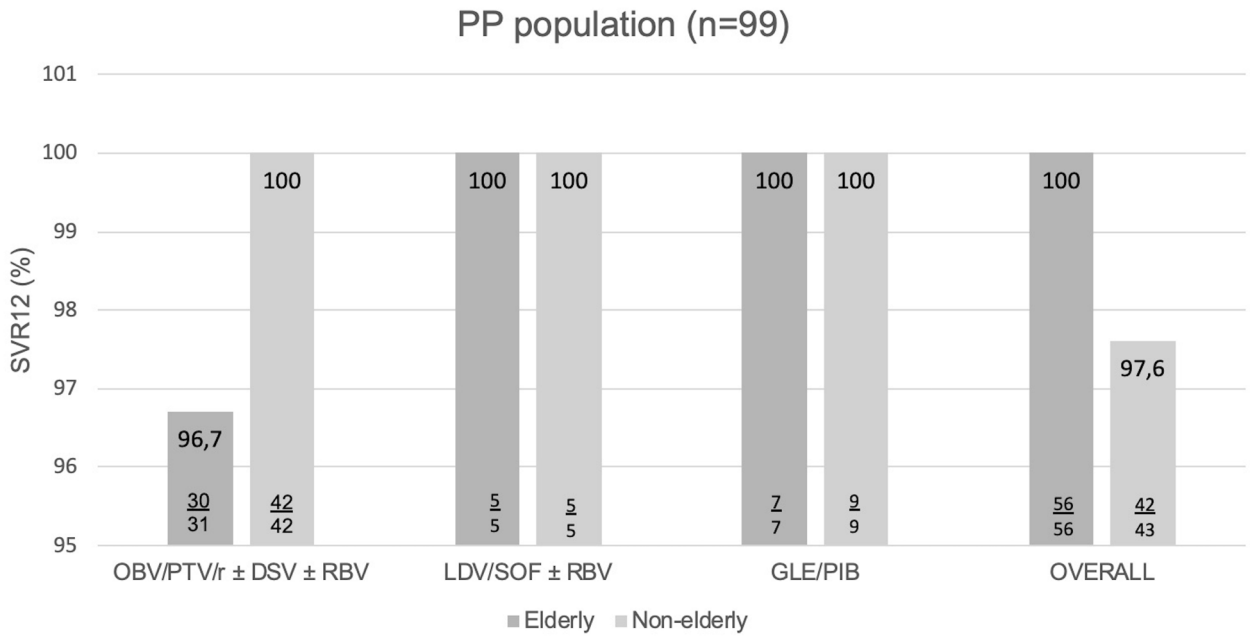
PIB treatment was started in 18% patients younger than 65 years of age. No statistically significant difference was observed between the groups in terms of the agents used in the treatment (p = 0.893). Of the 106 cases, 9 had diabetes mellitus, 10 had hypertension, 5 had coronary artery disease, and 7 had chronic renal failure.

Early virological response (EVR) was observed in 102 cases. EVR was 97/102 (95.1%) in all treatment regimens. It was detected as 53/57 (93.4%) in patients aged 65 years and older and 44/45 (97.8%) in patients younger than 65 years of age. No statistically significant difference was observed between both groups (p = 0.290).

A total of 106 and 99 cases were included in mITT and PP populations, respectively, for treatment outcome analysis. SVR-12 rates of patients aged 65 years and older were similar compared to patients younger than 65 years of age. PP analysis was 97.6% (42/43) vs. 100% (56/56) and mITT analysis was 91.3% (43/45) vs. 91.8% (56/61), respectively. SVR-12 could not be studied in seven cases as the patients of these cases did not attend follow-up examinations post treatment. SVR-12 rates are presented in Figures 3 and 4 according to age and mITT and PP analysis. No breakthrough was observed during treatment. Relapse was detected in a female patient aged 74 years at 24 weeks after treatment cessation. This patient in this case did not have prior treatment experience, was of genotype 1b, and received OBV + PTV/r ± DSV treatment.

In the present study, the levels of alanine aminotransferase, aspartate aminotransferase, and bilirubin significantly decreased and albumin levels

Figure 3. SVR12 rates according to DAA regimens in PP population by age groups



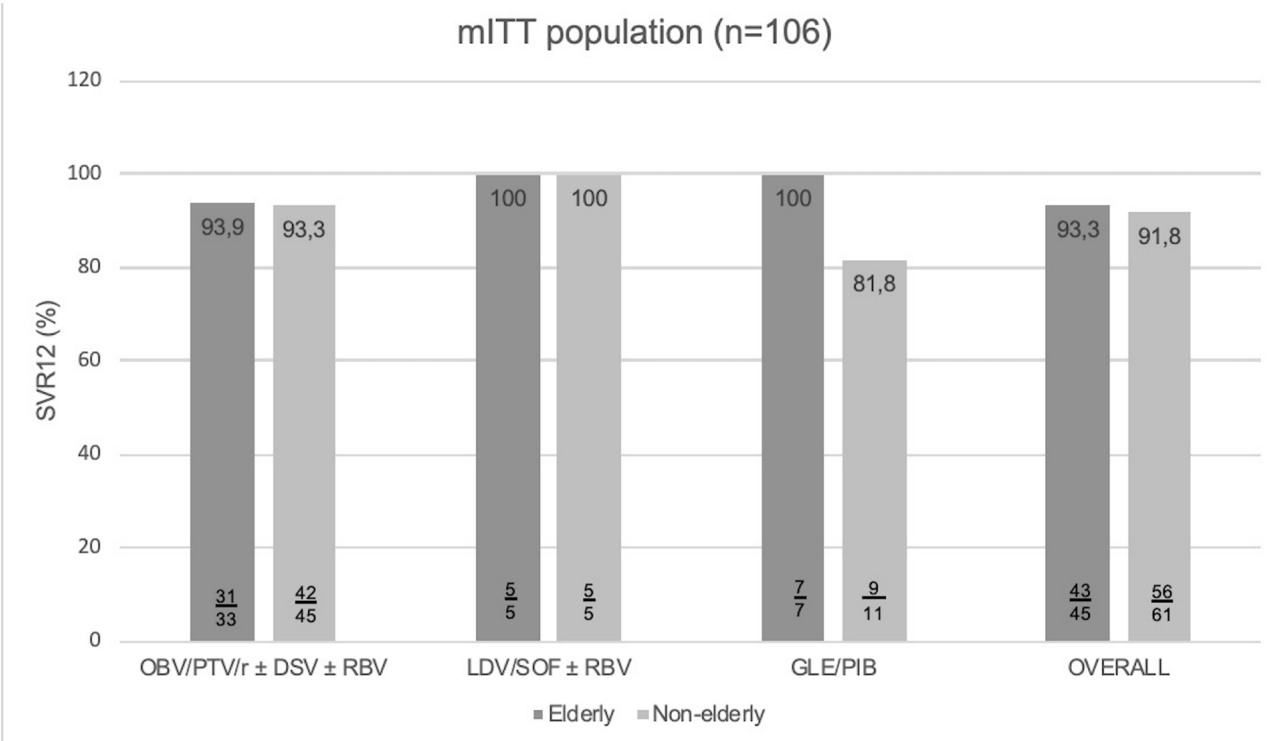
significantly increased with DAA treatment in both elderly and younger patients.

DISCUSSION

Elderly individuals have traditionally received less HCV treatment than young patients (11). In the meta-analysis of Yang et al., SVR rates of IFN/RBV treatment were found to be low in patients aged 65 years and older compared to patients younger than 65 years of age; in contrast, relapse was found to be significantly higher (12). Saab et al. reviewed four clinical trials and found that DAA and SVR-12 rates were similar between patients aged 65 years and older and patients younger than 65 years (13). Real-world data were used herein, and SVR-12 rates were found to be similar between patients aged 65 years and older and patients younger than 65 years treated with new DAAs Clinical and real-world studies, new DAAs have higher SVR rates than IFN-based treatments, and SVR-12 rates of new DAAs are above 90% (14-16). Real-world data on DAA treatment in elderly and advanced elderly patients is very limited. To the best of our knowledge, there is no other study comparing real-world data in Turkey on DAA treatment in patients aged 65 years and older and patients younger than 65 years of age. We believe that the present study is important because it is the first study to investigate real-world data on the elderly in Turkey.

Saab et al. retrospectively evaluated the results of four clinical trials. SVR was 98% in patients with HCV aged 65 years and older using LED/SOF GT-1 and 97% in patients under 65 years of age (13). Herein, SVR-12 was determined to be 100% - and 100% in both groups, respectively, owing to the small sample size. Sherigar et al. evaluated the results of 80 patients using LED/SOF in their study, and they found an SVR-12 rate of 94% (17). Dultz et al. found the SVR-12 rate to be 95% and 94% in non-cirrhotic and cirrhotic patients over 70 years of age receiving GT-1b and LED/SOF ± RBV treatment. In

Figure 4. SVR12 rates according to DAA regimens in mITT population by age groups



noncirrhotic and cirrhotic patients younger than 70 years of age, SVR-12 was 95% vs. 91%, respectively (14). In their studies including real-world data, Lens et al. found an SVR-12 rate of 96% in patients who received LED/SOF ± RBV treatment (15). In these studies, it was found that SVR-12 was high in elderly patients receiving LED/SOF ± RBV treatment.

Lens et al. found an SVR-12 rate of 98.3% with OBV + PTV/r ± DSV ± RBV treatment in elderly patients containing real-world data (15). Sheregar et al. investigated patients receiving OBV + PTV/r ± DSV ± RBV treatment and found an SVR-12 rate of 100% in patients aged 65 years and older as well as patients younger than 65 years (17). Herein, SVR-12 was found to be 93.9% (31/33) in patients aged 65 years and older and 93.3% in patients under 65 years of age. Dultz et al. found that SVR-12 was 91% vs. 91% in noncirrhotic and cirrhotic patients over 70 years of age who received GT1b and OBV + PTV/r ± DSV ± RBV treatment. SVR-12 was 93% vs. 94% in noncirrhotic and cirrhotic patients aged 70 years or younger (14). Although these studies show regional differences, the fact that SVR-12 is above 90% in elderly patients is important in terms of showing that chronic HCV cases are treatable regardless of age.

GLE + PIB have been found to be effective and safe in noncirrhotic cases in many phase III trials such as ENDURANCE 1-4 and SURVEYOR. These studies include patients over 65 years of age. These studies reported no failure of treatment with previous drug combinations and advanced age (18-20). Foster et al. examined real-world data in patients receiving GLE + PIB treatment, and found that SVR-12 was 97.9% in patients aged 65 years and older and 97.3% in patients younger than 65 years, and there was no statistical difference between the age groups (21). Herein, SVR-12 in patients receiving GLE + PIB treatment was determined to be 100%

in patients aged 65 years and older and 81.8% in patients younger than 65 years. Low SVR in patients younger than 65 years in the present study may be associated with the small sample size. For this reason, further studies with larger case series should be conducted in the elderly population in Turkey.

SVR rates can vary according to genotypes (GT). Sherigar et al. found that SVR rates with DAA were lower in the elderly with GT 1 genotype compared to younger patients (17). Backus et al. did not find a significant difference between treatment naive and treatment experienced elderly and young cases with GT 1 genotype; however, they found that SVR-12 was significantly lower in GT 2 treatment experienced elderly patients compared to young patients (22). In the study conducted by Su et al., GT 1 cases had higher SVR-12 than GT 2, 3, and 4 cases. In GT 3 cases, SVR-12 was lower than other genotypes (16). In the present study, there was no significant difference in SVR-12 rates between genotypes. This may be due to the small sample size in our study.

In our study, genotype 1b was the most common in the distribution of genotype in both age groups, but this rate was low in younger than 65 years, genotype 3 and 4 were found higher. We think that this may be due to the use of IV drugs and the increase in international contact.

Tapper et al. detected relapse in 44 patients who received LED + SOF treatment (23). Sherigar et al. detected treatment failure in 12 cases. Five of the cases were 65 years old and older and seven were younger than 65 years. They detected relapse in eight cases, partial response in three cases, and virological breakthrough in one case. They found that age was not a factor in both groups in terms of treatment failure and poor virological response. In five out of 12 patients with treatment failure, they detected HIV coinfection (17). In the present study, there were no cases of HIV coinfection. We detected relapse in one case aged 65 years and older. Therefore, we recommend that further multicentric studies with numerous cases should be conducted.

The limitations of this study include its retrospective design, investigation of regional data, and the small number of cases investigated. Another limitation is that the safety and side effects of DAAs were not evaluated herein.

CONCLUSION

In the present study, SVR rates were found to be similar in elderly patients compared to younger patients, but there is very limited information about the effectiveness and safety of new and recently approve; however, very limited information on DAAs is available in the Turkish elderly population. Although majority DAA clinical trials include advanced age populations, the proportion of elderly patients is small. This study presents the first real-world data examining patients aged 65 years and older and patients younger than 65 years in Turkey. Short treatment times with new DAAs can reduce drug-related side effects in the elderly. Therefore, we recommend that further multicentric studies that examine the safety, efficacy, and side effects of new DAAs in elderly people should be conducted.

REFERENCES

1. World Health Organization. Global Hepatitis Report; 2017. (Internet). Available from: https://www.who.int/hepatitis/publications/global-hepatitis-report2017/en/. Accessed: 06.08.2020.
2. Nelson PK, Mathers BM, Cowie B, et al. Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: results of systematic reviews. Lancet 2011; 378:571–83. (DOI:10.1016/s0140-6736(11)61097-0).
3. Global Burden Of Hepatitis C Working Group. Global burden of disease (GBD) for hepatitis C. J Clin Pharmacol 2004; 44(Suppl 1):20-9. (PMID: 14681338).
4. Averhoff FM, Glass N, Holtzman D. Global burden of hepatitis C: considerations for healthcare providers

in the United States. Clin Infect Dis 2012; 55(1):S10-5. (PMID: 22715208).

5. Tozun N, Ozdogan O, Cakaloglu Y, et al. Seroprevalence of hepatitis B and C virus infections and risk factors in Turkey: a fieldwork TURHEP study. Clin Microbiol Infect 2015; (11):1020-6. (PMID: 26163105).
6. Yang Z, Zhuang L, Yang L, et al. Efficacy and safety of peginterferon plus ribavirin for patients aged ≥65 years with chronic hepatitis C: a systematic review and meta-analysis. Clin Res Hepatol Gastroenterol 2014; 38:(Suppl 4):440–50 (PMID:24176812).
7. Abdel-Aziz F, Habib M, Mohamed MK, et al. Hepatitis C virus (HCV) infection in a community in the Nile Delta: population description and HCV prevalence. Hepatology 2000; 32(1):111–5. (PMID:10869297).
8. Thabut D, Le Calvez S, Thibault V, et al. Hepatitis C in 6,865 patients 65 yr or older: a severe and neglected curable disease? Am J Gastroenterol 2006; 101:1260-7. (PMID: 16771947).
9. Saab S, Rheem J, Sundaram V. Hepatitis C infection in the elderly. Dig Dis Sci 2015; 60(11):3170-80. (PMID:26008618).
10. Honda T, Katano Y, Shimizu J, et al. Efficacy of peginterferon-alpha-2b plus ribavirin in patients aged 65 years and older with chronic hepatitis C. Liver Int 2010; 30(4):527-37. (PMID:19523048).
11. El-Serag H, Kramer J, Duan Z, Kanwai F. Epidemiology and outcomes of hepatitis C infection in elderly US veterans. J Viral Hepat 2016; 23(9):687-96. (PMID:27040447).
12. Yang Z, Zhuang L, Yang L, et al. Efficacy and safety of peginterferon plus ribavirin for patients aged ≥ 65 years with chronic hepatitis C: A systematic review and meta-analysis. Clin Res Hepatol Gastroenterol 2014; 38(4):440-50. (PMID: 24176812).
13. Saab S, Park SH, Mizokami M, et al. Safety and efficacy of ledipasvir/ sofosbuvir for the treatment of genotype 1 hepatitis C in subjects aged 65 years or older. Hepatology 2016; 63(4):1112-9. (PMID:26704693).
14. Dultz G, Müller T, Petersen J, et al. Effectiveness and safety of direct-acting antiviral combination therapies for treatment of hepatitis C virus in elderly patients: results from the German Hepatitis C Registry. Drugs Aging 2018; 35(9):843–57. (PMID:30084012).
15. Lens S, Fernandez I, Rodriguez-Tajes S, et al. Interferon-free therapy in elderly patients with advanced liver disease. Am J Gastroenterol 2017; 112(9):1400–9. (PMID:28585554).
16. Su F, Beste LA, Green PK, Berry K, Ioannou GN. Direct-acting antivirals are effective for chronic hepatitis C treatment in elderly patients: a real-world study of 17 487 patients. Eur J Gastroenterol Hepatol 2017; 29(6):686–93. (PMID:28195877).
17. Sherigar JM, Gayam V, Khan A, et al. Clinical efficacy and tolerability of direct-acting antivirals in elderly patients with chronic hepatitis C. Eur J Gastroenterol Hepatol 2017; 29(7):767-76. (PMID:28346233).
18. Gane E, Poordad F, Wang S, et al. High Efficacy of ABT-493 and ABT-530 treatment in patients with HCV genotype 1 or 3 infection and compensated cirrhosis. Gastroenterology 2016; 151(4):651–659. (PMID:27456384).
19. Kwo PY, Poordad F, Asatryan A, et al. Glecaprevir and pibrentasvir yield high response rates in patients with HCV genotype 1–6 without cirrhosis. J Hepatol 2017; 67(2):263–71. (PMID:28412293).
20. Poordad F, Felizarta F, Asatryan A, et al. Glecaprevir and pibrentasvir for 12 weeks for hepatitis C virus genotype 1 infection and prior direct-acting antiviral treatment. Hepatology 2017; 66(2):389–97. (PMID:28128852).
21. Foster GR, Asselah T, Kopecky-Bromberg S, et al. Safety and efficacy of glecaprevir/pibrentasvir for the treatment of chronic hepatitis C in patients aged 65 years or older. PLoS One 2019; 14(1):e0208506 .(PMID:30601818).
22. Backus LI, Belperio PS, Shahoumian TA, Loomis TP, Mole LA. Effectiveness of sofosbuvir-based regimens in genotype 1 and 2 hepatitis C virus infection in 4026 U.S. Veterans. Aliment Pharmacol Ther 2015; 42(5):559-73. (PMID:26113432).
23. Tapper EB, Bacon BR, Curry MP, et al. Real-world effectiveness for 12 weeks of ledipasvir-sofosbuvir for genotype 1 hepatitis C: the Trio Health study. J Viral Hepat 2017; 24(1):22-7. (PMID: 27730717).

RESEARCH

THORACIC DEGENERATIVE DISC PATHOLOGIES IN GERIATRIC PATIENTS

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2020.186
2020; 23(4): 482-491

- Ayşe Serap AKGÜN[1]
- Arzu YAVAŞ DİNÇ[2]

CORRESPONDANCE
Arzu YAVAŞ DİNÇ
Medipol University School of Medicine, Department of Radiology, İstanbul, Turkey

Phone: +90212 912 25 25
e-mail: arzudinc0111@gmail.com

Received: Jun 25, 2020
Accepted: Sep 03, 2020

[1] Medipol University School of Medicine, Department of Radiology, İstanbul, Turkey

[2] Medipol University School of Medicine, Department of Physical Therapy and Rehabilitation, Istanbul, Turkey

Abstract

Introduction: This study investigates the incidence and localization of thoracic degenerative disc pathologies, such as bulging and herniation, in geriatric patients.

Materials and Methods: Between January 2015 and August 2019, a total of 171 patients were retrospectively examined in the study. The patients were admitted for dorsalgia and underwent magnetic resonance imaging (MRI) of the thoracic vertebra. All patients were examined for disc and endplate degeneration, bulging and/or disc herniation, and Schmorl nodes.

Results: Disc bulging/herniation was diagnosed in 534 (26%) of the overall total of 2052 intervertebral disc levels; 206 (10%) of these had bulging but no herniation. The location most commonly affected by bulging was T10-11 (n=46, 2.25%), followed by T11-T12 (n=45, 2.1%) Disc herniation was present in 329 (15.9%) of the levels; herniation was most common at T11-12 (n=51, 15.5%).

Conclusion: The intervention of music therapy was found to have an effect in reducing anxiety and increasing sleep quality of patients. Music therapy can be used as an alternative method of treating the anxiety and increasing the sleep quality of geriatric hematology patients.

Keywords: Geriatric Assessment; Back Pain; Thoracic Vertebrae; Magnetic Resonance Imaging

INTRODUCTION

Thoracic disc disease (TDD) is uncommon; it is estimated that less than 1% of all disc herniations occur in the thoracic region (1). However, several autopsy series have revealed an incidence of 7% to 15% (2, 3). The majority of thoracic pathologies emerge during the third to fifth decades of life. Disk degeneration is the main cause, but trauma is also considered a major factor (1). The clinical demonstration of a thoracic disc herniation (TDH) depends on its location and morphologic characteristics. This may lead to delayed diagnosis or misdiagnosis of TDH (4). According to previous literature, 75% of TDHs occur below T8, 3% of cases occur between T1 and T2, and less than 1% occur between T2 and T3 (5, 6). Cases with TDD usually present with upper back pain or pain radiating to a dermatome. However, the main initial symptom is nonspecific pain, followed by sensory and motor disturbances. Symptoms of spinal cord compression are observed in most patients with TDD at the time of diagnosis (7). Multiple imaging techniques have been used to diagnose this condition; however, as for most vertebral diseases, magnetic resonance imaging (MRI) is the ideal technique for assessing thoracic disc problems, since it is both non-invasive and very sensitive (7-9).

There is currently very little data about TDD in elderly people. Although symptomatic degenerative disc herniation occurs much less frequently in the thoracic spine than in other areas of the spine, the lack of research on the topic makes accurate diagnosis challenging (1). Moreover, there are few studies on pathology-related imaging of the thoracic spine (10-12). Therefore, the current study investigates the frequency of thoracic disc bulging/herniation in a group of elderly patients and seeks to determine the most common clinical presentations of such pathologies.

METHODS AND MATERIALS

Subjects

The study was planned as a retrospective study aimed at describing and characterizing the frequency of thoracic degenerative disc pathologies in a geriatric population. Participants were patients who presented at a physical medicine and rehabilitation outpatient clinic with upper back pain for more than 12 weeks and who were referred to the radiology department between January 2015 and August 2019.

The inclusion criteria of the study were: age 60 years and older and underwent an MRI scan of the thoracic vertebra due to complaints related to disc degeneration or to dorsalgia with suspected pathologies in the thoracic region. Patients with a chronic metabolic disorder, an infection, a malignancy, a compression fracture, or a previous surgery in the thoracic region were excluded. Patients with prominent kyphosis and/or rotoscoliosis were excluded as well.

This study was approved by the local ethics committee. The study was conducted in accordance with Good Clinical Practice and the Helsinki Declaration. Written and verbal informed consent was obtained from all participants.

Study Design

A total of 171 patients were included in the study. Each patient's thoracic vertebrae were scanned, resulting in a total of 2052 scanned levels (12disc levels). All T1- and T2-weighted sagittal and T2-weighted axial images were obtained with 1.5 T (Tesla) scanners (Magnetom; Siemens, Erlangen, Germany) and Philips Best (Netherlands). The following parameters were used: Sagittal T1 W (TR: 615/560, TE: 11/12, FOV: 320/220, slice thickness: 4/4 mm); sagittal T2 W (TR:3000/2930, TE: 83/110, FOV: 320/220, slice thickness: 4/4 mm); and axial T2 W (TR: 4340/4200, TE:109/140, FOV:160/200, slice thickness: 4/4 mm). These parameters were used for both MRI devices. A picture archiving and communication system was used (PACS, General Electric,

Chicago, IL, USA). All MR images were assessed by the same radiologist, who has ten years of experience in spinal neuroradiology. Two evaluations were done for each patient at an interval of one month to ensure intraobserver reliability.

Pathologies were characterized using updated lumbar disc nomenclature (13). The following pathologies were observed: protrusion, herniation, sequestration, bulging and extrusion, degeneration of the disc and the endplate, and Schmorl nodes. Intervertebral disc degeneration was determined using the Pfirrmann classification system, in which Pfirrmann grades I and II indicate no intervertebral disc degeneration, while Pfirrmann grades III, IV, and V indicate intervertebral disc degeneration (14). Changes in the endplate were evaluated using Modic classification and classified as type I, II, or III (15).

Statistical Analysis

The data were analyzed using the Statistical Package for the Social Sciences version 17 (SPSS Inc., Chicago, IL, USA). A Shapiro–Wilk test was used to check normality. Continuous variables were presented as the mean, standard deviation, and median (minimum–maximum) with regard to normality of distribution. Categorical variables were presented as frequency (percentage).

Table 1. Imaging findings by thoracic level and age group.

Age									H:
Disc Level	**60-69 (n:102)**		**70-79 (n:56)**		**>80 (n:13)**		**Total patients (n=171)**		
	B	**H**	**B**	**H**	**B**	**H**	**B**	**H**	**B+H**
T1-2	0	1	1	2	2	0	3	3	0
T2-3	1	3	1	6	2	1	4	10	0
T3-4	3	4	2	10	1	1	6	15	0
T4-5	1	6	1	11	1	2	3	19	0
T5-6	1	6	1	9	1	2	3	17	0
T6-7	4	11	4	18	1	5	9	34	3
T7-8	5	11	3	18	1	6	9	35	3
T8-9	9	13	7	14	4	3	20	30	4
T9-10	12	14	13	17	4	2	29	33	3
T10-11	23	21	18	25	5	4	46	50	7
T11-12	24	21	17	25	4	5	45	51	4
T12-L1	12	14	14	14	3	3	29	31	4
Total	**95**	**125**	**82**	**169**	**29**	**34**	**206**	**328**	**28**

H: Herniation; B: Bulging.

Table 2. Disc pathologies identified via MRI by intervertebral disc levels.

Disc Level	Bulging		Herniation			Total level	
	Bulging	Asymmetric bulging	Protrusion	Extrusion	Sequestration	n	%
T1-2	2	1	3	0	0	6	1.12
T2-3	3	1	10	0	0	14	2.62
T3-4	5	1	15	0	0	21	3.93
T4-5	2	1	19	0	0	22	4.11
T5-6	2	1	17	0	0	20	3.74
T6-7	8	1	34	1	0	44	8.22
T7-8	9	0	35	0	0	44	8.22
T8-9	20	0	30	0	0	50	9.35
T9-10	28	1	33	0	0	62	11.59
T10-11	46	0	48	1	1	96	17.94
T11-12	45	0	51	0	0	96	17.94
T12-L1	29	0	30	1	0	60	11.21
Total	**199**	**7**	**326**	**3**	**0**	**535**	**100,00**

RESULTS

A total of 171 participants (99 females and 72 males) were included in the study. The mean age of participants was 68.2±6.9 years. Of the 171 participants, 102 were aged 60 to 69 years (59%,65), 56were aged 70 to 79 years (32%,75), and 13were over 80 (7%,60).

Disc bulging or herniation was observed in 534 (26%) of the total 2052 intervertebral disc levels analyzed in this study. When evaluated separately, 206 (10%) discs demonstrated bulging. Bulging was most common at T10-11 (n=46, 2.2%), followed by T11-12 (n=45, 2.1%) and T9-10 (n=29, 1.4%). Disc herniation was present in 328 (15.9%) discs, most commonly at T11-12 (n=51,15.5%), followed by T10-11 (n=50,2.4%) and T7-8 (n=35, 1.7%). Bulging and herniation were least common at T1-2, with an incidence of only 0.1% (n=3). Table 1 shows the evaluation and frequency of disc pathologies at each thoracic intervertebral level for each age group. Higher age is related to higher grades of herniation at every level (Table 2).

In our study, 12 cases had single-level bulging and 19 had single-level herniation. Single-level bulging occurred most frequently at T10-11 (n=3), T11-12 (n=3), and T12-11 (n=3). Single-level herniation occurred most frequently at T6-7 (n=5), T7-8 (n=3), and T10-11 (n=3). A total of 194 cases had multilevel bulging; 309 cases displayed multilevel

Table 3. Frequency of single- and multilevel disc pathologies.

	Single level Bulging	Single level Herniation	Multilevel Bulging	Multi-level Herniation	Multi-level Bulging+Herniation
T1-2	0	0	3	3	0
T2-3	0	1	4	9	0
T3-4	1	0	5	15	0
T4-5	0	2	3	17	0
T5-6	0	0	3	17	0
T6-7	0	5	9	29	3
T7-8	0	3	9	32	3
T8-9	1	2	19	28	4
T9-10	1	0	28	33	3
T10-11	3	3	43	47	7
T11-12	3	2	42	49	4
T12-l1	3	1	26	30	4
Total	**12**	**19**	**194**	**309**	**28**

herniation, and 28 cases presented with both. Multilevel bulging was most common at T10-11 (n=43) and T11-12 (n=42). Multilevel herniation was most common at T11-12(n=49) and T10-11 (n=47). Multilevel bulging and herniation occurred together most commonly at T10-11(n=7). The frequency distributions of single- and multilevel disc pathologies are shown in Table 3.

All participants in the study presented with back pain. Forty-six participants had signs of neural compression. Of these 46 patients, 28 had herniation at multiple levels as well as a narrowed canal. One of these patients had a sequestrated disc, three had herniation at one level, six had herniation at two levels, four had herniation at three levels, and four had bulging at multiple levels.

An evaluation of disc degeneration at the thoracic level indicated that no participants had Pfirrmann grade 1 or 2 degeneration, 267 (13%,01) had grade 3 degenerations, 1628 (79%,34) had grade 4 degenerations, and 140 (6%,82) had grade 5 disc degeneration (Table 4).

In this study, endplate degeneration was found at 125 levels (6.09%), and Schmorl nodes were found at 439 levels (21.3%). Schmorl nodes were most common at T9-10, T10-11, T8-9, and T11-12 (in order of frequency) (Table 5).

DISCUSSION

This study was a retrospective investigation of 2052 levels of the thoracic spine in 171 geriatric patients

who underwent MRI examinations of the thoracic vertebrae. The most common findings were disc degeneration, bulging, and herniation. Disc herniation occurred most frequently at T11-12. Bulging was most frequent at T10-11. Endplate degeneration was present in 6.09% of the 2052 levels analyzed, and Schmorl nodes were identified in 21.3%.

Most TDHs are diagnosed in the third to fifth decades of life (1). Some studies have reported different ages of diagnosis; for instance, Sarsılmaz et al. found that thoracic disc pathologies were most frequent in the second and fourth decades (12). In this study, we examined patients in the sixth to eighth decades of life, and we accepted dorsalgia as an indication for thoracic vertebra MRI. MRI was used because of its high accuracy in diagnosing degenerative disc pathologies (1).

There are relatively few studies of age-related changes in the thoracic intervertebral discs. A previous retrospective study found that the prevalence of abnormal findings in the annuli, nuclei, and disc margins increases with increasing age, especially in the mid- and lower thoracic discs. Those authors suggest that disc recovery is unlikely after disc desiccation and height loss have occurred (16). Another study suggested a similar progression and found that developing degenerative changes became visible in imaging studies after 11 weeks (17). These results explain the increasing prevalence of thoracic disc pathologies with age. Similarly, our findings support a significant incidence of thoracic disc pathologies in patients over 60 years of age, especially in light of the reports by most literature that thoracic pathologies are very rare.

Table 4. Number of cases with each Pfirrmann grade by thoracic disk level.

	gr3	gr4	gr5	Total
T1-2	24	142	5	171
T2-3	23	142	6	171
T3-4	24	140	7	171
T4-5	21	142	8	171
T5-6	21	141	8	171
T6-7	21	133	15	171
T7-8	21	131	17	171
T8-9	22	130	16	171
T9-10	22	130	17	171
T10-11	22	132	14	171
T11-12	23	128	17	171
T12-l1	23	137	10	171
Total	**267**	**1628**	**140**	**2052**
	13.01%	**79.34%**	**6.82%**	

Table 5. Distribution of Schmorl nodes and endplate degeneration at all intervertebral levels.

Disc level	Number of Schmorl nodes	Disc level	Endplate degeneration (level numbers)
T1 inferior	7	T1-2	1
T2 superior	7		
T2 inferior	6	T2-3	2
T3 superior	6		
T3 inferior	6	T3-4	1
T4 superior	6		
T4 inferior	8	T4-5	3
T5 superior	8		
T5 inferior	11	T5-6	3
T6 superior	8		
T6 inferior	17	T6-7	14
T7 superior	15		
T7 inferior	32	T7-8	13
T8 superior	22		
T8 inferior	36	T8-9	20
T9 superior	26		
T9 inferior	37	T9-10	26
T10 superior	30		
T10 inferior	38	T10-11	22
T11 superior	29		
T11 inferior	31	T11-12	15
T12 superior	24		
T12 inferior	19	T12-L1	5
L1 superior	10		
Total	**439**		**125**

Previous studies have found that TDH is most common at the middle to lower segments of the thoracic vertebrae, with a ratio of about 75% (17, 18). Sarsılmaz et al. showed that two-thirds of disc bulging and herniation pathologies occur from T7-8 to T11-12. They also report that T6-9 is the most commonly affected level in patients under 50, while in older age groups, the most commonly affected levels are T10-12. Thus, they suggest that age-related changes in the vertebral column and ligaments may cause alterations in the localization of thoracic disc pathologies (12). Our findings are similar; we found that disc bulging and herniation are most common at T10-11 and T11-12 in patients over 60.

Another noteworthy finding of our study was that 36.2% of the patients had multilevel herniation. This incidence is higher than previously reported (about 20% to 26%) (4, 19, 20). Sarsılmaz et al. also found that 21.3% of participants had herniation at more than one level –consistent with previous literature but lower than our results (12). However, previous studies also suggest that thoracic disc pathologies increase with age. Increasing age coincides with more serious Modic and Pfirrmann grades. There is a strong correlation between changes in the endplates and in the intervertebral discs, as evidenced by changes in the MRI. The greater the level of disc degeneration, the closer the relationship between the Pfirrmann and Modic classification systems (21). Furthermore, we included patients with complaints suggesting thoracic disc degeneration, which may have disproportionally increased the number of patients with multilevel pathologies, as they are more likely to present at the hospital with complaints.

In our study, both Schmorl nodes and endplate degeneration were most common at the low thoracic intervertebral levels. These findings align with previous literature (12, 18). There are several theories that attempt to explain the formation of Schmorl nodes and their relationships with degenerative changes in the thoracic spine; however, the most popular explanation suggests that they occur when the cartilaginous endplate of the vertebral body is disrupted due to changes in physical properties. The most popular description suggests that Schmorl nodes occur when the cartilaginous endplate of the vertebral body is disrupted by physical changes (18, 22).

The present study has some limitations. First, we only included patients with dorsalgia. Previous studies have found that patients with thoracic disc pathologies have atypical presentations, such as abdominal pain, isolated chest pain, and isolated thoracic spine tenderness. Second, this is a retrospective study, which does not allow an investigation of causal relationships. Therefore, the frequency and severity of cases reported in this study may be higher than that in the general population of patients over 60. However, there are very few studies on this topic, and better characterization of thoracic disc pathologies is needed.

CONCLUSION

It is a given that thoracic disk pathologies are rare. However, they are not as rare nor as insignificant as previously suggested. They are known to cause severe neurological deficits, but their atypical clinical features make diagnosis difficult. To our knowledge, the present study is the most comprehensive characterization of thoracic disc pathologies in elderly patients. The results of our study indicate an increase in the prevalence of thoracic disc pathologies in elderly patients. Bulging, herniation, endplate changes, and Schmorl nodes occur more frequently at the lower intervertebral levels. Herniation and/or bulging at multiple levels are also more common than previously reported.

REFERENCES

1. Mcinerney J, Ball PA. The pathophysiology of thoracic disc disease. Neurosurgical focus 2000;9(4):1-8. (PMID: 16833239)
2. Arseni C, Nash F. Protrusion of thoracic intervertebral discs. Acta Neurochirurgica 1963;11(1):3-33. (PMID: 13794536)
3. Haley J, Perry J. Protrusions of intervertebral discs: study of their distribution, characteristics and effects on the nervous system. The American Journal of Surgery 1950;80(4):394-404. (PMID: 14771346)
4. Linscott MS, Heyborne R. Thoracic intervertebral disk herniation: a commonly missed diagnosis. The Journal of emergency medicine 2007;32(3):235-8. (PMID: 17394983)
5. Carson J, Gumpert J, Jefferson A. Diagnosis and treatment of thoracic intervertebral disc protrusions. Journal of Neurology, Neurosurgery & Psychiatry 1971;34(1):68-77. (PMID: 5551695)
6. Arce CA, Dohrmann GJ. Thoracic disc herniation: improved diagnosis with computed tomographic scanning and a review of the literature. Surgical neurology 1985;23(4):356-61. (PMID: 3975822)
7. Wilke A, Wolf U, Lageard P, Griss P. Thoracic disc herniation: a diagnostic challenge. Manual Therapy 2000;5(3):181-4. (PMID: 11034889)
8. Vanichkachorn JS, Vaccaro AR. Thoracic disk disease: diagnosis and treatment. JAAOS-Journal of the American Academy of Orthopaedic Surgeons 2000;8(3):159-69. (PMID: 10874223)
9. Wood KB, Garvey TA, Gundry C, Heithoff KB. Magnetic resonance imaging of the thoracic spine. Evaluation of asymptomatic individuals. The Journal of bone and joint surgery American volume 1995;77(11):1631-8. (PMID: 7593072)
10. Henkelman RM, Watts JF, Kucharczyk W. High signal intensity in MR images of calcified brain tissue. Radiology 1991;179(1):199-206. (PMID: 1848714)
11. Kasch R, Mensel B, Schmidt F, et al. Percutaneous disc decompression with nucleoplasty–volumetry of the nucleus pulposus using ultrahigh-field MRI. PloS one 2012;7(7):e41497. (PMID: 22848512)
12. Sarsılmaz A, Yencilek E, Özelçi Ü, Güzelbey T, Apaydın M. The incidence and most common levels of thoracic degenerative disc pathologies. Turkish Journal of Physical Medicine & Rehabilitation (2587-0823) 2018;64(2). (PMID: 31453506)
13. Fardon DF, Williams AL, Dohring EJ, Murtagh FR, Rothman SLG, Sze GK. Lumbar disc nomenclature: version 2.0: Recommendations of the combined task forces of the North American Spine Society, the American Society of Spine Radiology and the American Society of Neuroradiology. The Spine Journal 2014;14(11):2525-45. (PMID: 24768732)
14. Pfirrmann CW, Metzdorf A, Zanetti M, Hodler J, Boos N. Magnetic resonance classification of lumbar intervertebral disc degeneration. Spine (Phila Pa 1976) 2001;26(17):1873-8. (PMID: 11568697)
15. Modic MT, Masaryk TJ, Ross JS, Carter JR. Imaging of degenerative disk disease. Radiology 1988;168(1):177-86. (PMID: 3289089)
16. Goh S, Tan C, Price R, et al. Influence of age and gender on thoracic vertebral body shape and disc degeneration: an MR investigation of 169 cases. The Journal of Anatomy 2000;197(4):647-57. (PMID: 11197538)
17. Girard CJ, Schweitzer ME, Morrison WB, Parellada JA, Carrino J. Thoracic spine disc-related abnormalities: longitudinal MR imaging assessment. Skeletal radiology 2004;33(4):216-22. (PMID: 14991248)
18. Pfirrmann CW, Resnick D. Schmorl nodes of the thoracic and lumbar spine: radiographic-pathologic study of prevalence, characterization, and correlation with degenerative changes of 1,650 spinal levels in 100 cadavers. Radiology 2001;219(2):368-74. (PMID: 11323459)
19. Yue B, Chen B, Zou Y-w, et al. Thoracic intervertebral disc calcification and herniation in adults: a report of two cases. European Spine Journal 2016;25(1):118-23. (PMID: 26329651)
20. Giblin EM, Hochheiser GM. Thoracic disk herniation resulting in acutely progressing paraplegia in a pediatric patient. Pediatric emergency care 2008;24(8):550-3. (PMID: 18708901)

21. Rodrigues LMR, Yoshino CV, Costa AB. Lumbar alterations in magnetic resonance: correlation between Modic and Pfirrmann classifications. Coluna/Columna 2014;13(3):202-5. (DOI: 10.1590/s1808-18512014130300263)

22. Schmorl G. Über knorpelknötchen an den wirbelbandscheiben. Rofo Fortschr Geb Rontgenstr Neuen Bildgeb Verfahr 1928;38:265-79.

24. Bilgic S, Acaroglu R. Effects of listening to music on the comfort of chemotherapy patients. West J Nurs Res 2017: 39(6): 745-62. (PMID: 27515501).

25. Umbrello M, Sorrenti T, Mistraletti G, Formenti P, Chiumello D, Terzoni S. Music therapy reduces stress and anxiety in critically ill patients: a systematic review of randomized clinical trials. Minerva anestesiologica, 2019; 85(8): 886-98. (PMID: 30947484).

RESEARCH

THE ROLE OF FRAILTY IN PHYSICIANS' DECISIONS FOR SEVERE DISABILITY

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2020.187
2020; 23(4): 492-500

Cemile HAKİ[1]
Hakan DEMİRCİ[2]

Abstract

Introduction: We aimed to evaluate the correlation between disability approved by the medical board and frailty determined by the Edmonton Frail Scale, which is a tool used to assess frailty.

Materials and Method: We enrolled patients admitted to the neurology outpatient clinic of the Bursa Yuksek Ihtisas Training and Research Hospital between 1st-31st March 2019 for examination in order to obtain a disability report from the medical board.

Results: Cerebrovascular disease and dementia were more prevalent in older age, while epilepsy, cerebral palsy sequela and other neurological diseases were observed at a younger age. A strong correlation was observed between frailty analysis score and Balthazard disability percentage ($p < 0{,}001$, $r = 0{,}57$). Similarly, there was a correlation between the physicians' severe disability opinion and the Edmonton Frail index score. Scores for cognition, general health status, functional independence, frequency of forgetting to take prescription drugs, or indications of recent weight loss were higher for patients in the severe disability group who also had higher EFS scores. We found that EFS scores >8 correlate significantly with an increased risk of severe disability.

Conclusion: We conclude that use of the frailty analysis score in combination with Balthazard disability percentage for patients applying to the medical board could be practical and rational in evaluating the degree of disability and predicting severe disability. Since only patients who applied for medical board evaluation to the neurology clinic were included in our study, our results are relevant for neurology cases and cannot be generalized for all patients who applied for evaluation.

Keywords: Frailty; Social Support; Disability Evaluation; Frail Elderly; Cerebrovascular Disorders

CORRESPONDANCE

[1]Cemile HAKİ
Bursa Yuksek Ihtisas Training and Research Hospital, Department of Neurology, Bursa, Turkey

Phone: +905324713151
e-mail: cemilehaki@gmail.com

Received: Jun 17, 2020
Accepted: Nov 12, 2020

[1] Bursa Yuksek Ihtisas Training and Research Hospital, Department of Neurology, Bursa, Turkey

[2] Bursa Yuksek Ihtisas Training and Research Hospital, Department of Family Medicine, Bursa, Turkey

INTRODUCTION

A disabled person is defined as an "individual affected by environmental aspects and attitudes restricting his/her total and effective integration in society in equal conditions with other individuals due to various levels of loss in his/her physical, mental, spiritual and sensorial abilities" (1).

The "World Report on Disability," published in 2011, stated that 15.6% of the world's adult population (aged 18 and over) suffer from a disability. According to the "Turkey Disabled Research 2002" report, conducted by the Prime Ministry's State Institute of Statistics and the Prime Ministry Department for the Administration of the Disable, found that 12.29% of the Turkish population had some form of disability (2,3).

Living standards for disabled citizens and the quality of service provided to these individuals are two important indicators of a country's level of development. In Turkey, disabled persons can be admitted to a health care provider who is authorized to certify an annual disability report, which allows that individual to request a medical board report that is needed for claiming social benefits such as financial support, disability allowance, employment, education, disability retirement, and tax reductions. Those who receive medical board approval are evaluated by specialists in physical medicine and rehabilitation, internal medicine, ophthalmology, otorhinolaryngology, general surgery, neurology, and mental health, and their disability status is graded using the percentage scale (from zero to 100), according to disability rates tables. These regulations categorize individuals who are unable to fulfil their daily needs even if they receive help as severely disabled (or "fully dependent disabled") (1). Patients who are considered severely disabled ("fully dependent disability") are presented to the physicians on the committee.

Frailty is defined as a state of increased vulnerability to stress factors as a result of age-related decreases in physiological abilities (4). As frailty levels

Table 1. Distribution of chronic diseases by gender

Chronic Disease	Female (n=44)	Male (n=46)	p-value
Cerebrovascular Disease	18(40.90%)	15(32.60%)	0.414[a]
Epilepsy	5(11.40%)	9(19.60%)	0.283[a]
Dementia	12(27.30%)	6(13%)	0.092[a]
Parkinson Disease	1(2.30%)	1(2.20%)	1.00[b]
Cerebral Palsy Sequel	2(4.50%)	2(4.30%)	1.00[b]
Other Neurologic Disease	11(25%)	14(30.40%)	0.565[a]
Neuropathic Pain	5(11.40%)	7(15.20%)	0.591[a]
Hypertension	10(22.70%)	14(30.40%)	0.408[a]
Diabetes Mellitus	8(18.20%)	9(19.60%)	0.867[a]
Cardiac Disease	8(18.20%)	11(23.90%)	0.505[a]
Orthopedic Diseases	2(4.50%)	1(2.20%)	0.612[b]
Eye Diseases	3(6.80%)	1(2.20%)	0.355[b]
Psychiatric Diseases	5(11.40%)	4(8.70%)	0.737[b]
Other Diseases	18(40.90%)	15(32.60%)	0.414[a]

Data expressed asn (%), [a]: Pearson chi-square test, [b]: Fisher'sexactchi-square test

Note: More than one disease may occur in the same patient.

Table 2. Chronic disease and age correlation

Chronic Disease	n with the disease/ free from the disease	Positive	Negative	p-value[c]
CVD	33/57	68(44-89)	58(22-90)	0.003
Epilepsy	14/76	40(22-78)	65(24-90)	<0.001
Dementia	18/72	83(37-90)	58.50(22-89)	<0.001
Parkinson Disease	2*/88	60.50(37-84)	63(22-90)	NA
Cerebral Palsy Sequel	4/86	31.50(22-37)	63.50(24-90)	<0.001
Other Neurologic Diseases	25/65)	52(24-84)	66(22-90)	0.002
Neuropathic Pain	12/78	59(31-70)	64(22-90)	0.288
Hypertension	24/66	65(42-88)	62(22-90)	0.273
Diabetes Mellitus	17/73	63(48-84)	63(22-90)	0.351
Cardiac Disease	19/71	66(58-89)	59(22-90)	0.011
Orthopedic Diseases	3*/87	65(58-81)	63(22-90)	NA
Eye Diseases	4/86	73(36-84)	62.50(22-90)	0.478
Psychiatric Diseases	9/81	46(37-83)	63(22-90)	0.208
Other Diseases	33/57	62(24-90)	63(22-89)	0.947

For each chronic disease the data in the upper row is median age (minimum -maximum), n is the number of subjects having the disease /free from the disease.
*: Unit number in the group not enough for statistical analysis. [c]: Mann Whitney U test
Note: More than one disease may occur in the same patient.

increase with more exposure to stress factors, so too does the risk of hospitalization, falls, delirium, mortality, and morbidity (5,6). Frailty has become a more pressing issue as the world population continues to age, with levels of frailty between 4 and 59.1% having been reported (7). The prevalence of frailty among patients admitted to outpatient clinics in developing countries is particularly high, at 55 to 71% in Brazil and 28% in Peru (8). In Turkey, this rate is 39.2% (9).

There is no existing literature that applies the Edmonton Frail Scale (EFS)—which is used to assess frailty—to patients who are admitted to a medical board for disability evaluation in order to determine whether frailty levels can be used to predict approved disability status. The aim of this study is to evaluate the correlation between disability approval by a medical board in Turkey and frailty as detected by the EFS.

METHODS

Patients with a neurological disability who applied to the institutional health board of Bursa Yuksek Ihtisas Training and Research Hospital for the purpose of obtaining a disability report between the 1st and 31st March 2019, and had been admitted to the neurology outpatient clinic for examination, were included in the study. Patients under the age of 18, those who applied to obtain a medical committee report for job application, driver's license, gun license, rest report and status reports were excluded from the study.

For each patient, we recorded age, gender, diagnosis, comorbidity, disability rates, and severe disability status. Patients were also evaluated using the EFS. The patients' disability statuses, which were being presented to the medical board for evaluation, were calculated using the Balthazard formula, after they had been assessed by specialists from each of the divisions listed above. The Baltha-

Table 3. Relationship between Balthazard Disability Percentage and Edmonton Frail score

Edmonton Frail Scale		Disability Percentage (%)	
		Median (min: max)	p-value
Medication use 1	Yes(n=38)	67(36-89)	0.034[c]
	No(n=52)	57.50(22-90)	
Medication use 2	Yes(n=48)	72.50(22-90)	0.010[c]
	No(n=42)	53.50(24-78)	
Nutrition	Yes(n=22)	73.50(30-90)	0.003[c]
	No(n=68)	59.50(22-89)	
Mood	Yes(n=69)	64(24-90)	0.017[c]
	No(n=21)	52(22-89)	
Continence	Yes(n=46)	71(30-90)	<0.001[c]
	No(n=44)	56(22-83)	
Edmonton Frail Scale		**Disability Percentage(%)**	
		r_s	p-value
Cognition		0.49	<0.001
General health status 1		0.20	0.056
General health status 2		0.47	<0.001
Functional independence		0.53	<0.001
Social support		0.05	0.661
Functional performance		0.55	<0.001
Frailty analysis score		0.57	<0.001

Data is given as median(minimum: maximum). [c]: Mann Whitney U test

r_s: Spearman correlation coefficient

Medication use 1: Do you regularly use 5 or more different drugs?

Medication use 2: Do you forget to take your prescription medicines from time to time?

General Health 1: How many times were you hospitalized last year?

General Health 2: How would you describe your health in general?

zard formula is used to calculate degree of impairment for individuals with more than one disability (1). The EFS is a simple test that was developed by Rolfson et al. at the University of Alberta in Canada, consisting of 11 questions and a physical assessment (10). Turkish validity and reliability studies for the EFS were conducted by Aygor et al. (11). Our scale for this study consisted of 11 questions covering nine items: cognitive status, general health status, functional independency, social support, medication usage, nutrition, mood, continence, and functional performance. All items were assessed with one question, except general health status and medication usage, which used two questions. Cognitive status and functional performance were tested using the EFS; the timed-up-and-go test (TUGT) was used to assess functional performance; and the clock-drawing test was used to assess cognitive status (10). The EFS test is scored between 0-17, with the following categories: 0-4 – not frail; 5-8 – vulner-

Table 4. Relationship between frailty total and sub-group scores and severe disability status

Edmonton Frail Scale	Severe Disability		p-value
	Yes (n=33)	No (n=57)	
Cognition	2(0-2)	1(0-2)	<0.001[c]
General Health 1	0(0-1)	0(0-2)	0.088[c]
General Health 2	2(1-2)	1(1-2)	<0.001[c]
Functional independence	2(1-2)	1(0-2)	<0.001[c]
Social support	0(0-2)	0(0-2)	0.314[c]
Medication use 1	15(45.50%)	23(40.40%)	0.637[a]
Medication use 2	25(75.80%)	23(40.40%)	0.001[a]
Nutrition	14(42.40%)	8(14%)	0.003[a]
Mood	27(81.80%)	42(73.70%)	0.379[a]
Continence	28(84.80%)	18(31.60%)	<0.001[a]
Functional performance	2(0-2)	0(0-2)	<0.001[c]
Frailty Score	11(5-14)	6(1-13)	<0.001[c]

Data given as median (minimum: maximum) and n(%).
[a]: Pearson chi-square test, [c]: Mann Whitney U test

able; 7-8 – mild frailty; 9-10 – moderate frailty; and 11 and above – severe Frailty.

Assessment of disability rates for all patients were conducted as per the guidelines in the "Regulation on Disability Assessment for Adults," published in Official Gazette No.30692 on February 20, 2019. Approval for the study was received from the Bursa Yuksek Ihtisas Training and Research Hospital Ethics Committee (2011-KAEK-25 2019/02-21).

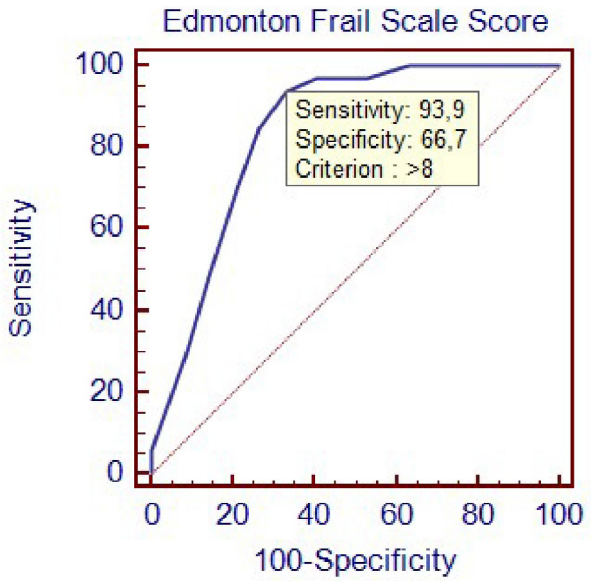
Statistical analysis

Based on the findings of this study, we conducted a post hoc power analysis using a large effect size, which was calculated by comparing the average EFS scores between severe disability status groups. Using an effect size of (d=1.56) with a sample size of 90 (n_1=57, n_2=33), we achieved an estimated power of 95% with a significance level of α= 0.05. A Kolmogorov-Smirnov test was used to assess whether the variables followed a normal distribution. Variables were reported as median (minimum: maximum) values. Based on the normality test results, a Mann Whitney U test was used to perform between-group comparisons. Categorical variables were compared using a Chi-square test or a Fisher's exact test. In order to estimate the sensitivity and specificity of EFS score values in predicting severe disability status, a receiver operator characteristic (ROC) curve analysis was performed. The reliability of the EFS was assessed using Cronbach's alpha (α) coefficient; the reliability of the EFS was determined as α=0.83. We used SPSS (IBM Corp., released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY) and MedCalc Statistical Software, trial version 16.4.3 (MedCalc Software bvba, Ostend, Belgium; https://www.medcalc.org; 2016) were used. A p-value of <0.05 was considered statistically significant.

RESULTS

Ninety people participated in the study. A total of 44 (48.8%) participants were female and 46 (51.1%) were male. The mean age of the participants was 60.5 ± 18.3 (min–max: 22–90) years. The median Edmonton Frail Scale (EFS) score was 9 (1-14). The median disability rate of the whole group was 87.5%

Figure 1. Receiver-operator characteristic (ROC) curves for determining the presence of severe disability. The area under the curve (AUC) for Edmonton Frail Scale Score is 0.84 with p<0.001.



(26–100%). In our study, cerebrovascular diseases (36.6%), dementia (20%), and epilepsy (15.5%) were among the most frequent causes of neurological disability. No statistical difference was observed between genders for cerebrovascular disease, epilepsy, or Parkinson's disease patients. Although dementia was more common among women, no statistically significant difference was observed (p>0.05). Distribution of chronic diseases by gender is shown in Table 1.

Table 2 shows that the median age for those with cerebrovascular disease or dementia was higher. Epilepsy was more common in younger participants, but cerebral palsy patients were on average the youngest. Correlation between chronic diseases and age are shown in Table 2.

Disability percentages were higher for patients who regularly used five or more different medications, as well as for those who forgot to take their prescription drugs, those who indicated that they had lost weight recently, those who frequently felt upset or depressed, and those who suffered from involuntary urination. An increase in disability percentages was detected in patients who had higher scores for cognition, general health status (based on the question, "In general, how would you describe your health?"), and functional independence. A significant parallel correlation was found between disability percentages and EFS score. The relationship between the Balthazard disability percentages and EFS scores is shown in Table 3.

Scores for cognition, general health status, functional independence, rates of forgetting to take prescription drugs, or indications of recent weight loss were higher for patients in the severe disability group; EFS scores were also higher for this group. The correlations between EFS scores and committee-certified disability status certified are included in Table 4.

A ROC curve analysis was performed to estimate the sensitivity and specificity of EFS scores in predicting the presence of severe disability, with a

cut-off point for EFS scores being set at >8 (see Figure 1). The area under the curve for the EFS score was 0.84 (sensitivity: 93.90%; specificity: 66.70%; p<0.001), indicating that EFS scores >8 correlate significantly with an increased risk of severe disability.

DISCUSSION

The power of the research was calculated as 95%. While cerebrovascular disease and dementia were more common in older participants, epilepsy, cerebral palsy, and other neurological diseases were observed in younger patients. A strong correlation was observed between EFS score and Balthazard disability percentage; there was also a correlation between physicians rating a patient as severely disabled and EFS index score.

There are not many studies on neurological disability in our country. One of the few, conducted by Çabalar et al. (12), reported that 10.87% of patients admitted to a medical board for evaluation were judged to be disabled because of their suffering from a neurological disease. another study by Benli Ar et al. (13) reported a figure of 22.3% for the same class of patients.

According to this research by Çabalar et al. (12), the highest mean age of any group admitted to the medical board with neurological disorders was for the group of dementia and Parkinson's disease patients. In our study, the highest mean age was for dementia patients, while the second highest was for cerebrovascular disease. Epilepsy was more common for younger patients, while the youngest admitted patients were those with cerebral palsy. The diseases that most often caused neurological disability were cerebrovascular diseases, dementia, and epilepsy, according to the studies by Çabalar et al. (12) and Evlice et al. (14). Similarly, we observed that the most common neurological diseases among patients admitted to the medical evaluation board were cerebrovascular diseases, dementia, and epilepsy.

Çabalar et al. (12) found that 56.2% of the neurologically disabled patients admitted to the medical board were male and 43.8% were female; Evlice et al. (14) found that 66% of neurological patients were men and 34% were women. In our study, however, 46 (51.1%) of the participants were male and 44 (48.85%) were female. We observed no statistical difference between genders for cerebrovascular disease, epilepsy, and Parkinson's disease patients. Although dementia was more prevalent among women, no statistically significant difference was detected.

There are several studies in existing literature that analyze the correlation between frailty and disability, with one study demonstrating a notable correlation between frailty and disability in farmers over 65 years of age who live in rural areas (15). It has also been observed that frailty and disability rates are higher in older adults with anorexia of aging than in those without anorexia of aging (16).

Studies have also shown that frailty is an independent risk factor for injury, complications, and mortality among surgical patients: Pre-operational frailty assessments have predicted complications and mortality following cardiac and abdominal operation (17-19), while frailty has also been associated with higher mortality in lung and kidney transplant candidates and during the liver transplant waiting period (20-22). In addition, frailty has been shown to be a strong prognostic factor for mortality in elderly patients admitted for acute coronary syndrome and is associated with lower survival rates in colorectal carcinoma patients (23,24).

In Turkey, documented severe disability is one criterion for receiving social support. Severe disability in patients ("fully dependent disabled" persons) is presented to a committee of physicians, who provide an opinion on disability status, with the possibility of different physicians having diverging opinions. We observed that patients with a frailty scale score >8 were more frequently certified as severely disabled, in line with Balthazard disability percentage assessments. This study also found

strong correlation between EFS scores and Balthazard disability percentages and a correlation between physicians' opinion of severe disability status and EFS index scores. Since the EFS is an easy and fast scale that can be applied by the nurse working with the physician in outpatient clinics, it may ease physicians' decision making process for severe disability.

To date, no studies have used the EFS to predict how a patient admitted to a medical board for disability status approval will be assessed. As the first study in the field to do so, this research study is valuable. A limitation of this study was that only one month of medical board data was analyzed. More valuable results could be obtained from long-term data analysis. We consider the strength of our research to be evident in its power analysis. Another important issue is that we conducted our study on patients who applied to the neurology outpatient clinic for evaluation by the health board. Therefore, our results are acceptable for neurology cases and cannot be generalized for all patients applying for health board evaluation.

In conclusion, we believe that the EFS, in combination with the Balthazard disability percentage assessment, could be a practical and rational method of assessing degree of disability and predicting severe disability status for patients whose disability status is being evaluated by a medical board.

REFERENCES

1. Regulation on Disability Assessment for Adults No. 30692 dated February 20, 2019. T. C. Official Gazette, Number: 30692. [Internet] Available from: https://www.resmigazete.gov.tr/eskiler/2019/02/20190220-2.htm. Accessed: 20.02.2019(in Turkish)
2. Organization WH, World report on disability 2011, World Health Organization 2011. [Internet] Available from: https://apps.who.int/iris/handle/10665/44575. Accessed: 20.02.2019
3. Devlet İstatistik Enstitüsü (DİE). Türkiye Özürlüler Araştırması 2002. Ankara: 2004
4. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. The lancet 2013;381(9868):752-62. (PMID: 23395245)
5. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences 2001;56(3):M146-M57. (PMID: 11253156).
6. Eeles EM, White SV, O'Mahony SM, Bayer AJ, Hubbard RE. The impact of frailty and delirium on mortality in older inpatients. Age Ageing 2012;41(3):412-6. (PMID: 22391613)
7. Collard RM, Boter H, Schoevers RA, Oude Voshaar RC. Prevalence of frailty in community-dwelling older persons: a systematic review. J Am Geriatr Soc 2012;60(8):1487-92. (PMID: 22881367).
8. Nguyen T, Cumming R, Hilmer S. A review of frailty in developing countries. J Nutr Health Aging 2015;19(9):941-6. (PMID: 26482697)
9. Eyigor S, Kutsal Y, Duran E, et al. Frailty prevalence and related factors in the older adult-FrailTURK Project. Age 2015;37(3):50. (PMID: 25948502)
10. Rolfson DB, Majumdar SR, Tsuyuki RT, Tahir A, Rockwood K. Validity and reliability of the Edmonton Frail Scale. Age Ageing 2006;35(5):526-9. (PMID: 16757522)
11. Aygör HE, Fadıloğlu Ç, Şahin S, Aykar FŞ, Akçiçek F. Validation of Edmonton Frail Scale into elderly Turkish population. Archives of Gerontology and Geriatrics. 2018;76:133–7.
12. Cabalar M, Tatlidede AD, Yazar T, Guveli B, Yayla V. Evaluation of the neurological disability rates in medical commission. Medical Journal of Bakırkoy 2011;7(4):142-6.(in Turkish)(DOI: 10.5350/BTDMJB201107404)
13. Benli AR, Cortuk M, Inci H, Benli NC. Evaluation of Causes Application on Medical Board. Konuralp Medical Journal 2016;8(3):167-72.(in Turkish) (DOI:10.18521/KTD.280035)

14. Evlice A, Demir T, Aslan K, et al. Disability at Neurological Diseases. Cukurova Medical Journal 2014;39(3):566-71.(in Turkish)(DOI:10.17826 / CUTF.78721)

15. Choi Y-S, Kim M-J, Lee G-Y, et al. The association between frailty and disability among the elderly in rural areas of Korea. Int J Environ Res Public Health 2019;16(14):2481. (PMID: 31336809)

16. Tsutsumimoto K, Doi T, Makizako H, et al. Aging-related anorexia and its association with disability and frailty. Journal of cachexia, sarcopenia and muscle 2018;9(5):834-43. (PMID: 30109778)

17. Dasgupta M, Rolfson DB, Stolee P, Borrie MJ, Speechley M. Frailty is associated with postoperative complications in older adults with medical problems. Arch Gerontol Geriatr 2009;48(1):78-83. (PMID: 18068828)

18. Tan K-Y, Kawamura YJ, Tokomitsu A, Tang T. Assessment for frailty is useful for predicting morbidity in elderly patients undergoing colorectal cancer resection whose comorbidities are already optimized. The American journal of surgery 2012;204(2):139-43. (PMID: 22178483)

19. Sündermann S, Dademasch A, Praetorius J, et al. Comprehensive assessment of frailty for elderly high-risk patients undergoing cardiac surgery. Eur J Cardiothorac Surg 2011;39(1):33-7. (PMID: 20627611)

20. McAdams-DeMarco M, Law A, King E, et al. Frailty and mortality in kidney transplant recipients. Am J Transplant 2015;15(1):149-54. (PMID: 25359393)

21. Singer JP, Diamond JM, Gries CJ, et al. Frailty phenotypes, disability, and outcomes in adult candidates for lung transplantation. Am J Respir Crit Care Med 2015;192(11):1325-34. (PMID: 26258797)

22. Lai JC, Feng S, Terrault NA, Lizaola B, Hayssen H, Covinsky K. Frailty predicts waitlist mortality in liver transplant candidates. Am J Transplant 2014;14(8):1870-9. (PMID: 24935609)

23. Blanco S, Ferrières J, Bongard V, et al. Prognosis impact of frailty assessed by the Edmonton Frail Scale in the setting of acute coronary syndrome in the elderly. Can J Cardiol 2017;33(7):933-9. (PMID: 28668143)

24. Meyers BM, Al-Shamsi HO, Rask S, et al. Utility of the Edmonton Frail Scale in identifying frail elderly patients during treatment of colorectal cancer. J Gastrointest Oncol 2017;8(1):32-38 (PMID: 28280606)

RESEARCH

PREVALENCE AND CLINICAL FEATURES OF CHRONIC CRITICAL ILLNESS IN THE ELDERLY POPULATION IN TURKEY

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2020.188
2020; 23(4): 501-508

Hilmi DEMİRKIRAN[1]
Başar ERDİVANLI[3]
Suna KOÇ[5]
Mustafa ÖZMEN[7]
Aydın ÇAĞAÇ[9]
Mustafa TUNCER[11]
Sinem BAYRAKCI[13]
Turkan BAHADIR[5]
İlhan BAHAR[15]
Sıddık KESKİN[17]
Emine UZUNOGLU[2]
Ulaş KARADAMAR[4]
Yakup TOMAK[6]
Necat ALMALI[8]
Mehmet Selim ÇÖMEZ[10]
Murat Emre TOKUR[12]
Orhan BİNİCİ[14]
Arzu Esen TEKELİ[1]
Buğra KARAKAŞ[16]
Hafize ÖKSÜZ[18]

CORRESPONDANCE

[1]Hilmi DEMİRKIRAN

Van Yuzuncu Yil University Faculty of Medicine, Department of Anesthesiology and Reanimation, Van, Turkey

Phone: +905336676188
e-mail: h.demirkiran@yyu.edu.tr

Received: Aug 29, 2020
Accepted: Nov 24, 2020

[1] Van Yuzuncu Yil University Faculty of Medicine, Department of Anesthesiology and Reanimation, Van, Turkey
[2] Istanbul Medipol University Mega Hospitals Complex, Department of Anesthesiology and Reanimation, Istanbul, Turkey
[3] Recep Tayyip Erdogan University Faculty of Medicine, Department of Anesthesiology and Reanimation, Rize, Turkey
[4] Private OFM Antalya Hospital, General Intensive Care Unit, Antalya, Turkey
[5] Biruni University Faculty of Medicine, Department of Anesthesiology and Reanimation, Istanbul, Turkey
[6] Sakarya University Faculty of Medicine, Anesthesiology and Intensive Care Unit, Sakarya, Turkey
[7] Private Corlu Vatan Hospital, General Intensive Care Unit, Tekirdag, Turkey
[8] Van Yuzuncu Yil University Faculty of Medicine, Department of General Surgery, Van, Turkey
[9] Van Yuzuncu Yil University Faculty of Medicine, Department of Neurology, Van, Turkey
[10] Hatay Mustafa Kemal University Tayfur Ata Sokmen Faculty of Medicine, Department of Anesthesiology and Reanimation, Hatay, Turkey
[11] Van Yuzuncu Yil University Faculty of Medicine, Department of Cardiology, Van, Turkey
[12] Kutahya Health Sciences University Evliya Celebi Training and Research Hospital, Internal Medicine Critical Care Unit, Kutahya, Turkey
[13] Gaziantep Provincial Directorate of Health Gaziantep Sehitkamil State Hospital, General Intensive Care Unit, Gaziantep, Turkey
[14] Harran University Faculty of Medicine, Department of Anesthesiology and Reanimation, Sanliurfa, Turkey
[15] Izmir Katip Celebi University Ataturk Training and Research Hospital, Internal Medicine Critical Care Unit, Izmir, Turkey
[16] Van Health Sciences University Van Training and Research Hospital, Anesthesiology Intensive Care Unit, Van, Turkey
[17] Van Yuzuncu Yil University Faculty of Medicine, Department of Biostatistics, Van, Turkey
[18] Kahramanmaras Sutcu Imam University Faculty of Medicine, Department of Anesthesiology and Reanimation, Kahramanmaras, Turkey

Abstract

Objectives: The definition of chronic critical illness in the elderly has not yet been determined. The aim of the study is to determine the prevalence and clinical features of chronic critical illness in the elderly population in Turkey.

Materials and Methods: Data from 16 intensive care units of public and private hospitals in Turkey were evaluated. Patients staying in the intensive care units for at least eight days between 2015 and 2017 and having at least one of the additional criteria were accepted as chronic critical illness and they were divided into two groups by age, those 65 and older and those under 65.

Results: The chronic critical illness patient rate in the intensive care units was 10.7%. Of chronic critical illness patients in the intensive care units, 60.9% were 65 years of age and older, and the mortality rate of patients 65 years and older was 70%. The frequencies of ischemic stroke and sepsis, the number of patients with comorbidities, and the mortality rate were higher in patients over 65 years of age, while the frequency of traumatic brain injury, presence of a major wound, tracheostomy, length of hospital stay and cost of care were higher in patients under 65 years of age.

Conclusion: We determined that prolonged mechanical ventilation, traumatic brain injury, tracheostomy and major wound presence in intensive care units patients 65 years and older increased hospital stay and costs. More work is needed to define chronic critical illness more clearly in elderly.

Keywords: Chronic Disease; Critical Illness; Intensive Care Unit; Aged; Turkey

INTRODUCTION

As a result of improvements in treatment in the intensive care unit (ICU), more patients survive acute critical illness. However, some of these patients have to live with long-term dependence on mechanical ventilation and other intensive care treatments (1). These patients who survive in the ICU and subsequently face a complex healing trajectory are described as chronic critical illness (CCI). It is increasingly recognized that patients with CCI are prone to psychological, physical, and cognitive dysfunction both during their stay in the hospital and after discharge (2). As a result of a recent consensus, patients who remained in the ICU for at least eight days and exhibited at least one of the following five conditions were defined as CCI: prolonged mechanical ventilation (PMV) >96 hours extended; tracheostomy; serious injuries and / or multiple organ failure; sepsis or others serious infections; ischemic stroke, intracerebral bleeding, or traumatic brain injury (TBI)(3).

The presence of various risk factors such as chronic kidney failure, frailty, repeated admissions to the ICU, and older age are indicators of poor prognosis in CCI patients (3). There has been an increase in the elderly population admitted to the ICU annually for the last two decades (4). The definition of CCI in the elderly has not yet been determined, thus preventing accurate analysis of elderly people with CCI.

Although there has been a comprehensive discussion of CCI in the elderly population worldwide, CCI in the elderly has not been studied much in Turkey. The aim of this multicenter study is to determine the prevalence, clinical features, and characteristics of CCI in the elderly population in Turkey.

MATERIALS AND METHODS

A retrospective crossectional study was conducted in five different regions of Turkey between July 2017 and June 2018. The study was approved by the Non-Interventional Van Yuzuncu Yil University Clinical Ethics Committee (June 20, 2017; No. 08). In addition, approval was obtained from the official administrations of the researchers they worked with who agreed to participate in the study. The medical records of patients treated in the ICU between 2015 and 2017 were evaluated. The study was registered at ClinicalTrials.gov (identifier: NCT03262883).

Patients staying in the ICU for at least eight days and having at least one of the additional criteria were accepted as CCI (PMV, tracheostomy, sepsis, major wound, stroke, or TBI). CCI patients included in the study were also divided into two groups, 65 years and older and under 65 years. Patients with illnesses other than CCI, length of ICU stay of ≤7 days, and age <18 years were excluded from the study.

Statistical Analysis

The data were evaluated in the IBM SPSS Statistics Standard Concurrent User V 25 (IBM Corp., Armonk, New York, USA) statistical program. For descriptive statistics, unit number (n), percent (%), mean ± standard deviation ($\bar{x}$ ± ss), median (M), smallest value (min), largest value (max), first quartile (Q1) and third quartile (Q3) and interquartile distance (IQR –Interquartile range) are given as values. Pearson Chi-square test was used to compare categorical variables between groups. In case of a difference in Pearson Chi-square test, two proportion z tests with Bonferroni correction were used. The normal distribution of data of numerical variables was evaluated by Shapiro–Wilk normality test and Q-Q graphs. Since the data did not show normal distribution, two groups were compared with Mann–Whitney U test and three groups were compared with Kruskal–Wallis analysis. A $p < .05$ value was considered statistically significant.

RESULTS

Among 23,272 patients admitted to ICUs during the study period, 2,493 (10.7%) were CCI. Demographic characteristics and the clinical features of the CCI patients are presented in Table 1.

PMV rate is high in both groups and shows similar distribution between groups ($p = .300$). The frequencies of ischemic stroke ($p < .001$) and sepsis ($p < .001$) in patients 65 years and older were significantly higher than in patients under 65 years (Table 2).

The number of patients with one, two, or three comorbid diseases in the 65 and older age group was significantly higher than in the under 65 age group. The mortality rate was higher in the 65 and older group (Table 3).

Comparison of PMV, TBI, major wound, sepsis and tracheostomy with mortality, duration of hospitalization and cost are given in table 4. The duration of hospitalization with PMV, sepsis and tracheostomy were significantly higher in both groups. The duration of hospital stay for those with TBI and major wound in the 65 and older age group was significantly longer. The mortality rate of patients with sepsis, tracheostomy and without TBI in the overall patient group were significantly higher.

DISCUSSION

There are no clear criteria for defining the transition of patients with CCI from the acute phase to the chronic phase (3). In this study, we have determined the CCI criteria as a stay in the ICU of eight or more days and at least one of the six clinical causes (major wound, sepsis, stroke, PMV, tracheostomy, or TBI) in accordance with the literature. Among 23,272 patients admitted to ICUs during the study period, 2,493 (10.7%) were CCI. The rate of CCI seen in our study is similar to the rates reported by other authors (5% to 15%) (5, 6). CCI-associated hospital mortality rates were 61% in the this study, 65% in a multicenter study in Brazil in 2015, and 50% in a study conducted in Mexico (7). The in-hospital mortality rate was 10% in a study conducted in New Zealand and Australia (8). In the US, which is a developed country, CCI-associated in-hospital mortality rate was 31% (9). Our mortality results are higher than those of developed countries and similar to those of developing countries.

Elderly patients account for 10 to 20% of all ICU admissions, and this number is growing steadily (10). In another study, the percent of patients over 65 years of age in the ICU was 53%, according to data from training hospitals (11). In our study, the rate of elderly CCI patients staying in the ICU was 60.9%, slightly higher than in other studies. PMV distribution was high in both groups and showed similar distribution between groups. The frequency of ischemic stroke and sepsis in patients 65 years and older was significantly higher than in patients under 65 years. The frequency of TBI, major wound presence, and tracheostomy was significantly higher in patients under 65 years of age. According to an observational study on the mortality rates of critically ill elderly patients admitted to the ICU, in-hospital mortality rates are between 24% and 40%, three-month mortality rates are between 39% and 41%, six-month mortality rates are between 37% and 51%, and one year mortality rates are between 44% and 68% (10). The one-year mortality rate was 73% in patients who had undergone mechanical ventilation for more than 14 days or underwent tracheostomy (12). In our study, the mortality rate of patients 65 years and older was 70%, and this rate was significantly higher than in those patients under 65 years old (47.6%).

PMV accounts for a large part of ICU costs (13). It is known that that elderly people are more sensitive to lung damage caused by PMV and the incidence of acute respiratory failure (ARF) increases significantly with age. Many studies have shown that age of patients requiring mechanical ventilation and ARF are independently associated with mortality (14, 15). In our study, the number of patients with chronic

Table 1. Chronic critical illness (CCI) Characteristics

Variables	n	%
Gender		
Male	1462	58.6
Female	1031	41.4
Age		
`x ± ss	65.5±18.7	
M (Q_1-Q_3)	70 (56-80)	
min-max	18-101	
Hospitalization year		
2015	557	22.3
2016	1071	43.0
2017	865	34.7
Number of Comorbid Diseases		
0	1354	54.3
1	777	31.2
2	299	12.0
3	56	2.2
4	7	0.3
Those with Comorbid Disease *		
COPD	426	17.1
DM	457	18.3
CHF	376	15.1
CLD	36	1.4
CRF	175	7.0
Cancer		
Solid Cancer	66	2.6
Hematological Cancer	6	0.2
Primary Hospital Diagnosis		
Respiratory Failure	472	18.9
Medical	696	27.9
Cardiac	395	15.8
Neurological disease	572	22.9
Surgery (post op)	141	5.7
Trauma	217	8.7
Chronic Disease Risk Factors *		
Prolonged Mechanical Ventilation	2369	95.0
Stroke		
Hemorrhagic Stroke	210	8.4
Ischemic Stroke	377	15.1
Traumatic Brain Injury	225	9.0
Major Wound	87	3.5
Sepsis	633	25.4
Tracheostomy	764	30.6
Undefined	39	1.6
Mediastinal	2	0.1
Permanent	195	7.8
Temporary	463	18.6

Discharge Status		
No	2146	86.1
Yes	347	13.9
Referral to a More Comprehensive Hospital		
No	2445	98.1
Yes	48	1.9
Referral to the Same Comprehensive Hospital		
No	2491	99.9
Yes	2	0.1
Transfer to Palliative Unit	2455	98.5
No	38	1.5
Yes		
Transfer to Service		
No	2466	98.9
Yes	27	1.1
Hospitalization Status In Intensive Care		
No	2438	97.8
Yes	55	2.2
Refuse Treatment		
No	2416	96.9
Yes	77	3.1
Survival		
Living	967	38.8
Died	1526	61.2
Time on Mechanical Ventilator (Days)		
`x ± ss	27.2±30.8	
M (Q_1-Q_3)	17 (10-33)	
min-max	0-355	
Time spent in intensive care (Days)		
`x ± ss	31.4±32.4	
M (Q_1-Q_3)	21 (13-37)	
min-max	8-384	
Length of hospital stay (Days)		
`x ± ss	34.9±36.4	
M (Q_1-Q_3)	23 (14-41)	
min-max	8-384	
Cost after the 8th day ($)		
`x ± ss	7774.8±12444.1	
M (Q_1-Q_3)	4104.6 (1655.9-9449.3)	
min-max	0.61-304252.9	
Money Paid by Insurance ($)		
`x ± ss	10116.2±11252.8	
M (Q_1-Q_3)	6358.6 (3753.4-12242.1)	
min-max	526.5-12242.1	

* Each disease was evaluated separately. COPD: Chronic Obstructive Pulmonary Disease, DM: Diabetes Mellitus, CHF: Chronic Heart Failure, CRF: Chronic Renal Failure, CLD: Chronic Liver Disease

Table 2. Comparison of Chronic Critical Illness Risk Factors, Hospitalization Times and Costs by Age.

	PMV n(%)		Stroke n(%)			TBI n(%)		MW n(%)		Sepsis n(%)		Tracheostomy n(%)		DHS	DHS in ICU	Cost
	No	Yes	No	HS	IS	No	Yes	No	Yes	No	Yes	No	Yes	M (Q_1-Q_3)	M (Q_1-Q_3)	M (Q_1-Q_3)
<65 (n=975)	43 (4.4)	932 (95.6)	791 (81.1)	87 (8.9)	97 (9.9)	841 (86.3)	134 (13.7)	924 (94.8)	51 (5.2)	767 (78.7)	208 (21.3)	643 (65.9)	332 (34.1)	25 (29)	22 (26)	4416.4 (9101.1)
≥65 (n=1518)	81 (5.3)	1437 (94.7)	1115[b] (73.5)	123[a] (8.1)	280[b] (18.4)	1427[b] (94.0)	91[b] (6.0)	1482[b] (97.6)	36[b] (2.4)	1093[b] (72.0)	425[b] (28.0)	1086[b] (71.5)	432[b] (28.5)	22 (26)	21(23)	3981.9 (9542.2)
χ^2, z	1.076		33.392			43.416		14.411		13.917		8.737		2.950	0.951	1.810
p	.300		<.001			<.001		<.001		<.001		<.001		.003	.341	.070

PMV, Prolonged Mechanical Ventilation; TBI, Traumatic Brain Injury; DHS, Duration of Hospital Stay (days); ICU, Intensive care unit; Cost, Cost after the 8th Day ($); HS, Hemorrhagic Stroke; IS; Ischemic Stroke. z: Mann–Whitney U test, χ^2: Chi-square test; The superscripts a and b indicate the difference of age groups between categories.

Table 3. Comparison of Number of Comorbidities, Types of Comorbidities, and Mortality by Age

	CD n(%)					COPD n(%)		DM n(%)		CHF n(%)		CLD n(%)		CRF n(%)		Cancer n(%)			Mortality n(%)	
	0	1	2	3	4	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	SC	HC	No	Yes
< 65 (n=975)	665[a] %68.2	221[a] %22.7	78[a] %8.0	10[a] %1.0	1[a] %0.1	870[a] %89.2	102[a] %10.8	855[a] %87.7	120[a] %12.3	904[a] %92.7	71[a] %7.3	959 %98.4	16 %1.6	931[a] %95.5	44[a] %91.4	937[a] %96.1	33[a] %3.4	5[a] %0.5	511[a] %52.4	464[a] %47.6
≥ 65 (n=1518)	689[b] %45.4	556[b] %36.6	221[b] %14.6	46[b] %3.0	6[a] %0.4	1197[b] %78.9	321[b] %21.1	1181[b] %77.8	337[b] %22.2	1213[b] %79.9	305[b] %20.1	1498 %98.7	20 %1.3	1387[b] %4.5	131[b] %8.6	1484[b] %97.8	33[a] %2.2	1[b] %0.1	456[b] %30.0	1062 %[b]70.0
χ^2	127.755					45.123		38.808		76.068		0.437		15.417		8.383			125.135	
p	<.001					<.001		<.001		<.001		.509		<.001		.015			<.001	

χ^2: Chi-square test; a and b superscripts show the difference between age groups between categories. COPD: Chronic Obstructive Pulmonary Disease. DM: Diabetes Mellitus. CHF: Chronic Heart Failure. CRF: Chronic Renal Failure, CLD: Chronic Liver Disease

obstructive pulmonary disease (COPD), longer PMV duration, and mortality were higher in the group over 65 years old. These findings confirm the results of previous studies.

Sepsis is common in ICUs and is associated with high morbidity rates. Development of sepsis is higher in patients with CCI remaining in the ICU (16). In our study, the cost values after the eighth day and the mortality rates of the patients with sepsis in both groups were significantly higher than for those without CCI. While the percentage of patients with sepsis younger than 65 years who died was 68.7%, this percentage was 84.2% in the 65 and older group.

It is known that the number of comorbid diseases increases with age. Patients with comorbidities in the ICU have higher in-hospital and long-term mortality rates (17). In our study, the number of patients with one, two, or three comorbid diseases in the 65 and older age group was significantly higher than in the group younger than 65 years old. The high mortality rate in the over 65 age group may be related to comorbid diseases as mentioned above. Studies have reported that PMV, age, presence of comorbidity, and sepsis increase mortality (18). The findings of this study reaffirm the results of previous studies.

In conclusion, this is the first study that describes the characteristics of CCI in the elderly population in Turkey. In this study, we observed that the mortality rate in ICU was high and mortality increased at the age of 65 and above. Moreover, we determined that

Table 4. Comparisons for Prolonged Mechanical Ventilation, Traumatic Brain Injury, Major Wound, Sepsis and Tracheostomy.

Variables	All patients				<65				≥65			
	No		Yes		No		Yes		No		Yes	
	M	IQR	M	IQR	M	IQR	M	IQR	M	IQR	M	IQR
Prolonged Mechanical Ventilation												
Hospital Duration (Days)	16.50	15	24.0	28	16.0	10	26.00	32	17	17	22	26
	z=6.157; p<.001				z=4.661; p<.001				z=4.177; p<.001			
Cost after the 8th day ($)	2211.2	6297.9	4202.2	7886.2	2355.1	4402.7	4524.1	9285.5	1774.2	6780.1	4016.9	7199.9
	z=4.742; p<.001				z=3.650; p<.001				z=3.161; p=.002			
	n	%	n	%	n	%	n	%	n	%	n	%
Survival												
Living	52	41.9	915	38.6	22	51.2	489	52.5	30	37.0	426	29.6
Died	72	58.1	1454	61.4	21	48.8	443	47.5	51	63.0	1011	70.4
	χ^2=0.544; p=.461				χ^2=0.028; p=.867				χ^2=1.994; p<.158			
Traumatic Brain Injury												
Hospital Duration (Days)	23	26	28	30	25	30	27.5	30	22	26	28	24
	z=1.645; p=.100				z=0.014; p=.989				z=2.005; p=.045			
Cost after the 8th day ($)	4016.9	7601.5	5429.1	8955.2	4324.8	8912.9	4777	9053	3942.8	7000.6	5965.8	8613.5
	z=2.473; p=.013				z=0.828; p=.408				z=2.413; p=.016			
	n	%	n	%	n	%	n	%	n	%	n	%
Survival												
Living	861	38.0	106	47.1	431	51.2	80	59.7	430	30.1	26	28.6
Died	1407	62.0	119	52.9	410	48.8	54	40.3	997	69.9	65	71.4
	χ^2=7.215; p=.007				χ^2=3.311; p=.069				χ^2=0.099; p=.753			
Major Wound												
Hospital Duration (Days)	23	27	24	27	25	31	22	30	22	26	31	26
	z=1.505; p=.132				z=0.226; p=.821				z=2.239; p=.025			
Cost after the 8th day ($)	4114.6	7791.1	4061.9	8125.5	4477.1	9119.5	3887.1	8348.1	3976.8	7069	4346.9	7950.0
	z=0.142; p=.887				z=0.349; p=.727				z=0.450; p=.653			
	n	%	n	%	n	%	n	%	n	%	n	%
Survival												
Living	921	38.3	46	52.9	478	51.7	33	64.7	443	29.9	13	36.1
Died	1485	61.0	41	47.1	446	48.3	28	35.3	1039	70.1	23	63.9
	χ^2=7.532; p=.006				χ^2=3.262; p=.071				χ^2=0.647; p=.421			
Sepsis												
Hospital Duration (Days)	23	26	24	28	24	30	26.5	30	22	26	22	27
	z=0.784; p=.433				z=1.171; p=.242				z=0.382; p=.703			
Cost after the 8th day ($)	3864.9	7240.3	4946.7	8264.5	4050.8	8401.1	5509.7	11864.2	3719.4	6715.1	4471.3	7626.2
	z=5.116; p<.001				z=4.092; p<.001				z=3.539; p<.001			
	n	%	n	%	n	%	n	%	n	%	n	%
Survival												
Living	835	44.9	132	20.9	446	58.1	65	31.3	389	35.6	67	15.8
Died	1025	55.1	501	79.1	321	41.9	143	68.7	704	64.4	358	84.2
	χ^2=114.949; p<.001				χ^2=47.466; p<.001				χ^2=57.232; p<.001			
Tracheostomy												
Hospital Duration (Days)	18	17	42	44	19	18	45	54	17	17	41	41
	z=24.241; p<.001				z=15.157; p<.001				z=18.787; p<.001			
Cost after the 8th day ($)	2807.5	4550.1	9805.9	12456.2	2733.4	4521.8	11052.1	14963.6	2870.2	4615.2	9081.7	11421.2
	z=22.804; p<.001				z=15.062; p<.001				z=17.006; p<.001			
	n	%	n	%	n	%	n	%	n	%	n	%
Survival												
Living	649	37.5	318	41.6	341	53.0	170	51.2	308	28.4	148	34.3
Died	1080	62.5	446	58.4	302	47.0	162	48.8	778	71.6	284	65.7
	χ^2=3.727; p=.054				χ^2=0.293; p<.588				χ^2=5.116; p=.024			

M: Median value. IQR: Distance between Quartiles. z: Mann–Whitney U test; χ^2: Chi-square test

PMV, TBI, tracheostomy, and major wound presence in the 65 and older age group increased hospital stay and costs. More work is needed to define CCI more clearly in elderly.

Acknowledgements

We would like to all clinician for this manuscript. There are no conflicts of interest in connection with this paper and the study was not use any sources of financial assistance.

REFERENCES

1. Polastri M, Comellini V, Pisani L. Defining the prevalence of chronic critical illness. Pulmonology 2020;26(3):119-20. (PMID: 31812701)
2. Herridge MS, Tansey CM, Matte A, et al. Functional disability 5 years after acute respiratory distress syndrome. N Engl J Med 2011;364(14):1293-304. (PMID: 21470008)
3. Carson SS. Definitions and epidemiology of the chronically critically ill. Respir Care 2012;57(6):848-56; discussion 56-8. (PMID: 22663962)
4. Laake JH, Dybwik K, Flaatten HK, et al. Impact of the post-World War II generation on intensive care needs in Norway. Acta Anaesthesiol Scand 2010;54(4):479-84. (PMID: 19930244)
5. Boniatti MM, Friedman G, Castilho RK, Vieira SR, Fialkow L. Characteristics of chronically critically ill patients: comparing two definitions. Clinics (Sao Paulo) 2011;66(4):701-4. (PMID: 21655767)
6. Nelson JE, Meier DE, Litke A, et al. The symptom burden of chronic critical illness. Crit Care Med 2004;32(7):1527-34. (PMID: 15241097)
7. Vásquez-Revilla HR, Revilla-Rodríguez E, Raymundo-Aguilar CA, Gaytan-Sánchez BM, Terrazas-Luna V. Epidemiological characteristics of patients with chronic critical illness. An ambispective observational study. Medicina Interna de México 2017;33(2):168-76. (in Spanish)
8. Iwashyna TJ, Hodgson CL, Pilcher D, et al. Timing of onset and burden of persistent critical illness in Australia and New Zealand: a retrospective, population-based, observational study. Lancet Respir Med 2016;4(7):566-73. (PMID: 27155770)
9. Kahn JM, Le T, Angus DC, et al. The epidemiology of chronic critical illness in the United States*. Crit Care Med 2015;43(2):282-7. (PMID: 25377018)
10. Guidet B, Leblanc G, Simon T, et al. Effect of Systematic Intensive Care Unit Triage on Long-term Mortality Among Critically Ill Elderly Patients in France: A Randomized Clinical Trial. JAMA 2017;318(15):1450-9. (PMID: 28973065)
11. Kwak SH, Jeong CW, Lee SH, Lee HJ, Koh Y. Current status of intensive care units registered as critical care subspecialty training hospitals in Korea. J Korean Med Sci 2014;29(3):431-7. (PMID: 24616595)
12. Heyland D, Cook D, Bagshaw SM, et al. The Very Elderly Admitted to ICU: A Quality Finish? Crit Care Med 2015;43(7):1352-60. (PMID: 25901550)
13. Milbrandt EB, Eldadah B, Nayfield S, Hadley E, Angus DC. Toward an integrated research agenda for critical illness in aging. Am J Respir Crit Care Med 2010;182(8):995-1003. (PMID: 20558632)
14. Bellani G, Laffey JG, Pham T, et al. Epidemiology, Patterns of Care, and Mortality for Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries. JAMA 2016;315(8):788-800. (PMID: 26903337)
15. Esteban A, Anzueto A, Frutos F, et al. Characteristics and outcomes in adult patients receiving mechanical ventilation: a 28-day international study. JAMA 2002;287(3):345-55. (PMID: 11790214)
16. Westphal GA, Vieira KD, Orzechowski R, et al. [Analysis of quality of life following hospital discharge among survivors of severe sepsis and septic shock]. Rev Panam Salud Publica 2012;31(6):499-505. (PMID: 22858817)
17. Stavem K, Hoel H, Skjaker SA, Haagensen R. Charlson comorbidity index derived from chart review or administrative data: agreement and prediction of mortality in intensive care patients. Clin Epidemiol 2017;9:311-20. (PMID: 28652813)
18. Rordorf G, Koroshetz W, Efird JT, Cramer SC. Predictors of mortality in stroke patients admitted to an intensive care unit. Crit Care Med 2000;28(5):1301-5. (PMID: 10834669)

RESEARCH

WHY SOME ELDERLY PEOPLE CANNOT USE THE HEARING AID

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2020.189
2020; 23(4): 509-514

Süleyman ERDOĞDU[1]

Abstract

Introduction: This study aims to investigate why some patients over 65 years of age cannot use their hearing aids.

Materials and Method: Hospital records between January 2018 and April 2019 identified 1,017 patients who received a hearing aid. Among them, 373 patients over the age of 65 were included in the study. It was questioned that they did not use the hearing aid.

Results: The reasons for not using the hearing aid are as follows: 9 patients couldnot distinguish sounds; 8 patients' cheap devices were not efficient; 6 patients showed a negative image so as not to be mentioned as disabled ; 6 patients' device battery runs out too quickly but use it as needd; 5 patients' device is making noise; 3 patients' device often fails; 3 patients reported it giving them headache; 2 patients feltirritated and that it injured theirear; 28 patients did not participate in the hearing rehabilitation program and did not contact the seller company to make the technical settings of the device.

Conclusion: Elderly patients complain that although they can hear voices, they have trouble understanding what the voices are saying, which are related but separate issues. Before applying the device, the age of the patient should be considered. All the details about the use must be taught to the person initially. It is very important to make technical adjustments depending on the software features of the device and routine control shouldbe included in the hearing rehabilitation program.

Key Words: Geriatrics; Presbycusis; Hearing Aids; Hearing Loss

CORRESPONDANCE

[1]Süleyman ERDOĞDU

Istanbul Haydarpasa Numune Training and Research Hospital, otorhinolaryngology, İstanbul, Turkey

Phone: +902165423232
e-mail: suleymanerdogdu@gmail.com

Received: Aug 27, 2020
Accepted: Nov 24, 2020

[1] Istanbul Haydarpasa Numune Training and Research Hospital, otorhinolaryngology, İstanbul, Turkey

INTRODUCTION

Hearing disorders due to old age are called 'presbycusis'. This disorder is an age-related physiological change of the sensorineural part of the hearing organ. Depending on the severity of the problem, the most common complaint of patients with presbycusis is not being unable to hear the sound but the difficulty to understand what is being said (1).

While the incidence of presbycusis is 24-40% between the ages of 65-74, this rate increases up to 40-66% after the age of 75. It is the third most common health problem in the geriatric population following high blood pressure and arthritis (2).

Hearing is the most important factor in the formation, development, and use of verbal communication. Presbycusis, affects the person not only organically but also psycho-socially and makes intense rehabilitation mandatory to provide the conditions that increase his/her quality of life. The first step toward rehabilitation is generally the selection of appropriate hearing aids. Otherwise, an unwise hearing aid recommendation will either be inadequate or destroy existing hearing over time. To get the most out of hearing aids, the use of the device should be binaural, the person should use the device as long as possible during the day, and both the patient and the patient's relatives should be well informed about the benefits of the device (3). Brooks stated that geriatric individuals need a longer adaptation period to hearing aids (4).

This study aims to investigate why some patients over 65 years of age do not use their hearing aids, even though they were prescribed and had already bought the devices.

MATERIALS AND METHODS

Ethical approval

This study has been approved by Haydarpasa Numune Training and Research Hospital Ethics Committee, Istanbul, Turkey. (date: 14.01.2019. no:2019/3).

Study design and population

We have studied a total number of 1017 patients requiring hearing aid who were admitted to Otorhinolaryngology outpatient clinic between January 2018 and April 2019. Age, gender and audiogram results were extracted from the hospital records. Age averages, air and bone track hearing threshold averages in the right and left ears as well as speech discrimination records were reviewed. 373 patients over 65 years of age were selected then (Tables 1-2). In one-on-one interviews, they were inquired about utilization of the hearing aids (Table 3), and their

Table 1. Audiogram Results of Patients

Mean±SD		Number of patients (N=1017)	Age 65≤ (N=373)
		Mean±SD	
Age		69.20 ±14.03 53.43 ±17.84	71.58±10.27 54.35 ±18.03
Right ear	AC		
	BC	43.49 ± 20.42	43.07±13.34
	SD	55.36 ±15.33	54.80±16.27
Left ear	AC	54.95±18.18	54.39±17.22
	BC	43.49±13.80	42.67±13.92
	SD	56.67±35.22	58.16±54.01

Table 2. Gender Distribution of Patients

n		Number of patients (N=1017)		Age 65≤ (N=373)	
		%	n	%	
Gender	**Female**	482	47.4	171	45.8
	Male	535	52.6	202	54.2

answers were recorded (Table 4). It was found out that among these 373 patients, 42 patients who had received digital hearing aids behind the ears could not use them.

The severity of the hearing loss according to audiogram results was classified as mild hearing loss in the 20-40 dB HL range, moderate in the 40-60 dB HL range, advanced in 60-80 dB HL range, and very high in the above 80 dB HL range (5).

Hearing aids constitute an important place in health expenditures even considering how the budgets are allocated by insurance institutions in the world and our country and the patients pay for their devices up to a certain extent. In a country with a population of around five million, like Finland, the amount paid for hearing aids is over 13 million Euros annually (6). In the USA in 1997, approximately 8% of individuals aged 65 experienced over use of hearing aids (7). In Turkey, this rate has remained relatively low. The rate of hearing aid usage is 4.7% according to Turkish Statistical Institute data (8).

In 2019, Turkey's population is approximately 83 million (83.154.997); 7.550.727 (9.1%) of the total population is aged 65 and over. Of these, 3.337.260 (8%) are male; 4.213.467 (10.2%) is female (9).

Statistical Analysis

Data were analyzed with SPSS (Statistical Package for the Social Sciences) 15.00 package program. Descriptive statistical methods (frequency, mean, standard deviation) were used to evaluate the data.

RESULTS

In our study, the audiograms of 373 patients over 65 years of age had moderate sensorineural hearing loss and speech discrimination means of 55-58%. The average age of the patients is 71.58 ± 10.27. Of these, 171 (45.8%) were women, and 202 (54.2%) were male (Table 2-3). The answers given by 42 patients who received the hearing aid but could not use it are listed in Table 3. Six of them stated that they used the device occasionally, rather than constantly because the battery was running out quickly. It was understood from the answers he/she gave that he/she did not use the device as a result of the communication between the company he/she purchased the device and these patients did not contact the hearing aid dispenser where they received the hearing aid battery regularly, did not adjust the device and did not receive rehabilitation training accordingly.

In response to question number 3, 17 patients stated that they bought low-quality devices, 9 patients had medium quality devices, and 5 patients

Table 3. Survey questions

1) Do you use the hearing aid?
2) What is your reason for not using the hearing aid?
3) What is the quality status of your hearing aid?
4) Did you contact the place where you bought your hearing aid?

Table 4. The Reasons for 42 Patients not Using the Hearing Aids

n	%	Complain
9	21.43	I can't distinguish sounds
8	19.05	I was able to buy a cheap device. It was not efficient.
6	14.29	Negative image: In order not to be called disabled
6	14.29	The device battery is running out quickly. I use it when I need it
5	11.90	The device is making noise.
3	7.14	The device frequently fails.
3	7.14	She's having a headache.
2	4.76	It causes irritation and soreness in my ear.

received high-quality devices. Most of the elderly patients' complained not from being unable to hear voices but having trouble understanding the words.

DISCUSSION

A complete ear-nose-throat examination for the diagnosis of presbycusis necessitates an audiologic examination, where pure tone air and bony conduction thresholds, speech threshold, and the ability to distinguish tolerance levels to pure-voice and speech are determined (1). A study determined that hearing loss impairs the quality of life in individuals, causes depressive symptoms, and reduces functional capacity (10). Yurtogullari et al. reported in their study that presbycusis is an important cause of dementia and leads to the rapid development of dementia, so it is important to monitor hearing loss in geriatric patients closely and regularly (11).

The hearing aid is an amplifier, not a discriminator. In other words; a digital hearing aid raises the intensity of the incoming sound in accordance with patient's hearing thresholds, but does not directly assist in distinguishing or understanding speech in sensorineural hearing loss. The hearing aid user needs to be told what they can and cannot get from the device. It should also be explained that there may be some adaptation difficulties in the first days of wearing the device, such as using glasses. For this purpose, adaptation and orientation programs are applied as much as needed (1).

It is very important to give right information before applying the device by explaining in detail that hearing and understanding are related but separate issues. Having an adequate fitting suitable for the hearing loss and expectations of the person and using the binaural device if the conditions are suitable will also minimize the possible complaints. Also, clogging the tip of the ear plug and clogging the filter introduces the need to change the device battery at frequent intervals, which has been a deterrent to the use of the hearing aid. There may be complaints, such as the difficulty of placing the device mold in the ear, plugging the mold end of the plug, and blockage of the filter. It is very important to have routine check-ups and make technical adjustments, depending on the software features of the device for the conditions it encounters at home, on the street, on the television, and in a telephone conversation.

For this purpose, it was recommended to send our patients to the centers where they initially purchased their devices to perform device settings and maintenance. The plugs in the outer ear canal and

ear mold were then cleaned and made available to the hearing aid.

Benett et al. (12) found that the problems encountered with hearing aid use are preventable and overcome problems with hearing aid application methods. A study conducted by Kahveci et al. (13) found that the method of hearing aid usage was not explained to the patients and the fact that the patients were older (70 and above) decreased the compliance to hearing aid use.

Orji et al (14) stated that 401.4 million people were in need of hearing aids. The great majority (83%) of them do not use hearing aids.

The rate of patients who were recommended and reported hearing aids but did not buy hearing aids was found to be 22% in one study and 31.9% in another study, and the high cost of devices was stated as the reason for not having a device (14-16). Hamurcu et al. (15) found 32%, Saatci et al. (8) 22% could not buy the device due to financial impossibilities. In our study, device cost is an important factor leading most of the patients to buy lower-quality devices. In their study, Hamurcu et al. (15) found a large group of patients who could not receive their device, even though the device was recommended. The reason for this is that the socioeconomic level of our country is low and the contribution paid by the social security is low, so most of the cost has to be covered by the patient. In our study, it was understood that 8 patients who bought cheap devices (19.05%) gave up using their devices because they had primitive technology.

A study by Mc Pherson (16) on affordable hearing aids investigated the effectiveness of the elderly and affordable over the counter devices to provide access to the many patients with hearing loss. They conclude that further research and more of these tools to provide improved rehabilitation results should be prioritized.

In their study, Saatci et al. (8) found that the most influential obstacle in the use of hearing aids is the external recognition of the device and the idea that it shows the user as elderly or disabled. This problem was detected in six patients (14.29%) in our study.

In their study, Hamurcu et al. (15) found the reasons for device incompatibility to be noise from the device, inability to speak in crowded environments, and infections occurring in the outer ear canal. In the study conducted by Kirkim et al. (17), the fact that device maintenance and use have difficulties, especially in elderly patients living alone, reduces the device's benefits.

Care should be taken to clean the ear mold, and an ear examination should be done periodically. It is seen that as the educational level increases, complaints about device use decrease.

Kenar et al. (18) stated that in a review examining the problems encountered in the use of hearing aids in the adult population, digital hearing aids, which have become widespread recently, decrease the usage problems considerably.

In the general evaluation of unilateral hearing aid users in the geriatric group, Senkal et al. (19) did not find a statistically significant effect of hearing aid usage time on the quality of life. In the same study, they found that the use of hearing aids increased their communication ability and strengthened self confidence.

The fact that the device is not an artificial ear but rather a headset should be explained to the patient, and all device related details should be taught to the user at the beginning.

CONCLUSIONS

Presbycusis is common in the geriatric population. It is recommended to use hearing aids for its rehabilitation. To receive maximum benefit from hearing aids, the use of the device should be binaural and the person should use the device as long as possible during the day. Our study showed that a

considerable percentage of the elderly population cannot use hearing aids even though having paid for them; and, the main reason for that was shown to be insufficient communication among physicians, audiologists and patients. Patients and their relatives should be informed about the benefits and usage of the device. They should be motivated to use the device. The doctor and audiologist should be informed about the problems in using the device. Most important of all, using the latest technology device should be encouraged.

REFERENCES

1. Ozkan S. Hearing, Voice and Speech Disorders in The Elderly. Turkish Journal of Geriatrics 1998;1(2):72-75. (in Turkish)
2. Aksoy S. Age-related hearing loss and auditory rehabilitation. Journal of Exercise Therapy and Rehabilitation 2015;4:1-2.(in Turkish)
3. Cakir O, Yildirim G, Kumral TL.et al. Presbycusis and Rehabilitation in Old Age. The Medical Journal of Okmeydanı Training and Research Hospital 2013;29(2):116-120. (DOI:10.5222/otd.supp2.2013.116). (in Turkish)
4. Brooks DN. The time course of adaptation to hearing aid use. Br J Audiol 1996;30(1):55-62. (PMID:8839367).
5. Jerger J, Jerger S. Measuring of hearing in adults. In: Paparella MM, Shumrick DA, eds. Otolaryngology, 2nd ed. WB Saunders, Philadelphia 1980. pp. 1226.
6. Akyildiz N. Ear Diseases and Microsurgery, vol.1. Scientific Medicine Publisher, Ankara, Turkey 1998, pp. 15-40.(in Turkish)
7. Cox RM, Alexander GC. The abbreviated profile of hearing aid benefit. Ear and Hearing 1995;16(2):176-86. (PMID:7789669).
8. Saatci O, Polat B, Cakir N. Hearing loss and stigma. Praxis of Otorhinolaryngology 2017;5(2):63-69. (DOI: 10.5606/kbbu.2017.83703).(in Turkish)
9. Turkish Statistical Institute. Population by Years. Age Group and Sex. Census of PopulationABPRS.2019.[Internet]Availablefrom: http://www.turkstat.gov.tr/UstMenu.do?metod=temelist. Accessed: 01.07.2020.
10. Lupsakko TA, Kautiainen HJ, Sulkava R. The non-use of hearing aids in people aged 75 years and over in the city of Kuopio in Finland. Eur Arch Otorhinolaryngol 2005; 262: 165-169.(PMID: 15133689).
11. Yurtogullari S, Kocan EG, Vural G, Gumusyayla S, Bababemez MA, Bozdemir K. The Relationship of Presbycusis with Cognitive Functions. Turkish Journal of Geriatrics 2020; 23(1): 75-81. (DOI: 10.31086/tjgeri.2020.140).
12. Bennett RJ, Lévesque AL, Meyer CJ, Eikelboom RH. Exploring Hearing Aid Problems: Perspectives of Hearing Aid Owners and Clinicians. Ear Hear 2018;39(1):172-187.(PMID: 28787315).
13. Kahveci OK, Miman MC, Okur E, Aycicek A, Sevinc S, Altuntas A. Hearing aid use and patient satisfaction. The Turkish Journal of Ear Nose and Throat 2011;21(3):117-121. (PMID: 21595614).(in Turkish)
14. Orji A, Kamenov K, Dirac N, Davis A, Chadha S, Vos T. Global and Regional Needs, Unmet Needs and Access to Hearing Aids. International Journal of Audiology 2020;59(3):1-8. (PMID: 32011190).
15. Hamurcu M, Sener BM, Atas A, Atalay RB, Bora F, Yigit O. Evaluation of Patients Satisfaction with Hearing Aids. Electronic Journal of Otolaryngology Head and Neck Surgery 2012;11(2):26-31.(in Turkish)
16. McPherson B, Wong ETL. Effectiveness of an affordable hearing aid with elderly persons. Disabil Rehabil 2005; 27: 601-609. (PMID: 16019870).
17. Kirkim G, Serbetcioglu MB, Mutlu B. Assessment of Patient Satisfaction for Hearing Aids Using the Turkish Version of International Outcome Inventory for Hearing Aids. Journal of Ear, Nose & Throat and Head & Neck Surgery 2008; 16(3): 101- 107.(in Turkish)
18. Kenar F, Bababemez MA. Problems encountered with hearing aids in adult population. Journal of ENT Updates 2015; 5(1): 41–47. (DOI:10.2399/jmu.2015001001).
19. Senkal OA, Kose A, Aksoy S. Assessment of Geriatric Patient's Satisfaction on Hearing Aids and Their Influence on Quality of Life. Turkish Journal of Geriatrics 2014 ;17 (4):389-396.(in Turkish)

RESEARCH

A PILOT STUDY OF CLINICAL PHARMACIST-LED MEDICATION REVIEW IN OLDER ADULTS ON POLYPHARMACY AND RECEIVING HOME HEALTH CARE SERVICES

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2020.190
2020; 23(4): 515-523

Semra MEMİŞ[1]
Mesut SANCAR[1]
Onursal VARLIKLI[2]
Betül AKÇAY[2]
Halide VAROL[2]
Sümeyra Lubeyne SÖYLEMEZ[1]
Mahmut Sabri MEDİŞOĞLU[2]
Betul OKUYAN[1]

CORRESPONDANCE

[1]Betul OKUYAN

Marmara University, Faculty of Pharmacy, Clinical Pharmacy Department, Istanbul, Turkey

Phone: +905333300353
e-mail: betulokuyan@yahoo.com

Received: Sep 22, 2020
Accepted: Nov 17, 2020

[1] Marmara University, Faculty of Pharmacy, Clinical Pharmacy Department, Istanbul, Turkey

[2] Republic of Turkey Ministry of Health, Kocaeli Provincial Health Directorate, Health Services at Home, Kocaeli, Turkey

Abstract

Introduction: This study aimed to evaluate the frequency and types of medication-related problems in older adults receiving home health care services that were identified through clinical pharmacist-led medication review.

Materials and Methods: This pilot study was conducted in patients ≥65 years of age who were on polypharmacy and receiving home health care services from May 15th, 2019 through October 30th, 2019 in Turkey. A multidisciplinary home care team, including physicians, nurses and clinical pharmacist, performed the home visits. Scores on the drug burden index, medication regimen complexity index, and medication appropriateness index, present of potentially inappropriate medications, and the medication-related problems were assessed.

Results: Among 100 older adults (74 females) with a mean age of 78.5±7.9 years, the median number of medications used was 7 (interquartile range: 5-9); the median scores of the drug burden index, medication regimen complexity, and medication appropriateness index were 0.5 (interquartile range: 0-0.8), 21 (interquartile range: 17-31), and 13 (interquartile range: 6-16.9), respectively. The problems identified were those related to 'drug selection' (66%), 'education and information' (58%) and 'monitoring' (33%). The health care team accepted 84.2% of the recommendations made by the clinical pharmacists.

Conclusions: The results suggested that clinical pharmacist-led cognitive services in a home health care services team could reduce medication-related problems in older adults on polypharmacy.

Keywords: Pharmacists; Home Care Services; Polypharmacy

INTRODUCTION

Older adults receiving home healthcare services with polypharmacy are susceptible to medication-related problem (1). A 'Medication Management Model' is defined as structured interprofessional services that involves clinical pharmacists and home health nurses (2). As a part of this interprofessional model developed for home health providers, home visits were conducted by pharmacists for home care patients on polypharmacy (≥9 medications) and a total of 2,482 medication-related problems were determined (3). The advantages of these pharmacy services conducted in the home setting have been reported as providing a comfortable place for discussing many issues, enabling the development of an accurate medication list and allowing functional medication administration for participants (3).

The home medicines review (HMR) is a community-based service that involves general practitioners and pharmacists in order to prevent, determine, and resolve medication-related problems in Australia (4). The drug burden index (DBI) (5) and medication appropriateness index (MAI) (6) are evidence-based tools that are used to demonstrate potential contribution of pharmacist-led HMR (4). Home health care services have recently been integrated into the health system in Turkey; however, pharmacists are not involved in the home care services team that includes physicians and nurses. A novel project was initiated in 2019 by the Kocaeli Provincial Health Directorate in cooperation with the Clinical Pharmacy Department of Marmara University Faculty of Pharmacy. This project aimed to provide education and training for pharmacists on cognitive services in home health care services and to develop clinical pharmacy services that could be integrated into the health care services in the home setting. As a part of this project, the present pilot study aimed to evaluate the potential impact of providing medication review in older adults on polypharmacy and receiving home health care services. For this purpose, the frequency and types of medication-related problems were determined through the clinical pharmacist-led medication review in older adults who were on polypharmacy and receiving home health care services, and acceptance rate of the pharmacists' recommendations by the health care team (the physicians and nurses) were assessed.

MATERIALS AND METHODS

Ethics Approval

The present study was approved by the Clinical Trial Ethics Committee of University of Health Sciences Kocaeli Derince Training and Research Hospital of (approval number: 2019-40, date: May 9th, 2019). The informed consents of the patients and/or their caregivers was obtained before the study.

Setting and Study Design

This descriptive cross-sectional pilot study was conducted from May 15th, 2019 through October 30th, 2019. Patients aged ≥65 years who were on polypharmacy (defined as concurrently used 4 or more medications based on previous study) (7) and receiving health care services in the home setting in the Kocaeli province of Turkey were eligible for participation.

Clinical Pharmacist-Led Medication Review

A multidisciplinary home care team including physicians and nurses performed weekly or daily visits to evaluate the patients. A clinical pharmacist joined the health care team within the time frame of the present study. During the home visits, the pharmacists interviewed with the older adults and/or their caregivers about their medications.

Data Collection

The data of the older adults regarding age, sex, number of years of education, history of falls, comorbidities, and hospital admissions during the previous six months were obtained from the med-

ical records. All medications, including medications with or without prescription and dietary supplements, were recorded for each patient and biochemical test results were also obtained from the medical records of each patient.

DBI scores were calculated for all patients. The DBI is an evidence-based tool that assesses the total exposure of older adults to anticholinergic and sedative medications (5). A previously published list was used as a reference to determine the minimum effective dose of medications (8).

The medication complexity of each patient was quantified using the Turkish version of the Medication Regimen Complexity Index (MRCI) (9). The MRCI is a 65-item valid tool that evaluates the medication complexity of patients according to the dosage forms, dosage frequency, and administration instructions of medications. Higher scores indicate more complex medication regimens (9).

Medication Related Problems

The appropriateness of all medications used by the patients was assessed with the MAI. This index contains 10 criteria, each of which is scored as appropriate, neutral, inappropriate, or unknown, and it yields a maximum potential score of 18. Lower scores indicate the appropriateness, whereas higher scores indicate inappropriateness of medication (6). The Potentially inappropriate medications (PIMs) used by the patients were determined with the 2019 American Geriatrics Society (AGS) Beers Criteria® (10) and TIME-to-STOP criteria (11).

The medication-related problems were determined by the clinical pharmacist-led medication review and listed by using the validated DOCUMENT classification system (12). The health care providers' (the physicians and the nurses) acceptance rate of clinical pharmacist's recommendations about the medication-related problems was recorded without evaluating the outcome of implementation these recommendations.

Statistical Analysis

The data analysis was performed using the Statistical Package for the Social Sciences for Windows (version 11; SPSS Inc., Chicago, IL, USA). The normality of data distribution was tested by using the Kolmogorov-Smirnov test. Data were expressed as median (interquartile range [IQR]) and mean and standard deviation (SD) for continuous variables and as frequency and percentage for categorical variables.

RESULTS

A total of 124 older adults who were receiving home health care services were visited during the study period, of which 19 had insufficient medication and clinical data, and five were not willing to participate in the study. Accordingly, the study was conducted in 100 older adults who were on polypharmacy and receiving home health care services. The mean age was 78.5±7.9 years; the majority of the patients were female (74%) and had less than eight years of education (97%). Nearly half of the patients (49%) had a hospital admission within the last six months, and 28 patients had a history of fall. The median total number of medications was 7 (IQR: 5-9). The median DBI score was calculated as 0.5 (IQR: 0-0.8). According to the DBI scores, a high exposure to anticholinergic and sedative medicines was determined in 22 older adults. The median total MRCI score was 21 (IQR: 17-31), and the median total MAI score was calculated as 13 (IQR: 6.0-16.9). The demographic and medical data of them included in the study are presented in Table 1.

Among the study patients, 40% were using PIMs according to the TIME-to-STOP criteria, and 7.0% of the all medications used (n=738) were PIMs. The MAI scores and the number of PIMs are presented in Table 2. At least one of the 2019 Beers Criteria® was determined in 53 of the patients receiving health care services in the home setting. The number of PIMs for the older adults receiving health care services in the home setting is summarized in Table 3.

Table 1. Demographic and medical data of older adults receiving home care services (number of patients=100)

	n
Age (years) Mean (SD)	78.5 (7.9)
Gender (%)	
Male	26
Female	74
Education (years) (%)	
<8	97
≥8	3
Hospital admission during last 6 months (%)	
Yes	49
No	51
History of Falls (%)	
Yes	28
No	72
Total number of medication Median (IQR)	7 (5-9)
DBI score Median (IQR)	0.5 (0-0.8)
DBI score	
0	35
<1	43
≥ 1	22
MRCI score Median (IQR)	21 (17-31)
MAI score Median (IQR)	13 (6.0-16.9)

SD: standard deviation; IQR: interquartile range DBI: drug burden index; MRCI: medication regimen complexity index; MAI: Medication Appropriateness Index

Table 2. Medication appropriateness index score and the number of PIMs (total number of medications= 738)

	A total number of medications (%)
MAI	
0	259 (35.1%)
1-2	298 (40.4%)
3-4	112 (15.1%)
≥5	59 (9.5%)
PIMs according to TIME-to STOP Criteria	
No	686 (93%)
Yes	52 (7%)
At least one PIM according to 2019 AGS Beers® Criteria	
Yes	90 (12.2%)
No	648 (87.8%)

MAI: Medication Appropriateness Index; PIM: potentially inappropriate medication; TIME to STOP: criteria for inappropriate medication use in Turkish older adults; AGS: American Geriatrics Society

For the older adults who were on polypharmacy, 329 medication-related problems were determined by the clinical pharmacist-led medication review, and 96% of the patients had at least one medication-related problem. Those problems were 'problems related to drug selection' (66%), 'problems related to education and information' (58%) and 'problems related to monitoring' (33%). Of the 329 recommendations of the pharmacists, 84.2% were accepted by the home health care team. The medication-related problems identified according to the DOCUMENT classification system for the patients

Table 3. PIMs in older adults receiving health care services at home setting (the number of patients=100)

PIMs according to TIME-to STOP Criteria	n
0	60
1	30
2	7
3	3
2019 AGS Beers Criteria® - PIM in Older Adults Due to Drug-Disease or Drug-Syndrome Interactions	
0	76
1	24
2019 AGS Beers Criteria® - PIM in Older Adult	
0	54
1	34
2	12
2019 AGS Beers Criteria® - Potentially Clinically Important Drug-Drug Interactions	
0	88
1	12
2019 AGS Beers Criteria® - Medications That Should Be Avoided or Have Their Dosage Reduced with Kidney Function of Older Patient	
0	98
1	2

PIM: potentially inappropriate medication; AGS: American Geriatrics Society; TIME to STOP: criteria for inappropriate medication use in Turkish older adults

are summarized in Table 4. The most commonly observed medication-related problems in older patients are summarized in Table 5.

DISCUSSION

The results of the present study, which investigated medication-related problems in older adults who were on polypharmacy and receiving home health care services, demonstrated that the majority of the patients (96%) had at least one medication-related problem determined by the clinical pharmacist. The problems identified were those related to 'drug selection' (66%), 'education and information' (58%) and 'monitoring' (33%). The health care team accepted 84.2% of the recommendations made by the clinical pharmacists.

The total number of medications was determined to be slightly lower than those reported in previous studies conducted in the home setting (13,14). Among our patients, the rate of those highly exposed to medications identified by the DBI was 22%. Similar to the results of the present study, the rate of exposure to medications identified by the DBI was shown to be nearly one fifth of them (15). In contrast, the rate of exposure to anticholinergic and/or sedative medications identified by the DBI in older patients has been reported to be higher in the community setting (7).

The median MRCI score was determined as 21 (IQR, 17-31) in the patients of this study; this finding was in parallel with the results reported in previous studies (16,17). However, the median total MAI score 13 [IQR, 6.0-16.9]) found in the present study was higher than that reported in previous studies (13,18).

In a retrospective study on community-dwelling older individuals (≥65 years; n=270) in Australia,

in which the effects of HMRs performed by pharmacists on prescribing appropriateness (13), were evaluated, the most common medication-related problems were reported as medications with no indication (22.0%), potential drug-drug interactions (14.3%) and problems related to dosage (13.0%). Additionally, the acceptance rate of the pharmacists' suggestions by the general practitioners was reported as 45.5% (13), a finding which was lower than the finding of the present study (84.2%). In contrast, similar to the rate found in the present study, the rate of receiving at least one PIM was reported to be 59% in patients with dementia living at home (19) and 40.4% in older home care patients in Japan (20). In a study conducted in Switzerland, 2.2% of all prescribed medications were identified as PIMs by clinical pharmacists in the patients transferred from hospital to home care (21). In Qatar, the ratio of patients receiving at least one PIM was 38.2% among older home care patients (22). In a study from Europe, overall, 19.8% of patients were reported to receive at least one PIM (23); the rate of those receiving at least one PIM was reported as 41.1% in the Czech Republic (23), and this rate was similar to the finding of the present study.

In a study performed to investigate the recommendations made by geriatric clinical pharmacists through medication reviews for patients with dementia living at home, the health care providers accepted 44% of the recommendations made by the geriatric clinical pharmacists (19); these recommendations included those related to the cessa-

Table 4. Medication-related problems identified according to DOCUMENT in the study population (the number of patients=100)

The type of medication related problems	The number of patients	The number of recommendations n(%)
Drug selection	66	111 (33.7)
Education or information	58	77 (23.4)
Monitoring	33	40 (12.1)
Toxicity or adverse reaction	29	38 (11.5)
Over or underdose	24	29 (8.8)
Compliance	21	27 (8.2)
Undertreated	7	7 (2.1)

Table 5. The most commonly determined medication related problems in the older adults receiving health care services at home setting (the number of patients=100)

The most commonly determined medication related problems	n
Problems related medication administration such as lack of information about how and when to take medications	72
Anticholinergic and sedative utilization that are resulted in ataxia, impaired psychomotor function, additional falls	50
Utilization of PPI more than 8 weeks	35
Combination of three or more CNS active agents concomitantly	11
Dose adjustment is required	13

PPI: proton pump inhibitors, CNS: central nervous system

tion of a drug, dose adjustment, and switching to a potentially safer alternative (19). In another study conducted among older adults receiving home care services and using at least five medications in the Netherlands, a total of 1,565 medication-related problems were determined (14). In contrast to the results of the present study, the most common medication-related problems were reported to be associated with medication selection (28%), untreated indication (26%), and monitoring (21%) (14). In a study from Canada, medication-related problems were detected in patients receiving home care services through pharmacist-led medication review (24). Moreover, the acceptance rate of the pharmacists' recommendations by the physicians was reported to be 69.9%, which was a lower rate than that found in the present study (84.2%), and the most common medication-related problems were identified as medication adherence problems (37.6%), unnecessary medication use (16.6%), need for an additional treatment (12.9%), and problems related to dosage (12.9%) (24). A randomized control trial in Jordan evaluated the effects of the medication management review service via home visits in the intervention group as compared with a control group through pharmacist-led medication review (25). The most common medication-related problems according to clinical pharmacists were reported to be associated with education (27.2%), inappropriate adherence (16.5%), and issues with monitoring (15.8%). At the end of the study, 85.0% of the medication-related problems identified by the clinical pharmacist in the intervention group were corrected (25).

The medications used by participants were evaluated in detail using the MRCI, MAI, DBI, and the PIMs and medication-related problems were also assessed; these could be considered as strengths of the study. Nevertheless, the present study has some limitations. First, the small sample size from a specific region could be considered a limitation. However, the potential impact of the pharmacist-led medication review on clinical and patient-related outcomes was not evaluated; this could be considered another limitation, which is attributed to the cross-sectional design of the study. This study presented a low evidence with current study design for potential impact of the pharmacists in the home care team. This study was determined the medication related problems and their frequency, and the acceptance rate of the pharmacist's recommendations. The future studies would be conducted to evaluate impact of these recommendations' implementation on the older patients' outcomes at home care setting.

This pilot study elucidates the potential impact of integrating the pharmacist into a health care team to determine and solve medication-related problems. These findings may be helpful in training the pharmacist for cognitive services such as medication review for older patients receiving home health care services. The findings of the present study could also encourage the development of programs and/or care models involving pharmacists for home health care services in Turkey and other countries where the development and implementation of clinical pharmacy services are ongoing.

Acknowledgments

None

Disclosure statement

We have no conflict of interest to declare.

REFERENCES

1. Meredith S, Feldman PH, Frey D, et al. Possible medication errors in home healthcare patients. J Am Geriatr Soc 2001;49(6):719-24. (PMID: 11454109).
2. Meredith S, Feldman P, Frey D, et al. Improving medication use in newly admitted home healthcare patients: A randomized controlled trial. J Am Geriatr Soc 2002;50(9):1484-91. (PMID: 12383144).
3. Reidt S, Morgan J, Larson T, Blade MA. The role of a pharmacist on the home care team: a collaborative model between a college of pharmacy and a visiting nurse agency. Home Healthc Nurse 2013;31(2):80-7; quiz 8-9. (PMID: 23314201).
4. Chen TF. Pharmacist-Led Home Medicines Review and Residential Medication Management Review: The Australian Model. Drugs Aging 2016;33(3):199-204. (PMID: 26961696).
5. Hilmer SN, Mager DE, Simonsick EM, et al. A drug burden index to define the functional burden of medications in older people. Arch Intern Med 2007;167(8):781-7. (PMID: 17452540).
6. Hanlon JT, Schmader KE, Samsa GP, et al. A method for assessing drug therapy appropriateness. J Clin Epidemiol 1992;45(10):1045-51. (PMID: 1474400).
7. Rankin A, Cadogan CA, Patterson SM, et al. Interventions to improve the appropriate use of polypharmacy for older people. Cochrane Database Syst Rev. 2018;9(9):CD008165. (PMID: 30175841).
8. Byrne CJ, Walsh C, Cahir C, Ryan C, Williams DJ, Bennett K. Anticholinergic and sedative drug burden in community-dwelling older people: a national database study. BMJ Open 2018;8(7):e022500. (PMID: 29982221).
9. Okuyan B, Babi B, Sancar M, et al. Validation of the Turkish version of medication regimen complexity index among elderly patients. J Eval Clin Pract 2016;22(5):732-6. (PMID: 26987572).
10. By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc 2019;67(4):674-94. (PMID: 30693946).
11. Bahat G, Ilhan B, Erdogan T, et al. Turkish inappropriate medication use in the elderly (TIME) criteria to improve prescribing in older adults: TIME-to-STOP/TIME-to-START. Eur Geriatr Med 2020;11(3):491-98. (PMID: 32297261).
12. Williams M, Peterson G, Tenni P, Bindoff I, Stafford A. DOCUMENT: a system for classifying drug-related problems in community pharmacy. Int J Clin Pharm 2012;34(1):43-52. (PMID: 22101425).
13. Castelino RL, Bajorek BV, Chen TF. Retrospective evaluation of home medicines review by pharmacists in older Australian patients using the medication appropriateness index. Ann Pharmacother 2010;44(12):1922-9. (PMID: 21119095).
14. Kwint HF, Faber A, Gussekloo J, Bouvy ML. The contribution of patient interviews to the identification of drug-related problems in home medication review. J Clin Pharm Ther 2012;37(6):674-80. (PMID: 22861493).
15. Zhang XL, Zhou S, Li XR, et al. Anticholinergic and sedative medications exposure in older patients: a cross-sectional study. Int J Clin Pharm 2019;41(5):1152-8. (PMID: 31392583).
16. Elliott RA, O'Callaghan C, Paul E, George J. Impact of an intervention to reduce medication regimen complexity for older hospital inpatients. Int J Clin Pharm 2013;35(2):217-24. (PMID: 23212732).
17. Saez de la Fuente J, Such Diaz A, Cañamares-Orbis I, et al. Cross-cultural Adaptation and Validation of the Medication Regimen Complexity Index Adapted to Spanish. Ann Pharmacother 2016;50(11):918-25. (PMID: 27371950).
18. Spinewine A, Swine C, Dhillon S, et al. Effect of a collaborative approach on the quality of prescribing for geriatric inpatients: a randomized, controlled trial. J Am Geriatr Soc 2007;55(5):658-65. (PMID: 17493184).
19. Melville BL, Bailey J, Moss J, et al. Description of Pharmacist Recommendations in the Caring for Older Adults and Caregivers at Home (COACH) Program. Sr Care Pharm 2020;35(1):38-46. (PMID: 31883544).
20. Hamano J, Tokuda Y. Inappropriate prescribing among elderly home care patients in Japan: prevalence and risk factors. J Prim Care Community Health 2014;5(2):90-6. (PMID: 24399442).
21. Meyer-Massetti C, Hofstetter V, Hedinger-Grogg B, Meier CR, Guglielmo BJ. Medication-related problems during transfer from hospital to home care: baseline data from Switzerland. Int J Clin Pharm 2018;40(6):1614-20. (PMID: 30291577).

22. Alhmoud E, Khalifa S, Bahi AA. Prevalence and predictors of potentially inappropriate medications among home care elderly patients in Qatar. Int J Clin Pharm 2015;37(5):815-21. (PMID: 25986290).

23. Fialová D, Topinková E, Gambassi G, et al. Potentially inappropriate medication use among elderly home care patients in Europe. JAMA 2005;293(11):1348-58. (PMID: 15769968).

24. Walus AN, Woloschuk DMM. Impact of Pharmacists in a Community-Based Home Care Service: A Pilot Program. Can J Hosp Pharm 2017;70(6):435-42. (PMID: 29299003).

25. Basheti IA, Al-Qudah RA, Obeidat NM, Bulatova NR. Home medication management review in outpatients with chronic diseases in Jordan: a randomized control trial. Int J Clin Pharm 2016;38(2):404-13. (PMID: 26960406).

RESEARCH

PREVALENCE AND TREATMENT APPROACHES OF IMPACTED TEETH IN OLDER ADULTS

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2020.191
2020; 23(4): 524-533

Hasan Onur ŞİMŞEK[1]
Gökhan ÖZKAN[2]
Umut DEMETOĞLU[1]

CORRESPONDANCE

[1]Hasan Onur Şimşek

Aydın Adnan Menderes University, Faculty of Dentistry, Oral and Maxillofacial Surgery, Aydın, Turkey

Phone: +90256 2133939
e-mail: hasanonursimsek@gmail.com

Received: Aug 04, 2020
Accepted: Nov 10, 2020

[1] Aydın Adnan Menderes University, Faculty of Dentistry, Oral and Maxillofacial Surgery, Aydın, Turkey

[2] Aydın Adnan Menderes University, Faculty of Dentistry, Oral and Maxillofacial Radiology, Aydın, Turkey

Abstract

Introduction: The primary aim of our study was to identify the problems caused by impacted teeth and to discuss treatment alternatives in older adults. The secondary aim of the study was to investigate the presence, frequency, and position of impacted teeth in older adults and to investigate the reasons for impaction.

Materials and Methods: The study included 79,733 patients who were admitted to the Aydın Adnan Menderes University, Faculty of Dentistry since December 2013. From these patients, 8,670 panoramic radiographs of patients aged 60 years and older were evaluated retrospectively.

Results: The most common impacted teeth were the third molar (453, 77.3%), canine (109, 18.6%), and premolar (13, 2.2%). There was a statistically significant difference between the presence of an impacted tooth and the outcome of treatment ($p<0.001$). Of the (216, 51.8%) patients for whom surgical tooth extraction was prescribed, (159, 38.1%) underwent extraction, while (57, 13.7%) patients refused treatment.

Conclusions: Routine follow-up should be recommended for asymptomatic teeth that do not cause significant problems in the adjacent teeth and surrounding tissues instead of prophylactic extraction in all age groups, especially in older adults.

Keywords: Tooth, Impacted; older adults; Radiography, Panoramic

INTRODUCTION

Advanced age is a physiological condition that causes social and health problems worldwide. Nowadays, significant changes are observed in population distribution charts. The overall progress of medical methods and living conditions has led to an increase in the average life span, especially in developed countries. According to the World Health Organization (WHO) and the United Nations (UN), the age group of 60 and over is considered older adults. By 2050, it is estimated that over 12% of people in the world will fit into this age group (1, 2). In certain areas of our territory, there are places where the older adults lives more longer in Turkey. This means older adults need more specific attention. It is necessary to plan required treatments while considering the physical and mental limitations of older adults, as well as their quality of life and needs (3).
For older adults who are still active, special dental treatments may be needed to provide function, phonation, and aesthetics. A number of surgical procedures may be required to regain the function of mastication in the elderly. In this study, reliable diagnosis, treatment concepts, and possible outcomes will be discussed for impacted teeth with different clinical characteristics. The sample size of the patient group differs from other studies in terms of searching for a diagnosis and treatment approaches. In the present study, the frequency of impacted teeth can be determined in older adults, and, at the same time, the clinician will learn treatment alternatives that can be administered in the presence of impacted teeth in older adults.

MATERIALS AND METHODS

The study included 79,733 patients who were admitted to the Aydın Adnan Menderes University, Faculty of Dentistry since December 2013. Among these patients, 8,670 panoramic radiographs of patients aged 60 years and older were evaluated retrospectively. The study was designed retrospectively in accordance with the principles of the Helsinki Declaration. The approval for the study was obtained from the Clinical Research Ethics Committee of Aydın Adnan Menderes University, Faculty of Dentistry (approval no.: ADÜDHF 2017-014).

Panoramic radiographs and demographic information such as age, gender, and systemic diseases of patients were obtained from patient records. The count and number of impacted teeth on the first panoramic radiographs of the patients were recorded. The position and depth of the impacted teeth, the presence of adjacent teeth, and the problems and pathological conditions of the impacted teeth and adjacent teeth, if any, were determined.

The depth of the impacted teeth according to the alveolar bone level was recorded as mucosa, partially impacted, or complete bone retention based on the enamel-cement boundary. The depth of impacted teeth to the occlusal plane was recorded according to the classification of Quek et al.: Class A, not impacted in bone, or the occlusal plane of the impacted tooth is at the same level as the adjacent tooth; Class B, partially impacted in bone, or the occlusal plane of the impacted tooth is between the occlusal plane and the cervical line of the adjacent tooth (if any part of the cementoenamel junction was lower than the bone level); or Class C, completely impacted in bone, or the occlusal plane of the impacted tooth is apical to the cervical line of the adjacent tooth (4). The angulations of impacted teeth were determined according to two lines drawn along the longitudinal axes of the impacted teeth and the sagittal plane. These were classified as vertical, mesioangular, horizontal, distoangular, buccolingual, and ectopic (other), based on Winter's classification (5, 6).

The patients' examination records and treatment procedures along with the demographic and descriptive data were analyzed. The treatment planned and administered for impacted teeth were noted from the patient records. The data were analyzed using the statistical software package SPSS 20.0 (Armonk, NY, IBM Corp.). Descriptive statistics were given as numbers and percentages. To determine the correlation between categorical variables,

Pearson's chi-squared test was performed. A p-value of <0.05 was considered statistically significant.

RESULTS

The mean age of the 8,670 patients aged 60 years and older included in the study was 66.23 years (std. error = 0.312). In the study, 179 (3.99%) of the 4,480 female patients and 238 (5.68%) of the 4,190 male patients had at least one impacted tooth. A total of 586 impacted teeth were detected, including at least one impacted tooth in 417 of the 8,670 patients participating in the study.

According to the International Classification of Diseases (ICD-11) endorsed by the WHO, of the 417 patients, 268 (64.2%) had circulatory system diseases and 126 (30.2%) had endocrine and metabolic disorders.

The most common impacted teeth were the third molars (453, 77.3%), canines (109, 18.6%), premolars (13, 2.2%), and other teeth (11, 1.9%). In the distribution of teeth by gender, there were 173 impacted maxillary teeth in the females and 144 impacted maxillary teeth in the males, while there were 73 impacted mandibular teeth in the females and 196 impacted mandibular teeth in the males. The distribution of teeth according to their numbers is shown in detail in Table I.

The effect of gender on impacted teeth was analyzed in terms of the presence of problems. Of the 179 female patients with impacted teeth, 42.5% had problems, while 57.5% didnot have problems. Of the 238 male patients with impacted teeth, 48.7% had problems, while 51.3% did not have problems. There was no statistically significant relationship between the presence of problems in impacted teeth, the depth of the impacted teeth, the angulation of the impacted teeth, treatment, and gender. Of the patients with impacted mandibular teeth, 71.8% were male and 28.2% were female, while of the patients with impacted maxillary teeth, 47.6% were male and 52.4% were female. There was a statistically significant difference between the type of impacted teeth (whether mandibular or maxillary) and gender (p<0.001) (Table II).

In the study, 288 patients had one impacted tooth, while 129 patients had more than one impacted tooth. The highest number of impacted teeth was five in one patient. There was no statistically significant relationship between the count of impacted teeth and gender (p=0.598). When the impaction depth and angulations of the teeth were

Table 1. Distribution of impacted tooth numbers by gender

Maxillary teeth number	Distribution			Mandibular teeth number	Distribution		
	Female	Male	Total		Female	Male	Total
13	29	17	46 (7.8%)	33	5	4	9 (1.5%)
15	2	0	2 (0.3%)	35	1	0	1 (0.2%)
18	46	47	93 (15.9%)	38	37	92	129 (22%)
21	1	0	1 (0.2%)	43	3	3	6 (1%)
23	33	15	48 (8.2%)	44	0	2	2 (0.3%)
25	1	2	3 (0.5%)	45	4	1	5 (0.9%)
28	57	61	118 (20.1%)	48	22	91	113 (19.3%)
sup	4	42	6 (%1)	sup	1	3	4 (0.7%)
TOTAL	**173**	**144**	**317 (%54)**	**TOTAL**	**73**	**196**	**269 (%46)**

Table 2. Data distribution table of impacted teeth by gender

Female n (%)		Gender		
		Male n (%)	p value	
Impacted Tooth Problem - Pathology	Yes	76 (42.5)	116 (48.7)	0.203
	No	103 (57.5)	122 (51.3)	
Treatment	Extraction	45 (25.1)	78 (32.8)	0.104
	Follow-up	114 (63.7)	144 (60.5)	
	Refusal of Treatment	20 (11.2)	16 (6.7)	
Impacted Tooth Mandible-Maxilla Classification	Mandible	46 (28.2)	117 (71.8)	< 0.001
	Maxilla	133 (52.4)	121 (47.6)	
Depth of Impacted Tooth	A	11 (6.1)	22 (9.2)	0.226
	B	40 (22.3)	64 (26.9)	
	C	128 (71.5)	152 (63.9)	
Angulation of Impacted Tooth	Vertical	54 (30.2)	64 (26.9)	0.869
	Mesioangular	67 (37.4)	82 (34.5)	
	Distoangular	23 (12.8)	36 (15.1)	
	Horizontal	24 (13.4)	38 (16)	
	Ectopic	8 (4.5)	14 (5.9)	
	Buccolingual	3 (1.7)	4 (1.7)	

analyzed, it was found that 165 (28.2%) teeth were vertical, 196 (33.4%) teeth were mesioangular, 80 (13.7%) teeth were distoangular, 100 (17.1%) teeth were horizontal, 31 (5.3%) teeth were ectopic, and 14 (2.4%) teeth were buccolingual. In terms of the depth of the impacted tooth, 46 (7.8%) teeth had mucosal retention without bone retention, 149 (25.4%) teeth had partial bone retention, and 391 (66.7%) teeth had bone retention (TableIII).

When the clinical and radiological findings of the impacted teeth were analyzed, no complications were observed in 323 (55.1%) teeth, while various problems were observed in 263 (44.9%) teeth. In terms of the complications of impacted teeth, it was found that 72 teeth were carious, 38 teeth were exposed into the mouth due to the use of a prosthesis, 67 teeth had pericoronitis, 52 teeth had an enlarged follicle, 16 teeth had cystic formations, and 18 teeth were malposed and microdontic. Of the teeth adjacent to the impacted teeth, 51 were carious and had root resorption and periodontal problems due to impacted teeth. The most common indications for impacted tooth extraction were pericoronitis in 53 (33.3%) teeth, caries in 38 (23.9) teeth, and prosthetic exposure in 28 (17.6%) teeth. Table 4 shows the distribution of problems and treatments of the impacted and adjacent teeth (TableIV).

When all the treatments administered to the patients due to impacted teeth were analyzed, it was found that the patients had indications for extraction or follow-up with a clinician. Of the 216 (51.8%) patients for whom surgical tooth extraction was prescribed, 159 (38.1%) underwent extraction, while 57 (13.7%) patients refused treatment. The decision not to extract was made for 370 patients, and those teeth were followed up on.

Table 3. Descriptive data of impacted teeth

	Description	Frequency	Percent %
Number of Impacted Teeth	1	288	69.1
	2	100	24.0
	3	19	4.6
	4	9	2.2
	5	1	0.2
	Total	417	100.0
Impacted Teeth Position-Angulation	Vertical Position	165	28.2
	Mesioangular Position	196	33.4
	Distoangular Position	80	13.7
	Horizontal Position	100	17.1
	Ectopic Position	31	5.3
	Buccolingual Position	14	2.4
	Total	586	100.0
Impacted Teeth Position-Bone	A: Not bony impacted	46	7.8
	B: Partially impacted	149	25.4
	C: Bony impacted	391	66.7
	Total	586	100.0

There was a statistically significant relationship between the presence of impacted tooth problems and the treatment outcome ($p<0.001$). Of the patients with impacted tooth problems, 59.7% underwent extraction, 22.4% were followed up on, and 17.9% refused treatment. Clinician follow-up was performed for the 311 (96.3%) impacted teeth without a problem. Problems were observed in 89.1% of the cases with an impacted tooth at the depth of the mucosa level, 71.3% of the cases with partial bone retention, and only 29.7% of the impacted teeth at the depth of bone level, and there was a statistically significant relationship ($p<0.001$). In terms of the mandibular-maxillary distribution of the impacted teeth and the presence of a problem, problems were detected in 59.4% of the impacted maxillary teeth and 48.9% of the impacted mandibular teeth, and there was a statistically significant relationship ($p=0.005$) (TableV).

DISCUSSION

When the current population data are analyzed, it shows that our geriatric population is rapidly increasing. It is extremely important to regain the functions of oral and surrounding tissues in order to increase the quality of life and awareness levels of older adults, as well as their participation in their social environments. Missing teeth are the most common clinical condition in the geriatric group (7). Because of the resultant increase in quality of life and sociocultural developments, dental rehabilitation needs to become more significant in this age group of patients. The examinations performed on our older adults showed that some patients were

Table 4. Presence of problem in impacted and adjacent teeth

Extraction		Treatment			Total	p value
		Clinician Follow-up	Refusal of Treat-ment			
Presence of impacted tooth problem	Caries	38(23.9%)	14(3.7%)	20(35%)	72(%12.3)	<0.001
	Prosthetic exposure	28(17.6%)	8(2.1%)	2(3.5%)	38(%6.5)	
	Pericoronitis	53(33.3%)	2(0.5%)	12(21%)	67(%11.4)	
	Enlarged follicle	11(6.9%)	30((8.1%)	11(19.2%)	52(%8.9)	
	Dentigerous cyst	14(8.8%)	0(0%)	2(3.5%)	16(%2.7)	
	Microdontia-Malposed	13(8.1%)	5(1.3%)	0(0%)	18(%3)	
	None	2(1.2%)	311(84%)	10(17.5%)	323(%55.1)	
Total		159	370	57	586	
Presence of adjacent tooth problem	Caries	6(3.7%)	3(0.8%)	3(5.2%)	12(2.0%)	0.029
	Root resorption	5(3.1%)	9(2.4%)	3(5.2%)	17(2.9%)	
	Periodontal problem	10(6.2%)	10(2.7%)	2(3.5%)	22(3.8%)	
	None	138(86.7%)	348(94%)	49(85.9%)	535(91.3%)	
Total		159	370	57	586	

aware of their impacted teeth and that others were unaware of them.

The primary aim of our study was to identify the problems caused by impacted teeth and to discuss treatment alternatives in older adults. The secondary aim of the study was to investigate the presence, frequency, and position of impacted teeth in older adults and to investigate the reasons for impaction. In the literature, most studies on impacted teeth include all age groups, not older adults alone (6, 8). The present study evaluated the impacted tooth status of only older adults. There are few studies specifically on impacted teeth in older adults (2, 9, 10). In their study on edentulous patients, Miloglu et al. (11) reported that 16 (5.6%) of 283 patients had impacted teeth. This study also examined other dental problems along with impacted teeth. Hastar et al. (10) reported that 6 of 106 (%5.7) patients over 60 years of age had impacted teeth. Canines and third molars are the most commonly encountered impacted teeth. Trybek et al. (2) found the prevalence of impacted teethto be 1.2% in older adults. The inclusion of only patients undergoing surgical procedures in the study may have contributed tothe low prevalence. The number of patients (8,670) included in our study is quite high compared to other studies. The prevalence of impacted teeth in older adults in our study (4.8%) was consistent with the general literature.

Another parameter that we examined in our study is the position of impacted teeth in the bone, since in most cases, eruption problems may occur in teeth that are not in their normal position (12). Pathological conditions may also occur in impacted teeth, leading to tooth position abnormalities. Despite the presence of various classifications, there is no tooth position classification that includes all teeth. Most studies on impacted teeth include impacted third molars, which are the most commonly encountered impacted teeth (13). In our study, we determined the positions of the teeth in the bone using the Pell and Gregory classification to deter-

mine tooth depth and Winter's classification to determine angular positioning. These are the most commonly used classifications in the literature for impacted teeth. Hashemipour et al. evaluated the position of impacted third molars based on the classification of Pell and Gregory and Winter. In their study, the authors reported that the most common angulation of impaction in the mandible was mesioangular impaction (48.3%), the most common angulation of impaction in the maxilla was vertical impaction (45.3%), and impaction in level IIA was the most common in both the maxilla and the mandible (14). Quek et al. (4) suggested that the mesioangular impaction of the mandibular third molar was the most common type of impaction (60%). In our study, all impacted teeth were examined, and the majority of the impacted teeth were the third molars, with the most common impaction in the mesioangular position. Examination of the eruption depth revealed that the most common type of impacted tooth was an impacted tooth with bone retention.

It can be predicted that bone retention that is too deep reduces the risk of complications in older adults. The extraction requirement for teeth with partial bone or mucosal retention may be high due to the potential of complications. This is thought to be related to the longer duration of prosthesis use by these patients and the exposure of impacted teeth in the mouth as a result of increased bone destruction and changes in the oral mucosa with ageing. Most of the symptomatic pathological problems caused by the third molars occur as a result of a partially erupted tooth. The problems associated with a complete bony impaction have a lower incidence.

Impacted teeth may cause pathologies both in themselves and in the adjacent teeth and surrounding tissues. Examples of such pathologies include root resorption of adjacent teeth, periodontal disease, pericoronitis, dental caries, odontogenic cysts and tumors, teeth under dental prostheses, jaw fracture, unexplained pain, and intracoronary resorption (2, 4, 8, 15–18). In a study, Gisakis et al. (8) reported that the following pathologies associated with impacted teeth occurred in all age groups: (a) caries of the impacted and/or adjacent teeth (93 cases, 9.9 %); (b) periodontal bone loss of the adjacent tooth more than 5 mm below the cementoenamel junction (242 cases, 25.7%); (c) root resorption of the adjacent tooth (183 cases, 19.5%); (d) an increase in the pericoronal space of the dental follicle more than 4 mm around the impacted tooth (116 cases, 12.3%); and (e) orthodontic complications. In our study, caries, prosthetic exposure, pericoronitis, enlarged

Table 5. Distribution of impacted tooth problems

Yes n (%)		Impacted Tooth Problem – Pathology		
		No n (%)	p value	
Treatment – Outcome	Extraction	157 (59.7)	2 (0.6)	< 0.001
	Follow-up	59 (22.4)	311 (96.3)	
	Refusal of Treatment	47 (17.9)	10 (3.1)	
Depth of Impacted Tooth	A	41 (89.1)	5 (10.9)	< 0.001
	B	106 (71.1)	43 (29.9)	
	C	116 (29.7)	275 (70.3)	
Impacted Tooth Mandible-Maxilla Classification	Mandible	137 (52.1)	131 (40.6)	0.005
	Maxilla	126 (47.9)	192 (59.4)	

dental follicles, cysts, malposition, and tooth shape anomalies were observed in the impacted tooth, while the pathological conditions associated with the tooth adjacent to the impacted tooth included caries, root resorption, and periodontal problems. These pathological conditions were found to be consistent with the general literature.

However, not every problem seen in impacted teeth is an indication for extraction. Older adults tend to be more medically complex and have higher risks associated with invasive treatments. Older adults requesting certain procedures can often invoke ethical dilemmas in which patient autonomy seemingly challenges nonmalfeasance or "do not harm" (19). A compilation of treatment options for impacted teeth is presented to assist dentists in discussing the sequelae of impacted teeth as well as the complications of treatment with their patients. A differential diagnosis for an impacted tooth is not possible without clinical assessment. The treatment options for the management of impacted teeth are categorized into four options: observation, intervention, relocation, and extraction (20). A surgical extraction is recommended when local factors are favorable. Trybek et al. stated that the indications for surgical extractions included prosthetic reasons (72%), pain symptoms related to pericoronal infection or a difficult tooth eruption process (22%), or caries (6%) (2).

In the present study, 10% of patients refused treatment or did not come to their appointment. Ikebe et al. (21) recommended different treatment options to their patients with missing teeth. According to this study, older adults generally preferred safer and simpler procedures. The risk of possible complications should be considered in surgical extraction in patients above 60 years (2, 22). Most of the complications associated with surgical extraction are postoperative problems: for example, alveolar osteitis, postoperative infection, and hematoma (2). With increasing age, various changes can be seen in the bone and, accordingly, in the alveolar bone. Volumetric reductions occur in the cortical and trabecular bones. As a result, the bone may become more brittle. A study by Chuang et al. investigating age as a risk factor showed a higher incidence of complications (18.3%). The most common complications were alveolar osteitis (7.4%), inferior alveolar nerve injury (1.6%), unexpected trismus (1.2%), and postoperative infection (1.1%) (23). The weakening of the mandible as a result of a reduction in bone elasticity during ageing may be the cause of the greater incidence of intraoperative fractures reported among patients in the fifth decade (24). For high-risk extractions (in older adults, with deep bony impaction, or with the presence of associated pathology), it may be necessary to offer specific diet instruction for at least four weeks postoperatively (24). The general contraindications for the extraction of impacted teeth can be grouped into three primary categories: advanced patient age, poor health, and surgical damage to adjacent structures (13). Some limitations of the study include a lack of knowledge about whether and how many of the patients' impacted teeth were extracted in the preadmission period and the carrying out of radiological examinations through panoramic radiographs.

CONCLUSION

While planning treatment approaches for impacted teeth in older adults who have multiple diseases and cannot manage their care, clinical problems should be considered. When impacted teeth remain in the mouth for a long time, it may cause various problems. However they can also stay in the jaws without any problems for many years. Routine follow-up should be recommended for asymptomatic teeth that do not cause significant problems in the adjacent teeth and surrounding tissues instead of prophylactic extraction in all age groups, especially older adults.

REFERENCES

1. United Nations, Deparment of Economic and Social Affairs, Population Division. World population prospects: The 2015 revision, Key Findings and Advance Tables. United Nations New York; 2015. [Internet]. Available from: https://population.un.org/wpp/Publications/Files/Key_Findings_WPP_2015.pdf. Accessed: 23.03.2020.
2. Trybek G, Chruściel-Nogalska M, Machnio M et al. Surgical extraction of impacted teeth in elderly patients. A retrospective analysis of perioperative complications–the experience of a single institution. Gerodontology 2016; 33: 410-415 (PMID: 25643646).
3. Hashemipour MA. Dental management and oral complications in elderly. Turkish Journal of Geriatrics 2009; 12(4): 198-201.
4. Quek S, Tay C, Tay K, Toh S, Lim K. Pattern of third molar impaction in a singapore chinese population: A retrospective radiographic survey. International Journal of Oral and Maxillofacial Surgery 2003; 32: 548-552 (PMID: 14759117).
5. Hou R, Kong L, Ao J et al. Investigation of impacted permanent teeth except the third molar in chinese patients through an x-ray study. Journal of Oral and Maxillofacial Surgery 2010; 68: 762-767 (PMID: 20307762).
6. Msagati F, Simon EN, Owibingire S. Pattern of occurrence and treatment of impacted teeth at the Muhimbili National Hospital, Dar es Salaam, Tanzania. BMC Oral Health 2013; 13: 37 (PMID: 23914842).
7. Uzun H, Nazlıel Çelenligil H. Medical, dental history and extraoral, intraoral and dental findings in the elderly. Turkish Journal of Geriatrics 2000; 3: 15-21(in Turkish).
8. Gisakis IG, Palamidakis FD, Farmakis ETR, Kamberos G, Kamberos S. Prevalence of impacted teeth in a Greek population. Journal of Investigative and Clinical Dentistry 2011; 2: 102-109 (PMID: 25426603).
9. Doğan BG, Gökalp S. Tooth loss and edentulism in the Turkish elderly. Archives of Gerontology and Geriatrics 2012; 54: e162-e66 (PMID: 22293677).
10. Haştar E, Yılmaz H, Orhan H. Findings from panoramic radiographs on the edentulous elderly patients. SDU The Journal of Health Science 2010; 1: 82-87 (in Turkish).
11. Miloglu Ö, Yasa Y, Bayrakdar I, Gungor H. Panoramic radiographic examination in a group of edentulous patients. J Dent Fac Atatürk Uni 2012; 22: 230-234 (in Turkish).
12. Şimşek HO, Kömerik N, Koca CG. Differences and similarities of third molar impaction in the mandible and in the maxilla. Journal of International Oral Health 2017; 9: 258-264 (DOI: 10.4103/jioh.jioh_150_17).
13. LJ Peterson. Principles of management of impacted teeth. In: Peterson LJ EEI, Hupp JR, Tucker MR (Eds). Contemporary Oral and Maxillofacial Surgery. 4th edition, CV Mosby, St. Louis, USA 2003, pp 184-213.
14. Hashemipour MA, Tahmasbi-Arashlow M, Fahimi-Hanzaei F. Incidence of impacted mandibular and maxillary third molars: A radiographic study in a southeast Iran population. Med Oral Patol Oral Cir Bucal 2013; 18: e140 (PMID: 23229243).
15. Şimşek-Kaya G, Melih-Ömezli M, Yapici G, Dayi E, Ertaş U. Prevalence of impacted premolars in a Turkish population and considerations for surgical treatment. Med Oral Patol Oral Cir Bucal 2011; 16: e781-6 (PMID: 21196868).
16. Özden B, Acikgoz A. Prevalence and characteristics of intracoronal resorption in unerupted teeth in the permanent dentition: A retrospective study. Oral Radiology 2009; 25: 6 (DOI: 10.1007/s11282-009-0003-3).
17. Patil S, Halgatti V, Khandelwal S, Santosh B, Maheshwari S. Prevalence of cysts and tumors around the retained and unerupted third molars in the Indian population. Journal of Oral Biology and Craniofacial Research 2014; 4: 82-87 (PMID: 25737923).
18. Yıldırım D, Şimşek HO, Karaturgut UE, Kapucuoğlu FN. Hypoesthesia due to a dentigerous cyst: A case report. Balıkesir Health Science Journal 2013; 2(2): 125-127 (in Turkish)
19. Wang TT, Wolff MS, Panchal N. The graying of America: Considerations and training needs for geriatric patient care. Journal of Oral and Maxillofacial Surgery 2019; 77: 1741-1742 (PMID: 31002788).
20. Frank CA. Treatment options for impacted teeth. The Journal of the American Dental Association 2000; 131: 623-632 (PMID: 10832256).
21. Ikebe K, Hazeyama T, Ogawa T et al. Subjective values of different age groups in japan regarding treatment for missing molars. Gerodontology 2011; 28: 192-196 (PMID: 20545773).
22. Baensch F, Kriwalsky MS, Kleffmann W, Kunkel M. Third molar complications in the elderly—a matched-pairs analysis. Journal of Oral and Maxillofacial Surgery 2017; 75: 680-686 (PMID: 28011325).

23. Chuang S-K, Perrott DH, Susarla SM, Dodson TB. Age as a risk factor for third molar surgery complications. Journal of Oral and Maxillofacial Surgery 2007; 65: 1685-1692 (PMID: 17719384).

24. Bodner L, Brennan PA, McLeod NM. Characteristics of iatrogenic mandibular fractures associated with tooth removal: Review and. analysis of 189 cases. British Journal of Oral and Maxillofacial Surgery 2011; 49: 567-572 (PMID: 20947226).

RESEARCH

A VALIDITY AND RELIABILITY STUDY OF THE TURKISH VERSION OF THE AMBIVALENT AGEISM SCALE

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2020.192
2020; 23(4): 534-545

Ahu ÖZTÜRK[1]
Leman Pınar TOSUN[1]
Gamze ÖZDEMİR[2]
Merve ÇAVUŞOĞLU[1]
Kenan ALPARSLAN[3]
Dilan POLAT[4]
Sercan KARLIDAĞ[5]
Anıl KABLANOĞLU[6]
Muharrem Ersin KUŞDİL[1]

CORRESPONDANCE

[1]Muharrem Ersin KUŞDİL

Bursa Uludağ University, Faculty of Arts & Sciences, Department of Psychology, Bursa, Turkey

Phone: +902242941871
e-mail: mekusdil@uludag.edu.tr

Received: Jul 31, 2020
Accepted: Dec 06, 2020

[1] Bursa Uludağ University, Faculty of Arts & Sciences, Department of Psychology, Bursa, Turkey

[2] Çanakkale Onsekiz Mart University, Faculty of Arts & Science, Department of Psychology, Çanakkale, Turkey

[3] Muş Alparslan University, Faculty of Arts & Science, Department of Psychology, Muş, Turkey

[4] Bartın University, Faculty of Literature, Department of Psychology, Bartın, Turkey

[5] Altınbaş University, School of Economics, Administrative and Social Sciences, Department of Psychology, İstanbul, Turkey

[6] Süleyman Demirel University, Faculty of Arts & Sciences, Department of Psychology, Isparta, Turkey

Abstract

Introduction: This study aimed to assess the psychometric properties of the Turkish version of the Ambivalent Ageism Scale, which measures 2 forms of ageism, namely benevolent and hostile ageism.

Materials and Methods: Data were collected from 222 adults through an online survey. Participants completed Turkish versions of the 13-item Ambivalent Ageism Scale and the Implicit Association Test adapted for ageism. Construct validity was assessed through confirmatory factor analyses. Internal consistency and split-half consistency were also calculated. Criterion validity was assessed by correlating ambivalent ageism and its subscales with implicit ageism scores.

Results: The results of confirmatory factor analysis of 12-items confirmed the original structure by exhibiting a good fit to the data (goodness of fit index = 0.93, $p < .001$, comparative fit index = 0.97, and root mean square error of approximation = 0.07). Internal consistency of the Ambivalent Ageism Scale and its 2 subscales were found to be satisfactory, with Cronbach's alpha being .89 for benevolent ageism (9 items), .79 for hostile ageism (3 items), and .89 for the total scale. Scale had a high split-half reliability coefficient (0.95). Implicit ageism positively correlated with ambivalent ageism (total score) and both benevolent ageism and hostile ageism (.22, .21, and .16, respectively). Except for cognitive assistance/protection, which was a sub-factor of benevolent ageism, no age and gender difference was found in any of the ageism scores.

Conclusion: It was decided that the Turkish version of the Ambivalent Ageism Scale is a valid and reliable measure of negative attitudes toward older adults.

Keywords: Ageism; Prejudice; Attitude; Reproducibility of Results

INTRODUCTION

Despite the increase in their lifespan in most countries of the world, including Turkey (1, 2), older adults continue to be viewed in a negative light; both in social life (3) and scientific literature (4) older adulthood is viewed as if it is associated with sickness, physical/mental deterioration, and closeness to death. This stereotyping, which ignores the substantial variation in several characteristics in aged individuals, ranging from physical condition to mental competencies, is called "ageism" (5). Ageism has not attracted as much attention as sexism and racism among researchers, and its existence and effects have not been made fully visible (6). Ageism is not always "hostile" and does not always cause "active harm." Ageism can also include "protectionist" behaviors, including "active facilitatory behaviors" (e.g., excessive/unwanted help) and "passive harm" (e.g., social exclusion) (7, 8). The first is referred to as "hostile ageism" (HA) and can be explained as antipathy toward older adults (6, 9). The latter is referred to as "benevolent ageism" (BA), and is characterized by patronizing behaviors (7, 9). Because the protective attitudes and behaviors are evaluated positively by most individuals, it can be more difficult to address the benevolent forms of ageism and their negative consequences (7, 10). Therefore, drawing exclusively upon the literature on sexism, Carry, Chasteen and Remedios differentiated the protective form from the hostile and named this as "ambivalent ageism" (AA), by combining benevolent and hostile prejudices. AA is assumed to arise out of the co-presence of both hostile and benevolent prejudices, similar to ambivalent sexism (7).

Carry, Chasteen, and Remedios have recently developed a 13-item Ambivalent Ageism Scale (AAS) in two studies and demonstrated that the scale had a two-factor structure (HA and BA) (7,10). In the first study, HA predicted belief that older adults were cold and incompetent, whereas BA predicted evaluations of older adults as warm. It was also found that participants with high BA but low HA were likely to view older adults as warm and less competent, confirming the idea that, similar to sexism, there are two forms of ageism, and that AAS is successful in measuring these elusive forms independently. Other studies that have used the AAS have demonstrated a positive correlation between employees' AA scores (total score for 13 items) and their attitudes toward the employment of older adults. Furthermore, AA has been found to be higher in youth and women, but has not been found to be related to educational level (11). In addition, BA has been observed to lead to a perception of behaviors toward older adults as just, even if they are not (10). In a recent study in Turkey, AA was found to be related to social identity motivations and predicted by belonging to a young group (12). One of the findings of a study using the visual screening task showed that adult participants (aged between 19 to 27) devoted less time for looking at older faces than the younger ones, implying that ageism may also have a physiological basis (13).

Another explanation regarding the elusive nature of ageism suggests that ageism is an "implicit attitude" (14). The measures of AA that are currently used in most prejudice research are generally based on self-reports and evaluate prejudices as "explicit attitudes" resulting from conscious, intentional, and controllable cognitive processes. "Implicit" attitude measures capture uncontrolled automatic cognitive processes (15). The most important advantage of an implicit measure is that, by limiting the participant's control over his/her responses, they produce results that are relatively free from social desirability and impression management strategies (16, 17). The Implicit Association Test (IAT) is the most commonly used instrument for measuring prejudice against groups such as people of African descent, women, and older adults (16). Past studies on ageism generally agree that young people are evaluated very positively, whereas older adults are perceived more negatively (18). In an online study of 70,000 people of various ages, it was found that implicit ageist attitudes, including those of older adults themselves,

were among the most common of all prejudiced attitudes and were much higher in magnitude than explicit ageist attitudes (14).

Current research on ageism in Turkey is predominantly based on explicit attitude scales that measure hostile ageist attitudes toward older adults. Although the prevalence of positive attitudes toward older adults is quite high (19), findings showing that even medical students do not prefer to work in geriatric clinics (20) and that nurses experience difficulties communicating with older adult patients (21) indicate that ageist attitudes cannot be fully captured with explicit attitude scales that focus primarily on the hostile form of ageism. More sophisticated instruments such as the AAS are needed to prevent the negative social and psychological consequences of ageism.

The aims of this study were as follows: (a) to assess the validity and reliability of the Turkish version of the AAS and (b) to cross-validate the AAS and its HA and BA subscales, using a recently developed implicit measure, namely the IAT.

MATERIALS AND METHODS

1. Study Sample and Procedure

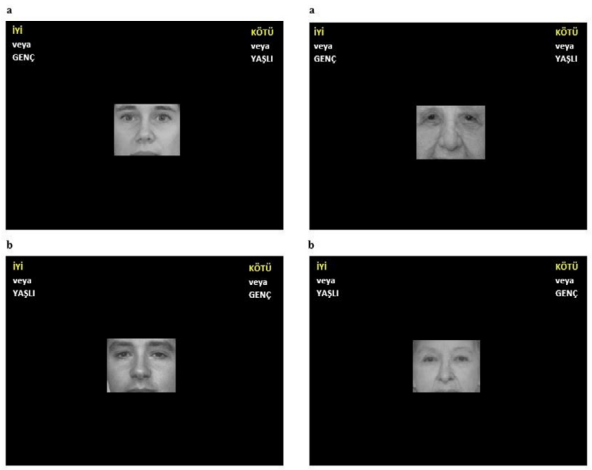
Data from the present study were collected as part of a larger study in which ageism was examined in the context of the coronavirus disease pandemic. The sample consisted of 226 individuals who were snowball-sampled using an online survey tool (Survey Monkey, SVMK Inc., San Mateo, CA, USA) between April and May 2020 in Turkey. After excluding two participants who did not complete the IAT and two others whose error rates and/or durations of response were above the acceptable limit, the final sample included 222 adults (142 women, 80 men; $\bar{x}_{age}$ = 32.93 years, standard deviation [SD] = 11.64). No age difference was found between women ($\bar{x}$ = 31.84, SD = 11.38) and men ($\bar{x}$ = 34.87, SD = 11.90), $t_{(220)}$ = -.1.87, p > .05). All participants completed the IAT (16) adapted for ageism, AAS (7), and sociodemographic questions, along with other scales that were used for other purposes in the online survey form. Participants were not compensated in any form for their participation.

2. Measures

The AAS. The AAS was developed by Cary et al. (7) and consists of nine items on BA and four items on HA. Their study revealed that it is possible to consider BA factor as having two sub-factors: Cognitive assistance/protection (CA/P) and unwanted help (UH). Responses for each item are based on a 7-point Likert scale (1 = Strongly Disagree; 7 = Strongly Agree). The original study reported internal reliability for the BA and HA subscales as α = .89 and α = .84, respectively, and the subscales were found to be highly correlated with each other (r = .62, p < .001). The entire scale also had good internal consistency (α = .91). Test-retest reliability was good for both subscales and the entire scale (r = .76 and .80, respectively). Turkish and English items are given in Appendix A and Appendix B, respectively.

The IAT. The IAT was developed by Greenwald (15,16) to measure implicit prejudice, and for this study participants completed an online version of the IAT for ageism (Inquisit, Millisecond Software, Seattle, WA, USA). The IAT requires the participant to respond as quickly and accurately as possible to seven blocks of stimuli (compatible and incompatible blocks), each consisting of 20 to 40 trials. During these trials, participants were asked to perform a categorization task, in which they sorted pleasant/unpleasant words and photographs of the faces of older/younger individuals (Figure 1). Target words and photographs appeared in the center of the screen, whereas categories are placed on either the left or right top corners. To assign items to the left category, participants pressed the "e" key, and for the right category, they pressed the "p" key. In the present study, the original test photographs of old and young faces and the Turkish versions of the pleasant and unpleasant words were used (for samples of the content, see Figure 1). The IAT produces a d score for the extent of the implicit association that ranges between 2 and -2. The d score indi-

Figure 1. Sample screenshots of the IAT, information about the trials, and examples of the words used.



Block	Number of trials	Phases[c]	Discrimination Task	Key Items	
				Left ('E')	Right ('P')
1	20	P	Face	Young	Old
2	20	P	Word	Pleasant[d]	Unpleasant[e]
3	20	C	Word + Face	Pleasant +Young	Unpleasant + Old
4	40	C	Word + Face	Pleasant + Young	Unpleasant + Old
5	20	P	New keys (switched)	Old	Young
6	20	C	Word + Face	Pleasant + Old	Unpleasant + Young
7	40	C	Word + Face	Pleasant + Old	Unpleasant + Young

Note. Adapted from Inquist Millisecond Software, https://www.millisecond.com/download/library/v5/iat/ageiat/ageiat.web

[a] Sample screens of 4th block; [b] Sample screens of 7th block; [c] P: Practice, C: Critical; [d] Joy (Neşe), Wonderful (Harika), Pleasure (Memnuniyet); [e] Agony (Izdırap), Terrible (Berbat), Awful (İğrenç)

cates the strength of associations (no association: 0-±0.15; low: ±0.15- ±0.35; moderate: ±0.35-±0.65; high ±0.65-±2). A positive score indicates that the participant tends to pair negative attributes more with older adults than with members of younger age groups, and a negative score indicates that the participant tends to pair positive attributes more with older adults than with members of younger age groups.

The IAT has been previously employed in Turkey by some studies using stimuli related to Turkish words (22, 23) and Turkish and Kurdish names (24). Şenyurt, Coşkun and Ünlü has reported that, although it depended on a different computational procedure, an open source Turkish IAT version that they developed had satisfactory psychometric qualities (25). Analyses of the data derived from the IAT in the present study showed that response times for compatible and incompatible blocks had good reliabilities (Cronbach alphas were .90 for each of the first and second compatible blocks; .86 for the first incompatible block and .94 for the second incompatible block).

Sociodemographic questions. The sociodemographic questions form included questions on age, gender, marital status, occupation, place of residence, education, and monthly income.

3. Translation of AAS Items and IAT Words

The words used in the IAT were translated to Turkish by two members of the research team who were native Turkish speakers and competent in English. The AAS items were translated by the same members of the research team and the final form was examined by another member to check for possible inconsistencies.

4. Data Analysis

All analyses were performed using SPSS version 23 (IBM Corp., Armonk, NY, USA) and AMOS (IBM Corp.). Construct validity was assessed through and confirmatory factor analyses. Cronbach alpha coefficients and the split-half reliability analysis were used for assessing the internal consistency. Assessment of criterion validity was done by correlating scores for AA and its subscales with IAT scores. Age and gender differences were examined by t-tests.

5. Ethical Issues

This study was approved by the Ethics Committee of Bursa Uludag University on July 27th, 2020 (reference number: 2020-05). All participants completed questionnaires anonymously after providing their consent online.

Table 1. Sociodemographic characteristics of the sample (N=222)

Variable	Frequency	%
Gender		
Women	142	64
Men	80	36
Age		
19-30 years	119	53.6
31-69 years	103	46.4
Marital status		
Single (unmarried, divorced, or widowed)	141	63.6
Married	81	36.4
Education		
High school or below	96	43.2
College	78	35.1
Graduate school	48	21.7
Occupation		
Student	76	34.2
Blue-collar work	18	8.1
White-collar work	76	34
Self-employment	15	6.9
Not working (unemployed, retired, or homemaker)	37	16.8
Living with a person who is over 65 years of age		
Yes	25	11.3
No	197	88.7
Residence		
Rural or small town	36	16.2
Small city	38	17.1
Large city	148	66.7
Income (monthly)		
Below 4000 ৳	61	27.5
4000-7000 ৳	75	33.8
Above 7000 ৳	86	38.7

RESULTS

Analysis of the sociodemographic characteristics of the sample revealed that the majority of the participants (64%) were women, single (64%), and had a high level of education (57%). Approximately 50% of the participants were actively employed. In addition, more than 75% of respondents resided in urban areas, and less than 12% were living with a relative aged 65 years or over (Table 1).

1. Construct Validity Analyses

First, exploratory factor analyses with two-factor and three-factor solutions were run independently using varimax and direct oblimin rotations. According the result of the analysis with the two-factor solution, one item (item #1) was need to be removed because it was loaded on both factors. On the other hand, according to the analysis with the three-factor solution, two items (items #1 and #13) were needed to be removed as they were loaded on multiple factors. Cary et al (7) suggested AAS neither being a two-factor nor three-factor scale. Rather, they suggested that it is a scale with higher order structure involving two factors (BA and HA), and one of those factors (BA) combining two sub-factors. The first one of BA sub-factors was composed of items measuring to what extent people agree that older adults need cognitive assistance/protection (CA/P), and the second one contained items measuring the agreement with the idea that older adults should be offered unwanted help (UH). In the current study, a higher order confirmatory factor analysis was conducted on 13 items to test Cary et al's (7) findings on AAS's higher order structure.

The cutoff values of a good fit for these indices were selected as >0.90 for the comparative fit index, <0.08 for the root mean square error of approximation, and <2.0 for the ratio of $\chi 2$ to degrees of freedom ($\chi 2$/df). The $\chi 2$/df ratio was preferred because $\chi 2$ statistics are known to be sensitive to sample size.

One item ("Old people are a drain on the health care system and the economy") was removed as it had a poor loading. In addition, four covariances (between the error terms of items 2 and 3, items 4 and 7, items 5 and 6 and items 8 and 9; see Figure 2) were added to the model as suggested by modification indices. The model was then re-tested. Factor loadings for this scale ranged between .62-.72 for UH sub-factor of BA, between .53-.73 for CA/P sub-factor of BA and between .66-.82 for HA (Figure 2). The scale with this higher-order structure had a good fit to the data ($\chi 2$ = 97.40, $\chi 2$/df = 1.99, goodness of fit index = .93, comparative fit index = .97, root mean square error of approximation = .07, and standardized root mean squared error = .04). Construct Reliability (CR) scores for main and sub-factors were all acceptable (.68 for CA/P; .82 for UH; .87 for BA and .79 for HA).

2. Reliability and Correlation Analyses

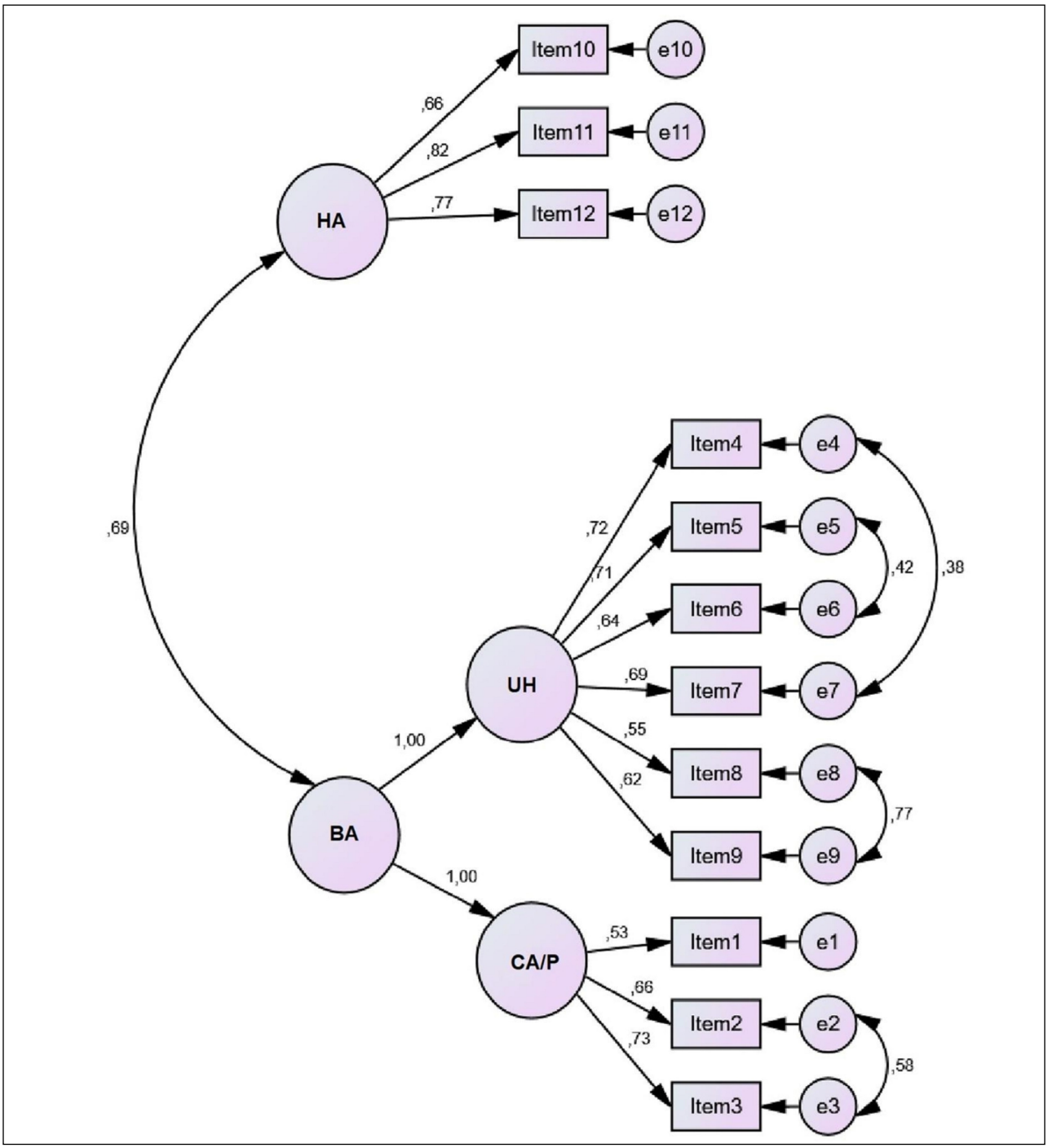
Cronbach's α coefficients with corrected total item correlations and item-total correlations were used to asses internal consistency. Corrected item totals for the entire scale ranged between .49 and .69. The reliability of both BA and HA was satisfactory, with Cronbach's α being .88 for the 9-item BA subscale, .79 for the 3-item HA subscale, and .89 for the entire scale. If any of the items were deleted, Cronbach's α for the entire scale varied between .87 and .89, showing that there was no need to discard any items. Cronbach's α for the two sub-factors of BA were .78 (CA/P) and .86 (UH). The split-half reliability for the two halves (even versus odd numbered items) of the scale was found to be satisfactory (.94).

Pearson correlations were calculated to examine the interrelations between the factors (Table 2). As in the original study, BA and HA were found to be positively correlated, $r = .57$, $p < .001$, two tailed.

3. Criterion Validity

Implicit ageism (IA), which was selected as a criterion for testing the validity of the AAS, was found to be positively correlated with AA (total score) and its subscales (Table 2). The correlation coefficient

Figure 2. Results of the confirmatory factor analysis of the 12-item Turkish version of the AAS.



HA: Hostile ageism, BA: Benevolent ageism, UH: Unwanted help, CA/P: Cognitive assistance/protection

between IA and HA was compared with the correlation coefficient between IA and BA using the interactive calculator developed by Lee and Preacher (26). The results showed that there was no significant difference between them ($z = .82$, $p > .05$).

4. Gender and Age Differences

Gender and age group (young vs. old) differences for the mean values of AA, HA, BA, CA/P, UH and IA were examined through correlation and independent t-test analyses. Age was negatively correlated only with CA/P (Table 2). To examine the age group differences, the sample was divided into two groups based on the sample's median age (30 years; young ≤ 30 years; old > 30 years). Results revealed no significant difference between age groups, whereas there was only one significant gender difference: CA/P score for women was higher than for men, $t_{(220)} = 2.19$, $p < .05$ (Table 3).

Table 2. Intercorrelations of study variables (N = 222)

	1	2	3	4	5	6	7
Age (1)	-	-.06	-.09	-.17**	-.03	.03	.01
Ambivalent ageism(AA) (2)		-	.93***	.82***	.92***	.74***	.22**
Benevolent ageism(BA) (3)			-	.84***	.95***	.57***	.21**
Cognitive assistance/protection(CA/P) (4)				-	.63***	.49***	.15*
Unwanted help(UH) (5)					-	.53***	.21**
Hostile ageism(HA) (6)						-	.16*
Implicit ageism(IA) (7)							-

*p < .05; ** p < .01; *** p < .001.

Table 3. Means and standard deviations of the AA, CA/P, UH, HA and the IAT scores for both gender and age (N=222)

	Gender					Age				
	Women (N =142)		Men (N = 80)			19-30 years (N =119)		31-69 years (N =103)		
	M	SD	M	SD	t	M	SD	M	SD	t
Ambivalent ageism (AA)	3.76	1.24	3.57	1.13	1.10	3.73	1.20	3.64	1.21	0.55
Benevolent ageism (BA)	3.95	1.34	3.63	1.23	1.74	3.90	1.31	3.75	1.31	0.82
Cognitive assistance/ protection (CA/P)	3.43	1.58	2.96	1.44	2.19*	3.43	1.60	3.06	1.47	1.74
Unwanted help (UH)	4.20	1.40	3.96	1.34	1.25	4.13	1.35	4.10	1.41	0.19
Hostile ageism (HA)	3.19	1.36	3.40	1.30	-1.12	3.24	1.36	3.31	1.32	-0.42
Implicit ageism (IA)	0.60	0.38	0.60	0.32	-0.07	0.62	0.32	0.58	0.39	0.86

Note. * p < .05

DISCUSSION AND CONCLUSIONS

Although another version of the AAS has recently been used for other purposes in Turkey (12), the present study is the first to report the psychometric qualities of a Turkish version of the scale in full detail and in relation to an implicit measure, namely the IAT. The study is a promising first step in the process of developing the Turkish version of AAS. The scores for AA, HA, BA, UH, CA/P and IA did not differ between genders and age groups, except for CA/P, suggesting that ageism may be a very common phenomenon across all individuals, as some social psychologists suggest (14). This finding is not consistent with the findings of two studies that did not employ implicit measures (11, 12); however, the general lack of significant differences in AA and IAT scores in relation to both gender and age is more plausible when the latent nature of both ambivalent and implicit forms of ageism are considered. In addition, unrepresentative nature of the present study's sample is somewhat compensated by the fact that the participants were recruited during the coronavirus disease pandemic, an unprecedented event that primed ageist attitudes in the minds of most people.

A final limitation of the present study is that, although AAS has been translated and used in Slovakia (27, 28), Poland (29) and India (30), a comparison of the psychometric qualities of Turkish version with those versions was not possible as detailed psychometric information regarding these applications were not reported in these studies.

We would like to thank Inquisit (Millisecond Software, Seattle, WA, USA) for providing free access to the IAT software during coronavirus disease pandemic.

REFERENCES

1. United Nations, Department of Economic and Social Affairs, Population Division. World Population Ageing 2019 [e-book] UN Publication; 2019. [Internet]. Available from: https://www.un.org/en/development/desa/population/publications/pdf/ageing/WorldPopulationAgeing2019-Highlights.pdf. Accessed: 27.06.2020.
2. Turkish Statistical Institute. Older People in Statistics, 2019. News Bulletin Number: 33712; 18 March 2020. [Internet]. Available from: https://data.tuik.gov.tr/Bulten/Index?p=Elderly-Statistics-2019-33712. Accessed: 09.11.2020.
3. Löckenhoff CE, De Fruyt F, Terracciano A, et al. Perceptions of aging across 26 cultures and their culture-level associates. Psychol Aging 2009; 24(4): 941-54. (PMID: 20025408)
4. N, Raz. The Aging Brain: Structural Changes and Their Implications for Cognitive Aging, In: Roger A. Dixon, Lars Bäckman, Lars-Göran Nilsson (Eds). New Frontiers in Cognitive Aging. 1st edition, Oxford University Press, New York, USA 2004, pp 115-33.
5. Butler RN. Age-ism: Another form of bigotry. Gerontologist 1969; 9(4): 243-6. (PMID: 5366225).
6. North MS, Fiske ST. An inconvenienced youth? Ageism and its potential intergenerational roots. Psychol Bull 2012; 138(5): 982-97. (PMID: 22448913)
7. Cary, LA, Chasteen AL, Remedios J. The ambivalent ageism scale: Developing and validating a scale to measure benevolent and hostile ageism. Gerontologist 2017; 57(2): e27-e36. (PMID: 27520730)
8. Cuddy AJC, Fiske ST, Glick P. The BIAS map: Behaviors from intergroup affect and stereotypes. J Pers Soc Psychol 2007;92 (4): 631-48. (PMID: 17469949)
9. North MS, Fiske ST. A prescriptive, intergenerational-tension ageism scale: Succession, identity, and consumption (SIC). Psychol Assess 2013; 25(3): 706–13. (PMID: 23544391)
10. AL Chasteen, LA Carry, Age Stereotypes and Age Stigma: Connections to Research on Subjective Aging, In: M Diehl, H. W. Wahl (Eds). Annual Review of Gerontology and Geriatrics Subjective Aging: New Developments and Future Directions. 35th edition, Springer Publishing Co, USA 2014, pp 99–119.
11. Búgelová T, Chupková L, Kratochvílová L. Ageism at work across three generations. Cross-Cultural Studies: Education and Science 2019; 4(4): 97-106. (DOI: 10.24411/2470-1262-2019-10067).
12. Taşdemir N. Young group identification and motives as predictors of ageism, aging anxiety, and life satisfaction. J Genet Psychol 2020; 180(4): 1-16. (PMID: 32580665)

13. Cangöz B, Altun A, Aşkar P, Baran Z, Mazman SG. Examining the visual screening patterns of emotional facial expressions with gender, age and lateralization. J Eye Mov Res 2013; 6(4): 1-15. (DOI:10.16910/jemr.6.4.3).

14. Nosek BA, Banaji MR, Greenwald AG. Harvesting implicit group attitudes and beliefs from a demonstration web site. Group Dyn-Theor Res 2002; 6(1): 101-15. (DOI: 10.1037/1089-2699.6.1.101).

15. Greenwald AG, Banaji MR. Implicit social cognition: Attitudes, self-esteem, and stereotypes. Psychol Rev 1995; 102(1): 4-27. (PMID: 7878162)

16. Greenwald AG, McGhee DE, Schwartz JL. Measuring individual differences in implicit cognition: the implicit association test. J Pers Soc Psychol 1998; 74(6): 1464-80. (PMID: 9654756).

17. Greenwald AG, Banaji MR, Rudman LA, Farnham SD, Nosek BA, Mellott DS. A unified theory of implicit attitudes, stereotypes, self-esteem, and self-concept. Psychol Rev 2002; 109(1): 3-25. (PMID: 11863040).

18. Chopik WJ, Giasson HL. Age differences in explicit and implicit age attitudes across the life span. Gerontologist 2017; 57(S2): S169-S177. (PMID: 28854609).

19. Şimşek H, Bahadır H, Bilgin AC. Physicians' attitudes towards the elderly: Ageism in a university hospital in Turkey. Turkish Journal of Geriatrics 2019; 22(1): 101-11. (DOI: 10.31086/tjgeri.2019150579).

20. Köse G, Ayhan H, Taştan S, İyigün E, Hatipoğlu S, Açıkel CH. Determination of the attitudes of students from different department in the field of health on the discrimination against the elders. Gülhane Med J 2015; 57(Suppl 2): 145-51. (in Turkish) (DOI: 10.5455/gulhane.152591).

21. Bulut E, Çilingir D. Attitudes of surgical nurses towards elderly. Turkish Journal of Geriatrics 2016; 19(4): 253-9.

22. Camcı, Y. (2015). The outgroup favoritism phenomenon in veiled and unveiled university students: An analysis of explicit and implicit attitudes via intergroup relations phenomenon. [Unpublished master's thesis, Bursa Uludag University, Bursa, Turkey]. (in Turkish). Available from: https://tez.yok.gov.tr/UlusalTezMerkezi/giris.jsp. Accessed: 10.11.2020.

23. Özdemir, G. (2015). My achievements are not mine: Imposter phenomenon in light of the social identity, social dominance and system justification theories. [Unpublished master's thesis, Bursa Uludag University, Bursa, Turkey]. (in Turkish). Available from: https://tez.yok.gov.tr/UlusalTezMerkezi/giris.jsp. Accessed: 10.11.2020.

24. Alparslan K Kuşdil ME. (in press). Kürt üniversite öğrencilerinin kimlik yönetim stratejileri ve dış-grup tarafgirliğinin kimlikle ilgili eylem ve hedeflerle ilişkileri: Açık ve örtük ölçümlerle bir inceleme. Türk Psikoloji Dergisi.

25. Şenyurt AY Coşkun H Ünlü E S. Örtük çağrışım testi'ni Türkçe'ye uyarlama çalışması. OPUS Uluslararası Toplum Araştırmaları Dergisi-International Journal of Society Researches 2020; 15(26), 1-17. DOI: 10.26466/opus.632149. Available from: https://dergipark.org.tr/tr/download/article-file/1133831. Accessed: 7.11.2020.

26. Lee IA, Preacher KJ. Calculation for the test of the difference between two dependent correlations with one variable in common [Computer software] 2013, September. [Internet] Available from: http://quantpsy.org/corrtest/corrtest2.htm Accessed: 27.06.2020.

27. Búgelová T, Chupková L, Kratochvílová L. Ageism at work across three generations. Cross-Cultural Studies: Education and Science 2019; 4 (4): 97-106. (DOI: 10.24411/2470-1262-2019-10067).

28. Čupková, L, Búgelová T, Fucsková Z. Attitudes towards the employment of seniors depending on the degree of ageism. Work and Organizational Psychology-2018 - Past, Present, and Challenges to The Future International Conference - Proceedings; Košice, Slovakia, 2019; 105–116. (ISBN 978-80-8152-713-5) [Internet] Available from: https://unibook.upjs.sk/img/cms/2019/FF/psychologia-prace-a-organizacie-web.pdf. Accessed: 3.11.2020.

29. Daniel F, Massano I, Galhardo A, Barroso I. Ambivalent and hostile ageism. 27th European Congress of Psychiatry, Warsaw, Poland, 6-9 April 2019. [Internet] Available from: http://repositorio.ismt.pt/bitstream/123456789/1030/1/Poster%20EPA19-Idadismo.pdf. Accessed: 3.11.2020.

30. Pramanik S, Biswal S. Ageism: A comparative study among young adults. IJARnD 2020; 5(5): 14–17. Available from: https://www.ijarnd.com/manuscripts/v5i5/V5I5-1140.pdf. Accessed: 3.11.2020.

Appendix A

Items of Turkish Version of AAS

1. Yaşlı insanlara bazı şeyleri yapmak için artık çok yaşlı olduklarını hatırlatmak iyi bir şeydir; yoksa sonunda başarısız olduklarında duyguları incinebilir.
2. Kendileri isteseler bile yaşlı insanların çalışmasına izin verilmemelidir; çünkü onlar topluma olan borçlarını çoktan ödemiş durumdadırlar.
3. Kendileri isteseler bile yaşlı insanların çalışmasına izin verilmemelidir; çünkü daha narin olduklarından kolayca hastalanabilirler.
4. Yaşlı insanlarla tane tane konuşmak iyidir; çünkü söyleneni anlamaları zaman alabilir.
5. Yaşlılara kötü haber vermekten kaçınılmalıdır; çünkü kolayca duygulanıp ağlayabilirler.
6. Yaşlı insanları toplumun acı gerçeklerinden korumak gerekir; çünkü bunlardan çok etkilenebilirler.
7. İlk seferde hemen anlayamadıkları için, yaşlı insanlara bazı şeyleri tekrar tekrar anlatmak daha iyidir.
8. Kendileri istemese bile, yaşlı insanlara her zaman yardım teklif edilmelidir.
9. Kendileri istemese bile, yaşlı insanlara alışverişlerinde yardım edilmelidir.
10. Yaşlıların çoğu, aslında iyi niyetli söz ya da davranışları yaşlı insanlara yönelik bir hakaret ya da ayrımcılık olarak yorumlarlar.
11. Yaşlı insanlar çok alıngan olurlar.
12. Yaşlı insanlar iş yerlerinde yaşadıkları sorunları abartmayı pek severler.

Appendix B

Items of English Version of AAS

1. It is good to tell old people that they are too old to do certain things; otherwise they might get their feelings hurt when they eventually fail.
2. Even if they want to, old people shouldn't be allowed to work because they have already paid their debt to society.
3. Even if they want to, old people shouldn't be allowed to work because they are fragile and may get sick.
4. It is good to speak slowly to old people because it may take them a while to understand things that are said to them.
5. People should shield older adults from sad news because they are easily moved to tears.
6. Older people need to be protected from the harsh realities of society.
7. It is helpful to repeat things to old people because they rarely understand the first time.
8. Even though they do not ask for help, older people should always be offered help.
9. Even if they do not ask for help, old people should be helped with their groceries.
10. Most old people interpret innocent remarks or acts as being ageist.
11. Old people are too easily offended.
12. Old people exaggerate the problems they have at work.
13. Old people are a drain on the health care system and the economy. (*)

(*) This item, with a factor load below 0.30 on CFA analysis, removed from the Turkish version of AAS.

RESEARCH

EFFECT OF MUSIC THERAPY ON ANXIETY AND SLEEP QUALITY OF GERIATRIC HAEMATOLOGICAL ONCOLOGY PATIENTS

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2020.193
2020; 23(4): 546-554

- Kübra GÖKALP[1]
- Mine EKİNCİ[1]

CORRESPONDANCE
Kübra GOKALP
Atatürk University, Faculty of Nursing,
Erzurum, Turkey

Phone: +904422314556
e-mail: kubragungormus2010@hotmail.com

Received: Jun 01, 2020
Accepted: Nov 10, 2020

[1] Atatürk University, Faculty of Nursing,
Erzurum, Turkey

Abstract

Introduction: Psychiatric symptoms that develop with the diagnosis of cancer are important in terms of affecting the severity of the patient's physical illness. This study was carried out to determine the effect of music therapy on anxiety and sleep quality of geriatric haematological oncology patients.

Materials and Methods: This experimental clinical trial, a pretest-posttest study, was conducted with 60 older hematologic cancer patients. The patients were sorted into control and experimental groups (n = 30 in the control group; n = 30 in the experimental group). Data was collected via a sociodemographic form, the Pittsburgh Sleep Quality Index, and the State-Trait Anxiety Inventory. The participants in the experimental group listened to music every day for one week while the control group was not exposed to any intervention.

Results: There was no statistically significant difference between the pretest Pittsburgh Sleep Quality Index and State-Trait Anxiety Inventory mean scores of the experimental and control groups. Pittsburgh Sleep Quality Index and State-Trait Anxiety Inventory mean score of the experimental group were lower than the control groups'.

Conclusion: The intervention of music therapy was found to have an effect in reducing anxiety and increasing sleep quality of patients. Music therapy can be used as an alternative method of treating the anxiety and increasing the sleep quality of geriatric hematology patients.

Keywords: Nursing; Hematology; Patients; Aged

INTRODUCTION

Cancer, followed by cardiovascular disease as the death cause, is one of the most serious health problems in the world, having adverse physical, psychological, social, and economic effects on individuals, families, and societies (1). According to the World Health Organization (WHO) and the International Agency for Research on Cancer, 18 million people were diagnosed with cancer worldwide in 2018, and 9 million of these cases constituted individuals 65 years and over (1). Hematological cancers constitute more than half of cancers in this age group (2). Although diseases such as leukemia, myeloma, and lymphoma are more likely to be seen in older adults than the young people, studies have concentrated on children because leukemia ranks first among childhood cancers (1).

Age is one of the important determinants of cancer, and the incidence of cancer is increasing as the older population increases (1). The percentage of older adults in Turkey has risen to 9.1%. It is predicted that if the rate of total fertility and death continues in the same way, the percentage of those 65 years old and over will increase to 10.2% in 2023 and 20.8% in 2050 (3). Considering that older patients have more difficulty adapting to environmental changes and innovations compared to younger patients, it could be predicted that the psychological problems of older cancer patients will increase in importance day-by-day (2, 4).

Psychiatric symptoms that develop with the diagnosis of cancer are important in terms of affecting the severity of the patient's physical illness, disease course, treatment response and the patient's quality of life and care (5). Research shows that nearly half of cancer patients have psychiatric disorders that need to be treated, such as anxiety, depression, organic psychiatric disorders, and personality disorders (2, 4). At the same time, sleep disorders are a common but often neglected problem in cancer patients (6). Medical treatments applied to a patient who is struggling with cancer (such as chemotherapy, radiotherapy, or surgical operations) could also be the cause of psychiatric symptoms, such as steroid treatment causing depression (7). Cancer requires holistic care and should receive multidisciplinary treatment (5-7). A consultation liaison psychiatry nurse should work in collaboration with other members of the treatment team, with holistic care given to the patient and their families (8). There are some complementary treatments for psychological symptoms like relaxation therapy, hypnosis, meditation/mindfulness-based stress reduction, yoga and acupuncture which among these the music therapy is also included (9). Music therapy, which is a psychosocial approach, complements the treatment of health problems, such as cancer, and is used as an alternative treatment (9, 10).

Music has been used in hospitals for a variety of reasons from the past to the present. It is known that music affects the areas in the human brain related to emotions such as happiness, joy, anger, and hate and has an important effect on human beings (9, 10). Music influences the limbic system of the brain, modulating endogenous opioids and oxytocin, producing relaxation and well-being; music also accelerates or slows breathing and changes a person's internal state; affects heart rhythm and blood pressure, reduces muscle tension and improves movement and coordination (9). These features of music are considered as therapeutic factors (8-10).

There are limited studies on older patients with hematologic cancers in the Turkish literature (4, 2). Considering the focus on children in previous studies on hematological cancers, this study is important in terms of determining the effectiveness of music therapy on anxiety and sleep quality experienced by older hematologic cancer patients and shedding light on nursing care (11). This study was the first one that explored the effectiveness of the music therapy on geriatric haematological oncology patients in Turkey.

The study hypotheses are as follows:

H1: Music therapy given to geriatric haemato-

Table 1. Demographic status of individuals in experimental and control groups

	Control Group		Experimental Group		
Characteristics	**n**	**%**	**n**	**%**	**p**
Gender					
Female	14	46.7	13	43.3	$\chi^2 = 0.67$
Male	16	53.3	17	56.7	p = 0.795
Marriage status					
Maried	24	80	22	73.4	$\chi^2 = 0.373$
Single	6	20	8	26.6	p = 0.542
Education level					
Primery school	19	63.3	20	66.6	$\chi^2 = 0.373$
High school	9	30	9	30	p = 0.946
Universty	2	6.7	1	3.4	
Diagnosis of disease					
1 year and ↓	11	36.7	13	43.3	$\chi^2 = 0.281$
2-4 year	11	36.7	10	30	p = 0.869
5 year and ↑	8	26.6	7	26.7	
Stage of cancer					
Stage II	14	46.7	17	56.7	$\chi^2 = 0.601$
Stage III	16	53.3	13	43.3	p = 0.438
Duration of stay in hospital					
14 day and ↓	6	20	4	13.4	$\chi^2 = 0.518$
15-20 day	16	53.4	18	60	p = 0.772
20 day and ↑	8	26.6	8	26.6	
	M ± SD				
Age (year)	72.13±4.03		73.14±4.18		MW-U = 153.500
					p = 0.630

$\chi 2$ = chi-square test. MW-U = MannWhitney U test.

logical oncology patients does not affect their levels of anxiety and sleep quality.

H2: Music therapy given to geriatric haematological oncology patients does affect their levels of anxiety and sleep quality.

MATERIALS AND METHODS

The study was conducted through an experimental method with pretest-posttest control group design from May–November 2015 with older hematologic cancer patients in Turkey. The study was conducted in a university hospital's hematology clinic in the

Table 2. A comparison of total pre-test and post-test PSQI score mean for individuals in the experimental group and the control group

Groups	Pre-test	Post-test	Within groups	
	M ±SD	M ±SD	t	p
Control group	14.50±2.70	13.87±2.90	t = 0.615	p = 0.543
Experimental group	14.56±2.00	10.67±2.73	t = 4.566	p = 0.000*
Between group				
t	t = -1.439	t = 3.819		
p	p = 0.161	p = 0.001*		

* $p < 0.05$

east of Turkey.

The population of the study consisted of older (65 years and over) hematologic cancer patients. On the basis of the power analysis, we determined the required sample size as total 54, including 27 patients each in the experimental and control groups, with 95% confidence interval, 90% power, and 5% error margin with a significance level of p = .05 (12). A total of 60 hematological cancer patients, 30 of whom were the control group and 30 of which were the experimental group, were included. The data collection tool was provided to the individuals who volunteered to participate in the study.

Inclusion criteria of the study:

- Having at least eleven days of inpatient treatment in hematology services.
- Receiving chemotherapy treatment.
- Being a host for disease II or III.
- Being able to cooperate and communicate
- Not using psychiatric or sleep medicine.
- Absence of radiation therapy.

Measurements

The Sociodemographic Form, the Pittsburgh Sleep Quality Index (PSQI), and the State-Trait Anxiety Inventory (STAI) were used for data collection. The participants in the experimental group listened to music every day for one week, while the control group did not listen to music during the study.

Sociodemographic Form

The Sociodemographic Form, created by the researchers, was consisted of seven questions (age, gender, marrital status, education level, the time since the diagnosis of disease, stage of cancer and the duration of stay in hospital) including ones to obtain the sociodemographic characteristics of the patients.

Pittsburgh Sleep Quality Index

The PSQI was used to assess the subjective sleep quality in all patients. The 18 items included in the scoring are grouped into 7 component points. Some of the components are specified with a single item, while others are obtained by grouping several substances. Each item is evaluated between 0–3 points. The total score has a value between 0–21. A higher score indicates a lower level of sleep quality (13). The reliability and validity of this scale for Turkey was determined in 1996 (14). Cronbach's alpha

reliability coefficient of the scale was found to be 0.80 (14). In this study, Cronbach's alpha reliability coefficient was 0.79.

State-Trait Anxiety Inventory

We measured anxiety using the STAI, developed by Spielberger, Gorsuch, and Lushene (1970) (15). The validity and reliability of this inventory for Turkey were determined in 1983 (16). The inventory has two separate scales with 20 items, each a four-point Likert type. The inventory consists of two parts: STAI-1, which measures the state anxiety (SA) level, and STAI-2, which measures the trait anxiety (TA) level. The total score obtained from both scales ranges from 20 to 80. A higher score indicates a higher level of anxiety. In this study, Cronbach's alpha reliability coefficient for the SA inventory was 0.84; the TA inventory's coefficient was 0.95.

Study Procedure

Data from the control group were collected first, to prevent any interference between patients, then data from the experimental group were collected. The interviewer primarily gave information to both groups and then the data were collected using the face-to-face interview technique in the clinic. The data were collected by interviewing each patient for a mean of 10 to 15 minutes in the hematological clinic.

The data were collected 48 hours after treatment because patients experienced intensive side effects related to the first 48 hours after chemotherapy treatment. On post chemotherapy days 3 to 10, we asked the participants to fill the Sociodemographic Form, PSQI, and STAI and recorded their responses.

The data from the control group were collected within the specified time frame using the data collection tools as mentioned above after implementation of routine in the clinic.

Data from the experimental group were collected after applying music therapy, and the data were collected using the same data collection tools as used for the control group. Music therapy was performed for the experimental group's members every day for one week

Application of Music Therapy

During the selection of the type of music compositions, the choice of music was designated by Oruc Güvenc who was a lecturer in the Department of Occupational Therapy at the Faculty of Health Sciences. He made a clinical psychology doctorate in music therapy at the Department of Psychiatry, the Cerrahpasa Faculty of Medicine. He founded Turkish Music Research and Promotion Group (TUMETA). He recommended Hejaz, Husseini and Neva compositions (nonverbal instrumental music) from the music and health series prepared by TUMATA (17). Hejaz composition has a therapeutic effect on bones, brain and children's diseases. It has a strong effect on the uro-genital system and kidneys. It gives a sense of humility. Husseini composition is useful for the heart, liver and stomach. It gives a sense of peace. Neva composition is useful in treating mental illnesses. It generates feelings of strength and heroism (17).

Patients laid back and listened to the music with earphones in their rooms. It was explained to the patients how to use their earphones and how to turn them on and off. The researchers observed the patients listening to music, without disturbing them. Each music therapy application took about 30-40 minutes every night for seven days. In the control group, three patients were unable to perform a post-test because one left the hospital early and the other two patients died in the hospital during treatment. In the experimental group, post-test data could not be collected from four patients because two of them were isolated because of the risk of infection, one patient died in the hospital during treatment, and one patient left the hospital early. New patients who met the inclusion criteria were included in the research as substitutes.

Statistical Analysis

The SPSS package program was used to evaluate the data. For the assessment of patients' descriptive characteristics percentage, arithmetic mean, and standard deviation were used. The chi-square test was also used to look at group homogeneity, and independent and dependent sample t-tests were used to analyze relationships among pretest–posttest scores in hematology patients. The level of significance was set at $p < .05$.

Ethical Considerations

After obtaining permission from the ethics committee of the Faculty of Health Sciences (approval number 2014-6/8), written permission was obtained from the hospital. The necessary information was given to the patients who took part in the study; their questions were answered and written permission was obtained from them. Since the use of humans in the study required protection of individual rights, informed consent, voluntary basis, and protection of confidentiality, which are relevant ethical principles, were realized.

RESULTS

Table 1 presents the characteristics of the control and experimental group. Regarding the sociodemographic status of the control and experimental group, the two groups were similar in terms of age, gender, marrital status, education level, the time since the diagnosis of disease, stage of cancer and the duration of stay in hospital ($p > .05$).

As seen in Table 2, there was no significant difference between pre-test and post-test PSQI mean scores of the control group patients ($t = .615$, $p = .543$). In contrast, the difference between the pre-test and post-test PSQI mean scores of the experimental group's patients was statistically significant ($t = 4.566$, $p = .000$).

The pre-test PSQI mean score of patients in the control group was 14.50±2.70, while the pre-test PSQI mean score of patients in the experimental group was 14.56±2.00. No statistically significant difference was found between pre-test mean of the groups ($t = -1.439$, $p = .161$). The post-test PSQI mean score of patients in the control group was 13.87±2.90, while the post-test PSQI mean score of patients in the experimental group was 10.67±2.73. Statistically significant difference was found between post-test mean of the groups ($t = 3.819$, $p = .001$).

According to Table 3, there was no statistically significant difference between the pre-test and post-test SA ($t = 1.782$, $p = .085$) and TA ($t = .143$, $p = .887$) mean scores of the control group. There was a statistically significant difference between the pre-test and posttest SA mean scores ($t = 4.715$, $p = .000$) and TA mean scores ($t = 2.630$, $p = .014$) of the hematology patients in the experimental group.

The post-test SA mean score of patients in the control group was 40.23±11.30, while the post-test SA mean score of patients in the experimental group was 35.43±10.12. The difference between the groups' post-test SA mean scores was statistically significant ($t = 3.799$ $p = .008$). The post-test TA mean scores of hematology patients in the control group was 35.90±9.82, while the post-test TA mean scores of the experimental group was 33.60±9.43. The difference between the groups' post-test TA mean scores was statistically significant ($t = 2.483$, $p = .019$).

DISCUSSION

This study found that music therapy had effects in reducing anxiety and increasing sleep quality. Music therapy, which is a psychosocial initiative, is used as a complementary and alternative treatment of health-related problems, such as cancer (10). It is a fact that music influences the emotional areas related to perceptions such as happiness, joy, sorrow, anger, and hatred in the human brain and has an important effect on humans in this regard. This feature of music is considered a therapeutic factor (9, 10).

In this study, it was found that the decrease between the pre-test and post-test PSQI scores of the experimental group was statistically significant; there was no statistically significant difference between the pre-test and post-test scores of the control group. This was consistent with the results of the related studies on sleep quality. Wang, Sun, and Zang (6) observed that music improved sleep quality in elderly people. Lafci, and Oztunc (18) found that relaxing classical music was an effective intervention in reducing sleeping problems. Blanaru, et al. (19) found that music therapy increased sleep efficiency in post-traumatic stress disorder patients. Kumar (20) studied music therapy's effect on the level of melatonin (a hormone affecting sleep and mood) in Alzheimer's patients; it was found that melatonin secretion increased after music therapy, and it was emphasized that music therapy was effective on the psychological and physiological characteristics of the patients. Thus, it can be concluded that music therapy can improve sleep quality in geriatric hematological oncology patients.

When the STAI score variations of both groups were examined, the decrease in the scores of the experimental group was significantly higher than the decrease in the scores of the control group. These findings parallel those of the existing literature. Zhou, et al. (21) found music therapy reduced depression and anxiety in female cancer patients. Palmer, et al. (22) similarly observed a significant decrease in anxiety levels of a group of women receiving music therapy who had surgery for the diagnosis or treatment of breast cancer. Rossetti, et al. (23) determined that music therapy for cancer patients resulted in decreased patient anxiety and distress. Bilgic, and Acaroglu (24) studied effect of listening to music on the comfort of chemotherapy patients; it was found that anxiety decreased after music. Umbrello, et al. (25) found that music therapy is associated with a reduction in anxiety of critically ill patients. This finding suggests that the music therapy intervention showed clinical efficacy for anxiety.

Therefore, music therapy that was given to various groups has been found to be effective in reducing anxiety and increasing sleep quality. The results of our study are in accordance with the results of the studies in the literature of geriatric haematological oncology patients. These results confirm the hypothesis H2, that "Music therapy given to geriatric haematological oncology patients does affect their levels of anxiety and sleep quality."

CONCLUSION

In this study, it was found that music therapy decreased PSQI and STAI mean scores of the experimental group. As a result of these findings it can be said that music therapy increases sleep quality and decreases the anxiety of geriatric oncology patients.

The findings of this study may provide a basis for future research with regard to evaluating the use of music therapy in the management of sleep quality and anxiety in various geriatric hematology patients. In line with this conclusion, it is suggested that music therapy be used in nursing practice. Nurses should use music therapy, which is a non-pharmacological method, in their practice because it is a safe and cheap method which may be used to treat sleep disorders and anxiety.

CONFLICT OF INTEREST STATEMENT

None

ACKNOWLEDGMENT

We would like to thank the geriatric oncology patients who participated in this study and deceaset Oruc Güvenc.

REFERENCES

1. International Agency for Research on Cancer 2018. [Internet] Available from: https://gco.iarc.fr/today/home. Accessed: 03.08.2020
2. Ovayolu O, Ovayolu N. Acupressure and fatigue in geriatric hematologic malignancies. J Health Sci Erciyes Uni 2017; 4(1): 69-78. (in Turkish). [Internet] Available from: https://pdfs.semanticscholar.org/4c5d/b378739ecb327168d8007c3a645fc5522cd2.pdf. Accessed:02.08.2020
3. Resaults of Population Censuses 1935-2000 and Results of Address Based Population Registiration System, 2007-2019. [Internet] Available from: http://www.tuik.gov.tr/UstMenu.do?metod=temelist. Accessed:05.08.2020.
4. Bostankolu O, Ozturk B, Coskun U, Buyukberber S, Benekli, M. Cancer chemotherapy in elderly patients. Int J Hematol and Oncol 2008; 18(3): 186-92. (in Turkish). [Internet] Available from: http://thod.org/pdf/PDF_333.pdf. Accessed:16.05.2020.
5. Nightingale CL, Rodriguez C, Carnaby G. The ımpact of music ınterventions on anxiety for adult cancer patients, a meta-analysis and systematic review. Integr Cancer Ther 2013; 12(5): 393-403. (PMID: 23625027).
6. Wang C F, Sun YL, Zang H X. Music therapy improves sleep quality in acute and chronic sleep disorders: A meta-analysis of 10 randomized studies. Int J Nursing Studies 2014; 51(1): 51-62. (PMID: 23582682).
7. Liu MC, Ko KT, Lee CS. Atypical depression associated with high-dose steroid treatment in an adolescent patient receiving liver transplantation. TaiwaN J Psychiatry 2019; 33 (2): 114-5. (DOI: 10.4103/TPSY.TPSY_21_19).
8. Yildirim S, Simsek E, Geridönmez K, Basma S, Vurak U. Examination of the knowledge and practices of nurses about consultation liaison psychiatry nursing. Journal Psychiatric Nurs 2019; 10(2):96-102. (DOI: 10.14744/phd.2019.21548).
9. Satija A, Bhatnagar S. Complementary therapies for symptom management in cancer patients. Indian J Palliat Care 2017; 23(4), 468-79.(PMID: 29123357).
10. Coban A. (Eds). Music Therapy, Music Therapy for Mental Health.1st edition, İstanbul, Timas Press, Turkey 2020, pp 126-350.
11. Bagcivan G, Uysal N, Karaaslan A, Kapucu S, Talas MS, Terakye G. Turkey between the years 2009-2013 which was published examination of oncology research in the field of nursing: systematic review. Turk J Oncol 2015; 30(Suppl 1): 5-15. (in Turkish). (DOI: 10.5505/tjoncol.2015.1195).
12. Capık C. Use of confirmatory factor analysis in validity and reliability studies. J Anatolia Nurs and Helath Sci 2014; 17(3): 196-205. (in Turkish) [Internet] Available from: https://dergipark.org.tr/en/download/article-file/29691. Accessed:28.07.2020.
13. Buysse DJ, Reynolds CF, 3rd Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiat Reserch 1989; 28: 193–213. (PMID: 2748771).
14. Agargun MY, Kara H, Anlar O. The validity and reliability of Pittsburgh Sleep Quality Index. Turkish Psychiatry Rev 1996; 7(Suppl 2): 107-15. (in Turkish) [Internet] Available from: http://www.turkpsikiyatri.com/en/default.aspx?modul=summary&id=210. Accessed:16.04.2020.
15. Spielberger CD, Gorsuch RL, Lushene RE. (Eds.). Manual for the State-Trait Anxiety Inventory. Palo Alto, Consulting Psychologists Press, USA 1970, pp 3-28.
16. Oner N, LeCompte A. State-Trait Anxiety İnventory Hand Book.1st edition, İstanbul, Bogazici University,Turkey 1983, pp 1-26.
17. Turkish Music Research and Promotion Group. [Internet] Available from: https://tumata.com/muzik-terapi/turk-muzigi-makamlari-ve-etkileri/. Accessed: 03.08.2020
18. Lafci D, Oztunc G. The effect of music on the sleep quality of breast cancer patients. Int J Caring Sciences 2015; 8(3): 633-40. [Internet] Available from: https://www.internationaljournalofcaringsciences.org/docs/14_Laftci_original_8_3.pdf. Accessed:16.04.2020.
19. Blanaru M, Bloch B, Vadaz L et al. The effects of music relaxation and muscle relaxation techniques on sleep quality and emotional measures among individuals with posttraumatic stress disorder. Ment Illn 2012; 4(13): 59–65. (PMID: 25478114).
20. Kumar AM. Music therapy ıncreases serum melatonin levels ın patients with alzheimer's disease. Altern Ther Health Med 1999; 5(6): 49-57. (PMID: 10550905).
21. Zhou K, Li X, Li J et al. A clinical randomized controlled trial of music therapy and progressive muscle relaxation training in female breast cancer

patients after radical mastectomy: Results on depression, anxiety and length of hospital stay. European J Oncol Nursing 2015; 19(1): 54-9. (PMID: 25181938).

22. Palmer JB, Lane D, Mayo D, Schluchter M, Leeming R. Effects of music therapy on anesthesia requirements and anxiety in women undergoing ambulatory breast surgery for cancer diagnosis and treatment: a randomized controlled trial. J ClinOncol 2015; 33(28): 3162-8. (PMID: 26282640).
23. Rossetti A, Chadha M, Torres BN et al. The impact of music therapy (MT) on anxiety in cancer patients undergoing simulation for radiation therapy (RT). Int J of Radiat Oncol Biol Phys 2017; 99(1): 103-10. (PMID: 28816136).
24. Bilgic S, Acaroglu R. Effects of listening to music on the comfort of chemotherapy patients. West J Nurs Res 2017: 39(6): 745-62. (PMID: 27515501).
25. Umbrello M, Sorrenti T, Mistraletti G, Formenti P, Chiumello D, Terzoni S. Music therapy reduces stress and anxiety in critically ill patients: a systematic review of randomized clinical trials. Minerva anestesiologica, 2019; 85(8): 886-98. (PMID: 30947484).

AMGEN®

prolia® denosumab

Osteoporoza karşı kesintisiz koruma için

Prolia®[1,2] 10 YIL

Referanslar: 1. Bone HG, et al. Lancet Diabetes Endocrinol. 2017;5:513-523. **2.** Lewiecki EM. Ther Adv Musculoskelet Dis. 2018 Nov; 10(11): 209–223.

PROLİA® 60 mg/ml SC Enjeksiyonluk Çözelti İçeren Kullanıma Hazır Enjektör Steril KISA ÜRÜN BİLGİSİ: **Formülü:** Her bir kullanıma hazır enjektör 1 ml çözelti içinde 60 mg denosumab içerir (60 mg/ml) **Endikasyonları:** Yüksek kırık riski olan postmenopozal osteoporozlu kadın ve erkek hastaların tedavisinde endikedir. Hormon ablasyonu uygulanmış olan nonmetastatik prostat kanserli veya meme kanseri nedeniyle adjuvan aromataz inhibitörü tedavisi gören yüksek kırık riskine sahip hastalardaki osteoporoz tedavisinde endikedir. Yüksek kırık riski olan yetişkin hastalarda uzun dönem glukokortikoid tedavisiyle ilişkili kemik kaybının tedavisinde endikedir. Kontrendikasyonlar: Hipokalsemi. Etkin maddeye ya da yardımcı maddelerin herhangi birine karşı aşırı duyarlılık. **Özel Kullanım Uyarıları ve Önlemleri:** Hipokalsemi tedaviye başlamadan önce yeterli kalsiyum ve D vitamini alımıyla düzeltilmelidir. Hipokalsemiye yatkın hastaların kalsiyum seviyelerinin klinik olarak izlenmesi önerilmektedir. Eşzamanlı glukokortikoid tedavisi, hipokalsemi için ilave bir risk faktörüdür. PROLİA® alan hastalarda hastaneye yatırılmaya yol açabilecek cilt enfeksiyonları (ağırlıklı olarak selülit) ortaya çıkabilir. Hastaların selülit belirtileri ve semptomları gelişmesi halinde hemen tıbbi kontrole gitmeleri tavsiye edilmelidir. Osteoporoz için PROLİA® alan hastalarda çene osteonekrozu (ÇO) ender olarak bildirilmiştir. PROLİA® tedavisi sırasında ağız hijyenine özen göstermeleri, rutin dental kontrollerini yaptırmaları ve PROLİA® ile tedavi sırasında dental mobilite, ağrı veya şişme ya da iyileşmeyen yaralar veya akıntı gibi herhangi bir oral semptom görüldüğü takdirde derhal bildirmeleri tavsiye edilmelidir. PROLİA® tedavisi sırasında ÇO ortaya çıkan hastalarda diş cerrahisi durumu kötüleştirebilir. Denosumab ile dış kulak kanalı osteonekrozu bildirilmiştir. Denosumab alan ve kronik kulak enfeksiyonlarının da aralarında olduğu kulak semptomları sergileyen hastalarda dış kulak kanalı osteonekrozu olasılığı düşünülmelidir. PROLİA® kullanan hastalarda atipik femur kırıkları bildirilmiştir. PROLİA® tedavisi sırasında hastalara baldır, kalça veya kasık bölgesindeki yeni veya anormal ağrılarını bildirmeleri önerilmelidir. Uzun dönem antirezorptif tedavi (denosumab ve bifosfonatlar dahil) kemiğin yeniden yapılanmasındaki anlamlı baskılanma sebebiyle çene osteonekrozu ve atipik femur kırıkları gibi advers sonuçlara ilişkin riskin artmasına katkıda bulunabilir. PROLİA® tedavisi gören hastalara denosumab içeren diğer tıbbi ürünlerle eşzamanlı tedavi uygulanmamalıdır (solid tümörden kemik metastazı bulunan erişkinlerde iskeletle ilişkili olayların önlenmesi için). Kullanıma hazır enjektörün iğne başlığı alerjik reaksiyonlara yol açabilecek kuru, doğal kauçuk (bir lateks türevi) içerir. PROLİA®, bir ml çözeltide 47 mg sorbitol içerir. Nadir kalıtımsal fruktoz intolerans problemi olan hastaların bu ilacı kullanmamaları gerekir. PROLİA®, 60 mg'da 1 mmol'den (23 mg) daha az oranda sodyum içerir, yani esasen 'sodyum içermez'. **Özel Popülasyonlara İlişkin Ek Bilgiler:** Böbrek yetmezliği: Şiddetli böbrek yetmezliği (kreatinin klerensi < 30 ml/dakika) olan hastalarda veya diyaliz hastalarında hipokalsemi gelişme riski daha yüksektir. Böbrek yetmezliğinin derecesi arttıkça hipokalsemi gelişme riski ve beraberinde paratiroid hormonlarında yükselme riski artar. Şiddetli böbrek yetmezliği olan veya diyaliz uygulanan hastalarda yeterli kalsiyum ve D vitamini alımı ile kalsiyum düzeylerinin düzenli olarak izlenmesi önemlidir. **İstenmeyen Etkiler:** Hipokalsemi: Pazarlama sonrası deneyimde PROLİA® alan hipokalsemi riski yüksek olan hastalarda seyrek olarak şiddetli semptomatik hipokalsemi vakaları bildirilmiştir. İlaçla ilişkili aşırı duyarlılık reaksiyonları: Pazarlama sonrasında PROLİA® alan hastalarda döküntü, ürtiker, yüzde şişme, eritemi ve anafilaktik reaksiyonları içeren, ilaçla ilgili seyrek aşırı duyarlılık olayları bildirilmiştir. **Diğer Tıbbi Ürünler ile Etkileşimler ve Diğer Etkileşim Şekilleri:** Bir etkileşim çalışmasında PROLİA® sitokrom P450 3A4 (CYP3A4) tarafından metabolize edilen midazolamın farmakokinetiğini etkilememiştir. Bu, PROLİA®'nın CYP3A4 tarafından metabolize edilen ilaçların farmakokinetiğini değiştirmemesi gerektiğini göstermektedir. Denosumabın ve hormon replasman tedavisinin (östrojen) birlikte uygulanmasına ilişkin herhangi bir klinik veri bulunmamaktadır ancak farmakodinamik etkileşim potansiyelinin düşük olduğu öngörülmektedir. Bir çalışmanın (alendronattan denosumaba) verilerine göre daha önce alendronat tedavisi uygulanmış olması osteoporozu olan postmenopozal kadınlarda denosumabın farmakokinetiğini ve farmakodinamiğini değiştirmemiştir. **Pozoloji ve Uygulama Şekli:** PROLİA®'nın 6 ayda bir, tek doz halinde (60 mg) subkutan enjeksiyon olarak uyluğa, karın duvarına ya da üst kola uygulanması önerilmektedir. Hastalara yeterli kalsiyum ve D vitamini desteği verilmelidir. Osteoporoz için antirezorptif tedavinin (denosumab ve bifosfonatlar dahil) optimal toplam süresi henüz belirlenmemiştir. Tedaviye devam etme ihtiyacı denosumabın bireysel hasta bazında yararları ve olası riskleri dikkate alınarak, özellikle 5 yıl veya daha uzun süreli kullanımdan sonra, periyodik olarak yeniden değerlendirilmelidir. Uygulama şekli: Uygulamanın enjeksiyon teknikleri konusunda yeterli eğitim almış biri tarafından yapılması gereklidir. Subkutan kullanıma yöneliktir. Uzun dönem glukokortikoid tedavisi alan ve şiddetli böbrek yetmezliği (GFR < 30 ml/dak) bulunan hastalara ilişkin veri yoktur. **Gebelik ve Laktasyon:** Gebelik kategorisi C'dir. Çocuk doğurma potansiyeli bulunan kadınlar/Doğum kontrolü: Kontrasepsiyon kullanmayan, çocuk doğurma potansiyeli bulunan kadınlarda PROLİA® kullanımı önerilmez. Kadınlara, PROLİA® tedavisi sırasında ve tedaviden sonra en az 5 ay boyunca hamile kalmamaları gerektiği bilgisi verilmelidir. Gebelik dönemi: PROLİA®'nın gebe kadınlarda kullanımına ilişkin yeterli veri mevcut değildir. Hayvanlar üzerinde yapılan araştırmalar üreme toksisitesinin bulunduğunu göstermiştir. İnsanlara yönelik potansiyel risk bilinmemektedir. Gebelik sırasında PROLİA® kullanımı önerilmez. . Laktasyon dönemi: Denosumabın insan sütüne geçip geçmediği bilinmemektedir. Emzirmenin durdurulup durdurulmayacağına ya da PROLİA® tedavisinin durdurulup durdurulmayacağına/tedaviden kaçınılıp kaçınılmayacağına ilişkin karar verilirken emzirmenin çocuk açısından faydası ve PROLİA® tedavisinin emziren anne açısından faydası dikkate alınmalıdır. Üreme yeteneği/Fertilite: Denosumabın insan fertilitesine etkileri hakkında veri mevcut değildir. **Doz Aşımı ve Tedavisi:** Klinik çalışmalarda doz aşımıyla ilgili bir deneyim yoktur. Klinik çalışmalarda 4 haftada bir 180 mg'a kadar dozlarda (kümülatif doz 6 ayda 1.080 mg'a kadar ulaşmıştır) denosumab uygulanmış ve herhangi bir ek advers etki görülmemiştir. **Raf Ömrü:** 36 ay. PROLİA®, orijinal kabında ve oda sıcaklığında (25 °C'ye kadar) 30 güne kadar saklanabilir. PROLİA® buzdolabından çıkarıldığında 30 gün içinde kullanılmalıdır. **Saklamaya Yönelik Özel Tedbirler:** 2°C-8°C arasında buzdolabında saklayınız. Dondurmayınız. Kullanıma hazır enjektörü ışıktan korumak için orijinal ambalajında saklayınız. Fazla çalkalamayınız. **Ticari Takdim Şekli ve Ambalajı**: Prolia® 60 mg/ml SC Enjeksiyonluk Çözelti İçeren Kullanıma Hazır Enjektör (1 korumalı enjektör), KDV Dahil Perakende Satış Fiyatı: 766,93 TL(19.02.2020 tarihi itibarıyla). **Ruhsat Sahibinin İsim ve Adresi:** Amgen İlaç Tic. Ltd. Şti. İş Kuleleri, Levent Mahallesi, Meltem Sok. No: 10 Kule: 2 Kat: 25 4.Levent Beşiktaş İstanbul. **Üretim Yeri:** Amgen Manufacturing Limited, ABD. **Ruhsat Tarihi ve Numarası:** 24.05.2013 - 136/17. **Güncel KÜB'ün Onaylanma Tarihi:** 25.12.2019. Reçete ile satılır. Daha geniş bilgi için firmamıza başvurunuz. **Materyal Onay Kodu:** OM-TUR-000124

PR-PRO-TUR-000017-10-2020

Turkish Journal of Geriatrics

2020; 23(4)