Turkish journal of GERIATRICS

Volume: 26 | Number: 1 | Year: 2023

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

TECHNICAL ASSISTANCE
Pelin ŞAHİN
BAYT Publishing Services

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: 31 March 2023

Turkish Journal of
GERIATRICS
Volume: 26 • Issue: 1 • Year: 2023

EDITOR-IN-CHIEF
Yeşim GÖKÇE KUTSAL

EDITORIAL BOARD

Alfonso CRUZ-JENTOFT	Peter FERRY	Önder İLGİLİ
Murat KOÇ	Sercan ÖZYURT	Clemens TESCH-ROEMER

International Advisory Board

Vladimir ANISIMOV	RUSSIA
Jean-Pierre BAEYENS	BELGIUM
Yitshal BERNER	ISRAEL
Harrison BLOOM	USA
C.J. BULPITT	UK
Robert N. BUTLER	USA
Roger Mc CARTER	USA
Mark CLARFIELD	ISRAEL
Cyrus COOPER	UK
Gaetano CREPALDI	ITALY
Michael FARTHING	UK
Marvin FORMOSA	MALTA
Ghada El-Hajj FULEIHAN	LEBANON
David GELLER	USA
Barry J. GOLDLIST	CANADA
Melvin GREER	USA
Gloria M. GUTMAN	CANADA
Carol HUNTER-WINOGRAD	USA
Alfenso JC JENTOFT	SPAIN
Vladimir KHAVINSON	RUSSIA
John KANIS	UK
Tom KIRKWOOD	UK
Jean-Pierre MICHEL	SWITZERLAND
John E. MORLEY	USA
Robert MOULIAS	FRANCE
Desmond O'NEILL	IRELAND
Sokrates PAPAPOULOS	HOLLAND
Mirko PETROVIC	BELGIUM
Russel REITER	USA
Rene RIZZOLLI	SWITZERLAND
Ego SEEMAN	AUSTRALIA
Walter O. SEILER	SWITZERLAND
Alan SINCLAIR	UK
Raymond C. TALLIS	UK
Adele TOWERS	USA
Guy VANDERSTRATEN	BELGIUM
Alan WALKER	UK
Ken WOODHOUSE	UK
Archie YOUNG	UK

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.

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 3000-4000 words (including 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.

INACCESSIBLE DOCUMENTS SUCH AS DISSERTATIONS, REPORTS, CONGRESS PROCEEDINGS, ABSTRACT BOOKS SHOULD NOT BE SHOWN AS REFERENCES.

1-Articles from journals

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).

2-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. (DOI: 10.1016/j.amepre.2018.09.006).

3-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.

4-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 DOI numbers) written according to the rules and of the journal (http://geriatri.dergisi.org/static.php?id=7).
11. Original articles should not exceed 4000 words (including 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: 26 • Issue: 1 • Year: 2023

Contents

EDITORIAL

FROM THE EDITOR IN CHIEF IX
Yeşim GÖKÇE KUTSAL

RESEARCH ARTICLES

FRAILTY AND RELATED FACTORS IN ELDERLY PATIENTS WITH CHRONIC KIDNEY DISEASE 1
Alper ALP, Hüseyin ELBİ, Aysun TORAMAN

THE RELATIONSHIP OF THE C-REACTIVE PROTEIN /ALBUMIN RATIO TO IN-HOSPITAL MORTALITY IN ELDERLY PATIENTS WITH NON-ST-ELEVATION MYOCARDIAL INFARCTION WHO HAVE UNDERGONE PERCUTANEOUS CORONARY INTERVENTION 12
Oğuz KILIÇ, Fatma ÖZPAMUK KARADENİZ, Fatih KAHRAMAN

EFFICACY OF EPIDURAL STEROID INJECTION IN ELDERLY PATIENTS: DOES DIAGNOSIS AFFECT TREATMENT SUCCESS? 20
Yücel OLGUN, Rekib SACAKLIDIR, Yasin OKUMUŞ, Savaş SENCAN, Osman Hakan GÜNDÜZ

A 30-DAY RISK ASSESSMENT OF GERIATRIC PATIENTS IN THE EMERGENCY DEPARTMENT: A COMPARISON OF ISAR AND TRST SCORES 27
Savaş SEZİK

COMPARISON OF THE EFFECTS OF INTRAOPERATIVE GOAL DIRECTED AND CONVENTIONAL FLUID MANAGEMENT ON THE INFERIOR VENA CAVA COLLAPSIBILITY INDEX AND POSTOPERATIVE COMPLICATIONS IN GERIATRIC PATIENTS OPERATED FROM PROXIMAL FEMORAL NAIL SURGERY 37
Dilara GÖÇMEN, Ceren KÖKSAL, Süheyla ABİTAĞAOĞLU, Arzu YILDIRIM AR

COMPARISON OF THE EFFECTS OF GENERAL ANESTHESIA AND DEEP SEDATION ON ANESTHESIA COMPLICATIONS AND MORTALITY IN ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY PROCEDURES 48
Elif BÜYÜKERKMEN, Ahmet YÜKSEK, Elif DOĞAN BAKI, Sezgin YILMAZ

KNEE ARTHRODESIS WITH COMPUTER-ASSISTED EXTERNAL FIXATOR SYSTEM AFTER PROSTHETIC JOINT INFECTION FOR ELDERLY POPULATION 60
Muharrem KANAR, Necmi CAM

THE EFFECTS OF LOW FLOW AND NORMAL FLOW DESFLURANE ANESTHESIA ON LIVER AND RENAL FUNCTIONS AND SERUM CYSTATIN C LEVELS IN GERIATRIC PATIENTS: A PROSPECTIVE RANDOMIZED CONTROLLED STUDY 68
Afife GÜLER KOL, Hacı Yusuf GÜNEŞ

EVALUATING THE ROLE OF VERTEBRAL ANATOMY EXAMINATION BY ULTRASONOGRAPHY BEFORE ADMINISTERING SPINAL ANESTHESIA IN GERIATRIC PATIENTS: A PROSPECTIVE RANDOMIZED TRIAL 79
Arda IŞIKER, Meryem ONAY, Alpaslan AKCAN, Ümit AKKEMİK, Mehmet Sacit GÜLEÇ

RELATIONSHIP BETWEEN THE AMOUNT OF AMALGAM FILLING AND COGNITION IN OLDER ADULTS 91
Savaş ÖZARSLANTÜRK, Mehmet İlkin NAHARCI, Numan AYDIN, Serpil KARAOĞLANOĞLU, Elif Aybala OKTAY

ASSESSMENT OF VESTIBULAR SYSTEM AND BALANCE FUNCTION IN PATIENTS WITH PSEUDOEXFOLIATION SYNDROME 100
Pelin KOÇDOR, Zeynep KAYAARASI ÖZTÜRKER, Osman Halit ÇAM

www.turkgeriatri.org

From The Editor In Chief

On behalf of the Editorial Board members of Turkish Journal of Geriatrics, I cordailly wish to thank the following reviewers who have helped to maintain and improve the quality of our journal during 2022.

Özlem AKİ, Berna ARDA, Sadık ARDIÇ, Didem ARSLANTAŞ, Ali ATAN, Yalım ATEŞ, Vildan AVKAN-OĞUZ, Saime AY, Semih AYDEMİR, Pınar AYDIN, Tolga Reşad AYDOS, Duygu AYHAN BAŞER, Okay BAŞAK, Mehmet Murad BAŞAR, Terken BAYDAR, Kutay BİBEROĞLU, Vildan BİNAY SAFER, Ayşe BORA TOKÇAER, Sedat BOYACIOĞLU, Banu BOZKURT, Selçuk BÖLÜKBAŞI, Banu CANGÖZ, Ahmet COŞAR, İlke COŞKUN BENLİDAYI, Nurettin Özgür DOĞAN, Aslı DÖNMEZ, Nurper ERBERK ÖZEN, Yasemin ERTEN, Erhan ESER, Nilay ETİLER, Ender GEDİK, Ayşe GELAL, Yeşim GÖKÇE KUTSAL, Gloria GUTMAN, Ahmet GÜDELOĞLU, Zafer GÜNENDİ, Rengin GÜZEL, Gülşen HASCELIK, Nur HERSEK, Önder İLGİLİ, Jale İRDESEL, Fuat KALYONCU, Zeynep Begüm KALYONCU ATASOY, Sevilay KARAHAN, Ayşe KARS, Hande KAYNAK, Semih KESKİL, Pembe KESKİNOĞLU, Gülce KİRAZLI, Murat KOÇ, Hakan KUMBASAR, Mahir KUNT, Ali KUTSAL, Demet OFLUOĞLU, Dilek OĞUZ, Abdullah OLGUN, Ebru ORTAÇ ERSOY, Serpil ÖCAL, Murat ÖZBEK, Tuğçe ÖZEKLİ MISIRLIOGLU, Işıl ÖZKOÇAK, Zerrin ÖZKÖSE, Şerefnur ÖZTÜRK, Mihrimah ÖZTÜRK, Sercan ÖZYURT, Nurdan PAKER, Gülden PEKCAN, Reyhan POLAT, Neslişah RAKICIOĞLU, İskender SAYEK, Meral SAYGUN, Hülya SUNGURTEKİN, Tijen ŞENGEZER, Sevilay ŞENOL ÇELİK, Tugan TEZCANER, Zahide TUNA, Canan ULUOĞLU, Oya ÜNAL ÖZDEMİR, Songül VAİZOĞLU, Orhan YILMAZ, Taner YILMAZ, İrfan YORULMAZ, Sevinç YÜCECAN and Faruk ZORLU.

Yeşim GÖKÇE KUTSAL

RESEARCH

FRAILTY AND RELATED FACTORS IN ELDERLY PATIENTS WITH CHRONIC KIDNEY DISEASE

Turkish Journal of Geriatrics
DOI: 10.29400/tjgeri.2023.325
2023; 26(1):1-11

Alper ALP[1]
Hüseyin ELBİ[2]
Aysun TORAMAN[3]

CORRESPONDANCE
[1]Alper ALP

Phone : +905303102244
e-mail : alperalp@mu.edu.tr

Received : Jan 09, 2023
Accepted : Mar 10, 2023

[1] Mugla Sitki Kocman University,Faculty of Medicine, Nephrology, Muğla, Turkey

[2] Celal Bayar University Faculty of Medicine, Family Medicine, Manisa, Turkey

[3] Celal Bayar University Faculty of Medicine, Nephrology, Manisa, Turkey

Abstract

Introduction: Chronic kidney disease and frailty are two crucial clinical conditions increasing in prevalence globally. Both lead to severe complications that increase mortality and morbidity in patients. Conditions that may potentiate frailty in chronic kidney disease patients may complicate the follow-up of chronic disease and complicate long-term survival in this patient group. In this study, we aimed to evaluate frailty and related factors in chronic kidney disease patients over 65 years of age who were on dialysis and who were not.

Materials and Methods: This cross-sectional study was carried out in geriatric chronic kidney disease patients followed in nephrology outpatient clinics or undergoing routine hemodialysis. Frailty was assessed using a scoring scale. Laboratory findings and their relationship with demographic and epidemiological data were investigated.

Results: One hundred eighty-eight patients aged 65 and over were included in our study. Of the patients, 92 were female, and 96 were male. The mean age was 72.86 years. We found frailty in 82 patients (43.6%). Female gender, over 75 years old, under dialysis treatment, low-income status, and low education level were parameters significantly associated with frailty. In the regression analysis, we found that economic status and dialysis were variables that independently affected frailty in chronic kidney disease patients.

Conclusions: In our study, the frequency of frailty was found to be high. Practical management and early assessment of frailty seem rational with the basic nephrological approach in patients with chronic kidney disease. Considering the high mortality rate among frail patients, we think these patients should be followed up more closely.

Keywords: Frailty; Aged; Renal Insufficiency, Chronic.

INTRODUCTION

With the increase in the elderly population globally and in Turkey, some geriatric syndromes with low awareness in previous decades have become more common. One of these geriatric syndromes is frailty (1).

Frailty is a dynamic entity with a decrease in physical, mental, and social life potentials advancing age and subsequent clinical, cognitive, and psychological negative consequences (2). It is a heterogeneous process that must be evaluated effectively in clinical practice, mainly because it causes an increase in morbidity and mortality in geriatric patients. Frail elderly patients have low physical performance abilities and a high probability of experiencing general health problems (3).

Chronic kidney disease (CKD) is a progressive, chronic clinical entity with various serious complications, an independent risk factor for cardiovascular disease, and a serious public health problem. Both morbidity and mortality are high among CKD patients, the incidence of which is increasing daily all over the world, and this creates a serious cost burden for health systems (4). However, many studies have shown that frailty increases in patients with CKD. It may be over 60% of patients receiving hemodialysis (HD) (2). Also, it was reported that frail patients had less planned dialysis initiation than a non-frail group (5).

As renal functions worsen, malnutrition and sarcopenia tend to increase in CKD patients due to uremic nausea and vomiting, insufficient oral intake due to gustatory changes, polypharmacy, concomitant chronic diseases, and strict diet practices. This challenging setting provides suitable grounds for frailty in patients (6). However, it has also been suggested that some non-pharmacological approaches may positively affect frail patients receiving hemodialysis. For example, some approaches as interventions to correct nutritional deficits and weight loss can help reduce the frailty level of patients. Therefore, early diagnosis of frailty is crucial in treatment management in CKD patients (2, 7).

It has been shown that mortality increases in frail patients in the pre-dialysis group and patients undergoing dialysis (5, 8). As the severity of the disease increases in CKD patients, the frequency of frailty also increases (6). In this study, we examined the frequency of frailty and related parameters in patients who were followed up for chronic kidney injury.

MATERIALS AND METHODS

Study design and participants

In this cross-sectional study, the G-Power program calculated the sample size at a 90% confidence level before the data collection phase. In this study, we planned to investigate CKD patients' frailty status risk factors. For this, a chi-square analysis was conducted. The study's effect size was 0.30; by taking the alpha value of 0.05 and the theoretical power of 0.90, the minimum number of samples was determined to be 183.

We evaluated 188 patients with CKD (stage II-VD), aged ≥65, who were followed up between 02/09/2018 and 04/01/2020 at the nephrology outpatient clinics at Manisa Celal Bayar University Hospital and Bakırçay University Çiğli Regional Education and Research Hospital. Patients with active solid organ or hematological malignancy, dementia or Alzheimer's disease, a history of cerebrovascular disease, physical limitations, hearing or speech difficulties, acute kidney injury, and hemodynamically unstable patients were excluded from the study.

Data collection tools

A sociodemographic data survey and the Edmonton Frail Scale (EFS) were administered to each patient.

Sociodemographic data survey

Demographic and epidemiological (age, gender, duration of disease) findings, basic biochemical tests, hemograms, sub-parameters, and comorbid conditions (diabetes, hypertension, chronic lung disease, and cardiovascular disease) were examined.

The Edmonton Frail Scale

The EFS is an assessment tool that can be used alone or in combination with other scales and can be easily applied to hospitalized and outpatients in assessing frailty, as defined by Rolfson et al. and validated in the Turkish population (9, 10). Those with a score of 0–4 were evaluated as non-frail, 5–6 apparently vulnerable, 7–8 as mildly frail, 9–10 as moderately frail, and 11 and above severely frail. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Statistical analysis

In the statistical analysis, when descriptive statistics were provided for normal distribution conditions, Student's t-tests and ANOVA were employed to compare the two independent groups in continuous data. The data obtained from the study were evaluated using SPSS 15.0. If the normal distribution conditions were not met, the Mann-Whitney U and Kruskal-Wallis tests were applied.

Ethical procedure

Permission was obtained from the local University Faculty of Medicine Health Sciences Ethics Committee (Manisa Celal Bayar University) with date and no. 30.05.2018/20.478.486. Each patient was informed about inclusion in the study, and their consent was obtained.

RESULTS

One hundred eighty-eight patients were included in the study. Of the patients, 96 were male. The patients who were aged between 65 and 99 years were included in the study. The mean height was 164.96 cm and weight 75.5 kg. Patients had a history of hypertension in 72.9%, chronic lung disease in 12.8%, diabetes mellitus in 47.3%, and cardiovascular disease in 41%. The patients living with their spouse comprised 53.2% of the total, while 21.3% were living with their spouse or children, 19.7% were living alone, and 5.9% were living in a nursing home (Table 1).

According to the CKD stages, the distribution was as follows: stage II 19 patients (10.1%), stage III 87 (46.3%), stage IV 46 (24.5%), and stage V 36 (19.1%). The mean hemoglobin level of the patients was 11.96 ± 1.93 g/dl (min. 7.1–max. 18 g/dl). Hemoglobin was found to be 12 g/dl > in 95 (50.5%) patients.

We found frailty in 82 (43.6%) patients when we combined frail patients according to the EFS with a holistic evaluation.

Among the frail patients, the female gender was significantly higher (64.6% vs 35.4%, $p = 0.001$). Women were more frail than men (7.11 ± 2.92 vs 5.3 ± 2.87, $p = 0.001$). However, this significance was unrelated to CKD staging by gender. Frailty was higher in patients over 75 years of age than in patients 75 years and younger ($p = 0.012$).

In the evaluation made according to the education level of the patients, it was observed that there was a significant difference between the groups in terms of frailty ($p = 0.001$). It was determined that primary school-educated and literate patients were more frail than other education levels ($p = 0.001$).

Table 1. Distribution of patient characteristics

Features		
	S/Ort.	% (or SS*)
Gender		
Female	92	48.9
Male	96	51.1
Age		
Mean	72.86*	6.41*
65-74 years	122	64.9
75-84 years	55	29.3
≥ 85 years	11	5.9
Education		
Primary school and Literate	149	79.3
Middle and High School	26	13.8
University	13	6.9
Marital status		
Married	128	68.1
Not married (widowed, divorced, never married)	60	31.9
Economical situation		
Equal to monthly income	97	51.6
Less than monthly income	70	37.2
More than monthly income	21	11.2
Chronic disease		
Yes	166	88.3
No	22	11.7
With whom she/he lives		
Alone	37	19.7
With his wife and children	140	74.5
Other (caregiver, nursing home)	11	5.9
Frailty status		
Non-frail	62	33.0
Vulnerable	44	23.4
Mild Frailty	32	17.0
Moderate Frailty	32	17.0
Severe Frailty	18	9.6
Dialysis application		
Yes	35	18.6
No	153	81.4

* mean

Table 2. Relationship of some parameters with frailty

	Nonfrail N (%)	Vulnerable N (%)	Frail N (%)	EFS total (mean)
Gender				
Female	17 (18.5)	22 (23.9)	53 (57.6)	7.11±2.92
Male	45 (46.9)	22 (22.9)	29 (30.2)	5.3±2.87
Age*				
≥ 75 years	12 (41.0)	18 (21.3)	36 (37.7)	6.94±2.82*
< 75 years	50 (18.2)	26 (27.3)	46 (54.5)	5.78±3.07
Education*				
Primary school and Literate	38 (25.5)	36 (24.2)	75 (50.3)	6.67±3.00**
Middle and High School	12 (46.2)	7 (26.9)	7 (26.9)	4.88±2.59
University	12 (92.3)	1 (7.7)	0 (0)	3.23±1.30
Marital status*				
Married	48 (37.5)	29 (22.7)	51 (39.8)	5.84±2.91*
Not married	14 (23.3)	15 (25.0)	31 (51.7)	6.93±3.15
Economic situation*				
Equal to monthly income	35 (36.1)	25 (25.8)	37 (38.1)	5.71±2.64
Less than monthly income	14 (20.0)	14 (20.0)	42 (60.0)	7.51±3.21
More than monthly income	13 (61.9)	5 (23.8)	3 (14.3)	3.95±2.03**
Chronic disease*				
Yes	51 (30.7)	40 (24.1)	75 (45.2)	6.36±3.02*
No	11 (50.0)	4 (18.2)	7 (31.8)	4.91±2.8
With whom she/he lives*				
Alone	15 (40.5)	11 (29.7)	11 (29.7)	5.35±2.69
With his wife and children	47 (33.6)	30 (21.4)	63 (45.0)	6.21±3.06
Other (caregiver, nursing home)	0 (0)	3 (27.3)	8 (72.7)	8.73±2.41**
Dialysis application*				
Yes	5 (14.3)	7 (20.0)	23 (65.7)	7.91±3.17*
No	57 (37.3)	37 (24.2)	59 (38.6)	5.79±2.86
BMI*				
Normal-weight	16 (28.1)	13 (22.8)	28 (49.1)	6.67±3.25
Overweight	34 (44.7)	18 (23.7)	24 (31.6)	5.43±2.99**
Obese	12 (21.8)	13 (23.6)	30 (54.5)	6.73±2.66

* p≤0.05, ** Post-hoc test was applied.

When the relationship with frailty was evaluated, those whose income was more than their expenses were less frail (p=0.001), and frailty was higher in patients with chronic diseases other than CKD than those without (p=0.03). Frailty varied significantly with whom the patients lived with a caregiver or at a nursing home (p=0.04).

Although there was no difference in frailty assessment according to the CKD stage, frailty was significantly higher in dialysis patients than in nondialysis patients (p=0.001) (Table 2). According to the body mass index (BMI), there was a significant difference between the groups in terms of frailty (p=0.014). Overweight patients were less frail than obese and normal-weight subjects (p=0.029). Smoking was present in 93 (49%) patients. No relationship was found between smoking and frailty.

When the relationship between hemogram parameter variables and frailty was evaluated, it was

Table 3. Evaluation of the relationship between hemogram sub-parameter variables and frailty

	Nonfrail	Vulnerable	Frail
Hgb*	12.68±2.05	12.32±1.78	11.21±1.65*
Htc*	38.75±6.10	37.97±5.50	34.73±5.21*
WBC	8.22±1.98	8.28±1.76	7.64±2.46
Neutrophil	5.39±1.64	5.33±1.46	5.07±2.05
Lymphocyte	1.97±0.88	2.00±0.79	1.77±0.67
Monocyte	0.58±0.25	0.62±0.18	0.57±0.26
Platelet	250.77±70.66	252.70±61.66	243.74±81.41
MCV*	101.10±10.39	88.97±6.68	88.78±7.29
MCHC*	32.71±1.02*	32.18±1.63	32.32±1.01
RDW	14.50±1.57	14.54±1.63	15.18±2.36
MPV	9.74±0.78	9.76±0.88	9.79±0.79
PLR	1.46±0.75	1.44±0.65	1.50±0.68
NLR	3.31±2.25	3.20±1.27	3.44±2.67
LMR	3.76±1.59	3.31±1.27	3.68±2.32
RDW/MPV	1.49±019	1.50±.026	1.56±0.27
RDW/platelet	6.51±0.19	6.22±2.45	7.00±3.32
MPV/platelet	4.45±3.10	4.14±1.28	4.56±2.12
MPV/lymphocyte	5.87±2.72	5.76±2.74	6.75±5.19

* p≤0.05, Post-hoc test was applied.

Hgb:Hemoglobin, Htc: Hematocrit,WBC: white blood cell, MCV: mean corpuscular volume, MCHC: mean corpuscular hemoglobin concentration, RDW: Red blood cell distribution width, MPV:mean platelet volume, PLR: platelet-lymphocyte ratio, NLR: neutrophil-to-lymphocyte ratio, LMR: lymphocyte-monocyte ratio

observed that hemoglobin and hematocrit levels were significantly lower in the frail group (Table 3). When CKD stage and hemogram parameters were assessed, it was found that anemia was seen significantly more frequently as the CKD stage increased. As the stage raised, there was an increase in neutrophil/lymphocyte (N/L) and MPV/lymphocyte ratios and a decrease in lymphocyte/monocyte ratio (Table 4).

Linear multiple regression analysis was performed to determine the extent to which the variables of age, marital status, economic situation, presence of chronic illness, with whom they lived, dialysis application, and BMI predicted the total EFS score. As a result of the first model, R2 = 0.341 was found. Since this model was found to have a good fit (Durbin-Watson: 1.930), a seven-variable model was chosen, as shown in Table 5. Due to the high and significant autocorrelation value (r = 0.584,

Table 4. Evaluation of the relationship between hemogram sub-parameters and CKD stage

	Stage II (N=19)	Stage III (N=87)	Stage IV (N=46)	Stage V (N=36)
Hgb*	13.14±2.33	12.57±1.58	11.56±1.66	10.34±1.69*
Htc*	40.35±7.19	38.76.±4.53	35.74±5.09	31.61±5.24*
WBC*	6.72±0.71*	8.38±0.21*	8.19±0.16	7.52±0.26
Neutrophil*	4.05±0.15*	5.43±0.17*	5.28±0.21	5.31±0.21
Lymphocyte*	1.96±0.61	2.03±0.79	1.95±0.92	1.42±0.38*
Monocyte	0.50±0.17	0.58±0.23	0.61±0.21	0.62±.032
Platelet	232.68±73.39	259.09±70.80	233.91±64.58	248.11±87.47
MCV	87.74±8.04	97.55±8.72	89.81±7.10	88.27±5.42
MCHC	32.60±1.06	32.31±1.32	32.31±1.18	32.71±0.97
RDW	15.00±2.17	14.58±2.21	14.76±1.67	15.32±1.63
MPV	9.75±0.78	9.77±0.91	9.61±0.83	9.98±0.41
PLR	126.43±46.11	143.95±66.25	134.76±63.33	185.09±85.36
NLR*	2.25±1.20*	3.12±2.03	3.53±2.70	4.22±2.87*
LMR*	4.30±1.52	3.77±1.45	3.76±2.82	2.71±1.13*
RDW/MPV	1.56±0.36	1.50±0.28	1.54±0.17	1.53±0.16
RDW/platelet	7.20±3.24	5.98±1.64	7.52±5.80	6.89±2.36
MPV/platelet	4.54±1.25	4.08±1.30	4.96±4.06	4.52±1.55
MPV/lymphocyte*	5.45±1.71	5.56±2.32*	6.70±6.87	7.64±2.53*

* p≤0.05, Post-hoc test was applied.

Hgb: Hemoglobin, Htc: Hematocrit, WBC: white blood cell, MCV: mean corpuscular volume, MCHC: mean corpuscular hemoglobin concentration, RDW: Red blood cell distribution width, MPV:mean platelet volume, PLR:platelet-lymphocyte ratio, NLR: neutrophil-to-lymphocyte ratio, LMR: lymphocyte-monocyte ratio

Table 5. Linear regression table

	R2	β	p
Edmonton Frailty Scale	0.584		
Coefficient			0.021
Age (0 < 75, 1 ≥75)		0.982	0.156
Marital status (0 married, 1 not married)		-0.950	0.203
Economic situation (0 income>expenditure, 1 equal)		**3.143**	**<0.001**
Chronic Disease (0, not present, 1 present)		0.639	0.490
Living with/in (0 others, 1 nursing home)		0.226	0.857
Dialysis (0 No, 1 Yes)		**2.030**	**0.009**
BMI (0 overweight, 1 other)		0.912	0.145

p = 0.000), it was decided to keep the economic situation and dialysis application variables in the model (Table 5).

DISCUSSION

Chronic kidney disease is a progressive, irreversible, and chronic disease that progresses with multiple complications, causing mortality and severe morbidity. According to 2017 data, CKD caused 1.2 million deaths, and 7.6% (1.4 million) of all cardiovascular (CV) deaths can be attributed to impaired renal function. Of all-cause mortality globally, CKD and CV deaths attributable to CKD account for 4.6% (11).

In a study in Turkey, the frailty rate in geriatric patients was found to be 36.2%. While findings such as a high prevalence of comorbid diseases, being widowed, and increasing age were significant, no significant correlation was found between age and educational status (10). In our study, the frequency of frailty in the CKD population was 43.6%. In some frailty prevalence studies in general and CKD populations in the aged group in Turkey and other countries, the results were variable (up to 73%) (12-14). It was thought that different health system practices among governments, socio-economic conditions, geopolitical variability, and the use of different scales for analyzing frailty may have affected these variations in the results.

It is known that frailty is higher in CKD patients than in other populations, and frailty in HD patients has also been reported to be associated with increased mortality (14). Chronic kidney disease and frailty syndrome may present with similar symptoms and signs. Our study did not find a significant relationship between glomerular filtration rate (GFR) level and CKD stage and frailty.

The relationship between creatinine-based GFR measurements and frailty and cognitive dysfunction has not consistently been demonstrated in cohort studies. The reason for this has been shown to be the variability of creatinine between individuals and its direct relationship with parameters such as malnutrition-muscle mass (15). We evaluated the results of our study in this direction and considered the heterogeneity in creatinine-based GFR measurements in the foreground. However, although no correlation was found between the CKD stage and the degree of frailty, frailty was

significantly higher in our patients who underwent hemodialysis than in those who did not.

In an Australian study in which 909 patients aged 65 and over were evaluated, the frequency of frailty assessed with the Frailty Index was 48%. Low income, female gender, obesity, and living alone were significantly correlated (16). Although the geographical and living conditions were very different, this study's data were compatible with ours. Many studies conducted in other populations have shown that frailty is higher in women. Similar findings, specifically in the CKD population, suggest that the female gender may be associated with frailty, regardless of the underlying disease type (17).

The frequency of frailty and its higher incidence in patients over 75 years were similar to some studies in our country. In a recent study, Çelebi et al. found the prevalence of frailty to be 40.8% in patients over 65 undergoing hemodialysis. The mean dialysis time was longer in this study than in our study (12). In a study by Inoue et al. that included 630 patients with CKD over 70, frail patients were significantly older than the pre-frail and robust groups (mean age 83, 77, and 72, respectively) (18). In the cohort study by Johnson et al., the frequency of frailty was 67.7% in 2,275 dialysis patients, while this rate was 44.4% in patients < 40 years of age and 78.8% in patients aged < 80 years of age (19).

Lifelong continuity of treatment in chronic dialysis patients, transportation to the center 3 days a week, and complications, such as hypotension, cramps, nausea-vomiting, arrhythmias, catheter infections, and blood flow problems that may occur during and after HD adversely affect the patients and lead to a deterioration in their quality of life (20). Our study did not show that frailty increased as the CKD stage increased, but HD patients were found to be more frail. This finding may be important in predicting increased complications in the HD group. In addition, frailty is associated with an increase in the frequency of hospitalization and a deterioration in the quality of life. Yoneki et al. emphasized that frailty in HD patients is essential in predicting bone loss (21). In the study by Nixon et al., 450 patients were evaluated (84 of them HD patients), and the frequency of frailty was found to be 33%. According to the results, frail patients were older, but there was no relationship between gender differences or dialysis and frailty.

Conflicting results have been found in the literature on the BMI frailty relationship. In a study by Laur et al., there was no significant difference in BMI between frail and non-frail women, while it was lower in frail men than in non-frail women (22). Our study showed a significant difference in frailty between the groups according to BMI. Overweight patients were less frail than obese and normal-weight patients.

As expected, lower socio-economic status is associated with greater frailty in the geriatric patient group (16). Considering current socio-economic conditions, the fact that frailty was higher in low-income patients was considered a predictable result in our study and was consistent with the literature. The increase in frailty with a high number of comorbid diseases can be evaluated in a similar context (23).

In recent years, it has been frequently mentioned that some hemogram parameters are correlated with different variables in many other patient populations. Of these, N/L elevation has been shown to be associated with the risk of progression, increased mortality, and inflammation in the CKD population (24). Studies have shown that it can also predict frailty in the geriatric population (25). In our study, however, no significant relationship was found with frailty, but there was a significant relationship between increased CKD stage and N/L elevation.

As a result, we would like to emphasize that it would be rational to show a closer and more effective approach to frailty in advanced-aged, low-income female patients undergoing hemodialysis due to the high risk of mortality and morbidity. We believe

that the presence of trained personnel, especially in center dialysis units, early detection of frailty, and taking precautions can lead to positive results. Our study could not find a significant relationship between the CKD stage and frailty. However, we still think closer follow-up in patients in the risk group for CKD progression would be appropriate (especially in making HD indication decisions and because of the high risk of CKD progression in frail patients).

Our study has some limitations. Patients were evaluated based on frailty in line with the purpose of the study, and not including sarcopenia or malnutrition investigation was a limitation. Other limitations of our study were the lack of evaluation of cognitive functions and the low number of patients. There is no agreed-upon scale among frailty scales applied explicitly to the CKD population. We used the EFS, which is valid globally. Different prevalences of frailty can be determined from different scales regarding geographical, socio-economic, and cultural differences. Which one is valid for which population can be revealed by more comprehensive studies with a large number of patients in which different scales are compared simultaneously?

Conflict of interest

The authors declare that no conflicts of interest are associated with this study.

REFERENCES

1. Akçiçek S, Sahin S, Aygör HE. Frailty. In:Savas S, editor. New Horizons in Geriatric Syndromes. 1st edition, Ege University Rectorate, Printing House Directorate, Turkiye 2018, p. 1–17. (in Turkish)
2. Nagaraju SP, Shenoy SV, Gupta A. Frailty in end stage renal disease: Current perspectives. Nefrologia. 2022;42(5):531–9. (PMID: 36792307)
3. Musso CG, Jauregui JR, Macías Núñez JF. Frailty phenotype and chronic kidney disease: a review of the literature. Int Urol Nephrol 2015;47(11):1801-7. (PMID: 26411428)
4. Pollock C, James G, Garcia Sanchez JJ, et al. Healthcare resource utilisation and related costs of patients with CKD from the UK: a report from the DISCOVER CKD retrospective cohort. Clin Kidney J 2022;15(11):2124-34. (PMID: 36325010)
5. Oki R, Hamasaki Y, Tsuji S, et al. Clinical frailty assessment might be associated with mortality in incident dialysis patients. Scientific reports. 2022;12(1):17651. (PMID: 36271111)
6. Kang SH, Do JY, Lee S-Y, Kim JC. Effect of dialysis modality on frailty phenotype, disability, and health-related quality of life in maintenance dialysis patients. PLOS One 2017;12(5):1-16. (PMID: 28467472)
7. Mayes J, Young HML, Blacklock RM, Lightfoot CJ, Chilcot J, Nixon AC. Targeted Non-Pharmacological Interventions for People Living with Frailty and Chronic Kidney Disease. Kidney and Dialysis. 2022; 2(2):245-61.
8. Merchant RA, Vathsala A. Healthy aging and chronic kidney disease. Kidney Res Clin Pract 2022;41(6):644-56. (PMID: 36328991)
9. Rolfson DB, Majumdar SR, Tsuyuki RT, Tahir A, Rockwood K. Validity and reliability of the Edmonton Frail Scale. Age and Ageing 2006;35(5):526-9. (PMID: 16757522)
10. Aygör HE, Fadıloğlu Ç, Şahin S, Aykar FŞ, Akçiçek F. Validation of Edmonton Frail Scale into Elderly Turkish Population. Arch Gerontol Geriatr 2018;76:133-137. (PMID: 29499529)
11. Bikbov B, Purcell CA, Levey AS, et al. Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2020;395:709-33. (PMID: 32061315)
12. Çelebi ZK, Erdoğmuş Ş, Turgut D. Determination of Frailty and Risk Factors in Elderly Hemodialysis Patients. Journal of Ankara University Faculty of Medicine 2020;73(1):26-30. (Doi: 10.4274/atfm.galenos.2020.14622). (in Turkish)
13. Nixon AC, Brown J, Brotherton A, et al. Implementation of a frailty screening programme and Geriatric Assessment Service in a nephrology centre: a quality improvement project. Journal of Nephrology 2020;34(4):1215-24. (PMID: 33040293)
14. Bao Y, Dalrymple L, Chertow GM, Kaysen GA, Johansen KL. Frailty, Dialysis Initiation, and Mortality in End-Stage Renal Disease. Archives of Internal Medicine 2012;172(14):1071-7. (PMID: 22733312)

15. Dalrymple LS, Katz R, Rifkin DE, et al. Kidney Function and Prevalent and Incident Frailty. Clin J Am Soc Nephrol 2013;8(12):2091-9. (PMID: 24178972)
16. Thompson MQ, Theou O, Yu S, Adams RJ, Tucker GR, Visvanathan R. Frailty prevalence and factors associated with the Frailty Phenotype and Frailty Index: Findings from the North West Adelaide Health Study. Australas J Ageing 2018;37(2):120-6. (PMID: 29205759)
17. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001;56(3):146-56. (PMID: 11253156)
18. Inoue T, Shinjo T, Matsuoka M, et al. The association between frailty and chronic kidney disease; cross-sectional analysis of the Nambu Cohort Study. Clin Exp Nephrol 2021;25(12):1311-8. (PMID: 34244892)
19. Johansen KL, Chertow GM, Jin C, Kutner NG. Significance of Frailty among Dialysis Patients. J Am Soc Nephrol 2007;18(11):2960-7. (PMID: 17942958)
20. Hsu C-C, Huang C-C, Chang Y-C, Chen J-S, Tsai W-C, Wang K-Y. A comparison of quality of life between patients treated with different dialysis modalities in Taiwan. PLoS One 2020;15(1):1-11. (PMID: 31907493)
21. Yoneki K, Kitagawa J, Hoshi K, et al. Association between frailty and bone loss in patients undergoing maintenance hemodialysis. J Bone Miner Metab 2019;37(1):81-9. (PMID: 29335796)
22. Laur O, Weaver MJ, Bridge C, et al. Computed tomography-based body composition profile as a screening tool for geriatric frailty detection. Skeletal Radiology 2022;51(7):1371-80. (PMID: 34862921)
23. Fried LP, Ferrucci L, Darer J, Williamson JD, Anderson G. Untangling the Concepts of Disability, Frailty, and Comorbidity: Implications for Improved Targeting and Care. J Gerontol A Biol Sci Med Sci 2004;59(3):255-3. (PMID: 15031310)
24. Mureșan AV, Russu E, Arbănași EM, et al. The Predictive Value of NLR, MLR, and PLR in the Outcome of End-Stage Kidney Disease Patients. Biomedicines 2022;10(6):1-13. (PMID: 35740294)
25. Xu W, Liang Y, Lin Z. Association Between Neutrophil-Lymphocyte Ratio and Frailty: The Chinese Longitudinal Healthy Longevity Survey. Frontiers in Medicine 2022;8:1-7. (PMID: 35047530)

RESEARCH

THE RELATIONSHIP OF THE C-REACTIVE PROTEIN /ALBUMIN RATIO TO IN-HOSPITAL MORTALITY IN ELDERLY PATIENTS WITH NON-ST-ELEVATION MYOCARDIAL INFARCTION WHO HAVE UNDERGONE PERCUTANEOUS CORONARY INTERVENTION

Turkish Journal of Geriatrics
DOI: 10.29400/tjgeri.2023.326
2023; 26(1):12−19

Oğuz KILIÇ[1]
Fatma ÖZPAMUK KARADENİZ[2]
Fatih KAHRAMAN[3]

CORRESPONDANCE

[1]Oğuz KILIÇ

Phone : +905300493033
e-mail : dr.kilicoguz@gmail.com

Received : Jan 23, 2023
Accepted : Mar 22, 2023

[1] Karaman Training and Research Hospital, Cardiology Clinic, Karaman, Turkey

[2] Karamanoglu Mehmetbey University, Cardiology Clinic, Karaman, Turkey

[3] Kütahya Evliya Celebi Training and Research Hospital, Cardiology Clinic, Kütahya, Turkey

Abstract

Introduction: Acute myocardial infarction is the most common cardiovascular disease and the cause of significant mortality worldwide. The C-reactive protein/albumin ratio, which measures inflammatory conditions, can be used to predict mortality. In this study, we aimed to investigate the relationship between in-hospital mortality and the C-reactive protein/albumin ratio in patients diagnosed with non-ST-elevation myocardial infarction who underwent interventional treatment at our hospital.

Materials and Method: Two hundred and ninety-seven elderly patients were included in the study. The information of the patients was obtained from the hospital database. The C-reactive protein/albumin ratio was calculated for each patient. We used regression analysis to investigate the relationship between the C-reactive protein/albumin ratio and in-hospital mortality.

Results: A univariate analysis showed that gender, ejection fraction, white blood cell, glucose, creatinine, systolic and diastolic blood pressure, heart rate, GRACE risk score, and CAR ratio were significant predictors of mortality (Table 2). All parameters were added to a multivariable logistic regression, and multivariable logistic regression analysis showed that the GRACE risk score (OR: 0.956, 95% CI: 0.941–0.971; p<0.001) and the C-reactive protein/albumin ratio (OR: 0.812, 95% CI: 0.661–0.998; p=0.048) were the only significant predictors of mortality. Furthermore, bivariate correlation analysis showed a weak but statistically significant correlation between GRACE risk score and C-reactive protein/albumin ratio (r=0.180, p<0.001).

Conclusion: We found a significant relationship between C-reactive protein/albumin and in-hospital mortality. C-reactive protein/albumin ratio can be used in clinical practice because it is inexpensive and easy to apply and has a strong prognostic value for elderly non-ST-elevation myocardial infarction patients.

Keywords: Myocardial Infarction; Albumin; Inflammation; Mortality.

INTRODUCTION

Acute myocardial infarction (AMI) is the most common cardiovascular disease worldwide and is a significant cause of mortality (1). Today, with the increase in life expectancy, both the elderly population and the incidence of AMI are increasing. Non-ST-elevation myocardial infarctions (NSTEMI) are more common than ST-elevation myocardial infarctions (STEMI) and unstable angina pectoris (UAP) (1,2). With the increase in recent years of well-equipped health centers providing both emergency interventional treatment and complementary health services, these patients may receive early treatment, yet mortality and morbidity are still high, resulting in high health expenditures.

It is known that age, gender, obesity, smoking, preferred treatment method (interventional, surgical, medical), additional diseases (diabetes mellitus, hypertension, hyperlipidemia, etc.), physical activity, long-term follow-up management, and patient compliance with treatment contribute to a patient's prognosis (2). The current approach to the management of mortality and morbidity after AMI focuses on stratifying patients according to their risk and using an appropriate prognostic factor to determine treatment steps.

Malnutrition is a risk factor for coronary artery disease (CAD). Many studies investigating the relationship between CAD and malnutrition have focused on hypoalbuminemia which is also a risk factor for the development of AMI (3). To our knowledge, there is no evidence demonstrating the prognostic value of low albumin levels in elderly patients diagnosed with NSTEMI.

Inflammation plays an important role in both the initiation and progression of the atherosclerotic process (3,4). Many studies have shown that the serum level of C-reactive protein (CRP), which is an inflammation marker, is correlated with the severity of atherosclerosis and plaque burden (4). It has also been found that the severity of myocardial damage and serum CRP levels are correlated after acute coronary syndrome (4,5).

The ratio of serum CRP level to albumin (CAR), which is considered a new indicator of inflammatory response, is thought to be a more accurate indicator than albumin and CRP levels alone in determining the prognosis of patients with many inflammatory diseases, such as sepsis, cancer, acute pancreatitis, and ulcerative colitis (5). In addition, the CAR ratio has been shown to predict stent restenosis in AMI patients during follow-up after interventional treatment (6). In this study, we aimed to investigate the relationship between in-hospital mortality and CAR in patients with a diagnosis of NSTEMI who underwent interventional treatment.

MATERIALS AND METHOD

Patient population

Our study is observational and retrospective. Two hundred and ninety-seven patients who applied to the emergency department of our clinic and who underwent interventional treatment in coronary angiography (CAG) with a diagnosis of NSTEMI were included by sequential screening. The study was approved by the local ethics committee and complies with the Declaration of Helsinki. Patient information was scanned retrospectively using the hospital registry system.

Patients who presented to the emergency department with chest pain and symptoms suggestive of ischemia (i.e., shortness of breath, palpitations, a squeezing sensation, fatigue, and dizziness), with cardiac enzymes exceeding the upper limit of normal, were included. Those with findings consistent with STEMI on electrocardiography, cardiac tamponade findings on echocardiography, acute valve pathology, aortic dissection and aneurysm, and systemic infection, and those who had taken medications (anti-inflammatory, antibiotic, statins, etc.) in the previous week were excluded.

The clinical features and laboratory data of the patients were recorded at the time of admission. Bedside echocardiography was performed on each patient. The left ventricular ejection fraction (LVEF) was calculated using the modified Simpson's method. The heart rhythm and heart rate of the patients were recorded. Demographics, fasting blood glucose levels, hemogram, kidney function parameters (urea, creatinine, glomerular filtration rate, and electrolyte levels), CRP, lipid profiles (low-density lipoprotein cholesterol [LDL-C]), high-density lipoprotein cholesterol [HDL-C]), triglyceride (TG) levels), albumin, and aspartate transaminase (AST) are among the clinical variables. Patients were considered hypertensive if their systolic blood pressure/diastolic blood pressure was greater than 140/90 mmHg on two or more measurements or if they were using any antihypertensive medication. Diabetes mellitus was defined as fasting blood sugar above 126 mg/dL, postprandial blood sugar above 200 mg/dL, glycosylated hemoglobin above 6.5%, or the use of any antidiabetic medication. Patients' CAR ratio was calculated and recorded upon admission.

Statistical analysis

All statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were defined as mean ± standard deviation, and categorical variables were defined as numbers and percentages. The Kolmogorov–Smirnov, and Shapiro–Wilk tests were used to determine the normal distribution. The independent samples t-test was used when parametric test conditions were met for independent group comparisons, and the Mann–Whitney U test was used when parametric test conditions were not met. The difference between categorical variables was analyzed using the chi-square test. Logistic regression (LR) analysis was used to find predictors of in-hospital mortality in NSTEMI. Univariate analysis was performed in the first step. Independent variables were found to be statistically significant (p-value less than 0.05), and clinically important parameters were added to binary multivariable logistic regression.

RESULTS

Of the 297 patients with NSTEMI who underwent percutaneous coronary intervention at our institution, 270 were discharged, and 27 patients died while in the hospital. When the two groups were compared, no statistical difference was found in terms of age, gender, hypertension, diabetes mellitus, hyperlipidemia, smoking, or history of CAD (Table 1). The group who died in the hospital showed lower LVEF (50% [40–55] vs. 40% [30–45]; p<0.001) and systolic blood pressure (130 mmHg [110–142] vs. 95.5 mmHg [86.5–128], p<0.001). Additionally, the group who died in the hospital showed higher values for heart rate (80/min [70–90] vs. 90/min [79–10]), p=0.008), peak troponin (0.4 ng/mL [0.09–1.78] vs. 2.2 ng/mL [1.1–7.7], p=0.001), and creatinine (0.94 mg/dl [0.77–1.20] vs. 1.39 mg/dl [1.05–1.66], p=0.047), and their GRACE risk score (148 [121–167] vs. 203 (169–233), p<0.001) was higher (Table 1). CAR (0.20 mg/g (0.06-0.76) vs. 0.71 mg/g (0.35-1.80), p=0.039) was statistically significant. In univariate analysis, gender, ejection fraction, WBC, glucose, creatinine, systolic and diastolic BPs, heart rate, GRACE risk score, and CAR ratio were found to be significant predictors of mortality (Table 2). All parameters were added to multivariable LR, and multivariable LR analysis showed that the GRACE risk score (OR: 0.956, 95% CI: 0.941-0.971; p<0.001) and CAR ratio (OR: 0.812, 95% CI: 0.661-0,998; p=0.048) were the only significant predictors of mortality. Furthermore, bivariate correlation analysis showed that a weak but statistically significant correlation between GRACE risk score and CAR ratio (r=0.180, p<0.001) (Table 2).

Table 1. Demographic and Clinical Characteristics of Patient Population

	Survivors (n=270)	Non-survivors (n=27)	p value
Age (years)	76 (70-82)	77 (73-86)	0.648
Gender male (n, %)	184 (%68.1)	21 (%77.8)	0.385
HT (n, %)	162 (60)	19 (70.4)	0.408
DM (n, %)	107 (39.6)	15 (55.6)	0.150
HL (n, %)	45 (16.7)	2 (7.4)	0.276
CRD (n, %)	55 (20.5)	6 (23.1)	0.800
Smoking (n, %)	58 (21.5)	4 (14.8)	0.665
CAD history (n, %)	142 (52.6)	19 (70.4)	0.104
LVEF (%)	50 (40-55)	40 (30-45)	**<0.001**
Systolic blood pressure	130 (110-142)	95.5 (86.5-128)	**<0.001**
Diastolic blood pressure	72.5 (68-72.5)	62.5 (59-70)	**0.002**
Heart rate (bpm)	80 (70-90)	90 (79-101)	**0.008**
Hemoglobin (mg/dl)	12.6±1.85	11.7±1.88	0.067
White blood cell 10^9/l	9 (7.2-11.1)	12.6 (9.4-15.9)	0.121
Glucose (g/dl)	121 (102-166)	170 (130-262)	**0.006**
Peak Troponin (ng/mL)	0.4 (0.09-1.78)	2.2 (1.1-7.7)	**0.001**
Peak CK-MB (U/L)	13.1 (4.3-43)	91.4 (14.2-196.3)	**0.002**
Creatinine (mg/dl)	0.94 (0.77-1.20)	1.39 (1.05-1.66)	**0.047**
Albumin (g/dl)	3.6 (3.2-3.9)	3.4 (3.1-3.7)	0.445
Total cholesterol (mg/dl)	173±46	162±44	0.202
LDL (mg/dl)	105±39	93±27	**0.021**
HDL (mg/dl)	41 (34-51)	36.5 (26-46)	0.869
Triglycerides (mg/dl)	109 (80-158)	113 (98-176)	0.242
CRP (mg/dl)	0.7 (0.2-2.8)	2.5 (1.1-6.3)	0.078
CRP to albumin ratio	0.20 (0.06-0.76)	0.71 (0.35-1.80)	**0.039**
GRACE risk score	148 (121-167)	203 (169-233)	**<0.001**

Continuous variables were summarized as mean ± SD, categorical variables were summarized as counts and percentages.
Abbreviations: HT: Hypertension, DM: Diabetes Mellitus, HL: Hyperlipidemia, CRD: Chronic Renal Disease, CAD: Coronary artery disease, LVEF: Left ventricular ejection fraction, LDL: Low density lipoprotein cholesterol, HDL: High density lipoprotein cholesterol, CRP: C-reactive protein.

Table 2. Independent Predictors of in-hospital mortality

Variables	Univariate analysis		Multivariable analysis	
	OR (95% CI)	p	OR (95% CI)	p
Gender (female)	0,611 (0,238-1.569)	0.306		
LVEF	1.087 (1.046-1.131)	**<0.001**		
WBC	0.836 (0.760-0.919)	**<0.001**		
GLUCOSE	0.994 (0.991-0.997)	**<0.001**		
CREATININE	0.690 (0.519-0.917)	**0.011**		
SBP	1.046 (1.024-1.068)	**<0.001**		
DBP	1.054 (1.019-1.091)	**0.002**		
HEART RATE	0.977 (0.959-0.994)	**0.010**		
GRACE RİSK SCORE	0.956 (0.941-0.970)	**<0.001**	0.956 (0.941-0.970)	**<0.001**
CAR	0.796 (0.670-0.947)	**0.010**	0.812 (0.661-0.998)	**0.048**

Abbreviations: LVEF: Left ventricular ejection fraction, WBC: White blood cell, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, CAR: C-reactive protein to albumin ratio

DISCUSSION

Our study is the first to investigate the relationship between in-hospital mortality and CAR ratio in elderly patients with NSTEMI who have undergone interventional treatment. Today, the prevalence of CAD is increasing with the prolongation of life expectancy and the increase in the elderly population (7). Despite the increase in both early interventional treatment and complementary health services in addition to medical treatment, mortality and morbidity are still high in these patients (8).

CRP, which is an acute-phase reactant, is used as a marker showing the presence of inflammation and tissue damage. The most common cause of CAD is atherosclerosis. The most important reason for the onset and progression of atherosclerosis is inflammation (9). Pro-inflammatory cytokines, which are released by immunological reactions in the initial stages of atherosclerotic plaque formation, increase the release of CRP from the liver (10). The predictive value of increased CRP levels for CAD has been emphasized in many studies. A study on healthy people showed that those with a plasma CRP level above 2 mg/L had a greater five-year risk of atherosclerotic cardiovascular disease than those with a CRP level of 0.5 mg/L or less (11). In another study, the long-term follow-up of approximately 700 patients hospitalized for AMI showed a significant correlation between CRP levels and mortality (12). In our study, the mean CRP value was higher in the group of patients who died in the hospital.

Hypoalbuminemia is a strong prognostic marker of inflammation and malnutrition. Recent studies have shown that a low albumin level is an independent risk factor for ischemic heart disease, heart failure, atrial fibrillation, stroke, and venous

thromboembolism (13). In the ARIC study, which included 14,506 patients, low albumin plasma levels were found to be associated with ischemic heart disease in the smoking group, independent of traditional risk factors and inflammation (14). In the Framingham Offspring Study, which included 4,506 people, a low plasma albumin level was an independent predictor of the first AMI during the 22-year follow-up period (15). In a recent study involving 7,647 individuals, low plasma albumin levels were strongly associated with the occurrence of a first or recurrent AMI, independent of traditional risk factors (16). Low albumin levels have also been associated with poor in-hospital outcomes in STEMI patients (17).

CAR is a new prognostic measure of inflammation associated with inflammation severity and mortality (17). Several studies have shown that increased CAR values have prognostic value for STEMI (18). Increased CAR values were also found to be associated with increased in-hospital mortality in STEMI patients (19). An increased CAR ratio was also associated with thrombus burden and a greater extent of coronary artery disease in AMI patients (20,21). Increased CAR levels were found to be associated with increased intent restenosis in STEMI patients (22,23). Increased CAR levels were also associated with increased contrast-induced nephropathy levels in NSTEMI patients (24). A study conducted in 2020 found that the CAR ratio predicted coronary microvascular dysfunction better than CRP and albumin levels alone in patients with celiac disease (25). Our study found that high CAR levels were associated with in-hospital mortality in elderly patients diagnosed with NSTEMI. In addition, CAR levels were also associated with a high GRACE risk score. The CAR ratio can reduce potential bias and can be used as a more reliable prognostic parameter than either CRP or albumin levels alone.

Limitations

The limitations of our study are, first, that it does not provide prognostic data due to its cross-sectional design. In addition, it is a single-center study that included a relatively small number of patients. In addition, some patients were excluded due to missing clinical data and/or laboratory variables. Finally, the presence of multiple comorbidities and vulnerabilities may have affected in-hospital mortality.

CONCLUSION

Our study investigates the association between CAR and in-hospital mortality in elderly patients following in-hospital treatment for NSTEMI. Multivariate regression analysis revealed a significant relationship between CAR and in-hospital mortality. The CAR ratio may have a stronger prognostic value than either CRP or albumin levels alone. It can be used in clinical practice because it is inexpensive and easy to apply and has a strong prognostic value in NSTEMI patients.

REFERENCES

1. Roth GA, Mensah GA, Johnson CO, et al. Global burden of cardiovascular diseases and risk factors, 1990–2019: update from the GBD 2019 study. J Am Coll Cardiol. 2020;76:2982–3021. (PMID: 33309175; PMCID: PMC7755038).
2. Ho PM, Lambert-Kerzner A, Carey EP, et al. Multifaceted intervention to improve medication adherence and secondary prevention measures after acute coronary syndrome hospital discharge: a randomized clinical trial. JAMA Intern Med. 2014;174(2):186-193. (PMID: 24247275).
3. Arques S. Serum albumin and cardiovascular diseases: a comprehensive review of the literature. Annales de Cardiologie et D'angéiologie 2018; 67 (2): 82-90. (PMID: 29544976).
4. Hansson GK. Inflammation, atherosclerosis, and coronary artery disease. N Engl J Med. 2005 Apr 21;352(16):1685-95. (PMID: 15843671).

5. Zhou T, Zhan J, Hong S, et al. Ratio of C-reactive protein/albumin is an ınflammatory prognostic score for predicting overall survival of patients with small-cell lung cancer. Scientific Reports 2015; 5: 10481. (PMID: 26084991; PMCID: PMC4471724).
6. Karabağ Y, Çağdaş M, Rencuzogullari I, et al. Usefulness of the C-reactive protein/albumin ratio for predicting no-reflow in ST-elevation myocardial infarction treated with primary percutaneous coronary intervention. European Journal of Clinical Investigation 2018; 48 (6): e12928. (PMID: 29577260).
7. Virani SS, Alonso A, Aparicio HJ, et al. Heart disease and stroke statistics 2021 update: a report from the American Heart Associationexternal icon. Circulation. 2021;143:e254–e743. (PMID: 33501848).
8. Rosamond WD, Chambless LE, Heiss G, et al. Twenty-two-year trends in incidence of myocardial infarction, coronary heart disease mortality, and case fatality in 4 US communities, 1987-2008. Circulation. 2012;125:1848–1857. (PMID: 22420957; PMCID: PMC3341729).
9. Alexander RW. Inflammation and coronary heart disease. N Engl J Med 1994; 331:468-9. (PMID: 8035844).
10. Bataille R, Klein B. C-reactive protein levels in humans in vivo. Arthritis Rheum 1992; 35:982-4. (PMID: 1642664).
11. Ridker PM, Cushman M, Stampfer MJ, Tracy RP, Hennekens CH. Plasma concentration of C-reactive protein and risk of developing peripheral vascular disease. Circulation 1998; 97:425-8. (PMID: 9490235).
12. Nikfardjam M, Mullner M, Schreiber W, Oschatz E, Exner M. The association between C-reactive protein on admission and mortality in patients with acute myocardial infarction. J Intern Med 2000; 247(3):341-5. (PMID: 10762450).
13. Kanaan GN, Harper ME. Cellular redox dysfunction in the development of cardiovascular diseases. Biochim Biophys Acta 2017 Nov;1861(11 Pt A):2822–9. (PMID: 28778485).
14. Nelson JJ, Liao D, Sharrett AR, et al. Serum albumin level as a predictor of incident coronary heart disease: the Atherosclerosis Risk in Communities (ARIC) study. Am J Epidemiol 2000 Mar 1;151(5):468–77. (PMID: 10707915).
15. Djoussé L, Rothman KJ, Cupples LA, Levy D, Ellison RC. Serum albumin and risk of myocardial infarction and all-cause mortality in the Framingham Offspring Study. Circulation 2002 Dec 3;106(23):2919–24. (PMID: 12460872).
16. Yang Q, He YM, Cai DP, Yang XJ, Xu HF. Risk burdens of modifiable risk factors incorporating lipoprotein (a) and low serum albumin concentrations for first incident acute myocardial infarction. Sci Rep 2016 Oct 17;6:35463. (PMID: 27748452; PMCID: PMC5066202).
17. Bicciré FG, Pastori D, Tanzilli A, et al. Low serum albumin levels and in-hospital outcomes in patients with ST segment elevation myocardial infarction. Nutr Metab Cardiovasc Dis. 2021 Sep 22;31(10):2904-2911. (PMID: 34344545).
18. Askin L, Tanriverdi O, Tibilli H, Turkmen S. Prognostic value of C-reactive protein/albumin ratio in ST-segment elevation myocardial infarction. Interv Med Appl Sci. 2019 Oct 7;11(3):168-171. (PMID: 36343286; PMCID: PMC9467334).
19. Söğüt O, Akdemir T, Can MM. Prognostic value of the C-reactive protein to albumin ratio in patients undergoing primary percutaneous coronary intervention for ST-segment elevation myocardial infarction. Turk J Med Sci. 2021; 51: 1281-1288. (PMID: 33453709; PMCID: PMC8283510).
20. Çağdaş M, Rencüzoğullari I, Karakoyun S, et al. Assessment of Relationship Between C-Reactive Protein to Albumin Ratio and Coronary Artery Disease Severity in Patients With Acute Coronary Syndrome. Angiology. 2019 Apr;70(4):361-368. (PMID: 29172653).
21. Duman H, Çinier G, Bakırcı EM, et al. Relationship Between C-Reactive Protein to Albumin Ratio and Thrombus Burden in Patients With Acute Coronary Syndrome. Clin Appl Thromb Hemost. 2019 Jan-Dec;25:1076029618824418. (PMID: 30808220; PMCID: PMC6715111).
22. Aksu U, Gulcu O, Aksakal E, et al. The association between CRP / Albumin ratio and in-stent restenosis development in patients with ST-segment elevation myocardial infarction. J Clin Lab Anal. 2019 May;33(4):e22848. (PMID: 30737841; PMCID: PMC6528603).
23. Rencuzogullari I, Karabağ Y, Çağdaş M, et al. Assessment of the relationship between preprocedural C-reactive protein/albumin ratio and stent restenosis in patients with ST-segment elevation myocardial infarction. Rev Port Cardiol (Engl Ed). 2019 Apr;38(4):269-277. (PMID: 31104927).

24. Satilmis S, Karabulut A. Value of C-Reactive Protein/Albumin Ratio in Predicting the Development of Contrast-Induced Nephropathy in Patients With Non-ST Elevation Myocardial Infarction. Angiology. 2020 Apr;71(4):366-371. (PMID: 32000500).

25. Ranzani OT, Zampieri FG, Forte DN, Azevedo LC, Park M. C-reactive protein/albumin ratio predicts 90-day mortality of septic patients. PLoS One 2013;8:e59321. (PMID: 23555017; PMCID: PMC3595283).

RESEARCH

EFFICACY OF EPIDURAL STEROID INJECTION IN ELDERLY PATIENTS: DOES DIAGNOSIS AFFECT TREATMENT SUCCESS?

Turkish Journal of Geriatrics
DOI: 10.29400/tjgeri.2023.327
2023; 26(1):20-26

Yücel OLGUN[1]
Rekib SACAKLIDIR[1]
Yasin OKUMUŞ[2]
Savaş SENCAN[1]
Osman Hakan GÜNDÜZ[1]

CORRESPONDANCE

[1]Rekib SACAKLIDIR

Phone : +905538044082
e-mail : rakipsacakli@hotmail.com

Received : Dec 17, 2022
Accepted : Feb 06, 2023

[1] Marmara University School of Medicine, Division of Pain Medicine, Department of Physical Medicine and Rehabilitation, istanbul, Turkey

[2] Marmara University School of Medicine, Department of Physical Medicine and Rehabilitation, istanbul , Turkey

Abstract

Introduction: Epidural steroid injections are a preferred interventional pain treatment for patients with low back pain. Our aim was to investigate the effectiveness of epidural steroid injections treatment in elderly patients and to examine the effect of patients' diagnosis on the treatment success.

Materials and Methods: Patients over the age of 65 who underwent epidural injections between January 2020 and January 2022 were retrospectively screened. The patients were divided into three groups according to their diagnosis: disc herniation, spinal stenosis, and failed back surgery syndrome. Numeric rating scale scores of all patients before the procedure, at three weeks, and at three months were noted.

Results: A total of 234 patients were included in the study. Of these, 89 had disc herniation, 98 had spinal stenosis, and 47 had a history of failed back surgery. There were no significant differences between the groups in terms of age, gender, symptom duration, pre-procedural pain score, medical treatment, radiation dose, and procedure duration. Although a significant improvement was detected in pain scores at all follow-ups in all groups, these scores were found to be significantly lower in the disc herniation group than the spinal stenosis and failed back surgery groups at the three-week and month follow-ups.

Conclusions: Epidural steroid injections has been found to be effective in back pain in elderly. In addition, elderly patients with disc herniation had a better response to treatment than those with spinal stenosis and failed back surgery. Further prospective and long-term follow-up studies are needed to support these results.

Keywords: Aged; Low Back Pain; Injections, Epidural; Spinal Stenosis; Failed Back Surgery Syndrome.

INTRODUCTION

Low back pain (LBP) is a common health problem in elderly patients, and its prevalence varies between 21% and 75% (1). LBP causes difficulties in performing daily activities in elderly patients and is responsible for a high rate of functional limitations (1,2). Lumbar spinal stenosis (LSS) and disc herniation (LDH) are common causes of LBP in elderly patients (3). Treatment options for LBP include conservative treatment, interventional pain procedures, and surgery (4).

Lumbar epidural steroid injections (ESIs) are a preferred interventional pain procedure for patients with LBP who do not respond to conservative treatment (5). It is performed using a caudal, interlaminar, or transforaminal approach. ESI is an effective treatment option in the short and medium term in selected cases evaluated clinically and radiologically (6). However, there are few studies on the efficacy of ESIs in elderly patients (7,8). Curatolo et al. showed that ESIs are effective in the long term in patients over 65 years of age (7). In another study, it was shown that ESIs improved pain and functionality for three months in patients over 65 years of age with LSS (8). To the best of our knowledge, the effect of the cause of LBP (failed back surgery, disc herniation, or spinal stenosis) on treatment success in elderly patients has not been investigated. Accordingly, our aim was to investigate the effectiveness of ESI treatment in patients over 65 years of age and to examine the effect of patients' diagnosis on the treatment success.

MATERIALS AND METHODS

Design and study population

The study was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants. After receiving approval from the institutional ethics committee (Ethic approval: 02.09.2022/1151), a retrospective evaluation of patients who received fluoroscopy-guided ESI between January 2020 and January 2022 was conducted in a tertiary hospital pain management center.

The data on all patients were collected from hospital medical documents (demographic data, numeric rating scale (NRS) scores, type of procedure, and medical treatment). The inclusion criteria were individuals aged > 65 years who had an ESI (lumbar interlaminar, lumbar transforaminal, or caudal approaches). Patients with a history of major psychiatric disorders, a diagnosis of malignancy, missing three-week and three-month follow-ups, and without demographic or clinical data were excluded from the study. The patients were divided into three groups according to their diagnosis as LDH, LSS, and failed back surgery syndrome (FBSS). The NRS scores of all patients before the procedure, at the third week, and at the third month were noted. A 50% or more reduction in NRS score at follow-up was accepted as treatment success (9).

Statistical analysis

Statistical analyses were performed using SPSS version 22.0 software (IBM Corp., Armonk, NY). Continuous variables were expressed as means (standard deviation) and medians (interquartile range), while categorical variables were expressed as numbers and frequencies. The chi-square test was used to compare categorical variables. The Shapiro–Wilk test was used to analyze the normal distribution of quantitative data. A repeated measure analysis of variance (ANOVA) was used to analyze changes over time with treatment, and Bonferroni correction was employed for multiple comparisons. Statistical significance was accepted at a p-value <.017 for Bonferroni correction; and otherwise, a p-value <.05 was considered statistically significant.

RESULTS

A total of 234 patients were included in the study. Of these patients, 89 had LDH, 98 had LSS, and 47 had a history of FBSS. The average age of the patients in the LDH and FBSS groups was 72, while the average age of the patients in the LSS group was 74. There was no significant difference between the three groups in terms of age, symptom duration, BMI, gender, medical treatment, pre-procedural NRS, radiation dose, and procedure duration (Table 1).

The mean pre-procedural NRS score of all patients was 8.24, and the NRS scores of the patients at the third week and third month were 4.20 and 4.51, respectively (Table 2). In all groups, a significant improvement was found in NRS scores in the first hour, third week, and the third month compared to the pre-procedural NRS ($p<0.001$). Although significant improvements were detected in NRS scores at all follow-ups in all three groups, the scores were found to be significantly lower in the LDH group than in the LSS and FBSS groups

Table 1. Demographic and clinical data between the groups

Variable value	LDH (n:89)	LSS (n:98)	FBSS (n:47)	p
Age (years)	72.21± 5.61	74.02 ± 6.57	72.44 ± 6.65	0.113
BMI (kg/m^2)	29.91 ± 5.89	30.56 ± 6.24	29.72 ± 4.57	0.603
Pre NRS	8.08 ± 1.24	8.18 ± 1.15	8.55 ± 0.921	0.156
Symptom duration (m)	17.72 ± 5.44	18.95 ± 5.65	20.10 ± 6.05	0.245
Procedure time	47.63 (13-197)	41.46 (17-150)	52.56 (17-186)	0.142
Radiation dose	8.22 ± (0.38-37.6)	8.71 ± (0.48-96.5)	13.14 ± (0.15-65.4)	0.095
Gender (n / %)				
Male	28 (31.5)	25 (25.5)	14 (29.6)	0.299
Female	61 (68.5)	73 (74.5)	33 (70.4)	
Neuropathic pain medications (n)				
Pregabalin	11	24	10	0.098
Gabapentin	23	31	14	0.102
Duloksetin	8	11	8	0.370
Opioid	12	14	7	0.405

Lumbar Disc Herniation (LDH), Lumbar Spinal Stenosis (LSS) and Failed Back Surgery Syndrome (FBSS)

Table 2. Time Changes of NRS Scores LDH, LSS and FBSS Group

	Mean ± Std. Deviation	p
LDH.NRS.Pre[1]	8.09 ± 1.25	<0.001[a]
LDH.NRS.Post[2]	0.79 ± 0.34	
LDH.NRS3.week[3]	3.15 ± 2.55	
LDH.NRS3.month[4]	3.36 ± 3.02	
LSS.NRSPre[1]	8.17 ± 1.20	<0.001[b]
LSS.NRSPost[2]	0.55 ± 0.23	
LSS.NRS3.week[3]	4.60 ± 3.11	
LSS.NRS3.month[4]	4.95 ± 3.16	
FBSS.NRSPre[1]	8.49 ± 0.89	<0.001[c]
FBSS.NRSPost[2]	1.17 ± 0.90	
FBSS.NRS3.week[3]	4.83 ± 3.01	
FBSS.RS3.month[4]	5.07 ± 3.30	
Total.NRSPre[1]	8.24 ± 1.15	0.001[d]
Total.NRSPost[2]	0.71 ± 0.34	
Total.NRS3.week[3]	4.20 ± 2.95	
Total.NRS3.month[4]	4.51 ± 3.25	

[a]Post hoc tests: 1-2, 1-3, 1-4 significant ;[b]Post hoc tests: 1-2, 1-3, 1-4 significant ;[c]Post hoc tests: 1-2, 1-3, 1-4 significant; [d]Post hoc tests: 1-2, 1-3, 1-4 significant; Pre:Before ESI ; Post: 1. Hour after ESI

Table 3. NRS change between groups at 3.th week and 3.th month follow-up

	Group 1	Group 2	Mean (SD)	Mean (SD)	p
NRS.Pre	LDH	LSS	8.09 ± 1.25	8.17± 1.20	1.000
	LDH	FBSS	8.09 ± 1.25	8.49± 0.86	0.175
	LSS	FBSS	8.17 ± 1.20	8.49± 0.86	0.383
NRS3.Week	LDH	LSS	3.15 ± 2.55	4.60 ± 3.11	**0.007**
	LDH	FBSS	3.15 ± 2.55	4.83 ± 3.01	**0.009**
	LSS	FBSS	4.60 ± 3.11	4.83 ± 3.01	1.000
NRS3.Month	LDH	LSS	3.36 ± 3.02	4.95 ± 3.16	**0.007**
	LDH	FBSS	3.36 ± 3.02	5.07 ± 3.30	**0.014**
	LSS	FBSS	4.95 ± 3.16	5.07 ± 3.30	1.000

Lumbar Disc Herniation (LDH), Lumbar Spinal Stenosis (LSS) and Failed Back Surgery Syndrome (FBSS)

at the three-week and three-month follow-ups (Table 3). No major complications were detected during the procedures. There were two minor complications in the LDH and LSS groups and one minor complication in the FBSS group.

DISCUSSION

ESIs have been found to be an effective and safe treatment option for LBP in elderly patients (7,8,10). In particularly, elderly patients with LBP due to LDH or LSS have been shown to benefit from ESI (7,8). The present study investigated the effectiveness of ESI treatment in patients over 65 years of age and examined the effect of patients' diagnosis on treatment. It was found that ESI resulted in a statistically significant pain improvement in elderly patients at the three-month follow-up. In addition, the NRS pain scores of the patients with LDH at the third week and third month after treatment were significantly lower than those in the LSS and FBSS groups.

Curatolo et al. showed that pain and functionality were better in the group that underwent ESI compared to the control group at the 24-month follow-up in elderly patients (7). Tasdogan et al. reported that ESI was effective based on a three-month follow-up of 44 elderly patients with LSS (8). Similarly, ESI was found to be effective in a one-month follow-up of 16 elderly patients with LSS (10). In the current study, the three-month pain scores of 234 patients with LBP after ESI were evaluated retrospectively. The three-week and three-month pain scores were significantly lower than the preprocedural pain scores. This result supports other studies on ESI in elderly patients (8,10). In addition, no major complications were detected, and only five patients (2.1%) had minor complications. In this respect, ESIs may be beneficial for patients of advanced age, as they are an effective treatment option with a low complication rate (11).

Manchikanti et al. published a systematic review of transforaminal ESI for LBP and lower extremity pain. The study examined lumbar disc herniation, spinal stenosis, discogenic pain, and FBSS. Strong evidence of the efficacy of ESI was found in the disc herniation group, moderate evidence in the spinal stenosis group, and poor evidence in the postsurgery syndrome group (12). Smith et al. presented a systematic review of ESI as a treatment for lumbar radicular pain. They found strong evidence that ESI is effective in treating lumbar radicular pain due to disc herniation. Low-quality evidence has been found for ESI treatment for radicular pain due to spinal stenosis (13). Rivest et al. also investigated the effect of ESI treatment on LDH and LSS and found that the treatment success of the LDH group was better than that of the LSS group (14). In the present study, although a significant improvement was detected in all patient groups over 65 years of age with lumbar ESI, a significant difference was found between the LDH group and the LSS and FBSS groups at the third month. The LDH patients benefited most from lumbar ESI, followed by LSS patients and then the FBSS group. While this study supports the data in the literature, it also provides information about the success of the treatment based on the diagnosis. The better ESI response in patients with LDH may be due to different pain mechanisms in the pathologies of these diseases. In patients with LSS, steroid injection provides membrane stabilization and pain relief (15), but mechanical and vascular compression does not improve with steroid injection (16). Meanwhile, in FBSS, multiple mechanisms, such as inflammation, mechanical compression, fibrosis, and arachnoiditis cause pain (17), and ESI is especially effective for relieving pain due to inflammation. As inflammation is the main cause of LDH-induced pain, steroid injection, which suppresses inflammation, is effective (18). Therefore, better results may be obtained with ESI in patients with LDH compared to those with LSS and FBSS.

The prevalence of LBP in the elderly is 21%–75% (1), and it is more common in women than in men. Similarly, in the present study, most of the patients who applied to the outpatient clinic and underwent ESI were women. The patients mostly received gabapentin, pregabalin, opioids, and duloxetine, and the rates of drug use were similar in all groups. The rate of opioid use was found to be 8% in elderly patients who underwent ESI for LSS (8), which supports our results. It has been observed that amitriptyline treatment is not desirable in the elderly because of its cardiac and antimuscarinic side effects (19,20).

This study has a number of limitations. First, it is a retrospective study with short-term results. Second, the grades of disc herniation and spinal stenosis were not measured. Further, differences between ESI types in the patient groups were not evaluated. Finally, patients' comorbidities were not evaluated. Conversely, the strength of the study is the large number of patients, and to the best of our knowledge, it is the first study to evaluate ESI treatment success according to diagnosis in elderly patients.

CONCLUSION

ESI is a preferred treatment for LBP in elderly patients because of its effectiveness and low complication rate. In this study, elderly patients with LDH showed a better response to treatment than those with LSS and FBSS. Further prospective and long-term follow-up studies are needed to support these results.

REFERENCES

1. de Souza IMB, Sakaguchi TF, Yuan SLK, et al. Prevalence of low back pain in the elderly population: a systematic review. Clinics (Sao Paulo) 2019;74: e789. (PMID: 31664424)
2. Edmond SL, Felson DT. Function and back symptoms in older adults. Journal of the American Geriatrics Society 2003;51: 1702-1709. (PMID: 14687347)
3. Tarulli AW, Raynor EM. Lumbosacral radiculopathy. Neurol Clin 2007;25: 387-405. (PMID: 17445735)
4. Wong AYL, Karppinen J, Samartzis D. Low back pain in older adults: risk factors, management options and future directions. Scoliosis Spinal Disord 2017;12: 14. (PMID: 28435906)
5. Manchikanti L, Knezevic E, Knezevic NN, et al. A Comparative Systematic Review and Meta-Analysis of 3 Routes of Administration of Epidural Injections in Lumbar Disc Herniation. Pain Physician 2021;24: 425-440. (PMID: 34554683)
6. Friedrich JM, Harrast MA. Lumbar epidural steroid injections: indications, contraindications, risks, and benefits. Current sports medicine reports 2010;9: 43-49. (PMID: 20071921)
7. Curatolo M, Rundell SD, Gold LS, et al. Long-term effectiveness of epidural steroid injections after new episodes of low back pain in older adults. Eur J Pain 2022;26: 1469-1480. (PMID: 35604636)
8. Tasdogan AM, Kilic ET. Outcome Measurements for Pain Relief in Elderly Patients with Spinal Stenosis Undergoing Epidural Steroid Injection: Is Conservative Approach an Option? Turk Neurosurg 2020;30: 734-738. (PMID: 32530487)
9. Ghahreman A, Ferch R, Bogduk N. The efficacy of transforaminal injection of steroids for the treatment of lumbar radicular pain. Pain Medicine 2010;11: 1149-1168. (PMID: 20704666)
10. Przkora R, Kinsky MP, Fisher SR, et al. Functional Improvements Utilizing the Short Physical Performance Battery (SPPB) in the Elderly after Epidural Steroid Injections. Curr Pain Headache Rep 2019;23: 14. (PMID: 30796532)
11. Sencan S, Sacaklidir R, Gunduz OH. The Immediate Adverse Events of Lumbar Interventional Pain Procedures in 4,209 Patients: An Observational Clinical Study. Pain Med 2022;23: 76-80. (PMID: 34347099)
12. Manchikanti L, Buenaventura RM, Manchikanti KN, et al. Effectiveness of therapeutic lumbar transforaminal epidural steroid injections in managing lumbar spinal pain. Pain Physician 2012;15: E199-245. (PMID: 22622912)
13. Smith CC, McCormick ZL, Mattie R, et al. The Effectiveness of Lumbar Transforaminal Injection of Steroid for the Treatment of Radicular Pain: A Comprehensive Review of the Published Data. Pain Med 2020;21: 472-487. (PMID: 31343693)

14. Rivest C, Katz JN, Ferrante FM, et al. Effects of epidural steroid injection on pain due to lumbar spinal stenosis or herniated disks: a prospective study. Arthritis Care Res 1998;11: 291-297. (PMID: 9791328)

15. Johansson A, Hao J, Sjölund B. Local corticosteroid application blocks transmission in normal nociceptive C-fibres. Acta Anaesthesiol Scand 1990;34: 335-338. (PMID: 2167604)

16. Shamov T, Al-Hashel JY, Rousseff RT. Fluoroscopic Epidural Steroid Injection: Pain Relief in Discogenic Sciatica Versus Lumbar Spinal Stenosis. A Study on Middle Eastern Patients. Acta Medica (Hradec Kralove) 2020;63: 73-78. (PMID: 32771072)

17. Van Buyten J-P, Linderoth B. "The failed back surgery syndrome": Definition and therapeutic algorithms – An update. European Journal of Pain Supplements 2010;4: 273-286. (DOI: 10.1016/j.eujps.2010.09.006)

18. Mulleman D, Mammou S, Griffoul I, et al. Pathophysiology of disk-related sciatica. I.--Evidence supporting a chemical component. Joint Bone Spine 2006;73: 151-158. (PMID: 16046173)

19. McCue RE. Using tricyclic antidepressants in the elderly. Clin Geriatr Med 1992;8: 323-334. (PMID: 1600482)

20. Sacaklidir R, Şencan S, Gündüz OH. The Effect of the Covid-19 Pandemic on Lumbar Epidural Steroid Injections in Elderly Patients: One Year Data. Turkish Journal of Geriatrics 2022; 25(2): 230-235 (DOI: 10.31086/tjgeri.2022.280)

RESEARCH

A 30-DAY RISK ASSESSMENT OF GERIATRIC PATIENTS IN THE EMERGENCY DEPARTMENT: A COMPARISON OF ISAR AND TRST SCORES

Turkish Journal of Geriatrics
DOI: 10.29400/tjgeri.2023.328
2023; 26(1):27-36

Savaş SEZİK[1]

Abstract

Introduction: The aim of this prospective observational study was to compare the predictive ability of the Triage Risk Stratification Tool and Identification of Seniors at Risk in identifying elderly people at risk of adverse outcomes (return to the emergency department, hospital admission, and death) within 30 days following discharge from the emergency department.

Materials and Methods: 396 patients aged between 65 and 98 (mean 76.89±7.59) accessing the emergency department were evaluated over a 1-month period. Both screening tool were administered in the emergency department by emergency specialist physicians. Risk factors were assigned a score based on their regression co-efficient estimate and a total risk score was created. This score was evaluated for sensitivity and specificity.

Results: Of the 396 participants, 198 (50%) were female. A significant correlation was not observed between risk of adverse outcomes and characteristics of the participant (p>0.005). The Identification of Seniors at Risk (cutoff of ≥3) was positive in 61.3% of the patients, whereas 79% were Triage Risk Stratification Tool-positive (cutoff of ≥2). The two scores were significantly correlated and had similar areas under the receiver operating characteristic curves in predicting hospital admission (Identification of Seniors at Risk, 0.63; Triage Risk Stratification Tool, 0.59).

Conclusions: The predictive accuracy of the scoring systems for hospital admission after 30 days was significant at cutoff values of ≥3 for Identification of Seniors at Risk and ≥2 for Triage Risk Stratification Tool. The Identification of Seniors at Risk had slightly higher sensitivity and lower specificity than the Triage Risk Stratification Tool.

Key Words: Emergency Service, Hospital; Geriatric Assessment; Risk Assessment; Aged.

CORRESPONDANCE

[1]Savaş SEZİK

Phone : +905059442335
e-mail : savassezik@gmail.com

Received : Feb 11, 2023
Accepted : Mar 22, 2023

[1] Odemis State Hospital, Emergency Service, Izmir, Turkey

INTRODUCTION

The population of elderly people who pose great risk for hospitalization, unintended admission to the emergency department (ED) and death are enormously growing, resulting in huge economic and accommodation encumbrance for the healthcare organizations. Conducive to recognition of these target groups, healthcare workers need to perform some sort of risk evaluation to concentrate their exertions, taking into account that the elderly people are far reaching diversified in terms of operating and disease load. We do lack enough specialized units in our EDs to receive geriatric patients. We also do not have specific care providers for these patients. Certain standards should be established in care areas for this age group of patients who are also physiologically fragile due to their age. One of these standards should be scoring systems to be used in emergency services. Unfortunately, the importance of these scoring systems is not considered. With the increase in the elderly population, both admission to the ED and the economic burden brought about will increase significantly. In many countries, various measures have been tried to identify risk groups, prevent recurrent presentations, and reduce the economic burden. Efforts have been done to evolve different scoring systems to recognize risk groups, and these are being modified over time. In many countries, readmission rates are discussed as quality indicators; therefore, governments seek various ways to take measures (1).

There isn't enough agreement in the literature regarding the most proper introductory try-out examinations to be used. Several screenings for risk, including the Identification of Seniors at Risk (ISAR), the Dismiss of the Aged people from the urgent section (ED) and lately the Silver Code, have been advanced to point out older ED patients bearing more risk. The ISAR and the Triage Risk Screening Tool (TRST) are two of the most conventional risk assessment implements for elderly patients admitted to ED. The foretelling accuracies of the ISAR and TRST scores are sustained, remarking replicability of these scores (2).

The ISAR was developed to pick out seniors at risk of disadvantageous health consequences, including but not limited to functional turn down, admission to the ED, being inpatient, staying in hospital for longer term and finally morbidity during three, six and nine months after being admitted into ED with a discontinued score of 2 (3). ISAR screening foresees a broad spectrum of unfavourable health results, such as morbidity, hospital readmission, assets utilizing and corporeal or cognitive function (4). The ISAR score consists of six uncomplicated bipartite questions (functional decline, mortality, hospitalization, community service utilization), making it momentary, straightforward, and bearable for patients and health workers (5). Assuming patients have two or more positive responses (≥ 2 scores) on the ISAR screening test indicates an increased risk for the geriatric population. This test can be applied for advanced geriatric evaluations and treatments to improve prognosis and reduce the likelihood of poor outcomes (6). The anticipating credibility of the ISAR regarding death and complicate results was marked as poor to fair. It is not acceptable to employ ISAR test solely for picking up elderlies at risk of unfavourable outcomes in the ED (7). It should be used while taking clinical conclusions and for the purpose of the levelling and adoption of patients to be part of clinical assessments (4).

The TRST test was enhanced to recognize aged ED patients with higher possibility of returning to the ED, staying in hospital, or admission to a convalescent home between 30- and 120-days after dismissing from ED of hospital (8). The TRST should not be implied alone to recognize seniors at risk of ED revisits or inpatient (9). The goal of the attending examination was to compare the ISAR with the TRST in terms of performance in predicting 30-day return to ED, hospital admission and death in elderly who admitted to the ED.

METHODS

Study design, follow-up and end point

The ED of Odemis State Hospital treats approximately 200,000 patients per year. All patients who were above 65 years old and admitted to our ED facility and were followed up in the monitored observation unit were put into in the evaluation analysis. Patients who did not give their approval for the use of their information for scientific grounds in writing or vocally were eliminated from the bracket. Demographic and social input (age, sex, education, family status, decreased functional capacity, residency, arrival at the ED and contact person) and stay in the ED were extracted from the electronic documentation of all entries to our ED between 1 November 2022 and 1 December 2022. Outcomes were confirmed through telephone follow-up by emergency specialist physicians within one month of the index ED visit (1 December 2022 to 1 January 2023). The primary end-points were return to the ED, hospital admission or death.

Measurements

Same individual (SS) carried out both the diagram reviews and data obtainment. The ISAR is a risk assessment implement which consist of six components used to identify aged patients posing higher risk of unfavourable results after an admittance to the ED. ISAR is a self-report implement consist of six straightforward "yes/no" elements regarding functional reliance, current hospitalization, flawed reminiscences and sight, and polypharmacy. The overall scale span is between 0 to 6, as each component is scored as 1 if the patient demonstrates having a difficulty and 0 provided reports not (5). The five-item (cognitive disability; strained walking, recorded moving hardship and plummet, taking five or more medicaments, treatment history or documented ED entries, and assessment by the health worker of other reasons) TRST rule submits a feasible score between 0 and 5 (each element scoring 1 if existing or 0 if not attending) (8).

The author ascertained that ISAR and TRST scores of at least 2 identify patients who has greater risk for adverse outcomes.

Statistical methods

Frequencies and percentages were assigned for categorical changeable, while average, standard deviation (SD), median and range (minimum–maximum) values were provided for numerical variables as descriptive statistics. The relationship between two categorical variables was analysed applying Pearson's chi-squared assessment. Group comparisons for arithmetic variables were performed with the dependent sample t-test or the Mann–Whitney U test. In the Mann–Whitney U test evaluation, significance, and cut-off values for ISAR and TRST scores were determined only for the hospital admission value at the end of 30 days. The receiver operating characteristic (ROC) curve was implied to assay the scores' capability to assess the relationship between screening tools (ISAR ≥ 3 and TRST ≥ 2). The area under the curve (AUC) was summarized with 95% confidence intervals (CIs). The ROC curves of the scores were compared implying DeLong's test for two correlated ROC curves. The Youden index was applied to ascertain the break off point that optimized the variable's discerning capability by providing equal value to sensitivity and specificity. Rigorous binomial confidence limits were determined for sensitivity, specificity and positive and negative predictive values for scores transformed into binary based on cut-off values.

Ethical considerations

The study was confirmed, and the ethics commission of Izmir Katip Celebi University's Non-Interventional Clinical Studies Institutional Review Board deferred the necessity of obtaining informed written consent from patients (#0253).

RESULTS

In the present study, 396 patients (mean age 76.89 ± 7.59, interquartile range 65–98; 50% men) were enrolled. Their characteristics are summarized in Table 1. The mean age of the males was 71 ± 6.65, and the mean age of the females was 78.08 ± 8.27. The most common isolated presentation complaints were dyspnoea, abdominal pain and cough, as determined in 68 (17.2%), 19 (4.8%) and 8 (2%) persons, respectively. The three most common final diagnoses were chest diseases in 101 (25.5%), cardiovascular diseases in 86 (21.7%) and neurological diseases in 54 (13.6%). The ED outcomes were discharge in 261 (65.9%), hospitalization in 98 (24.7%), transfer to another hospital in 28 (7.1%), refusal of treatment in 8 (2%) and death in 1 (0.3%). The hospital outcomes were discharge in 104 (26.2%), death in 21 (5.3%) and referral in 1 (0.3%). The outcome of the referred patient is unknown. The numbers of returns to the ED, hospitalizations, deaths, decreases in functional capacity and clinic visits at the end of 30 days are shown in Table 2. The average length of stay in the ED was 5.11 hours. The mean ISAR score was 3.08, and the mean TRST score was 2.67. The correlation coefficient between ISAR and TRST was 0.657. There were no significant differences in ISAR and TRST scores for sex, age, marital status, living environment, level of education, mode of application, 30-day hospitalization, return to the ED or death status ($p > 0.05$).

Table 1. Participant baseline characteristics

Demographic and social data		N	%
Gender	Female	198	50
	Male	198	50
Family Status	Married	223	56.3
	Widow/er	167	42.2
	Divorced	3	0.8
	Unmarried	3	0.8
Education	Did not go to school	134	33.8
	Primary	252	64.4
	Secondary	2	0.5
	High	5	1.3
Residency	Alone	27	6.8
	With spouse	141	35.6
	Extended family	210	53.0
	Other	18	4.6
Arrival at the ED	With 112(911)	130	32.8
	Own possibilities	264	66.7
	Other	2	0.5
Contact person	Self	34	8.6
	Relative	355	89.6
	Neighbors	2	0.5
	Other	5	1.3

Table 2. Evaluation of the participants at the end of 30 days

Criteria	Yes (n, %)	No (n, %)	ISAR score* p	TRST score* p
Return to ED	125 (3.4)	249 (66.6)	0.233	0.174
Hospital admission	43 (11.5)	331 (88.5)	**0.004**	**0.042**
Death	13 (3.5)	361 (96.5)	0.059	0.295
Decreased functional capacity	73 (19.5)	301 (80.5)	0.265	0.371
Outpatient admission	242 (64.7)	132 (35.3)	0.127	0.187

ISAR: Identification of Senior at Risk, TRST: Triage Risk Screening Tool

Among the patients included in the study, 22 people (mean age was 80.41 years), including 12 females (mean age was 82.08 years), 10 males (mean age was 78.40 years), 1 in the emergency department and 21 in the hospital after the emergency department died. The primary end point at 30 days was evaluated in a total of 374 participants (mean age was 76.68 years), 186 women (mean age was 77.82 years) and 188 men (mean age was 75.56 years). While 11.5% of the patients (n = 43) in our cohort were admitted to hospital, 33.4% (n = 125) returned to the ED within 30 days. There were 13 deaths (3.5%) within 30 days (4%). No significant relationship was observed between the primary endpoints and the characteristics of the participants (age, gender, education, family status, residency, arrival at the emergency department) ($p > 0.005$). ISAR screening of the 396 ED patients revealed that 294 (± 1.26) were ISAR positive (≥ 2), and 102 (± 0.47) were ISAR negative (< 2). TRST screening of the 396 ED patients showed that 313 (± 1.32) were TRST positive (≥ 2), and 83 (± 0.28) were TRST negative (< 2). Table 3 shows the predictable value of ISAR (≥ 2) and TRST (≥ 2) for the primary end points for 374 patients. A significant correlation was observed for hospital admissions.

Table 3. Predictable value of ISAR and TRST for primary end points for 374 patients.

	Screening Tools											
	ISAR						TRST					
Primary end points	**Sensitivity (%)**	**Specificity (%)**	**PPV (%)**	**NPV (%)**	**AUC (95%CI)**	**P**	**Sensitivity (%)**	**Specificity (%)**	**PPV (%)**	**NPV (%)**	**AUC (95%CI)**	**P**
Return to ED	80	30.9	36.8	75.5	0.53 (0.47-0.59)	0.23	84.8	24.9	36.2	76.5	0.54 (0.48-0.60)	0.18
Hospital admission	88.4	29.3	14	95.1	0.63 (0.55-0.71)	**0.005**	90.7	23.3	13.3	95.1	0.59 (0.50-0.67)	**0.04**
Death	92.3	28	4.4	99	0.65 (0.52-0.77)	0.63	92.3	22.2	4.1	98.8	0.58 (0.44-0.72)	0.30

AUC: Area Under the Curve, CI: Confident Internal, ISAR: Identification of Senior at Risk, NPV: Negative Predictive Value, PPV: Negative Predictive Value, TRST: Triage Risk Screening Tool, ED: Emergency Department

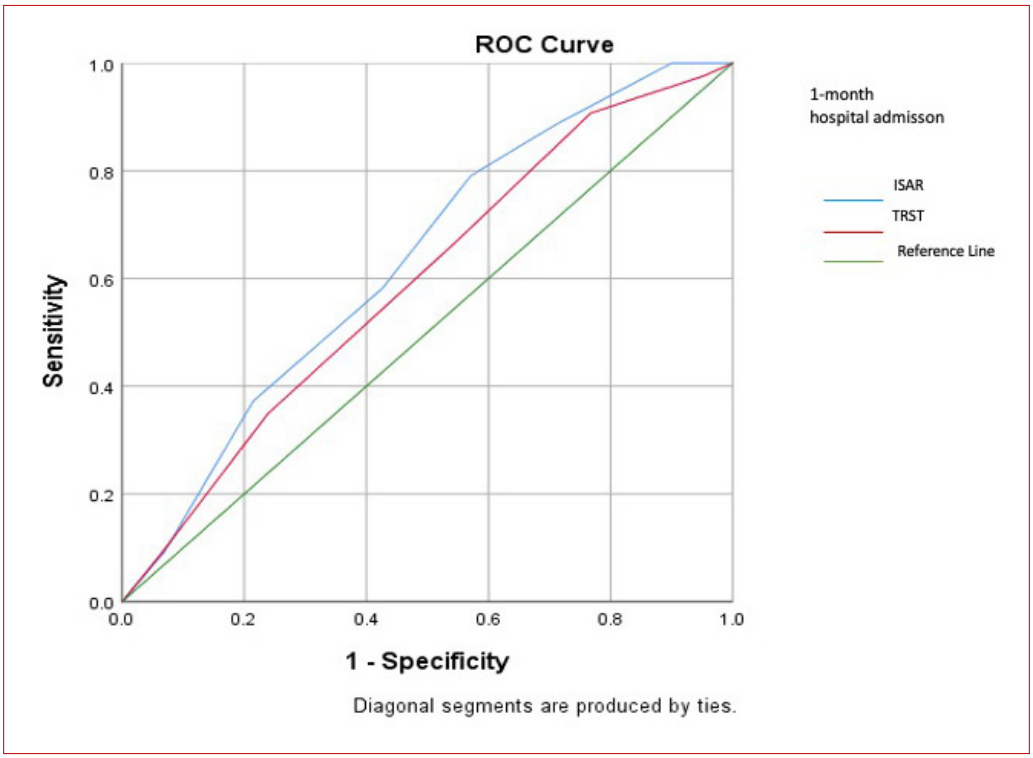

Figure 1. Receiver operating characteristic (ROC) curve of Identification of Seniors at Risk (ISAR) and Triage Risk Screening Tool (TRST) in predicting the 1-month hospital admission of 43 older patients. The ISAR shows an area under the curve of 0.63 (95% CI 0.55-0.71), where as the TRST shows an area under the curve of 0.59 (95% CI 0.50-0.67)

In this study, when comparing the predictive ability of the ISAR and TRST for the primary endpoint, significance was found only for hospital admissions. The optimum subjective ISAR cut-off score for hospital admission was ≥ 2, with a sensitivity of 88.4% and a specificity of 29.3%. Using the subjective ISAR tool, the AUC was 0.66. The optimum objective ISAR-related hospital admission cut-off score for screening was ≥ 3, with a sensitivity of 79.1% and a specificity of 42.9%. Using the objective ISAR-related tool, the AUC was 0.63. The optimum subjective and objective cut-off for TRST was ≥ 2. The ISAR showed slightly better performance in predicting 30-day hospital admission compared with the TRST, as shown in Figure 1. ISAR ≥ 3 showed an AUC of 0.63 (95% CI 0.55–0.71), a positive predictable value of 15.2% and a negative predictable value of 94%. TRST ≥ 2 showed an AUC of 0.59 (95% CI 0.50–0.67), with a sensitivity of 90.7%, a specificity of 23.3%, a positive predictable value of 13.3% and a negative predictable value of 95.1%.

DISCUSSION

The predictability of two risk assessment tools (ISAR and TRST) in terms of adverse clinical outcomes (return to ED, hospital admission and mortality) during 30 days in aged patients who presented to the ED was evaluated. Schwab et al. examined five scoring systems in their review, including 12 studies related to unplanned readmission at the end of 30 days. In that review, in which AUC values were

reported to be betwixt 0.445 and 0.69, the ISAR and TRST scoring systems were studied and confirmed (2).

In a meta-analysis of ISAR scoring including 32 studies, Galvin et al. reported as 0.83 (95% CI 0.75–0.90) for hospitalization and 0.97 (95% CI 0.89–0.99) for morbidity. In our study, these values were 0.88 and 0.92, respectively. Although these values were close to each other, the difference may have been due to the heterogeneity of the studies in the review (10). Buurman et al. (11) expressed predictive validity for the return to the ED of ISAR120. Sensitivity was 56%, and specificity was 4%; positive predictive value (PPV) was 19%, and negative predictive value (NPV) was 90%; AUC of the ROC curve was 0.59 (95% CI 0.51–0.67). In our study, sensitivity was higher (80%), and the AUC value was similar.

Since it is more difficult to estimate the risk over a long-term interval in older individuals, it is expected that the one-month estimation of our study will be higher than that of the six-month period. In their study using Revised ISAR (ISAR-R), McCusker et al. reported a sensitivity of 81% and a specificity of 40% for ED return at 90 days for the cut-point of 2+ in 386 patients. They defined the specificity value as low (5). In a review in which Galvin et al. included 32 studies, at 30 days, pooled appraises of sensitivity at a cut-off point of ≥ 2 were 81%, and specificity was 29% for ED return (10). In their study conducted with 333 patients in a population similar to the one in our study, Demir Akca et al. (12) reported that one-month sensitivity was 69%, and specificity was 40% for ISAR. In our study, these values were 80% and 30.9%, respectively. These values are compatible with the results of the review by Galvin et al. and McCuster et al. and have higher sensitivity values, unlike the results reported by Demir Akca et al. a higher sensitivity value indicates higher accuracy in identifying high-risk patients.

In a study conducted with 794 patients over 70 years of age, AUC values for return to ED were found to be 0.49 for ISAR and fTRST after 30 days. For hospitalization, these values were reported as 0.62 for ISAR and 0.56 for fTRST (13). In another study conducted with 200 patients over the age of 67, the AUC values were evaluated for the same period (1 month) and the same outcomes (return to ED, hospitalization) and were found to be 0.50 and 0.62 for ISAR. For TRST, both values were reported as 0.55 (14). In a study in which 2,057 people over 65 years of age were evaluated prospectively, the one-month AUC values for getting back to the ED and hospitalization calculated as 0.63 and 0.61, and 0.68 and 0.66, respectively, for ISAR and TRST (15). In our study, these values were as follows: return to ED ISAR 0.53 (0.47–0.59), TRST 0.54 (0.48–0.60); hospital admission ISAR 0.63 (0.55–0.71), TRST 0.59 (0.50–0.67). The results of our study were similar to Gretarsdottir et al. and Heeren et al. and lower than that of Salvi et al. We think that the lower values in our study, which was conducted with individuals of similar mean age, may have been due to the smaller size of the sample.

Rizka et al. (16) reported that for one-month mortality for 771 patients, the ISAR showed an AUC of 0.62 (95% CI 0.57–0.68), whereas the TRST showed an AUC of 0.58 (95% CI 0.52–0.64). Salvi et al. (15) reported a one-month mortality AUC for ISAR of 0.74 and for TRST of 0.68 in 2,057 individuals. In our study, these values were 0.65 (0.52–0.77) for the ISAR and 0.58 (0.44–0.72) for the TRST. The results of our study are similar to those reported by Rızka et al. and lower than those reported by Salvi et al. Although we have a similar sample size as the study of Rizka et al., our study has a much higher sample size than Salvi et al. We can say that as the number of samples increases, the level of predictability increases.

Studies reveal that the predictive value for the ISAR at 30–90 and 120 days ranges from moderate to poor, while the TRST has average diagnostic correctness at 30 days (11, 15–20). In the study by Suffoletto et al. (21) conducted with 202 patients, 84% of the participants had an ISAR score ≥ 2,

with up to 91% of sensitivity and almost 19% of specificity. In our analysis, in which the AUC value was 0.66, the rate of poor outcomes was 23% at the end of 30 days. Researchers found a cut-off value of ≥ 3 in the optimal objective ISAR risk scoring for poor outcomes (revisit-hospitalization and death). According to this cut-off value, specificity increases to 40% (21). In our study, for ISAR score ≥ 2 in 74% of the participants, ED sensitivity was 80%, and specificity was 30.9%; death sensitivity was 92.3%, and specificity was 28%; and sensitivity was 88.4%, and specificity was 29.3% for hospitalization.

The AUC values were similar to those in our study. In our study, the cut-off value of the ISAR score for hospital admission was ≥ 3. The specificity at this cut-off value was very close to the value found by Suffoletto et al. (21). As the cut-off value of the ISAR score increased, the specificity increased.

The anticipating ability of the ISAR and TRST at the common cut-off ≥ 2 points to recognize seniors at risk for return to the ED, hospital admission and mortality for adverse health outcomes is limited. In our study, significant results were obtained only for hospital admission in predictive ability analyses for ISAR cut-off ≥ 2–6 and TRST cut-off ≥ 2–5. The cut-off value for hospital admission was evaluated as ≥ 3 for the ISAR and ≥ 2 for the TRST. Although similar results were obtained for cut-off ≥ 2 values (sensitivity, specificity, AUC) for both scores, as stated in the paragraphs above, the different cut-off points determined for predictive ability emphasize the originality of the study.

Strengths and Limitations

The major limitation of our study was that it included to only one centre. At the end of 30 days, evaluations made by telephone were recorded, so they depended on the responses of the interviewees. These responses may not be objective.

One of the strengths of the study was that it was a prospective study, and three risks of unfavourable results (return to ED, hospital admission and death) were evaluated. In an ageing community, a narrower endpoint, such as one month, is required to look over the unbiased impact on the return to ED. The more protracted the observation period, the likelier new illnesses or aggravation of co-morbidities will bias the initial outcomes. Another fortitude of our review was that multivariable regression analysis was carried out to check for feasible confounders, which lowered bias. As a result of these analyses, different cut-off points were determined from the literature for both screening tools.

CONCLUSION

The risk scoring of the geriatric patient group needs to be reconsidered in order to reduce re-presentations to the ED, as well as the financial burden of these presentations, and patients in the risk group should be identified and followed up more closely. Although the ISAR and TRST have various limitations, they can be used as simple, standardized, auxiliary instruments to differentiate elderly patients during clinical decision making and practice and to identify high-risk patients. Both instruments demonstrated poor foretelling ability, however the ISAR presented greater attainment in anticipating the one-month hospital admission of elderly patients visiting the ED.

Meeting presentations

None.

Funding

None.

Declaration of competing interest

None of the authors has a conflict of interest to declare.

REFERENCES

1. Fischer C, Lingsma HF, Marang-van de Mheen PJ et al. Is the Readmission Rate a Valid Quality Indicator? A Review of the Evidence. PLoS One 2014, 9(11): e112282. (DOI: 10.1371/journal.pone.0112282).
2. Schwab C, Hindlet P, Sabatier B, Fernandez C, Korb-Savoldelli V. Risk scores identifying elderly inpatients at risk of 30-day unplanned readmission and accident and emergency department visit: a systematic review. BMJ Open 2019; 9(7): e028302. (DOI: 10.1136/bmjopen-2018-028302).
3. Theou O, Campbell S, Malone ML, Rockwood K. Older adults in Emergency Department with Frailty. Clin Geriatr Med 2018;34(3):369-386. (DOI: 10.1016/j.cger.2018.04.003)
4. Edmans J, Bradshaw L, Gladman JRF et al. The Identification of Seniors at Risk (ISAR) score to predict clinical outcomes and health service costs in older people discharged from UK acute medical units. Age Ageing 2013; 42(6): 747–753. (DOI: 10.1093/ageing/aft054).
5. McCusker J, Warburton RN, Lambert SD, Belzile E, de Raad M. The Revised Identification of Senior at Risk screening tool predict readmission in older hospitalized patients: a cohort study. BMC Geriatr 2022; 22(1): 888. (DOI: 10.1186/s12877-022-03458-w).
6. 6.Singler K, Heppner HJ, Skutetzky A, Sieber C, Christ M, Thiem U. Predictive validity of the Identification of seniors at risk screening tool in a German emergency department setting. Gerontology 2014; 60(5): 413-419. (DOI: 10.1159/000358825).
7. Yao JL, Fang J, LouQQ, Anderson RM. A systematic review of the identification of seniors at risk (ISAR) tool for the prediction of adverse outcome in elderly patients seen in the emergency department. Int J Clin Exp Med 2015;8(4):4778-4786.
8. Lalla R, Sammy I, Paul J, Nunes P, Ramcharitar Maharaj V, Robertson P. Assessing the validity of the Triage Risk Screening Tool in a third world setting. J Int Med Res 2018;46 (2):557-563. (DOI: 10.1177/0300060517714935).
9. Cousins G, Bennett Z, Dillon G, Smith SM, Galvin R. Adverse outcomes in older adults attending emergency department: systematic review and meta-analysis of the Triage Risk Stratification Tool. Eur J Emerg Med 2013; 20(4): 230-239. (DOI: 10.1097/MEJ.0b013e3283606ba6).
10. Galvin R, Gilleit Y, Wallace E, Cousins G, Bolmer M, Rainer T, Smith SM, Fahey T. Adverse outcomes in older adults attending emergency departments: a systematic review and meta-analysis of the Identification of Seniors At Risk (ISAR) screening tool. Age Ageing. 2017; 46(2): 179-186. (DOI: 10.1093/ageing/afw233).
11. Buurman BM, van den Berg W, Korevaar JC, Milisen K, de Haan RJ, de Rooij SE. Risk for poor outcomes in older patients discharged from an emergency department: feasibility of four screening instruments. Eur J Emerg Med 2011; 18(4): 215-220. (DOI: 10.1097/MEJ.0b013e328344597e).
12. Demir Akca AS, Kafadar D, Kahveci FO, Buyukuysal MC, Akca F. Performance of Identification of Senior at Risk tool to predict unplanned revisits to the emergency department in 6 month was low in predictive accuracy: A single-center study. Hong Kong J Emerg Med 2020; 28(2): 72-78. (DOI:10.1177/1024907920914811).
13. Heeren P, Devriendt E, Wellens NIH, Deschodt M, Flamaing J, Sabbe M, Milisen K. Old and new Geriatric Screening Tools in a Belgian Emergency Department: A diagnostic accuracy study. J Am Geriatr Soc 2020; 68(7): 1454-1461. (DOI: 10.1111/jgs.16503).
14. Gretarsdottir E, Jonsdottir AB, Sigurthorsdottir I et al. Patients in need of comprehensive geriatric assessment: The utility of the InterRAI emergency department screener. Int Emerg Nurs 2021; 54(5): 100943 (DOI: 10.1016/j.ienj.2020.100943).
15. Salvi F, Morichi V, Lorenzetti B et al. Risk stratification of older patients in the emergency department: comparison between the Identification of Seniors at Risk and Triage Risk Screening Tool. Rejuvenation Res 2012; 15(3): 288-294. (DOI: 10.1089/rej.2011.1239).
16. Rizka A, Harimurti K, Pitoyo CW, Koesnoe S. Comparison between the Identification of Seniors at Risk and Triage Risk Sccreening Tool in predicting mortality of older adults visiting the emergency department: Result from Indonesia. Geriatr Gerontol Int 2020; 20(1): 47-51. (DOI: 10.1111/ggi.13817).
17. Graf CE, Giannelli SV, Herrmann FR et al. Identification of older patients at risk of unplanned readmission after discharge from the emergency department: comparison of two screening tools. Swiss Med Wkly 2012; 142:1–9. (DOI: 10.57187/smw.2012.13327).

18. Di Bari M, Salvi F, Roberts AT et al. Prognostic stratification of elderly patients in the emergency department: a comparison between the 'Identification of Seniors at Risk' and the 'Silver Code'. J Gerontol A Biol Sci Med Sci 2012; 67(5): 544–550. (DOI: 10.1093/gerona/glr209).

19. Deschodt M, Wellens NIH, Braes T et al. Prediction of functional decline in older hospitalized patients: a comparative multicenter study of three screening tools. Aging Clin Exp Res 2011; 23(5-6): 421–426. (DOI: 10.1007/BF03325237).

20. Yim VWT, Rainer TH, Graham CA, Woo J, Lan FL, Ting SM. Emergency department intervention for high-risk elders: identification strategy and randomised controlled trial to reduce hospitalisation and institutionalisation. Hong Kong Med J 2011; 13(Suppl. 3): 4–7.

21. Suffoletto B, Miller T, Shah R, Callaway C, Yealy DM. Predicting older adults who return to the hospital or die within 30 days of emergency department care using the ISAR tool: subjective versus objective risk factors. Emerg Med J 2016; 33(1): 4-9. (DOI: 10.1136/emermed-2014-203936).

RESEARCH

COMPARISON OF THE EFFECTS OF INTRAOPERATIVE GOAL DIRECTED AND CONVENTIONAL FLUID MANAGEMENT ON THE INFERIOR VENA CAVA COLLAPSIBILITY INDEX AND POSTOPERATIVE COMPLICATIONS IN GERIATRIC PATIENTS OPERATED FROM PROXIMAL FEMORAL NAIL SURGERY

Turkish Journal of Geriatrics
DOI: 10.29400/tjgeri.2023.329
2023; 26(1):37-47

Dilara GÖÇMEN[1]
Ceren KÖKSAL[1]
Süheyla ABİTAĞAOĞLU[1]
Arzu YILDIRIM AR[1]

CORRESPONDANCE

[1]Dilara GÖÇMEN

Phone : +905413439438
e-mail : dilaragocmen@yahoo.com

Received : Feb 19, 2023
Accepted : Mar 17, 2023

[1] Fatih Sultan Mehmet Training and Research Hospital, Anesthesiology and Reanimation, İstanbul, Turkey

Abstract

Introduction: Avoiding undesirable effects of hyper- and hypovolemia is important in geriatric hip fracture patients perioperatively. In our study, we aimed to compare the effects of intraoperative goal directed and conventional fluid therapy on inferior vena cava collapsibility index, postoperative complications and 30-day mortality in these patients.

Materials and Methods: 60 patients aged 65 and over who underwent proximal femoral nail surgery were included in the study.Patients were randomized into two groups; Goal Directed and Conventional Therapy groups. Patients in the Goal Directed Therapy Group were monitored with a MostcareTm (Vygon, VytechHealth, Padova, Italy) haemodynamic monitor. Fluid therapy was applied by targeting Pulse Pressure Variation <10%, Stroke Volume Variation <13%. In the Conventional Therapy group fluid management was administered to the patients according to the 4-2-1 rule. Before anesthesia and leaving the recovery room, inferior vena cava collapsibility index measurements was performed by ultrasonography.

Results: Postoperative inferior vena cava collapsibility index was higher in the Conventional group. Total administered crystalloid fluid volumes were similar in both the groups and more colloids were used in the Goal Directed Therapy group. Intraoperative urine output was observed more in the Goal Directed Therapy group. Postoperative hospital stay was shorter in the Goal Directed Therapy group. There was no significant difference in terms of 30-day mortality and postoperative complications.

Conclusion: According to our study, intraoperative targeted fluid herapy provides optimal postoperative intravascular volume and shortened the postoperative hospital stay.

Keywords: Femoral Fractures; Vena Cava, Inferior; Hemodynamic Monitoring; Fluid Therapy; Postoperative Complications.

INTRODUCTION

It is estimated that the annual number of hip fracture cases will exceed 6 million in 2050, with the rapid increase in the aging population of the world (1).

Advanced age, comorbidities, dehydration, malnutrition and decreased functional and cognitive functions pose a risk for postoperative complications in patients admitted to the hospital due to hip fracture Considering age, frailty and high cardiovascular risk in the geriatric patient group, it is possible that they are resuscitated with insufficient fluid before, during and after surgery, because of the fear of increase in left ventricular failure due to excessive fluid administration (2). Optimization of perioperative haemodynamics and fluid management is important to reduce this risk.

Therefore, managing these high-risk patients using static parameters may reveal the undesirable effects of postoperative hypovolemia and hypervolemia. Vasoconstriction due to hypovolemia may lead to decreased oxygen delivery, decreased tissue perfusion and dysfunction of the peripheral organs. Along with glycocalyx damage due to hypervolemia, tissue oedema, impaired tissue perfusion, local inflammation, delayed wound healing, wound infection and anastomotic leaks can be observed (3). There is no clear consensus on how to perform optimal fluid management in this population, which has many comorbidities and is at a high risk for postoperative complications.

The research for an optimal fluid regimen to avoid intravascular volume overload and maximize tissue perfusion has brought individualized targeted fluid replacement therapies with the help of technology (4). In the approach of goal directed therapy (GDT) approach, parameters such as stroke volume variation (SVV), pulse pressure variation (PPV) and cardiac output (CO) related to global O2 distribution are measured to improve tissue perfusion and clinical outcomes. Replacement with crystalloids, colloids, blood products, or vasopressors is adjusted according to the targeted physiological variables in the dynamic process (5). Developments in recent years have drawn attention to the future of non-invasive or less invasive devices (6).

The inferior vena cava collapsibility index (cIVC) is an easy, bedside, rapid measurement method. It can be used as an indicator of fluid response and as a guide for fluid management in critically ill patients with spontaneous breathing. (7–9). The inferior vena cava (IVC) is a vein with a low intravenous pressure and high collapsibility. Its diameter is modified by the intravascular volume status, right heart function, and respiration (10). During each respiratory cycle, the IVC contracts and relaxes. With the negative pressure resulting from inspiration, venous return to the heart increases in patients and the IVC collapses (9) . With expiration, the IVC diameter increases again and returns to the basal value. An increase or decrease in the collapsibility of the vessel guides the evaluation of the clinical status of the patient. IVC ultrasound has advantages over other fluid response measuring methods it is non-invasive, inexpensive, widely available, can be obtained with minimal training, and can be combined with heart and lung ultrasound to provide a complete sonographic picture of the patient (11).

Although the necessity of providing adequate intravascular volume in intraoperative fluid management is obvious, an optimal fluid management guideline has not yet been established for geriatric and emergency cases with high mortality. The primary aim of our study was to compare the effects of goal directed and conventional fluid management on cIVC in patients undergoing proximal femoral surgery. In addition, evaluation of the amount of fluid administered, blood products, number of perioperative hypotensive events, intraoperative haemodynamics, intraoperative urine output, amount of bleeding, postoperative complications (cardiac, respiratory, renal, etc.), postoperative 30-day mortality, nausea

and vomiting score, postoperative hospitalization days, and comparisons were performed.

MATERIALS AND METHODS

This study was conducted at the Fatih Sultan Mehmet Training and Research Hospital of the Ministry of Health Health Sciences University between July 2021 and November 2021 after obtaining clinical trials (NCT05154435) and ethics committee approval from Istanbul Kartal Koşuyolu High Specialization Training and Research Hospital (2021/14/548).

Sixty patients over 65 years of age, who were scheduled for PFN surgery and had an American Society of Anesthesiologists Physical Evaluation Classification (ASA) score of 1-3 were included in our prospective, randomized, controlled study.

Patients with cardiac arrhythmia, advanced heart and aortic failure, chronic renal failure need for dialysis, advanced obstructive or restrictive respiratory diseases, active lower/upper respiratory tract infection, body mass index (BMI)>35, and IVC that could not be clearly visualized by ultrasonography were excluded from the study.

The patients were randomized into two groups CON (n=30) and GDT (n=30) and the patients were not informed about the group to which they belonged. The study protocol was explained to all patients. A consent form was signed by the patients who volunteered to participate in the study. Patients in both the groups underwent routine electrocardiography (ECG), saturation (SpO2), non-invasive blood pressure and depth of anesthesia monitoring with a bispectral index (BIS) (BIS Complete 2 channel monitoring system Medtronic Limited., UK) probe. All patients were sedated with 1 mg/kg fentanyl (Talinat 50 mcg/10 ml 1 amp, Vem İlaç Sanayi ve Ticaret Ltd.Şti.). Invasive arterial monitoring was performed under sterile conditions, and preoperative blood gas analysis was performed. Systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP), heart rate (HR), BIS and SpO2 were recorded every 15 min. IVC ultrasonography was performed in all patients by an experienced anesthesiologist who was blinded to the study. The patient was placed in the supine position, with a convex probe (5 MHz) from the subxiphoid region, that measured the diameter of the IVC inspirium and expirium (EsaoteSpA, Genova-Italy) and the collapsibility index was recorded. All measurements were made by the same anesthesiologist. The IVC was visualized along the longitudinal axis in the subxiphoid position. The intrahepatic segment of the IVC was visualized as it entered the right atrium. The IVC diameter was measured 3-4 cm from the junction of the IVC and the right atrium or 2 cm caudal to the hepatic vein-IVC junction. The M mode was placed perpendicular to the IVC and the IVC was monitored for approximately 10 s over two or three respiratory cycles. The maximum IVC diameter (IVC dmax) was measured at the end of expiration from the inner margin of the vessel wall to the inner rim. The minimum IVC diameter (IVC dmin) was measured and recorded at the end of inspiration. The IVC collapsibility index was calculated as the difference between the maximum and minimum IVC diameters divided by the maximum IVC diameter and was expressed as a percentage. ([IVCdmax–IVCdmin]/IVCdmax×100%).

1-2 mg/kg propofol (Propofol 1% fresenius, FreseniusİlaçSan. ve Tic. Ltd. Şti.), 0.6 mg/kg rocuronium (Muscuron 50 mg/5 ml, KoçakFarma) and 1 mg/kg fentanyl (Talinat 50mcg /10ml 1 amp, Vemİlaç) were administered intravenously to all participants during anesthesia induction. Mechanical ventilation initiated with an oxygen-air mixture with an end-tidal CO_2 value (EtCO2) 35-45, 5 cmH_2O positive end-tidal pressure, 8 ml/kg tidal volume, 2 lt flow rate and 40% oxygen. Anesthesia was maintained with 3-5% desflurane (Suprane 240 ml solution, Eczacıbaşı-Baxter) and 0.25-1 mcg/kg/min remifentanil (Ultiva 5 mg flk, Glaxo Smith

Kline). The aim was to maintain the BIS value between 40 and 60. A balanced electrolyte solution (Eczacıbaşı-Baxter) was used as the maintenance fluid for both the groups. All patients were warmed perioperatively with an active air blown heating blanket and body temperature monitoring was performed. All patients were normothermic.

Patients in the targeted fluid therapy group (GDT Group) were monitored with a MostcareTM (Vygon, VytechHealth, Padova, Italy) haemodynamic monitor after arterial cannulation. CO, SVV, PPV, systemic vascular resistance index (SVRI), arterial elastance (Ea) measurements, and SAB, DAB, MAP, KTA and SpO2 values were monitored. Fluid therapy every 15 min was planned in accordance with our algorithm.

PPV <10%, CI >2.5 L/min/m^2, SVV <13%, and mean arterial pressure >65 mmHg were targeted. If the patient's parameters were within these limits, 4 ml/kg/h balanced crystalloid infusion was administered. When SVV was >13%, 4 ml/kg hydroxyethyl starch (HES) (Voluhes, Hes 130/0.4% 6% Solution for Iv Infusion 500 ml Polifarma) was administered for 5 min and a crystalloid infusion was administered as 8 ml/kg/h. The fluid response was re-evaluated after 15 min (Figure 1). The aim was that the amount of HES administered to the patient within 24 h should not exceed 1000 ml. In case of SVV >13%, CI <2.5 L/min/m^2, MAP <65 mmHg, 0.1-0.2 mcg/kg/min norepinephrine (Cardenor 4 mg/4 ml VEM) infusion was started.

Fluid deficit due to fasting time was calculated in accordance with the 4-2-1 rule for patients in the CON group. (4 ml/kg/hr for the first 10 kg, 2 ml/kg/hr for the second 10 kg, 1 ml/kg/hr for each subsequent kg). Half of the calculated fluid volume was given in the first hour; the remaining half was given at the 2nd and 3rd hours. Bleeding was replaced with HES equal to the amount of bleeding or three times of balanced crystalloid fluid.

In both the groups, intraoperative hypotension (MAP <65 mmHg) was first intervened with 5 mg ephedrine (0.05 g/ml ampoule, Osel İlaç San. ve Tic. A.Ş.) The dose of remifentanil was reduced by 25%. If no response was obtained, 5 mg ephedrine was added and 4 ml/kg crystalloid was administered intravenously (IV) in 15 min. This was recorded as a hypotensive event. When blood loss of more than 20% of the total blood volume or Hb <8 g/dl was detected acutely, erythrocyte suspension and fresh frozen plasma replacement was planned at a ratio of 2:1.

All patients were treated with 1 g paracetamol (Paracerol 10 mg/ml, PF polyfarma), and 1 mg/kg tramadol (Tramosel 100 mg/2 ml, HaverFarma) 20 min before end of the surgery for postoperative analgesia, and 4 mg ondansetron (Zofer 4 mg/ 2 ml, Adeka) for prophylaxis of nausea was administered intravenously. At the end of the surgery, before awakening, all patients underwent a femoral nerve block with 20 ml of 0.25% bupivacaine and a lateral femoral cutaneous nerve block with 5 ml of 0.25% bupivacaine (Buvacin 5 mg/ml VEM) under ultrasound guidance. After the block was applied, the inhalation anesthetic was discontinued and the patients were ventilated with oxygen-air at a flow rate of 6 lt/min and 80% oxygen. In order to reverse the neuromuscular blockade, 0.02 mg/kg atropine and 0.05 mg/kg neostigmine (Neostigmine 0.5 mg/ml ampoule, Adeka) were administered IV after observing the tachycardia response of the patient with a spontaneous respiratory effort.

The amount of crystalloid and colloid administered during the surgery, the amount of inotrope, ephedrine, and atropine, if given; and the amount of blood and blood product transfusions, bleeding and urine output were recorded.

After extubation patient was taken to the post anesthesia care unit (PACU). Postoperative cIVCmeasurements were made in the PACU by the anesthesiologist who performed the preoperative measurements, and the measurements were recorded. The patients were monitored by a PACU nurse who was blinded to the study. Visual

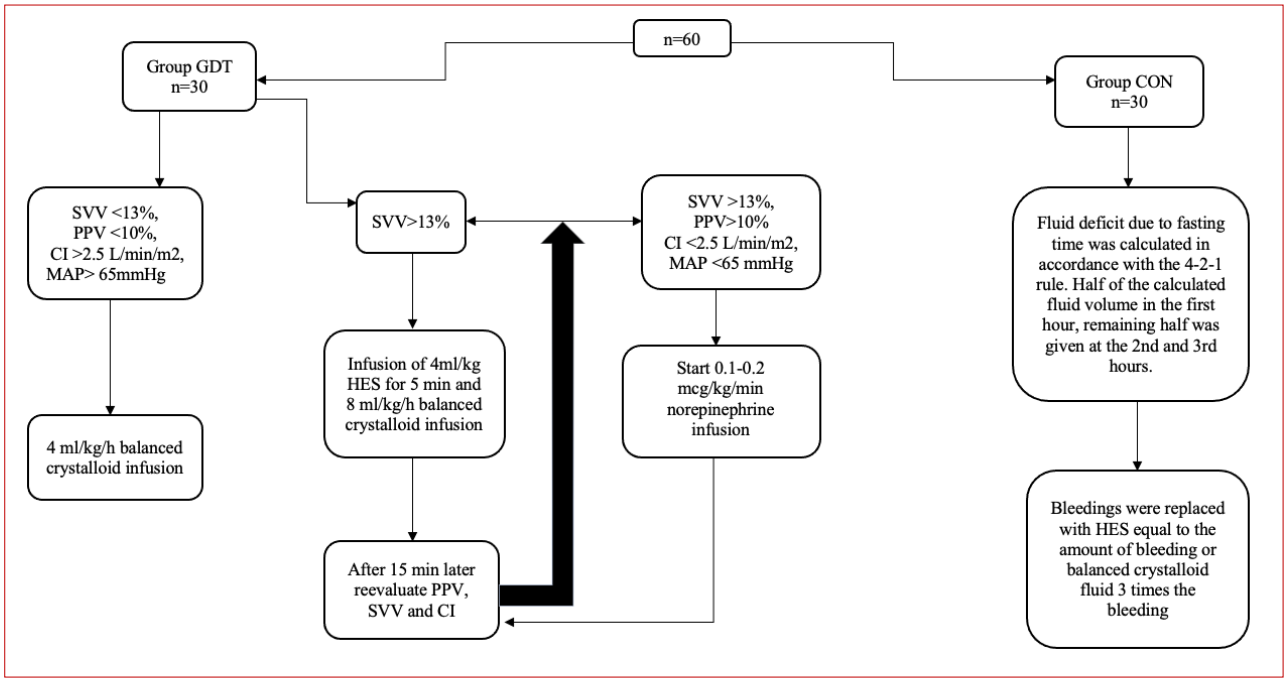

Figure 1. Group GDT and Group CON fluid management

SVV: Stroke Volume Variation, PPV: Pulse Pressure Variation, MAP: Mean Arterial Pressure, CI: Cardiac Index, HES: Hydroxyethyl Starch

analogue scale (VAS) scores, nausea and vomiting status were recorded. Control postoperative blood gas was obtained before arterial cannula removal in the PACU. Control of postoperative biochemistry values (AST, ALT, creatinine) were taken at the 4th postoperative hour in the service.

For the evaluation of the level of nausea, a 4-scale postoperative nausea and vomiting (PONV) scale was used: "0 = no nausea, 1 = mild nausea, 2 = moderate nausea, 3 = severe nausea".

Before discharge, the patients were questioned regarding cardiovascular, respiratory, neurological, gastroenterological, infective, haemorrhagic and renal complications. The patients were called on the 30th postoperative day and the 30-day mortality was assessed.

The Shapiro-Wilk test was used to examine whether the data showed normal distribution in the statistical analysis. Mann-Whitney U test was used to the compare the two groups for normally distributed data. Repeated measurements between groups were compared by calculating the percent change value (percentage change = (last measurement - first measurement) / first measurement) compared to the initial measurement. the Friedman test was used for intergroup comparisons. In the case of significance, Bonferroni correction was applied in pairwise comparisons. In addition, the paired t-test and Wilcoxon signed -rank test were used to compare pre- and post- measurements of dependent variables. Pearson's Chi-square test, Fisher's Exact Chi-square test, and Fisher-Freeman-Halton test were used to the analyze the categorical data. The significance level was set at as α=0.05. Statistical analysis of the data was performed using the IBM SPSS Statistics for Windows version 23.0 (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.).

RESULTS

Sixty-three patients aged 65 years and older were evaluated in our study. One patient was excluded from the study due to covid positivity in the last 3 months, one patient currently covid positive, and one patient due to discontinued of perioperative arterial monitoring. Data were evaluated in 60 patients: 71% (n=43) were female and 29% (n=17) were male. Sex distrubution, age, ASA scores, weight, anesthesia and duration of surgery of the groups were similar (Table 1).

There was no significant difference in the SAP, DAP, HR and BIS parameters between the groups at 0, 30, 60 and 90 min.

When the IVC expiratory diameter of the patients was measured, no significant difference was found between the two groups in the preoperative measurements (Table 2). In the postoperative measurements, the IVC expiratory diameter was found to be larger in the GDT group ($p<0.05$). In intragroup comparisons, postoperative measurements were wider when the pre- and postoperative IVC expiratory diameters were compared in the GDT group ($p<0.001$). There was no significant difference between pre- and postoperative IVC expiratory diameters in the CON group ($p=0.825$).

When the IVC inspirium diameter was examined, the two groups were found to be similar in preoperative measurements. In the postoperative measurements, the diameter of the IVC inspirium was wider in the GDT group ($p<0.001$). In intragroup measurements, the postoperative IVC inspirium diameter was wider in the GDT group ($p<0.001$). Pre- and postoperative IVC expiratory diameters were similar in the CON group.

When both groups were examined in terms of the IVC collapsibility index, they were found to be similar in their preoperative measurements. In the

Table 1. Comparison of Patients between Groups in terms of Demographic Data, ASA, Anesthesia Duration and Surgery Duration

		Group GDT n=30	Group CON n=30	P Value
Gender %	Female	n=22(%73)	n=21 (%70)	0.774[1]
	Male	n=8 (%27)	n=9 (%31)	
ASA %	1	n=0 (%0)	n=1 (%3)	0.492[2]
	2	n=2 (%6)	n=0 (%0)	
	3	n=28 (%94)	n=29 (%97)	
Age (years) (mean±SD)		80±8	80±7.9	0.8[3]
Weight(kg) (mean±SD)		64.8±10	65.6±12	0.797[3]
Anesthesia duration (min) Median(min-max)		110 (75-120)	105 (60 -125)	0.138[4]
Surgery time (min) Median (min-max)		95 (60-110)	90 (55-110)	0.112[4]

[1]Pearson Chi-Square, [2]Pearson Chi-square test, [3]t-test, [4]Asymp. Sig. (2-tailed), ASA: American Society of Anesthesiologists Physical Assessment Classification, SD: Standard Deviation, Min: Minimum, Max: Maximum.

postoperative measurements, cIVC was lower in the GDT group ($p<0.05$). In the intragroup comparison, preoperative measurements were higher than the postoperative measurements in both the groups ($p<0.05$).

No significant difference was observed between GDT and CON groups when the total volume of crystalloid administered was compared. The Total colloid amount, total bleeding, and total urine output were found to be higher in the GDT group ($p<0.05$). The total amount of blood products administered was similar between the two groups. The number of intraoperative hypotensive events was similar in both the groups (Table 3).

When the patients were examined in terms of postoperative hospitalization days, it was found that the patients in the GDT group were discharged within a shorter time ($p<0.05$). When the 30-day mortality was questioned, one patient in the GDT group was admitted to the hospital on the 7th postoperative day due to respiratory distress and was intubated. The patient, who tested positive for Covid-19, died on the 17th day. There was no significant difference between the groups in 30-day mortality. When examined in terms of postoperative complications, complications developed in a total of 5 patients. Of these patients, two had infective, two had respiratory complications, one had infective and haemorrhagic complications. There was no significant difference between the groups ($p=0.671$).

The Friedman test was used to compare the 0th, 30th, 60th and 90th values of SVV, PPV, and CO in the GDT group, and there was a significant difference (Table 4). Bonferroni correction was applied for pairwise comparisons. There was a significant difference among the values recorded between SVV 0 and 30 minutes and between SVV 0 and 60

Table 2. Comparison of Inferior Vena Cava (IVC) Expirium, IVC Inspirium Measurements and Collapsibility Indices Within and Between Groups

		Group GDT n=30	Group CON n=30	P value
IVC Expirium (cm) Mean±SD	Preop	1.18±0.32	1.30±0.29	[1]0.130
	Postop	1.33±0.33	1.31±0.31	[1]0.02*
	Δ	0.14±0.18	-0.01±0.01	
	P vaue	<0.001*	0.825	
IVC Inspirium (cm) Mean±SD	Preop	0.57±0.26	0.53±0.17	[1]0.499
	Postop	0.81±0.27	0.58±0.17	<[1]0.001*
	Δ	0.53±0.35	0.14±0.31	
	P value	<[1]0.001*	[1]0.055	
Collapsibility Index (%) Mean±SD	Preop	52.70±10.42	59.57±7.66	[1]0.0052
	Postop	38.90±7.25	55.60±9.98	<[1]0.001*
	Δ	-0.25±0.13	-0.06±0.16	
	P value	<[1]0.001*	[1]0.028*	

IVC: Inferior Vena Cava, Preop: preoperative measurement, Postop: Postoperative measurment, Δ: percentage change between preoperative and postoperative measurements. SD: Standard Deviation, *: $p<0.05$, [1]: t-test.

Table 3. Comparison of Intraoperatively Given Crystalloid, Colloid, Total Bleeding, Total Urine Output, Total Amounts of Blood Product Given, Number of Hypotensive Events, Postoperative Hospitalization Days, 30-Day Mortality and Postoperative Complications

		Group GDT n=30	Group CON n=30	P value
Total Crystalloid volume (ml) Med(min-max)		1175 (800-1600)	1125 (700-1650)	[1]0.75
Total Colloid Volume (ml) Med(min-max)		250 (0-650)	0 (0-550)	<[1]0.001*
Total Bleeding Volume (ml) mean± SD		163±38	145±78	[1]0.018*
Total Urine Output (ml) Med(min-max)		100 (0-400)	0 (0-400)	[1]0.007*
Total Given Blood Product(ml) Med(min-max)		0 (0-350)	0 (0-350)	[1]0.42
Number of Hypotensive Events Med(min-max)		1 (0-2)	1 (0-2)	[1]0.204
Postoperative Hospitalization Day Median (min-max)		2 (1-5)	3 (2-21)	[1]0.015*
Postoperative Complications %	no	93 (n=28)	90 (n=27)	0.671[1]
	yes	7 (n=2)	10 (n=3)	
30-Day Mortality %	yes	3 (n=1)	0 (n=0)	1.00[2]
	no	97 (n=29)	30 (n=30)	

*: p<0.05, [1]: Mann-Whitney U Test, [2]: Chi-square test, Med: Median, Min: Minimum, Max: Maximum, SD: Standard deviation

Table 4. Group GDT Stroke Volume Variation (SVV) / Pulse Pressure Variation(PPV) / Cardiac Output (CO) / Systemic Vascular Resistance Index (SVRI) / Arterial Elastance (Ea)

	0. min	30. min	60. min	90. min	P Value
SVV Med (min-max)	22 (7-30)	12 (3-30)	7 (5-46)	6 (4-17)	<[1]0.001*
PPV Med (min-max).	22 (8-43)	11 (4-34)	9 (4-31)	7 (4-11)	<[1]0.001*
CO Med (min-max)	4.60 (3.30-8.10)	4.40 (3.10-6)	4.15 (3.10-5.30)	4.20 (3.10-5.1)	[1]0.019*
SVRI Med (min-max)	1677 (948-2890)	1283 (846-3269)	1272 (958-2680)	1155 (833-1603)	<[1]0.001*
Ea Med (min-max)	1.85 (1.1-2.20)	1.48 (0.83-2.96)	1.15 (0.78- 2.70)	1.20 (0.64-1.919	<[1]0.001*

Time-Related Change and 0-90 min Comparison

[1]: Related-Samples Friedman's Two Way Analysis of Variance By Ranks, *:[1]p<0.05*, SVV: Stroke Volume Variation, PPV: Pulse Pressure Variation, SVRI: Systemic Vascular Resistance Index, Ea: Arterial Elastance, Med: Median, Min: Minimum, Max: Maximum

min ($p<0.05$). SVV values measured at 90th and 60th min were similar ($p=0.8$). SVV values measured at 30 and 60 min were similar ($p=0.07$).

PPV 0-30, 0-60, 0-90: there was a significant difference in the measurements between the30th and 90th min ($p<0.05$). the values recorded between 60-90 min and 30-60 min were found to be similar.

When AST, ALT and creatinine values were compared between the groups, no significant differences were observed in pre- and postoperative measurements. In the intragroup comparison, AST and ALT values were found to be higher postoperatively in the GDT group. In the CON group, no significant difference was observed between the pre- and postoperative measurements in the intragroup comparison. In intragroup comparisons of creatine, the postoperative value measured in CON group was found to be lower than the preoperative value ($p<0.05$). In the GDT group, intragroup pre- and postoperative creatine measurements were similar.

Postoperative nausea and vomiting were not detected in any patient in either group. All the patients were transferred from the PACU to the service. When examined in terms of the method of discharge from the hospital, all patients in both the groups were discharged with full recovery. Postoperative 30th min VAS score of the patients in both the groups were similar.

DISCUSSION

In our study that examined the effects of targeted and traditional fluid management on cIVC and postoperative complications in geriatric patients who underwent proximal femoral surgery, the postoperative cIVC in the targeted therapy group was found to be lower and within euvolemic limits than that in the traditional fluid management group. The cIVC was found to be within the hypovolemic limits in patients followed up using the conventional method. Postoperative IVC inspiratory and expiratory diameters were larger in the targeted therapy group.

While the amount of intraoperative crystalloid infusion was similar, the amount of colloid infusion was higher in the GDT group. While urine output was higher in the GDT group, postoperative creatinine values were similar in both the groups. While there was no significant difference between the two groups in terms of postoperative complications and 30-day mortality, hospital stay was shorter in the GDT group.

There was no significant difference between the two groups in terms of postoperative nausea and vomiting, exit site from PACU and hospital, pre- and postoperative ALT, AST and blood gas values.

In their study, Airepetan et al. evaluated the fluid responsiveness in spontaneously breathing patients in the intensive care unit, and reported that a cIVC ≥42% showed an increase in CO after fluid infusion (9). Szabo et al. reported that a preoperative cIVC ≥50% was associated with post-induction hypotension in their study of 83 spontaneously breathing patients who were scheduled for non-cardiac surgery (12). Nagdev et al. reported that a cIVC ≥ 50% was associated with a CVP ≤8mmHg, in their study with 73 spontaneously breathing patients who were scheduled for central catheterization for CVP measurement for different reasons in the emergency department (13). In our study, postoperative cIVC was 38% in the GDT group, and 55% in the CON group. In parallel with different studies in the literature, a cIVC value of 55% in the CON group can be considered hypovolemia. The high cIVC diameter measured in the CON group may indicate inadequate intraoperative fluid therapy. A lower urinary output supports this finding. Patients undergoing hip surgery may need more pre- and perioperative volume support due to reasons such as dehydration in the preoperative period, prolonged fasting and inability to take oral fluids during surgical preparation, and existing or worsening malnutrition. However, due to common

comorbidities and fragility in advanced age, it is recommended that this volume be given at an optimal level, with appropriate and enough fluid, without causing hypervolemia.

In a meta-analysis of 23 studies performed by Rollins et al in which major abdominal surgery was performed, it was reported that a decrease in the length of hospital stay was found in patients who underwent perioperative targeted fluid therapy, compared to the traditional method; however, no significant difference in mortality was observed between the groups (14). Che et al. reported that postoperative complications were lower in patients who underwent individualized fluid therapy than in those who underwent standard fluid management, and that there was no significant difference between the length of hospital stay and the volumes of fluid administered (15). In a review of 2159 patients by Michard et al. who underwent fluid management with non-calibrated pulse contour analysis methods, the total amount of colloid was found to be higher than that in the control group, and the amount of crystalloid was found to be less than that in the control group. Postoperative morbidity was lower in the targeted therapy group (16).

In our study, no significant differences were observed between GDT and CON groups in terms of postoperative complications. Similar to the studies of Rollins et al., the length of hospital stay was found to be lower in the GDT group, and there was no significant difference in postoperative mortality between the two groups. We believe that our exclusion of patients with an ASA score of 4 and those with advanced cardiac, respiratory and organ failure may have affected this finding. In addition, we believe that increasing sample size will be more appropriate for the evaluation of postoperative mortality and complications.

In our study, unlike Michard et al., no significant differences were observed between the crystalloid volumes given between the groups, while more colloids were given in the GDT group. We believe that the lower cIVC value in the GDT group in preoperative measurements may be due to less fluid requirement compared to the CON group. If equal cIVC were measured in both the groups, it is possible that the total amount of fluid administered would differ.

One of the limitations of our study was that while colloid was administered to reach the targeted parameters in the GDT group, colloid was administered only in case of bleeding in the CON group. While the study was being planned, this protocol was followed in the GDT group in order to reach the target SVV and PPV values in a short time during which the surgery continued. Colloids stay longer in the intravascular space and are more suitable as volume expanders. Since the fluid management of the patients in the CON group was performed using traditional methods, a colloid routine was not added to the protocol. Another limitation was the exclusion of patients who may require postoperative intensive care. Increasing the number of patients and the inclusion of high-risk cases in the study could provide different results in terms of 30-day mortality and postoperative complications. Major complications were examined in our study, and the fact that they were not evaluated in detail in terms of minor complications can be considered among the limitations of our study. In our study, postoperative complications were evaluated during the acute period prior discharge, had it been evaluated over a longer period of time, different results could have been obtained.

The fluid management is an important concern for elderly patients in order to decrease the mortality and morbidity rate. The cIVC may be useful for this aim and although there are some limitations this research may show the usefullnes of using this index for elderly management.

Targeted fluid therapy may be safe and beneficial for the intraoperative follow-up of patients scheduled for high-risk major surgery. Larger studies are needed to determine its effects on postoperative mortality and morbidity, organ perfusion.

REFERENCES

1. Kannus P, Parkkari J, Sievänen H, Heinonen A, Vuori I JM. Epidemiology of hip fractures. Bone. 1996;Jan;18:57–63. (DOI: 10.1016/8756-3282(95)00381-9).
2. Sinclair S, James S, Singer M. Intraoperative intravascular volume optimisation and length of hospital stay after repair of proximal femoral fracture: randomised controlled trial. BMJ. 1997 Oct;315(7113):909–12. (DOI: 10.1136/bmj.315.7113.909).
3. Kendrick JB, Kaye AD, Tong Y, Belani K, Urman RD, Hoffman C, et al. Goal-directed fluid therapy in the perioperative setting. J Anaesthesiol Clin Pharmacol. 2019 Apr;35(Suppl 1):S29–34. (DOI: 10.4103/joacp.JOACP_26_18).
4. Edwards MR, Grocott MP. Perioperative Fluid and Electrolyte Therapy. In Gropper MA, Cohen NH, Eriksson LI (eds). Miller's Anesthesia. 9th edition, Elsevier, Philadelphia 2019, pp 1513-14.
5. Chong MA, Wang Y, Berbenetz NM, McConachie I. Does goal-directed haemodynamic and fluid therapy improve peri-operative outcomes?: A systematic review and meta-analysis. Eur J Anaesthesiol. 2018 Jul;35(7):469–83. (DOI: 10.1097/EJA.0000000000000778).
6. Tsai Y-F, Liu F-C, Yu H-P. FloTrac/Vigileo system monitoring in acute-care surgery: current and future trends. Expert Rev Med Devices. 2013 Nov;10(6):717–28. (DOI: 10.1586/17434440.2013.844464).
7. Preau S, Bortolotti P, Colling D, Dewavrin F, Colas V, Voisin B, et al. Diagnostic Accuracy of the Inferior Vena Cava Collapsibility to Predict Fluid Responsiveness in Spontaneously Breathing Patients With Sepsis and Acute Circulatory Failure. Crit Care Med. 2017 Mar;45(3):e290–7. (DOI: 10.1097/CCM.0000000000002090).
8. Thanakitcharu P, Charoenwut M, Siriwiwatanakul N. Inferior vena cava diameter and collapsibility index: a practical non-invasive evaluation of intravascular fluid volume in critically-ill patients. J Med Assoc Thai. 2013 Mar;96 Suppl 3:S14-22. (PMID: 23682518)
9. Airapetian N, Maizel J, Alyamani O et al. Does inferior vena cava respiratory variability predict fluid responsiveness in spontaneously breathing patients? Crit Care. 2015 Nov 13;19:400. (DOI: 10.1186/s13054-015-1100-9).
10. Zhang Q, Wang X, Su L, Zhang H, Chai W, Chao Y, et al. Relationship between inferior vena cava diameter ratio and central venous pressure. J Clin Ultrasound. 2018 Sep;46(7):450–4. (DOI: 10.1002/jcu.22586).
11. Long E, Oakley E, Duke T, Babl FE. Does Respiratory Variation in Inferior Vena Cava Diameter Predict Fluid Responsiveness: A Systematic Review and Meta-Analysis. Shock. 2017 May;47(5):550–9. (DOI: 10.1097/SHK.0000000000000801).
12. Szabó M, Bozó A, Darvas K, Horváth A, Iványi ZD. Role of inferior vena cava collapsibility index in the prediction of hypotension associated with general anesthesia: An observational study. BMC Anesthesiol. 2019;19(1):1–8. (DOI: 10.1186/s12871-019-0809-4).
13. Nagdev AD, Merchant RC, Tirado-Gonzalez A, Sisson CA, Murphy MC. Emergency department bedside ultrasonographic measurement of the caval index for noninvasive determination of low central venous pressure. Ann Emerg Med. 2010 Mar;55(3):290–5. (DOI: 10.1016/j.annemergmed.2009.04.021).
14. Rollins KE, Lobo DN. Intraoperative Goal-directed Fluid Therapy in Elective Major Abdominal Surgery: A Meta-analysis of Randomized Controlled Trials. Ann Surg. 2016 Mar;263(3):465–76. (DOI: 10.1097/SLA.0000000000001366).
15. Che L, Zhang XH, Li X, Zhang YL, Xu L, Huang YG. Outcome impact of individualized fluid management during spine surgery: a before-after prospective comparison study. BMC Anesthesiol. 2020 Jul;20(1):181. (DOI: 10.1186/s12871-020-01092-w).
16. Michard F, Giglio MT, Brienza N. Perioperative goal-directed therapy with uncalibrated pulse contour methods: impact on fluid management and postoperative outcome. Br J Anaesth. 2017 Jul 1;119(1):22-30. (DOI: 10.1093/bja/aex138).

RESEARCH

COMPARISON OF THE EFFECTS OF GENERAL ANESTHESIA AND DEEP SEDATION ON ANESTHESIA COMPLICATIONS AND MORTALITY IN ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY PROCEDURES

Turkish Journal of Geriatrics
DOI: 10.29400/tjgeri.2023.330
2023; 26(1):48-59

Elif BÜYÜKERKMEN[2]
Ahmet YÜKSEK[1]
Elif DOĞAN BAKI[3]
Sezgin YILMAZ[4]

CORRESPONDANCE
[1]Ahmet YÜKSEK

Phone : +905326580351
e-mail : mdayuksek@hotmail.com

Received : Dec 22, 2022
Accepted : Feb 24, 2023

[1] Derince Education and Research Hospital, Anesthesiology and Reanimation, Kocaeli, Turkey

[2] Afyonkarahisar State Hospital, Anesthesiology and Reanimation, Afyonkarahisar, Turkey

[3] Afyon University of Health Sciences , Anesthesiology and Reanimation, Afyonkarahisar, Turkey

[4] Afyon University of Health Sciences , General Surgery, Afyonkarahisar, Turkey

Abstract

Introduction: Endoscopic retrograde cholangiopancreatography is extremely painful and uncomfortable when performed without anesthesia. However, the type of anesthesia to be applied remains a matter of debate. In this study, general anesthesia and sedation procedures were compared in endoscopic retrograde cholangiopancreatography performed by the same anesthesia and surgical team over a 5-year period.

Materials and Method: Patients aged over 65 years were divided into two groups, general anesthesia and sedation, and their data were analyzed retrospectively. Anesthesia complications, surgical complications, duration of the procedure, need for intensive care, and length of hospital stay and intensive care needs were compared between groups in 2812 patients.

Results: Data from 1885 patients were analyzed. The procedure time and hospital stay were shorter, and anesthesia-related complication rate was lower in the general anesthesia group. Although not statistically significant, mortality was higher, and the need for intensive care was similar to the sedation group. The complication rate significantly increased in patients aged over 75 years

Conclusion: Endoscopic retrograde cholangiopancreatography can be performed under deep sedation or general anesthesia. The experience of the anesthetist is an important factor for this choice. The use of sedation in geriatric patients is associated with more complications that require airway interventions. In addition, anesthesia complications due to prolonged procedures were more common in the sedation group. Conclusion: In our study, it was observed that general anesthesia was safer for endoscopic retrograde cholangiopancreatography procedures performed in geriatric patients by an experienced anesthesia and surgical team.

Keywords: Geriatrics; Cholangiopancreatography; Anesthesia, General; Deep Sedation.

INTRODUCTION

Endoscopic retrograde cholangiopancreatography (ERCP) refers to the direct cannulation of the ampulla of vater in the second part of the duodenum with or without the use of a guide wire by dilating or creating a sphincterotomy through an upper gastrointestinal system endoscope with an oblique view; visualization of the biliary system and/or pancreatic duct under the scope by providing an opaque material through this cannula; and obtaining images at the desired stages. ERCP is widely used in the diagnosis and treatment of bile duct pathologies and has wide clinical benefits (1). ERCP is performed in > 500,000 cases per year in the United States alone. The complexity of ERCP is also increasing. Anesthesia plays an important role during ERCP procedures. In recent years, there has been an increase in both the number and diversity of patients in non-operating room anesthesia and day case surgeries, including ERCP procedures. Increasingly, older patients are receiving non-operating room anesthetic procedures. This has led to the search for safer anesthesia methods. However, despite the increasing numbers of cases and centers, anesthesia applications and sedation protocols in ERCP procedures cannot be standardized (2). The fact that the team that performs sedation in endoscopic procedures in different countries differs from anesthesiologists makes it difficult to reach a consensus. An important point with no consensus is the type of anesthesia used. Different studies have advocated general and deep sedation (3,4). Geriatric patients are related groups that require attention in terms of anesthesia, are prone to complications, and may have increased mortality, morbidity, and cost (5,6).

ERCP is painful and usually requires sedation and analgesia. However, the patient population in which this procedure is applied is mostly the elderly, rendering this procedure difficult in terms of both anesthesia and surgery. There are limited studies that consider each parameter in small patient groups; however, there are few studies with large patient groups (7). The effects of general anesthesia and deep sedation on mortality in ERCP are unclear in the literature. For this reason, in our study, a large group of patients who underwent ERCP procedures by a single experienced anesthesia and surgical team were examined, and ERCP procedures in geriatric patients in which general anesthesia and deep sedation were applied were compared in terms of procedure time, complications, and patient characteristics.

MATERIAL AND METHODS

After obtaining permission from the local ethics committee (Ethics Committee Decision No: 2021/175) and permission to use the hospital archives, the computer records of patients over 65 years of age, out of a total of 2812 patients who underwent ERCP under anesthesia in the ERCP unit of our hospital between December 31, 2015 and December 31, 2020, were analyzed retrospectively. Repetitive ERCP procedures during the same hospitalization were determined asthe exclusion criteria (Figure 1). Age, sex, American Society of Anesthesiologists (ASA) Classification score, additional disease, airway evaluations and Mallampati scores, laboratory results, patient information and anesthesia type (general-deep sedation), duration of the procedure, and complications of surgery or anesthesia from our records, early period (first 7 days) mortality, and anesthetic drugs used were recorded as procedural information. Anesthesia duration was defined as the time from the onset of anesthesia to awakening and recovery of the patient. ERCP time was defined as the time between insertion and removal of the ERCP probe. All procedures were performed by a single anesthesia team and a surgical team. The surgical and anesthesia team had at least 10 years of ERCP and non-operating room anesthesia experience, and worked regularly in the same unit. Nausea and vomiting, anaphylaxis or allergic reaction,

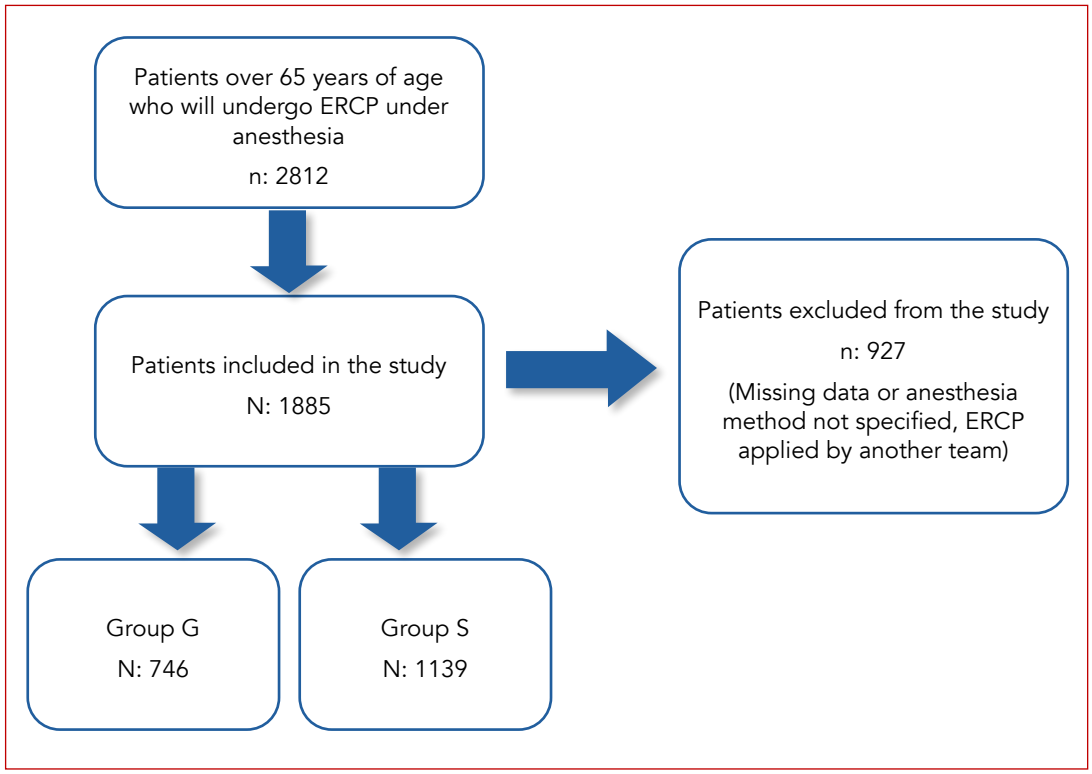

Figure 1. Study Flow Chart

cardiovascular collapse, cardiac arrest, prolonged hypotension for 1 min, bronchospasm, desaturation under anesthesia, postoperative desaturation, tooth damage, and anesthesia complications were recorded. Pancreatitis, bleeding, perforation, and other surgical complications were also recorded. Failure of the procedure due to anesthesia (such as anesthesia complication in the patient before the procedure and interruption of the procedure due to anesthesia-related problems) was recorded as present or absent. Procedures requiring removal of the endoscope and airway intervention were recorded as anesthesia-induced interruptions.

In all patients, according to national guidelines, 3-channel electrocardiography, automated non-invasive blood pressure, pulse oximetry, and temperature monitoring were performed before the procedure until the 30th minute after recovery (8). The depth of anesthesia was monitored using electroencephalography-based monitoring (bispectral index [BIS]). The anesthetics administered to the patients were adjusted according to the BIS values or the patient's response to the procedure, within the framework of our protocols. EtCo2 monitoring was applied to patients in the general anesthesia group but not in the sedation group. All patients received supplemental oxygen via nasal cannula (3 L/min) during the periprocedural period. The patients were divided into those who received deep sedation (Group S) and those who received general anesthesia (Group G). Deep sedation was defined as a patient who could respond to repetitive painful stimuli and whose cardiovascular and respiratory functions were preserved. Patients in Group S who needed general anesthesia after the start of the procedure were

recorded as needing airway intervention. During anesthesia, analgesia was provided with fentanyl or remifentanil in all patients. Propofol was used as an intravenous induction agent and ketamine was used together with propofol in the sedation group. A neuromuscular block was applied with rocuronium before endotracheal intubation in patients in Group G, and sugammadex was used in the reverse procedure.

Demographic data, such as age, sex, ASA score, complication development rate, length of hospital stay, early period (first 7 days) mortality, and need for intensive care, were compared between the groups.

Statistical analysis

IBM SPSS Statistics version 22 was used for all statistical analyses. First, the normality of the data distribution was evaluated (IBM Corp. IBM SPSS Statistics for Windows, version 22.0; Armonk, NY: IBM Corp.). Data are expressed as the mean and standard deviation. The Mann–Whitney U test and Student's t-test were used to compare quantitative data. The chi-square test was used to compare categorical variables. It was also expressed as a percentage when comparing the groups. Statistical significance was set at $P < 0.05$.

RESULTS

In our study, the computer records of 1885 patients aged 65 years and over, out of a total of 2812 patients who underwent ERCP under anesthesia in the ERCP unit of our hospital between 31.12.2015 and 31.12.2020, were retrospectively analyzed. ERCP procedures were divided into two groups: those performed under general anesthesia (Group G, n=746) and those performed under deep sedation (Group S, n=1139). The sex, age, and ASA classification of the patients are shown in Table 1. Group G included 418 female patients and 328 male patients, while Group S included 626 female and 513 male patients. There were no significant sex differences between the two groups (p=0.647, Table 1). The majority of the patients were in the ASA II group, and the mean age was as follows: Group G= 75.92±7.07 and Group S= 76.75±7.23

Table 1. Patients' gender and ASA status

	Group G (n = 746)	**Group S (n = 1139)**	**Total (n = 1885)**	**p**
Gender (female / male, n)	418 / 328	626 / 513	1044 / 841	0.647
Age, year, n	75.92±7.07	76.75±7.23	76.42±7.18	0.023
ASA I, n	100	100	200	**0.000**
ASA II, n	342	834	1176	
ASA III, n	272	201	473	
ASA IV, n	32	4	36	

Group G; patients underwent general anesthesia, Group S; patients underwent sedation
ASA ; American Society of Anesthesiologists.

Table 2. Comparison of patients according to the mortality, postoperative exit, hospital stay and ERCP duration

	Group G (n = 746)	Group S (n = 1139)	Total (n=1885)	p
Mortality, (n (%)				
Exitus, n	38	47	85	
% within mortality	44.7	55.3		
% within anesthesia	5.1	4.1		
% of total	2	2.5	4.5	
				0.322
Alive, n (%)	708	1092	1800	
% within mortality	39.3	60.7		
% within anesthesia	94.9	95.9		
% of total	37.6	57.9	95.5	
Anesthesia complications	38%5	89%7.8	127	**0.021**
Surgical complications	22	41	63	0.113
Postoperative exit				
Service room, n (%)	663	1009	1672)	0.847
% within mortality	39.7	60.3		
% within anesthesia	88.9	88.6		
% of total	35.2	53.5	88.7	
ICU, n (%)	83	130	213	0.882
% within mortality	39	61		
% within anesthesia	11.1	11.4		
% of total	4.4	6.9	11.3	
Hospital stay, day,				
median (min-max)	3 (1-30)	21 (1-52)	2 (1-52) 3.94 ± 4.35	**0.000**
mean ± SD	3.98 ± 3.95	3.92 ± 4.59		
ERCP duration, minute				
median (min-max)	30 (15-75)	50 (10-90)	45 (10-90) 41.80±11.3	**0.000**
mean ± SD	35.99 ± 8.70	45.60 ± 11.3		

Group G; patients underwent general anesthesia, Group S; patients underwent sedation, ICU; intensive care unit, SD; standart deviation, ERCP; Endoscopic retrograde cholangiopancreatography

(Table 1). It was observed that the sedated patients were older (p=0.023).

The mortality rate was 4.5% among all patients, and 44.7% of the patients who died were in the general anesthesia group and 55.3% were in the sedation group. While the mortality rate in Group G was 5.1%, it was 4.1% in Group S. There were no statistically significant differences between the two groups in terms of mortality. No significant differences were observed (p=0.322, Table 2). After the procedure, 11.3% of all patients were admitted to the intensive care unit and 88.7% were discharged to the hospital. While 39.7% of those admitted to the ward were in the general anesthesia group, 60.3% were in the sedation group, 39% of those admitted to the intensive care unit were in the general anesthesia group, and 61% were in the sedation group (p=0.847). While the need for intensive care in Group G patients was 11.1%, the need for intensive care was 11.4% in Group S patients and 11.3% on average. There was no significant difference between the two groups in terms of discharge or intensive care need (p=0.847, Table 2).

Desaturation was observed during postoperative recovery in 16 (2.1%) patients in Group G. Intraoperative desaturation was not observed in the general anesthesia group. Hypotension was observed during the induction of anesthesia in 22 patients (2.9%). No other complications of anesthesia were observed. The total number of complications was 38. In Group S, 55 (4.8%) patients had intraoperative desaturation, 19 (1.6%) patients had postoperative desaturation, and 15 (1.3%) patients experienced hypotension during anesthesia induction. A total of 89 complications were observed in the sedation group. Complication rates were significantly different between Group G and S patients. (p=0.021). Surgical complications were observed in 22 Group G and 41 Group S patients. There was no difference between the two groups in terms of surgical complications (p=0.113). The length of hospital stay and ERCP duration were significantly lower in the general anesthesia group than in the sedation group (p<0.001 and p<0.001, respectively; Table 2). While anesthesia-related interruption was not observed during ERCP in Group G patients, the procedure was interrupted for anesthesia intervention in 35 patients in Group S (<0.001). While there was no significant correlation between the development of complications in patients according to ERCP duration (p=0.336) and sex (p=0.537), a significant correlation was observed between age and complications (p<0.001). The mean age of the patients who developed complications was 83.94±6.5 years, while the mean age of the patients who did not develop complications was 75.88±6.9 years. While the complication rate was 1.7% in patients aged < 75 years, this rate increased to 10.6% in those aged > 75 years. A significant relationship was observed between age and complications (p<0.001).

According to the results obtained here, fewer anesthesia complications, shorter hospital stay, and shorter ERCP duration were observed in patients who underwent general anesthesia during the ERCP procedure. The need for intensive care, mortality, and surgical complications were similar to those of deep sedation.

DISCUSSION

The main findings of the current study include the following: 1) mortality and need for postoperative intensive care in ERCP procedures did not differ among the groups (p=322 and p=0.847, respectively); 2) length of hospital stay and ERCP duration were found to be significantly lower in the general anesthesia group than in the sedation group (p<0.001); and 3) fewer anesthesia complications were observed under general anesthesia (p=0.021). These findings show that general anesthesia is safer in terms of ERCP procedures.

In our study, the procedures in Group S were performed using propofol, midazolam, and ketamine. In a study evaluating the analgesic needs of ERCP patients, two-thirds of sedated patients experienced pain. Therefore, short-acting sedative agents may be beneficial for patients (9,10). Dexmedetomidine is a good option because it protects the airway better; however, it has a cost disadvantage (10). Propofol is another widely used and proven safe agent. Studies show that propofol is a safe option in non-operating room sedation procedures (11). In our study, propofol was preferred in both groups. Ketamine, on the other hand, requires a more complicated approach because it increases secretion; therefore, glycoprolate or atropine is needed, or midazolam is needed to reduce its hallucinogenic effects. In addition, hypertension in our study patients, similar in other geriatric patients, is an important limitation for the use of ketamine. Remifentanil, on the other hand, can be a good analgesic for daily procedures with its short duration of action. We think that remifentanil will be used more widely in the target of comfortable and safe anesthesia.

Mild sedation or conscious sedation has been abandoned in painful procedures such as ERCP. Propofol-based monitoring of anesthetic care can be used. However, patients often require deep sedation. In addition, there is a risk of inability to maintain spontaneous respiration under propofol, the need for respiratory support, and desaturation during deep sedation. In this respect, general anesthesia seems to be safer in ERCP, as the risks of desaturation and loss of the airway are lower. In our study group, airway intervention, hypotension, or desaturation developed during sedation in 7.8% of patients in Group S. The ERCP procedure was interrupted in 35 patients. Complications requiring intraoperative airway intervention were not observed in patients in Group G. With neuromuscular blocks used in general anesthesia, residual neuromuscular block is an important risk factor and may cause respiratory complications in the postoperative period. In a study conducted by Amornyotin et al.(12) with 158 patients, airway intervention was required in 26.6% of ASA I–II group patients and 28.8% of ASA III–IV group patients. Desaturation, upper airway obstruction, hypotension, and bradycardia were determined as the causes. In addition, pulse oximetry may delay the recognition of desaturation during apneic periods in patients under sedation.

Since our study patients were most frequently in the ASA II and III groups and included the geriatric patient group, the rate of airway problems as high as one-third in the Amornyotin's study is not an acceptable rate (12). Turning intubated patients in the prone position is also risky. Extubation and airway complications associated with the procedure were also observed. However, in inexperienced teams, the risk of airway loss is as important a possibility as a complication related to patient position. At this point, endotracheal intubation may be safe. Although there are some studies in the literature about the use of the laryngeal mask airway in the prone position and loss and management of the airway, the use of a laryngeal mask in the prone position does not seem practical in procedures such as ERCP, where the airway is shared with the surgical team (13). When we compared our study groups, we observed that airway complications were more common in patients under sedation.

Procedure duration and success

A significant proportion of ERCP procedures are abandoned early owing to insufficient anesthesia, and the success of the procedure increases twofold under general anesthesia (14). The experience of the surgical team is as important as that of the anesthesiologist for the success of the procedure. Poor cooperation among sedated patients may affect their level of success. Unsuccessful attempts increase surgical complications as well as prolonged anesthesia and anesthetic complications. However, no significant correlation was found between the

development of complications and the duration of ERCP in our groups. However, the duration of anesthesia is an independent risk factor for cardiovascular and respiratory complications in procedures performed under sedation under perioperative conditions (15). In our study, the duration of the procedure in the sedation group was nearly doubled and was significantly higher. Since prolonged procedures are associated with increased anesthetic drug doses, it is expected to increase post-anesthesia complications. It has been shown that the procedure is shorter in Group G patients. These results bring general anesthesia to the forefront in order to perform it successfully and in a short time.

Although the initiation of general anesthesia was slower than that of sedation, the procedures under general anesthesia in our study were significantly shorter than those in the deep sedation group. The effect of these two groups on ERCP unit turnover time could not be investigated because of the retrospective nature of the study owing to low evidence. However, it can be thought that general anesthesia will not be a waste of time for the ERCP unit, because of the shorter procedure time, less interruption of the procedure, and lower complication rates (15). For this reason, it is thought that the general anesthesia method may be superior for patient turnover in ERCP units. In addition, the use of sugammadex in the conversion of neuromuscular blocks has contributed to a short review (16). Turnover time may also need to be considered as a factor in the choice.

Effect of ASA score

In a study involving 1023 patients, the total mortality rate was 0.88% in patients with ASA III and higher, who expected difficult intubation, and who excluded depths of anesthesia other than "light propofol-based general anesthesia." (17). In an eight-year study, the relationship between ASA and mortality was examined in approximately 1.5 million endoscopy and ERCP procedures, and no correlation was observed between ASA and mortality for ERCP procedures (18). In another study involving geriatric patients, it was shown that elderly (>80) patients had higher ASA scores (3-4), but no correlation was found between ASA, Age, Gender and mortality. According to other findings, it was shown that these elderly patients had lower Charlson Comorbidity Indexes compared to younger patients, which was interpreted as older patients were more selectively treated and patients with high comorbidities were avoided (19).

Although it is known that the duration of the procedure under anesthesia is an independent risk factor for respiratory and cardiovascular complications, Goudra et al. stated that the procedures were shorter in patients with high ASA scores and longer procedures were performed in low-risk patients. This suggests that there is a selectivity in the duration of the procedure according to the ASA score or patient risk. However, the results of the high ASA score and the combination of anesthesia type were not analyzed clearly in these studies (20). In our study, while the mean mortality was 4.1% in Group S patients, it was 5.1% in Group G patients. There was no difference between the groups in terms of mortality and need for postoperative intensive care. However, while there were 32 ASA IV patients in Group G, only four patients in Group S were in the ASA IV class and ASA scores were significantly different between the groups. There were no restrictions in terms of ASA scores and additional diseases in the study patients. General anesthesia was preferred in patients with high ASA scores. Although this finding was not significant, it may be the reason for the slightly higher mortality in the general anesthesia group. When evaluated together with the literature, this suggests that the two techniques may be similar in terms of mortality in geriatric patients, and general anesthesia may be preferred in patients with high ASA scores (21).

Factors that can affect complication rates

In a study conducted with 458 patients, 89.7% of the patients underwent deep sedation and 10% of them underwent ERCP under general anesthesia; 3.7% of the sedation group was converted to general anesthesia, and the procedure had to be terminated early in one patient. The BMI and ASA scores of the general anesthesia group were higher, and the postoperative complications were similar (22). Cote et al. conducted a similar study with 799 patients and showed that male sex, high BMI, and ASA score were risk factors for airway problems (23). Based on these results, the authors suggest that both methods can be used in non-obese and uncomplicated patients. In our study, 1885 patients were examined, and it was found that the length of hospital stay was significantly higher in the sedation group, and the rates of anesthesia-related complications were still higher. In our study, the ASA scores of the general anesthesia group were higher, but we could not find any difference in terms of sex. When the three studies were evaluated together, general anesthesia was safer in those with high ASA scores. Another point to be considered here is which factors, other than the type of anesthesia, affect the high complication rates of anesthesia. Therefore, in our regression analysis, age and the development of surgical complications were also associated with anesthesia complications. Although all our study patients were over 65 years of age, the complication rate in patients over 75 years of age increased significantly to 10.6%. In terms of surgical complications, factors such as the effect on the duration of the procedure and the effect on the patient's hemodynamics can be considered the cause or result of anesthesia complications.

After ERCP, the rates of bacteremia, pancreatitis, sepsis, hemorrhage, and duodenal perforation can be as high as 8%. Anesthesia complications include hemodynamic complications, airway problems, aspiration, drug reactions, and death (15). To analyze this situation, it may be necessary to analyze surgical indications and complications. When evaluated together in both groups, intraoperative desaturation complications were most common in 4.8% of sedation patients, followed by 2.9% intraoperative hypotension under general anesthesia, postoperative desaturation under general anesthesia (2.1%), and sedation. Postoperative desaturation (1.6%) and hypotension (1.3%) were observed following sedation. Other undesirable conditions, defined as complications, were not observed in the medical records. Surgical complications were similar in both groups. In one study, the most common anesthesia-related complication was hemodynamic instability (37.01%), followed by desaturation (11.65%) (24). The complication rates in this study were considerably higher than those in the present study.

Who should apply sedation?

In both anesthesia methods, it is a prerequisite to have an experienced anesthesiologist, appropriate equipment, and personnel for non-operating-room anesthesia. The complication rate was higher than the operating room for anesthesia procedures outside the operating room. Since the cases in our study were performed by a single surgical and anesthesia team, both teams are highly experienced. In this case, it increased the reliability of our results and explained the low complication rates. In some centers, sedation is provided by physicians who are not anesthesiologists during ERCP or other endoscopic procedures (25). While American and British anesthesia societies advocate that sedation procedures should only be performed by an experienced anesthesia team, surgery and gastroenterology societies do not agree with this situation, and the practice still remains controversial. The common point is that when a patient needs general anesthesia, he also needs an anesthesiologist (26). In some centers, anesthesiologists working inrotation provide non-

operating room anesthesia. However, the effect of this situation on the results remains unclear. However, in some studies, it has been reported that both the duration of work and the cost of a hospital caused an increase of 760 thousand dollars in sedation administered by non-anesthesiologists who do not have experience in non-operating room anesthesia (27). Deep sedation is associated with risks of airway interventions, oxygenation problems, and loss of spontaneous breathing by ASA (28). For this reason, the same monitoring and anesthesia care as general anesthesia are recommended in national and international guidelines at this level of sedation (8,26).

Hospitalization and intensive care

Prolonged postoperative hospital stay may be due to more than one reason. In our study, patients in the sedation group had significantly longer hospital stays. A striking finding of our study was that 83 (11.1%) of the 746 patients in the general anesthesia group and 130 (11.4%) of the 1139 patients in the sedation group were admitted to the intensive care unit. The type of anesthesia did not significantly change the need for intensive care. Surgical clinics and post-procedure treatment plans for these patients may have also been effective in determining their intensive care needs.

Due to the retrospective nature of our study, there are some limitations. First, no randomization was conducted for patient selection. General and deep sedation preferences changed periodically, depending on the conditions of the ERCP unit. The comfort and preferences of patients were not analyzed in this study. Patients with missing data were excluded from the study to increase the reliability of the data. For this reason, although 2812 patient files were examined, data from 1885 patientswere used for analysis (Figure 1). However, the number of patients examined here is high, which has not been found in many studies in the literature.

In our study, end-tidal carbon dioxide monitoring was not used as a standard in the sedation group or this application has not been recorded. Based on retrospective data, this process is not clear, this gap should also be considered as a shortcoming for evaluating patient outcomes. Our study patients were sedated under non-objective and objective monitoring such as BIS, hemodynamic and respiratory responses, and response to surgery. Accordingly, the effect of the end-tidal carbon dioxide values on the results is not clear. Therefore, an important limitation of our study is the non-standard use of this monitor. However, although the use of capnography is undisputed, how to use it is a matter of debate, Many open-ended points show that end-tidal carbon dioxide monitoring is still open to many researches, such as the fact that non-anesthesiologist physicians who are not familiar with this monitoring also give sedation depending on the conditions, Which value should be taken as the threshold for end-tidal carbon dioxide values in patients who will receive sedation, is the threshold value or the trend safer? (29,30). From this point of view, we think that our findings will contribute to an ongoing gap in the literature. Our large patient group followed by BIS in sedated procedures can be compared in many studies with patients sedated by end-tidal carbon dioxide. Another limitation of our study was that the complexity of ERCP procedures was not classified. Some procedures are inherently more challenging for surgeons than others. The Quality Committee of the American Society of Gastrointestinal Endoscopy divided the procedures into four classes according to their difficulties (23), which may have affected the duration of the procedure. However, such a large number of patients and a significant difference in the level of statistical significance appeared to reduce this effect. The doses of anesthetic drugs used were naturally different between the sedation and general anesthesia groups. However, this point would be the subject of a different study. In the current

study, complications and mortality were compared between general anesthesia and sedation procedures in a large patient group as the primary goal. However, more than one subparameter that may affect the high complication rate can be identified through further tests. Therefore, we believe that a prospective study will contribute to this area. The strengths of our study are that we included all geriatric patients without restriction in terms of ASA score and comorbidities; all patients in both groups were recruited in a single center, without rotation, with a team experienced in both anesthesia and surgery; and inclusion of a large patient group compared to that in studies in the literature.

CONCLUSION

Team experience is at the forefront of ERCP procedures in geriatric patients, both in increasing the success of the treatment and in reducing the complication rates. Deep sedation and general anesthesia did not affect mortality or the need for intensive care. However, general anesthesia seems to be safer in patients with high ASA scores. General anesthesia significantly reduced the length of hospital stay and ERCP procedure time. Complications related to general anesthesia are reduced, while the duration of the procedure is shortened. In this respect, general anesthesia appears superior to deep sedation. Nevertheless, the choice of anesthesia should be considered on a patient basis in line with the priorities, and it would be beneficial to make a choice in line with the experience of the team and conduct more randomized controlled clinical studies to strengthen the results.

Acknowledgments: None

Conflict of interest: None

REFERENCES

1. Yılmaz S, AkıcıM, ŞimşekM, Okur N, ErşenO, Tuncer AA. Endoscopic retrograde cholangiopancreatography for biliary system parasites. Turk J Surg. 2018;34(4):306–310. (PMID: 30664430).
2. Kandemír A, Arabul M, Çelik M, Alper E, Vatansever S, Ünsal B. Assessment of gastrointestinal endoscopic procedures in aged patients.Turk J Geriatr. 2013;16(1):43–47. (in Turkish).
3. Ministry of Health Okmeydanı Training and Research Hospital Anesthesia and Reanimation Clinic,.GeriatricAnesthesia. Turk J Geriatr. 2007;10(1):49–56. (in Turkish).
4. Goudra BG, Singh PM. Anesthesia for ERCP. In: Goudra BG, Duggan M, Chidambaran V, VenkataHariP K, Duggan E, Powell M, Singh PM (Eds). Anesthesiology: A practical approach. 1st ed., Springer International Publishing AG, part of Springer Nature.Cham; 2018.p. 175–88.(Doi:10.1007/978-3-319-74766-8)
5. Yüksek A, Büyükerkmen E. Anesthesia in ERCP procedures. In: Akaydin M, Bektaş H, Dolay K, Yilmaz S (Eds).Surgical ERCP applications. Akademisyen Bookstore Ankara 2020. p. 9–13. (in Turkish).
6. Thosani N, Banerjee S. Deep sedation or general anesthesia for ERCP? Dig Dis Sci. 2013;58(11):3061–3063. (PMID: 23990001).
7. Doğan Baki E, Yüksek A, Bezen BA, Saritaş TB, Sivaci R. Retrospective analysis of anesthesia in geriatric patients during endoscopic retrograde cholangiopancreatography. Turk J Geriatr. 2018;21(2):225–230. (Doi: 10.31086/tjgeri.2018240423). (in Turkish).
8. Turkish Society of Anesthesiology and Reanimation, Guide to Non-Operating Room Anesthesia Iyilikçi L, Ökesli S (Eds). [e-book]. TSAR December 2015 [Internet].Available from: https://www.tard.org.tr/assets/kilavuz/1.pdf. Accessed: 20.06.2022].(in Turkish).
9. Heuss LT, Froehlich F, Beglinger C. Nonanesthesiologist-administered propofol sedation: from the exception to standard practice. Sedation and monitoring trends over 20 years.Endoscopy. 2012;44(5):504–511. (PMID: 22389232).
10. Bayram A, Erkan GN, Talih G et al. The alpha-2 receptor agonist dexmedetomidine attenuates vancomycin-induced acute kidney injury. Bratisl Lek Listy. 2019;120(6):429-433. (PMID: 31223023).

11. Riphaus A, Stergiou N, Wehrmann T. Sedation with propofol for routine ERCP in high-risk octogenarians: a randomized, controlled study. Am J Gastroenterol. 2005;100(9):1957–1963. (PMID: 16128939).

12. Amornyotin S, Kachintorn U, Chalayonnawin W, Kongphlay S. Propofol-based deep sedation for endoscopic retrograde cholangiopancreatography procedure in sick elderly patients in a developing country. TherClin Risk Manag. 2011;7:251–255. (PMID: 21753887).

13. Kwee MM, Ho YH, Rozen WM. The prone position during surgery and its complications: a systematic review and evidence-based guidelines. Int Surg. 2015;100(2):292–303. (PMID: 25692433).

14. Ah Mew N, Simpson KL, Gropman AL, et al. Urea Cycle Disorders Overview. In: GeneReviews®. University of Washington, Seattle, Seattle (WA); 1993. (PMID: 20301396).

15. Garewal D, Vele L, Waikar P. Anaesthetic considerations for endoscopic retrograde cholangio-pancreatography procedures. Curr Opin Anaesthesiol. 2013;26(4):475–480. (PMID: 23635608).

16. De Robertis E, ZitoMarinosci G, Romano GM, et al. The use of sugammadex for bariatric surgery: analysis of recovery time from neuromuscular blockade and possible economic impact. Clinicoecon Outcomes Res. 2016;8:317–322. (PMID: 27418846).

17. Hormati A, Aminnejad R, Saeidi M, Ghadir MR, Mohammadbeigi A, Shafiee H. Prevalence of anesthetic and gastrointestinal complications of endoscopic retrograde cholangiopancreatography. Anesth Pain Med. 2019;9(4):e95796. (PMID: 31754612).

18. Enestvedt BK, Eisen GM, Holub J, Lieberman DA. Is the American Society of Anesthesiologists classification useful in risk stratification for endoscopic procedures? Gastrointest Endosc. 2013 Mar;77(3):464-71.(PMID: 23410699)

19. Galeazzi M, Mazzola P, Valcarcel B, Bellelli G, Dinelli M, Pasinetti GM, Annoni G. Endoscopic retrograde cholangiopancreatography in the elderly: results of a retrospective study and a geriatricians' point of view. BMC Gastroenterol. 2018 Mar 14;18(1):38. (PMID: 29540171)

20. Goudra BG, Singh PM, Sinha AC. Anesthesia for ERCP: Impact of Anesthesiologist's Experience on Outcome and Cost. Anesthesiol Res Pract. 2013;2013:570518. (PMID: 23781243)

21. Celik JB, Topal A, Erdem TB, İnci KA.A comparison of two different sedation techniques in geriatric patients for endoscopic urological surgery.Turk J Geriatr. 2012;15(1):55–60. (in Turkish).

22. Garewal D, Powell S, Milan SJ, Nordmeyer J, Waikar P. Sedative techniques for endoscopic retrograde cholangiopancreatography. Cochrane Database Syst Rev. 2012;6(6):CD007274. (PMID:22696368)

23. Barnett SR, Berzin T, Sanaka S, Pleskow D, Sawhney M, Chuttani R. Deep sedation without intubation for ERCP is appropriate in healthier, non-obese patients. Dig Dis Sci. 2013;58(11):3287–3892. (PMID: 23877477).

24. Coté GA, Hovis RM, Ansstas MA, et al. Incidence of sedation-related complications with propofol use during advanced endoscopic procedures. ClinGastroenterolHepatol. 2010;8(2):137–142. (PMID:19607937).

25. Jeurnink SM, Steyerberg EW, Kuipers EJ, Siersema PD. The burden of endoscopic retrograde cholangiopancreatography (ERCP) performed with the patient under conscious sedation. SurgEndosc. 2012;26(8):2213–2219. (PMID: 22302536).

26. Hinkelbein J, Lamperti M, Akeson J, et al. European Society of Anaesthesiology and European Board of Anaesthesiology guidelines for procedural sedation and analgesia in adults. Eur J Anaesthesiol. 2018;35(1):6–24. (PMID: 28877145).

27. Goudra BG, Singh PM, Sinha AC. Anesthesia for ERCP: impact of anesthesiologist's experience on outcome and cost. Anesthesiol Res Pract. 2013;2013:570518. (PMID: 23781243).

28. Saricaoğlu F. Akinci Sb, Süheyla at, Çağlar Ö, Aypar Ü. The effects of anesthesia techniques on postoperative mortality in elderly geriatric patients operated for femoral fractures. Turk J Geriatr. 2012;15(4):434–438. (in Turkish).

29. B. Goudra, L. Penugonda, R. Speck and A. Sinha. Comparison of Acoustic Respiration Rate, Impedance Pneumography and Capnometry Monitors for Respiration Rate Accuracy and Apnea Detection during GI Endoscopy Anesthesia. Open Journal of Anesthesiology. 2013;3(2): 74-79. doi: 10.4236/ojanes.2013.32019.

30. Ciocîrlan M. Is capnography mandatory during sedation for endoscopy? Endosc Int Open. 2016 Mar;4(3):E352-3.(PMID: 27004255)

RESEARCH

KNEE ARTHRODESIS WITH COMPUTER-ASSISTED EXTERNAL FIXATOR SYSTEM AFTER PROSTHETIC JOINT INFECTION FOR ELDERLY POPULATION

Turkish Journal of Geriatrics
DOI: 10.29400/tjgeri.2023.331
2023; 26(1):60−67

Muharrem KANAR[1]
Necmi CAM[2]

Abstract

Introduction: This study aimed to evaluate the effectiveness of a computer-assisted circular external fixator used to achieve arthrodesis in elderly patients with failed infected total knee arthroplasty.

Materials and Methods: Retrospectively 11 patients who treated with arthrodesis between 2015 and 2020 were included in the study. The average age was 73.5 ±4.73 years (65–81). All patients had recurrent infections after total knee arthroplasty. Radiologic evaluations, the time for fusion, shortening of extremities, visual analog scale scores, Oxford knee scoring system, lower extremity functional scale of all patients were compared pre-and post-operatively. complications of the technique were noted.

Results: The mean follow-up was 33.7 ±12.85 (12–52) months. Fusion was achieved in all patients. The average limb length discrepancy after removal of the fixator was 46±0.78 (36–61) mm. The mean visual analog scale score measured pre-op was 6.91±0.94 (5–8), and after fixator removal they were measured as 2.36±0.92 (1–4). The mean Oxford knee score was 10.27±2.68 (4–14) pre-operatively and 28.64±2.69 (23–32) postoperatively. The mean, lower extremity functional scale was 17.06±9.38 (7.5–33.8) pre-operatively and 38.54±12.22 (21.3–56.3) postoperatively. No joint infection recurrence was seen post-operatively.

Conclusion: Arthrodesis is a suitable option for elderly patients with limited mobilization who are tired of repeated revision surgeries. Due to its high fusion and low complication rate, computer-assisted circular external fixator is an effective method in the treatment of difficult knee arthrodesis required after infected total knee arthroplasty.

Key Words: Arthroplasty, Replacement, Knee; Reoperation; Infection; Arthrodesis; External Fixators.

CORRESPONDANCE

[1]Muharrem KANAR

Phone : +905325100418
e-mail : dr.kanar@hotmail.com

Received : Nov 05, 2022
Accepted : Feb 06, 2023

[1] Şişli Hamidiye Etfal Training and Research Hospital, Orthopaedics And Traumatologia, Istanbul, Turkey

[2] Şişli Hamidiye Etfal Training and Research Hospital, Orthopaedics and Traumatologia, Istanbul, Turkey

INTRODUCTION

Infection of knee arthroplasty is feared and is one of the most catastrophic complications for that can accompany above-knee amputation. It can be seen at a rate of 0.4–2%, and it is quite difficult to treat (1).

Knee arthrodesis is a salvage procedure for end-stage periprosthetic joint infections. Also, massive bone and soft tissue loss and extensor mechanism disruption are caused by repeated operations or in cases of a patient's refusal to undergo revision arthroplasty after infected knee arthroplasty (2).

The main goals of knee arthrodesis in infected total knee arthroplasty (TKA) are to provide pain relief and stability of the extremity. Many methods have been described to achieve solid knee fusion: canulated screws, intramedullary nails, plate osteosynthesis, and external fixation, with rates of fusion ranging from 29% to 100%. The ideal method should have a high fusion rate with a low complication rate, minimal visits to the hospital, and a reduction in the need for further treatment. Normal anatomical alignment should be restored. It has been accepted that rigid fixation and compression reduce failure rates. The success of arthrodesis is determined by the patient's bone stock, independent of the technique and indication (3).

Arthrodesis of the knee can provide a stable and painless extremity on which patients can walk. The patient also had better functional outcomes than those encountered with amputation or suppressive antibiotic treatment. Therefore, arthrodesis procedures can be a choice for the management of persistent infection after failed multiple-stage revision arthroplasty (4).

Studies have shown that the success rates of TKA have increased. Therefore, the indication of total knee arthroplasty has expanded, and it has begun to be performed more in younger patients (5).

Because of the increasing knee arthroplasty, we believe that requirement the revision knee arthroplasty and arthrodesis will probably increase. In this study, we aimed to investigate the effectiveness of a computer-assisted circular external fixator (Ca-CEF) system for achieving knee arthrodesis in patients with failed infected TKA.

MATERIALS AND METHODS

In this study, we retrospectively evaluated elderly patients with infected knee arthroplasty who were treated with knee arthrodesis by a Ca-CEF (Spiderframe Tasarımmed, İstanbul, Turkey) between June 2015 and September 2020 and at least followed up six months after fixator removal in the Health Sciences University, Orthopaedic and Traumatology department , Şişli Hamidiye Etfal Training and Research Hospital. The exclusion criteria were the patient who was out of follow-up before the treatment was completed, the patient under 65 years, and the knee arthrodesis was not based on periprosthetic infection. Twelve patients who underwent arthrodesis after failed knee arthroplasty were retrospectively analyzed from hospital archive records. One patient died due to COVID-19 while his treatment was ongoing, and his follow-up was not completed. This patient was excluded from the study group. Eleven patients were included in our study; eight of the patients were female, and three were male. The average age was 73.5±4.73 (65–81) years. All patients had recurrent infections after TKA. Patients over 65 years with infected knee arthroplasty who has at least one major criteria of MSIS criteria (6), who did not recover despite at least three surgeries, and who accepted arthrodesis were included in the study.

The study protocol was approved by the Şişli Hamidiye Etfal Training and Research Hospital Ethics Committee (date: 02/02/2021, number:3119). Written informed consent was obtained from the patients or their legal guardians of each patient. The study was conducted according to the principles of the Declaration of Helsinki.

Surgery was performed by anteromedial parapatellar approach, which had also been used in previous arthroplasty surgery, was used. Firstly, spacers were removed, and joint debridement was applied to the patients then bone surfaces were prepared to improve the contact area by an electrical saw. Ca-CEF was applied, and intraoperative compression of the bone was performed in the operating room.

Postoperatively x-ray was evaluated for correct angulation of any plane or compression by Ca-CEF, if needed. The patients were mobilized by full weight bearing using crutches on the day after the operation. Systemic antibiotic treatment was started according to the post-operative positive cultures. After six weeks of systemic antibiotherapy, clinical and laboratory findings evaluated oral antibiotherapy according to the recommendations of the infectious disease consultation. Time for solid bone fusion, limb alignment and shortening of extremities (mm), recurrence of infection, visual analog scale (VAS), Oxford knee scoring (OKS) and lower extremity functional scale (LEFS) scores of all patients were compared pre-op and post-op (six months after fixator removal). Minor and major complications of the technique were noted.Patients details are summarized in Table 1.

RESULTS

The mean follow-up was 33.7 ±12.85 (12–52) months, and fusion was achieved in all patients. The average time for fusion was 7.7±1.84 months (5–11 months). (Figure 1). The average limb length discrepancy after removal of the fixator was 46±0.78 (36-61) mm. The mean VAS score measured pre-op was 6.91±0.94(5–8), after fixator removal 2.36±0.92(1–4). The average patient hospital stay was 16.8 (6–29) days. Mean OKS was 10.27±2.68 (4–14) pre-operatively, and 28.64±2.69 (23–32) postoperatively. Mean LEFS was 17.06±9.38 (7.5-33.8) pre-operatively, and 38.54±12.22 (21.3-56.3) was post-operatively. The decrease in the post-op VAS score and the increase in OKS and LEFS scores were found to be statistically significant compared

Table 1. Details of patients

Patient	Age	Gender	Side	Culture results	Follow -up (months)	Fusion time (months)	Shortness (mm)
1	72	Male	Left	MRSA	12	8	45
2	74	Female	Right	Candida albicans	21	7	55
3	65	Male	Right	Polimikrobial	52	9	36
4	71	Female	Left	Enterococcus fecalis	23	5	48
5	76	Male	Right	Klebsiella pneumoniae	34	6	5
6	79	Female	Right	Staphylococcus epidermidis	37	6	4
7	69	Female	Left	Pseudomonas aeruginosa	20	11	61
8	70	Female	Left	MRSA	43	6	44
9	77	Female	Right	Polimikrobial	39	9	38
10	76	Female	Left	Polimikrobial	44	10	41
11	81	Male	Left	Escherichia coli	46	7	54

MRSA: methicillin-resistant Staphylococcus aureus

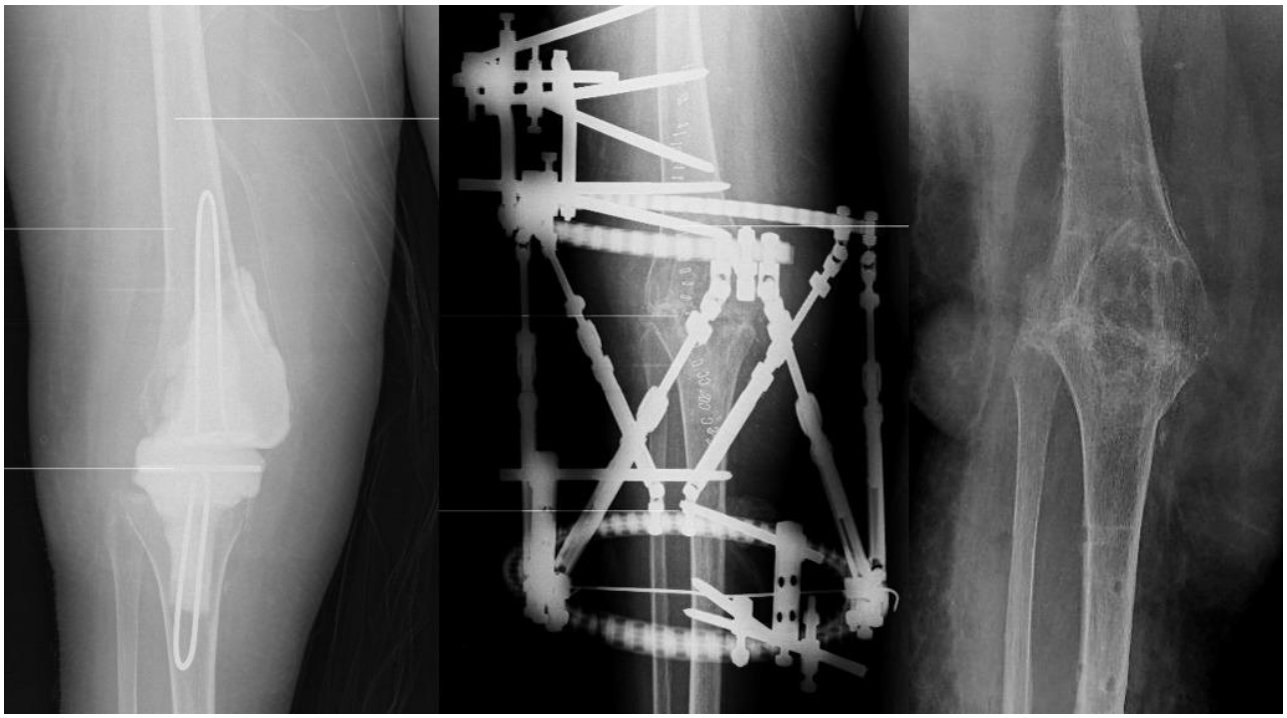

Figure 1. X-ray images before arthrodesis, after Ca-CEF application and after fixator removal are seen

to the pre-op values of the patients. Descriptive statistical results are summarized in Table 2.

Almost all patients had a low-grade pin-tract infection that treated with local wound care and antibiotherapy. Only two patients had to pins removed with local anesthesia. Clinically, all patients had stable knee arthrodesis, all patients were able to walk on their own, even four of them could walk without crutches during the last follow-up. No patient had a stress fracture or a refracture

Table 2. Statistical analysis of pain and functional scores

		Mean±SD	Min-Maks (Median)	p
VAS	Pre-op	6.91±0.94	5-8 (7)	0,003#
	Post-op	2.36±0.92	1-4 (2)	
	Variation Mean.±SD %95 CI)	4.55±1.29 (3.68-5.41		
OKS	Pre-op	10.27±2.68	4-14 (11)	<0,001*
	Postop	28.64±2.69	23-32 (29)	
	Variation Ort.±SD %95 CI)	18.4±1.9 (17.1-19.6)		
LEFS	Pre-op	17.06±9.38	7.5-33.8 (13.8)	<0,001*
	Post-op	38.54±12.22	21.3-56.3 (40)	
	Variation Ort.±SD %95 CI)	21.5±7.6 (16.4-26.6)		

VAS: Visual Analog Scale, OKS: Oxford Knee Scoring , LEFS: lower extremity functional scale
*Paired t Test #Wilcoxon Test

after fixator removal during the follow-up. No joint infection recurrence was seen in any of the patients. All patients reported mild pain but did not need any pain medication.

The alignment of fusion was noted mechanical axis deviation (MAD) from medially varus was noted as "+" and valgus was noted as "-". Mean coronal alignment was -2.4 mm and the range was + 2 to (-7) and mean sagittal plan alignment was 4.6 degrees (range was 0–10 degrees procurvatum). There was no recurvatum deformity.

Statistical analysis

SPSS 15.0 for Windows program was used for statistical analysis. Descriptive statistics were given as number and percentage for categorical variables, mean, standard deviation, median, minimum, maximum for numerical variables. When the differences of numerical variables in the dependent group provided the normal distribution condition, the Paired t test was analyzed with the Wilcoxon test when the condition was not met. The alpha significance level was accepted as $p<0.05$.

DISCUSSION

Revision after failed infected knee arthroplasty results in a higher complication rate, with a more unfavorable outcome in terms of pain and function. Multiple surgeries may be required (7). These patients also face potentially disastrous complications including above-the-knee amputation, and unfortunately death (8). Especially in elderly patients in order to avoid these complications, as a salvage surgery, the knee arthrodesis option should not be ignored.

Arthrodesis is a widely accepted surgery for failed TKA when further revisions are not desired for geriatric population. Recurrent infections, extensive bone defects, ligament instability, lack of extensor mechanism, and insufficient soft tissue coverage of the knee may require arthrodesis of the knee joint as a curative procedure for limb salvage. Arthrodesis restores good limb loading, reduces pain, eliminates infection and generally well tolerated by the elderly patients (9). Studies in the literature mention that even after achieving successful knee arthrodesis using any of various techniques, some patients have continued to experience mild pain but acceptable functionality (10). This also observed in our current study. All patients reported mild pain but did not need any medication.

Many techniques have been described for knee arthrodesis. External fixators (monolateral, circular), intramedullary nails, plates and screws are among the surgical methods that can be used. Each technique has its own positive and negative aspects. Regardless techniques stable and painless extremity with the eradication of infection is the main goal of knee arthrodesis after failed infected TKA. For a successful fusion the infection should be controlled, soft tissue problems should be eliminated. Two-stage procedure has high fusion rate of arthrodesis (11). We prefer two-stage procedure with Ca-CEF for high fusion rate.

An ideal arthrodesis should achieve a high rate of fusion with a low complication rate, allow early mobilization, and achieve normal anatomical alignment of the limb. The use of plate and screw is not preferred because of not allowing early weight bearing, soft tissue problems, and high infection recurrence rate. Most of the publications recommended intramedullary nail or external fixator in arthrodesis surgeries after infected TKA (11).

Intramedullary nail provides good stability, well tolerated and allows early weight bearing (11). Apart from this, there are also disadvantages compared to external fixators. Surgery time of the arthrodesis by intramedullary nail procedure is longer than the external fixator and reaming of the femur and tibia increases the risk of pulmonary embolism and can spread the infection along the medullary canal (9,12).

Therefore, the insertion of a long intramedullary nail is a challenging operation with a high risk of

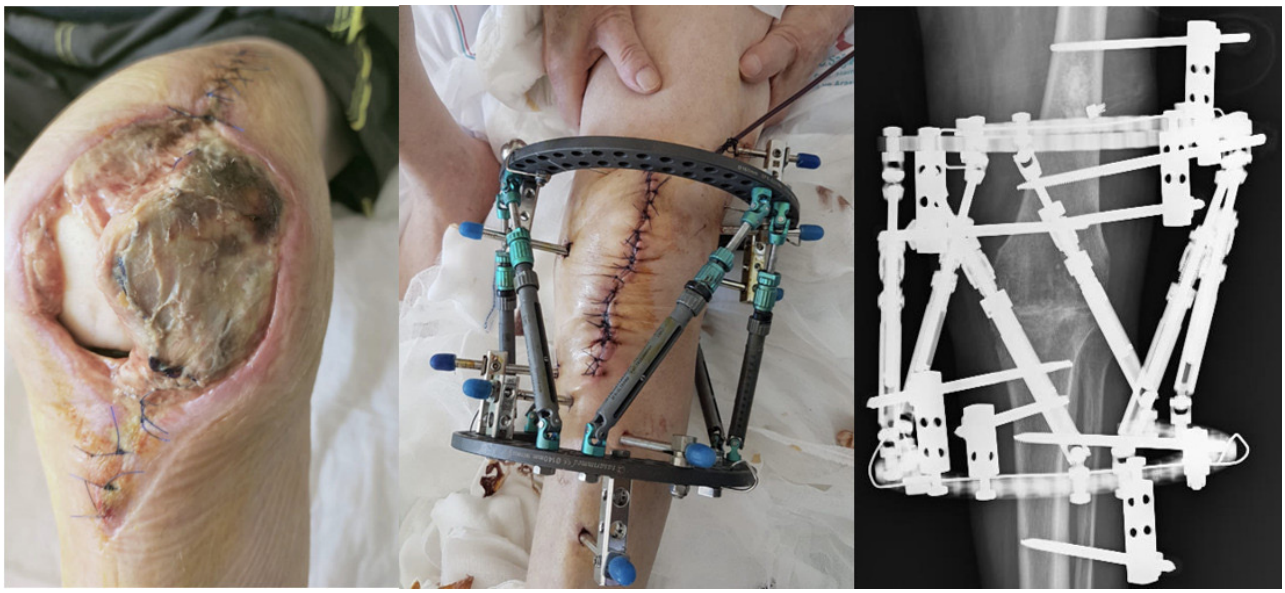

Figure 2. Patient who treated by Ca-CEF with soft tissue problem after infected TKA is seen

proximal femur fracture (12). In addition, external fixation provides intraoperative flexibility; it can be used in cases when medullary canal of femur has already been obliterated by an implant or anatomic deformities. It also allows performing reconstructive procedures in which cases had soft tissue problems. (Figure 2). External fixators are more advantageous in terms of infection recurrence because of there is no implant that remains in the body (10,11).

Parratte et al. reported complete remission of infection with external fixator arthrodesis in infected TKA (13). Also, in our patient group no infection recurrence was seen. When the results of arthrodesis applied with intramedullary nail after infected knee prosthesis are examined in the literature, fusion rates vary between 73.7% and 100%, and the average limb length discrepancy rates are between 28mm and 55mm (14-17). In our case series fusion was achieved in all patients and the average limb length discrepancy was 46mm. None of the patients requested limb-lengthening surgery, early removal of the fixator was their priority. The effective compression in the Ca-CEF while increasing the shortness, also positively affects to our fusion rates.

The fusion time of knee arthrodesis is longer than normal bone fracture healing (2). Comfort was decreased in external fixators when compared to internal fixations. Because of this treatment with fixators can negatively affects the social and emotional status of the patient (18). Some patients may even request the termination of the fixator without waiting for the completion of the treatment. There was no such request in our elderly patients. Because they were motivated when their pain subsided and they could walk on their own.

Classic complications of external fixators such as pin-tract infections and pin loosening, can often be seen. Klinger et al. conducted a study of 18 patients in which 100% developed pin-tract infections (19). In our study, pin-tract infection was observed in all patients, but most recovered with local wound care and antibiotic therapy. Only two patients had pin loosening in the proximal region. In these patients, loosened pins were removed with the help of local

anesthesia under outpatient conditions, and no additional surgical procedure was required. We predicted this in our patients and kept the number of Schanz applied to the proximal region to more than normal.

It is recommended to perform knee arthrodesis in 5-8 degrees of valgus, 0-15 degrees of flexion and 5-10 degrees of external rotation (2). When arthrodesis is performed with an intramedullary nail, this arthrodesis occurs with 2–5 degrees of varus, which theoretically causes same-side hip arthritis (20). In our study, an average of -2.1 mm MAD (valgus) was obtained after the fusion was completed. Using the advantage of Ca-CEF ability to correct in all directions, we achieved the desired arthrodesis angles in the fusion. There is no consensus on which position arthrodesis should be performed for the sagittal plane of knee arthrodesis. In our study, arthrodesis was planned in full extension with the aim of preventing the increase of shortness.

Artodesis can be applied with many external fixator systems. Although monolateral fixators are comfortable, but they are not very suitable for weight bearing. On the other hand, wires and Schanz screws at different angles in Ilizarov and other circular fixators resist high stability and dynamic axial stability versus torsional forces (20,21)

Full load with a circular fixator allows axial compression in the arthrodesis side axially, even after surgery, that increases bone regeneration. Ca-CEF systems, which can provide more rigid fixation according to the classical Illizarov systems and can be defined as a more advanced current version of the circular fixators, allow for the easy correction of deformities during the arthrodesis process in the post-operative period (22).

The indication of total knee arthroplasty is expanded, and it has begun to be performed more often in younger patients (5) Therefore, we believe that the need for arthroplasty revisions and arthrodesis surgeries will increase, and this study may be inspire for future studies with a larger sample.

Small sample size and retrospective design are limitations of our study .

We aimed to achieve better results by combining the stability of IM nails and the success of conventional ex-fixes in infection using Ca-CEF. This was supported by the fact that fusion was achieved in all patients and no recurrence of infection was observed.

In conclusion, Arthrodesis is a suitable option for elderly patients with limited mobilization who are tired of repeated revision surgeries. Due to its high fusion and low complication rate, Ca-CEF is an effective method in the treatment of difficult knee arthrodesis required after infected TKA.

REFERENCES

1. Peersman G, Laskin R, Davis J, et al. Infection in total knee replacement: a retrospective review of 6489 total knee replacements. Clin Orthop Relat Res. 2001;(392):15-23. (PMID: 11716377)
2. Balci HI, Saglam Y, Pehlivanoglu T, Sen C, et al. Knee Arthrodesis in Persistently Infected Total Knee Arthroplasty. J Knee Surg. 2016;29(7):580-88. (PMID: 26683977)
3. Vlasak R, Gearen PF, Petty W. Knee arthrodesis in the treatment of failed total knee replacement. Clin Orthop Relat Res. 1995;(321):138-44. (PMID: 7497659)
4. Wu CH, Gray CF, Lee GC. Arthrodesis should be strongly considered after failed two-stage reimplantation TKA. Clin Orthop Relat Res. 2014;472(11):3295-304. (PMID: 24488752)
5. Lonner JH, Hershman S, Mont M. Total knee arthroplasty in patients 40 years of age and younger with osteoarthritis. Clin Orthop Relat Res. 2000;(380):85-90. (PMID: 11064977)
6. Parvizi J, Zmistowski B, Berbari EF, et al. New definition for periprosthetic joint infection: from the Workgroup of the Musculoskeletal Infection Society. Clin Orthop Relat Res. 2011;469(11):2992-4. (PMID: 21938532)
7. Roman MD, Russu O, Mohor C, et al. Outcomes in revision total knee arthroplasty . Exp Ther Med. 2022;23(1):29. (PMID: 34824637)

8. Sierra RJ, Trousdale RT, Pagnano MW. Above-the-knee amputation after a total knee replacement: prevalence, etiology, and functional outcome. J Bone Joint Surg Am. 2003;85(6):1000-4. (PMID: 12783994)

9. Spina M, Gualdrini G, Fosco M, Giunti A. Knee arthrodesis with the Ilizarov external fixator as treatment for septic failure of knee arthroplasty. J Orthop Traumatol. 2010;11(2):81-8. (PMID: 20425133)

10. Mahmoud SS, Sukeik M, Alazzawi S, et al. Salvage Procedures for Management of Prosthetic Joint Infection After Hip and Knee Replacements. Open Orthop J. 2016 30;10:600-614. (PMID: 28144373)

11. Robinson M, Piponov HI, Ormseth A, et al. Knee Arthrodesis Outcomes After Infected Total Knee Arthroplasty and Failure of Two-stage Revision With an Antibiotic Cement Spacer. J Am Acad Orthop Surg Glob Res Rev. 20183;2(1):077. (PMID: 30211377)

12. Mabry TM, Jacofsky DJ, Haidukewych GJ, et al. Comparison of intramedullary nailing and external fixation knee arthrodesis for the infected knee replacement. Clin Orthop Relat Res. 2007;464:11-5. (PMID: 17471102)

13. Parratte S, Madougou S, Villaba M, et al. Knee arthrodesis with a double mono-bar external fixators to salvageinfected knee arthroplasty: retrospective analysis of 18 knees with mean seven-year follow-up. Rev Chir Orthop Repar Appar Mot2007;93(4):373–80. (PMID: 17646819)

14. De Vil J, Almqvist KF, Vanheeren P, Boone B, Verdonk R. Knee arthrodesis with an intramedullary nail: a retrospective study. Knee Surg Sports Traumatol Arthrosc. 2008 Jul;16(7):645-50. (PMID: 18373081)

15. Incavo SJ, Lilly JW, Bartlett CS, Churchill DL. Arthrodesis of the knee: experience with intramedullary nailing. J Arthroplasty. 2000 Oct;15(7):871-6. (PMID: 11061447)

16. Leroux B, Aparicio G, Fontanin N, et al. Arthrodesis in septic knees using a long intramedullary nail: 17 consecutive cases. Orthop Traumatol Surg Res. 2013 Jun;99(4):399-404. (PMID: 23623438)

17. Bargiotas K, Wohlrab D, Sewecke JJ et al. Arthrodesis of the knee with a long intramedullary nail following the failure of a total knee arthroplasty as the result of infection. Surgical technique. J Bone Joint Surg Am. 2007 Mar;89 Suppl 2 Pt.1:103-10. (PMID: 17332129)

18. Benson ER, Resine ST, Lewis CG. Functional outcome of arthrodesis for failed total knee arthroplasty. Orthopedics. 1998 Aug;21(8):875-9.(PMID: 9731669)

19. Klinger HM, Spahn G, Schultz W,. Arthrodesis of the knee after failed infected total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2006;14(5):447-53. (PMID: 16133442)

20. Conway JD, Mont MA, Bezwada HP. Arthrodesis of the knee. J Bone Joint Surg Am. 2004;86(4):835-48. (PMID: 15069154)

21. Van Rensch PJ, Van de Pol GJ, Goosen JH, et al. Arthrodesis of the knee following failed arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2014;22(8):1940-8. (PMID: 23708381)

22. Tan B, Shanmugam R, Gunalan R, et al. A Biomechanical Comparison between Taylor's Spatial Frame and Ilizarov External Fixator. Malays Orthop J. 2014;8(2):35-9. (PMID: 25279090)

Turkish Journal of Geriatrics
DOI: 10.29400/tjgeri.2023.332
2023; 26(1):68-78

Afife GÜLER KOL[1]
Hacı Yusuf GÜNEŞ[1]

RESEARCH

THE EFFECTS OF LOW FLOW AND NORMAL FLOW DESFLURANE ANESTHESIA ON LIVER AND RENAL FUNCTIONS AND SERUM CYSTATIN C LEVELS IN GERIATRIC PATIENTS: A PROSPECTIVE RANDOMIZED CONTROLLED STUDY

CORRESPONDANCE

[1]Hacı Yusuf GÜNEŞ

Phone : +905065357166
e-mail : hyusufgunes@hotmail.com

Received : Nov 30, 2022
Accepted : Feb 19, 2023

[1] Van Yuzuncu Yıl University, Faculty of Medicine, Department of Anesthesiology and Reanimation, Van, Turkey

Abstract

Introduction: Aging is a physiological process and the elderly population is increasing. In parallel to the increasing of the elderly population, the number of geriatric patients who required an invasive procedure or surgical intervention under anesthesia are also increasing. The geriatric patients who are frailty and have a loss of functional reserve in all organ systems are more sensitive to anesthetic agents. The purpose of this research was to investigate whether low flow desflurane anesthesia also affects hepatic and kidney functions, in elderly patients.

Methods: After approval from the local ethics committee, the patients were divided into two groups; as the low flow desflurane anesthesia group and the normal flow desflurane anesthesia group using the closed-envelope method. Calibration and leakage tests of the anesthesia device (Primus, Drager) were performed before anesthesia. Heamodynamics parametres, peripheral oxygen saturation, and bispectral index monitoring were performed to all patients in operating room. The blood samples were collected before anesthesia induction, after surgery, and at the postoperative 24th hour. The serum alanine aminotransferase and aspartate aminotransferase levels were measured to assess the liver damage. The serum creatinine, blood urea nitrogen, and cystatin C levels were measured to assess the kidney function.

Results: The serum alanine aminotransferase, aspartate aminotransferase, blood urea nitrogen, creatinine and cystatin C levels and hemodynamic parameters, peripheral oxygen saturation and bispectral index values were similar in both groups.

Conclusions: It was concluded that low-flow desflurane anesthesia does not adversely affect liver and kidney functions in geriatric patients and is as safe as normal-flow desflurane anesthesia.

Keywords: Anesthesia; Cystatin C; Desflurane; Aged; Kidney; Liver.

INTRODUCTION

Aging, which is a physiological process; it is characterized by loss of functional reserve in all organ systems, regression in anabolic processes, and increase in catabolic processes (1). In parallel to the increase in the life expectancy of geriatric patients, it is predicted that we will provide medical treatment under anesthesia to more and more elderly patients (2). Low-flow anesthesia an inhalation technique applied with a semi-closed rebreathing system, has a rebreathing rate of at least 50% (3, 4). With this anesthesia technique, cost is reduced, environmental pollution is lower, and the humidity and temperature of the inhaled gases can be protected (5, 6). Volatile anesthetic agents such as sevoflurane and desflurane are commonly used in anesthesia practice (7). They affect hepatic blood flow and cardiac output to varying degrees. For this reason; liver and kidney functions are also affected. In addition, teh metabolic rates and excretion in the liver and kidneys are also a determining factor in their effects on liver and kidney functions. Sevoflurane undergoes defluorination in the kidneys to form inorganic fluoride ions. The carbon dioxide absorber converts sevoflurane to compound A. Both inorganic fluoride and compound A were associated with nephrotoxicity. The renal excretion rates of inhalation agents and their stability to degradation by standard carbon dioxide absorbents are also effective on renal function (8,9). Desflurane, which is highly proof to defluorination, has not been associated with nephrotoxicity (10). The hepatotoxic effects of inhalation agents may vary according to their effects on hemodynamic parameters and hepatic blood flow, and their metabolism rates in the liver (11). Does low-flow desflurane anesthesia affect liver and kidney functions in elderly patients who are frail and have losses of functional reserve in their organ systems? The aim of this study is to investigate the effects of low-flow and normal flow desflurane anesthesia on hepatic and kidney functions in geriatric patients.

MATERIALS AND METHODS

This prospective, randomized-controlled study (ClinicalTrials ID: NCT05414721) was conducted following the approval of the Faculty of Medicine's ethics committee at Yuzuncu Yil University (April 16, 2021; Decision no: 05-27). Writen consent from the patients was obtained.

Sixty patients, aged 65 years of age or older and undergoing elective surgery (other than thoracic surgery and neurosurgery), duration of the surgery longer than 1 hour and physical status I-III according to the American Society of Anesthesiologists (ASA) were included. Patients were excluded if they exhibited cardiorespiratory disease, uncontrolled diabetes mellitus, coagulopathy, signs of infections, and/or abnormality in preoperative liver and kidney functions; if they used nephrotoxic or hepatotoxic drugs, if they displayed major bleeding in surgery (> 1000 cc); and/or if they suffered from chronic alcoholism, active drug use, and/or withdrawal symptoms.

The cases were using the closed envelope method divided into two groups: the low-flow desflurane anesthesia group (Group D; n=30) and the normal-flow desflurane anesthesia group (Group N; n=30) (Figure 1).

Calibration and leakage tests of the anesthesia device (Primus, Drager) were performed before anesthesia. The leak test was also repeated manually for each patient. Alarm settings of the anesthesia device, inspired oxygen concentration (FiO_2) lower limit 30%, inspired CO_2 upper limit 3%, end-tidal carbon dioxide ($etCO_2$) upper limit 45 mmHg, disconnection alarm 5 cmH2O lower than peak pressure, occlusion alarm 30 cm H_2O, and expiratory gas volume were adjusted to be 500 mL below the desired minute volume (MV). Soda lime (Sorbo-lime, Berkim, Turkey) was used as a carbon dioxide absorbent. The color and dryness of the carbon dioxide absorber was controled frequently and changed at appropriate times. A disposable

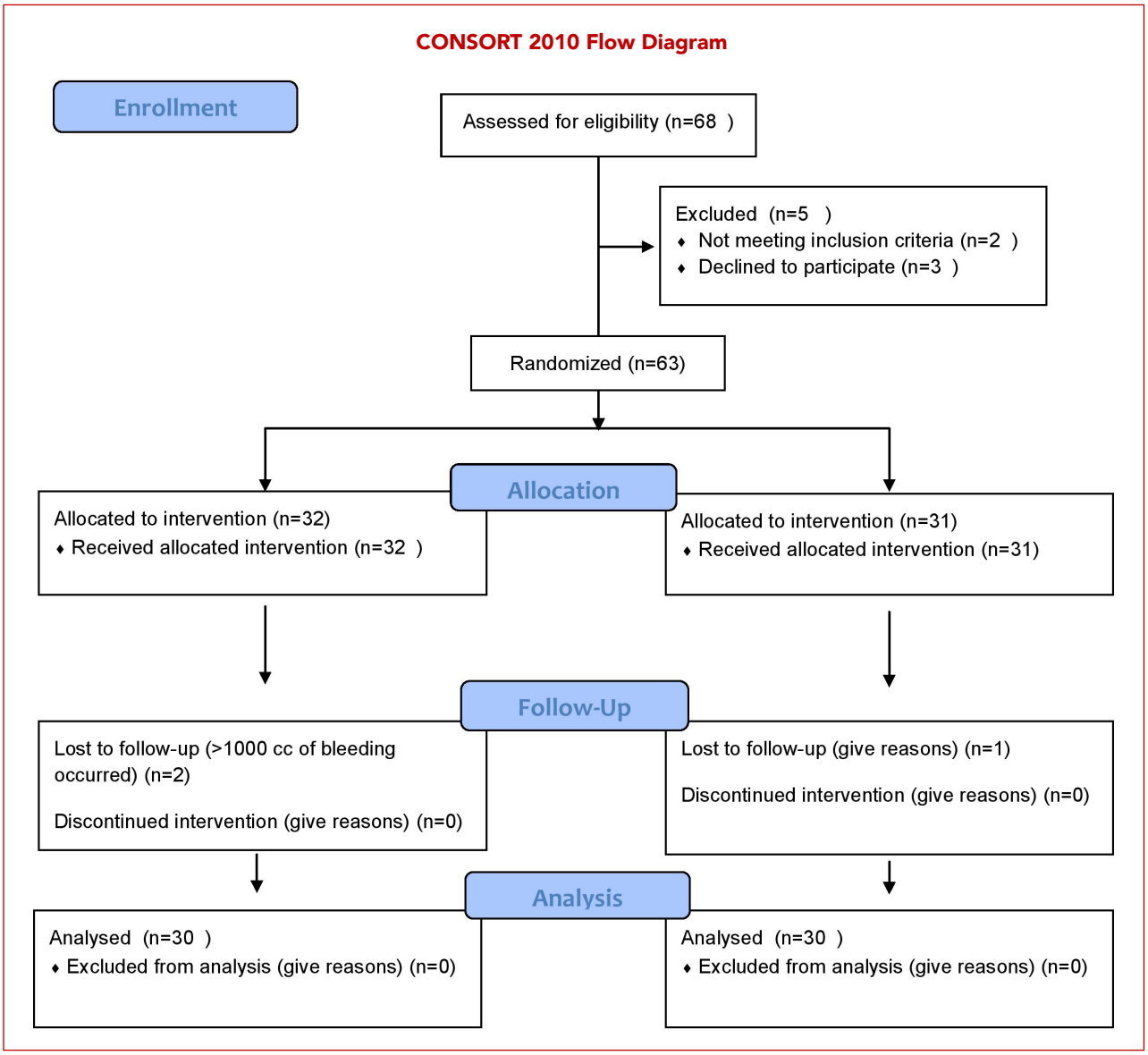

Figure 1. CONSORT 2010 Flow Diagram

bacterial filter and anesthesia circuit were used for every patient.

All patients underwent non-invasive blood pressure, heart rate (HR), electrocardiography (ECG) and peripheral oxygen saturation (SpO2) monitoring in the operating room. We also measured the depth of anesthesia in all patients using a bispectral index (BIS) monitor (A-2000 Aspect medical systems, USA). BIS values were kept between 40 and 60 throughout all operations.

Preoxygenation was performed with 100% O_2 for 3 minutes to all cases. After administering 0.03 mg/kg midazolam, 1.5 mcg/kg fentanyl, 2 mg/kg propofol, and 0.6 mg/kg rocuronium bromide,

endotracheal intubation was carried out. All patients were ventilated in volume-controlled, mechanical ventilation mode with 12 breaths/min, 6-8 mL/kg tidal volume, I:E ratio 1:2, and 5 cm H_2O positive end-expiratory pressure (PEEP). The $EtCO_2$ was maintained at 30-40 mmHg. Patients in both groups were given a mixture of 50% O_2 + 50% air + 6-7% desflurane at a 4 L/min fresh gas flow rate (FGF) until the minimum alveolar concentration (MAC) value achieved +1, at which time Group D's FGF was reduced to 0.5 L/min and FiO_2 was increased to 60% (60% O_2 + 40% air + 8% desflurane), and Group N's FGF was reduced to 2 L/min and the FiO_2 was reduced to 40% (40% O_2 + 60% air + 6% desflurane). In both groups, the MAC value was kept in the range of 0.9-1.1 by titrating the concentration of desflurane. During all surgeries, the patients' FiO_2, fractional inspirium carbon dioxide pressure ($FiCO_2$), $etCO_2$, fractional inspirium desflurane concentration, fractional expirium desflurane concentration, and MAC values were continuously monitored.

Because geriatric patients are more sensitive to hypoxia, it was not acceptable for the inspiratory O_2 concentration to fall below 35%. In this case, the amount of O_2 in the fresh gas increased by 10%. If the inspiratory O_2 ratio did not exceed 35% despite intervention, the low flow desflurane anesthesia was terminated and the operation continued with normal flow anesthesia in the patients who were excluded from the study. After intubation, a Foley catheters were used in all patients to monitor intraoperative urine flow.

The patients' blood pressure (non-invasive), SpO_2, and BIS values were monitored and recorded before and after induction, at the start of low flow desflurane anesthesia, and every 5 minutes thereafter during the operations.

The vaporizer was closed approximately 10–15 minutes before the end of the surgery. The FGF was increased to 6 L/min and ventilation was continued manually with 100% FiO_2. When the MAC value of desflurane reduced to 0.1-0.3 and the BIS value reached 80 in the anesthesia device, the neuromuscular blockade was reversed using atropine sulphate (0.015 mg kg−1) and neostigmine (0.03 mg kg−1). Patients who had spontaneous ventilation were extubated.

The patients were monitored for side effects such as medication allergies, nausea and vomiting, tremor and agitation, and complications such as hypoxia, hypercarbia, hypoventilation, and insufficient depth of anesthesia, both during the procedure and in the postoperative period.

The blood samples were collected before anesthesia induction, after surgery, and at the 24th hour, postoperatively by venepuncture. Samples were immediately centrifuged at 2000 rpm for 10 minutes, and the supernatant was used for biochemical analysis such as levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST), blood urea nitrogen (BUN) and creatinine. The levels of ALT, AST, BUN and creatinine were analyzed within 30 minutes after sampling. The cystatin C levels were measured in the serum. For serum separation, blood was centrifuged at 4000 rpm for 10 minutes. The obtained serum was transferred to Eppendorf tubes and stored at -80°C until biochemical analysis. The serums stored at -80°C were thawed at room temperature for analysis. Serum cystatin C was measured on the Abbott Architect C16000 fully automatic analyzer using the multiagent cystatin C kit (Milan, Italy).

Statistical analysis

Descriptive statistics are presented as mean, median, minimum, maximum, standard deviation, frequency and percentage values. The normality of the variables were compared with Kolmogorov-Smirnov test. The Mann-Whitney U test and independent-samples t-test were used in the analyses of the quantitative data in independent groups. The chi-squared test was used in the analysis

of the qualitative data in independent groups. When the conditions for the chi-squared test were not met, the Fisher's exact test was used. Statistical significance value was accepted as $p<0.05$ in all tests. Statistically significance level was considered as 5%. The Statistical Package for Social Science (SPSS) version 27.0 was used for data analysis.

RESULTS

Age, gender, ASA scores, smoking rates, and duration of anesthesia and surgery were found to be similar in both groups ($p > 0.05$) (Table 1-2).

Hemodynamic parameters, SpO_2 and BIS values

The HR, SpO_2 and BIS values measured at all times were similar in both groups ($p > 0.05$). In Group D, systolic blood pressure (SBP) values measured at the first minute after extubation ($p = 0.042$) were higher than Group N. In addition, mean blood pressure (MBP) values that measured at the 40th minute ($p = 0.038$) and at the first minute after extubation ($p = 0.035$) were significantly higher than group N. In Group N, diastolic blood pressure (DBP) values measured at the 5th minute after anesthesia

Table 1. Demographic characteristics in groups (mean ± SD).

		Group N		Group D		p
		Mean±SD/ n-%	Median	Mean ±SD/ n-%	Median	
Age (year)		69.6 ± 5.2	68.5	70.5 ± 5.9	68.0	0.731†
Gender	Female	11	36.7 %	9	30.0%	0.584‡
	Male	19	63.3 %	21	70.0%	
Height (cm)		169.5± 9.5	168.5	171.8±9.9	174.5	0.428†
Weight (kg)		73.0 ± 9.8	72.0	74.1±11.4	74.5	0.690†
BMI (kg/m^2)		25.4 ± 2.3	25.0	25.0±2.7	24.7	0.626†

Values are mean ± standard deviation and medians [interquartile range]. †Mann–Whitney U-test. ‡Chi-square test. †Independent sample t-test. SD: Standard deviation, BMI: Body Mass Index

Table 2. ASA scores, smoking rates, and the duration of anesthesia and surgery of patients.

		Group N				Group D				p
		Mean±SD/n-%			Medyan	Mean±SD /n-%			Medyan	
ASA Scores		2.2	±	0.6	2.0	2.1	±	0.5	2.0	0.349†
Smoking	(-)	21		70.0 %		22		73.3%		0.774‡
	(+)	9		30.0 %		8		26.7%		
Duration of Anesthesia (min)		113.8	±	13.0	110.0	116.0	±	16.6	115.0	0.868†
Duration of Surgey (min)		103.7	±	12.7	100.0	105.5	±	16.1	105.0	0.885†

Values are mean ± standard deviation and medians [interquartile range]. †Mann–Whitney U-test. ‡Chi-square test. SD: Standard deviation, min: Minute

induction (p = 0.035) were significantly higher than in Group D. The SBP, DBP and MBP values that measured at all other times were similar in both groups (p > 0.05).

Hepatic and renal functions

The serum ALT, AST, BUN, creatinine and cystatin C levels measured pre anesthetic period, at the end of surgery and at the postoperative 24th hour were like in both groups (p > 0.05). Intragroup comparisons, serum ALT, BUN, creatinine and cystatin C levels measured at different times were also similar (p > 0.05). There was a significant increase in serum AST values that measured at the postoperative 24th hour in both groups compared to before anesthesia induction period values (Group N, p = 0.049; Group D, p = 0.028) (Table 3) (Graph 1).

Table 3. Comparison of serum ALT, AST, BUN, creatinine and cystatin C values measured at the different times in groups.

	Group N		Group D		p
	Mean±SD	Median	Mean±SD	Median	
ALT (U/L)					
Pre-Induction	20.2±9.9	17.0	19.9±9.7	17.0	0.982†
Post Extubation	20.5±11.1	18.5	19.3±10.2	17.5	0.662†
Change seen compared to Pre-Induction period (p)	0.713 w		0.927 w		
Postoperative 24th hour	22.3±12.1	19.0	20.5±11.4	17.5	0.520†
Change seen compared to Pre-Induction period (p)	0.914 w		0.714 w		
AST (U/L)					
Pre-Induction	20.6±6.2	18.5	20.2±8.0	18.0	0.473†
Post Extubation	22.6±8.1	20.1	21.5±11.1	16.7	0.162†
Change seen compared to Pre-Induction period (p)	0.608 w		0.085 w		
Postoperative 24th hour	24.0±8.6	21.5	23.4±10.4	21.0	0.505†
Change seen compared to Pre-Induction period (p)	***0.049*** w		***0.028*** w		
BUN (mg/L)					
Pre-Induction	18.1±5.9	17.2	19.3±4.2	20.5	0.201†
Post Extubation	17.2±4.6	17.3	17.9±4.5	18.0	0.662†
Change seen compared to Pre-Induction period (p)	0.105 w		0.345 w		
Postoperative 24th hour	18.4±7.3	17.7	18.7±4.7	18.2	0.482†
Change seen compared to Pre-Induction period (p)	0.472 w		0.665 w		

Table 3. Comparison of serum ALT, AST, BUN, creatinine and cystatin C values measured at the different times in groups.

Creatinine (mg/dL)					
Pre-Induction	0.84±0.18	0.80	0.89±0.16	0.86	0.201 †
Post Extubation	0.82±0.23	0.76	0.84±0.21	0.81	0.539 †
Change seen compared to Pre-Induction period (p)	0.055 w		0.666 w		
Postoperative 24th hour	0.86±0.24	0.80	0.90±0.27	0.81	0.450 †
Change seen compared to Pre-Induction period (p)	0.113 w		0.604 w		
Serum Cystatin C (mg/L)					
Pre-Induction	1.12±0.24	1.11	1.18±0.17	1.17	0.160 †
Post Extubation	1.12±0.33	1.15	1.16±0.28	1.16	0.673 †
Change seen compared to Pre-Induction period (p)	0.171 w		0.593 w		
Postoperative 24th hour	1.18±0.35	1.10	1.22±0.28	1.14	0.359 †
Change seen compared to Pre-Induction period (p)	0.914 w		0.234 w		

Values are mean ± standard deviation and medians [interquartile range]. †Mann–Whitney U-test. ‡Chi-square test. SD: Standard deviation. wWilcoxon test. AST: Aspartate aminotransferase. ALT: Alanine aminotransferase. BUN: Blood urea nitrogen. (p): P Value

Side effects and complications

Nausea, vomiting, tremor, agitation and complication rates were alike in both groups (p> 0.05).

DISCUSSION

The study's major finding is that low flow and normal flow desflurane anesthesia did not cause a significant change in serum AST, ALT, BUN, creatinine, and cystatin C levels in geriatric patients. However, in the intragroup comparison, we found a statistically significant increase in AST values measured at the postoperative 24th hour compared to the AST values measured before anesthesia induction in both groups.

The low - flow anesthesia decrease loss of humidity and heat from the patients' airway during anesthesia. Maintains intraoperative body temperature in geriatric patients. It has been reported that it allows to minimize the incidence of complications due to hypothermia. In contrast to high-flow anesthesia in elderly patients with severe comorbidities, the low-flow anesthesia technique has been reported to make better early mobilization conditions. It has been stated that low-flow desflurane anesthesia is effective and safe in routine geriatric surgeries and minimally affects the liver functions (12,13).

The modern anesthesia devices used today have high patient safety standards and monitors that can analyze the anesthetic gas components continuously and in detail. In addition, the increase in knowledge about the pharmacodynamics and pharmacokinetics of inhalation anesthetics has facilitated the safer application of low-flow anesthesia (14). While

applying low-flow anesthesia, the airway pressure, volume, and concentrations of inspired and expired gases, FiO_2, and MAC value of the volatile agent should be monitored continuously. The alarm limits should be followed carefully (15, 16). We used the Drager Primus anesthesia device (Drager® Medizin technik, Lubeck, Germany), which allows for safely making these measurements.

Many studies have investigated how anesthesia methods applied with varied FGF affect hemodynamics. Elmacioglu et al. (17), in their study in which they applied desflurane anesthesia with 0.5, 1, and 2 L/min FGF, compared hemodynamic parameters and stated that there was not meaningful difference among the groups. Ceylan et al. (18) stated that perioperative MBP changes in both groups remained within normal limits in their study in which they applied low-flow desflurane and sevoflurane anesthesia. They reported that the perioperative MBP values remained within normal limits and were similar in patients who received low-flow desflurane and sevoflurane anesthesia. Xie et al. (19) reported that desflurane was associated with more stable hemodynamic results in their study in which they applied low-flow desflurane, sevoflurane, and enflurane anesthesia.

Systolic, diastolic, and mean blood pressures of the patients were closely monitored. There was not observed meaningful difference among the groups except the 5th and 40th minutes after anesthesia induction and the 1st minute after extubation. We observed that these differences in hemodynamic parameters did not exceed 20% of the preoperative measured values and remained within the clinically normal limits. The groups' HR and SpO_2 values as measured in all times throughout the surgery were found to be similar.

The serum levels of ALT and AST are mostly measured to assess liver damage. The half-lives of ALT and AST are approximately 47 and 17 hours, respectively. The AST and ALT levels measured within 24–48 hours after the anesthesia procedure provide information about changes in perioperative hepatic functions (20). Ebert and Arain (21) compared low-flow sevoflurane, low-flow desflurane, and intravenous propofol anesthesia, stated that there were significant increases in plasma AST levels in groups given volatile anesthetics. However, they reported that the values remained within the normal reference range. Bosna et al. (20) stated that low and high flow desflurane anesthesia had similar effects on serum ALT and AST levels measured in the postoperative period. Park et al. (22) compared postoperative AST values with preoperative AST levels in a study in which they compared high- and low-flow desflurane anesthesia. Postoperative AST levels increased significantly in both groups; however, this increase was clinically insignificant as the measured values remained within the normal reference range.

In this study, serum ALT and AST levels measured before anesthesia induction, after extubation, and at the postoperative 24th hour were detected to be similar in both groups. However, we observed a significant increase in both groups when the AST levels measured at the 24th postoperative hour were compared with the AST levels measured before inducing anesthesia. Despite the increase in AST levels, AST values remained within the normal reference range.

Serum creatinine, urea, BUN, creatinine clearance, and urine glucose and protein can be used to assess renal functions. In recent studies, serum cystatin C values were also used to evaluate renal functions, and are stated to be more sensitive. One study stated that, when glomerular filtration rate (GFR) fell below 80 mL/m^2 in intensive care patients, there was a 48% increase in the serum creatinine level and an 88% increase in the serum cystatin C level (23). When serum creatinine levels and serum cystatin C levels were compared in patients with acute renal failure, it was reported that serum cystatin C values increased in more patients

and were more correlated with GFR compared to creatinine (24-27). Eger et al. (28) compared 8-hour normal flow sevoflurane and desflurane anesthesia in their study. They measured BUN and creatinine levels at the 24th and 48th hours after anesthesia and compared them with the values before anesthesia. They reported that there was no significant increase in either group. Ebert and Arain (24) compared low-flow sevoflurane, low-flow desflurane anesthesia, and intravenous propofol anesthesia, and reported that postoperative creatinine levels did not change in any of the groups and BUN levels decreased significantly. Yildirim et al. (29) compared the urea and creatinine values measured before surgery, after extubation, and at the postoperative 24th and 48th hours in patients receiving low-flow sevoflurane, desflurane and isoflurane anesthesia. When they compared the urea and creatinine levels inter- and intra-group, they stated that they were similar in both groups. Duymaz et al. (30) compared the effects of low-flow sevoflurane and desflurane anesthesia on the kidneys in their study. They compared the serum urea, creatinine and cystatin C values measured at the end of the surgery and postoperative 24th hour with the preoperative values, they reported that there was no significant difference intra- and inter gruop. A Foley catheter was used in all patients to monitor intraoperative urine flow. Oliguria (< 0.5 ml/kg/hr) was not observed in any patient. Serum creatinine, BUN and cystatin C levels were found to be similar in both intra- and inter-group comparisons.

In low-flow anesthesia, BIS monitoring can be used to minimize the risk of anesthesia awareness. Akbas et al. (31) stated that they found BIS values to be similar in both groups in their study in which they compared low-flow and normal-flow desflurane anesthesia in morbidly obese cases. In this study, we also observed that the mean BIS values did not exceed 60 and BIS values were similar in both groups.

The superiorities of this study

The management of geriatric anesthesia is special in terms of anesthesia applications and difficult to manage. In a literature review, we could not find enough studies on low-flow anesthesia in geriatric patients. We believe that our study is one of the few studies investigating whether low-flow desflurane anesthesia affects liver and kidney functions in geriatric patients.

Limitations of the study

The heterogeneity of surgical operations and the small number of patients were considered as limitations of the study.

In conclusion, the present study showed that low-flow desflurane anesthesia did not adversely affect liver and kidney functions in geriatric patients. It has also shown that it provides sufficient depth of anesthesia in the intraoperative period, does not cause hemodynamic instability, and is as safe as normal-flow desflurane anesthesia.

REFERENCES

1. RJ Lofrumento. Overview of Aging and its Demographics, In: Frederick E. Sieber (ed). Geriatric Anesthtesia. 1st edition, McGraw-Hill Medical, USA 2006; pp 3-11.
2. Türkmen A, Turgut N. Geriatric Anesthesia. Turkish Journal of Geriatrics 2007; 10(1): 49-56. (in Turkish)
3. Baum JA, Aitkenhead AR. Low-flow anaesthesia. Anaesthesia, 1995; 50; 37-44. (PMID: 7485917)
4. Eger EI. II. Uptake and distribution, In: Miller RD (ed). Miller's Anesthesia. 6th edition, Philadelphia: Elsevier Churchill Living Stone; USA 2005, pp 131-53.
5. Baum JA. Low-flow anesthesia: theory, practice, technical preconditions, advantages, and foreign gas accumulation. Journal of Anesthesia 1999; 13(3): 166-74. (PMID: 14530937)
6. Baum J. Low flow anesthesia. Der Anaesthesist, 1994; 43(3): 194–210. (PMID: 8179170)
7. Young CJ, Apfelbaum JL. Inhalational anesthetics: desflurane and sevoflurane. J Clin Anesth. 1995; 7(7):564–77. (PMID: 8652167)

8. Kobayashi Y, Ochiai R, Takeda J, Sekiguchi H, Fukushima K. Serum and urinary inorganic fluoride concentrations after prolonged inhalation of sevoflurane in humans. Anesth Analg. 1992; 74(5):753–7. (PMID: 1567045)

9. Keller KA, Callan C, Prokocimer P, Delgado-Herrera L, Friedman MB, Hoffman GM, et al. Inhalation toxicity study of a haloalkene degradant of sevoflurane, Compound A (PIFE), in Sprague-Dawley rats. Anesthesiology. 1995; 83(6):1220–32. (PMID: 8533915)

10. Smiley RM, Ornstein E, Pantuck EJ, Pantuck CB, Matteo RS. Metabolism of desflurane and isoflurane to fluoride ion in surgical patients. Can J Anaesth. 1991; 38(8):965–8. (PMID: 1752017)

11. Soliman R, Yacoub A, Abdellatif M. Comparative effect of desflurane and sevoflurane on liver function tests of patients with impaired hepatic function undergoing cholecystectomy: A randomized clinical study. Indian Journal of Anaesthesia. 2020; 64(5):383-390. (PMID: 32724246)

12. Lebanidze NG, Peshkov TG. Induced hypothermia during low-flow anesthesia in elderly patients. Georgian medical news. 2006; (133):27-31. (PMID: 16705220)

13. Lebanidze NG, Peshkov TGRecovery after low-flow anesthesia in elderly patients. Georgian Medical News. 2006; (135):63-5. (PMID: 16905812)

14. Yıldız TS, Baykara N, Bozkurt N, et al. The effect of clonidine on tremor in low-flow desflurane anesthesia. Turk J Anaesthesiol Reanim, 2005; 33(1): 29-35. (in Turkish)

15. Toğal T, Ayas A, Demirbilek S, et al. Comparison of the fresh gas flows adjusted to the body weights in patients undergoing low flow anaesthesia either with isoflurane or desflurane. Turk J Anaesthesiol Reanim 2004; 32(2): 91-99. (in Turkish)

16. Brattwall M, Warrén-Stomberg M, Hesselvik F, Jakobsson J. Brief review: theory and practice of minimal fresh gas flow anesthesia. Can J Anaesth. 2012; 59(8): 785-97. (PMID: 22653840)

17. Elmacioglu MA, Goksu S, Kocoglu H, Oner U. Effects of flow rate on hemodynamic parameters and agent consumption in low-flow desflurane anesthesia: An open-label, prospective study in 90 patients. Curr Ther Res Clin Exp. 2005; 66(1): 4-12. (PMID: 24672107)

18. Ceylan A, Kırdemir P, Kabalak A, et al. Comparison of arterial carboxyhemoglobin, heamodynamic and recovery characteristics of low flow desflurane and sevoflurane anesthesia. Gulhane Med J. 2004; 46(4): 291-297. (in Turkish)

19. Xie G, Jiang H. Clinical study of desflurane on low flow anesthesia compared with sevoflurane and enflurane. Chinese medical journal 1997; 110(9): 707-710.(PMID: 9642331)

20. Bosna G, Ekinci O, Yılmaz A, et al. Comparison of the Effects of Low-flow and High-Flow Anesthesia on Hemodynamics, liver and Renal Function Tests. Haydarpaşa Numune Medical Journal 2015; 55 (1): 37-44. (in Turkish)

21. Ebert TJ, Arain SR. Renal responses to low flow desflurane, sevoflurane and propofol patients. Anesthesiology 2000; 93(6): 1401-1406.(PMID: 11149433)

22. Park SY, et al. The safety and efficacy of minimal-flow desflurane anesthesia during prolonged laparoscopic surgery. Korean journal of anesthesiology, 2012; 63(6): 498-503. (PMID: 23277809)

23. Le Bricon T, Leblanc I, Benlakehal M, et al. Evaluation of renal function in intensive care: plasma cystatin C vs. creatinine and derived glomerular filtration rate estimates. Clin Chem Lab Med. 2005; 43(9): 953-7. (PMID: 16176176.)

24. Villa P, Jiménez M, Soriano MC, Manzanares J, Casasnovas P. Serum cystatin C concentration as a marker of acute renal dysfunction in critically ill patients. Crit Care. 2005; 9(2): 139-43. (PMID: 15774046)

25. Randers E, Erlands EJ. Serum cystatin C as an endogenous marker of the renal function; a review. Clin Chem Lab Med 1999; 37(4): 389-95. (PMID: 10369108)

26. Laterza OF, Price CP, Scott MG. Cystatin C: an improved estimator of glomerular filtration rate? Clin Chem. 2002; 48(5): 699-707. (PMID: 11978596)

27. Grubb A. Diagnostic value of analysis of cystatin C and protein HC in biological fluids. Clin Nephrol. 1992; 38(11):20-7. (PMID: 1284235)

28. Eger EI 2nd, Koblin DD, Bowland T,et al. Nephrotoxicity of sevoflurane versus desflurane anesthesia in volunteers. Anesth Analg. 1997; 84(1):160-8. (PMID: 8989018.)

29. Yıldırım A, Göksu H, Toprak GÇ, et al. The safety and quality of low flow anaesthesia with isoflurane, sevoflurane and desflurane. Fırat Medical Journal 2006; 11(3): 170-174. (in Turkish)

30. Duymaz G, Yağar S, Özgök A. Comparison of effects of low-flow sevoflurane and low-flow desflurane anaesthesia on renal functions using cystatin C. Turk J Anaesthesiol Reanim. 2017; 45(2):93-97. (PMID: 28439441)

31. Akbas S, Ozkan AS. Comparison of effects of low-flow and normal-flow anesthesia on cerebral oxygenation and bispectral index in morbidly obese patients undergoing laparoscopic sleeve gastrectomy: a prospective, randomized clinical trial. Wideochir Inne Tech Maloinwazyjne. 2019; 14(1):19-26. (PMID: 30766625)

Turkish Journal of Geriatrics
DOI: 10.29400/tjgeri.2023.333
2023; 26(1):79–90

Arda IŞIKER[1]
Meryem ONAY[2]
Alpaslan AKCAN[3]
Ümit AKKEMİK[4]
Mehmet Sacit GÜLEÇ[2]

CORRESPONDANCE

[1]Meryem ONAY

Phone : +905063436101
e-mail : dr.meryemonay@hotmail.com

Received : Feb 11, 2023
Accepted : Mar 22, 2023

[1] Kırklareli Training and Research Hospital, Anesthesiology and Reanimaiton, Kırklareli, Turkey

[2] Eskisehir Osmangazi University Faculty of Medicine, Anesthesiology and Reanimation, Eskisehir, Turkey

[3] Eskisehir City Hospital, Anesthesiology and Reanimation, Eskisehir, Turkey

[4] Eskisehir City Hospital, Algology, Eskisehir, Turkey

RESEARCH

EVALUATING THE ROLE OF VERTEBRAL ANATOMY EXAMINATION BY ULTRASONOGRAPHY BEFORE ADMINISTERING SPINAL ANESTHESIA IN GERIATRIC PATIENTS: A PROSPECTIVE RANDOMIZED TRIAL

Abstract

Introduction: This study evaluated the importance of examining neuraxial anatomy by preprocedural ultrasonography to ensure effective spinal anesthesia administration, which can be technically challenging in geriatric patients owing to their physiological and pathological conditions.

Materials and Methods: Geriatric patients with an American Society of Anesthesiologists' physical classification of I–III undergoing elective surgery under spinal anesthesia were included. The patients were divided into two groups: the anatomical landmark-guided group and the ultrasound-assisted group. Spinal block application times, number of attempts and number of needle redirections were recorded.

Results: Among the studied patients, 29 and 30 patients were included in the anatomical landmark-guided group and the ultrasound-assisted group groups, respectively. There was no significant difference in the mean age of the patients in the ultrasound-assisted group (74.6 ± 7.41 years) and the anatomical landmark-guided group (75.6 ± 7.52 years). Assisted procedure time and total operative time were significantly shorter in the anatomical landmark-guided group than in the ultrasound-assisted group ($p<0.001$ and $p<0.05$, respectively); however, spinal application times and number of trials and needle redirections were significantly lower in the ultrasound-assisted group than in the anatomical landmark-guided group ($p<0.05$ and $p<0.05$, respectively).

Conclusion: Preprocedural ultrasonography before spinal anesthesia administration increases the first-attempt success rate and decreases the number of attempts and needle redirections in geriatric patients.

Keywords: Geriatrics; Anesthesia, Spinal; Ultrasonography

INTRODUCTION

With improvements in the health care system and patient care services worldwide, life expectancy has increased, and the proportion of elderly people is gradually increasing. According to the World Health Organization, patients over the age of 65 years are defined as geriatric patients (1, 2). Many geriatric patients have more than one chronic disease and at least one disease that requires surgery. Due to existing comorbidities, spinal anesthesia is usually preferred to protect the airway and cognitive functions, especially in lower extremity and lower abdominal surgeries, in geriatric patients. Studies have shown that the incidences of deep vein thrombosis and pulmonary embolism and the amount of postoperative bleeding are lower when spinal anesthesia is administered instead of general anesthesia (3, 4).

The failure rate of spinal anesthesia in geriatric patients ranges between 8% and 14%. High failure rates can be attributed to difficulty in administering spinal anesthesia due to physiological and pathological changes such as disk degeneration, decrease in bone mass, facet joint hypertrophy, spinal degeneration, spinal deformities, ossifications in spinal ligaments, and narrowing of the interspinous spaces (5). Therefore, because multiple attempts at administering spinal anesthesia are required in geriatric patients, complications such as postdural headache, neurological damage, spinal hematoma, and bloody cerebrospinal fluid (CSF) often occur (5, 6). Ultrasonography (USG) is a noninvasive, portable and radiation-free imaging modality that is prominently used in clinical practice. Its widespread use and easy accessibility make USG a suitable method for examining neuraxial blocks.

The aim of this study was to evaluate the effect of examining neuraxial anatomy by preprocedural USG examination on the effectiveness of spinal anesthesia in geriatric patients, which is challenging due to physiological and pathological conditions.

MATERIALS AND METHODS

This prospective and randomized controlled study was approved by the Ethical Committee of Osmangazi University (decision number: 2020/39). Patients were informed about the study protocol, and verbal and written informed consent was obtained. Patients with an ASA physical classification of I-III, who were 65 years and older and underwent an elective operation under spinal anesthesia were included in the study. Patients in whom spinal anesthesia was contraindicated, including those with histories of an allergy to local anesthesia, coagulation disorder, infection at the site of intervention, and lumbar surgery, and those who were unwilling to participate in the study were excluded. Patients in both groups were taken to the operating room and underwent standard monitoring (electrocardiogram, pulse oximetry, and noninvasive blood pressure). Intravenous cannulation was performed, and intravenous drip of normal saline was connected. The patients in both groups were placed in a sitting or lateral decubitus position, depending on the type of anesthesia desired.

Patients were divided into two groups based on the preprocedural examination method used: the anatomical landmark-guided group (ALGG) and the ultrasound-assisted group (UAG). Imaging was performed using a convex probe [Philips Medical Systems, Seattle, WA, United States] in both groups. The "Covidien Devon Skin Marker with a Regular Tip" was used for skin marking. A computer-generated table of random numbers and the closed envelope method were used for the randomization of patients to these two groups.

ALGG: After positioning the patient, the upper border of the iliac crest and the spinous processes of the vertebrae were palpated and marked. The location of the L4–L5 was estimated by extending the mark on the upper border of the iliac crest transversely to the vertebral column. One level above or below the spinous processes was palpated,

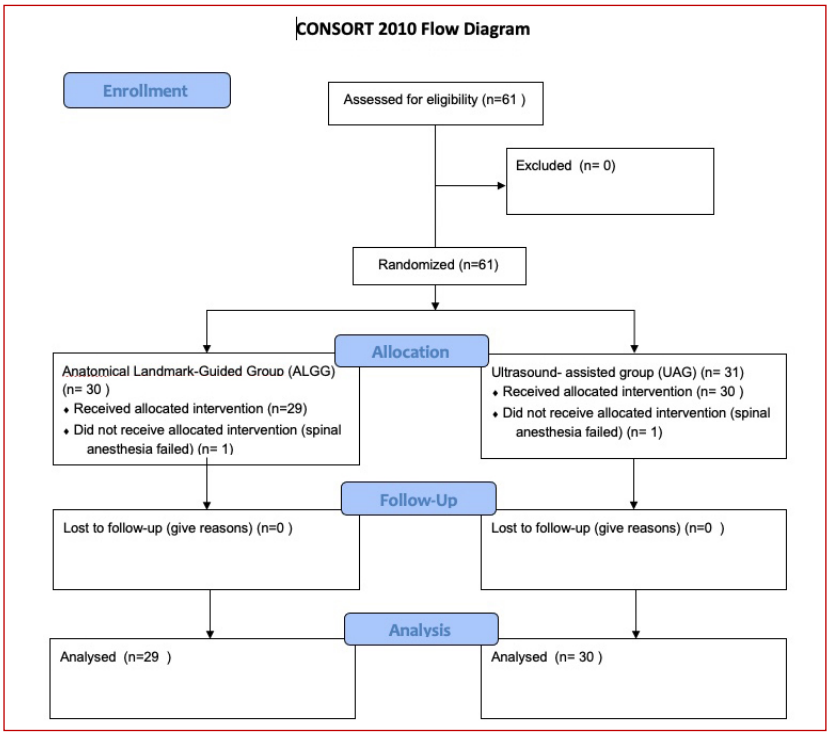

Figure 1. CONSORT flow diagram of the patients

and the most appropriate entry site, either L3-4 or L4-5, was determined by the practitioner. These points were marked straight over the transverse line and then connected to each other by a vertical line to determine the entry point. After ensuring sterile conditions, spinal anesthesia was administered to the patients. While maintaining the same position, the level of the spinal needle entry site was checked with the convex probe of the USG to determine the distance between the intrathecal space and the skin (Figure 1).

UAG: After positioning the patient, the convex probe of the USG was placed transversely over the sacrum and advanced to the cephalus, and the location of the L4-5 was detected. The image was moved to the center of the screen. The midpoint of the top edge and side edge of the probe were marked with a tissue pen. After determining the distance between the intrathecal space and the skin (ID), the upper mark was extended caudally, and the lateral mark was extended straight toward the vertebral column. The intersection point of the two lines was considered the entry point. The image was sharpened by tilting the probe. The entry angle of the spinal needle was determined based on the angle at which the image was the sharpest. After sterile conditions were ensured, spinal anesthesia was administered (Figure 2).

The patients in both groups were placed in the surgical position, and the study was terminated after the spinal block's success was evaluated. USG imaging and spinal blocking were performed by the same person (A.I). A maximum of three attempts at the same level and five attempts in total were allowed. Spinal anesthesia procedures that could not be performed after 5 attempts were recorded as failed spinal anesthesia. In the case of blood tap by the spinal needle, another interspinous interval was used. In a failed block, a paramedian approach and general anesthesia were applied before the surgery.

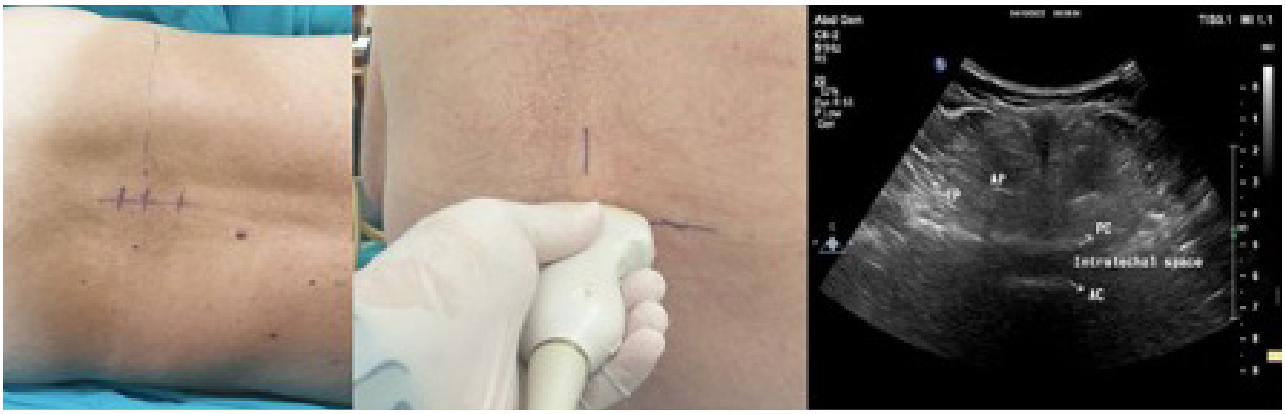

Figure 2. Anatomical marking, USG marking and USG image

Spinal block application time (SAT), the number of attempts, and the number of needle redirections were recorded for each patient. SAT was defined as the time lapsed between the entry of the needle into the skin until the appearance of clear CSF. The number of attempts was defined as the number of times the needle entered the skin. The number of needle redirections was defined as the number of times the needle was directed cephalad caudally or laterally under the skin without being removed. Anatomical marking time (AMT) was recorded for the ALGG, and ultrasound-assisted marking time (UMT) was recorded for the UAG.

Sample Size and Statistical Analysis

The research was based on the comparison of two independent groups, and an independent samples t test was used in the background for power analysis. With 80% power and a 5% type I error rate, the minimum sample size was calculated as 27 people per group and 54 people in total (5).

For statistical analysis of the findings obtained in the study, we used the Statistical Package for Social Sciences for Windows 24.0 program. Mean, standard deviation, median, minimum–maximum values, and interquartile range (IQR) were used to present descriptive statistics.

Pearson chi-square and Fisher's exact tests were used to compare 2 × 2 cells. The conformity of the variables to a normal distribution was analyzed by histograms and the Shapiro–Wilk test.

Independent samples t tests were used to evaluate normally distributed parametric independent variables. One-way ANOVA was used to analyze normally distributed independent variables in more than two groups. The Mann–Whitney U test was used to evaluate nonnormally distributed nonparametric independent variables. The Kruskal–Wallis analysis test was used to evaluate nonnormally distributed independent variables in more than two groups.

The relationship between variables was evaluated using the Pearson correlation test and Spearman correlation test for normally distributed parametric and nonnormally distributed nonparametric data, respectively. The statistical significance level was set at $p < 0.05$.

RESULTS

Of the 59 patients who were included in the study, 30 and 29 patients were added to the UAG and ALGG, respectively. However, spinal anesthesia could not be performed in one patient in each group. These patients were recorded as having failed spinal anesthesia (Figure 1).

Table 1. Demographic Data

		UAG (n:30)			ALGG (n:29)			p
		n		%	n		%	
*Sex	Female	9		30	11		37.9	0.52
	Male	21		70	18		62.1	
*BMI Group	Underweight	2		6.7	1		3.5	0.73
	Normal weight	11		36.7	13		44.8	
	Overweight	17		56.6	15		51.7	
		n	**Range Avg**	**IQR**	**n**	**Range Avg**	**IQR**	**p**
**Age (year)		30	28.60	12	29	31.45	10	0.52
**BMI (kg/m^2)		30	30.82	6	29	29.16	9	0.71
		n	**Mean**	**ss**	**n**	**Mean**	**ss**	**p**
***ID (cm)		30	5.17	0.57	29	5.17	0.62	0.37

*Chi Square Test **Mann-Whitney U Test, *** Independent-Samples T Test

UAG: Ultrasound-Assisted Group, ALGG: Anatomical Landmark-Guided Group BMI: Body Mass Index, ID: Intrathecal Distance, cm: centimeter, kg: kilogram

The study sample included geriatric patients with a mean age of 75.12 ± 0.96 years. The mean age of the patients in the UAG and in the ALGG was 74.6 ± 7.41 and 75.6 ± 7.52 years, respectively, with no statistical significance (Table 1). The ASA classes of the preoperative patients were I in 6.8% (n: 4), II in 42.4% (n: 25), and III in 50.8% (n: 30). There was no statistically significant difference between the groups in terms of surgical operation or level and position of spinal anesthesia (Table 2).

Assisted procedure time and total operative time were significantly shorter in the ALGG than in the UAG ($p < 0.001$ and $p < 0.05$, respectively); however, spinal application times were significantly shorter in the UAG than in the ALGG ($p < 0.05$). The number of attempts and the number of needle redirections were significantly lower in the UAG than in the ALGG ($p < 0.05$; Table 3).

The success rates of the spinal block at the first attempt were 93% (n = 28) and 69% (n = 20) in the UAG and the ALGG, respectively. The probability of success at the first attempt was also higher in the UAG than in the ALGG ($p < 0.05$; Table 2). Although the spinal block was effective, general anesthesia was induced after 35 minutes in one patient in the UAG due to patient noncompliance.

The correlation analysis of AMT data showed a moderately significant positive correlation between AMT and SAT ($r = 0.381$; $p < 0.05$) and a significant positive correlation between AMT and total time ($r=0.608$; $p<0.001$).

Table 2. Characteristics of Blocks

		UAG (n:30)		ALGG (n:29)		p
		n	%	n	%	
Type of surgery	Orthopedic Surgery	11	36.7	17	58.6	0.52
	Urological Surgery	17	56.6	7	24.1	
	Other Surgical Procedures	2	6.7	5	17.3	
Interspace level used for dural puncture	L 3-4	0	0.0	4	6.8	0.052
	L 4-5	30	100.0	25	93.2	
Patient Position	Sitting	15	50.0	14	48.3	0.89
	Lateral decubitus	15	50.0	15	51.7	
Blood Tap By The Spinal Needle	No	29	96.7	24	82.8	0.09
	Yes	1	3.3	5	17.2	
Electric-Like Feeling	No	27	90.0	27	91.5	0.51
	Yes	3	10.0	2	8.5	
Number of attempts	One	28	93.3	20	69.0	0.016[a]
	More than one	2	6.7	9	31.0	

[a] $p<0.05$

Table 3. Characteristics of the procedure

	UAG (n:30)			ALGG (n:29)			p
	n	Range Avg	IQR	n	Range Avg	IQR	
APT (sec)	30	42.82	11.70	29	16.74	9.45	<0.001[β]
SAT (sec)	30	24.70	11.68	29	35.48	25.05	0.016[a]
Total Time (sec)	30	34.48	30.23	29	25.36	30.70	0.041[a]
Number of Attempts	30	26.33	0	29	33.79	1	0.014[a]
Number of Needle Redirections	30	25.67	1	29	34.48	1	0.026[a]

Mann-Whitney U Test
[a] $p<0.05$, [β] $p<0.001$
APT: Assisted procedure time, SAT: Spinal block application time, sec: Second

The correlation analysis of UMT showed no significant correlation between UMT and age, body mass index (BMI), ID, SAT, number of attempts, and number of guidance ($p > 0.05$), while a significant positive correlation was found between UMT and total time ($r = 0.593$; $p = 0.001$).

The correlation analysis of ID and demographic characteristics of the patients revealed a moderately significant negative correlation between age and ID ($r = 0.288$; $p < 0.05$) and a moderately significant positive correlation between ID and height ($r = 0.270$; $p < 0.05$), weight ($r = 0.433$, $p < 0.001$), and BMI ($r = 0.301$; $p < 0.05$). There was no significant difference in intrathecal distances between BMI groups ($p > 0.05$).

After marking the spinal intervention site, the predicted anatomical level was checked with USG in ALGG ($n = 29$). The level was correctly predicted in 22 patients (75.9%), and incorrectly predicted in seven patients (24.1%).

No significant difference was found between the groups in terms of blood tap by the spinal needle and electric-like feeling during spinal anesthesia ($p > 0.05$). The incidence of blood tap by the spinal needle increased as the number of spinal anesthesia attempts increased ($p < 0.05$). Electric-like feelings increased as the number of attempts and number of redirections increased ($p < 0.05$).

DISCUSSION

This study focuses on proposing a suitable method for administering spinal anesthesia in geriatric patients, which can otherwise be challenging owing to their physiological and pathological conditions. The mean age of the studied patients was 75.12 ± 0.96 years, which was higher than the age range included in the previous studies that investigated the use of preprocedural USG for spinal anesthesia in geriatric patients. It was found that neuraxial ultrasonography improved spinal anesthesia effectiveness in geriatric patients. It was observed that using USG could decrease the procedure time and number of attempts and redirections required for spinal anesthesia and increase the total procedure time with increased assisted procedure time.

The number of geriatric patients seeking health care services is increasing worldwide, leading to anesthesiologists developing special care techniques for elderly patients. Such patients needing surgery require a higher level of perioperative care due to the tendency of multiple comorbid chronic diseases increasing the risk of postoperative complications (7). The most appropriate anesthetic technique for geriatric patients is still controversial. Although spinal anesthesia can reduce the risks of postoperative and intraoperative complications, shorten the hospital stay, and decrease the risk of in-hospital mortality, there was no significant difference in postdischarge and 30-day mortality when compared to those associated with general anesthesia (7-9). However, a shorter hospital stay and fewer complications have made spinal anesthesia more cost effective than general anesthesia (10).

Spinal anesthesia is the most commonly used regional anesthesia technique, particularly in orthopedic, urological, and obstetric anesthesia. The increasing number of attempts and redirections decreases patient satisfaction, and also increases the likelihood of spinal anesthesia-related complications such as low back pain, postspinal headache, neurological damage, and spinal and epidural hematoma (11, 12). Therefore, reducing the number of attempts during spinal anesthesia will be beneficial in preventing complications and increasing patient satisfaction.

Different approaches for administering spinal anesthesia in geriatric patients have always interested anesthesiologists due to the growing elderly population and the challenges faced by patients. Different approaches have been introduced to overcome this challenge. Rabinowitz

et al. reported that the paramedian approach was more successful than the median approach in continuous anesthesia in geriatric patients (13). Park et al. showed that neuraxial ultrasonography in the paramedian approach improved spinal anesthesia performance in elderly patients (14).

With advances in ultrasound technology and the widespread use of USG in anesthesia applications, the use of USG for neuraxial blocks has become popular among anesthesiologists. In this study, we compared the effectiveness of preprocedural USG examination of neuraxial anatomy and the classic anatomical marking method on the success of spinal anesthesia in geriatric patients scheduled for spinal anesthesia. Failure to reach the subarachnoid space within the recommended number of attempts and needle redirections was defined as failed spinal anesthesia. Spinal anesthesia could not be performed in one patient in the ALGG and in the UAG, and general anesthesia was initiated for these patients. There was no significant difference between the groups in terms of the incidence of failed spinal anesthesia.

In a meta-analysis, Jiang et al. evaluated the first-attempt success of preprocedural neuraxial ultrasonography in obstetric patients. It was reported that ultrasonography improved the first-attempt success rate only in patients who were difficult to palpate (15). As palpation is difficult due to the anatomy of geriatric patients, the first-attempt success rate of spinal anesthesia was significantly higher with USG, which was similar to the observed success rate with UAG in this study.

The preferred intervertebral spaces for spinal anesthesia are L4–5, L3–4, and L5–S1. Although the medulla spinalis usually ends at L1–2, Soleiman et al. showed that the medulla spinalis can extend to the L3 vertebra and is usually at a lower level in elderly patients (16). The level determined by anatomical landmarks may differ from the predicted level. In a study by Broadbent et al. that evaluated the ability of anesthesiologists to estimate the lumbar interval with magnetic resonance, the correct estimation was made in only 29% of cases. In 51% of cases, the marked range was one level above the correct range (17). Furness et al. showed that the use of USG and palpation in determining the intervertebral level provided 71% and 27% accuracy, respectively (18). Inadequate anatomical landmarks and the medulla spinalis terminating at a more caudal level with increasing age may lead to complications during intrathecal injections. In the present study, intrathecal injections were made outside the predicted range with ultrasonography in 24.1% of spinal anesthesia procedures that were performed with the guidance of anatomical landmarks. This relatively low rate may be related to the experience and expertise of our surgeons who administer spinal anesthesia. Although studies have shown that ultrasonography is more successful in detecting the correct range than anatomical landmarks, it should be noted that ultrasonography is not completely reliable. This suggests that USG-assisted spinal anesthesia may prevent possible complications by identifying a safe intervertebral space.

In studies wherein the vertebral axis was examined from the longitudinal and transverse axes, the mean time required to identify the vertebral axis with USG was 95 seconds in patients with abnormal spinal anatomy and 117 seconds in elderly patients in whom the paramedian approach was used (14,19). In the present study, only the transverse axis was evaluated in a mean time of 42 seconds. The first-attempt dural puncture success rate is similar to that in previous studies, and the total procedure time is shorter, suggesting that the use of USG in clinical practice for spinal anesthesia will gain prominence.

The effect of USG guidance in spinal anesthesia on the success of first-attempt punctures and the number of attempts and needle redirections is still controversial. In the study by Lim et al. that evaluated the use of USG before spinal anesthesia

procedures in the general population, USG did not significantly reduce the number of successful first-attempt punctures or the number of attempts and needle redirections (20). While Marvan et al. (21) obtained similar results, Srinivasan et al. (22) compared the classic anatomical landmark method with the paramedian approach from L5–S1 and the USG-assisted method and showed that USG did not reduce the number of attempts or needle redirections for successful puncture; however, the first-attempt success rate was higher in the USG-assisted method. Contrary to these results, the success rate of USG at the first attempt in elderly patients and in patients with lumbar scoliosis and a history of previous lumbar surgery was higher and the number of attempts and redirections was lower (19,23). This discrepancy among various studies may be due to differences in the patient groups that were studied and the practitioner's experience in the use of USG. Therefore, patients aged ≥ 65 years for whom such procedures were challenging in terms of positioning and physiopathological changes were selected in the present study. In the UAG, the rate of successful spinal anesthesia on the first attempt was higher than that in the ALGG, and the number of attempts and needle redirections was significantly lower.

In this study, the marking time for spinal anesthesia was significantly shorter in the ALGG than in the UAG. However, spinal anesthesia was performed in a significantly shorter time in the UAG. Although the longer marking time was partially compensated by a shorter duration of spinal anesthesia in the UAG, the total procedure time was significantly shorter in the ALGG than in the UAG. In a study by Chin et al. conducted on adults with a BMI>35 kg/m^2 and difficult anatomical landmarks such as poor spinous process palpation, moderate to severe lumbar scoliosis, or with a history of lumber spinal surgery, marking time and total time were longer in the USG, but spinal anesthesia was performed in a shorter time (24). Park et al. compared anatomical landmarks and USG-assisted paramedian spinal anesthesia in geriatric patients and found that while the marking and total times were longer, the time taken for spinal anesthesia was shorter in the USG-assisted method, which was similar to the result obtained in this study. In contrast, a previous study demonstrated that adults with an abnormal spinal anatomy exhibited similar total procedure times in both groups. Although administering spinal anesthesia can be complicated in older patients, lateral curvatures and rotational changes in the spine of patients with scoliosis and unclear or even absent anatomical landmarks in patients with a history of lumbar spinal surgery can make this procedure more complicated and require more time (14, 19).

In our study, it was observed that the duration of spinal analgesia and the number of attempts increased in the geriatric patients in the ALGG, whose anatomical marking time was prolonged. There was a moderate positive correlation among the anatomical marking time, the duration of spinal application, and the number of attempts. The importance of the quality of anatomical landmarks for the success of spinal anesthesia was previously emphasized by Filho et al. (6). Therefore, more effort and time were required for spinal anesthesia in patients with palpation difficulty, which was an expected result. In the UAG, no significant correlation was found among the marking time, time taken for spinal anesthesia, and number of attempts. Therefore, the results suggest that USG reduces the time taken and number of attempts for spinal anesthesia, especially in patients in whom anatomical landmarks are difficult to identify.

The use of USG during spinal anesthesia can guide the practitioner by showing the distance of the intrathecal space. Şahin et al. compared USG and classic anatomical landmark methods in obese and nonobese pregnant women and found that the intrathecal distance was significantly larger in the obese group than in the nonobese pregnant

women (25). In this study, no significant difference was found in the BMI groups in terms of intrathecal distance, but there was a moderate positive correlation between BMI and intrathecal space. The lack of a significant difference between BMI groups may be attributed to the lower average BMI values in this study than those included in the study by Şahin et al. Nevertheless, there was a moderate negative correlation between age and intrathecal space. The intrathecal space is closer to the skin in geriatric patients, suggesting that reviewing the needle entry site and direction before increasing the needle depth during unsuccessful spinal anesthesia attempts can prevent possible trauma.

In their study comparing the USG-assisted method with the anatomical landmark-guided paramedian method, Park et al. found no significant difference between the groups in terms of electric-like feeling, paresthesia, and blood tap by the spinal needle (14). Similarly, no significant difference was found between the groups with respect to electric-like feeling and blood tap by the spinal needle. However, in this study, the likelihood of developing radicular pain increased as the number of attempts and redirections increased, and encountering blood tap by the spinal needle increased as the number of attempts increased. Complications of spinal anesthesia are rare, and the sample size of the present study was insufficient to evaluate the rate of complications between the groups, which explains the lack of a significant difference between the groups. It is theoretically correct that USG can reduce the number of attempts and redirections, resulting in fewer complications of spinal anesthesia, such as low back pain, postspinal headache, neural damage, and spinal and epidural hematoma, which are risk factors for multiple interventions. However, further studies with large patient populations are needed to validate this.

There are a few limitations of this study. Due to the nature of the study, patients who were examined by USG imaging and administered spinal anesthesia could not be blinded. For practicality, the intrathecal distance was only transversely maintained with a convex USG probe. Longitudinal, paramedian or simultaneous spinal anesthesia was not preferred. In the UAG, the angle of probe insertion into the skin during imaging was based on the anesthesiologist's memory and not on measurements.

In conclusion, our results show that neuraxial USG facilitates spinal anesthesia application in elderly patients. Compared with preprocedural anatomical landmarks, USG has a high first-attempt success rate and requires fewer attempts and needle redirections. The reduced number of attempts and needle redirections is expected to lead to a reduction in the complications of this procedure. Randomized controlled trials with larger patient groups are required to validate these results.

Conflicts of interest

The authors certify that there are no conflicts of interest with any financial organization regarding the material discussed in the manuscript.

Acknowledgment

None to declare

Authors' contributions

All authors have read and approved the final version of the manuscript.

REFERENCES:

1. Bose R. Physiology and Anesthesia for Elderly Patients. In: Ehrenfeld JM, Urman RD, Segal S (Eds). Anesthesia Student Survival Guide: A Case-Based Approach. Springer New York Dordrecht Heidelberg London, 2010. p. 369-80.
2. Organization WH. Psychogeriatrics: report of a WHO scientific group [meeting held in Geneva from 19 to 23 October 1970]. [Internet] Available from: https://apps.who.int/iris/handle/10665/40993/ global_health.pdf. Accessed:25.10.2022.

3. Memtsoudis SG, Sun X, Chiu Y-L, et al. Perioperative Comparative Effectiveness of Anesthetic Technique in Orthopedic Patients. Anesthesiology. 2013;118(5):1046-58. DOI: 10.1097/ALN.0b013e318286061d

4. Rodgers A, Walker N, Schug S, et al. Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: results from overview of randomised trials. Bmj. 2000;321(7275):1493. DOI: 10.1136/bmj.321.7275.1493

5. Narkhede HH, Kane D, Parekh V, Hemantkumar I. A cohort study of anatomical landmark-guided midline versus pre-procedure ultrasound-guided midline technique of spinal anesthesia in elderly patients undergoing orthopedic surgery. Journal of Anaesthesiology, Clinical Pharmacology. 2019;35(4):522. DOI: 10.4103/joacp.JOACP_396_17

6. de Oliveira Filho G, Gomes H, Da Fonseca M, Hoffman J, Pederneiras S, Garcia J. Predictors of successful neuraxial block: a prospective study. European Journal of Anaesthesiology (EJA). 2002;19(6):447-51. DOI: 10.1017/s0265021502000716

7. Lim B-G, Lee I-O. Anesthetic management of geriatric patients. Korean journal of anesthesiology. 2020;73(1),8-29. DOI: 10.4097/kja.19391

8. Chen DX, Yang L, Ding L, Li SY, Qi YN, Li Q. Perioperative outcomes in geriatric patients undergoing hip fracture surgery with different anesthesia techniques: A systematic review and meta-analysis. Medicine. 2019;98(49). DOI: 10.1097/MD.0000000000018220

9. Helwani MA, Avidan MS, Abdallah AB, et al. Effects of regional versus general anesthesia on outcomes after total hip arthroplasty: a retrospective propensity-matched cohort study. JBJS. 2015;97(3):186-93. DOI: 10.2106/JBJS.N.00612

10. Memtsoudis SG, Poeran J, Zubizarreta N, et al. Do hospitals performing frequent neuraxial anesthesia for hip and knee replacements have better outcomes? Anesthesiology: The Journal of the American Society of Anesthesiologists. 2018;129(3):428-39. DOI: 10.1097/ALN.0000000000002299

11. Charuluxananan S, Sriprajittichai P, Sirichotvithyakorn P, Rodanant O, Kyokong O. Factors related to patient satisfaction regarding spinal anesthesia. Journal of the Medical Association of Thailand= Chotmaihet thangphaet. 2003;86:S338-43.

12. Rhee WJ, Chung CJ, Lim YH, Lee KH, Lee SC. Factors in patient dissatisfaction and refusal regarding spinal anesthesia. Korean journal of anesthesiology. 2010;59(4):260-264. DOI: 10.4097/kjae.2010.59.4.260

13. Rabinowitz A, Bourdet B, Minville V, et al. The paramedian technique: a superior initial approach to continuous spinal anesthesia in the elderly. Anesthesia & Analgesia. 2007;105(6):1855-7. DOI: 10.1213/01.ane.0000287655.95619.fa

14. Park S-K, Yoo S, Kim WH, Lim Y-J, Bahk J-H, Kim J-T. Ultrasound-Assisted vs. landmark-guided paramedian spinal anaesthesia in the elderly: a randomised controlled trial. European Journal of Anaesthesiology (EJA). 2019;36(10):763-71. DOI: 10.1097/EJA.0000000000001029

15. Jiang L, Zhang F, Wei N, Lv J, Chen W, Dai Z. Could preprocedural ultrasound increase the first-pass success rate of neuraxial anesthesia in obstetrics? A systematic review and meta-analysis of randomized controlled trials. Journal of Anesthesia. 2020: 34(3), 434-444. DOI: 10.1007/s00540-020-02750-6

16. Soleiman J, Demaerel P, Rocher S, Maes F, Marchal G. Magnetic resonance imaging study of the level of termination of the conus medullaris and the thecal sac: influence of age and gender. Spine. 2005;30(16):1875-80. DOI: 10.1097/01.brs.0000174116.74775.2e

17. Broadbent C, Maxwell W, Ferrie R, Wilson D, Gawne-Cain M, Russell R. Ability of anaesthetists to identify a marked lumbar interspace. Anaesthesia. 2000;55(11):1122-6. DOI: 10.1046/j.1365-2044.2000.01547-4.x

18. Furness G, Reilly M, Kuchi S. An evaluation of ultrasound imaging for identificationof lumbar intervertebral level. Anaesthesia. 2002;57(3):277-80. DOI: 10.1046/j.1365-2044.2002.2403_4.x

19. Park S-K, Bae J, Yoo S, et al. Ultrasound-Assisted Versus Landmark-Guided Spinal Anesthesia in Patients with Abnormal Spinal Anatomy: A Randomized Controlled Trial. Anesthesia & Analgesia. 2020;130(3):787-95. DOI: 10.1213/ANE.0000000000004600

20. Lim Y, Choo C, Tan K. A randomised controlled trial of ultrasound-assisted spinal anaesthesia. Anaesthesia and intensive care. 2014;42(2):191-8. DOI: 10.1177/0310057X1404200205

21. Rizk MS, Zeeni CA, Bouez JN, et al. Preprocedural ultrasound versus landmark techniques for spinal anesthesia performed by novice residents in elderly: a randomized controlled trial. BMC anesthesiology. 2019;19(1):208. DOI: 10.1186/s12871-019-0882-8

22. Srinivasan KK, Leo A-M, Iohom G, Loughnane F, Lee PJ. Pre-procedure ultrasound-guided paramedian spinal anaesthesia at L5–S1: Is this better than landmark-guided midline approach? A randomised controlled trial. Indian journal of anaesthesia. 2018;62(1):53. DOI: 10.4103/ija.IJA_448_17

23. Geng J, Chen X, Wang X, Guo X, Li M. Ultrasound imaging increases first-attempt success rate of neuraxial block in elderly patients. Zhonghua yi xue za zhi. 2016;96(43):3459-63. DOI: 10.3760/cma.j.issn.0376-2491.2016.43.004

24. Chin KJ, Perlas A, Chan V, Brown-Shreves D, Koshkin A, Vaishnav V. Ultrasound imaging facilitates spinal anesthesia in adults with difficult surface anatomic landmarks. Anesthesiology: The Journal of the American Society of Anesthesiologists. 2011;115(1):94-101. DOI: 10.1097/ALN.0b013e31821a8ad4

25. Sahin T, Balaban O, Sahin L, Solak M, Toker K. A randomized controlled trial of preinsertion ultrasound guidance for spinal anaesthesia in pregnancy: outcomes among obese and lean parturients. Journal of anesthesia. 2014;28(3):413-9. DOI: 10.1007/s00540-013-1726-1

RESEARCH

RELATIONSHIP BETWEEN THE AMOUNT OF AMALGAM FILLING AND COGNITION IN OLDER ADULTS

Turkish Journal of Geriatrics
DOI: 10.29400/tjgeri.2023.334
2023; 26(1):91–99

Savaş ÖZARSLANTÜRK[1]
Mehmet İlkin NAHARCI[2]
Numan AYDIN[3]
Serpil KARAOĞLANOĞLU[3]
Elif Aybala OKTAY[3]

CORRESPONDANCE

[1]Savaş ÖZARSLANTÜRK

Phone : +905057050920
e-mail : savasozarslanturk@yahoo.com

Received : Sep 28, 2022
Accepted : Feb 07, 2023

[1] University of Health Sciences, Gulhane Faculty of Dentistry, Department of Dentomaxillofacial Radiology, Ankara, Turkey

[2] University of Health Sciences, Gulhane Faculty of Medicine & Gulhane Training and Research Hospital, Division of Geriatrics, Ankara, Turkey

[3] University of Health Sciences, Gulhane Faculty of Dentistry, Department of Restorative Dental Treatment, Ankara, Turkey

Abstract

Introduction: This study aimed to evaluate the relationship between dental amalgam filling and cognition in older adults.

Materials and Methods: A total of 169 patients aged 65 years and above were recruited from a geriatric outpatient clinic. Their socio-demographic and chronic disease data were recorded. All patients underwent oral examinations. Amalgam filling index scores were calculated for individuals with amalgam fillings. The participants were divided into a study group [amalgam (+)] and a control group [amalgam (–)] based on their amalgam-filling statuses. For sub-analysis, the amalgam-filled group was categorised according to high (≥4.191) and low (<4.191) mean index scores. Standardised mini-mental test, clock drawing test and Lawton–Brody instrumental activities of daily living scale were conducted for all patients.

Results: About 46.2% (n=78) of participants were female, mean age was 69.6 ± 6.3 years and 53.7% (n=89) had amalgam fillings. There was no significant difference in the standardised mini-mental test, clock drawing test and Lawton–Brody instrumental activities of daily living scale scores between the study and control groups (all p>0.05), or in all test scores between participants with high and low amalgam scores in the group with amalgam fillings.

Conclusions: This study showed that dental amalgam fillings were not associated with cognitive decline in older adults.

Keywords: Aged; Cognitive Dysfunction; Dental Amalgam.

INTRODUCTION

Dental amalgam has been used in dentistry for 150 years because of its low cost, ease of application, durability and bacteriostatic effects (1). It is formed by combining approximately 50% mercury as a liquid with a mixture of powdered silver, copper, zinc and tin (2). The popularity of amalgam has decreased in recent years, especially because of the harmful effects of mercury on health, environmental pollution and aesthetic concerns (3). Mercury exposure from amalgam depends on both the number of amalgam fillings present and the total surface area of the exposed amalgam (4). Mercury vapour released from amalgam fillings increases with oral functions, such as chewing, taking hot drinks and brushing (5). Most inhaled mercury vapour passes into the circulatory system and is excreted from the body, but some accumulates in the brain, kidneys and other body tissues (6). The blood mercury level in individuals with amalgam fillings is approximately 3–5 times higher in urine and 2–12 times higher in body tissues than in individuals without amalgam fillings (7). The half-life of mercury in the brain can also extend up to 18 years (8).

Because of its lipophilic property, mercury crosses the blood-brain barrier into the brain and central nervous system. This chemical element can cause demyelination, autonomic dysfunction, sensory nerve conduction delay, abnormal neuronal migration and abnormal cell division in the central nervous system (6). Some studies have examined the relationship between Alzheimer's disease (AD), a neurodegenerative disorder and the most common cause of dementia, and mercury (9). Although a cross-sectional study showed that amalgam filling increases the risk of AD in older females, there is also a contrary finding in another report showing no relationship (10). Blood mercury levels were also found to be high in Parkinson's disease, another neurodegenerative disease (11).

However, studies on the effects of mercury on the cognitive state of healthy individuals are limited. Investigating this relationship in healthy individuals with amalgam fillings before possible mercury-induced cognitive impairment may add value to the current literature. This study aimed to examine the relationship between dental amalgam filling and cognitive status in cognitively intact older adults.

MATERIALS AND METHODS

Subjects who visited the geriatric outpatient clinic between February 2020 and June 2021 were prospectively included in this study. The inclusion criteria were as follows: age ≥ 65 years, must be literate, absence of dementia, absence of any psychiatric disease and volunteering for the study. The exclusion criteria were visual and/or hearing impairment and total tooth deficiency. In this study performed in accordance with the principles of the Declaration of Helsinki, all patients provided written informed consent and the local ethics committee approved the study (2019/99).

Data collection

Age, gender, educational status, current smoking and alcohol use and existing chronic diseases (cardiovascular diseases, diabetes, hypertension, chronic obstructive pulmonary disease, liver diseases, kidney diseases, stomach diseases, cancer and AIDS) were recorded using case data follow-up forms. The individual's burden of disease was measured using the modified Charlson comorbidity index (MCCI), which assigned a weighted score to each of 19 comorbid conditions based on the relative risk of 1-year mortality (12).

Amalgam-filling score evaluation

Each tooth containing an amalgam restoration was evaluated according to the location and number of filling surfaces, with reference to the "location index scores" section in the "criteria for

dental amalgam index scores" table in Saxe et al. (9). The location index score was calculated by the same dentist who performed the oral examinations. The location and surface number of amalgam fillings in existing amalgam-filled teeth were included in the evaluation. The occlusal surfaces scored higher than the surfaces other than the occlusal surface. The occlusal amalgam restorations in molars scored higher than those in premolars because the molars had larger surface areas.

Subjects (n = 80; 47%) who did not have amalgam fillings in their teeth, who declared that they had not had an amalgam filling in the last 10 years or who had an amalgam-filled tooth extracted (n = 80; 47%) were included in the control group. All participants were divided into a study group, amalgam (+) and a control group, amalgam (–), based on their amalgam-filling statuses. For further analysis, the amalgam-filled group was divided into two categories after the mean amalgam score was determined (high: ≥ 4.191; low < 4.191).

Cognitive and functional assessments

The standardised mini-mental test (SMMT), clock drawing test (CDT) and Lawton–Brody instrumental activities of daily living (IADL) scale scores were administered to both groups by the same geriatrician.

SMMT is a universal, short, useful and standardised neuropsychological tool for measuring cognitive domains, including orientation, registration, attention and calculation, recall and language (13). Total scores on the SMMT range from 0 to 30, with lower scores indicating worse cognitive statuses.

CDT is a simple and fast applicable test for evaluating the cognitive abilities of comprehension, visual memory, executive function, planning, numerical sequencing, knowledge and abstract thinking (14, 15). Its reliability in detecting the early stages of cognitive dysfunction is high (15). In scoring out of six points, a low score indicates a poor cognitive status (16).

Lawton–Brody IADL assesses independent daily living skills in eight areas: using the phone, shopping, preparing meals, cleaning the house, washing laundry, travelling, accepting responsibility for taking medication and coping with financial affairs (17). Total IADL scores range from 0 to 8, with a lower score indicating a functional disability (17).

Statistics

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) 22.0 (IBM SPSS Inc., Chicago, IL) software. Results were presented as absolute numbers, percentages and mean ± standard deviation, as appropriate. Categorical variables between amalgam (+) and amalgam (-) groups were compared using chi-square tests. After testing for normality of distribution of continuous variables via the Kolmogorov-Smirnov test, Student's t-test and Mann–Whitney U-test were used for normally distributed and non-normally distributed data, respectively. To make a comparison based on the amount of amalgam filling within the amalgam (+) group, an amalgam filling average ($\bar{x}$ = 4.191) was taken and this value was accepted as "normal". Then, the amalgam-filled group was divided into two categories; "low" for those below the amalgam-filling average and "high" for those equal to or above the average.

RESULTS

A total of 169 participants were included in the study (mean age 69.6 ± 6.3 years; females 53.8%; mean MCCI score 4.3 ± 1.6). About 52.7% (n = 89) of the sample had amalgam fillings in their teeth (Table 1). Since we did not have enough cases aged 85 and over, we formed two age groups, 65-74 and 75 and over. When we compared these two age groups according to whether or not they

Table 1. Comparison of cognition and function according to amalgam-filling statuses.

Tests	Amalgam (+) (n = 89)	Amalgam (-) (n = 80)	T/U	p
Age (years)	69.2 ± 5.9	70.0 ± 6.7	-0.885	0.377
65-74 years	76 (53.5)	66 (46.5)	0.263	0.608
+75 years	13 (48.1)	14 (51.9)		
Gender (female)	42 (47.2)	49 (61.3)	3.351	0.067
Current smokers, n (%)	7 (7.9)	10 (12.5)	1.000	0.317
Current alcohol users, n (%)	5 (5.6)	5 (5.3)	0.030	0.862
MCCI, mean ± SD	4.2 ± 1.6	4.2 ± 1.6	-0.924	0.357
SMMT	26.7 ± 3.5	27.1 ± 3.0	3326.50	0.456
CDT	4.4 ± 1.7	4.5 ± 1.5	-0.28	0.779
IADLs	7.33 ± 1.45	7.39 ± 1.35	3549	0.966

*MCCI: Modified Charlson comorbidity index, CDT, clock drawing test; SMMT, standardised mini-mental test; IADLs, Lawton–Brody instrumental activities of daily living scale. Values given in bold indicate statistically significant results ($p < 0.05$).

Table 2. Comparison of cognition and function according to amalgam-filling statuses at different education levels.

Education	Tests	Amalgam (+)	Amalgam (-)	T/U	p
Illiterate		N = 8	N = 5		
	SMMT	24.8 ± 3.0	25.40 ± 1.34	18.00	0.833
	CDT	2.13 ± 1.81	2.60 ± 1.34	16.00	0.622
	IADLs	6.25 ± 2.61	6.60 ± 1.14	17.50	0.724
Primary/Middle school		n = 39	n = 49		
	SMMT	25.7 ± 4.5	26.9 ± 2.3	843	0.338
	CDT	4.15 ± 1.83	4.55 ± 1.37	-1.17	0.247
	IADLs	7.13 ± 1.66	7.53 ± 0.79	903	0.596
High school		n = 24	n = 21		
	SMMT	27.54 ± 2.0	27.3 ± 4.6	192.50	0.167
	CDT	4.7 ± 1.2	4.5 ± 1.7	0.33	0.743
	IADLs	7.5 ± 0.7	7.1 ± 2.2	251.50	0.981
University		N = 18	N = 5		
	SMMT	28.6 ± 1.0	29.4 ± 0.9	-1.62	0.120
	CDT	5.61 ± 0.7	5.4 ± 0.9	0.57	0.578
	IADLs	7.9 ± 0.4	8.0 ± 0.0	42.50	0.857

*CDT, clock drawing test; SMMT, standardised mini-mental test; IADLs, Lawton–Brody instrumental activities of daily living scale. Values given in bold indicate statistically significant results ($p < 0.05$).

had amalgam fillings, there was no significant difference. (p = 0.608) (Table 1). No difference was found between the amalgam (+) and amalgam (–) groups in terms of demographic and clinical data. The SMMT, CDT and Lawton–Brody IADL scores did not differ significantly between the groups (p = 0.779, p = 0.456 and p = 0.966, respectively) (Table 1).

When all participants were grouped according to their educational levels and compared according to their amalgam-filling statuses at an equal educational level, SMMT, CDT and Lawton–Brody IADL scores were similar (all p > 0.05) (Table 2).

When the effect of gender status on the results was evaluated, there was no significant difference between SMMT, CDT and IADL scores for female (p = 0.403, p = 0.653, p = 0.866, respectively) and male participants (p = 0.785, p = 0.227, p = 0.551, respectively) according to whether or not they had amalgam fillings (Table 3).

Tablo 3. Comparison of cognition and function according to gender.

Gender	Tests	Group	n	$\bar{X}$	S	Sd	T/U	P
Female	SMMT	Amalgam (+)	47	26.04	3.75	76	647.50	.403
		Amalgam (-)	31	26.48	3.64			
	CDT	Amalgam (+)	47	3.81	1.93	76	-.45	.653
		Amalgam (-)	31	4.00	1.67			
	IADLs	Amalgam (+)	47	7.00	1.79	76	713.50	.866
		Amalgam (-)	31	7.13	1.41			
Male	SMMT	Amalgam (+)	42	27.48	3.11	89	995.50	.785
		Amalgam (-)	49	27.43	2.57			
	CDT	Amalgam (+)	42	5.07	1.20	89	885.50	.227
		Amalgam (-)	49	4.78	1.31			
	IADLs	Amalgam (+)	42	7.69	.81	89	977.00	.551
		Amalgam (-)	49	7.55	1.29			

CDT, clock drawing test; SMMT, standardized mini-mental test; IADLs, Lawton–Brody instrumental activities of daily living scale. Values given in bold indicate statistically significant results (p < 0.05).

Table 4. Comparison of cognition and function according to amalgam-filling scores among patients with amalgam-fillings.

Tests	Low score (n = 57)	High score (n = 32)	T/U	p
SMMT	27.6 ± 2.0	25.1 ± 4.9	570	0.920
CDT	6.3 ± 4.1	5.9 ± 4.1	861.50	0.619
IADLs	4.8 ± 1.5	3.7 ± 1.9	2.91	0.632

*CDT, clock drawing test; SMMT, standardised mini-mental test; IADLs, Lawton–Brody instrumental activities of daily living scale. Values given in bold indicate statistically significant results ($p < 0.05$).

When we compared the amalgam (+) cases according to their amalgam-filling scores, no significant differences were found between those with "low" amalgam-filling scores and those with "high" amalgam-filling scores for the SMMT, CDT and Lawton–Brody IADL scores ($p = 0.920$, $p = 0.619$ and $p = 0.632$, respectively) (Table 4).

DISCUSSION

This study, which focused on the neurotoxic effects of mercury-containing amalgam fillings, found that the presence of amalgam fillings in the teeth of older adults was not associated with cognitive or functional changes. Gender status and educational level did not play a role in these relationships. In addition, higher scores in amalgam-filled patients were not associated with cognitive or functional decline. This finding is original and deserves attention in several ways. Our findings provide additional insights into understanding cognitive functions in older adults with amalgam fillings, emphasising that the need for an amalgam-filling replacement in this population may be unnecessary except it is in a particularly poor condition.

In recent years, there has been growing interest in investigating the effect of amalgam filling on functionality. Our study shows that amalgam restorations are not associated with cognitive and physical functions in older adults. Consistent with our results, no significant side effects of amalgam restorations were found in a study on the effects of amalgam on mental health involving 129 individuals aged ≥ 75 years (18). In another study involving 587 participants, researchers analysed the relationships between the number of surfaces restored with dental amalgams and indices predicting somatic health, mental health and memory functions. They found no adverse effects of dental amalgam on physical or mental health (19). However, a recent study conversely reported that amalgam fillings caused a significant increase in serum mercury and plasma microRNA (124–3p, 125–5p and 127–3p) levels. The increase in microRNA levels, a possible biomarker of different neurodegenerative diseases (AD and Parkinson's), might be due to amalgam filling–induced mercury exposure, which increases susceptibility to neurological diseases (20). Likewise, another study described the neurobehavioral effects of exposure to low levels of mercury from dental amalgams (21). More research is needed to determine the effect of amalgam on neurocognitive functions.

In this study, we focused on an almost unstudied clinical exploration: the potential effect of amalgam

load on cognitive function in cognitively intact older adults. Our findings indicate that dental amalgam filling or high-filling scores may not be associated with decreased cognitive functions in older adults. The lack of changes in cognitive functions accompanying the stability of activities of daily living also shows that our findings are consistent. Given the aforementioned cognitive stability, our results might be useful in future studies to develop strategies for amalgam-filling replacements to improve the quality of life in older adults.

Many studies in different age groups have shown that amalgam restorations do not cause cognitive dysfunction or that no significant relationships exist between cognitive impairments and amalgam restorations (11,22). However, methodological errors have drawn attention in most studies (8). For example, in a study by Björkman et al. (19), people who were completely edentulous or who had other dental treatments were classified as amalgam free. What seems to have been overlooked is that amalgam-free individuals (toothless or with crowns and bridges) may have had amalgam fillings in the past, with correspondingly longer exposures than individuals with amalgam fillings. Likewise, methodological errors were made by Ahlqwist et al. (23). They did not use a truly amalgam-free group as a control, because that group's past amalgam exposures were not taken into account. The amalgam-filled group was also physically and psychologically healthier than the amalgam-free group (23).

With these results, whether the participants have amalgam fillings or not according to gender does not make a significant difference at these three test levels. In our study, SMMT, CDT and IADL scores of women exposed to amalgam fillings were lower than those who were not exposed, but this was not statistically significant. Sun et al (24) found that women exposed to amalgam fillings were 1,132 times more likely to develop Alzheimer's disease than those who were not exposed. On the other hand, Kukull et al (25) reported that there was no association between gender and the onset of Alzheimer's disease.

This study had several limitations and strengths. Because of its cross-sectional design, our study and findings do not reveal a causal relationship. Since we collected cases in geriatric outpatient clinics, our findings cannot be generalised to older adults living in the whole community. Moreover, it is possible that incomplete or inaccurate information may have been provided by participants without amalgam fillings regarding not receiving an amalgam filling in the last 10 years or not receiving extractions of amalgam-filled teeth. The self-reported recall might have led to the underreporting of dental histories in older adults but using medical records to confirm the information minimised selection bias.

On the other hand, the dental examination of the cases was performed by the same dentist, the geriatric evaluation was performed by the same geriatrician, and the accuracy and completeness of the recorded data are the strengths of our study.

CONCLUSION

Our study shows that the presence and amount of dental amalgam filling are not associated with cognitive dysfunction in older adults. Although it has not been fully proven that amalgam fillings cause damage to neurological, immunological and other organs, it is surmised that their mercury content may cause these problems. Despite its cost-effective use and long history in dentistry, the safety of amalgam as a restorative material is still debatable. Evaluation of the risk-benefit balance of other filling materials such as directly placed composite, composite/ceramic inlays or glass ionomer cements, which can be alternatives to amalgam could be new promising area of interest. More detailed research on these alternatives and amalgam filling is required.

REFERENCES

1. Berry TG, Summit JB, Chung AK, Osborne JW. Amalgam at the new millennium. J Am Dent Assoc 1998; 129:1547-56. (PMID: 9818572).
2. Shenoy A. Is it the end of the road for dental amalgam? A critical review. J Conserv Dent 2008;11(3):99-107. (PMID: 20142895).
3. Dunne SM, Gainsford ID, Wilson NH. Current materials and techniques for direct restorations in posterior teeth. Part 1: Silver amalgam. Int Dent J 1997; 47:123-36. (PMID: 9448798).
4. Brownawell AM, Berent S, Brent RL et al. The potential adverse health effects of dental amalgam. Toxicological Reviews 2005;24(1):1-10. (PMID: 16042501).
5. Svare CW, Peterson LC, Reinhardt JW et al. The effect of dental amalgams on mercury levels in expired air. J Dent Res 1981;60(9):68-71. (PMID: 6943160).
6. Clarkson TW. The three modern faces of mercury. Environ Health Perspect 2002;110 (Suppl. 1):11-23. (PMID: 11834460).
7. Kingman A, Albertini T, Brown LJ. Mercury concentrations in urine and whole blood associated with amalgam exposure in a US military population. J Dent Res 1998; 77:461-71. (PMID: 9496919).
8. Mutter J, Naumann J, Walach H, Daschner F. Amalgam risk assessment with coverage of references up to 2005, Review. Gesundheitswesen. German 2005;67(3):204-16. (PMID: 15789284).
9. Saxe SR, Wekstein MW, Kryscio RJ et al. Alzheimer's disease, dental amalgam and mercury. JADA 1999; 130:191-9. (PMID: 10036842).
10. Fung YK, Meade AG, Rack EP, Blotcky AJ. Brain mercury in neurodegenerative disorders. J Toxicol Clin Toxicol 1997; 35:49-54. (PMID: 9022652).
11. Dantzig PI. Parkinson's disease, macular degeneration and cutaneous signs of mercury toxicity. J Occup Environ Med 2006; 48:656. (PMID: 16832218).
12. Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index, J Clin Epidemiol 1994;47(11): 1245-51. (PMID: 7722560).
13. Folstein MF, Folstein S, Mc Hugh PR: "Mini Mental State" A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975; 12:189-98. (PMID: 1202204).
14. Amodeo S, Mainland BJ, Herrmann N, Shulman KI. The times they are a-Changin': Clock drawing and prediction of dementia. J Geriatr Psychiatry Neurol 2015;28(2):145-55. (PMID: 25319477).
15. Rakusa M, Jensterle J, Mlakar J. Clock drawing test: a simple scoring system for the accurate screening of cognitive impairment in patients with mild cognitive impairment and dementia. Dement Geriatr Cogn Disord 2018;45(5-6):326-34. (PMID: 30036864).
16. Shulman KI: Clock-drawing: is it the ideal cognitive screening test? Int J Geriatr Psychiatry 2000; 15: 548–61. (PMID: 10861923).
17. Lawton MP, Brody EH. Instrumental activities of daily living (IADL) scale: original observer-rated version. Psychopharmacol Bull 1988; 24:785-91. (PMID: 3249785).
18. Saxe SR, Snowdon DA, Wekstein MW et al. Dental amalgam, and cognitive function in older women: Findings from the nun study. JADA 1995;126(11):1495-501. (PMID: 7499646).
19. Björkman L, Pedersen NL, Lichtenstein P. Physical and mental health related to dental amalgam fillings in Swedish twins. Community Dentistry and Oral Epidemiology 1996;24(4):260-7. (PMID: (8711034).
20. Tunçdemir MT, Yerlikaya FH. The Relationship Between Plasma MicroRNAs and Serum Mercury Levels in Patients with Amalgam Filling and Dentists. Selcuk Dent J 2021; 8:736-43. (DOI: 10.15311/selcukdentj.800489).
21. Echeverria D, Aposhian HV, Woods JS et al. Neurobehavioral effects from exposure to dental amalgam Hg(o): New distinctions between recent exposure and Hg body burden. FASEB. J.1998;12: 971-80. (PMID: 9707169).
22. DeRouen TA, Martin MD, Leroux BG et al. Neurobehavioral effects of dental amalgam in children: A randomized clinical trial. JADA 2006; 295(15):1784-92. (PMID: 16622140).
23. Ahlqwist M, Bengtsson C, Lapidus L, Gergdahl IA, Schutz A. Serum mercury concentration in relation to survival, symptoms, and diseases: results from the prospective population study of women in Gothenburg, Sweden. Acta Odontol Scand 1999; 57:168-74. (PMID: 10480284).

24. Sun YH, Nfor ON, Huang JY, Liaw YP. Association between dental amalgam fillings and Alzheimer's disease: a population-based cross-sectional study in Taiwan. Alzheimer's Research & Therapy 2015; 7(1):65. (PMID: 26560125).

25. Kukull WA, Higdon R, Bowen JD et al. Dementia and Alzheimer disease incidence: a prospective cohort study. Arch Neurol. 2002; 59:1737-46. (PMID: 12433261).

RESEARCH

ASSESSMENT OF VESTIBULAR SYSTEM AND BALANCE FUNCTION IN PATIENTS WITH PSEUDOEXFOLIATION SYNDROME

Turkish Journal of Geriatrics
DOI: 10.29400/tjgeri.2023.335
2023; 26(1):100−106

Pelin KOÇDOR[1]
Zeynep KAYAARASI ÖZTÜRKER[2]
Osman Halit ÇAM[1]

CORRESPONDANCE

[1]Pelin KOÇDOR

Phone : +905324722529
e-mail : pelinkocdor@gmail.com

Received : Feb 16, 2023
Accepted : Mar 23, 2023

[1] Baskent University, Otorhinolaryngology Head and Neck Surgery, Istanbul, Turkey

[2] Baskent University, Ophthalmology, Istanbul, Turkey

Abstract

Introduction: This study aims to evaluate the balance and vestibular system of patients with pseudoexfoliation syndrome.

Materials and Method: A prospective case–control study was performed in a university hospital. The study population consisted of 37 patients (16 patient group, 21 control group). The Modified Clinical Test of Sensory Interaction Balance was performed in four conditions: 1) eyes open, firm surface; 2) eyes closed, firm surface; 3) eyes closed, foam surface; and 4) eyes open, foam surface. The Equilibrium Score, Anteroposterior Stability Index, Mediolateral Stability Index were employed for all conditions in both groups. Scores were compared between and within groups. Additionally, the physical activity of the patients with pseudoexfoliation syndrome was assessed using questionnaires based on the Turkish versions of the Modified Falls Efficacy Scale and the Physical Activity Scale for the Elderly.

Results: There were no significant differences in terms of stability index and equilibrium scores with eyes open or closed conditions between the two groups; the only difference was in the mean mediolateral stability index score in the eyes open, firm surface condition with low scores in the pseudoexfoliation group (p=0.01). In the group analysis, patients with pseudoexfoliation had a significant increase in the equilibrium scores when their eyes were closed in the firm and foam surface conditions (p=0.001 for both).

Conclusion: The central nervous system redistributes its dependence on sensory information when vision is compromised in patients with pseudoexfoliation syndrome. Their somatosensory input might deteriorate in some way but not the vestibular system.

Keywords: Dizziness; Glaucoma; Aged.

INTRODUCTION

Pseudoexfoliation syndrome (PES) is characterized by deposition of microfibrillar material mainly in the anterior segment of the eye. Gradual accumulation of this material in the outflow pathways may cause a common and severe type of chronic open-angle glaucoma (1). Exfoliative material can also be found in the connective tissue of blood vessels and internal organs, such as the lungs, kidneys, liver, and inner ear (2). The prevalence of PES varies by country: 4% in England, 4.7% in Germany, 6.3% in Norway, 7.2% in Turkey, 9.6% in Iran, 12% in Russia, 16.1% in Greece, 22% in Finland, and 29% in Iceland (3). In Scandinavia, 20–25% of those over the age of 60 and 40% of those over the age of 80 are affected by PES (4). Both population-based and pedigree-based studies have shown that genetic factors contribute to the pathogenesis of PES (1).

Although PES is a systemic disease, the initial diagnosis is often made by an ophthalmologist (5). Several studies demonstrated the presence and accumulation of pseudoexfoliative material in the inner ear using electron microscopy and immunohistochemical methods, suggesting a connection between vestibular end-organ damage and PES (5-7). However, there are few studies demonstrating the involvement of the vestibular system in terms of postural balance (3,8).

Balance is maintained by complex interactions among visual, vestibular, and somatosensory inputs, and its impairment can have a substantial impact on an individual's ability to perform daily activities. Although studies suggest that balance relies greatly on visual input, which is connected to musculoskeletal coordination, proprioceptive function, and neural information integration (9), the vestibular end organs also have a similar significant effect on balance. It is possible that the vestibular part of the inner ear is involved in PES and the balance system may be affected by the accumulation of pseudoexfoliative material in the end organs.

Therefore, in this study, we evaluated the vestibular system with the Modified Clinical Test of Sensory Interaction Balance (M-CTSIB) in patients with PES. The M-CTSIB is a modified version of the original clinical test of sensory interaction balance that evaluates the contribution of the visual, somatosensory, and vestibular systems to postural control (10). The Equilibrium Score (ES), Anteriorposterior Stability Index (APSI), and Mediolateral Stability Index (MLSI) were also employed. The ES indicates the overall coordination of the visual system, vestibular system, and proprioceptive sensations for maintaining standing posture. APSI and MLSI scores relate to more biomechanical aspects of postural stability; like weight and ankle moment, than the ES and are also subunits of the ES (11). To our knowledge, this is the first study using the M-CTSIB for the evaluation of the vestibular system in patients with PES. Additionally, we aimed to assess the physical activity of patients with PES using questionnaires based on the Turkish versions of the Modified Falls Efficacy Scale (MFES) (12) and the Physical Activity Scale for the Elderly (PASE) (13) since physical activity is connected with postural stability and balance.

MATERIALS AND METHOD

This study was reviewed and approved by the institutional review board of the Baskent University Ethics Committee. The tenets of the Helsinki Declaration were followed throughout the study. Informed consent was obtained from each participant before all procedures.

A prospective case–control study was conducted at our university hospital. The study population consisted of 37 patients (18 male, 19 female), 16 of whom were diagnosed with PES. The PES group included patients over the age of 65 diagnosed with PES without any glaucomatous optic nerve or visual field changes within the previous year and with best-corrected visual acuity of 20/40 or more in the Snellen chart. The control group included

patients over the age of 65 with best-corrected visual acuity of 20/40 or more in the Snellen chart. Exclusion criteria for both groups were any ocular pathology other than cataracts and previous ocular surgery other than cataract surgery in the proposed study eye, diseases of the ear (acoustic neuroma, Meniere's disease, chronic otitis media, ototoxic or vestibulotoxic medication history, cholesteatoma, and any ear surgery) except presbycusis, any neurological disease that can cause central vertigo, and any disease or surgery that can affect the lower extremities.

All subjects underwent a complete ophthalmic examination, including best-corrected visual acuity, applanation tonometry, slit-lamp biomicroscopy, indirect ophthalmoscopy under dilated pupil conditions, and Humphrey Swedish Interactive Thresholding Algorithm SITA Standard 24-2 visual field testing. PES was identified based on modest changes on the lens surface and pupil margin, as well as poor pupillary dilation and pigment-related symptoms, such as pigment dispersion and pupillary atrophy. After the complete ophthalmic evaluation, patients eligible for the study were referred to the otorhinolaryngology clinic for the application of the Turkish versions of the MFES and PASE questionnaires followed by the M-CTSIB, which was conducted under the following four conditions:

1. Standing on firm surface with eyes open; three balance systems (visual, somatosensory, and vestibular) are fully engaged to evaluate baseline condition.
2. Standing on firm surface with eyes closed; visual input is eliminated to evaluate vestibular and somatosensory systems.
3. Standing on foam surface with eyes open; somatosensory input is purposely eliminated with the compliant surface.
4. Standing on foam surface with eyes closed; both somatosensory and visuals systems are purposely eliminated.

During the test conditions, the patients kept their arms at their sides. If the patients opened or closed their eyes, lifted their arms away from their bodies, or lost their balance during the 30-second test, the timer was stopped. If numerous trials were required, the trial times were averaged to calculate the score.

Three trials were performed in each condition, and the mean of the three trials was taken as the final measurement. M-CTSIB measurements included the ES, which quantifies the center of postural stability under each condition, as well as APSI, MLSI, and Overall Stability Index (OSI) scores, which are derived from the summation of the degrees of tilt calculated in the anteroposterior and mediolateral axis. The mean scores of the three trials were analyzed.

Statistical Analysis

The SPSS 25.0 (IBM SPSS Statistics for Windows, Version 25.0) package program was used for the statistical analysis of the data. Categorical measurements were summarized as numbers and percentages, and continuous measurements were presented as means and standard deviations (as median and minimum–maximum when required). Chi-square or Fisher test statistics were used to compare categorical variables. In comparing continuous measurements between the groups, the distributions were controlled, and the student's t-test was used for the parameters that showed normal distribution according to the number of variables. The Mann-Whitney U test was used for the parameters that did not show normal distribution. When the expected frequencies were below 20%, to include these frequencies in the analyses, the Monte Carlo Simulation Method was used. The statistical significance level was taken as $p<0.05$ and $p<0.01$ in all tests.

RESULTS

A total of 16 PES patients (9 male, 7 female) and 21 healthy volunteers (9 male, 12 female) were included in the study (Table1). There were no statistically significant differences between these two groups in terms of age, Body Mass Index, and MFES and PASE scores ($p>0.05$ for all).

There were no significant differences between the groups in terms of the mean values of the APSI, MLSI, OSI, and ES measurements in the foam surface condition, regardless of whether their eyes were open or closed. However, in the firm surface condition, there was a significant decrease in the mean MLSI in the eyes open condition in the PES group when compared to the control group ($p=0.01$) (Table 2). There were no significant differences between male and female participants in both groups with respect to the stability indexes and ES.

In the group analysis, PES patients had a significant increase in the ES when their eyes were closed in the firm and foam surface conditions ($p=0.001$ for both) (Table 3). There were no significant

Table 1. Demographic distribution of patients

		Control	PES	Total
Male	n	9	9	18
	%	50.0%	50.0%	100.0%
Female	n	12	7	19
	%	63.2%	36.8%	100.0%
Total	n	21	16	37
	%	56.8%	43.2%	100.0%

Table 2. Mean values of Mediolateral stability index (MLSI) scores according to the surface and eyes condition.

	CONTROL (n=21)	PES (n=16)	p-value
Eyes Open Firm Surface MLSI	0.56±0.27	0.43±0.15	**0.010**
Eyes Closed Firm Surface MLSI	0.49±0.3	0.42±0.18	0.390

Table 3. Mean values of ES according to the surface and eyes condition. ES: Equilibrium Score

	CONTROL (n=21)	PES (n=16)
Eyes Open Firm Surface ES	53±12.47	50.14±17.24
Eyes Closed Firm Surface ES	61.93±13.17	59.3±12.04
p-value	0.078	**0.001**
Eyes Open Foam Surface ES	45.4±17.34	44.95±17.85
Eyes Closed Foam Surface ES	42.08±18.92	48.86±22.19
p-value	0.615	**0.001**

differences in the ES regardless of whether the eyes were open or closed in the control group. There were no statistically significant differences in the stability index scores in both groups.

DISCUSSION

According to our findings, when visual input is eliminated, PES patients showed a higher ES in firm and foam surface conditions within the group analyses. When compared to the control group, they showed worse MLSI scores on a firm surface, indicating that their somatosensorial systems, but not the vestibular system, deteriorated in some way.

The advantage of the M-CTSIB is that it is designed to assess the level of use of each sensory input when more than one sensory system is affected in older individuals. When standing on a foam surface, the somatosensorial system is disabled and balance control is maintained with information from the visual and vestibular systems. However, when attempting to maintain balance on a firm surface, the somatosensory system is activated. To our knowledge, this is the first study to use the M-CTSIB for the evaluation of the vestibular system in individuals with PES (PubMed search terms: "pseudoexfoliation, balance, M-CTSIB" on 01/10/2022.) Several research studies have revealed that the accumulation of pseudoexfoliation material in the cochlea causes sensorineural hearing loss (14-17). However, few investigations assessed the involvement of the vestibular system, which is another component of the inner ear. Bilgec et al. observed pathological findings in the vestibular system, including in the saccule, vestibular nerve, and semicircular canal; however, they did not observe balance problems (8). Turgut et al. obtained similar results, revealing that the visual and proprioceptive systems compensate for balance even when vestibular function is impaired (3). The aforementioned studies relied mostly on the bithermal caloric, Romberg, Unterberger, Dix-Hallpike, and Vestibular evoked myogenic potential (VEMP) tests to assess vestibular function. These tests are helpful before performing more objective tests but are not as precise as the M-CTSIB. We could have used a combination of the caloric test and M-CTSIB, which would have been more helpful for the evaluation of the vestibular system; however, it would have been very disturbing and exhausting for the study participants since they were presented only for the eye exam and the caloric test would have caused a real spinning sensation. Interestingly, the mean age in both studies was under 65. Since PES incidence increases markedly with age (4), and the mean age in our study group was 74, the increasing amount of elastic fiber components accumulation may have a time-dependent impact on the balance system.

In our study, stability index scores (mediolateral, eyes open) on a firm surface were different for the PES and control groups, suggesting that visual input is less likely to increase the vestibular and somatosensory contribution to postural stability. Shabana et al. demonstrated that glaucoma patients aged 40-66 years exhibited greater somatosensory contributions to postural stability to maintain a steady stance when compared with controls (18). However, Black et al. found a significant association between glaucomatous visual impairment and postural sway in older adults (19). While our results are comparable with those of Black et al., our study group consisted of individuals with PES and not glaucoma.

Our study also found that vision is not contributing to balance in older persons with PES because there were significant differences in the ES regardless of surface condition. Kotecha et al. showed that during silent standing conditions on firm surfaces, patients with a visual impairment might make better use of nonvisual inputs to maintain balance (20). Our study confirms their results. The central nervous system redistributes its dependence on sensory data when available information is compromised, even in older people (19, 21).

In one study, the combination of PES and glaucoma resulted in poor balance on foam and firm surfaces, demonstrating that glaucomatous visual field loss contributes to balance limitations that cannot be compensated for by the somatosensory and vestibular systems (22). Another study reported that balance was worse in glaucoma patients with greater visual field damage under foam surface and firm surface conditions (23).

Our results showed that individuals with PES have the same physical activity and the same fear of falling scores as their peers. Previous studies have shown that patients with glaucoma had worse scores on the fear of falling questionnaires compared to control subjects (20,21). Ramulu et al. (22) and De Luna et al. (23) revealed that fear of falling mediates the relationship between vision loss and physical activity restrictions.

The main limitation of our study was the low patient number. Also, we did not run the full vestibular test battery due to time constraints and patient intolerance. The addition of VEMP tests and video head impulse test (vHIT) could have added more specific information to improve our understanding of the difference in MLSI and APSI scores for the PES and control groups on a firm surface and supplied more information about the location of fibrillar deposition in the vestibular system.

In conclusion, PES patients demonstrated a high ES in firm and foam surface conditions when visual input was removed. Since the ES was high, we may conclude that the central nervous system redistributes its dependence on sensory information when vision is compromised in patients with PES. This suggests that balance control is not compromised in this patient group. They displayed lower MLSI scores on hard surfaces compared to those in the control group but not in the other stability index scores in any other condition, which suggests that their somatosensory input might deteriorate in some way but not the vestibular system.

Acknowledgements

We would like to express our very great appreciation to Emel Isik and Oguzhan Cetin for helping with data collection of this research work. Their willingness to give their time so generously has been very much appreciated.

REFERENCES

1. Schlotzer-Schrehardt U, Pasutto F, Sommer P, et al. Genotype-correlated expression of lysyl oxidase-like 1 in ocular tissues of patients with pseudoexfoliation syndrome/glaucoma and normal patients. Am J Pathol. 2008; 173: 1724-1735. (DOI: 10.2353/ajpath.2008.080535).
2. Elhawy E, Kamthan G, Dong CQ, Danias J. Pseudoexfoliation syndrome, a systemic disorder with ocular manifestations. Hum Genomics. 2012; 10: 6-22. (DOI: 10.1186/1479-7364-6-22).
3. Turgut B, Alpay HC, Kaya MK, Oger M, Celiker U, Yalcin S. The evaluation of vestibular functions in patients with pseudoexfoliation syndrome. Eur Arch Otorhinolaryngology. 2010; 267: 523-527. (DOI: 10.1007/s00405-009-1093-6).
4. Astrom S, Linden C. Incidence and prevalence of pseudoexfoliation and open-angle glaucoma in northern Sweden: I.Baseline report. Acta Ophthalmol Scand. 2007; 85: 828-831. (DOI: 10.1111/j.1600-0420.2007.00992.x).
5. Schlötzer-Schrehardt UM, Koca MR, Naumann GO, Volkholz H. Pseudoexfoliation syndrome Ocular manifestation of a systemic disorder? Arch. Ophthalmol. 1992; 110: 1752–1756. (DOI: 10.1001/archopht.1992.01080240092038).
6. Tryggvason G, Jonasson F, Cotch MF, et al. Hearing in older adults with exfoliation syndrome/exfoliation glaucoma or primary open-angle glaucoma. Acta Ophthalmol. 2016; 94: 140-147. (DOI: 10.1111/aos.12914).
7. Streeten BW, Li ZY, Wallace RN, Eagle RC Jr, Keshgegian AA. Pseudoexfoliative fibrillopathy in visceral organs of a patient with pseudoexfoliation syndrome. Arch Ophthalmol. 1992; 110: 1757–1762. (DOI: 10.1001/archopht.1992.01080240097039).
8. Bilgec MD, Kucukcan NE, Birdane L, Incesulu A, Yildirim N. Evaluation of the vestibulocochlear system in patients with pseudoexfoliation syndrome.

Turk J Ophthalmol. 2021; 51: 156-160. (DOI: 10.4274/tjo.galenos.2020.14892).

9. Tobis JS, Block M, Steinnhaus-Donham C, et al. Falling among the sensorially impaired elderly. Arch Phys Med Rehabil. 1990; 71: 144-147. (PMID: 2302048).
10. Aksoy S, Boru A, Kilic RT. Posturografi, In: Fazil Necdet Ardic. Vertigo. 2rd Edition, US Akademi TR 2019 pp 113-151.
11. Chaudhry H, Findley T, Quigley KS, et al. Postural stability index is a more valid measure of stability than equilibrium score. J Rehabil Res Dev. 2005; 42: 547-56. (DOI: 10.1682/jrrd.2004.08.0097).
12. Okuyan CB, Bilgili N, Kitis Y. Validity and reliability of the Turkish version of the modified falls efficacy scale of in older adults. J Gerontol Geriatr Res. 2018; 7: 494. (DOI: 10.4172/2167-7182.1000494).
13. Ayvat E, Kilinc M, Kirdi N. The Turkish version of the physical activity scale for the elderly (PASE): its cultural adaptation, validation and reliability. Turk J Med Sci. 2017; 47: 908-915. (DOI: 10.3906/sag-1605-7).
14. Yazdani S, Tausi A, Pakravan M, Faghihi AR. Sensorineural Hearing Loss in pseudoexfoliationsyndrome. Ophthalmology. 2008; 115: 425429. (DOI: 10.1016/j.ophtha.2007 .10.038).
15. Papadopoulos TA, Naxakis SS, Charalabopoulou M, Vathylakis I, Goumas PD, Gartaganis SP. Exfoliation Syndrome related to sensorineural hearing loss. Clin Exp Ophthalmol. 2010; 38: 456–461. (DOI: 10.1111/j.1442-9071.2010.02289.x).
16. Samarai V, Samarei R, Haghighi N, Jalili E. Sensory-neural hearing loss in pseudoexfoliation syndrome. Int J Ophthalmol. 2012; 5: 393–396. (DOI: 10.3980/j.issn.2222-3959.2012.03.28).
17. Turacli ME, Ozdemir FA, Tekeli O, Gökcan K, Gerçeker M, Dürük K. Sensorineural hearing loss in pseudoexfoliation. Can J Ophthalmol. 2007; 42: 56-9. (PMID: 17361242).
18. Shabana N, Cornilleau-Peres V, Droulez J, Goh JC, Lee GS, Chew PT. Postural stability in primary open angle glaucoma. Clin Experiment Ophthalmology. 2005; 33: 264-73. (DOI: 10.1111/j.1442-9071.2005.01003.x).
19. Black AA, Wood JM, Lovie-Kitchin JE, Newman BM. Visual impairment and postural sway among older adults with glaucoma. Optometry and Vision Science. 2008; 85: 489-497. (DOI: 10.1097/OPX.0b013e31817882db).
20. Kotecha A, Richardson G, Chopra R, Fahy RTA, Garway-Heath DF, Rubin GS. Balance control in glaucoma. Invest Ophthalmol Vis Sci. 2012; 53: 7795-7801. (DOI: 10.1167/iovs.12-10866).
21. Horak FB, Hlavacka F. Somatosensory loss increases vestibulospinal sensitivity. J Neurophysiol. 2001; 86: 575-585. (DOI: 10.1152/jn.2001.86.2.575).
22. Ramulu PY, van Landingham SW, Massof RW, Chan ES, Ferrucci L, Friedman DS. Fear of falling and visual field loss from glaucoma. Ophthalmology. 2012; 119: 1352-1358. (DOI: 10.1016/j.ophtha.2012.01.037).
23. De Luna RA, Mihailovic A, Nguyen AM, Friedman DS, Gitlin LN, Ramulu PY. The association of glaucomatos visual field loss and balance. Transl Vis Sci Technol. 2017; 6: 8. (DOI: 10.1167/tvst.6.3.8).

Turkish Journal of Geriatrics
2023; 26(1)

FROM THE EDITOR IN CHIEF
Yeşim GÖKÇE KUTSAL

RESEARCH ARTICLES

FRAILTY AND RELATED FACTORS IN ELDERLY PATIENTS WITH CHRONIC KIDNEY DISEASE
Alper ALP , Hüseyin ELBİ, Aysun TORAMAN

THE RELATIONSHIP OF THE C-REACTIVE PROTEIN /ALBUMIN RATIO TO IN-HOSPITAL MORTALITY IN ELDERLY PATIENTS WITH NON-ST-ELEVATION MYOCARDIAL INFARCTION WHO HAVE UNDERGONE PERCUTANEOUS CORONARY INTERVENTION
Oğuz KILIÇ, Fatma ÖZPAMUK KARADENİZ, Fatih KAHRAMAN

EFFICACY OF EPIDURAL STEROID INJECTION IN ELDERLY PATIENTS: DOES DIAGNOSIS AFFECT TREATMENT SUCCESS?
Yücel OLGUN, Rekib SACAKLIDIR, Yasin OKUMUŞ, Savaş SENCAN, Osman Hakan GÜNDÜZ

A 30-DAY RISK ASSESSMENT OF GERIATRIC PATIENTS IN THE EMERGENCY DEPARTMENT: A COMPARISON OF ISAR AND TRST SCORES
Savaş SEZİK

COMPARISON OF THE EFFECTS OF INTRAOPERATIVE GOAL DIRECTED AND CONVENTIONAL FLUID MANAGEMENT ON THE INFERIOR VENA CAVA COLLAPSIBILITY INDEX AND POSTOPERATIVE COMPLICATIONS IN GERIATRIC PATIENTS OPERATED FROM PROXIMAL FEMORAL NAIL SURGERY
Dilara GÖÇMEN, Ceren KÖKSAL, Süheyla ABİTAĞAOĞLU, Arzu YILDIRIM AR

COMPARISON OF THE EFFECTS OF GENERAL ANESTHESIA AND DEEP SEDATION ON ANESTHESIA COMPLICATIONS AND MORTALITY IN ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY PROCEDURES
Elif BÜYÜKERKMEN, Ahmet YÜKSEK, Elif DOĞAN BAKI, Sezgin YILMAZ

KNEE ARTHRODESIS WITH COMPUTER-ASSISTED EXTERNAL FIXATOR SYSTEM AFTER PROSTHETIC JOINT INFECTION FOR ELDERLY POPULATION
Muharrem KANAR, Necmi CAM

THE EFFECTS OF LOW FLOW AND NORMAL FLOW DESFLURANE ANESTHESIA ON LIVER AND RENAL FUNCTIONS AND SERUM CYSTATIN C LEVELS IN GERIATRIC PATIENTS: A PROSPECTIVE RANDOMIZED CONTROLLED STUDY
Afife GÜLER KOL, Hacı Yusuf GÜNEŞ

EVALUATING THE ROLE OF VERTEBRAL ANATOMY EXAMINATION BY ULTRASONOGRAPHY BEFORE ADMINISTERING SPINAL ANESTHESIA IN GERIATRIC PATIENTS: A PROSPECTIVE RANDOMIZED TRIAL
Arda IŞIKER, Meryem ONAY, Alpaslan AKCAN, Ümit AKKEMİK, Mehmet Sacit GÜLEÇ

RELATIONSHIP BETWEEN THE AMOUNT OF AMALGAM FILLING AND COGNITION IN OLDER ADULTS
Savaş ÖZARSLANTÜRK, Mehmet İlkin NAHARCI, Numan AYDIN, Serpil KARAOĞLANOĞLU, Elif Aybala OKTAY

ASSESSMENT OF VESTIBULAR SYSTEM AND BALANCE FUNCTION IN PATIENTS WITH PSEUDOEXFOLIATION SYNDROME
Pelin KOÇDOR, Zeynep KAYAARASI ÖZTÜRKER, Osman Halit ÇAM