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■ Sibel EYİGÖR[1]
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REVIEW

SARCOPENIA: AGAIN AND UPDATED

Abstract

Sarcopenia is defined as, skeletal muscle dysfunction associated with age, chronic diseases, cancer, nutrition problems and physical inactivity. The pathophysiology of sarcopenia seems to involve degeneration of neurogenic, musculogenic, synaptogenic and vasculogenic systems, mitochondrial dysfunction, metabolic factors and inflammatory mechanisms. Early detection of sarcopenia in older adults and patients is important to prevent morbidity, functional decline and death and the diagnosis requires assessment of muscle mass, muscle strength and physical performance. The strongest evidences in the treatment of sarcopenia are probably associated with the positive effects of resistance exercises on muscle strength, muscle mass and physical performance. Also protein intake needs to be increased. Positive results have been reported on supplementation with leucine, β-hydroxy β-methylbutyrate, Omega 3 and Vitamin D. Antioxidant intake naturally from food is recommended. There are promising studies related to angiotensin receptor blockers, oral anti-diabetic drugs. Interventions to prevent sarcopenia, treatment of the primarily responsible disease, suppression of inflammation, and treatment of metabolic syndromes constitute the basic components of a successful treatment.

Keywords: Sarcopenia; Physical Functional Performance; Muscle Strength; Aged.

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INTRODUCTION

Derived from Greek "sarx" for flesh and "penia" for loss/poverty, sarcopenia was first discovered by Leonardo da Vinci as seen in his drawings (1,2). Although three decades have passed since, it was first defined in 1989 and its clinical details and diagnosis are still controversial. While its first definition was age-related loss of muscle mass, it was agreed later, to be a skeletal muscle dysfunction associated with age, chronic diseases, cancer, nutrition problems and physical inactivity (2, 3). Recently, this clinical situation is being mentioned to exist even in the paediatric group (4).

And based on these facts, the definition was updated by Cruz Jentoft and Sayer as: sarcopenia is a progressive and generalised skeletal muscle disorder involving the accelerated loss of muscle mass and function that is associated with increased adverse outcomes including falls, functional decline, frailty, and mortality (3).

While the prevalence of sarcopenia is approximately 25% in those under 70 years of age, it goes up to 50% in the elderly aged 80 years and over (5). Its prevalence was found to be 46 % in geriatric care units and it is also prevalent in patients with hip fracture (71%), or long term hospitalizations (6-8). However, it should be noted that, the prevalence of sarcopenia may differ depending on the diagnostic criteria, cut-off values and measurement method chosen.

The reason underlying the fact that a new study on sarcopenia has been published almost every day in the last 30 years and it has become such a trend is that sarcopenia is associated with mortality, morbidity and quality of life (9, 10).

PATHOPHYSIOLOGICAL MECHANISMS

The point we have arrived today based on research is that, sarcopenia is a result of a combination of complex multifactorial processes. The pathophysiology of sarcopenia seems to involve degeneration of neurogenic, musculogenic, synaptogenic and vasculogenic systems, mitochondrial dysfunction, metabolic factors and inflammatory mechanisms. All these mechanisms have impacts on sarcopenia, but it is still difficult to establish a causal relationship between these mechanisms and their impacts on the muscle (11-13).

Although it is mostly associated with old age, there are many comorbidities that contribute to the development of sarcopenia (14). The relationship between diseases and sarcopenia gains a new dimension with a new study being conducted every day. It has been found to be associated with nutritional deficiencies, hormonal alterations, metabolic dysfunctions, inactivity (immobilization, sedentary life style), bone-joint diseases (osteoarthritis, osteoporosis, etc.), endocrine diseases (thyroid diseases, androgen deprivation, etc.), neurological diseases, kidney and liver diseases, cardiovascular and respiratory diseases, cancer, inflammatory diseases, cognitive impairment, and drug side effects as well as genetic and environmental factors (15,16). When such factors result in a loss of muscle mass and strength, patients are faced with weakness and a decline in mobility and physiologic functions. Sarcopenia is also associated with frailty and an increased incidence of falls (17, 18). Thus, it is a major challenge in rehabilitation clinics and should be addressed diligently (14,18).

DIAGNOSTIC CRITERIA

It should be kept in mind that, the core of the sarcopenia condition involves quantitative and qualitative losses of skeletal muscle (19).

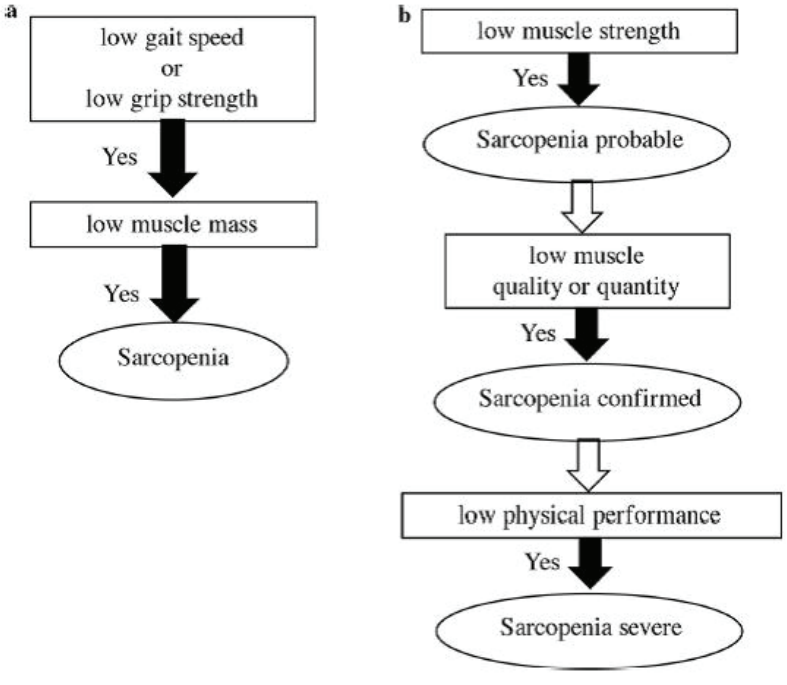
Since the time it was first identified, various study groups have tried to establish new definitions and diagnostic steps. Criteria for sarcopenia has been a matter of debate for a long time, and there are more than 6 criteria for diagnosis (20). The criteria developed by the European Working Group on Sarcopenia in Older People (EWGSOP)

(15) and the Foundation for the National Institutes of Health - Sarcopenia Project (21) are the most widely used ones. Studies being conducted in Asia also use the criteria of the Asian Working Group for Sarcopenia (AWGS) for diagnosis besides the others (22). These criteria are still being improved and updated, the most recent update being in 2019 (15). This process will obviously continue and working groups will keep coming up with new definitions and criteria (23). Based on the information currently available, the diagnosis of sarcopenia requires assessment of muscle mass, muscle strength and physical performance. Although a low muscle mass was initially considered essential for diagnosis by EWGSOP, later studies have shown that a change in muscle strength is more predictive of adverse outcomes. Therefore, a need has arisen to issue EWGSOP2, a new version updated based on clinical and scientific evidences (Figure 1) (13).

Early detection of sarcopenia in older adults and patients is important to prevent morbidity, functional decline and death (24, 25). Although it was given the code M62.84 in the International Classification of Diseases system very recently, the criteria proposed for the diagnosis of sarcopenia are still not widely used and can easily escape the attention in clinical practice (11, 26).

The symptoms and signs of general weakness, loss of muscle mass (visual), low walking speed, weight loss, muscle strength depletion in the arms/legs, fatigue, falls, mobility disorder, loss of energy, and difficulties in activities of daily living need to be considered red flags, raising alerts for a sarcopenia screening. If these symptoms are present, the guidelines of EWGSOP (15) recommend screening of patients for sarcopenia using SARC-F. If the SARC-F score turns out 4 and over, a muscle strength test is recommended and if there is a problem in muscle strength, then a "probable sarcopenia" diagnosis can be made. If probable sarcopenia is detected, treatment is recommended. In case there is a problem in muscle strength, a muscle quality and quantity assessment is suggested, and if a problem is found, a diagnosis of "sarcopenia" can be made. In case a physical

Figure 1. Sarcopenia assessment algorithm.



performance disorder is also present in the above algorithm, then a diagnosis of "severe sarcopenia" can be made. A hand grip strength or chair stand test is recommended for muscle strength assessment and a gait speed, short physical performance battery, timed up and go test, 400 mt walk or long distance corridor walk test for physical performance measurement (15).

Currently there have been some methods for evaluation of sarcopenia focusing on body composition imaging modalities such as, whole-body dual-energy X-ray absorptiometry, computed tomography (CT), and magnetic resonance imaging (MRG). But the there are controversial issues, including the lack of consensus and standardization of the disease definition, imaging modality, measurement methods, and diagnostic cutoff points (27).

Recent revised European consensus on definition was as follows (Figure 1) (13, 15):

Probable sarcopenia is identified by Criterion 1.

Diagnosis is confirmed by additional documentation of Criterion 2.

If Criteria 1, 2 and 3 are all met, sarcopenia is considered severe.

(1) Low muscle strength

(2) Low muscle quantity or quality

(3) Low physical performance.

Unfortunately, one can say that, there is not adequate data for muscle quality assessment although it is a very important parameter. However, recent studies suggest that early assessment of muscle quality will be of crucial importance to prevent sarcopenia in the future (13).

Validated tests and tools for current use are listed by the European consensus as; SARC-F for screening sarcopenia risk, calibrated handheld dynamometer for muscle strength, chair rise test, body mass index (BMI) for muscle quantity, MRG, CT and also Dual-energy X-ray absorptiometry (DXA) for muscle quantity/mass, Bioelectrical impedance analysis (BIA) for Appendicular Skeletal Muscle Mass. Gait speed, Short Physical Performance Battery (SPPB), the Timed-Up and Go test (TUG) for the evaluation of physical performance are recommended (15).

New methods are being tested for validity, reliability and accuracy and may play a relevant role in the future. Such as; lumbar 3rd vertebra imaging by computed tomography, mid-thigh muscle measurement, psoas muscle measurement with CT, muscle quality measurement (MRI and CT), creatine dilution test, ultrasound assessment of muscle, specific biomarkers or panels of biomarkers. Since quality of life is a very considerable issue, "Sarcopenia and Qality of Life (SarQoL)" identifies and predicts sarcopenia complications that may later impact the patient's quality of life (15).

TREATMENT OPTIONS

Treatment of advanced PC has improved recently. As the diagnostic criteria to identify patients with sarcopenia are debatable, potential treatment options also become obscure. The options in the literature are unfortunately unable to meet our needs due to their side effects and lack of evidences. Data on the mechanisms, efficacy and safety of pharmacological therapies are not satisfactory.

The strongest evidences in the treatment of sarcopenia are probably associated with the positive effects of resistance exercises on muscle strength, muscle mass and physical performance (13). An individual's general physical activity level is also important (28). An hour of increase in daily sitting time is reported to increase the risk of sarcopenia by 33% (29). Therefore, it is of utmost importance for protection to increase the level of daily physical activity as much as possible. Weekly physical activity for 150 minutes at a moderate level or for 75 minutes at an intense level is recommended (30). Rehabilitation physicians need to put their effort into planning tailor-made exercise programs, either community-based or home-based as appro-



priate.

According to general consensus reports and evidences at a lower level, protein intake needs to be increased to 1-1.5 g/kg/day to achieve an optimal health condition in the elderly. Daily protein amount should be proportioned between meals and particularly taken within the first 2-3 hours following an exercise (for muscle protein synthesis stimulation). Reports suggest that daily intake can be increased up to 2 g/kg in the cases of an injury, a severe disease, or a proinflammatory/catabolic process.

Positive results have been reported on supplementation with leucine and its metabolite β-hydroxy β-methylbutyrate (HMB) due to their contribution to protein synthesis (13, 31). HMB has been shown to improve muscle mass and to preserve muscle strength and function in older people with sarcopenia or frailty (17, 18, 32). Positive results have also been obtained with Omega 3 support but without sufficient evidence. A combination of resistance exercises and nutritional supplements is reported to have more apparent protective and healing effects (28). Vitamin D supplementation specifically for sarcopenia was found to have insufficient evidence, though there is evidence that persons with low vitamin D levels may improve their strength with vitamin D supplementation (33). Since oxidative stress is also in the aetiology of sarcopenia, use of antioxidants (vitamin E, Selenium, vitamin C, etc.) can also be considered. However, antioxidant intake naturally from food is recommended more. Specific or popular diet regimens have not produced a significant outcome. There are very promising studies related to angiotensin receptor blockers in the literature. Some oral anti-diabetic drugs are also reported to be helpful in preventing sarcopenia. Interventions to prevent sarcopenia, treatment of the primarily responsible disease, suppression of inflammation, and treatment of metabolic syndromes constitute the basic components of a successful treatment (13, 14, 34, 35).

High-dose testosterone increases muscle power and function, but has a number of potentially limiting side effects. Other drugs in clinical development include selective androgen receptor molecules, ghrelin agonists, myostatin antibodies, activin type 2 receptor antagonists, angiotensin converting enzyme inhibitors, beta antagonists, and fast skeletal muscle troponin activators (34, 35). At present, there is insufficient evidence that anabolic steroids or newer pharmacological agents (ghrelin, anti-myostatin antibodies) should be used to treat sarcopenia.

However, promising results still cannot be obtained due to side effects of some therapies and inefficacy of some others. An effective pharmacological treatment is still not available due to the quality of the studies in the literature, heterogeneous groups involved and a large amount of factors affecting sarcopenia.

CONCLUSION

It is well shown that, sarcopenia is associated with multiple adverse outcomes such as comorbidities, poor physical performance, physical disability, depression, hospitalisation, functional decline and falls, causing the patients having worse quality of life. Indicating the importance of preventative and interventional management strategies for managing sarcopenic individuals (36).

Unavailability of distinct diagnostic criteria for sarcopenia leads to confusion in selecting a treatment option. The point that needs to be stressed is that it often escapes the attention in clinical practice and successful treatment results cannot be achieved due to its complex nature. Data on the mechanisms, efficacy and safety of pharmacological therapies are not satisfactory. But nowadays diagnosis, treatment, and prevention of sarcopenia is likely to become part of routine clinical practice. And designing effective preventive strategies that people can apply during their lifetime is of primary concern today (3).

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RESEARCH

CAN CHOLECYSTECTOMY BE PERFORMED AS SAFELY IN ELDERLY PATIENTS AS IT IS IN YOUNG PATIENTS?

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Abstract

Introduction: In this study, we aimed to compare the surgical outcomes between elderly and young patients undergoing surgery for gallstone disease and determine variations in patient characteristics, if any.

Materials and Method: Data of patients who underwent surgery for gallstone disease at a single center between 2010 and 2018 were analyzed retrospectively. Two patient groups were evaluated: patients <65 years and ≥65 years. Patient characteristics, preoperative outpatient clinic data, surgical data, and postoperative data were collected.

Results: In total, 1,198 patients with a mean age of 54.77 ± 15.03 (15–91) years were assessed. Comorbid conditions, including cardiovascular disease, pulmonary disease, renal disease, and diabetes mellitus were significantly more common in elderly patients ($p<0.001$). Acute cholecystitis in the preoperative period was noted in 15.36% of young patients and in 30.4% of elderly patients ($p<0.001$). Need for emergency surgery was higher in elderly patients than in young patients [13.86% (47) and 9.31% (80), respectively] ($p=0.021$). Laparoscopic cholecystectomy and open cholecystectomy were performed in 98.37% and 1.04% of young patients, respectively, and in 92.62% and 3.53% of elderly patients, respectively ($p<0.001$). Among factors affecting the length of hospital stay in elderly patients, the duration of hospitalization was significantly longer in elderly patients who underwent emergency surgery, open surgery, needed additional surgery, and who had high American Society of Anesthesiologists scores ($p<0.001$, $p<0.001$, $p=0.013$, $p<0.001$, respectively).

Conclusion: Complications rates associated with cholecystectomy are similar between young and elderly patients when appropriate surgical preparations are performed. Surgery for gallstone disease can be performed safely in elderly patients with low morbidity and mortality rates.

Keywords: Gall Stone; Cholecystectomy; Aged.



INTRODUCTION

Surgical procedures for gallstone disease (GD) are the most common abdominal procedures performed in elderly patients (1-3). The reluctance by surgeons to perform surgery for elderly patients stands out because of the fact that increased age is an independent risk factor for complications that may arise in elderly patients requiring surgery (4-5).

In addition to this negative prediction, some studies emphasize that complicated GD is more common in elderly patients (4,5), whereas other studies report that complicated GD is less common in elderly patients with early intervention for the symptomatic disease (6-8).

The United Nations estimates that in 2019, individuals aged >65 years will constitute 11% of the population and by 2050, 16% will be over age 65(9). The Turkish Statistical Institute (TUIK) announced that of the total population in Turkey, the ratio of the elderly population increased from 7.7% in 2013 to 8.5% in 2017 and that the expected life expectancy of an individual reaching the age of 65 is 17.8 years (10). The increasing elderly population brings with it increased health problems. Gallstone disease is one of them.

The aim of this study was to compare the surgical results of the elderly patients who underwent surgery for GD with the young patient group and to investigate complication development, length of hospital stay, and return to daily activities.

MATERIALS AND METHOD

This study is a retrospective single-center cross-sectional study. The data of 1,273 patients who underwent surgery for GD between 2010 and 2018 at our medical center were reviewed retrospectively. Seventy-five patients were excluded from the study because they underwent GD secondary to their original surgery.

Retrospective data were obtained from the computer-based data system of the hospital where the study was conducted. These data in the system were transferred to a database created by the researchers. These include demographic data such as age and gender of the patients, surgical notes such as surgical indications, degree of urgency, American Society of Anesthesiologists (ASA) score, type of surgery, duration of surgery (time between entry into and exit from the operating room), and length of hospital stay. Comorbidities of the patients in terms of cardiovascular disease, pulmonary disease, renal disease, and diabetes mellitus were retrieved from the database and recorded. Additionally, history of biliary tract diseases and interventions and previous abdominal surgery was obtained from the records. Lastly, data on postoperative complications were recorded in the hospital registry system as determined by the surgeons.

This study was performed using data of patients who underwent emergency and elective surgery for primary GD. Patients were operated on by four surgeons. Patients who were diagnosed with acute cholecystitis (AC), presented to the hospital within 72 h after the onset of abdominal pain, whose examination findings localized in the right upper quadrant, who had a C-reactive protein (CRP) level of <10 mg/dl and blood leukocyte count of <18,000 cells/µl, and those whose gallbladder wall thickness was <1cm on ultrasonography underwent emergency surgery. The initial surgical treatment in these patients was laparoscopic cholecystectomy (LC). Patients who had complaints for a longer term and presented to the hospital after 72 h and those with high CRP and leukocyte levels were hospitalized and placed under follow-up. These patients were administered parenteral antibiotics (third generation cephalosporin or ciprofloxacin and metronidazole for anaerobic activity) and fluid treatment along with symptomatic treatment and followed up with discontinuation of oral intake. Patients whose complaints regressed and who did not develop complications were

scheduled for elective surgery 4–6 weeks after discharge. However, patients who had a complicated disease, such as gallbladder perforation, at the time of admission and those whose complaints did not regress or who developed complications despite therapy underwent emergency surgery. Owing to the lack of an interventional radiology unit at our hospital, patients for whom cholecystostomy was indicated were referred to other medical centers for cholecystostomy with their own wish after being informed about surgical treatment and cholecystostomy, and patients who did not wish to undergo cholecystostomy were treated with emergency surgery. Open cholecystectomy (OC) was preferred inpatients who underwent delayed emergency cholecystectomy.

This study was approved by the Medical and Health Sciences Research Ethics Committee of Başkent University (Project number: KA19/03) and was supported by the research fund of Başkent University. As this was a retrospective cross-sectional study, informed consent was not obtained from the patients.

STATISTICS

The data obtained from the study was analyzed using the Statistical Package for Social Science software version 15.0. Numbers and percentages were used to present numeric variables. Descriptive statistics were expressed in number and percentage. A Chi-square test was used to compare data, including descriptive characteristics and perioperative and postoperative outcomes, of patients. A p value <0.05 was considered statistically significant.

RESULTS

The study included 1,198 patients. The mean age of the patients was 54.77±15.03 (15–91) years. Of note, 28.3% (339) of the patients were aged ≥65years and 71.7% (859) were aged <65 years. The mean age of the patients was 47.97±11.76 (18–64) years in the <65 age group and 72.01±5.77 (65–91) years in the ≥65 age group. Female patients were significantly higher in number in both the elderly and young groups (p=0.006) (Table 1).

While most of the ASA I group patients were young, the majority of the ASA II group patients were in the elderly group and all ASA III patients were in the elderly group (p<0.001). The comorbid conditions, including cardiovascular disease, pulmonary disease, renal disease, and diabetes mellitus, were significantly more common in the elderly patients (p<0.001) (Table 1).

Although 15.36% of young patients had an episode of AC in the preoperative period, the rate of AC in elderly patients was 30.4% (p<0.001). Preoperative choledocholithiasis occurred in 2.79% of patients in the young group and 5.30% of patients in the elderly group (p=0.033). A history of preoperative pancreatitis was present in 0.93% of patients in the young group and 1.04% of patients in the elderly group. The rate of preoperative endoscopic retrograde cholangiopancreatography (ERCP) was 1.86% in the young group and 3.83% in the elderly group (p=0.045) (Table 1).

When the surgical diagnoses of patients in the elderly group were evaluated, the need for emergency surgery was observed to be higher owing to both AC and gallbladder perforation (p=0.038 and p=0.038, respectively) (Table 2).

The mean operation time was shorter in the young group than in the elderly group (80.45±26.71 and 88.14±33.87, respectively) (p<0.001). The need for emergency surgery was higher in the elderly group than in the young group [13.86% (47) and 9.31% (80), respectively] (p=0.021) (Table 3).

LC and OC were performed in 98.37% and 1.04% of patients in the young group, respectively, and in 92.62% and 3.53% of patients in the elderly group, respectively (p <0.001). The rate of conversion from LC to OC was 0.58% in the young group and 3.83% in the elderly group (p<0.001) (Table 3).



Table 1. Demographic data, clinical features, and associated diseases.

Age groups	<65 (n=859)	≤65 (n=339)	p
Sex (female/male)	605/254	211/128	0.006
Mean age	47.97±11.76	72.01±5.77	<0.001
ASA score			
I	610 (71.01%)	60 (17.69%)	<0.001
II	249 (28.98%)	269 (79.35%)	<0.001
III	0	10 (2.94%)	<0.001
Comorbidity			
Cardiovascular disease	196 (22.81%)	248 (73.15%)	<0.001
Pulmonary disease	23 (2.67%)	30 (8.84%)	<0.001
Renal disease	3 (0.34%)	5 (1.47%)	0.031
Diabetes mellitus	93 (10.82%)	86 (25.36%)	<0.001
Preoperative choledocholithiasis	24 (2.79%)	18 (5.30%)	0.033
Preoperative pancreatitis	8 (0.93%)	6 (1.76%)	0.224
Preoperative ERCP	16 (1.86%)	13 (3.83%)	0.045
Preoperative choledocholithiasis treatment without ERCP	9 (1.04%)	6 (1.73%)	0.311
Acute cholecystitis episode	132 (15.36%)	102 (30.4%)	<0.001
History of lower abdominal surgery	140 (16.29%)	49 (14:45%)	0.430
History of upper abdominal surgery	32 (3.72%)	11 (3.24%)	0.782

ASA: American Society of Anesthesiologists. ERCP: Endoscopic retrograde cholangiopancreatography.

Drain usage was more frequent in the elderly group than in the young group (10.02% and 4.65%, respectively) (p=0.001). The mean length of hospital stay was shorter in the young group that in the elderly group (1.06±0.36 days and 1.27±0.98 days, respectively) (p<0.001) (Table 3).

Incisional hernia, intestinal injury, bleeding, biliary leakage, and common bile duct injury were the complications that occurred during the postoperative period, and no significant difference was observed between the groups (Table 4).

Postoperative choledocholithiasis occurred at a rate of 0.46% and 1% in the young and elderly group, respectively. Only one patient in the young group developed postoperative pancreatitis. Postoperative ERCP requirement was 0.23% in the young group and 1.76% in the elderly group (p=0.003) (Table 4).

Table 2. Diagnoses.

	<65 (n = 859)	≥65 (n = 339)	p
Symptomatic cholelithiasis	759 (88.35%)	288 (84.95%)	0.110
Acute cholecystitis	77 (8.96%)	44 (12.97%)	0.038
Acalculous cholecystitis	1 (0.11%)	0	0.530
Gallbladder perforation	1 (0.11%)	3 (0.88%)	0.038
Polyp in gallbladder	17 (1.97%)	4 (1.17%)	0.342
Polyp + symptomatic cholelithiasis	4 (0.46)	0	0.208

Table 3. Surgery data.

		<65 years (n = 859)	≥65 (n = 339)	p
Anesthesia (GA/RA)		857/2	339/0	0.374
Duration of surgery (minutes)		80.45±26.71	88.14±33.87	<0.001
Type of surgery	Emergency	80 (9.31%)	47 (13.86%)	0.021
	Elective	779 (90.69%)	292 (86.14%)	
Additional Surgery		21 (2.44%)	19 (5.6%)	0.005
Hospital stay (days)		1.06 ± 0.36	1.27±0.98	<0.001
Method of surgery				
Open		9 (1.04%)	12 (3.53%)	<0.001
Laparoscopic		845 (98.37%)	314 (92.62%)	
Conversion to open surgery		5 (0.58%)	13 (3.83%)	<0.001
Drain Usage		40 (4.65%)	34 (10.02%)	0.001

GA: General anesthesia. RA: Regional anesthesia.

When the patient groups were compared, the factors that affected the duration of surgery in the elderly patient group were a high number of previous episodes, emergency surgery, conversion to open surgery, and a higher rate of initial open surgery decision. In addition, the length of hospital stay was longer for patients who developed complications. However, there was no significant difference in the length of hospital stay between patients with a history of previous surgery and a history of an episode of cholecystitis (p=0.618 and p=0.093, respectively) (Table 5).

DISCUSSION

Studies show that life expectancy is increasing in the world and in Turkey, where it has reached 65 years of age (9,10). Prevalence of gallbladder stone is 50% in patients aged 70 and over and gallbladder disease is the most common cause of



acute abdominal pain in elderly patients (11,12). In this retrospective study, 28.3% of patients who underwent surgery for primary GD between 2010 and 2018 were under the age of 65. These patients constituted almost one-third of the total number of patients operated for GD. Given the increase in the elderly population in the world and in Turkey, findings of the present study indicate that the number of elderly patients needing surgical intervention for GD will increase.

Fukami et al. (2014) reported that AC occurred with more severe inflammation in elderly patients, and for this reason, elderly patients had a longer recovery period after undergoing surgical treatment for AC. However, they stated that this did not make a difference in postoperative morbidity and length of hospital stay compared with young people (13). Huber et al. (1983) and Kuy et al. (2011) reported that the clinical outcomes of elderly patients requiring emergency cholecystectomy for GD were poor (14,15). In the present study, emergency cholecystectomy was performed in 13.86% of patients in the elderly group, and 44.7% of these patients were hospitalized for more than 1 day regardless of the type of surgery ($p<0.001$). This rate was 7.9% for elderly patients undergoing elective cholecystectomy. According to these results, both surgical procedure and presence of comorbidities in elderly patients undergoing emergency cholecystectomy adversely affect the length of hospital stay and recovery. Consistent with the literature, the results of the present study also showed that both the surgical process and the presence of comorbidities adversely affected the duration of hospital stay and time to recovery in elderly patients undergoing emergency cholecystectomy. In addition, in this study, the duration of hospital stay was significantly longer in the elderly patient group compared with the younger patient group in relation to the type of surgery, degree of urgency, and comorbidities ($p < 0.001$).

The frequency of AC episodes was significantly higher in elderly patients, but this did not affect the length of hospital stay. With the technological improvement of laparoscopy devices and the increase in surgical experience, the threshold of surgeons to convert to open surgery increases. Therefore, there is an increasing tendency to complete the surgery laparoscopically.

Elective cholecystectomy was performed in 32% of elderly patients in the study by Magnuson et al. (1997), whereas the rate was as high as 73.2% in the study by Majeski et al. (2004) (16,17). The reason for this was that all patients in their clinic with acalculous cholecystitis who had symptomatic cholelithiasis or whose gallbladder ejection fraction was <35% were scheduled for elective surgery (17). Nielsen et al. (2014) stated that age was independently associated with poor outcomes and that there morbidity and mortality rates will be low if patients with symptomatic gallstones undergo surgery before inflammatory complications occur (18). Yetkin et al. (2009) did not report a significant difference between elderly and young patients in terms of frequency of emergency surgery and found that the requirement for emergency surgery was more frequent especially in patients aged >80 years (19). A similar situation also affected the decision to convert from laparoscopy to open surgery (19). In our study, the rate of emergency cholecystectomy was 9.31% in young patients and 13.86% in elderly patients ($p=0.021$). Similarly, the rate of conversion to OC in the present study was 0.58% in young patients and 3.83% in elderly patients ($p<0.001$). We believe that early detection of the symptoms of GD and recommending elective surgery will enable patients to experience less morbidity during the postoperative period. No mortality was observed in patients in this study. Morbidities of patients were independent of their comorbidities, and no difference was observed between the young and elderly patient groups.

LC is considered to be the gold standard treatment for patients operated for GD; it has the advantages of less postoperative pain, short recovery period, fast return to normal activity, and good

cosmetic outcomes compared with OC (14). In most studies, this method has been recommended for elderly patients as well as for young patients (18-20). In most cholecystectomy studies, patients operated with closed surgery were reported to have lower mortality rates and shorter hospital stay, but primary OC is preferred more commonly in elderly patients. There as on for this is gallbladder disease being a more severe disease and the low threshold of surgeons for converting to open surgery during laparoscopy in elderly patients (19-21).

Fukami et al. (2014) stated that the most important reason for conversion to open surgery is the presence of a history of previous upper abdominal surgery. The second most common reason was reported to be the occurrence of perioperative cardiopulmonary problems (13). Therefore, they preferred to start the procedure primarily with open surgery in high-risk patients (13). Surgeons in the institution where these retrospective data were obtained were found to primarily prefer open surgery in patients with high cardiopulmonary risk undergoing delayed emergency surgery. In a Danish-based investigation by Majeski et al. (2004), the most common cause of conversion to open surgery was adhesion due to AC, whereas previous abdominal surgery and cardiopulmonary diseases were reported as the minor causes (17). Conversion to open surgery is reported to be between 3.6% and 25% in elderly patients according to various studies (17,18). Majeski et al. (2004) argued that there should be conversion to open surgery when Calot's triangle dissection is difficult and unsafe or when there is an accompanying intra-abdominal disease, and that the patient's age and accompanying medical diseases should not prevent the removal of the gallbladder using laparoscopic techniques (17). In our study, the rate of conversion to open surgery was 4.28% in elderly patients and 0.58% in young patients, and the most common reason for conversion to open surgery was adhesions arising from AC. Adhesions caused by previous abdominal surgery did not affect conversion to open surgery. Furthermore, conversion to open surgery did not occur due to cardiopulmonary causes. It was determined that the adhesions due to previous abdominal surgery did not affect the decision to convert to open surgery and there was no conversion to open surgery because of cardiopulmonary reasons.

In this retrospective study, it was found that surgeons evaluated the patients primarily with magnetic resonance cholangiopancreatography (MRCP) when bile duct stones were detected or suspected based on clinical, laboratory, and ultrasonography (US) findings before LC. It was determined that the surgeons referred our patients to ERCP for bile duct stones detected with this methodology. In the elderly group, 5.3% of the patients were evaluated with the preoperative diagnosis of choledocholithiasis, and 3.83% of these patients needed ERCP after MRCP. This rate was found to be significantly higher compared with the young patient group (2.79% vs. 1.86%, p = 0.045).

In a study investigating choledocholithiasis after LC, Anwar et al. (2004) reported that choledocholithiasis occurred in 2.5% of patients postoperatively, but only 1.84% of these patients with a clinically significant disease required treatment (22). In this study, postoperative choledocholithiasis was detected in 0.46% of patients in the young patients and in 1.17% of patients in the elderly group. In the young group, only two needed ERCP, whereas all elderly patients underwent ERCP. Postoperative ERCP requirement was higher in the elderly group patients (p= 0003). None of these patients had problems during follow-up after ERCP, and they did not require additional surgical procedures. The rate of postoperative ERCP requirement due to choledocholithiasis was 0.47% in all our patient groups.

In this study, the mean operation time was longer in the elderly group. When the patient groups were compared, it was observed that the high number of episodes and high number of patients



undergoing emergency surgery, conversion to open surgery or starting with open surgery in the elderly group were factors affecting the operation time in the elderly patient group. It was observed that the factors affecting the operation time were similar to those reported in the literature (6,8,17). Additionally, the surgeons' tendency to use laparoscopic surgery instead of open surgery with advances in and increasing experience on laparoscopic technology is among the factors reported in several studies (8,18,20). In addition, one of the reasons for prolonged duration of surgery was the need for performing additional procedures in the same session. Notably, 5.29% of patients in the elderly group and 2.44% in the young group underwent additional surgery (p=0.005).

Although it has been described in the literature that cholecystectomy without drainage is ideal, the use of closed drainage systems has traditionally been reported to allow early detection of possible injuries and leaks; however, there are no objective criteria on drain use (23,24). In a retrospective study of 250 patients who underwent elective LC, Gürer et al. (2013) reported that drainage was used in 20.4% of the patients, and when the patients were compared in terms of intra-abdominal fluid loculation in their postoperative follow-ups, it was found that drainage was not necessary (24). Kim et al. (2014) retrospectively evaluated 457 patients who underwent LC for acute inflammatory gallbladder disease and reported that drainage was used only when there was concern for bile leakage and the use of drainage did not affect morbidity and mortality (25). In the meta-analysis of Picchio et al. (2019), it was emphasized that insertion of drainage for suspected biliary leakage after laparoscopic cholecystectomies due to AC was unnecessary, but the authors indicated that it would be appropriate to prove this with high-quality randomized controlled studies (26). The complication rates after laparoscopic cholecystectomy in elderly patients were reported to be between 5% and 15% and mortality was reported to be between 0% and 1% (27,28). In this retrospective study, the complication rate was 1.16% in the young patient group and 1.76% in the elderly patient group, and there was no significant difference between the groups. In this institution, from which retrospective data were obtained, closed drainage systems are used for early postoperative detection of bile leakage not detected perioperatively after difficult cholecystectomies performed in the presence of severe infection, and for draining hemorrhage and inflammatory fluid accumulation. In the present study, drain usage was found to be higher in the elderly patient group because of the reasons mentioned (p = 0.001).

In this study, the length of hospital stay was found to be significantly longer in elderly patients who underwent emergency surgery, those who underwent open surgery, those who developed complications, those who underwent additional surgical procedures, and who had high ASA scores. The frequency of AC episodes was significantly higher in elderly patients but did not affect the length of hospital stay. The threshold of surgeons for conversion to open surgery has increased with technological improvements in laparoscopy devices and increase in surgical experience. Therefore, there is an increasing tendency to complete the surgery laparoscopically.

There are certain limitations of this study. Because of the retrospective nature of this study, the complications were evaluated based only on the complications encountered. This created a limitation in the comparison of the elderly and the young patient groups for the other complications reported in the literature. Another limitation was the referral of patients with high ASA scores (ASA 4–5) and patients in need of interventional radiology to another center. The absence of this patient group also had an effect on the low complication rates and no mortality in our sample. Additionally, because of missing data during the retrospective evaluation, certain classifications based on the Tokyo Guidelines could not be included in the

study. This situation both limited the formation of objective criteria for evaluating the severity of the disease and also led to a limitation in the classification of the surgical technique selected by the surgeons during surgery. In addition, the socioeconomic status of the patient group presenting to the hospital was middle to high because it is a foundation hospital. Therefore, the findings may not be generalizable to the Turkish society.

CONCLUSION

The rate of complications associated with cholecystectomy is similar between young and elderly patients provided that appropriate surgical preparation is performed. We determined that a high number and high severity of cholecystitis episodes and a history of previous surgery in elderly patients increased the rate of conversion to open surgery. Patients who undergo emergency surgery, open surgery, and additional surgery and have high ASA scores have a longer length of hospital stay. Our preferred method is open surgery in the presence of delayed emergency surgery and high comorbidity in the elderly patient group. Because of the aforementioned factors, the duration of hospital stays and return to daily activities is significantly longer in elderly patients than in younger patients. Within the bounds of these possibilities, surgical treatment for GD can be performed safely in elderly patients with low morbidity and mortality rates.

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RESEARCH

DEATH ANXIETY AND CONCEPT OF GOOD DEATH IN THE ELDERLY

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Abstract

Introduction: We aimed to determine what elderly individuals think about good death and their level of anxiety about death in order to guide people and families working with elderly individuals.

Materials and Method: 420 volunteer elderly participated in the study. Questionnaires were conducted using face to face interview technique. The measured values were calculated as arithmetic mean and standard deviation, while values determined by counting as number and percent. The significance of the difference between the means of the groups was evaluated using the T-test for 2-independent samples for two measured values, the One-Way ANOVA test for comparison of three and more measured variables, and the Tukey's post-hoc test for determining the factor that caused the significance.

Results: The importance given to psychosocial and spiritual aspect, personal control and clinical aspect of death were found to be high in elderly individuals, having a near death experience and having children are factors that increase death anxiety of elderly people. Elderly women have higher death anxiety, and death anxiety decreases with age. It was found that thinking of death frequently increases death anxiety.

Conclusion: As a decent and fair life befitting human dignity is an indispensable right for all people, decisions regarding the last period of life and the desire for a good death are equally indispensable rights for all people and all age groups, and applications in practice should be shaped according to these needs.

Key Words: Aged; Anxiety; Death; Attitude.

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INTRODUCTION

Although death and life are understood as opposing concepts, they actually constitute a whole in human life. Namely, death, which means the end of life, is also defined in some sources as the purpose of life and actually complements life. In different cultures, societies and disciplines, very different definitions of death have been made, which also vary depending on the personality, age, religion and cultural position of the individual. The common points in all these definitions include the loss of ability of the living organism to regenerate itself and the inevitable end of life by complete dysfunction of one or more vital organs. Individually and socially, death has never been viewed as a simple event (1-4). Death alone is a cause of concern both for the individual himself/herself and his/her relatives. Understanding the cause of this anxiety and knowing how to reduce it will comfort both the individual and the family emotionally. For this reason, studies have been carried out on people from all age groups on how they want to die in an attempt to determine what is important for people at the time of death. Consequently, although not spoken, people have some expectations about their own deaths, and meeting these expectations is one of the factors that reduce anxiety (3-7). Especially older individuals are more associated with the concept of death as they are closer to the end of their life expectancy, and it is a fact that mortality rate at younger ages is lower compared to that of the elderly. Knowing the thoughts of elderly people about the concept of good death and their anxiety levels about death is important for the relatives of the elderly and healthcare professional groups working with the elderly. Knowing the elderly individuals' wishes about death and providing them a death as they wish will reduce the spiritual burden on family and health personnel and allow them to deal with this situation more easily. Therefore, in this study, we aimed to determine what elderly individuals think about good death and their level of anxiety about death in order to guide people and families working with elderly individuals.

METHOD

Sampling

The population of the study consists of individuals aged 65 and over who live in the city center of Burdur. According to the address-based population registration system for 2018, the population of Burdur city center aged 65 and over is 12.378. In the study, the sample size was calculated as 378 individuals in Epi-info software with a 5% acceptable error level, 95% confidence interval and 50% probability of occurrence within the main mass. The questionnaires were applied using face-to-face interview technique to 420 volunteer participants aged 65 years and over who presented to the Burdur State Hospital outpatient clinics between April 01, 2017 and October 01, 2018.

Data Collection Tools

1. Socio-demographic characteristics data form: A questionnaire created by us including questions such as gender, age, marital status, number of children, family type, educational status, whether they think of death frequently, whether they had near-death experience (past heart attack, serious accident requiring long-term intensive care, a history of injury and/or surgery, having a fatal disease such as cancer, etc.).

2. Death Anxiety Scale (DAS): In the study, the Death Anxiety Scale (DAS) was used to determine anxiety levels of the elderly individuals; this scale was developed by Templer in 1970 (8), and its validity and reliability study for Turkish population was conducted by Akça (9).

3. Good Death Scale (GDS): The scale was developed by Schwartz et al. in 2003 to determine the concept and characteristics of a good death (10). The Turkish validity and adaptation of the scale, which consists of 17 questions and 3 sub-dimensions, was conducted by Fadıloğlu and Menekli (11).

Ethical Dimension of Research

Before initiating the study, ethical approval was obtained from the Mehmet Akif Ersoy University Non-Interventional Research Ethics Committee (No: GO2017/76).

Statistical Evaluation

The data obtained from the study were analyzed using the "SPSS 20.0 for Windows" software, and the measured values were calculated as arithmetic mean and standard deviation, while values determined by counting as number and percent. The significance of the difference between the means of the groups was evaluated using the T-test for 2-independent samples for two measured values, the One-Way ANOVA test for comparison of three and more measured variables, and the Tukey's post-hoc test for determining the factor that caused the significance. Cronbach's alpha was used to determine the consistency of the scales, the Pearson correlation method was used to determine the relationship between the scales, and the Kruskal-Wallis analysis was used for data without normal distribution.

RESULTS

When the demographic characteristics of the elderly participating in the study were examined, it was determined that 26.6% of the participants had a near-death experience (previous heart attack, conditions requiring long-term intensive care, having a fatal disease such as cancer), 53.6% of them were female, the mean age was 72.5±1.2, 99.1% of them had children, and 41.6% of them were educated at primary school level (Table 3).

Table 1. Elderly individuals' thoughts on death anxiety.

Answers for the Death Anxiety Scale	Correct n (%)
1. I am very afraid of dying.	301 (71,6)
2. I'm often troubled with the fact that time passes so fast.	236 (56,1)
3. I'm afraid when I think I will undergo surgery.	385 (91,6)
4. I often think about how short life really is.	320 (76,1)
5. Life after death worries me greatly.	380 (90,4)
6. I'm really afraid of having a heart attack.	400 (95,2)
7. Appearance of a corpse terrifies me.	51 (12,1)
8. Talking about outbreak of a world war scares me.	73 (17,3)
9. I'm afraid of dying in agony.	403 (95,9)
10. I'm not afraid of dying.	119 (28,4)
11. I feel there is nothing to fear for me in the future.	230 (54,7)
12. I don't have a particular fear of getting cancer.	227 (54)
13. I don't get nervous when people talk about death.	318 (75,7)
14. The thought of death never worries me.	65 (15,4)
15. The thought of death comes to my mind occasionally.	325 (77,3)



The DAS scores of the participants were examined, and the total death anxiety score was determined as 8.62±2.75 (moderate anxiety). The DAS Cronbach's alpha value was 0.804, and the consistency was found to be good. It was determined that more than 90% of elderly individuals were afraid of dying in agony, having a heart attack and having surgery (Table 1).

Table 2. Elderly individuals' view on concept of good death.

Answers for the Death Anxiety Scale		**Correct n (%)**	**Correct n (%)**
Psychosocial and spiritual subdimension (3.63±0.66)	Family and doctors observing one's wishes (4)	3,47	0,71
	Peaceful death (6)	3,83	0,62
	Presence of beloved ones (7)	3,68	0,63
	Meeting one's spiritual needs (8)	3,81	0,62
	Ability to accept death (9)	3,72	0,68
	Having a chance to complete one's important tasks (10)	3,89	0,78
	Having an opportunity to say goodbye to loved ones (11)	3,93	0,61
	Being at home (12)	3,22	0,78
Personal control subdimension (3.28±0.51)	Having intact mental functioning until death (15)	3,43	0,63
	Having control of bodily functions until death (16)	2,96	0,88
	Ability to communicate until death (17)	3,47	0,83
Clinical subdimension (3.41±0.81)	Having a painless or substantially painless death (1)	3,92	0,81
	Short death time (2)	3,37	0,76
	Sudden and unexpected death (3)	3,34	0,81
	Natural death without technical means (5)	3,11	0,68
	Death during sleep (14)	3,31	0,77

In this study, the consistency of the subdimensions of the good death scale, which was applied to determine which dimensions of death were given importance, was measured, and the Cronbach's alpha value was 0.888 for psychosocial and spiritual subdimension, 0.889 for personal control subdimension, and 0.823 for clinical subdimension, hence they were found to be quite consistent. It was determined that the importance given to psychosocial and spiritual aspect, personal control and clinical aspect of death, which are subdimensions of the scale, were found to be high in elderly individuals (Table 2).

Table 3. Factors affecting the concept of good death and death anxiety according to sociodemographic characteristics (Univariate analysis)

Sociodemographic Characteristics		Number-Percent n (%)	GDS Subdimensions			Death Anxiety
			Psychosocial & Spiritual	Personal Control	Clinical	
			Mean±SD	Mean±SD	Mean±SD	Mean±SD
Age	a.65-74 b.75-84 c.85 and above	256 (%60,9) 121 (28,8) 43 (10,3)	3,51±0,55 3,58±0,56 3, 60±0,48	3,37±0,68 3,25±0,61 3,25±0,51	3,48±0,67 3,46±0,62 3,36±0,61	9,82±2,69 8,99±3,02 7,56±3,16
		(p)	a-b=0,278 a-c=0,387 b-c=0,392	a-b=0,196 a-c=0,189 b-c=0,436	a-b=0,173 a-c=0,192 b-c=0,296	a-b=0,009 a-c=0,001 b-c=0,006
Gender	Male Female (p)	195 (46,4) 225 (53,6)	3,57±0,74 3,78±0,52 (0,005)	3,08±0,81 3,41±0,59 (0,002)	3,21±0,73 3,44±0,64 (0,004)	6,69±2,29 8,97±3,16 (0,005)
Income status	a. Less than expenses b. Equal to expenses c. More than expenses	56 (13,4) 324 (77,1) 40 (9,5	3,54±0,45 3,50±0,46 3,52 ±0,48	3,27±0,64 3,15±0,62 3,21±0,53	3,38±0,63 3,40±0,61 3,36±0,67	8,22±2,69 8,39±3,02 8,26±3,16
		(p)	a-b=0,478 a-c=0,362 b-c=0,322	a-b=0,563 a-c=0,186 b-c=0,391	a-b=0,216 a-c=0,196 b-c=0,288	a-b=0,716 a-c=0,821 b-c=0,842
Marital status	Married Single Divorced/Widowed	307 (73) 4 (0,9) 109 (26,1)	3,74±0,51 3,89±0,54 3,71±0,56	3,38±0,71 3,29±0,74 3,39±0,71	3,32±0,69 3,39±0,60 3,31±0,41	8,14±2,99 7,82±3,35 8,97±3,46
		(p)	a-b=0,338 a-c=0,197 b-c=0,480	a-b=0,356 a-c=0,361 b-c=0,342	a-b=0,123 a-c=0,344 b-c=0,112	a-b=0,268 a-c=0,198 b-c=0,212
Child	Yes No (p)	416 (99,1) 4 (0,9)	3,79±0,58 3,51±0,51 (0,001)	3,56±0,71 3,24±0,79 (0,001)	3,37±0,56 3,17±0,65 (0,004)	9,59±2,18 7,42±3,17 (0,003)
Educational status	a.Primary school b.Middle school c.High school d.University (p)*	175 (41,6) 165 (39,3) 44 (10,5) 36 (8,6)	175 (41,6) 165 (39,3) 44 (10,5) 36 (8,6) >0,05	3,39±0,88 3,25±0,76 3,18±0,68 3,20±0,43 >0,05	3,46±0,63 3,47±0,74 3,46±0,57 3,35±0,10 >0,05	7,64±2,53 8,70±3,09 8,60±3,33 7,95±3,89 >0,05
Thinking about death frequently	Yes No (p)	320 (76,1) 100 (23,9)	3,84±0,59 3,80±0,56 (0,973)	3,34±0,18 3,23±0,53 (0,694)	3,41±0,68 3,37±0,50 (0,783)	7,89±3,17 9,69±2,62 (0,001)
Near-death experience	Yes No (p)	112 (26,6) 308 (73,4)	3,96±0,67 3,11±0,45 (0,001)	3,33±0,67 3,26±0,51 (0,003)	3,44±0,62 3,31±0,46 (0,003)	9,52±2,85 7,87±3,09 (0,001
Total		420 (100,0)	3,64±0,56	3,25±0,75	3,47±0,66	8,94±3,05

According to our research results, having a near death experience and having children are factors that increase death anxiety of elderly people. Elderly women have higher death anxiety, and death anxiety decreases with age. It was found that thinking of death frequently increases death anxiety (Table 3).



Table 4. Factors affecting concept of good death and death anxiety (Multivariate analysis).

GDS Subdimensions			Death Anxiety B (95% CI) p
Psychosocial and Spiritual Dimension B (95% CI) p	Personal Control B (95% CI) p	Clinical B (95% CI) p	
Near-death experience: 0,355 (0,081-0,623) 0,001 Gender: 0,254 (0,067-0,252) 0,005 Child: 0,177 (0,017-0,340) 0,001	Near-death experience: 0,360 (0,076-0,613) 0,003 Gender: 0,444 (0,089-0,788) 0,002 Number of children: 0,227 (0,021-0,249) 0,001	Near-death experience: 0,399 (0,077-0,713) 0,003 Gender: 0,375 (0,118-0,527) 0,004 Child: 0,186 (0,077-0,393) 0,004	Near-death experience: 0,350 (0,087-0,719) 0,001 Gender: 0,415 (0,188-0,522) 0,005 Child: 0,196 (0,063-0,397) 0,003 Age: 0,296 (0,051-0,403) 0,003 Thinking of death frequently: 0371 (0,058-0,881) 0,001
Linear regression (backward regression): df: 14; R:0.41; R2: 0.19 Dubin Watson: 0.897, ANOVA; p=0.013	Linear regression (backward regression): df: 14; R: 0.47; R2: 0.21 Dubin Watson: 0.948, ANOVA; p=0.015	Linear regression (backward regression): df: 14; R:0.43; R2: 0.17 Dubin Watson: 0.823, ANOVA; p=0.017	Linear regression (backward regression): df: 14; R: 0.56; R2: 0.25 Dubin Watson: 1.972, ANOVA; p=0.011

In the study, it was found that according to the results of multivariate analysis, the importance given to all subdimensions of the concept of good death by female participants, those with near-death experience and those with children was statistically significantly higher (Table 4).

Table 5. Good Death Scale subdimensions and Death Anxiety correlations.

GDS Subdimensions and Death Anxiety	Mean	Standard Deviation	1	2	3	4
Psychosocial and spiritual subdimension (1)	3,63	0,66	1			
Personal control subdimension (2)	3,28	0,51	r= 0,78*	2		
Clinical subdimension (3)	3,41	0,81	r= 0,81*	r= 0,73*	3	
Death anxiety (4)	8,62	2,75	r= 0,51**	r= 0,47**	r= 0,53**	4

When the correlations of the good death scale subdimensions were examined, it was found that the correlations of all subdimensions with each other were positive and highly significant, and there was a positive and moderately significant relationship between the subdimensions and death anxiety (Table 5).

DISCUSSION

Death is one of the important issues that will continue to shape our lives as long as life itself continues to exist. Advances in science, technology and health have not eliminated people's helplessness, loneliness and anxiety in the face of death. Being aware that the end of life is approaching causes people to spend this period with despair and anxiety (2, 12).

Many studies have shown that age is the variable that is most associated with death anxiety. There are many studies that show that death anxiety decreases with increasing age in elderly individuals (1, 13). This aspect of our study is consistent with these studies in the literature (Table 3, $p \leq 0.005$)

In most studies on death anxiety and gender, as in our study, women's death anxiety was higher than that of men, and the difference was statistically significant (Table 3, $p \leq 0.005$) (14). Although the difference between anxiety scores was statistically insignificant in some of these studies, it was found that the mean score of women was higher than that of men (1, 15).

In some previous studies, the relationship between educational status, income and marital status and death anxiety was examined, and contradictory results were obtained (9, 15-17). In our study, we did not determine a statistically significant relationship between death anxiety and marital status, educational status and income in the elderly (Table 3, $p \geq 0.05$).

Studies have shown that the frequency of thinking about death increases death anxiety in the elderly (16,17). We have similarly found that as the frequency of thinking about death increases, death anxiety increases significantly in the elderly, and our findings are consistent with the literature (Table 3, $p \leq 0.001$).

In our study, unlike the other studies in the literature, we questioned whether the participants had children and had near-death experiences. We found that those with children ($p \leq 0.003$) and those with a near-death experience ($p \leq 0.001$) had a higher rate of death anxiety than those without (Table 3).

In our study, we investigated, along with death anxiety, how a good death should look like for elderly individuals. One's point of view on how a good death should look like is closely related to how one wants to spend his/her last moments. In many studies on good death, how a good death should be having been questioned in different age groups and cultures (3,4,12,18). In our literature review and research results, we have found that some topics on the idea of good death were the same for all societies and all segments of society. During the examinations of the answers to questions about the concept of good death in the clinical subdimension of the good death scale used in our study, we found that the highest score was received for the option "having a painless or substantially painless death" (3.92 ± 0.81) (19-22), which was consistent with the literature, while the highest score in the personal control subdimension was received for the option "ability to communicate until death" (3.47 ± 0.83) (21, 23), and in the psychosocial and spiritual dimension "having an opportunity to say goodbye to loved ones" (3.93 ± 0.61) (2, 12, 20); these results are consistent with the literature.

In our study, we found that as the importance given to all subdimensions of good death increased, the death anxiety increased positively, and all subdimensions of good death had a significant correlation among themselves (Table 5); all the answers given to all subdimensions were statistically significantly correlated with gender (female), having children and having near-death experience (Table 4). In these aspects, our study is consistent with the literature (10, 12, 22, 24). Although Schwartz found that the subdimensions of good death had a significant relationship with variables of age, income and marital status (10), in our study we did not determine a significant re-



lationship between subdimensions of good death and the variables of age, income, marital status, thinking of death frequently. We found no significant relationship between the dimensions (Table 3). We think that this is due to the fact that our research was limited only to elderly individuals. However, in the relevant literature on the subject, it can be seen that the relationship between good death and variables such as age, income, marital status, frequency of thinking about death and having near-death experience varies (7, 22, 24, 25).

Even though death is a concept existing in our lives like life, we do not like talking much about it. It seems that there is no definition of death that will fit all cultures and societies. Although there are many studies about anxiety and depression in elderly individuals in Turkey, there are very few studies on death anxiety, good death and the last period of life. Considering the average life expectancy in humans, studies conducted in order to explain death anxiety and how a good death should be from the perspective of elderly individuals, whom we see close to death, will be guiding for both families and professional groups working with the elderly since our research results have revealed that there are universal findings about how people want to spend their last moments, and the most important one is a painless death. As a decent and fair life befitting human dignity is an indispensable right for all people, decisions regarding the last period of life and the desire for a good death are equally indispensable rights for all people and all age groups, and applications in practice should be shaped according to these needs.

Disclosure Statement

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RESEARCH

CLINICAL CHARACTERISTICS AND FACTORS AFFECTING MORTALITY IN ELDERLY PATIENTS ADMITTED TO RESPIRATORY INTENSIVE CARE UNIT

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Abstract

Introduction: The number of geriatric patients being followed up in intensive care units (ICUs) has increased because of increased elderly population in our country and worldwide. This study aimed to investigate the clinical/laboratory features of patients aged over 65 years hospitalized in respiratory ICUs and to ascertain factors affecting mortality.

Materials and Method: Patients hospitalized in the respiratory ICU of Adnan Menderes University Medical Faculty between January 1, 2017 and January 1, 2018 were included. Patients aged 65 years and over were classified as the Elderly group, whereas those aged under 65 years were classified as the Non-Elderly group. The groups were compared for demographic, clinical, and laboratory characteristics. Parameters affecting mortality in the Elderly group were also evaluated.

Results: The mean age of 57 patients in the Non-Elderly group was 55.15 ± 9.57 years, and that of 101 patients in the Elderly group was 76.55 ± 7 years. In the Elderly group, urea and creatine levels were higher and pH was lower; the predicted mortality rate and Acute Physiology and Chronic Health Evaluation (APACHE) II score were higher; however, mortality rates were similar. Factors affecting mortality were hypoalbuminemia, high APACHE II score, and vasopressor requirement.

Conclusion: The albumin level, APACHE II score, and VP requirement are more important for prediction of mortality in respiratory intensive care patients when compared to age.

Key Words: Geriatrics; Mortality; APACHE.

INTRODUCTION

Human lifespan has concurrently prolonged with improvements in the field of health in the last century, which has progressively increased the number of elderly individuals (1). In Turkey, the population aged 65 years and over has increased by 16% in the last 5 years and reached 8.8% of the total population in 2018. It is estimated that this figure will be 10.2% by 2023 (2). With an increase in the elderly population, the frequency of presentation of elderly patients to health institutions, and therefore, hospitalization in either a hospital or ICUs has increased (3). Approximately 27% of the hospitalized patients aged 65 years and over have a requirement for ICU follow-up, and 21%–51% of patients admitted to ICUs are in the elderly age group (4, 5). In our country, there is a progressively increasing interest in data related to elderly population hospitalized in ICUs; however, the number of studies on this subject is limited (6-8).

We aimed to evaluate the demographic, clinical, and laboratory characteristics of elderly patients hospitalized and followed up in respiratory ICU and to ascertain factors affecting mortality in the elderly patients.

MATERIALS AND METHOD

The study was conducted by retrospective evaluation of data of 179 patients hospitalized in the respiratory ICU of Adnan Menderes University Medical Faculty between January 1, 2017 and January 1, 2018. The study was approved by the Non-invasive Clinical Research Ethics Committee of Adnan Menderes University, Turkey (Protocol number: 2019/97). The informant consent was not obtained because of the retrospective nature of the study. After excluding 21 patients with either missing data or an ICU stay less than 24 h, 158 patients were included in the study. The patients aged under 65 years were categorized as the Non-Elderly group and those aged 65 years and over as the Elderly group. Data of the patients such as age, gender, body mass index (BMI), comorbidities, diagnosis, the type and duration of ventilator treatment, vasopressor (VP) requirement, duration of hospitalization in ICU, the Acute Physiology and Chronic Health Evaluation (APACHE) II score, predicted mortality rate, and whether mortality had occurred or not were recorded. The APACHE II scoring system is one of the systems used in the determination of mortality rate and efficacy of treatment in ICUs (9). For calculating the APACHE II score, the most abnormal values obtained in the ICU within the first 24 h were considered. In addition to age, body temperature, mean arterial pressure, heart rate, respiratory rate, oxygenation (when fraction of inspired oxygen (FiO2) ≥ 0.5, alveolar–arterial gradient; when FiO2 < 0.5, partial oxygen pressure (PaO2)), serum bicarbonate (HCO3) value, serum sodium, potassium, and creatinine values, leukocyte count, hematocrit value, and the Glasgow Coma Scale score were used. The APACHE II score and the predicted mortality rate were calculated using computer software.

The biochemical parameters involving urea, creatine, alanine aminotransferase, aspartate aminotransferase, total bilirubin, direct bilirubin, protein, and albumin; the hematological parameters involving leukocyte, neutrophil, and lymphocyte counts, neutrophil/lymphocyte ratio (NLR), hemoglobin (Hb), platelet count, mean platelet volume (MPV), and red cell distribution width (RDW); and the blood gas parameters of the patients such as pH, PaO2, partial carbon dioxide pressure, oxygen saturation and HCO3, and also C-reactive protein (CRP), and procalcitonin values were recorded.

Statistical Analysis

Descriptive statistics for quantitative variables were specified as mean ± standard deviation for normally distributed variables and as median (25th–75th percentiles) for non-normally distributed variables. Descriptive statistics for qualitative variables were specified as frequency (%). Comparison between quantitative variables was analyzed by conducting Student t- or Mann–Whit-



ney U-test. The dependence between qualitative variables was determined by chi-square analysis. Logistic regression (LR) analysis was used to determine factors affecting mortality. A $p < 0.05$ was considered statistically significant.

RESULTS

The mean age of the patients was 55.15 ± 9.57 years in the Non-Elderly group and 76.55 ± 7 years in the Elderly group, consisting of 57 patients and 101 patients, respectively. Forty-one (71.9%) non-elderly patients and 69 (68.3%) elderly patients were male ($p = 0.635$). The two groups were similar in terms of BMIs ($p = 0.439$). The most common indications for hospitalization in both groups were pneumonia and exacerbation of chronic obstructive pulmonary disease (COPD) ($p = 0.770$ and $p = 0.655$, respectively). The presence of comorbidities had similar and very high rates in both groups (Non-Elderly group: 94.7%, Elderly group: 94.1%; $p = 0.583$). COPD, hypertension, and diabetes mellitus were the most common comorbidities in both groups, and the incidence of the comorbidities except that of heart failure (HF) was similar in both groups ($p > 0.05$). The incidence of HF was significantly higher in the Elderly group ($p = 0.006$) than in the Non-Elderly group. The mean duration of hospitalization was 14.68 ± 12.89 days in the Non-Elderly group and 16.43 ± 14.82 days in the Elderly group. Even though the duration of hospitalization was found to be relatively longer in the Elderly group, a statistically significant difference between the two groups was not present ($p = 0.580$). Invasive mechanical ventilation (IMV) was performed in 31 (54.4%) patients in the Non-Elderly group and in 46 (45.6%) in the Elderly group ($p = 0.286$). The mean number of days that the patients were kept intubated was 11.64 ± 10.05 days in the Non-Elderly group and 14.34 ± 16.77 days in the Elderly group ($p = 0.685$). Non-invasive mechanical ventilation (NIMV) was performed in 35 (61.4%) patients in the Non-Elderly group and in 74 (73.3%) in the Elderly group ($p = 0.122$). NIMV was performed for an average of 9.42 ± 10.03 days in the Non-Elderly group and for an average of 11.31 ± 8.68 days in the Elderly group ($p = 0.190$). While VP requirement occurred in 11 (19.3%) of non-elderly patients during their follow-up period, it was detected in 26 (27.7%) patients in the Elderly group ($p = 0.358$). The predicted mortality rate and the APACHE II score calculated during admission to the ICU were statistically significantly higher in the Elderly group ($p = 0.010$ and $p = 0.008$, respectively) then in the Non-Elderly group. Mortality occurred in 14 (24.6%) patients in the Non-Elderly group and in 30 (29.7%) patients in the Elderly group ($p = 0.489$). Demographic data of the patients are shown in Table 1.

Among the hematological, biochemical, and blood gas parameters analyzed during admissions of both groups of patients to the ICU, the urea and creatine values were statistically significantly higher, and the pH value was significantly lower in the Non-Elderly group compared with the Elderly group ($p = 0.004$, $p = 0.002$, and $p = 0.036$, respectively). The two groups were similar with respect to all the remaining parameters (Table 2).

When LR analysis was performed to determine the factors affecting mortality, hypoalbuminemia, increased APACHE II score, and VP requirement were found to be associated with mortality (sensitivity 63.3%, specificity 95.5%, and overall accuracy rate 83.2%) (Table 3).

DISCUSSION

The number of elderly patients followed up in ICUs has been progressively increasing because of an increased elderly population (3-5). In our study, 63.9% of patients in the respiratory ICU were aged 65 years and over. The ratio of elderly patients followed in ICUs differs from study to study conducted in our country. For example, Topeli et al. (6), in their study, reported that 48.6% of patients followed in ICU were aged 65 years and over; whereas, Doğan et al. reported it as 51% and Uysal et al.

Table 1. The demographic data of the Elderly and Non-Elderly Patient Groups.

Parameter	Non-Elderly Group (n:57)	Elderly Group (n:101)	p-value
Age [years]	55.15±9.57	76.55±7	<0.001
Gender n (M/F)	41/16	69/32	0.635
BMI [kg/m2]	24.16 (22.49-28.83)	24.91 (21.96-26.57)	0.117
Diagnosis n (%)			
Pneumonia	38 (66.7)	65 (64.4)	0.770
COPD	13 (22.8)	20 (19.8)	0.655
PTE	4 (7)	7 (6.9)	0.984
TBC	1 (1.8)	2 (2)	0.920
OHS	1 (1.8)	2 (2)	0.920
IPF exacerbations	0 (0)	3 (3)	0.189
Bronchiectasis	0 (0)	2 (2)	0.285
Comorbidities n (%)	54 (94.7)	95 (94.1)	0.583
Duration of hospitalization (days)	12 (5-18.5)	12 (6-20.5)	0.580
Vasopressor requirement n (%)	11 (19.3)	26 (25.7)	0.358
Predicted mortality rate	16.2 (10-26.3)	21 (11.4-35.6)	0.010
APACHE II score	13 (8.5-17)	15 (10.5-20.5)	0.008
IMV n (%)	31 (54.4)	46 (45.6)	0.286
The duration of staying intubated (days)	9 (4-15)	7.5 (2-15.25)	0.685
NIMV n (%)	35 (61.4)	74 (73.3)	0.122
The duration of NIMV (days)	7 (4-12)	9 (4.5-18)	0.190
Mortality n (%)	14 (24.6)	30 (29.7)	0.489

M/F: Male/female, BMI: Body mass index, COPD: Chronic obstructive pulmonary disease, PTE: Pulmonary thromboembolism, TBC: Tuberculosis, OHS: Obesity hypoventilation syndrome, IPF: Idiopathic pulmonary fibrosis, APACHE: Acute Physiology, Assessment and Chronic Health Evaluation, IMV: Invasive mechanical ventilation, NIMV: Non-invasive mechanical ventilation.

as 38% (7, 8). Similar ratios have been reported in studies conducted in countries other than Turkey. In the study conducted by Fuchs et al. (10), 45.7% of patients followed in ICU were aged 65 years or over; whereas, it was reported as 55% in the study by Angus et al. (11). In our study, the most frequent causes of hospitalization were pneumonia and COPD exacerbations (65.2% and 20.9%, respectively) in patients both over and below 65 years of age. Even though cardiovascular disorders have been reported as the leading cause of hospitalization of elderly patients in ICUs (3), patient population varies in accordance with the type of ICU. The most common diagnosis at admission was reported as pneumonia in a study which evaluated 3,050 patients who had been hospitalized in ICUs because of respiratory causes (12). Likewise, Akın et al. (13) reported that the most common diagnosis at admission was pneumonia in patients aged 65 years and over hospitalized in the medical ICU.



Table 2. The laboratory parameters of the Non-Elderly and Elderly Groups.

Parameter	Non-Elderly Group (n:57)	Elderly Group (n:101)	p-value
Urea (mg/L)	47 (30-66)	59 (38-95)	0.004
Creatine (mg/dL)	0.69 (0.54-0.83)	0.84 (0.63-1.3)	0.002
ALT (U/L)	21 (12.5-36.5)	15 (10.5-31)	0.154
AST (U/L)	23 (14.5-42.5)	21 (13.5-36)	0.104
T. Bilirubin (mg/dL)	0.6 (0.39-0.79)	0.6 (0.4-0.9)	0.493
D. Bilirubin (mg/dL)	0.28 (0.18-0.45)	0.32 (0.21-0.54)	0.598
Protein (g/dL)	5.65±0.89	5.72±0.85	0.597
Albumin (g/dL)	2.77±0.61	2.7±0.54	0.536
CRP (mg/L)	108.51±86.52	104.84±74.46	0.993
Procalcitonin (ng/mL)	0.59 (0.1-1.57)	0.26 (0.11-0.71)	0.826
Leukocyte (x103/µL)	11.98±6.39	13.3±6.3	0.196
Neutrophil (x103/µL)	10.12±5.93	11.25±62.6	0.241
Lymphocyte (x103/µL)	1.15 (0.5-1.62)	1000 (595-1475)	0.270
NLR	8 (5.28-17.29)	9.74 (5.79-17.69)	0.882
Hb (g/dL)	10.94±2.23	10.62±1.84	0.405
PLT (x103/µL)	224 (163.5-301)	256 (190.5-331.5)	0.419
MPV (fL)	9.73±1.31	9.79±1.07	0.598
RDW (%)	15.86±2.54	16.09±1.9	0.295
pH	7.42 (7.35-7.48)	7.39 (7.30-7.45)	0.036
PaO2 (mmHg)	64 (56.5-92.9)	67 (57-94)	0.981
PaCO2(mmHg)	43 (35.8-67.25)	48 (37.55-63)	0.860
HCO3 (mEq/L)	29 (25-34)	27 (23-31)	0.068
SaO2 (%)	92.5 (89-96)	93 (87.5-96.5)	0.259

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, T: Total, D: Direct, CRP: C-reactive protein, NLR: Neutrophil / lymphocyte ratio, Hb: Hemoglobin, PLT: Platelet, MPV: Mean platelet volume, RDW: Red cell distribution width, (PaO2): Partial oxygen pressure, (PaCO2): Partial carbon dioxide pressure, HCO3: Bicarbonate, (SaO2): Oxygen saturation.

Table 3. The laboratory parameters of the Non-Elderly and Elderly Groups.

Risk factor	OR	Lower	Upper	p-value
APACHE II	0.852	0.771	0.942	0.002
Hypoalbuminemia	23.430	4.504	121.871	<0.001
Vasopressor requirement	6.448	1.674	24.837	0.007

APACHE: Acute Physiology, Assessment and Chronic Health Evaluation

Because our study was conducted in the respiratory ICU, our patient population most commonly comprised patients hospitalized for pneumonia and COPD exacerbations.

Various studies have reported that the mortality rate is higher in elderly patients hospitalized in ICUs (7, 10, 14). In a study by Rosenthal et al. (15), age was reported to be related to mortality, independent of the severity of the disease and other prognostic factors. Likewise, in a study by Hamel et al. (16), it was reported that mortality increased with age after correction of various parameters such as gender, race, baseline functional status, disease severity, aggressiveness of treatment, and socio-economic status. However, even though the predicted mortality rate and the APACHE II score were significantly higher in patients aged 65 years and over in our study, the mortality rates of both groups were similar. There are also studies in the literature stating that age is not separately effective on mortality (13, 17, 18). In various studies, it has been reported that age was not associated with poor prognosis in ICU patients, and prognosis was more likely related to disease severity and functional status before the onset of the disease (19,20). We also consider that the severity of the underlying disease more likely affects mortality rather than age and believe that with appropriate treatment and follow-up, mortality in elderly patients would be the same as in young patients.

In our study, the mortality rate was found to be 24.6% in patients under 65 years of age and 29.7% in those aged 65 years and over; the overall mortality rate was 27.8%. Different mortality rates have been reported in the literature. In a study by Rockwood et al. (21), the 1-year mortality was reported as 31% and 49% under and over 65 years of age, respectively. In a study conducted by Topeli et al. (6), the mortality rate was found as 32.5% in patients younger than 65 years and 38.7% in patients aged 65 years and over. The higher mortality rates in these studies may be due to the heterogeneity of patients followed in ICUs. Moreover, the mortality rate in ICU varies according to the characteristics of the followed patient population and the experience of the healthcare staff. Following a similar patient group in ICU would contribute to achieve a more experienced ICU healthcare staff, which would cause a positive effect on patient recovery. In a study by Doğan et al. (7), it was determined that while the mortality rate was 54.6% in 2008, it decreased to 33.1% with turning over the management of ICU to Anesthesiology Department in 2009.

In our study, when the laboratory data were analyzed, it was found that the urea and creatine values were higher and the pH was lower in the Elderly group. We suggest that these may have originated from impairment of renal function and its related effect on blood gases with advanced age. It has been shown in the medical literature that renal functions and blood gas parameters



were affected in elderly patients (22). The association of hypoalbuminemia with mortality has been shown before (23). In our study, hypoalbuminemia was determined to be an effective factor in mortality, which was in accordance with the literature. The APACHE II scoring system is a significant predictor of mortality (9). In the study conducted by Rordorf et al., it was shown in intensive care patients that the APACHE II score was a predictor of mortality (24). In our study also, the elevation of the APACHE II score was determined to be a factor effective on mortality. The requirement of VP support in patients during the follow-up period in ICU indicates a hemodynamic disorder and has been reported to be associated with mortality (25). In our study also, we determined that the requirement of VP support affected mortality.

As a conclusion, we suggest that the albumin level, APACHE II score, and VP requirement should be used rather than age for prediction of mortality in patients followed up in the respiratory intensive care unit, and more detailed studies should be conducted on this subject.

Conflicts of interest

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

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RESEARCH

FORENSIC TRAUMATIC CASES IN THE GERIATRIC POPULATION

Abstract

Introduction: Physiological and metabolic changes arising in elderliness may increase the risk of trauma. The causes of trauma and trauma severity may vary with age. We aimed to determine the causes of trauma, traumatic lesions, and permanent damage status in the geriatric population by analyzing forensic trauma cases.

Materials and Method: Subjects were randomly selected from patients aged ≥65 years whose forensic evaluation was performed at the department of forensic medicine. The sample size was determined with Epi-Info version 7 software. SPSS Windows 20.0 software was used to analyze the data.

Results: Of the patients, 68.9% were male and 31.1% were female, with a mean age of 72.8 ± 6.11 years. Among them, 53.8% and 46.2% were exposed to trauma due to non-accidental causes and an accident, respectively. Such accidental injuries most commonly occurred due to traffic accidents (78%) and falls (16.7%), whereas non-accidental injuries most commonly occurred due to intentional injuries (96.1%). Accidental and non-accidental injuries were most commonly seen in females and males, respectively. The injury severity score was higher for accidental injuries. Minor and major injuries were observed in 95.1% and 4.9% patients, respectively, according to the injury severity score. Of the major injuries, 42.9% were in the head and neck region.

Conclusion: According to our results, non-accidental traumas in the geriatric population are similar to those in other age groups, whereas injuries due to falls increase in the former with a decrease in physiological reserves. Trauma severity appears to be more severe in accidental injuries.

Keywords: Geriatrics; Forensic Sciences; Wounds and Injuries; Violence; Accidents, Traffic.

INTRODUCTION

Physiological and metabolic changes occur in elder age. These changes increase the risk of trauma. Of those admitted to the emergency department because of trauma average 12% are >65 years (1-3). At the same time, 25%–28% of deaths in individuals aged ≥65 years are associated with trauma (4). The causes of trauma and trauma severity may vary with age. In the geriatric population, traumas such as pedestrian injuries due to traffic accidents and falls primarily occur in relation to a decrease in physiological reserves (5).

Studies evaluating forensic trauma cases in the geriatric population are relatively limited. The studies examining traumas in the geriatric population usually include data from single centres in secondary or tertiary care institutions. Furthermore, it is difficult to determine whether permanent disability develops in these cases because it requires a long follow-up period during the wound healing process. According to the Turkish Penal Code, medico-legal evaluations are made at the end of the wound healing process. All findings related to the traumas; to which the cases were exposed, are identified with medico-legal evaluation. The treatment of these cases has been completed in several different secondary or tertiary health care institutions, and the origin of the trauma (whether it was an accidental or non-accidental one) has been determined by the judicial authorities. Therefore, investigation of trauma cases in the geriatric population undergoing medico-legal evaluation may provide comprehensive information about the traumas of these cases. For these reasons, in this study, we retrospectively evaluated forensic trauma patients aged ≥65 years; who were admitted to the department of forensic medicine and who had undergone a forensic medical evaluation. We aimed to determine the causes of trauma, traumatic lesions, trauma severity, and traumatic permanent damage status specific to forensic cases in the geriatric population.

MATERIALS AND METHODS

Sample size

The sample size was initially determined to be 260 with Epi-Info version 7 software at a confidence interval of 99% with an expected prevalence of 12%. The sample size was determined as 286 cases found (6).

Patient selection

A total of 286 patients ≥65 years old who had undergone medico-legal evaluation because of trauma were randomly selected. Their age, gender, cause of trauma, traumatic lesions, injury severity, and permanent disability status were analyzed by scanning the year 2018 and earlier records of the Forensic Medicine Department of the Ataturk University. The injury severity score (ISS) is an anatomical trauma scoring system that best demonstrates mortality and morbidity in the geriatric population (7). The distribution of trauma according to anatomical regions and trauma severity in the patients were evaluated according to the ISS (8). Traumatic lesions were analyzed in terms of forensic medicine according to the guideline for the forensic evaluation of wounding crimes defined in Turkish Criminal Law.

Statistical analysis

Following data collection, the data were recorded in Microsoft Excel 2010 and SPSS Windows 20.0 software was used for data analysis. The normality test of the data was carried out with skewness and kurtosis values. The z-score was obtained by dividing the skewness and kurtosis values by their standard errors (9). Further, the percentage, mean, and standard deviation values of the data were calculated. The chi-square test was used to analyze comparisons between the groups, and the student's t-test was used to analyze the paired comparisons. A p-value < 0.05 was considered statistically significant.

This study was conducted in accordance with Good Clinical Practice guidelines and the princi-



ples of the Declaration of Helsinki. Ethics committee approval was obtained for this study (Ethics No: 26.09.2019/09).

RESULTS

Of the patients analyzed in this study, 68.9% (n = 197) were male and 31.1% (n = 89) were female. The oldest patient was 97 years old, and the mean age was 72.8 ± 6.11 years. Of the patients, 46.2% (n = 132) were exposed to trauma due to an accident, whereas 53.8% (n = 154) were exposed to trauma because of non-accidental causes. The causes of the patients' trauma are shown in Table 1.

When traumas caused by accidental and non-accidental causes were compared, it was found that the patients injured because of accidents were 2 years older than those injured because of non-accidental causes. Furthermore, accidental injuries were more common in females, whereas non-accidental injuries were more common in males ($p = 0.002$). The ISS was found to be higher for accidental injuries ($p < 0.001$). At the same time, it was found that bone fractures were more common in accidental injuries ($p < 0.001$), and patients who were injured because of accidents were mostly treated as inpatients ($p < 0.001$). The variables of accidental and non-accidental injuries are shown in Table 2.

When traumatic lesions in the patients were examined according to anatomical region, they were found to be located in a single anatomical region in 95% (n = 272) of cases and in multiple anatomic regions in 5% (n = 14) of cases. Of the isolated injuries, 56% (n = 152) were located in superficial regions of the cutaneous and subcutaneous tissue. Regarding the patients, 95.1% (n = 272) had minor injuries and 4.9% (n = 14) had major injuries according to the ISS. The severity of the injuries determined according to the ISS are shown in Table 3.

When the bone fractures were analyzed, it was found that 32.4% (n = 46) of patients had lower extremity fractures, whereas 12% (n = 17) had upper extremity fractures. The bone fractures detected in the patients are shown in Table 4.

According to the results of the forensic reports that evaluated to Turkish Panel Code 11% (n = 31) of the patients had a life-threatening injury [head

Table 1. Distribution of cases according to the causes of trauma.

		% (n)
Accidental injury	Traffic accident pedestrian	16.8 (48)
	Traffic accident-passenger	19.2 (55)
	Fall	7.7 (22)
	Industrial accident	1.4 (4)
	Injury-associated hypothermia	0.4 (1)
	Hot milk scald burns	0.4 (1)
	Hot water scald burns	0.4 (1)
Non-accidental injury	Physical assault	51.6 (148)
	Firearm injury	0.7 (2)
	Stab wounds	1.4 (4)

Table 2. Evaluation of accidental with non-accidental injury.

Variables		Accidental injury	Non-accidental injury	p-value
			% (n=132)	% (n=154)
Age	Mean (±sd)	73.9 (±6.6)	71.8 (±5.4)	0.002
Gender	Male	41.1 (81)	58.9 (116)	0.011
	Female	57.3 (51)	42.7 (38)	
Trauma severity	Mean ISS score (±sd)	6.6 (±7.3)	2.29 (±4.4)	<0.001
	ISS 0-15	42.9 (111)	57.1 (148)	<0.001
	ISS 16 <	77.8 (21)	22.2 (6)	
Bone fracture	No	31.7 (59)	68.3 (127)	<0.001
	Yes	73 (73)	27 (27)	
The hospitalization	No	32.8 (67)	67.2 (137)	<0.001
	Yes	79.3 (65)	20.7 (17)	

Table 3. Localization and severity of traumatic injuries according to the ISS scor.

	Location of trauma	Mean the ISS score	Minor trauma [a]	Major trauma [b]
			% (n)	% (n)
Isolated	Head or neck	16	3.1 (9)	2.1 (6)
	Face	2.4	6.3 (18)	
	Thorax	13	5.6 (16)	
	Abdominal or pelvic content	9	0.3 (1)	
	Ekstremities or pelvic girdle	5.7	19.2 (55)	
	Skin and the subcutaneous tissue	1	57.3 (167)	
Multiple	Head or neck, Face		0.7 (2)	0.3 (1)
	Face, Thorax		0.3 (1)	0.3 (1)
	Head or neck, Abdominal or pelvic content			0.3 (1)
	Head or neck, Ekstremities or pelvic girdle			0.3 (1)
	Thorax, Ekstremities or pelvic girdle			0.3 (1)
	Face, Ekstremities or pelvic girdle		0.7 (2)	
	Ekstremities or pelvic girdle, Skin and the subcutaneous tissue		0.3 (1)	
	Face, Thorax, Ekstremities or pelvic girdle			0.3 (1)
	Head or neck, Face, Thorax, Ekstremities or pelvic girdle			0.7 (2)
	Total		95.1 (272)	4.9 (14)

a: Cases with ISS score between 0-15, b: Cases with ISS score of 16 or higher (8).



Table 4. . Distribution of the bone fractures detected in the cases.

Facial bones	29 (20.4)
Femur	18 (12.7)
Tibia-fibula	16 (11.3)
Ribs	15 (10.6)
Cranium	13 (9.2)
Radius-ulna	11 (7.8)
Vertebral colon	10 (7)
Foot-ankle	10 (7)
Pelvis	5 (3.5)
Clavicle	5 (3.5)
Hand-wrist	4 (2.8)
Humerus	2 (1.4)
Scapula	2 (1.4)
Patella	2 (1.4)
Total[a]	142 (100)

a: Some cases have more than one fracture. Therefore, the number of fractures is higher than the number of cases.

and neck region (n = 19), thoracic region (n = 11) and abdomen region (n = 1)]. From the forensic aspect, 9.5% (n = 29) of all patients and 26% (n = 26) of those with a bone fracture were found to have permanent damage. Of all the cases of permanent damage, 80% (n = 23), 10% (n = 3), 7% (n = 2), and 3% (n = 1) were developed because of limited range of motion, craniectomy defects, paraplegia, and loss of vision, respectively. It was found that permanent damage was primarily caused by accidental injuries and fractures of the long bones of the extremities ($p < 0.001$).

DISCUSSION

As the age increases, geriatric individuals experience a decrease in perception and attention, mental and motor activity, sensory functions such as vision and hearing, and postural structure impairment. These pathophysiological changes cause elderly individuals to become exposed to more trauma (5). Although the female population is higher in the geriatric age group, the incidence of trauma is higher in males (10, 11). In the present study analyzing forensic trauma cases in the geriatric population, the number of male patients was found to be higher. More exposure to trauma in males may be associated with a more active social life. In addition, another factor that increases the risk of exposure to trauma in the geriatric population is increased opportunities for active living (12, 13).

Traffic accidents and falls are the most common causes of accidental trauma in the geriatric population, and pedestrian injured due to traffic accidents are more commonly seen in the this population (14-17). In our study, traffic accidents were the most common cause of injury because of accidents, and the number of patients facing pedestrian injured due to traffic accidents was slightly higher. Among the accidental injuries, the second most common cause was found to be falls. Falls and domestic accidents are considered indicators of balance disorders, visual problems, and other neurological problems in the geriatric age group (18). The frequency of traffic accidents and falls increases in the geriatric age group (15-17). Other accidental injuries identified in our study such as occupational accidents, hot water scald burns, and milk scald burns were also determined to be traumas associated with physiological disabilities. In our study, it was found that the patients injured because of accidents were 2 years older than those injured because of non-accidental causes. Accordingly, we can speculate that traumatic injuries due to accidents increase with age.

The other group, consisting of 53.8% of the patients, had faced non-accidental injuries. In studies investigating forensic medical evaluation cases, it can been seen that non-accidental injuries such as physical assault, sharp object injuries, and gunshot injuries account for approximately half of the traumas in all age groups (11, 19). In the geriatric

population, physical assault seems to be the most common cause of non-accidental trauma.

According to the ISS anatomical trauma scoring system, 95.1% of the patients had minor traumas primarily located in superficial regions of the cutaneous and subcutaneous tissues. Although the number of major injuries was low, they were most commonly located in the head and neck region. In line with the literature, minor traumas were mostly detected in cases of physical assault, whereas major traumas were mostly identified in traffic accidents (18). Traffic accidents result in high-energy traumas, leading to more bone fractures, more major trauma, and more inpatient treatment of patients. Although the number of minor traumas is higher, minor traumas due to increased comorbidity in the elderly may result in more serious consequences and higher rates of mortality and morbidity (20-22). In geriatric traumas, the most important cause of death is head trauma (23). In our study, major injuries were most commonly located in the head and neck region, and, from the forensic aspect, the majority of life-threatening injuries were also identified in this region.

Traumas are one of the major causes of permanent damage development in the musculoskeletal system (24). It has been stated that the rate of anatomic loss or functional impairment arising in elderly individuals because of traumatic causes varies between 25% and 47%, and these patients cannot return to their pre-event conditions (25). In our study, we found permanent damage in 9.5% of the geriatric population according to forensic medical evaluation. A significant portion of the permanent injuries was a limited range of motion due to extremity and pelvic bone fractures. The rates of permanent damage that we determined in the patients with bone fractures were similar to those in the literature (11). According to forensic medical evaluation, an organ or extremity identified as traumatized should have lost at least 10% of its anatomic structure and/or function to be considered permanently damaged. With increasing comorbidity in the geriatric population, nearly complete recovery may not be possible, especially in skeletal system fractures. Therefore, the rate of permanent damage in the geriatric population may be even higher when patients with less anatomic loss or functional impairment are included.

In conclusion, according to our results, the most common cause of non-accidental trauma in the geriatric population is physical assault, which has a similar rate in all age groups. Furthermore, pedestrian injured due to traffic accidents and fall-related traumas are the major causes of accidental injuries in the geriatric population. Sensory, perceptual, and physical disabilities developing with increasing age make older individuals more vulnerable to environmental dangers. With increasing comorbidity, traumas may result in more severe consequences. Measures taken for the living space and in consideration of the physiological disability of the geriatric population can reduce the rates of accidental traumas and disabilities.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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RESEARCH

EVALUATION OF EPICARDIAL FAT AND CAROTID AND FEMORAL INTIMA-MEDIA THICKNESSES IN GERIATRIC PATIENTS WITH END-STAGE RENAL DISEASE

Abstract

Introduction: Although atherosclerotic cardiovascular diseases and cardiovascular risks are known to increase in patients with end-stage renal disease, it is not clear whether these risks increase in the geriatric patient population as well. This study aims to evaluate these risks in geriatric patients with end-stage renal disease by evaluating epicardial fat and carotid and femoral intima-media thicknesses, known as markers, for subclinical atherosclerosis and cardiovascular risks.

Materials and Methods: This cross-sectional study included 52 patients who started to receive chronic hemodialysis treatment after the age of 65 years (mean age 73.92±5.63) years with end-stage renal failure and 51 healthy volunteers (mean age: 74.49±4.63 years). Epicardial fat and carotid and femoral intima-media thicknesses were measured and compared between these groups.

Results: Carotid intima-media and epicardial fat thicknesses were significantly higher in the patient group than in the control group (0.91±0.08 vs. 0.71±0.1 mm, p<0.001 and 0.84±0.17 vs. 0.75±0.17 cm, p=0.01, respectively). However, no significant difference was observed in femoral intima-media thickness between the two groups (0.58±0.07 vs. 0.56±0.97 mm, p=0.266). Correlation analysis revealed a significant positive correlation between the duration of dialysis and epicardial fat and carotid intima-media thicknesses (r=0.611, p<0.001 and r=0.337, p=0.015, respectively). Furthermore, regression analysis revealed a significant relationship between the duration of dialysis and carotid intima-media thickness (β=0.657, p=0.001).

Conclusion: Epicardial fat and carotid intima-media thicknesses increase in geriatric patients with end-stage renal disease but with no significant changes in femoral intima-media thickness, indirectly suggesting that subclinical atherosclerosis and cardiovascular risks are increased in these patients.

Keywords: Atherosclerosis; Echocardiography; Kidney disease; Ultrasonography.



INTRODUCTION

Chronic renal failure has recently become a common public health problem in the elderly population (1). Despite diagnostic and therapeutic advancements, the number of patients with end-stage renal disease (ESRD) requiring renal replacement therapy is increasing every year. Therapeutic advancements and prolonged patient survival cause an increase in geriatric population in this patient group (2-3). Cardiovascular diseases are the most important cause of mortality and morbidity in patients with ESRD. The most common group of cardiovascular diseases observed in this patient group is atherosclerotic cardiovascular diseases (ASCVD) (4).

The epicardial adipose tissue is the adipose tissue found between the visceral pericardial layer of the heart and myocardium. The success of using the thickness of this tissue for determining cardiovascular risks has been demonstrated in many studies (5). Similarly, carotid intima-media thickness (CIMT) and femoral intima-media thickness (FIMT) are parameters that demonstrate the risk of subclinical atherosclerosis and successfully predict the risk of cardiovascular events in many studies (6-7).

Although the risk of ASCVD is increased in all patients with ESRD, it is not clear how this risk occurs in geriatric patients. Therefore, this study aims to evaluate the risks of subclinical atherosclerosis and cardiovascular events in geriatric patients with ESRD by evaluating epicardial fat thickness (EFT), CIMT and FIMT, which are considered to be the predictors of these risks.

MATERIAL AND METHODS

The study was designed as a cross-sectional study. The records of patients receiving chronic hemodialysis treatment at the outpatient clinic of hospital were examined. A total of 52 patients who started to receive chronic hemodialysis treatment after the age of 65 years and 51 healthy volunteers (control group) with similar demographic characteristics were included. The healthy participants had normal findings in treadmill test, myocardial perfusion scintigraphy, and coronary computed tomography (CT) that were conducted in the last one-year.

Exclusion criteria: Patients <65 years of age; those with known ASCVD (coronary artery disease, previous cerebrovascular event, or peripheral artery disease), patients who started to receive chronic hemodialysis treatment before the age of 65 years, hypertension, diabetes mellitus, known malignancy, chronic liver disease, connective tissue disease, hypothyroidism, hyperthyroidism, chronic steroid use, severe heart-valve disease or heart failure, history of heart surgery or smoking, familial hyperlipidemia, autoimmune disease, chronic renal failure and receiving peritoneal dialysis, and previous renal transplantation; or those with insufficient image quality or refusal to participate in the study were not included.

The participants in the patient group were diagnosed with chronic renal failure by a nephrologist according to the guidelines (8). Standard 2-dimensional (2D) echocardiography was performed by a cardiologist, and EFT was measured and recorded. CIMT and FIMT measurements were performed by radiologists. The selection of the patients and control group individuals was conducted by a nephrologist. Cardiologist and radiologist who measured EFT, CIMT and FIMT were blinded to the study.

Baseline demographic, anthropometric, and laboratory values of the participants in both groups were measured and recorded. EFT, CIMT and FIMT were recorded, and the differences between the two groups were evaluated for statistical significance.

Routine 2D echocardiography, conventional spectral Doppler ultrasonography, and epicardial fat thickness data

A Philips EPIQ 7 (Seattle, U.S.A) ultrasound system and Philips X5-1 (Seattle, U.S.A) probe (broadband transducer) were used for echocardiographic

evaluations. The evaluations were performed using standard 2D and Doppler evaluations according to the recommendations of the American Society of Echocardiography and European Association of Cardiovascular Imaging. The ejection fraction (EF) was calculated using the modified Simpson method (9).

EFT is defined as the echo-free area between the free wall of the myocardium and the visceral layer of the pericardium. In this study, EFT was measured in the parasternal long-axis imaging at the end of the diastole and at three cardiac beats, perpendicular to the right ventricular free wall (Figure-1A) (10).

Carotid and femoral ultrasonography

A Siemens Acuson S1000 (Erlangen, Germany) ultrasound system and Siemens 9L4 (Erlangen, Germany) probe (broadband transducer) were used for ultrasonographic evaluations. CIMT was manually measured from the far walls of left and/or

Figure 1. Measurements of epicardial fat thickness on the free wall of the right ventricle from the parasternal long-axis views (A) and carotid (B) and femoral (C) intima-media thicknesses at the far wall of common carotid/femoral arteries.

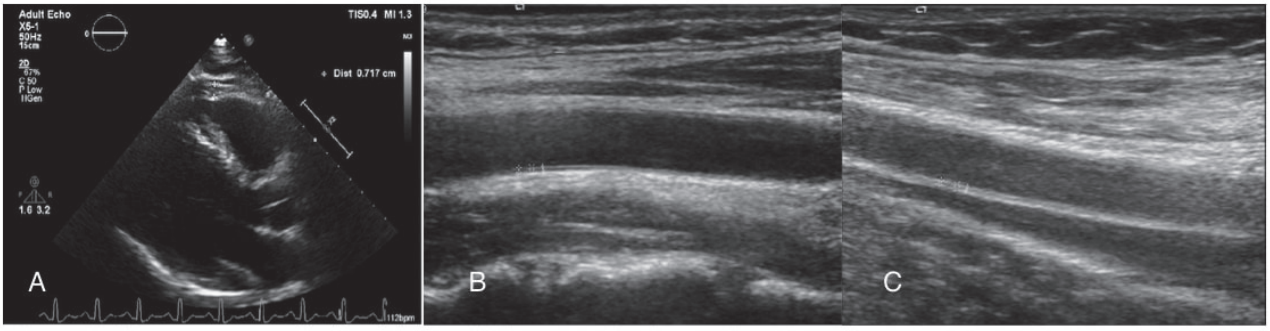
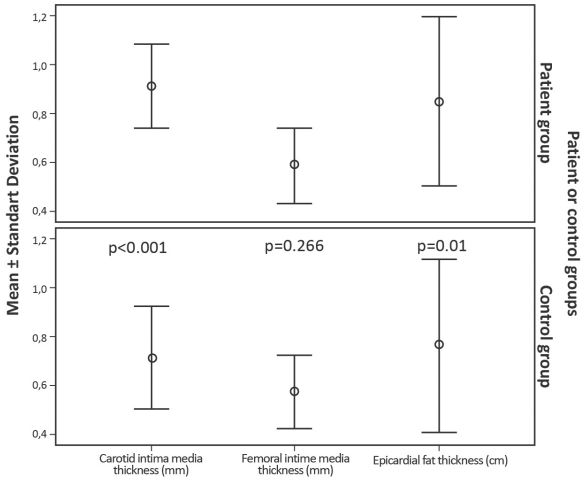


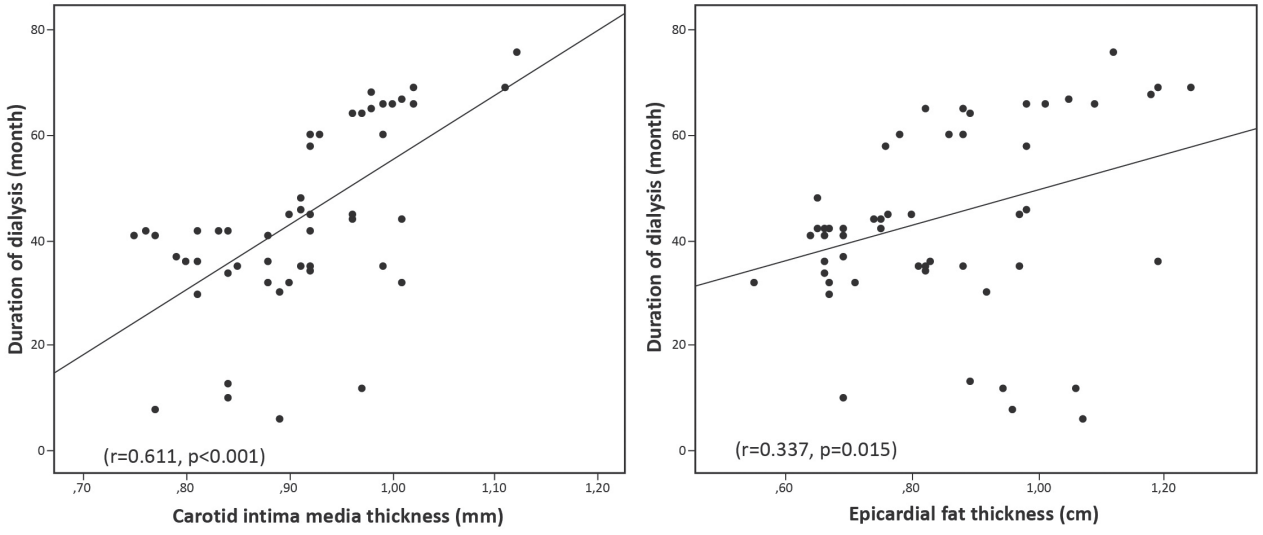
Figure 2. Comparison of carotid and femoral intima-media and epicardial fat thickness measurements between the groups.



right common carotid arteries (opposite side of arteriyovenous dialysis fistula for patient group, both side for control group), at a region 10 mm proximal to the carotid bifurcation. Measurements were conducted on B-mode duplex ultrasound in a longitudinal plane. CIMT was measured on this image at three adjacent sites, 1 mm apart (Figure-1B). In addition, on B-mode duplex ultrasound, the mean FIMT at the far wall of the left or right common femoral arteries (opposite side of arteriyovenous dialysis fistula for patient group, both side for control group), was manually measured manually at three adjacent sites, 1 mm apart (Figure-1C).

The study was conducted in accordance with the criteria of the Helsinki Declaration, and approval was obtained from the local ethics committee (KA19/259). After providing detailed information about the study, written informed consent was obtained from all participants.

Figure 3. Correlation analyses between carotid intima-media and epicardial fat thicknesses and the duration of dialysis.



Statistical analyses

All parameters were evaluated using SPSS software (SPSS version 21.0; SPSS Inc., Chicago, IL, USA). Continuous variables were tested for normal distribution using Kolmogorov–Smirnov test. The results, including normally distributed variables, were expressed as mean ± standard deviation; whereas on-normally distributed variables were expressed as medians and interquartile ranges. Categorical variables were shown as absolute values and percentages. Independent sample t-test was used to compare the two groups with respect to the variables with normal distribution and homogeneous group variance. The variables that showed a non-homogenous distribution were compared using the Mann–Whitney U-test. Categorical variables, such as clinical characteristics, of the groups were compared using the chi-square test. Spearman's or Pearson correlation tests were used to determine the degrees of association between continuous variables. Independent determinants of variables were determined using standard multiple linear regression analysis.

RESULTS

A total of 103 individuals, including 52 patients with ESRD (mean age: 73.92±5.63 years) and 51 healthy volunteers (mean age: 74.49±4.63 years), were included in this study. There was no statistically significant difference between patient and control groups in terms of baseline clinical characteristics ($p>0.05$). The clinical characteristics of both groups are shown in Table I.

Both CIMT and EFT were significantly higher in patient group than in the control group (0.91±0.08 vs. 0.71±0.1 mm, $p<0.001$ and 0.84±0.17 vs. 0.75±0.17 cm, $p=0.01$, respectively). However, there was no significant difference in FIMT between the two groups (0.58±0.07 vs. 0.56±0.97 mm, $p=266$). Figure-2 shows the comparison of CIMT, FIMT and EFT measurements between the groups.

Table II shows the results of correlation analyses and linear regression analysis between age, body mass index, systolic blood pressure, diastolic blood pressure, fasting plasma glucose, EF, duration of dialysis, low-density lipoprotein (LDL), high-den-

Table 1. Baseline clinical characteristics of the study population.

	Patients (n=52)	Control (n=51)	p
Age (years)	73.92±5.63	74.49±4.63	0.579
Sex, female gender, n (%)	23 (44.23)	19 (37.25)	0.471
Body mass index (kg/m2)	23.35±2.58	23.49±2.28	0.779
Hemoglobin (gr/dL)	11.19±0.99	11.47±0.87	0.144
White blood cell (/mm3)	7931±1131	7841±1061	0.678
Platelets (100/mm3)	310 (IQR=53)	315 (IQR=46)	0.229
Na (mmol/L)	136.15±2.87	136.24±2.77	0.884
K (mmol/L)	3.94±0.34	3.9±0.27	0.553
EF (%)	55.33±2.94	55.08±1.92	0.613
LDL (mg/dL)	131.19±9.4	131,65±10.17	0.814
HDL (mg/dL)	42.23±3.64	41.45±3.83	0.292
Triglyceride (mg/dL)	148 (IQR=60)	141 (IQR=56)	0.157
SBP (mmHg)	130.08±12.13	127.25±11.71	0.233
DBP (mmHg)	65±6.1	62.84±7.76	0.121
CRP (mg/L)	2.76±1.18	2.6±1.09	0.474
Heart rate (beat/min)	78.83±9.84	75.55±10.26	0.101
ALT (U/L)	31.17±4.84	30.69±4.87	0.612
FPG (mg/dL)	102.58±9.34	101.92±9.67	0.727

ALT: Alanine aminotransferase, CRP: C-reactive protein, DBP: Diastolic blood pressure, EF: Ejection fraction, FPG: Fasting plasma glucose, HDL: High density lipoprotein, IQR: Interquartile range, K: Potassium, LDL: Light density lipoprotein, Na: Sodium, NA: Non available, SBP: Systolic blood pressure.

sity lipoprotein, triglyceride, hemoglobin, C-reactive protein, and CIMT and EFT measurements. Correlation analysis showed a statistically significant positive correlation between the duration of dialysis and CIMT and EFT, as shown in Figure-3 ($r=0.611$, $p<0.001$ and $r=0.337$, $p=0.015$, respectively). No significant correlation was observed between other variables. Moreover, in multiple linear regression analysis, there was a statistically significant relationship between the duration of dialysis and CIMT ($\beta = 0.657$, $p=0.001$). No significant relationship was found between other variables.

DISCUSSION

This is the first study that evaluates CIMT, FIMT and EFT in geriatric patients ESRD. Our study demonstrated that EFT and CIMT were significantly higher in the patient group than in the control group; however, there was no statistically significant difference between the two groups in terms of FIMT, suggesting indirect cardiovascular risks may be higher in geriatric patients with ESRD. However, the development of atherosclerosis in carotid arteries may occur earlier than the development of atherosclerosis in femoral arteries in this patient group.

Table 2. Correlation and multiple linear regression analysis of epicardial fat and carotid intima media thicknesses and various clinical variables.

	Correlation analysis				Multiple linear regression analysis			
	EFT		CIMT		EFT		CIMT	
Variables	r	p	r	p	β	p	β	p
Age	-0.148	0.296	0.103	0.469	-0.038	0.784	0.027	0.851
BMI	0.075	0.595	-0.14	0.324	0.076	0.611	-0.085	0.571
SBP	0.215	0.126	-0.087	0.538	0.124	0.557	-0.113	0.59
DBP	0.194	0.168	-0.041	0.771	0.052	0.805	-0.007	0.975
FPG	0.116	0.413	0.241	0.085	0.08	0.589	0.264	0.075
EF	0.139	0.325	-0.142	0.315	0.019	0.911	-0.016	0.926
DD	0.337	0.015	0.611	<0.001	0.32	0.072	0.657	0.001
LDL	0.165	0.243	-0.105	0.458	0.106	0.488	-0.061	0.689
HDL	0.257	0.066	0.23	0.101	0.097	0.643	0.175	0.409
TRG	0.054	0.702	0.041	0.775	0.109	0.385	0.012	0.923
Hb	0.094	0.507	-0.07	0.624	0.094	0.507	-0.493	0.624
CRP	0.225	0.108	-0.054	0.704	0.225	0.108	-0.054	0.704

BMI: Body mass index, CRP: C-Reactive protein, DBP: Diastolic blood pressure, DD: Duration of dialysis, EF: Ejection fraction, FPG: Fasting plasma glucose, Hb: Hemoglobin, HDL: High density lipoprotein, LDL: Light density lipoprotein, SBP: Systolic blood pressure, TRG: Triglyceride.

It has been known for many years that cardiovascular risk is increased in patients with chronic renal failure (11). In recent years, in addition to traditional risk factors, impaired renal function is considered to be a risk factor for coronary artery disease and cardiovascular event development (12). However, it is not clear why cardiovascular risks increase in patients with renal failure. Chronic inflammation, oxidative stress, and increased angiogenesis could be the reason for the increased risk of atherosclerosis in these patients (12). A study showed that proinflammatory cytokines are released more than epicardial fat tissue in patients with coronary artery disease (13). Many studies have demonstrated an increase in EFT in patients with ESRD (14-15). The cytokines released from the epicardial adipose tissue directly adjacent to the coronary arteries in the epicardial region may cause an increased risk of atherosclerosis and thus an increased risk of cardiovascular events. Oxidative stress is another mechanism responsible for increased risk other than infiltration. Previous studies have shown a positive correlation between EFT and serum oxidant content and a negative correlation with anti oxidant content (16-17).

Echocardiography, CT, and magnetic resonance imaging (MRI) are three different imaging methods that can be used to measure epicardial adipose tissue thickness. Each of the three imaging methods has its advantages and disadvantages. Among these methods, echocardiography is the most preferred method because it is economical and easily accessible and does not use radiation. The disadvantage, however, is that it is operator-dependent and allows only 2D evaluation. Moreover, it is impossible to obtain a healthy echocardiographic

evaluation in obese people and individuals with poor image quality (10,15,18). MRI is the gold standard method for the evaluation of epicardial fat. The advantages include the measurement of total adipose tissue, absence of radiation, and use of contrast media. The disadvantages are that it is expensive, not easily accessible, and cannot be used in patients with cardiac devices and implants. The advantages of CT, with high sensitivity and specificity in epicardial adipose tissue measurement, include allowing the measurement of total adipose tissue and a direct assessment of cardiovascular risk by calculating coronary calcium score. The main disadvantage is the use of radiation as well as nephrotoxic contrast agents in its application (18).

CIMT is another marker showing the risk of subclinical atherosclerosis. Its success in predicting cardiovascular events has been demonstrated by many studies (6). There are many mechanisms responsible for increasing the risk of atherosclerosis in ESRD, such as sharing the same risk factors, increased inflammation, renin–angiotensin and over-activation of the sympathetic system, and degradation of LDL oxidation (19).

Although MRI and CT can be used to evaluate carotid plaques and intima-media, ultrasonography is the most commonly used diagnostic method, which is considered to be a low-cost, noninvasive, and easily applicable imaging method. Carotid MRI, which has higher reproducibility than ultrasonography, has several disadvantages because it is expensive to conduct and not easily applicable. A good correlation has been shown between MRI and ultrasonography in the evaluation of wall area, thickness, and plaque index (20). CT is not a frequently preferred method for the evaluation of carotid plaque and intima media due to its in adequacy in evaluating dense calcified plaques and calcified plaques, low transfer of contrast media to lipid and fibrotic tissues, the presence of radiation, and use of contrast media. However, a study has shown that CIMT and carotid plaques can be evaluated using multi-detector row CT angiography (21).

Different risk factors affecting the development of atherosclerosis may have different effects on different artery segments. For example, a study has shown that smoking and diabetes are more effective than other risk factors in the development of femoral atherosclerosis (22). In another study, hyperlipidemia and high blood pressure were found to be more associated with femoral atherosclerosis than with other risk factors (23). According to the results of our study, the development of femoral atherosclerosis in geriatric patients with ESRD may start later. Long-term prospective studies with more patients may be needed to evaluate this clearly.

Study limitations

This was a cross-sectional study, and therefore long-term results are currently unknown. Moreover, it was a single-centered study, with a relatively small number of patients; therefore, the study results should be confirmed with more patients and multi-centered studies. The epicardial adipose tissue was evaluated using 2D echocardiography; therefore, evaluation of total epicardial fat volume was not possible; however, studies have shown that 2D measurement in front of the right ventricle correlates with the total fat volume (10). In our study, although the operators performing ultrasonographic evaluations blindly evaluated the patient and control groups, the fact that these measurements are operator-dependent is another limitation of this study.

CONCLUSION

EFT and CIMT are significantly higher in geriatric patients with ESRD than in the control group. Therefore, cardiovascular risks may be higher in this patient group. However, no significant difference was observed between the two groups in terms of FIMT, suggesting that femoral atherosclerosis may develop later in patients with geriatric ESRD.



Conflict of Interest, Disclosure Statement

The authors declare that they have no conflicts of interest. The authors have indicated they have no financial relationships relevant to this article to disclose

Ethical Approval: All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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RESEARCH

RETROSPECTIVE ANALYSIS OF COST AND FACTORS AFFECTING MORTALITY IN ELDERLY PATIENTS IN THE INTENSIVE CARE UNIT

Abstract

Introduction: The older population of the world continues to grow. Currently, 8.5% of people worldwide are above 65 years, leading to an increased frequency of intensive care unit admission. This study aimed to assess the cost and factors affecting mortality in elderly patients.

Materials and Methods: This retrospective cohort study included patients aged over 65 years admitted to the tertiary intensive care unit. The demographics including age, gender, body mass index, comorbidities, Glasgow coma scale scores, acute physiology and chronic health evaluation II, the Charlson comorbidity index scores, diagnosis, blood gas analysis results, type of mechanical ventilation, length of stay in the intensive care unit (ICU), time of death and cost of ICU stay were obtained from the government electronic mortality declaration system.

Results: This study evaluated 1401 patients with a mean age of 75.73 ± 6.92, where the mean BMI was 25.31 ± 7.03. Most of the patients (n=714, 51%) belonged to the 65–75 years old group while 569 (40.6%) belonged to the 75–85 years old group and 118 (8.4%) were over 85 years old. Mortality rates were the following: 28-day mortality rate, 41.7%; 1-year mortality rate, 66.4% and 2-year mortality rate, 75%. The mean cost of ICU stay was 7992.95 ± 10166.33 ₺, and the mean cost of hospital stay was 8211.28 ± 10172.41 ₺.

Conclusion: It is shown that comorbidities increased as age advanced, and sepsis remains the leading cause of death in short-term and long-term periods in the elderly population admitted to the ICU.

Keywords: Critical Care; Sepsis; Comorbidity; Mortality; Mechanical Ventilation; Aged.

INTRODUCTION

Technological advancements and improved health care resulted in increasing human lifespan. Therefore, the world population is progressively getting older. The admission of elderly and very elderly patients to the intensive care unit (ICU) has increased in developed countries (1). The short-term outcomes after ICU may be associated with illness severity, comorbidities, performance status of the patient and the quality of care. Despite previous studies, 'age' effect remains to be a debate where health-care professionals are still reluctant in admitting the elderly to the ICU (2). The severity of illness is the leading predictor of mortality rates in the ICU, ranging between 6.4 and 40% in different ICUs. Several studies focus on 30-day mortality, where 1-year and 2-year mortality rates seem to be more relevant. The discharge from the ICU of the elderly appears to be the beginning of the treatment strategy, since it is most likely crucial to hold the elderly outside of the ICU (3).

Moreover, ICU stay was seven times longer in patients above 75 years of age than in patients aged 65 years, and mechanical ventilation requirement was reported to be 10 times higher in patients over 85 years than in patients below 55 years (4,5). Besides the challenging medical care of the elderly, ICU cost accounts for 20–30% of hospital care costs. Several questions remain unanswered, such as the controversial benefit of ICU care for the elderly.

This study primarily aimed to evaluate the clinical characteristics and outcome in elderly patients, and the secondary goal was to define the independent predictors of ICU mortality. Lastly, particular focus was on medico-economic implications.

MATERIALS AND METHODS

This retrospective cohort study was approved by the Scientific Study Committee by a Health Sciences University Chest Diseases and Thoracic Surgery Training and Research Hospital Ethics Committee (Date, 30.04.2019/ No: 066), and patients above 65 years admitted to the tertiary ICU between October 2014 and October 2016 were enrolled in this study.

Data

Patient's data were collected from the hospital database. Age, gender, body mass index (BMI), comorbidities, Glasgow coma scale (GCS) score, acute physiology and chronic health evaluation (APACHE) II scores, the Charlson comorbidity index (CCI) score, diagnosis, blood gas analysis results, type of mechanical ventilation (MV) applied in intensive care unit (invasive or noninvasive), length of ICU stay, time of death and cost of ICU stay were obtained from the government electronic mortality declaration system.

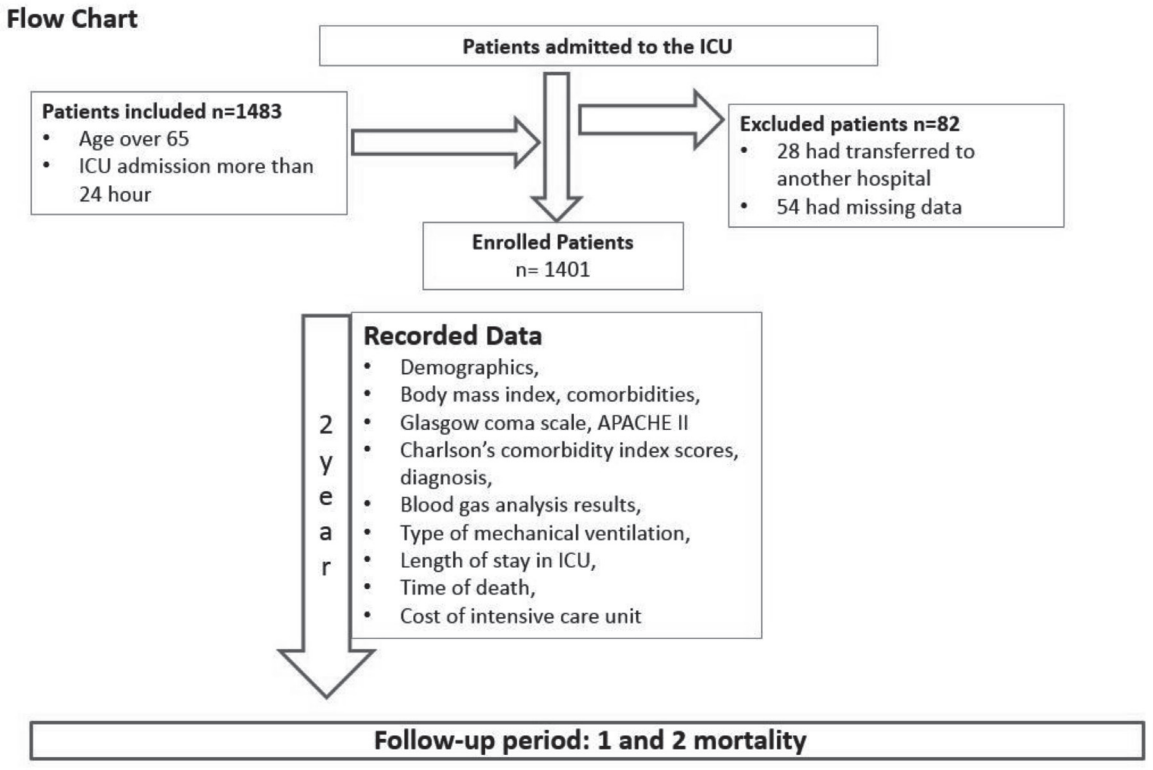
Statistical Analysis

The distribution of the variables was analysed using Kolmogorov–Smirnov test, and the quantitative data were presented as mean and standard deviation where qualitative data were given as median (interquartile range [IQR] 25%–75%) values and also with numbers and percentage. The relationship between variables was determined using either Pearson (r) or Spearman's (ρ) correlation analysis. Long-term mortality risk factors were analysed by multivariate regression analysis, and the age groups and type of MV were compared by one-way ANOVA test. Intragroup comparisons were analysed using Tukey's HSD test. Independent samples t-test was used to compare the GCS, CCI and APACHE II scores. Categorical data was analysed using chi-square test. Data were statistically analysed using the Statistical Package for Social Sciences (SPSS) version 20 programme. The significance level was determined to be $p<0.05$.

RESULTS

This study included 1401 patients. Figure 1 shows the recruitment of the patients. The mean age of the patients was 75.73 ± 6.92, where the mean BMI

Figure 1. Flow chart of the study.



was 25.31 ± 7.03. Most of the patients (n=714, 51%) belonged to the 65–75 years old group, while 569 (40.6%) belonged to the 75–85 years old group and 118 patients (8.4%) were over 85 years old. The diagnosis of the patients on admission were the following: pulmonary diseases (n=1058, 75.5%), cardiac diseases (n=778, 55.5%), renal diseases (n=398, 28.4%) and neurological diseases (n=350, 25%). Majority of the patients were referred from the emergency room (ER) (n=705, 50.3%), where chest disease was the second one (n=581, 41.5%). Table 1 presents the medical characteristics of the patients. The mean ICU stay was 9.63 ± 8.45 days, with a minimum of 1 and a maximum of 57 days. The patients' mean survival time starting with the day admitted to the ICU was 374.31 ± 497.98 days with a minimum value of 1 and a maximum of 1935 days. A total of 497 (35.5%) of the patients died in the ICU, and 904 (64.5%) died after discharge. Table 2 shows the comparison of the GCS and APACHE II and CCI scores of patients who died in the ICU and after discharge. A positive weak correlation was detected between age and CCI score (ß=0.340, $p<0.001$). The frequency of comorbidities among the age groups is shown in Table 3. A multivariate regression analysis of the age; presence of any of the comorbidities including pulmonary diseases (PD), cardiac diseases (CD), neurological diseases

Table 1. Characteristics of the patients.

	Mean±SD	Median	IQR
Age (years)	75.73±6.92	75	11
BMI (kg/m2)	25.31±7.03	23	8
CCI score	5.45±1.62	5	2
APACHE II score	25.92±8.03	24	11
GCS score	12.29±4.24	15	4
	Hypoxia (n, %)	Hypoxia + Hypercarbia (n, %)	Metabolic disturbance (n, %)
Type of BGA	420 (30%)	826 (59%)	155 (11%)

BMI, body mass index; CCI, Charlson comorbidity index; APACHE, acute physiology and chronic health evaluation; GCS, Glasgow coma scale; BGA, blood gas analysis.

Table 2. APACHE II, CCI, and GCS score comparisons.

	Patients died in ICU	Patients died after discharge	p
APACHE II score	30.87±8.05	23.2±6.59	<0.001*
CCI score	5.98±1.78	5.16±1.44	<0.001*
GCS score	10.58±4.82	13.23±3.56	<0.001*

*p<0.05. Independent samples t test.

(ND), renal diseases (RD), malignancy, mechanical ventilation (no MV, NIMV or IMV), ARDS, sepsis, hypertension and diabetes mellitus as possible predictors of survival time starting from ICU admission to the time of death in the ICU; 28-day mortality; 1-year mortality and 2-year mortality is displayed in Table 4. A positive moderate correlation was noted between APACHE II score and ICU mortality, while a negative moderate correlation was observed between APACHE II score and survival time (ρ=0.458, p<0.001; ρ=−0.461, p<0.001, respectively). A positive weak was detected between CCI and ICU mortality, and a negative weak correlation was found between CCI and survival time (ρ=0.232, p<0.001; ρ=−0.282, p<0.001, respectively). Moreover, a negative weak correlation was observed between GCS on admission and ICU mortality, while a positive weak correlation was noted between GCS on admission and survival time (ρ=−0.318, p<0.001; ρ=0.354, p<0.001, respectively). Table 5 displays the relationship between MV and age groups and scores. Mortality rates were found in the following order: 28-day mortality rate, 41.7%; 1-year mortality rate, 66.4% and 2-year mortality rate, 75%. Patients with MV had a mortality rate of 40.5% in 28 days, 62.5% in 1 year and 70.2% in 2 years. The costs of hospital and ICU stay according to age groups are summarised in Table 6. The mean cost of ICU stay was 7992.95 ± 10166.33 ₺, and the mean cost of hospital stay was 8211.28 ± 10172.41 ₺.



Table 3. The distribution of comorbidities among age groups.

	Total (n=1401) n (%)	65 – 75 years (n=714) n (%)	75 – 85 years (n=714) n (%)	> 85 years (n=714) n (%)	p
PD	1058 (75.5)	574 (80.4)	418 (73.5)	66 (55.9)	<0.001*
CD	778 (55.5)	361 (50.6)	337 (59.2)	80 (67.8)	<0.001*
ND	350 (25)	133 (18.6)	169 (29.7)	48 (40.7)	<0.001*
RD	398 (28.4)	172 (24.1)	178 (31.3)	48 (40.7)	<0.001*
Malignity	241 (17.2)	159 (22.3)	75 (13.2)	7 (5.9)	<0.001*
MV	1295 (92.4)	667 (93.4)	523 (91.9)	105 (89)	0.221
ARDS	39 (2.8)	24 (3.4)	11 (1.9)	4 (3.4)	0.262
Sepsis	384 (27.4)	182 (25.5)	171 (30.1)	31 (26.3)	0.185
DM	379 (27.1)	199 (27.9)	151 (26.5)	29 (24.6)	0.708
HT	785 (56)	373 (52.2)	331 (58.2)	81 (68.6)	0.001*

*p<0.05.

Chi-square test. PD, pulmonary diseases; CD, cardiac diseases; ND, neurological diseases; RD, renal diseases; MV, mechanical ventilation; ARDS, acute respiratory distress syndrome; DM, diabetes mellitus; HT, hypertension.

Table 4. Multivariate regression analysis.

	Mortality in ICU (ß, p)	28-days mortality (ß, p)	1-year mortality (ß, p)	2-years mortality (ß, p)
Age (years)	–	0.038, 0.088	0.093, <0.001*	0.069, 0.007
PD	-0.106, <0.001*	-0.097, <0.001*	-0.055, 0.034*	-0.051, 0.059
CD	0.043, 0.044*	0.061, 0.008*	–	–
ND	–	0.061, 0.008*	0.123, <0.001*	0.095, <0.001*
RD	0.267, <0.001*	0.255, <0.001*	0.173, <0.001*	0.144, <0.001*
Malignity	0.120, <0.001*	0.128, <0.001*	0.185, <0.001*	0.160, <0.001*
MV	0.121, <0.001*	0.105, <0.001*	0.073, 0.002*	0.060, 0.018*
ARDS	0.051, 0.017*	0.054, 0.014*	–	–
Sepsis	0.365, <0.001*	0.351, <0.001*	0.241, <0.001*	0.191, <0.001*
DM	–	–	-0.045, 0.055	–
HT	-0.048, 0.028*	-0.076, 0.001*	–	–

*p<0.05. PD, pulmonary diseases; CD, cardiac diseases; ND, neurological diseases; RD, renal diseases; MV, mechanical ventilation; ARDS, acute respiratory distress syndrome; DM, diabetes mellitus; HT, hypertension. Death in ICU: The model explained 62.1% of the variance (F=109.327, p<0.001).

28-days mortality: The model explained 61.4% of the variance (F=84.074, p<0.001). **1-year mortality**: The model explained 47.6% of the variance (F=50.914, p<0.001). **2-years mortality**: The model explained 38.7% of the variance (F=35.116, p<0.001).

acute respiratory distress syndrome; DM, diabetes mellitus; HT, hypertension.

Table 5. The effect of mechanical ventilation on the scores and survival time.

	No MV (n=106	NIMV (n=516)	IMV (n=779)	p
65 – 75 years	47 (6.6%)	277 (38.8%)	390 (54.6%)	0.443
75 – 85 years	46 (8.1%)	192 (33.7%)	331 (58.2%)	
> 85 years	13 (11%)	47 (39.8%)	58 (49.2%)	
Stay in ICU (days)	5.34±4.99	7.26±5.19	11.79±9.81	<0.001*
Survival time (days)	557.3±551.14	576.35±533.44	215.38±399.86	<0.001*
GCS score	13.66±2.95	14.4±1.84	10.71±4.82	<0.001*
CCI score	5.37±2.04	5.14±1.44	5.67±1.63	<0.001*
APACHE II score	21.11±5.96	21.3±5.08	29.64±7.93	<0.001*

*p<0.05. One-way ANOVA test. Tukey's HSD test.
Intragroup comparisons for the stay in ICU: No MV-NIMV (p=0.066); No MV-IMV (p<0.001); NIMV-IMV (p<0.001).
Intragroup comparisons for survival time: No MV-NIMV (p=0.922); No MV-IMV (p<0.001); NIMV-IMV (p<0.001).
Intragroup comparisons for GCS score: No MV-NIMV (p=0.165); No MV-IMV (p<0.001); NIMV-IMV (p<0.001).
Intragroup comparisons for CCI score: No MV-NIMV (p=0.352); No MV-IMV (p=0.177); NIMV-IMV (p<0.001).
Intragroup comparisons for APACHE II score: No MV-NIMV (p=0.963); No MV-IMV (p<0.001); NIMV-IMV (p<0.001).

Table 6. The cost distribution according to the use of mechanical ventilation.

	No MV (n=106	NIMV (n=516)	IMV (n=779)	p
Cost of Hospital Stay	4421.97±5130.9	6651.16±7824.3	9511.85±11459.14	<0.001*
Cost of ICU stay	4854.57 8460.27	5422.69±6245.22	9096.85±10692.66	<0.001*

*p<0.05. One-way ANOVA test. Tukey's HSD test.
Intragroup comparisons for cost of hospital stay:
No MV-NIMV (p=0.313); No MV-IMV (p=0.002); NIMV-IMV (p=0.001).
Intragroup comparisons for cost of ICU stay: No MV-NIMV (p=0.850); No MV-IMV (p<0.001); NIMV-IMV (p<0.001).

DISCUSSION

This study showed that PD, CD and HT are the leading cause of ICU admission among the elderly population, where CD, ND, RD and HT have increased with the advancing age and PD and malignancy decreased. The evident causes of death in the ICU appears to be RD and sepsis, those are the same in 28-days. Moreover, 1-year and 2-year mortality were considerably associated with sepsis, RD and malignancy in the elderly population in the ICU. Patients with NIMV had a longer survival compared to patients with IMV or without MV. However, MV (NIMV or IMV) lengthened ICU stay and increased the cost of hospital and ICU stay. It is also detected that higher APACHE II score was associated with increased ICU mortality rate and longer survival time. Life expectancy has increased in the developed countries, raising the number of ICU admissions. The prognosis prediction of the elderly in the ICU has been investigated by sev-



eral studies, including that of Somme et al. that showed the intensity of the illness evaluated by APACHE II score could be the most important predictor in short-term mortality in elderly patients. The authors also reported that age and limited daily activities might be the possible predictors of the long-term mortality (5). Several studies reported the same result; that is, severity of the illness was the only predictor for short-term mortality (1,6,7). Despite the abovementioned studies, recent analysis conducted on large populations demonstrated that the medical condition of the patient in the hospital is more likely associated with in-hospital death rather than age (8). Moreover, Flaatten et al. showed that age had a minimal effect on ICU survival (9). This study revealed that considering the age as a single variable in the equation could be an underestimation compared to the condition of the patient associated with diseases they had. However, age is a factor indirectly affecting the observed frequency of the disease, leading a change on the balance by a path that did not exist in the account. Studies have demonstrated that ageing is associated with an increased susceptibility to PD (10,11). Despite the study's limited sample population, it was shown that PD and malignancy frequency decreased related to advancing age. This outcome could be associated with the low number of patients > 85 years of age, which might be higher than the sum of the patients in the 75–85 years and > 85 years groups. In contrast, advanced age is evidently related to malignancy. This is also confirmed by the present study (11). Inevitably, life expectancy is shorter in a patient diagnosed with cancer who also requires ICU treatment associated with accompanying disorders, and age is also related to prolonged MV in the elderly (12).

Furthermore, physiologic changes may occur in the cardiovascular system of elderly patients. Stage 1 diastolic dysfunction is a normal alteration of ageing. Left ventricular outflow may be depleted under stress conditions by a change in the structural integrity of the ventricular space called 'sigmoid septum'. Ageing leads to reduced maximal cardiac output; decreased inotropy, lusotropy and chronotropy and lower tissue extraction of oxygen (13). Renal changes are mainly caused by the decreased extraction of sodium levels, triggering older patients to be more prone to volume fluctuations. Diminished baroreceptor sensitivity is also a negative factor for pressure control of the cardiovascular system. Moreover, ageing affects cognitive functions, resulting in difficulty in memory, executive functioning and processing speed. Immobility is another loss of functioning during ageing observed in 82% of the patients above 85 years. Immobility and sedentary lifestyle impair the physiologic changes on other systems. It is noted that early mobility and physical exercise are fundamental in improving the functionality of the elderly patients (14-16). This study demonstrated that the frequencies of CD, ND, RD and HT increased with advancing age, also noted in previous studies mentioned above.

Nevertheless, the overall ICU mortality was affected by sepsis, a known cause of death which is the most likely cause of admission and the most common cause of death in the ICU and has been currently indicated as the final common route to death from infection (17). It has a high mortality rate ranging from 11.9% to 47.2% (18). In this study, sepsis had the single factor associated with the overall, 28-day, 1-year and 2-year mortality with a higher correlation coefficient than the other variables including RD and malignity. Despite the development of detailed sepsis guidelines for those requiring early diagnosis and prompt administration of therapy to prevent single- or multiple-organ dysfunctions, sepsis remains to be the most challenging syndrome worldwide. Recent developments in the management of sepsis have decreased mortality rates by 20 to 30% in the last decades; however, complexity of therapy for sepsis results in high costs (19-21). Moreover, the treatment of elderly patients admitted to the ICU could be challenging due to various factors. This

group of patients has a lower life expectancy, high mortality rates and high health-care costs, increasing with advancing age. In this study, the mortality rates were 41.7%, 66.4% and 75% in 28-day, 1-year and 2-year mortality, respectively. Higher mortality rates indicated that the severity of comorbidities accompanying complications in ICU could increase with advancing age. The bigger percentage of patients admitted to the ICU was comprised of elderly patients above 75 years. The use of recent technologies, which are also expensive, is increasing and expands the health-care costs accompanied by increased ICU admission (22).

The use of MV holds higher ICU costs (23). Similar to this information, this study showed that MV requirement extends the ICU and hospital stay that also increase cost. An interesting finding of this study is that MV seemed to shorten survival time; however, MV is a technique performed in respiratory failure. The lower survival time may be considerably associated with the severe comorbidities leading to the use of MV. Several studies have been conducted on the prediction of ICU mortality, resulting in a highly valuable scoring system called APACHE II (22). The relationship between APACHE II score and mortality and survival time in elderly patients is a known condition in which the APACHE II score defines the patient's mortality risk on admission.

Overall, this study showed the causes of ICU death by utilising the elderly population, the association between the advanced age and comorbidities and the effects of MV on the ICU stay and cost. These data provide baseline and local information that might be enhanced by gathering data from distinct hospitals and regional areas.

This study had some limitations. First, the blood gas analysis data could be obtained in detail provided there is additional information on the patient's condition; unfortunately, we were not able to obtain such data from the hospital database. Second, our data did not include the patient's functional status after discharge. Third, the admission policy variation across countries may lead to restrict the generalizability of the results.

Therefore, this study revealed that comorbidities increased along with advancing age, and sepsis is still the leading cause of death in short-term and long-term periods in the elderly population admitted to the ICU. Further studies with large sample size may be conducted to elucidate this outcome.

CONFLICT OF INTEREST

All authors declared that there is no conflict of interest.

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RESEARCH

DO SURGICAL PATIENTS OLDER THAN 90 YEARS MORE BENEFIT FROM INTENSIVE CARE UNIT?

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Abstract

Introduction: The number of elderly patients followed in intensive care units is increasing day by day. In the literature, there are a limited number of studies covering patients aged 90 and over. We aimed to investigate the epidemiologic characteristics and clinical outcomes of elderly patients aged ≥90 years admitted to intensive care unit.

Materials and Methods: In this study, medical records of patients aged ≥90 years admitted to intensive care unit, between January 2015 and January 2018, were retrospectively reviewed. Demographic data, reason for admission (medical or surgical), Acute Physical and Chronic Health Evaluation II (APACHE II) score, need for and duration of mechanical ventilation, need for inotropic agents, duration of intensive care unit stay, and mortality rate were recorded.

Results: A total of 107 nonagenarians were evaluated. The mean age of the patients was 92.65 ± 2.36 years, and 72 of them were women. The mean score of APHACHE II was 23.6 ± 7.2. Most patients were admitted due to medical reasons (n = 82, 76.63%). Sixty-four of the medical patients, and four of the surgical patients had died in the intensive care unit (n = 68, 63.55%). APACHE II score, need for and the duration of mechanical ventilation, need for inotropic agents, the duration of intensive care unit stay, and the mortality rate were higher in medical patients than in surgical patients.

Conclusions: The mortality rates of the medical patients were high; nevertheless, we believe that surgical patients more benefit from intensive care unit follow-up.

Keywords: Aged; Patient; Intensive Care Unit; Mortality.

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INTRODUCTION

The world population is ageing rapidly, and according the Turkey Statistical Institute data, 0.11% of the total population was aged ≥90 years in 2018 (1). In conjunction with the increase in the number of the elderly population, the number of elderly patients requiring intensive care unit (ICU) admission is on the rise. Elderly patients form an essential part of the patients admitted to ICU (2). These patients need follow-up in ICU due to acute exacerbations of existing chronic diseases or following a surgical procedure. Although nonagenarians, namely individuals aged ≥90 years represent a small subgroup, they are at high risk of death. In the literature, many studies frequently evaluating patients aged 65 years or ≥80 years can be found (3,4). However; only a few studies on elderly patients in ICU have included nonagenarians (5-7). Therefore, this study investigated the epidemiologic characteristics and outcomes of elderly patients aged ≥90 years who were admitted to ICU.

MATERIALS AND METHODS

This study was approved by the Ethics and Research Committee of Karabuk University (No:77192459-050.99-E.1826). From 1 January, 2015 to 1 January, 2018, the medical records of patients aged ≥90 years admitted to the ICU of Karabuk University Hospital, Turkey, for ≥24 h were reviewed in this retrospective observational study. For patients with multiple ICU admissions, only the first admission was considered. All patients aged < 90 years, as well as those admitted to the cardiac ICU were excluded. The ICUs of Karabuk University Training and Research Hospital are closed ICUs where patients are treated by full-time critical care physicians.

The following parameters were recorded; age, sex, comorbidities, hospital stay prior to the ICU admission, the main reason for the ICU admission (medical; respiratory, gastrointestinal, neurological, renal diseases, cardiopulmonary resuscitation, sepsis, or surgical; unscheduled or scheduled surgery), Acute Physical and Chronic Health Evaluation II (APACHE II) score on ICU admission, need for and duration of mechanical ventilation (MV), need for inotropic agents, duration of ICU stay and mortality rate.

Statistical analysis: Statistical analyses were performed using SPSS 14.0. Quantitative variables were reported as mean standard deviation (SD). Nominal variables were expressed as number and percentages. The mean data were compared using the Student's t test. Categorical data were compared using the chi-square test or Fisher's exact test upon compatibility. $P<0.05$ was considered statistically significant.

RESULTS

During the three years, 3257 patients were admitted to the ICU. A total of 124 patients were aged ≥90 years. Of these patients, 10 who were discharged before 24 h of ICU admission, and 7 with missing data were excluded. Thus, 107 (3.29%) patients participated in the study.

The mean age of the patients was 92.65 ± 2.36 years. Women comprised most of the patients (n=72, 67.29%). The mean APACHE II scores on ICU admission were 23.6 ± 7.2. A total of 96 (89.72%) patients had at least one comorbid disease. The main comorbidities were systemic arterial hypertension, heart disease, diabetes mellitus, respiratory diseases, neurodegenerative disease, and chronic renal failure.

Most patients were admitted to the ICU for medical reasons (n=82, 76.64%). Respiratory diseases (56.10%), neurological diseases (14.63%), and cardiopulmonary resuscitation (12.19%) were the most frequent medical causes. 25 patients (23.36%) were accepted for surgical reasons, of which 24% underwent unscheduled surgery.

A total of 82 patients (76.64%) were mechanically ventilated, and the mean MV duration was

9.23 ± 2.8 days. Moreover, 73 patients (68.22%) patients required inotropic treatment and 8 patients (7.47%) underwent RRT. The mean duration of ICU stay was 11.82 ± 3.9 days (Table 1). Sixty-four of the medical patients, and four of the surgical patients had died in the intensive care unit (n = 68, 63.55%).

When we grouped the patients as medical and surgical, we found that the APACHE II score, need for MV, MV duration, need for inotropic agents, duration of ICU stays, and mortality rate were higher in medical patients than in surgical patients (Table 2).

DISCUSSION

In the study, nonagenarians represented approximately 3.29% of ICU admissions, and the ICU mortality rate was 63.55%. Few studies have analyzed the outcome of the nonagenarians. Sim et al. examined 155 patients aged ≥90 years, and reported ICU admission rates and ICU mortality rates were 0.92% and 32.3%, respectively (7). Rellos et al. found that the proportion of nonagenarians in ICU was 1.1%, with an ICU mortality of 20 % (8). Becker et al. reported these rates as 1.1% and 18.3%, respectively (6).

Table 1. Patients' general characteristics and clinical data.

Variables		
Age (years), mean±SD		92.65 ± 2.36
Sex (female/male), n (%)		72/35 (67.29/32.71)
Comorbidities, n(%)	**Systemic arterial hypertension**	66 (61.68)
	Diabetes mellitus	42 (39.25)
	Heart disease	52 (48.59)
	Respiratory diseases	36 (33.64)
	Neurodegenerative disease	32 (29.90)
	Chronic renal failure	12 (11.21)
	Others	22 (20.56)
Admission category n(%)	**Medical**	82 (76.64)
	Surgical	25 (23.36)
APACHE II score, mean ± SD		23.6 ± 7.2
Need for MV, n(%)		82 (76.64)
Duration of MV (days), mean±SD		9.23 ± 2.8
Need for inotropes, n(%)		73 (68.22)
Need for RRT, n(%)		8 (7.47)
Duration of ICU stay(days), mean±SD		11.82 ± 3.9
Mortality, n(%)		68 (63.55)

Data are stated as mean ± standard deviation (mean ± SD) or patient number and percentage (n, %). APACHE II: Acute Physical and Chronic Health Evaluation, MV: Mechanical ventilation, RRT: Renal replacement therapy, ICU: Intensive care unit.



Table 2. Comparison of demographic and clinical data of the medical and surgical patients.

	Medical (n=82)	Surgical (n=25	P value
Age (years), mean ± SD	93.68±2.8	91.54±3.2	0.13
Female sex, n (%)	57 (69.51)	15 (60)	0.87
APACHE II score, mean ± SD	28.48±6.1	19.22±8.5	<0.001*#
Need for MV, n(%)	76 (92.68)	6 (24)	<0.001†#
Duration of MV (days), mean ± SD	11.64±2.8	1.45±1.1	<0.01*#
Need for inotropes, n(%)	68 (82.92)	5 (20)	<0.001†#
Need for RRT, n(%)	6 (7.31)	2 (8)	0.18
Duration of ICU stay(days), mean ± SD	14.46±2.5	3.16±3.1	<0.01*#
Mortality, n(%)	64 (78.04)	4 (16)	<0.001†#

Data are stated as mean±standard deviation (mean ± SD) or patient number and percentage (n, %). APACHE II: Acute Physical and Chronic Health Evaluation, MV: Mechanical ventilation, RRT: Renal replacement therapy, ICU: Intensive care unit. *Student's t test, †Pearson's chi-square test, #Statistically significant difference between groups.

Although chronological age is associated with higher rates of ICU mortality, other studies have found the severity of illness, reason for admission, and comorbidities to be more important risk factors than age itself (9-11).

The outcome of very elderly patients varies depending on the reasons for ICU admission. In previous studies, the mortality rate has been reported to be higher in medical patients than in surgical patients. Bagshaw et al. reported that after scheduled surgery, the ICU and hospital mortality rate were 12 and 25 %, respectively (12). Other studies have found the, rates were 38 and 64 % for medical patients and 45 and 55 % for unscheduled surgery patients (9,13). In the present study, the ICU mortality rate was higher in medical patients (78.04%) than in surgical patients (16%).

Mechanical ventilation and inotropic support have been associated with mortality in patients admitted to ICU (14). In an ongoing Indian study, mechanical ventilation and inotropic support proved to increase mortality in geriatric patients (15).

Sim et al. have found that high Simplified Acute Physiology Scoring II scores, poor nutritional status, high glucose, use of vasopressors, and DNR orders should be considered as significant predictors of mortality in very elderly ICU patients (7). In a study on 104 patients aged >85 years, van den Noortgate et al. found inotropes as an independent risk factor in mortality (16). Orsini et al. found that advanced age, critical illness, cardiopulmonary resuscitation, and needs for mechanical ventilation and/or vasopressor therapy are independent risk factors associated with adverse outcome in elderly patients admitted to ICU (14). Similar to these results, this investigation revealed that medical patients had higher APACHE II score, need for MV, need for inotropes, and mortality rate.

There are noteworthy several limitations to the present study. First, this was a single-centre, non-randomised retrospective study. The long-term outcome of patients could not be assessed

because of the retrospective nature of the study. Last, because ICU management can be different in each hospital, we cannot generalise our findings.

Although patients aged ≥90 years are a small subgroup of the elderly population, their numbers are increasing. Elderly patients have high ICU mortality, but studies have shown that only age does not affect mortality. In our study, we found that the mortality rates of medical patients were high. Nevertheless, we believe that surgical patients benefit more from ICU follow-up.

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This report received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. The authors have no competing interests to declare regarding the publication of this paper.

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RESEARCH

DIAGNOSIS AND MORTALITY OUTCOMES OF THREE DIFFERENT GERIATRIC AGE GROUPS IN THE INTENSIVE CARE UNIT: 10–YEAR RETROSPECTIVE ANALYSIS

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Abstract

Introduction: In addition to bringing many physiological changes with it, aging is a period in which morbidity and mortality rates increase due to the increase in the incidence of chronic diseases and malignant diseases. The aim of this study was to determine the prevalence of conditions requiring intensive care and the mortality incidence based on geriatric age groups followed-up in the intensive care unit.

Materials and Method: Three different geriatric age groups were formed out of the 65 years old and older patients (n=5932) included in the study as young old (65–74 years), middle old (75–84 years) and oldest old (85 years and older). In each group, disease prevalence and mortality rate by diagnostic groups were analysed.

Results: The resulting diagnostic groups were found to be at different rates in different age groups ($p = 0.01$ $p < 0.05$). Malignancy was high in young elderly patients ($p = 0.01$ $p < 0.05$), while cardiovascular diseases were higher in other groups ($p = 0.01$ $p<0.05$). Patients admitted to the intensive care unit with cardiac arrest had the highest mortality rate ($p = 0.01$ $p<0.05$).

Conclusion: Geriatric patients constitute an important part of intensive care patients, therefore the mortality rate is high. In all three groups, 30–day mortality results were highest in patients with cardiac arrest followed by sepsis and cardiovascular diseases, respectively.

Keywords: Geriatrics; Intensive Care Units; Mortality; Age groups; Prevalence.

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INTRODUCTION

The World Health Organisation defines old age as the beginning of the chronological age of 65 years. Besides bringing several physiological changes, aging increases the rate of morbidity and mortality due to an increased incidence of chronic and malignant diseases. Furthermore, geriatric patients have a high incidence of chronic diseases developing because of diabetes and hypertension (1–3). Moreover, elderly individuals have a higher rate of acute kidney injury compared with young people (4) and are, therefore, at an increased risk of renal failure. Notably, diabetes and hypertension are the two most common causes of chronic renal failure (5). The most common comorbidities observed in the intensive care unit (ICU) are hypertension, heart failure and diabetes mellitus (6). In addition, trauma is associated with increased morbidity and mortality rates in geriatric individuals (7, 8). Moreover, weakened immunity, chronic diseases and organ physiology changes make geriatric patients susceptible to infections, such as sepsis and bacteremia (9). Notably, the fact that the age and preoperative albumin levels were found to be significantly correlated with hospital length of stay and 30-day ICU admissions (10) indicates the need for intensive care in the geriatric age group and the elderly with chronic diseases. Given that the geriatric population in the United States is expected to increase from 52 million in 2018 to 95 million in 2060 (11), a corresponding increase in the geriatric patient population needing intensive care can be expected as well in the future. Until date, no guidelines or recommendations have been suggested for geriatric intensive care, and no randomized controlled studies have been performed (12). The mortality rate of elderly patients in the ICU is not only related to age but also the decrease in functional reserves and age-related physiological weakness (12). Various disease groups may come into prominence in three different geriatric age groups depending on the possible pathophysiology and aging. Determining mortality rates for diagnostic groups may provide insight for disease prevention and geriatric disease groups at risk. Therefore, this study determined the prevalence of conditions requiring intensive care and the mortality incidence in geriatric age groups followed in the ICU.

MATERIALS AND METHOD

Study population

This study was conducted in accordance with the Declaration of Helsinki from 2008 to 2017 after obtaining approval from the Institutional Ethics Committee (Date of Approval-Protocol No: 10.10.2019-22/14).

This research was conducted as a single-center retrospective descriptive study by scanning the data in the electronic health records system (SARUS) of 17819 patients who were treated in the ICU (Reanimation Intensive Care Unit, Surgical Intensive Care Unit) of our Level 3 hospital. Of these, 8639 patients (mean ± SD: 76.64 ± 8.32 years, 62% were females) aged 65 years and above were included in the study. Overall, 2707 patients were excluded from the study because of an uncertain diagnosis. Finally, the study was conducted on 5932 patients over 65 years of age who had a definite diagnosis. Notably, patients under 65 years of age were excluded from the study.

Assessments

Patients included in the study (n = 5932) were grouped into the following three different geriatric age groups: young-old (65–74 years), middle-old (75–84 years) and oldest-old (85 years and above). Accordingly, various diagnostic groups were formed based on the most frequent causes of mortality in each of the three geriatric age groups, such as cardiovascular diseases (acute coronary syndrome, heart failure, etc), malignancies (cancers of brain, larynx, lung, stomach, colon, bladder and kidneys), cerebrovascular diseases (stroke, intracerebral haemorrhage, etc), gastrointestinal diseases (non-malignant liver, biliary tract diseases, inflam-

matory and haemorrhagic diseases of the stomach and intestine), trauma (multiple fractures, hip fractures, etc), urinary system (non-malignant pathologies of the urinary system) and other diseases. Differently from cardiovascular disease diagnostic group, cardiac arrest diagnostic group was formed according to the results of the emergency code blue calls made from the other departments of the hospital. Age-based analyses of various diagnostic groups were performed to determine the indication for intensive care admission and the 30-day mortality rate of each diagnostic group. Geriatric patients admitted to the ICU for postoperative follow-up were excluded from the study.

Statistical analysis

The descriptive statistics of the groups were calculated as frequency and percentage values to examine the relevant data. Chi-square analysis (Fisher's exact test) was performed to explore the diagnoses according to patient characteristics. The Bonferroni method was used to identify the group that created the difference in different groups. In the study, p values less than 0.05 were considered statistically significant. SPSS 22.0 software was used for analysis.

RESULTS

2236 (38%) of the 5932 study patients in the ICU were men, and 3696 (62%) were women. The number of patients in three study groups was as follows: 2444 (41%) young-old (70.02 ± 6.42), 2488 (42%) middle-old (79.35 ± 5.23) and 1000 (17%) oldest-old patients (89.50 ± 15, 12). Overall, 2389 (40%) patients passed away, and 3543 (60%) patients were transferred from the ICU to the ward.

Our study detected that geriatric patients were treated in the ICU for the following conditions: 1323 patients (22.3%) for cardiovascular diseases, 883 (14.9%) for malignancies, 807 (13.6%) for gastrointestinal diseases, 754 (12.7%) for acute respiratory failure, 536 (9%) for cerebrovascular diseases, 534 (9%) for trauma, 219 (3.7%) for pneumonia, 173 (2.9%) for sepsis, 155 (2.6%) for chronic renal failure, 125 (2.1%) for urinary system diseases, 113 (1.9%) for ileus, 91 (1.5%) for cardiac arrest, 65 (1.1%) for diabetes mellitus, 63 (1.1%) for high fever, 47 (0.8%) for acute renal failure and 44 (0.7%) for burns (Table 1).

The diagnostic groups of young-old patients had statistically different incidence rates ($p = 0.01$, $p < 0.05$) (Table 2). Identified in 504 patients (20.6%), malignancy had the highest rate.

The diagnostic groups of middle-old patients had statistically different incidence rates ($p = 0.01$, $p < 0.05$) (Table 3). Identified in 589 patients (23.7%), cardiovascular diseases had the highest rate.

The diagnostic groups of oldest-old patients had statistically different incidence rates ($p = 0.01$, $p < 0.05$) (Table 4). Identified in 239 patients (23.9%), cardiovascular diseases had the highest rate.

Furthermore, the 30-day mortality rates of geriatric age groups varied for different diagnostic groups ($p = 0.01$, $p < 0.05$) (Table 5). Cardiac arrest, sepsis and cardiovascular diseases are the most common causes of mortality. Although the incidence of acute renal failure was at 0.7 and urinary system diseases at 1.5% in the over 85 years old patient group, mortality rates were significantly higher compared to other geriatric age groups, being 85.7% and 53.3%, respectively.

In the young and middle old geriatric groups, mortality rates of patients diagnosed with pneumonia were found to be higher than patients diagnosed with acute respiratory failure.

DISCUSSION

The fact that 8639 patients (48.4%) in our study were aged 65 years and above indicates the importance of intensive care treatment in geriatric age groups. Per the literature, the rate of ICU admission of elderly patients was noted to be 46% (6),



Table 1. Patient characteristics and diagnostic groups.

Sex	**n**	**% Percentage**
Male	2236	37.7
Female	3696	62.3
Age (mean ± SD)	n	% Percentage
65-74 years of age (70.02 ± 6.42)	2444	41.2
Age 75-84 years (79.35 ± 5.23)	2488	41.9
85 years and older (89.50 ± 15.12)	1000	16,9
Treatment Result	**n**	**% Percentage**
Exitus	2389	40,3
Discharge	3543	59,7
Diagnosis	**n**	**% Percentage**
Cardiovascular Disease	1323	22.3
Malignancy	883	14.9
Gastrointestinal Diseases	807	13.6
Acute Respiratory Failure	754	12.7
Cerebrovascular Diseases	536	9.0
Trauma	534	9.0
Pneumonia	219	3.7
Sepsis	173	2.9
Chronic Renal Failure	155	2.6
Urinary System	125	2.1
Ileus	113	1.9
Cardiac Arrest	91	1.5
Diabetes Mellitus	65	1.1
High Fever	63	1.1
Acute Kidney Failure	47	0.8
Burn	44	0.7

Table 2. Analysis of Diagnosis Distribution of 65-74 Age Group.

Age	Diagnosis	n	Percentage %	p
65-74	Malignancy	504	20.6	0.01
	Cardiovascular Disease	495	20,3	
	Acute Respiratory Failure	339	13.9	
	Gastrointestinal Diseases	307	12.6	
	Cerebrovascular Diseases	203	8.3	
	Trauma	172	7.0	
	Sepsis	77	3.2	
	Pneumonia	73	3.0	
	Urinary System	67	2.7	
	Chronic Renal Failure	51	2.1	
	Ileus	40	1.6	
	Cardiac Arrest	39	1.6	
	High Fever	25	1.0	
	Burn	21	0.9	
	Diabetes Mellitus	16	0.7	
	Acute Kidney Failure	15	0.6	

*Single ratio chi-square analysis was performed.

which corresponds to the rate of 48.4% observed in our study. Our study determined the mortality rate in geriatric intensive care patients to be 40%. In a study that did not discriminate between adult and geriatric age, the mortality rate was observed to be 19.6% (13). Among the 5932 patients included in the study, the proportion of female geriatric patients was determined to be high with 3696 female patients (62%). Notably, the young-old and middle-old patient groups exhibited proportionality with 2444 (41%) and 2488 (42%) patients in the groups, respectively. Per the literature, the prevalence of geriatric patients over the age of 80 in the ICU is 20% (14), whereas our study observed that the rate of patients aged 85 and above was 16.9%.

Malignancy was high in the young-old and young-old male patient groups, whereas cardiovascular diseases were observed to be high in the other groups.

Notably, advanced age increases the mortality rate even if the existing morbidity is controlled (15). When we evaluated the 30-day mortality rates of geriatric intensive care patient groups, the mortality rate was the highest in all three geriatric age groups admitted to the ICU with the diagnoses of



Table 3. Analysis of the Distribution of Diagnosis in 75-84 Age Groups.

Age	Diagnosis	n	Percentage %	p
75 - 84	Cardiovascular Disease	589	23.7	0.01
	Gastrointestinal Diseases	373	15.0	
	Malignancy	303	12.2	
	Acute Respiratory Failure	295	11.9	
	Cerebrovascular Diseases	233	9.4	
	Trauma	212	8.5	
	Pneumonia	96	3.9	
	Chronic Renal Failure	79	3.2	
	Sepsis	66	2.7	
	Ileus	56	2.3	
	Urinary System	43	1.7	
	Cardiac Arrest	38	1.5	
	Diabetes Mellitus	34	1.4	
	High Fever	30	1.2	
	Acute Kidney Failure	25	1.0	
	Burn	16	0.6	

*Single ratio chi-square analysis was performed.

cardiac arrest, closely followed by sepsis, cardiovascular diseases and acute renal failure. In our study, the mortality rate was 40% (n = 2389), whereas other studies noted it to be 37% (16) and 52.3% (6) in patients in the critical intensive care. In a prospective study conducted on patients in the ICU with an average age of 84 years, the 30-day mortality rate was 41.9% (17). In another study, the 30-day mortality was determined to be 43.7% (15). Per the literature, the mortality rate of cardiovascular disease was 66.6% (18), whereas our study observed it to be 57.90% in the middle-old geriatric group. Notably, our study determined that the mortality rates of sepsis and acute renal failure were identical. A study that analysed this occurrence demonstrated that sepsis was the most common cause of acute renal failure (19). In our study, in the geriatric group aged over 85 years, the mortality rate was higher than 85% in patients with high fever and acute renal failure, probably secondary to sepsis. A retrospective study in the literature conducted on ICU patients over 85 years of age determined the sepsis-related survival rate to be 38.5% (20), whereas in our study, the survival and mortality rates were 30% and 70%, respectively. The literature revealed a trauma-related mortality rate of 15.5% in geriatric

Table 4. Analysis of the Distribution of Diagnosis in 85 and Older Age Groups.

Age	Diagnosis	n	Percentage %	p
85 years and older	Cardiovascular Disease	239	23.9	0.01
	Trauma	150	15.0	
	Gastrointestinal Diseases	127	12.7	
	Acute Respiratory Failure	120	12.0	
	Cerebrovascular Diseases	100	10.0	
	Malignancy	76	7.6	
	Pneumonia	50	5.0	
	Sepsis	30	3.0	
	Chronic Renal Failure	25	2.5	
	Ileus	17	1.7	
	Diabetes Mellitus	15	1.5	
	Urinary System	15	1.5	
	Cardiac Arrest	14	1.4	
	High Fever	8	0.8	
	Acute Kidney Failure	7	0.7	
	Burn	7	0.7	

*Single ratio chi-square analysis was performed.

patients over 80 years of age, whereas our study identified this rate to be 10.70% (16, 21).

CONCLUSION

Geriatric patients constitute a significant fraction of intensive care patients, thereby increasing the mortality rate. Regarding the disease prevalence in the three different geriatric age groups in ICU, malignancy was prominent in young-old geriatric patients, whereas the incidence of cardiovascular disease increased in middle-old and oldest-old geriatric patients.

Mortality rates of the patients in young and middle old geriatric groups diagnosed with pneumonia are at high levels, respectively, 47.9%(35) and 58.3%(56). In all three groups, the 30-day mortality results were highest in patients with cardiac arrest, followed by sepsis and cardiovascular diseases. Therefore, in individuals who are 85 years and older, caution should be taken in case of acute renal failure and high fever, bearing in mind the possibility of high mortality, and such instances warrant appropriate treatment management strategies. Nonetheless, when treating critically ill elderly patients in the ICU, well-organized team

Table 4. Analysis of the Distribution of Diagnosis in 85 and Older Age Groups.

Diagnosis	Age						P
	65-74		75 - 84		85 years and older		
	n	Mortality	n	Mortality	n	Mortality	Mortem
Acute Kidney Failure	10	66.70%	12	48.00%	6	85.70%	0.01*
Acute Respiratory Failure	117	34.50%	107	36.30%	66	55.00%	
Diabetes Mellitus	7	43%-80%	5	14.70%	2	13.30%	
Gastrointestinal Diseases	58	18.90%	116	31.10%	38	29.90%	
Ileus	15	37.50%	19	33.90%	7	41.20%	
Cardiac Arrest	37	94.90%	36	94.70%	13	92.90%	
Cardiovascular Disease	274	55.20%	341	57.90%	170	71.10%	
Chronic Renal Failure	19	37.30%	40	50.60%	10	40.00%	
Malignancy	95	18.80%	93	30.70%	23	30.30%	
Pneumonia	35	47.90%	56	58.30%	27	54.00%	
Sepsis	60	77.90%	51	77.30%	21	70.00%	
Cerebrovascular Diseases	75	36.90%	121	51.90%	60	60.00%	
Trauma	38	22.10%	35	16.50%	16	10.70%	
Urinary System	5	7.50%	9	20.90%	8	53.30%	
Burn	8	38.10%	3	18.80%	2	28.60%	
High Fever	7	28.00%	9	30.00%	7	87.50%	

*Chi-square analysis was used to analyse mortality rates and Bonferrioni post hoc test was used to analyse different groups.

management can substantially reduce morbidity and mortality.

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CONFLICT OF INTEREST:

No conflict of interest was declared by the authors.

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RESEARCH

THE RELATIONSHIP OF PRESBYCUSIS WITH COGNITIVE FUNCTIONS

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Abstract

Introduction: Presbycusis, age-related hearing loss, is one of the most common diseases in geriatric patients. The present study aims to achieve early diagnosis of presbycusis, prevent cognitive disorders, avoid social isolation, and provide guidance for the treatment.

Materials and Method: Presbycusis was diagnosed by routine biochemical, hormone, and audiological tests in patients aged ≥50 years with hearing loss who were admitted to the ear-nose-throat outpatient clinic. Cognitive impairment was examined by a neurologist; all patients received the Mini-Mental State Examination and Clock Drawing Test. Patients with dementia caused by metabolic and toxic disorders, and patients with depression who scored >10 on Beck's depression scale were excluded from the study.

Results: This prospective study was conducted between February 2016 and June 2017. A total of 73 patients were included in the study; the mean ± SD age was 71.44 ± 8.12 (min–max: 48-88) years; 42.5% (n = 31) were men and 57.5% (n = 42) women. Following age correction, the Mini-Mental State Examination score of patients with hearing loss was lower than those without (Corrected Z = 2.229; p = 0.026). The Clock Drawing Test score was lower in patients with hearing loss than those without (Corrected Z = 3.302; p < 0.001).

Conclusion: The present study revealed that presbycusis is neglected but significant cause of dementia and leads to its rapid development. Close and regular monitoring of hearing loss in geriatric patients and enhancement of social awareness on this issue are important factors for preventing dementia.

Keywords: Presbycusis; Cognitive Dysfunction; Dementia.

INTRODUCTION

According to the United Nations (UN) data anticipates that by 2020 world's population of individuals over 65 years of age will be 698 million (9.3% of the whole population) (1). In Turkey, however, the population of individuals over 65 years of age was 7.3% in 2011 and this ratio has been speculated to reach up to 17.6% in 2050 (2). Worldwide approximately 328 million adults suffer from hearing impairment, approximately 1/3 of the population over 65 years of age have been affected by hearing loss (3). According to the data of WHO, when the total of healthy years missed due to disability is evaluated, presbycusis ranks third among the causes leading to this loss (4).

Hearing problems are extremely common in elderly individuals, with a general prevalence of 23-48% over 65 years of age. The most common cause of hearing loss is presbycusis, which is progressive and bilateral high-frequency hearing loss. It physiologically occurs during the third decade and at high frequencies (5). It begins to influence the frequencies involving speech spectrum by the fifth decade. In most cases, people around the individuals recognize the hearing loss before the individual himself/herself. Difficulties in perceiving fast speech and having difficulties in recognition and differentiation of words in noisy media are generally described in the history. Therefore, admission complaints are as "hearing but not being able to understand the speech". Presbycusis is an exclusion diagnosis. It should be excluded through evaluating etiologies that may lead to hearing loss in elderly (6). Environmental factors (exposure to noise, use of ototoxic medications, alcohol intake, chronic diseases like diabetes, trauma, otological diseases etc.) and genetic factors are effective in development of presbycusis (7-10).

Presbycusis has been shown that influence life quality negatively by leading to situations such as limitation in social activities, loneliness, isolation, communicative disorders and dissatisfaction with family (11-13). There is also an association between presbycusis and dementia. Risk of developing dementia is increased two-fold in individuals with slight hearing loss, three-fold in individuals with moderate hearing loss and five-fold in those with severe hearing loss, compared to individuals with normal hearing functions (14). Hearing loss also leads to decrement in cognitive functional capacity of individuals (15).

It is clear that screening of hearing disorders are not sufficiently performed; it is performed in primary health care services routinely but to some extent. Patients unfortunately, cannot think that they should ask for help for such an issue. There are many screening tests for hearing; whispered voice test is the simplest in which a physician stands outside the visual field and 30 cm away from the relevant ear of the patient, and the patient is supposed to repeat at least 50% of the words whispered. While a screening test, the gold standard is audiometric measurement; if patients cannot hear voices at 1000 or 2000 Hz frequency with one or both ears, patients must be then referred to an ENT specialist. Hearing function is recommended to be checked up annually. By this means, early detection of presbycusis becomes possible and s/he can be closely followed-up for risk of potential dementia and preventive measures can be taken.

MATERIAL AND METHOD

Our study was conducted in a prospective manner between the dates of February 2016 to June 2017 in accordance with the principles determined in the Declaration of Helsinki. The study was approved by the Ethics Committee of Ankara Training and Research Hospital (2016/4/13-129). Patients over 50 years of age with suspected hearing loss who admitted to ENT outpatient clinic were examined by an ear-nose-throat specialist for presbycusis through exclusion of other potential causes. Routine biochemical and hormone tests and audiological tests were performed. The patients were assessed with minimental test (MMT)



and clock drawing tests by a neurologist who was unaware of the audiological tests. Accompanying diseases, organic and metabolic causes which may lead to dementia were excluded, Beck's depression scale was applied to the patients for exclusion of depression and those received scores over 10 were excluded from the study.

Statistical Analyses

Distribution of age and MMT score in the study was examined by using Shapiro-Wilk test. Age was summarized as mean ± standard deviation (mean±s), MMT and clock drawing scores were summarized as median (min-max). Categorical variables such as gender ere expressed as n (%).

Age, MMT and clock drawing test scores by hearing loss were compared by using Mann-Whitney U test. While age varies among groups and there was a statistically and clinically significant difference between MMT and clock drawing test scores, MMT and clock drawing scores by hearing loss were re-compared after corrected according to age. Changes in scores after a 6-month period was calculated as (Initial score – 6th month score)/(initial score) for MMT, because there were 0s in the initial values, as (initial score – 6th month score) for clock drawing test. Changes in the scores also were compared after age correction. While the data did not meet ANCOVA assumptions, age correction was performed with nonparametric ANCOVA and results of this test were provided. Three patients were excluded from the analysis because of advanced dementia. While ages of housewives and retired individuals were similar, their MMT and clock drawing tests were compared without any correction. A p-value of less than 0.05 was considered to show statistical significance.

Table 1. Demographical features.

	Mean±S n	Min-Max %
Age	**71.44±8.12**	**48-88**
Gender		
Male	31	42.5
Female	42	57.5
Educational Level		
Illiterate	1	1.4
Primary school	24	32.9
Secondary school	5	6.8
High school	23	31.5
Graduate school	20	27.4
Status of Employment		
Housewife	24	32.9
Retired	46	63.0
Employed	3	4.1

Table 2. Features Regarding Hearing Loss and Dementia.

	Baseline	6th Month
MMT Score [median (range)]	28 (17-30)	27 (16-30)
MMT group [n (%)]		
Moderate	1 (1.4)	3 (41)
Slight	13 (17.8)	20 (27.4)
Normal	59 (80.8)	50 (68.5)
Clock Drawing Test Score [median (range)]	7 (0-7)	6 (0-7)

IBM SPSS Statistics 21.0 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) program was used for statistical analyses and calculations.

RESULTS

The study was conducted between the dates February 2016 to June 2017. 83 patients over 50 years of age were included in the study. Ten patients with severe dementia were excluded from the study.

Of the patients included in the study; 31 were male (42.5%) and 42 were female (57.5%). Mean age of the 73 patients was 71.44±8.12 years (min-max:48-88) (Table 1). Of the patients; 32.9% (n=24) were primary school graduate and 31.5% (n=23) were high school graduate. It was determined that 46 patients (63.0%) were retired and 3 patients (4.1%) were employed. It was observed that 47 (64.4%) of the patients had hearing loss, MMT results of 59 (80.8%) were normal and Magnetic Resonance Imaging (MRI) results of 34 (46.6%) were normal.

MMT and Clock Drawıng test results were presented in Table 2 at baseline and 6th month results. The mean MMT score was 28 at baseline and 27 at the end of the 6th month. The Clock Drawing Test Score was 7 at the beginning and 6 at the end of the 6th month (Table 2).

Median age was 74 years (min-max:50-88) in patients with hearing loss and 69 years (min-max: 48-75) in patients without hearing loss. Ages of patients with hearing loss were observed to be higher ($Z=4.315$; $p<0.001$).

Median initial MMT score was 26 (min-max: 17-30) in patients with hearing loss and 29 (min-max: 26-30) in patients without hearing loss (Table 3). With corrected according to age, MMT score of patients with hearing loss was determined to be lower compared to those without hearing loss (Corrected $Z=2.229$; $p=0.026$).

Median sixth month MMT score was 25 (min-max: 16-29) in patients with hearing loss and 29 (min-max: 26-30) in patients without hearing loss (Table 3). With corrected according to age, when sixth month MMT scores were compared, scores of patients with hearing loss were observed to be lower (Corrected $Z=3.980$; $p<0.001$).

Sixth month MMT score in patients with hearing loss was determined to be reduced by a median of 7.14% (min-max: 0.0%-15.0%) compared to the initial score (Table 3). The median of this change in patients without hearing loss was 0% (min-max: 3.85%- 7.14%). When the percentage of change in MMT scores were compared between the two groups with corrected according to age, the difference between them was determined to be sig-

Table 3. Comparison of results of MMT test and clock drawing test by hearing loss.

	Hearing Loss		Corrected	
	No	Yes	Z; p	Z; p
Initial MMT				
Median (min-max)	29 (26-30)	26 (17-30)	4.036; <0.001	2.229; 0.026
6th Month MMT				
Median (min-max)	29 (26-30)	25 (16-29)	5.575; <0.001	3.980; <0.001
MMT difference (%)*				
Median (min-max)	0.00 (-3.85–7.14)	7.14 (0.00-15.00)	6.063; <0.001	4.776; <0.001
Initial Clock Drawing Test				
Median (min-max)	7 (6-7)	6 (0-7)	4.348; <0.001	1.891; 0.059
6th Month clock drawing test				
Median (min-max)	7 (0-7)	5 (0-7)	4.463; <0.001	3.302; 0.001
Clock drawing difference**				
Median (min-max)	0 (0-7)	0 (-6–2)	1.565; 0.118	3.863; <0.001

*(initial score-6th month score)/(initial score)*100. ** initial score-6th month score.

Table 4. Comparison of MMT and clock drawing test scores.

	Hearing Loss		Corrected	
	No	Yes	Z; p	Z; p
Initial MMT				
Median (min-max)	29 (26-30)	26 (17-30)	4.036; <0.001	2.229; 0.026
6th Month MMT				
Median (min-max)	29 (26-30)	25 (16-29)	5.575; <0.001	3.980; <0.001
MMT difference (%)*				
Median (min-max)	0.00 (-3.85–7.14)	7.14 (0.00-15.00)	6.063; <0.001	4.776; <0.001
Initial Clock Drawing Test				
Median (min-max)	7 (6-7)	6 (0-7)	4.348; <0.001	1.891; 0.059
6th Month clock drawing test				
Median (min-max)	7 (0-7)	5 (0-7)	4.463; <0.001	3.302; 0.001
Clock drawing difference**				
Median (min-max)	0 (0-7)	0 (-6–2)	1.565; 0.118	3.863; <0.001

*(initial score-6th month score)/(initial score)*100. ** initial score-6th month score.

nificant (Corrected Z=4.776; p<0.001). MMT score in patients with hearing loss was determined to decrease more.

After corrected according to age, it was concluded that patients with and without hearing loss were similar in regard to the initial clock drawing test (Corrected Z=1.891; p=0.059). 6th month clock drawing score was lower in patients with hearing loss (corrected Z=3.302; p<0.001). When the change in clock drawing score was examined, it was determined that more reduction occurred in patients with hearing loss (Corrected Z=3.863; p<0.001).

There were no differences between retired individuals and housewives I terms of age, MMT score, clock drawing score and changes in these scores at the 6th month compared to the beginning (p>0.05, Table 4).

DISCUSSION

Individuals with hearing loss had a higher risk of impaired cognitive functions and presence of dementia (16-17). In our study, both initial and 6th month MMT scores and clock drawing scores were compared, in evaluations by the end of 6th month, particularly patients with presbycusis were determined to have a statistically significant reduction in both of two scores. Hearing loss over 60 years of age is more than 30% as is shown in previous study. Similarly, in our study, median age was 74 years (min-max:50-88) in patients with hearing loss and 69 years (min-max: 48-75) in patients without hearing loss. Ages of patients with hearing loss were observed to be higher (Z=4.315; p<0.001). This can be a risk factor for dementia (18).

Hearing loss is independently associated with dementia. Larger studies are need to determine whether hearing loss is a marker for early-stage dementia or a modifiable risk factor for dementia. When the increment in elderly population worldwide and in our country is taken into consideration, it is extremely crucial to pay attention to this health issue, presbycusis, whose determination is extremely easy. Referral of patients with hearing impairment detected by taking this into consideration in primary health care services to relevant specialties is of vital importance in regard to public health by reducing risk of potential dementia.

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RESEARCH

THE INVESTIGATION OF THE USE OF EMERGENCY MEDICAL SERVICES FOR GERIATRIC PATIENTS DUE TO SUICIDE

Abstract

Introduction: Ageing is a physiological process, and inevitable psychological and physical changes occur after the age of 65 in every individual. Elderly suicide is a crucial public health concern that is still largely ignored worldwide. The purpose of this study is to investigate the use of emergency medical services by geriatric patients due to suicide.

Materials and Method: We obtained the demographic and clinical information of the patients from the records. We retrospectively examined the data of all patients, who are 65 and older, enrolled in Turkey for the suicide attempt between September 2018 and August 2019.

Results: Our study included 769 cases. There was a statistically significant difference between the two genders in terms of the number of completed suicides ($p < 0.001$). The most common suicide method was drug use (30.8%). In total, 36.7% of women and 62.7% of men used violent methods for suicide. We found a statistically significant difference between the groups in terms of violent method usage ($p < 0.001$). There was a statistically significant difference between the age groups in terms of completed suicide percentages ($p = 0.008$), and the cases reported from urban and rural areas in terms of mortality ($p < 0.001$).

Conclusion: The percentage of completed suicides increases with age, and the careful evaluation of suicide attempts is vital in reducing the risk of suicide-related death. The process starting from the moment of notification of suicide attempt to the emergency dispatch centre must be managed effectively and quickly by trained and experienced medical teams.

Key words: Emergency Treatment; Health Services for the Aged; Suicide.

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INTRODUCTION

Ageing is a physiological process, and inevitable psychological and physical changes occur after the age of 65 in every individual who successively reaches this age. According to the World Health Organization's old age report published in 2015, the elderly population in the world is expected to grow twice its present size in 2050. Therefore, interventions aiming at improving the geriatric health in the future health policies of the countries are highly recommended. Elderly suicide is a crucial public health concern that is still largely ignored worldwide. Suicide rates have been reported to be higher among the elderly in all the countries. The highest rate of suicide was reported in the individuals who were 70 years and older. (1-3)

Pre-hospital emergency medical services (EMS) are known to be the first medical contact with the patients who are at a risk of suicide, especially in the rural areas. (4) A study conducted in Valencia reported that 6,537 suicide-related emergency calls were received over the course of 7 years, of which 142 were completed suicides. (5) However, it is stated that suicide attempts are under-reported, even in countries with an advanced registration system. It is also reported that the cases treated by emergency health services are often more critical. (6) Considering that some of the suicide-related emergency calls are also refused to be taken to the hospital, the notifications made to the emergency dispatch centres provide reliable data on suicide attempts. (7) The fact that EMS providers receive adequate training on this issue is also considered as a crucial point in terms of preventing suicides. (4)

In our knowledge, although various studies have been published in some of the provinces and territories of our country for the use of EMS for suicide-related emergencies, a study reflecting the general state has not been published yet. Therefore, the purpose of this study is to investigate the use of EMS by geriatric patients due to suicide. By examining the pre-hospital records, we aimed to reveal not only the completed suicides but also the data on all suicide attempts reported to the emergency dispatch centres. Thus, we also aimed to contribute to the planning of preventive and therapeutic health services to be provided to the geriatric individuals in the vulnerable and disadvantaged group for suicide.

MATERIALS AND METHOD

This study is designed as a cross-sectional epidemiological study. After obtaining the approval of Başkent University Medical and Health Sciences Research Board (project no: KA19/318), we applied to the Ministry of Health for permission. After receiving the necessary permission, we obtained the demographic and clinical information of the patients from the records of the Emergency Health Automation System (ASOS). We retrospectively examined the data of all patients, who are 65 and older, enrolled in Turkey for the suicide attempt between September 2018 and August 2019. We recorded the date, month, season, time, the rural–urban distinction and the provinces from which the calls were made to the emergency dispatch centres by the patients. We determined the age, age group, gender, on-site mortality and suicide methods of the patients. The use of drugs, chemicals or natural gas and jumping into the water were considered as the cases of non-violent suicide, whereas the use of a sharp or blunt object and firearms, self-hanging, jumping in front of a moving motor vehicle (car or train, etc.), jumping from high places and self-immolation were considered as the cases of violent suicide. (8)

We conducted our study on the 769 calls made due to suicide between the dates mentioned above.

Statistical Analysis

We evaluated whether the data showed a normal distribution with the help of graph and Kolmogorov–Smirnov test. We presented descriptive statistics as number (n), percentage (%), median and interquartile range. The Mann–Whitney U test was employed to assess the numerical data, which

did not fit the normal distribution in the paired group comparisons, whereas the Chi-square test was employed to assess the categorical data. Patients were divided into three groups according to their ages: 65–74 years (young-old), 75–84 years (middle-old) and 85 years and older (oldest-old) as described by Koo et al. (9) p <0.05 was considered statistically significant.

RESULTS

Our study included 769 cases of patients, who are 65 years and over and have a history of suicide attempts or completed suicide between 01.09.2018 and 31.08.2019 in Turkey. In total, 34.5% (n = 265) of the cases were female. The median age of the total cohort was 72 (11) years. The median age of the females was 71 (11) years, whereas the median age of the males was 72 (11) years. We did not find any statistically significant difference between the female and male groups in terms of age (p = 0.812).

We divided the patients into three groups. Accordingly, there were 472 patients (61.4%) in the 65–74 age group, 217 patients (28.2%) in the 75–84 age group and 80 patients (10.4%) aged in the group of 85 years and older.

Of these, 54.7% (n = 421) of these cases were reported between 8.00 and 15.59 hours, 32.6% (n = 251) were reported between 16.00 and 23.59 hours and 12.6% (n = 97) were reported between 00.00 and 07.59 hours. The seasonal distribution of cases was as follows: summer had 31.1% (n = 239), autumn had 22% (n = 169), winter had 20.8% (n = 160) and spring 26.1% of the cases (n = 201).

In total, 68.9% (n = 530) of the cases were reported from the urban areas, whereas the rural areas reported 31.1% (n = 239) of the cases. The distribution of cases by seven geographical regions of Turkey is presented in Table 1. Most of the cases were reported from the Marmara region (26.9%), which is the most crowded geographical region of Turkey.

In total, 68.9% (n = 530) of the cases were suicide attempts, whereas 31.1% (n = 239) of these cases were completed suicides. In other words, 31.1% of the cases lost their lives.

Table 2 shows the comparison of completed suicide and attempted suicide cases by gender. There was a statistically significant difference between the two genders in terms of the number of completed suicides (p <0.001). In total, 37.1% of suicides in males were completed suicides.

Table 1. Distribution of suicide cases aged 65 and over by seven geographical regions of Turkey.

Geographical Region	Number	%
Marmara	207	26.9
Aegean	184	23.9
Mediterranean	99	12.9
Central Anatolian	124	16.1
Black Sea	94	12.2
Eastern Anatolian	40	5.2
Southeastern Anatolian	21	2.7
Total	769	100

Table 2. Distribution of suicide attempts and completed suicide cases by gender.

Gender	Suicide attempts	Completed suicides	Total	p value
Female	213 (80.4%)	52 (19.6%)	265 (100%)	<0.001*
Male	317 (62.9%)	187 (37.1%)	504 (100%)	
Total	530 (68.9%)	239 (31.1%)	769 (100%)	

*Chi-square test

Table 3. Distribution of cases by suicide methods.

Suicide methods	Gender n (%)		Mortality n (%)		Total n (%)
	Female	Male	Non-survivor	Survivor	
Drug use	120(45.3)	117(23.2)	0(0)	237(100)	237(30.8)
Chemical use	30(11.3)	42(8.3)	1(1.4)	71(98.6)	72(9.4)
Sharp or blunt object	10(3.8)	46(9.1)	3(5.4)	53(94.6)	56(7.3)
Self-hanging	53(20)	142(28.2)	157(80.5)	38(19.5)	195(25.4)
Firearms	1(0.4)	75(14.9)	57(75)	19(25)	76(9.9)
Jump in front of a moving motor vehicle (car-train, etc.)	2(0.8)	3(0.6)	2(40)	3(60)	5(0.7)
Jumping from high places	20(7.5)	23(4.6)	13(30.2)	30(68.8)	43(5.6)
Natural gas	1(0.4)	5(1)	2(33.3)	4(66.7)	6(0.8)
Burning himself/herself	2(0.8)	1(0.2)	1(33.3)	2(66.7)	3(0.4)
Jumping into water	2(0.8)	3(0.6)	0(0)	5(100)	5(0.7)
Drugs + chemicals	2(0.8)	8(1.6)	0(0)	10(100)	10(1.3)
Drug use + sharp or blunt object	0(0)	1(0.2)	0(0)	1(100)	1(0.1)
Chemical use + sharp or blunt object	2(0.8)	2(0.4)	0(0)	4(100)	4(0.5)
Self-hanging + jumping from high places	0(0)	1(0.2)	0(0)	1(100)	1(0.1)
Others	20(7.5)	35(6.9)	3(5.5)	52(94.5)	55(7.2)
Total	265(100)	504(100)	239(31)	530(68.9)	769(100)

*n: number

Table 3 summarizes the cases according to the suicide methods. According to the observations, the most common suicide method was drug use (30.8%). This was followed by suicides done by self-hanging (25.4%) and using firearms (9.9%). The most common suicide method in women was drug use with 45.3%, whereas the most common method was self-hanging in men (28.2%). In total, 36.7% of women (n = 90) and 62.7% of men (n = 294) used violent methods for suicide. By comparing the two

Table 4. The mortality according to age groups.

Age group	Completed suicides	Suicide attempts	Total	p value
65-74 years	132 (28%)	340 (72%)	472 (100%)	0.008
75-84 years	71 (32.7%)	146 (67.3%)	217 (100%)	
85 years and older	36 (45%)	44 (55%)	80 (100%)	
Total	239 (31.1%)	530 (68.9%)	769 (100%)	

groups, we found a statistically significant difference between the groups in terms of violent method usage ($p < 0.001$).

Table 4 shows the mortality according to age groups. Accordingly, there was a statistically significant difference between the age groups in terms of completed suicide percentages ($p = 0.008$). We used paired group comparisons by employing Bonferroni correction to determine which groups stem from the difference. We found that the difference was between the age groups of 65–74 and 85 years and older ($p = 0.002$).

The mortality rates in urban and rural areas were 24.2% and 46.4%, respectively. There was a statistically significant difference between the cases reported from urban and rural areas in terms of mortality ($p < 0.001$).

DISCUSSION

The results of our study revealed the characteristics of suicide attempts and completed suicides of geriatric individuals in our country. Accordingly, the ratio of completed suicides to suicide attempts was 1:2.2. The suicide attempts were higher in the males (65.5%). Besides, the number of completed suicides was significantly higher in men than in women ($p < 0.001$). In our country, Ozer et al. reported a higher percentage (74.5%) of men committing suicide than women in a study of completed suicides of geriatric population. (10) In 2018, the Turkey Statistical Institute has announced that the number of suicides by males in the general population was higher than women (2391 vs. 770). (11) Our results are consistent with the literature. In addition, the suicide rates in men in the geriatric age group were reported to be higher than the general age group. (12) In the general population, unlike our study, suicide attempts were higher in the females. (13)

The suicide rates in the geriatric age group are reported to be highest in the age group of 75 years and over. (12) Our study determined most of the cases of suicide (61.4%) in 65-74 years group. Besides, the completed suicide proportion was the lowest in this group (28%). This proportion was the highest in 85 years and older group (45%).

A study, which evaluated the suicide attempts in all the age groups in Sanliurfa, Turkey, found that nearly half of the cases (49.8%) occurred between 16.00 and 24.00 hours. (14) In our study, cases were concentrated between 08.00 and 16.00 (54.7%). We believe that this difference is because all the mentioned cases in the first study were under 65 years of age. From this observation, we can conclude that the cases in the geriatric age group are intensified when the family members are not at home.

Akkaya-Kalayci et al. found that the suicide attempts were most common in summer (30.6%) in Istanbul. They examined suicide attempts of young individuals between the ages of 15 and 25. (15) In



our study, although the ages of the cases were a lot different from this study, suicides were most common in summer (31.1%). A study conducted by Nazari Kangavari et al in Iran showed that the number of completed suicides was higher in the months of summer. (16)

Senol et al. reported that 65.5% of the patients who applied to the emergency department for suicide chose using drugs as a suicide method. (17) Dilbaz et al. showed that the most commonly used suicide methods were excessive use of drug, chemicals or sharp objects, self-hanging, jumping from high places, and killing self by a firearm. (18) The most common suicide methods reported in our study were drug use, self-hanging and killing self by firearms. Violent (62.7%) and completed suicides (37.1%) were more common in men, and the most common methods were self-hanging, drug use and killing self by firearms. Ozer et al. found that self-hanging was the most common method in the completed suicides among geriatric population. (10) Besides, violent methods were reported to be used more frequently by males as shown in our study. (12)

In our study, we found that most suicides (68.9%) were reported from the urban areas, but we also found that completed suicides were considerably higher in the rural areas ($p < 0.001$). In the United States, it was found that the rates of suicide were higher in rural areas than in urban areas (20 vs. 11 per hundred thousand). (19) Although it has been suggested that the more widespread use of firearms in the rural areas may be a reason for high rates of suicides, the reasons for this situation remain unclear. (20) In our study, the most common method in completed suicides in rural areas was self-hanging ($n = 74$), followed by killing self with a firearm ($n = 30$). In countries and states where access to firearms is not easy under the law, suicide rates were found to be less. It is stated that limiting the possession of firearms will reduce the suicide-related mortality even if it does not change the total number of suicide attempts. (12)

The strength of our study is that it includes a large sample and demographic information on both suicide attempts and completed suicides. Given the difficulties in accessing data on suicide attempts, the generalizability of our results is stronger than the previous studies that only involve a hospital emergency department or psychiatry clinics. There are some limitations in our study: the suicide attempt data of EMS are the only considered data in our study, and it does not include suicide attempt cases of people, who applied to the hospital with their means and did not apply to any other health service. There were no data on the marital status, socioeconomic information, educational status, previous physical or psychiatric diseases, suicide attempts, addictions and medications of the patients included in the study. Therefore, other risk factors reported in the previous suicide-related studies could not be analyzed. We believe that acquiring this information in future prospective studies at the national scale will be beneficial in revealing the preventable causes of suicide.

CONCLUSION

In conclusion, the completed and attempted suicide frequencies were higher in males. The drug use was the most common suicide method among geriatric individuals. The men used violent methods more than women. Most of the suicide cases were in the young-old age group. The completed suicide proportion was the highest in the oldest-old age group. The mortality rates were higher in rural areas than in urban areas.

The percentage of completed suicides increases with age, and the careful evaluation of suicide attempts is vital in reducing the risk of suicide-related death. EMS is the medical unit, which is firstly contacted by most of the geriatric patients with suicide attempts. The process starting from the moment of notification of suicide attempt to the emergency dispatch centre must be managed effectively and quickly by trained and experienced

medical teams. (21) Taking into consideration the importance of EMS records in terms of suicide statistics and risk factors, the results of our study can be used for the planning of protective measures in this area. Further studies are needed to determine the risk factors related to geriatric suicides.

CONFLICT OF INTEREST

The authors declared that there was no conflict of interest.

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RESEARCH

ATTITUDES AND BEHAVIORS OF ELDERLY INDIVIDUALS TOWARDS END-OF-LIFE DECISIONS

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Abstract

Introduction: Elderly individuals frequently face end-of-life decisions. These decisions create moral burden for the family and health personnel. Aim of this study is determine the opinions of elderly about end-of-life decisions, which will act as a guide for physicians and families in clinical decision-making processes.

Materials and Method: Standardized Mini Mental Test was applied to 650 elderlies, and 448 participants with a test score 27 or more were interviewed between 1 May 2017 and 1 January 2019 using questionnaires including sociodemographic data form and scenarios that would determine their end-of-life decisions. Only statistically significant ($P \leq 0.05$) results were presented in the results section.

Results: 72.5% (n=325) of the participants stated that they should be informed about medical diagnosis, 70.1% (n=314) stated that decision of informing the family should be left to patient and physician should inform the patient in any case. It was found that being familiar with the physician for a long time was important in fulfilling patient requests, and 79% (n=354) of the participants could consider leaving a living will and appointing a medical guardian.

Conclusion: Not talking to elderly patients with the judgment that they will not understand the concepts of elderly care, not seeing them as a decision-maker in treatment and care decisions, letting relatives make the decisions and applying these decisions are unacceptable attitudes for elderly individuals who have good mental health.

Keywords: Ageds; Advance Directives; Clinical Decision-Making; Physician-Patient Relations; Attitude.

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INTRODUCTION

Since elderly individuals are closer to end of their expected lives, they are more likely to face situations where difficult decisions about health care have to be given. Therefore, when elderly people need health care, they frequently face end-of-life situations and they are often unable to make these decisions themselves. End-of-life care decisions often lead to additional stress, especially for elderly patients, and often don't reflect the patient's wishes correctly (1, 2). Who should be decision-maker in these situations? Herein, does the fact that care is pre-planned by patient, having left a living will, or having proxy to decide on their behalf facilitates their end-of-life decision making and care? All these questions make concepts of living will, advance directive, and durable power of attorney more prominent in elderly care.

Although concepts and practices such as living will, advanced directives, and durable power of attorney seem to overlap, the rationale for applying each in clinical setting and related application methods differ. End-of-life treatment preferences, future care choices, interviews with family and health care staff can be considered as part of advanced directives. Advanced directives should be clear and specific enough to guide the future clinical decisions. Living will direct the physicians about situations in which the patient wants to stop or withdraw his/her life support. Living will can only be used in fatal diseases and patient has to be aware of the decision and his/her medical condition. The situation is slightly different for durable power of attorney. Here, patient is unable to make decisions on his or her own, and appoints a proxy who can make medical decisions on his or her behalf. In contrast to the living will, the patient can be suffering from mental capacity loss or fatal disease in this case (2, 3). Individuals suffering from mental or physical capacity loss as a result of accidents, illnesses, or serious disabilities that may happen in the future will also cause difficulties in communication. For this reason, it is important that individuals declare the practices that they want or don't want to be performed on them while they are healthy, or declare who they want to be decision-maker when they become unable to make decisions for themselves. Furthermore, it's also true that participation of elderly individuals in medical decisions isn't at the desired level even if they don't have mental problems. Families ask physicians to tell them the diagnosis first (4, 5). However, Article 24 of the Patient Rights Regulation in our country requires the consent of the patient in medical interventions and it is essential for the patient to know its illness (6). This situation is sometimes just the opposite. Physicians prefer to talk with the family of older adults instead of themselves, for reasons such as lack of time, thinking that the patient cannot understand its condition, or feeling uncomfortable while saying the undesirable diagnosis, which completely eliminates the decision-making of an older adult having good mental health. However, it should be known that such practices contradict the Patient Rights Regulation in our country because Article 24 of the regulation indicates "even in cases where the legal representative's consent is sufficient, the young or restricted patient shall be enabled to participate in the information process and decisions about the treatment as much as possible to the extent that it can understand what has been told and is allowed to speak" (Patient Rights Regulation, Article 24) (6). In addition, for recurrent diseases where the competency is lost from time to time (which is frequently encountered in older adults due to dementia), there is the phrase in the same regulation that "prior requests of a patient, who is unable to explain its request during a medical intervention, regarding the medical intervention shall be taken into consideration". For this reason, it is important to know the decisions, wishes, and attitudes of elderly patients, who are at the last stage of their lives, about their ends, which will save the patient and family from many legal and ethical dilemmas. There are concerns about their deputies to decide on their behalf, as well as the predictable nature of both the serious illnesses of older adults and the

decrease in their cognitive and voluntary abilities. This reveals significant benefits in the use of advance directives of the older adults for their care. Such directives include Authorization Statement - Representative Consent documents and Testament. Interestingly, most of the empirical research on both proxy decisions and advance directives focused on older adults. Unfortunately, such research in our country has not been made specifically for age groups. The lack of applications such as the living will, advance directive, durable power of attorney and the fact that their legal grounds have not been yet prepared are also important obstacles regarding the end of life decisions. In our country, there are a limited number of studies examining physician and patient attitudes regarding end-of-life decisions. Odabasi and Buken's study, "Informed Consent and Ethical Decision Making at the End of Life: Hacettepe Example", is an important resource for discussing the ethical decisions of physicians and patients at the HUTF hospital and the problem of autonomy. In the case of Hacettepe, physicians and patients prefer the authority and decision-making of the family and physician to the autonomy of the patient (7).

There are no studies in Turkey that reveal the opinions of elderly individuals about being told about bad diagnosis, living will, and durable power of attorney. Therefore, in this study, we tried to determine the opinions of elderly individuals about end-of-life decisions to act as a guide to physicians and families in clinical decision-making processes.

MATERIALS AND METHOD

Sampling

The population of the study consisted of elderly individuals living in the city center of Burdur. Considering the population of 11,360 individuals, prevalence of 50%, sampling error rate of 0.05 and confidence interval of 95.0%, the minimum sample size, which represents the population in the Epi-info programme, was calculated to be 378. In this study, Standardized Mini Mental Test (SMMT) was applied to 650 people aged 65 years and over. Face-to-face interviews were conducted and questionnaires were applied to total of 448 volunteer participants with a test score of ≥27 between May 1, 2017 and January 1, 2019, and only statistically significant results ($P \leq 0.05$) were presented in the Results section.

Data Collection Tools

SMMT was developed by Folstein et al. in 1975 for the grading of cognitive disorders (8). Turkish validity and reliability of test was studied by Gungen et al. (2002) and normative values were determined. The patient receives a maximum of 30 and a minimum of 0 points at the end of the test. The critical score here is 27 or 24. Patients with a score below 27 are considered to have cognitive impairment (9).

Sociodemographic data form prepared by researchers was used to collect data such as age, gender, marital status, education, social security, and income status of participants.

Scenarios in the questionnaire form used in this study to determine attitudes of elderly individuals towards end-of-life decisions were applied to participants by obtaining the necessary permissions from Ruhnke et al. (2000), which was adapted to Turkish by Buken and Balseven (10, 3). These scenarios questioning end-of-life decisions were selected because they are far from medical terminology and easy to understand for older adults and are designed to measure attitudes only, independent of acts and practices of the current country.

Analysis of Data

All statistical analyses were performed using Statistical Package for The Social Science v20.0. Descriptive analyses and Chi Square analysis were used to evaluate the data.

Ethical considerations

This study was approved by Ethics Committee of Mehmet Akif Ersoy University



(Date:08.03.2017-Number: GO2017/55).

RESULTS

The examination of the demographic characteristics of the participants revealed that 38.2% were male, 33.3% were primary school graduates, 62.5% were married, 100% had a regular income, 83% had social security, and 53.1% had income equal to their expenses. The mean age of the participants was 71.6 ± 3.4 and mean SMMT score was 29.6 ± 0.2 (Table 1).

Table 1. Sociodemographic Characteristics of the Participants.

Characteristic	Groups	Number (n)	Percentage (%)
Age Group	65-74	305	68,1
	75 and over	143	31,9
Sex	Female	277	61,8
	Male	171	38,2
Marital Status	Married	280	62,5
	Widowed	154	34,4
	Divorced	14	3,1
Education	Illiterate	83	18,5
	Primary School	149	33,3
	Middle and High school	64	14,2
	University	152	33,9
Regular Income	Yes	448	100
	No	0	0
Social Security	Yes	372	83
	No	76	17
Income Status	Less than expenses	134	29,9
	Equal to expenses	238	53,1
	More than expenses	76	17
Mini Mental Test Score	27	5	1,1
	28	31	6,9
	29	174	38,8
	30	278	53,2

When participants' opinions about diagnosis being told to patient were examined, it was found that 72.5% of the participants considered that the patient should be told the truth. In addition, the responses given for different situations in Scenario 1 were found to be statistically significant in terms of some sociodemographic variables (Table 2).

Table 2. Scenario 1: Suppose you have advanced stage cancer that can't be treated.

Situation 1.1. The doctor should inform you about your disease. The doctor should let you decide whether or not to disclose this information to your family. Do you agree?				
Sociodemographic characteristics		n (%) *	I agree** n (%)	P
Age Group	65 -74 75 or above	305 (68.1) 143 (31.9)	226 (74) 99 (69.2)	0,01
Education	Primary school or below Middle – High school University or above	232 (52) 64 (14,2) 152 (33,8)	157 (67.6) 34 (53.1) 134 (88.1)	0,05
Social Security	Yes No	372 (83) 76 (17)	279 (75) 46 (60.5)	0.01
Marital Status	Married Single	280 (62,5) 168 (37,5)	240 (85.7) 85 (50.8)	0,001
Situation 1.2. The doctor should inform your family about your disease, and not you. Your family should decide whether you should be told about your disease. Do you agree?				
Sociodemographic characteristics		n (%) *	I agree** n (%)	P
Age Group	65 -74 75 or above	305 (68.1) 143 (31.9)	75 (24.5) 55 (38.4)	0.001
Education	Primary school or below Middle – High school University or above	232 (52) 64 (14,2) 152 (33,8)	95 (40.9) 29 (45.3) 16 (0.1)	0.0001
Marital Status	Married Single	280 (62,5) 168 (37,5)	67 (23.9) 63 (37.5)	0.01
Income Status	Less than expenses Equal to expenses More than expenses	134 (29,9) 238 (53,1) 76 (17)	50 (37.3) 70 (29.4) 10 (13.1)	0.005
Situation 1.3. Suppose your family is aware of your illness and that they don't want the doctor to give you information about your illness. The doctor should still inform you about your illness. Do you agree?				
Sociodemographic characteristics		n (%) *	I agree** n (%)	P
Age Group	65 -74 75 or above	305 (68.1) 143 (31.9)	226 (74) 99 (69.2)	0,01
Education	Primary school or below Middle – High school University or above	232 (52) 64 (14,2) 152 (33,8)	157 (67.6) 34 (53.1) 134 (88.1)	0,05
Social Security	Yes No	372 (83) 76 (17)	279 (75) 46 (60.5)	0.01
Marital Status	Married Single	280 (62,5) 168 (37,5)	240 (85.7) 85 (50.8)	0,001
Gender	Female Male	277 (61.8) 171 (38.2)	163 (58.8) 151 (88.3)	0.005

*Column percentage **Row percentage



According to the answers in scenario 2, it is seen that being familiar with the physician for a long time is important for elderly individuals. In addition, the responses given for different situations in Scenario 2 were found to be statistically significant in terms of some sociodemographic variables (Table 3).

Table 3. Scenario 2: Suppose you have gastric cancer that will result in death within six weeks and you have pain that can't be relieved. You ask the doctor for a large dose and amount of painkillers to end your life.

Situation 2.1. Let us assume that the doctor is seeing you for the first time and receives general information about your illness.				
Situation 2.1.1. The doctor should give you this large dose and amount of medication. Do you agree?				
Sociodemographic characteristics		n (%) *	I agree** n (%)	P
Age Group	65 -74 75 or above	305 (68.1) 143 (31.9)	80 (26.2) 67 (46.8)	0,001
Education	Primary school or below Middle – High school University or above	232 (52) 64 (14,2) 152 (33,8	96 (41.3) 21 (32.8) 30 (19.7)	0,001
Marital Status	Married Single	280 (62,5) 168 (37,5)	100 (35.7) 47 (27.9)	0,001
Income Status	Less than expenses Equal to expenses More than expenses	134 (29,9) 238 (53,1) 76 (17)	40 (29.8) 96(40.33) 11 (14.4)	0.01
Situation 2.2. The same situation, but this time, let us assume that the doctor has known you for 20 years.				
Situation 2.2.1. The doctor should give you this large dose and amount of medication. Do you agree?				
Sociodemographic characteristics		n (%) *	I agree** n (%)	P
Age Group	65 -74 75 or above	305 (68.1) 143 (31.9)	180 (59) 64 (44.7)	0.05
Education	Primary school or below Middle – High school University or above	232 (52) 64 (14,2) 152 (33,8)	165 (71.1) 25 (39) 54 (35.5)	0.005
Marital Status	Married Single	280 (62,5) 168 (37,5)	200 (71.4) 44 (26.1)	0.0001
Social Security	Yes No	372 (83) 76 (17)	230 (61.8) 14 (18.4)	0.0001

*Column percentage **Row percentage

Based on the answers given to Scenario 3, it was determined that 79% (n = 354) of the participants thought about leaving a living will and appointing a medical proxy.

Table 4. Scenario 3. Let us assume that your condition has suddenly worsened one day because of your illness and that you are unable to make decisions on medical interventions to be performed on you. In such a case, you talked to your family when your health was still good, you told your family about any interventions you didn't want to be performed (e.g. cardiopulmonary resuscitation, respiratory support, etc.), but your family doesn't support your thoughts.

Situation 3.1. Would you consider leaving a living will and appointing a medical proxy to make medical decisions on your behalf?				
Sociodemographic characteristics		n (%) *	I agree** n (%)	P
Age Group	65 -74 75 or above	305 (68.1) 143 (31.9)	270 (88.5) 84 (58.7)	0,05
Education	Primary school or below Middle – High school University or above	232 (52) 64 (14,2) 152 (33,8)	150 (64.6) 59 (92.1) 145 (95.3)	0,05
Marital Status	Married Single	280 (62,5) 168 (37,5)	240 (85.7) 84 (50)	0,001

*Column percentage **Row percentage

When the responses given by the participants to the scenarios are examined, it can be seen that age group, education, and marital status are common variables that are statistically significant in all scenarios ($P \leq 0.05$).

DISCUSSION

The main purpose of planning end-of-life treatment and care decisions in advance is to ensure that patient, family, and physician discuss the best treatment options and are prepared for certain medical conditions, and make the best possible medical decisions at the time (11). One of the most important problems in the physician-patient relationship in our country is that the decisions for the treatment are mostly taken by the relatives and/or physician of the patient instead of the patient. This situation becomes more evident in the decisions taken about the termination of life (12). In their cross-cultural study comparing attitudes of American, Japanese, Arab and Turkish physicians regarding the last period of life, Buken and Odabasi (2013) found that the fact that physicians knew their patients caused differences in attitudes about physician-assisted suicide. However, knowing the patient for a long time in Saudi Arabia, which is a Muslim country like ours, did not change the physician attitude regarding physician-assisted suicide (13, 14). In other Islamic countries such as ours, the common thought about end-of-life treatment and care is that if the treatment will not improve the patient's condition or quality of life, life support can be interrupted or terminated. It has been reported that the patient population at the end of life is largely comprised of older adults. However, even if life support is terminated, nutrition is not terminated or interrupted. Even with the possibility of Double Effect, pain relief is advocated but euthanasia is never accepted. The fact that the physician knows its patient has been reported to accelerate the decision-making process in the treatment and care protocol (15). In study of Kellog et al. found that the physician and the patient who were familiar with each other facilitated the end-of-life treatment and care process. Because the doctor knows the treatment preferences of the patient he or she has known for years, and it was found that the majority of elderly people wanted to be told about their medical diagnoses (78%) (16). Kelner's study in Canada showed that a large proportion of patients (76%) wanted to be told

about their medical diagnosis and take active role in medical treatment decisions (17). In this respect, the results of present study are consistent with the literature, and it was found that the majority of elderly participants in Turkey wanted to know their medical diagnoses and be a decision maker when making medical decisions (Table 2, Table 3).

Based on the results of our study, it was found that 79% of the participants would consider leaving a living will after being explained what a living will was (Scenario 3). Although these concepts are new in Turkey and we don't see them often in practice, the situation in other countries isn't so different either. During their interviews in Canada, Heyland et al. found that 76.3% of elderly thought about end-of-life decisions before being hospitalized but only 11.9% acted on these thoughts and left a living will, 30.3% discussed these decisions with physicians (18). In the study of Gamble et al. in North Carolina, it was found that 64% knew what living will was, none of them filled out a living even though the government had a program related to it, and only two participants (3%) discussed end-of-life treatment and care preferences living their doctors. In the same study, it was found that 93% of the participants wanted to have a family member or spouse as their medical proxy when they couldn't make decisions for themselves (4). In another study of 76 elderly individuals in the UK, it was found that 82% of the participants didn't hear the terms of living will, instructions, or advanced directives before, and only 4 people out of 13 who had heard what living will be correctly defined the term, and 75% of the participants preferred relatives or spouses, 5% preferred friends, and 20% preferred their doctors as medical proxy (19). In our study, these rates were 58.9% for family, 38.6% for physician, and 2.5% for friends. In addition, we found that married participants, aged between 65 and 74 years, with social security and a university education or above wanted to take an active part in their end-of-life treatment preferences, they wanted to be informed first about their diagnosis, and they wanted to decide whether the diagnosis should be told to the family (Table 2, Situation 1.1). It was determined that elderly individuals who had more income than their expenses didn't agree with the idea that the medical diagnosis should be told to the family first and the family should decide whether the diagnosis should be told to them or not (Table 2, Situation 1.2). It was also found that male participants between the ages of 65 and 74, with social security and a university education or above considered that the physician should inform them about their diseases even if their family didn't want this information to be disclosed to them (Table 2, Situation 1.3). Similar to our findings, when we look at other studies in the literature, we see that married elderly people with high educational level and above average income status want to play an active role in end-of-life treatment and care decisions, and think that the medical diagnosis should be told to them as it will create a pressure and burden on family members and spouses (5, 17, 19). On the other hand, regarding the practices in some Middle Eastern countries, it is known that undesirable diagnosis is reported to the family and then to the patient in Iran, and the family decides to tell the diagnosis to the patient (20). tendency to act in line with the principle of beneficence is common in Saudi Arabia, but family members are reported to be given priority in telling about the diagnosis of the disease (21). In our study, we determined that patients who have been familiar with their physicians for a long time think that the physicians should fulfill their wishes and requests. Based on the answers given to Scenario 2, it was found that being familiar with the physician for a long time was a factor in fulfilling the request for high doses of painkillers and they thought that the physician should give them these high doses of drugs since they had been familiar with the physician for a long time (Table 3). As well as in our study, the research in Hacettepe, mentioned above, revealed that knowing the physician for a long time increased the rate of asking for high doses of pain killer (7). Kellog also found that elderly people who

are familiar with their physicians talk about their end-of-life treatment and care preferences more easily with their physicians and think that the physician should fulfill their wishes (16). In terms of living will and appointing a medical proxy, we found that married participants between the ages of 65 and 74 with a university education or above were considering leaving a living will and appointing a medical proxy, which was consistent with the literature (Table 4) (11, 16, 18).

Within the traditional social structure of Turkey, it is the duty of first-degree relatives (spouses, children, grandchildren, etc.) to look after the elderly in the family who are in need of care, and decisions about elderly are largely made by those who assume this responsibility, with the idea that the elderly will benefit from them. All kinds of problems are discussed with the person or people who assume the care needs of elderly individuals. Although this is regarded as normal for elderly individuals who are unable to make decisions on their behalf, the fact that the family doesn't know what the elderly individual would decide on if he or she were able to make a decision puts the family under a moral burden. Our results and other studies in literature show that family and patient decisions often contradict with each other. Therefore, elderly individuals filling out a statement of authorization will eliminate the dilemmas associated with the appointment of a medical proxy and end-of-life treatment and care decisions. During the provision of health services, the standards of courtesy, providing information, and dealing with the health, well-being, and peace of a person shouldn't change according to age. Based on the results of our study, not talking to elderly individuals with the judgment that they will not understand the concepts of elderly care, not seeing them as a decision-maker in treatment and care decisions, allowing close relatives to make the decisions and applying these decisions are unacceptable attitudes, especially for elderly people with good mental health. The most important point here is to ensure that elderly people take part in decision making processes by establishing the right communication channel, preparing an appropriate communication environment, explaining things to the elderly in a language that they will understand and repeating these often if necessary, allowing them to ask questions, and, if necessary, providing psychological support. Fair treatment not only necessitates equal treatment, but also providing patients with different treatment options, if necessary, based on their specific needs.

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RESEARCH

EVALUATION OF POSTOPERATIVE COMPLICATIONS IN ELDERLY PATIENTS UNDERGOING PLASTIC SURGERY ACCORDING TO THE MODIFED CLAVIEN-DINDO CLASSIFICATION

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Abstract

Aim: Although age is not encountered as a contraindication for surgery, performing the surgical procedures in shortest time possible is essential in order to avoid complications and facilitate management of the coexisting comorbidities. The aim of this study is to determine the complication rates and to evaluate the risk factors according to the modified Clavien Dindo classification in elderly patients over 80 years of age who received plastic and reconstructive surgery.

Material and Method: 184 patients over 80 years of age who were treated in the Plastic Reconstructive and Aesthetic Surgery Clinic between January 2015 and December 2018 were included in the study. The diseases were examined in five different groups consisting of acute or chronic wound (pressuresores, diabetic wounds, vascular trauma, trauma, etc.), malignant skin tumors, benign skin tumors, craniomaxillofacial trauma and others (hand trauma, temporamandibular joint dysfunction,etc.).

Results: When the complications were evaluated, it was observed that a total of 50 patients had medical or surgical complications. According to the Dindo Clavien classification, the most common complication was vascular compromise of flaps or wounds tha tnecessitated debridement application under local anesthesia in 17 patients with stage IIIA. The total complication rate was 27.1%.

Conclusion: Age is not a contraindication for the elderly in cases when plastic surgery procedures should be performed. Evaluating comorbidities and the preoperative medical conditions delicately, choosing the appropriate anesthesia method and performing the shortest possible surgical procedure with the aim of shorten the duration of surgery is essential in order to reduce and prevent postoperative complications in elderly patients.

Keywords: Aged; Complication; Surgery.

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INTRODUCTION

Life expectancy is increasing worldwide as a result of the improvement in socioeconomic status as well as development of medical and surgical treatments. These demographic changes lead to increased proportions of old and elderly people in the general population.

Therefore, the applicability and number of surgeries considered to be risky in elderly patients are increasing. This can lead to impaired functional organ capacity in elderly patients and increased rates of complication (1,2). Although age is not typically considered a contraindication for surgery, performing the surgical procedures in the shortest time possible is essential to avoid complications and facilitate management of coexisting comorbidities (3,4).

The Clavien classification system is frequently used to provide standardization for patients to be informed of complications and for grading and evaluating complications. This classification was first established by Clavien et al. (5) in 1992 to evaluate complications of general surgical procedures. Because this classification system did not consider the duration of hospitalization and was insufficient in classifying life-threatening complications as well as evaluating permanent complications, it was modified by Dindo and Clavien (6) in 2004.

Finlayson and Birkmeyer retrospectively evaluated operative mortality in millions of patients aged 65–99 years who underwent major elective surgeries and found that the mortality rate increased with age and the surgical mortality rate in patients over 80 years was twice as high as that in patients aged 65–69 years (7).

To the best of our knowledge, there are no studies in the literature researching the complications and risk factors of elderly patients undergoing surgical interventions in the field of plastic surgery. This study aims to determine the complication rates and evaluate the risk factors according to the modified Clavien–Dindo classification in elderly patients aged over 80 years who underwent plastic and reconstructive surgeries.

MATERIALS AND METHOD

After the approval of the local ethics committee, 184 patients over 80 years of age who were treated in the plastic reconstructive and esthetic surgery clinic between January 2015 and December 2018 were included in the study. Clinical data obtained from the hospital management information system and patient records involving age, gender, type of disease, laboratory parameters (hemoglobin, albumin, and white blood cell count), systemic diseases (hypertension, diabetes, pulmonary diseases, and cardiovascular diseases), treatment method (conservative or surgery), surgical procedure, anesthesia type, postoperative complications, and hospitalization period were retrospectively evaluated. Only the initial applications were considered in patients who had recurrent applications. The diseases were examined in five different groups consisting of acute or chronic wound (pressure sores, diabetic wounds, vascular trauma, trauma, etc.), malignant skin tumors, benign skin tumors, craniomaxillofacial trauma, and others (hand trauma, temporamandibular joint dysfunction, etc.).

The comorbidity status of the patients was evaluated utilizing the American Society of Anesthesiologist (ASA) performance status (PS). ASA PS is a scoring system used to describe the risk of anesthesia.

The laboratory parameters of the patients were taken into consideration in their first hospital visits, and abnormal values were controlled following consultations to the relevant departments during hospitalization. Conservative care was given predominantly to the patients in the wound group by means of dressings and vacuum-assisted closure (VAC) therapy. Surgical treatment was performed especially in skin tumor patients under local or general anesthesia as excision–primary repair as well as reconstruction with graft and/or flap ac-

cording to tumor size and the resultant defect following tumor removal. Complication rates were evaluated according to the Clavien–Dindo classification (Table 1).

In the present study, according to the Clavien–Dindo classification, follow-up of the performed surgical procedure (flap circulation follow-up, wound care, hemorrhage, hematoma, etc.) was accepted as grade 1, while additional drug use for systemic diseases (hypertension, diabetes mellitus [DM], etc.) was accepted as grade 2. Surgical procedures performed under local anesthesia (e.g., wound debridement) were accepted as grade 3A, while surgical procedures performed under general anesthesia were accepted as grade 3B.

Statistical methods

All data were analyzed using the SPSS 24.0 statistical package program. Minimum, maximum, mean, and median values were calculated.

Fisher's exact test was used compare the complication rates between independent variables. Multiple logistic regression analysis was performed to evaluate the risk factors in postoperative complications. P□0.05 values were considered as statistically significant. Odds ratios (ORs) and 95% confidence intervals of the variables were determined.

RESULTS

One hundred and eighty-four patients over 80 years of age were included in the study. The mean age of the patients was 88 (80–99 years); 88 (47.82%) were females, and 96 (52.17%) were males. The mean hemoglobin value was calculated as 11.9 (8.3–16.4), while the mean white blood count value was 9.28 (3.77–60.28), and the mean value of albumin was 3.52 (1.2–4.9). Systemic diseases of the patients were also determined (Table 2). During the hospitalization period, the necessary departmental consultations were requested, and appropriate treatments were initiated subsequently.

According to the type of diseases, it was found that the highest number of patients were treated for malignant skin tumor (105 patients), followed by wounds (DM, peripheral vascular disease, pressure sore, and trauma), craniomaxillofacial traumas, benign skin tumors, and others (hand trauma, temporamandibular joint dysfunction, etc.) (Table 3). The majority of patients with malignant and benign skin tumors were treated by surgical intervention under local or general anesthesia, while wounded patients were treated with conventional dressings or VAC after debridement.

When the patients were evaluated according

Table 1. Clavien–Dindo classification.

Grade	Complication
1	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions
2	Requiring pharmacological treatment with drugs other than those allowed for grade 1 complications
3A	Requiring surgical, endoscopic, or radiological intervention not under general anesthesia
3B	Requiring surgical, endoscopic, or radiological intervention under general anesthesia
4A	Single-organ dysfunction (including dialysis)
4B	Multiorgan dysfunction
5	Death of a patient



Table 2. Patient characteristics.

Patients	Number (n = 184)
Age (years)	
Mean	88±2.34
Range (min-max)	80–99
Sex	
Female, n (%)	88 (47.8%)
Male, n (%)	96 (52.1%)
ASA PS	
≤2, n (%)	89 (73.5%)
≥3, n (%)	32 (26.4%)
Hemoglobin (g/dL)	
Mean	11.9±1.26
Range (min-max)	8.3–16.4
Leukocytes (white blood cells) (µL)	
Mean	9.28±3.62
Range (min-max)	3.77–60.28
Albumin (g/dL)	
Mean	3.52±1.35
Range (min-max)	1.2–4.9
Systemic Disease	
Hypertension	72
Diabetes mellitus	56
Pulmonary disease	18
Cardiovascular disease	68

Minimum: min, maximum: max

Table 3. Distribution of disease types.

Disease	Number of Patients
Malign skin tumor	105
Wound (diabetes mellitus; pressure sore)	56
Maxillofacial trauma	5
Benign tumor	6
Other	12
Total	184

Table 4. Distribution of patients according to treatment modality, anesthesia type, and duration of surgery

Patients	Number (n)
Treatment modality	
Surgery	121
Medical treatment/wound care	63
Surgical Method	
Tumor excision + primary repair	64
Skin graft	28
Local flap	13
Debridement	8
Fracture repair	3
Amputation	3
Tendon repair	2
Anesthesia type	
Local	94
General	27
Operation duration (min)	
< 60	80
≥ 60; < 120	32
≥ 120	2

to treatment method, it was observed that 121 patients were treated surgically, while the other patients were followed with medical treatment or dressing. When surgical treatment methods were considered, primary repair after skin tumor excision was found to be the most frequent, followed by skin grafting, local flap, debridement, and fracture repair procedures.

Of the patients undergoing surgical treatment, 94 had local anesthesia, and 27 had undergone surgery under general anesthesia. Local anesthesia was mostly preferred since it is more appropriate for the prevention of complications due to existing systemic diseases in elderly patients. The operation length was mostly less than 60 min, just as the operation length was longer than 120 min only in two patients (Table 4).

Table 5. Complication distribution by the Dindo–Clavien classification

Clavien–Dindo Grade	Years				
	2015	2016	2017	2018	Total
I	2	3	6	4	15
II	2	3	3	2	10
IIIA	1	7	6	3	17
IIIB	1	3	2	2	8
Total	6	16	17	11	50

I—Flap follow-up: follow-up surgical procedure; II—Additional medical treatment following the performed surgical procedure besides systemic diseases such as diabetes and hypertension; IIIA—Additional surgery (wound debridement) under local anesthesia; IIIB—Wound debridement under general anesthesia; IV and V—not seen.

Table 6. Effect of Risk Factors on Complications.

Risk Factors	Complications (n:50) %27.1	Univariate p
Diabetes		
Absent	48 (%36.9)	= 0.16
Present	2 (%3.70)	
Pulmonary Disease		
Absent	47 (%28.31)	= 0.09
Present	3 (%5.55)	
Cardiovasculare Disease		
Absent	48 (%41.37)	= 0.18
Present	2 (%2.94)	
Hypertension		
Absent	47 (%40.17)	= 0.12
Present	3 (%4.16)	
Type of Disease		
Malign skin tumor	17 (%16.1)	
Wound (diabetes mellitus; pressure sore)	28 (%50)	< 0.05
Maxillofacial trauma		
Benign tumor	1 (%25)	
Other	1 (%16.6)	
Operating room time (min)	3 (%25)	
< 60		
≥ 60; < 120	18 (%22.5)	
≥ 120	30 (%93.75)	< 0.05
ASA PS	2 (%100)	
≤2		
≥3	18 (%20.2)	
	32 (%100)	< 0.05



Table 7. Risk Factors for Postoperative Complications.

Variables	OR	95% CI	p-values
ASA PS			
≤2, n (%)	1 (ref)		
≥3, n (%)	2.64	1.32-5.23	0.01
Operation duration (min)			
< 60	1 (ref)		
≥ 60; < 120	2.19	1.19-3.37	
≥ 120	4.76	1.90-8.79	< 0.05
Types of disease			
Other*	1 (ref)		
Ulcer**	2.72	1.53-4.87	0.01

* Others: traumatic injuries, tumors, orscars ** Ulcers: PAD, pressure ulcers, necrotizing fasciitis, other ulcers (those associated with diabetes, collagen, radiation, etc.)

When the complications were evaluated, it was observed that a total of 50 patients had medical or surgical complications. According to the Dindo–Clavien classification, the most common complication was vascular compromise of the flaps or wounds that necessitated debridement application under local anesthesia in 17 patients with stage IIIA. Medical complications were observed in patients who underwent surgery lasted more than 60 min via general anesthesia and also in patients who received additional drug medication due to hypertension and cardiovascular disease (Table 5). The total complication rate was 27.1%.

Surgical and medical complications were found to be related with ASA PS, duration of operation and type of disease. Increased complication rates were determined in patients with peripheral arterial disease, pressure ulcers, and other types of ulcers as well as patients whose ASA PS≥3, and duration of surgical operation was longer than 60 minutes. (P <0.05) (Table 6,7).

DISCUSSION

Compatible with that of the world, the elderly population in our country is also increasing. According to recent researches in Turkey, from 2012 to 2016, the elderly population (aged ≥65) increased by 17.1%, and the elderly population became 6,651,503, while it was 5,682,003 in 2012. It has been demonstrated that 60.3% of the elderly population were within the 65–74 age group, while 32.5% of the elderly were between 75 and 84, and 7.1% of them were ≥ 85 years old in 2012. The distribution of the elderly population in 2016 was as follows: 61.5% were between 65 and 74 years old, 30.2% were in the 75–84 age group, and 8.2 % were ≥ 85 years old (8).

There is also an outstanding increase in diseases such as chronic ulcers and skin tumors related to aging. In order to improve the quality of life in patients with such disorders, hospitalization time and surgical operation rates are also increasing. Therefore, it is crucial to evaluate the risk factors for postoperative complications in elderly patients (4,9).

Aging is characterized by progressive atrophy, fibrosis, and loss of elasticity in organs and tissues. Elderly patients have different characteristics in terms of physiological, pharmacological, psychological, and social aspects when compared to young patients (9,10). Evers et al. emphasized that

the effect of age on different organs and systems generally did not affect normal functions, and they also denoted that organs of the elderly met the basal needs when there is no chronic disease in the elderly concurrently with the decreased functional reserve capacity (11). In case of stress, elderly people cannot respond well enough. Surgery and anesthesia are also a source of stress. According to the American Society of Anesthesiologists classification, age alone is not a strong factor in the emergence of side effects due to anesthesia (12,13). Age is a minor risk factor. Examination of comorbid diseases are mainly associated with age is essential (14). The most important factors affecting perioperative morbidity and mortality in the elderly are the presence comorbid diseases of the cardiovascular, pulmonary, endocrine, and neurological systems and presence of malnutrition as well as immune system disorders (9,15). In this study, the vast majority of the patients had a history of at least one or more chronic diseases.

Nowadays, the rate of surgical interventions in the elderly population is increasing due to the development of surgical methods, operative techniques, and improved postoperative care. Meticulous preoperative assessment, individualized optimal surgical technique, and proper anesthetic method are crucial in geriatric surgery. To decrease anesthesia-related issues, preoperative evaluation, accurate assessment of existing comorbidities as well as the main surgical problem, and selection of the appropriate drugs and anesthetic method are gaining importance (1,9,16). In our study, local anesthetics was administered in 51% of the patients by injection, while general anesthesia was used in 14.6%.

Chung et al. reported that patients had fewer postoperative confusion and delirium after regional anesthesia in geriatric patients compared to those who had general anesthesia. Lower morbidity rates and less blood loss and postoperative thromboembolic complication rates have been reported after regional anesthesia (17). A decrease in perfusion of the skin and soft tissue in the elderly patients makes them more sensitive to pressure-induced ischemia. Reduction of cardiac and respiratory functions is further worsened by the cardiodepressive effect of inhaled drugs. Drug elimination is prolonged along with impaired liver and kidney functions. The sensitivity of the cerebral cortex to narcotic and hypnotics increases in advanced ages (18).

Fukui et al. has shown that the duration of operation has the strongest effect on the risk of complications in terms of both medical and surgical complications in elderly patients undergoing plastic surgery procedures. In addition, they reported that low serum albumin levels increased the frequency of complications, especially in patients with ulcers (pressure sores, PAD, necrotizing fasciitis, and diabetic ulcers), and they developed more frequent postoperative complications compared to other patients (19). In our study, it is seen that there was a significant relationship between the complication rates and the disease type, just as the correlation between the duration of surgical operation and ASA ps score.

According to the Dindo–Clavien classification, the most common complication was observed in 17 patients of grade III as impaired flap circulation necessitated debridement under local anesthesia. Moreover, patients who needed additional medical treatments were found to be composed of the ones who underwent operation via general anesthesia over 60 min and/or those having comorbidities.

As a result, age is not a contraindication for the elderly in cases when plastic surgery procedures should be performed. Evaluating comorbidities and the preoperative medical conditions delicately, choosing the appropriate anesthesia method, and performing the surgical procedure with the aim of shortening the duration of surgery are essential in order to reduce and prevent postoperative complications in elderly patients.



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RESEARCH

EVALUATION OF DIGOXIN LEVELS IN ELDERLY PATIENTS IN A TRAINING HOSPITAL: AN 11-YEAR FOLLOW-UP

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Abstract

Introduction: Digoxin monitoring is important in the elderly because of the toxicity risk. The aim of this study was to evaluate the orders made by different units for digoxin monitoring in the elderly.

Materials and Method: Digoxin orders and results in patients aged over 65, patients' demographic characteristics, such as age and gender, the unit from which the order was made, and patients' pre-diagnoses were retrospectively recorded. Patients were divided into young-old, middle-old, and very-old groups, and the results were divided into subtherapeutic, therapeutic, and toxic levels.

Results: The percentage of young-old, middle-old, and very-old patients was 39.4%, 45.3%, and 15.3%, respectively. Women were more (64.3%) and their median age and digoxin concentrations were higher ($p<0.001$). Outpatients' median digoxin concentrations were lower than inpatients' median digoxin concentrations ($p<0.001$). A proportion of 46.6% of all digoxin levels were therapeutic; 29.2% were subtherapeutic; and 24.2% were toxic. Subtherapeutic levels in males and toxic levels in females predominated ($p<0.001$). Toxic levels were higher in inpatients, and subtherapeutic levels were higher in outpatients ($p<0.001$). The highest rate of therapeutic levels was observed in young-old patients (48.7%), while toxic levels were observed most frequently in very-old patients (28.1%). The highest number of digoxin orders in elderly patients was from the emergency department (44.2%).

Conclusion: In elderly patients, more than half of the serum digoxin orders were inappropriate. These results significantly changed according to gender, outpatient or inpatient status, age, and the ordering unit. Changes in digoxin pharmacokinetics, especially in the geriatric period, require physicians to be vigilant of subtherapeutic drug concentrations.

Keywords: Aged; Geriatrics; Digoxin; Drug monitoring.



INTRODUCTION

The prevalence of heart failure and the risk of atrial fibrillation increase with age (1). Digoxin can be an appropriate agent to treat systolic dysfunction, high ventricular rate, and atrial fibrillation in the elderly. The elderly population appears to experience comparable symptom improvement and hospitalization reduction to younger populations from the use of digoxin for heart failure management (1, 2). However, digoxin has a complex pharmacokinetic profile, narrow therapeutic range, and high risk of toxicity. Also, pharmacological properties of digoxin may vary significantly between men and women (3). According to the Digitalis Investigation Group, the risk of all-cause mortality and all-cause hospitalization was lower than placebo in patients with digoxin concentrations of 0.5-0.9 ng/mL, and mortality increased significantly to 12% in those with digoxin concentrations ≥1.2 ng/mL. Therefore, serum levels need to be monitored to optimize therapeutic performance, detect noncompliance, and reduce toxicity (4, 5). Digoxin toxicity may mimic certain symptoms of heart disease, and measuring the plasma concentration in cases in which toxicity is suspected may help confirm a diagnosis. The recognition of digoxin toxicity is more difficult in elderly patients than in younger patients (6). When digoxin is used in elderly patients, the specific geriatric pharmacokinetics of the drug must be considered. Changes in serum digoxin levels require further evaluation in elderly patients because of significant risks specific to comorbid diseases, sex, electrolyte disturbances, and drug interactions. In addition, elderly patients are especially susceptible to digoxin toxicity (2, 5). Patients over 70 years of age may show clinical signs of digoxin toxicity despite having digoxin concentrations within the recommended therapeutic range. Increased age is most likely associated with enhanced susceptibility to digoxin toxicity due to unknown pharmacodynamic changes (7, 8). Digoxin is in the top five causes of emergency department admissions due to adverse drug reactions (9), and it is among the top three drugs that cause emergency department admissions in patients over 65 years (10).

Serum digoxin concentration is the most commonly ordered therapeutic drug monitoring test globally (11). Despite many clinical trials, studies evaluating digoxin orders specifically in the elderly are uncommon. The aim of this study was to evaluate the orders made by different units in elderly patients aged over 65 years and to evaluate the eleven-year data of these results according to age groups, sex, and inpatient or outpatient status.

MATERIALS AND METHOD

Study design

This was a retrospective, descriptive study. This study began after its approval by the Local Ethics Committee for Non-Interventional Research and was performed in accordance with the Declaration of Helsinki. Between 1 January 2008 and 31 December 2018, the data for serum digoxin orders in patients over the age of 65 sent to the Medical Biochemistry Laboratory in Health Sciences University Izmir Bozyaka Training and Research Hospital to be studied from different departments and polyclinics were collected from the hospital electronic medical record and analysed. The demographic characteristics, such as age and sex, of the patients, unit from which the order was made, pre-diagnosis codes of the patients according to the International Classification of Diseases-10 (ICD-10) codes, order time, and serum digoxin levels were recorded. In the study, since there were multiple digoxin measurements on behalf of the same patient, a demand-based evaluation was performed in both inpatients and outpatients. Patients older than 65 years were divided into young-old (65-74 years), middle-old (75-84 years), and very-old (85 years and older) groups, and the results were grouped as subtherapeutic (<0.8 ng/mL), therapeutic (0.8-2 ng/mL), and toxic (>2 ng/mL) levels.

Methods

Serum samples were analysed spectrophotometrically (Beckman-Coulter, Digoxin, OSR6404) with the Olympus AU-680 autoanalyzer (Beckman-Coulter, Fullerton, USA) in the Medical Biochemistry Laboratory, and the results are expressed in ng/dL. Two levels of internal quality control were used daily at each shift change. In addition, external quality control was performed monthly. The detection limit of the method used in the study was 0.14 ng/dL, and the maximum measurement value was 5 ng/dL. The samples with higher concentrations were diluted according to the manufacturer's instructions and re-measured.

Statistical analysis

Data are presented as frequencies (n) and percentages (%) or medians and interquartile ranges. The medians were compared using the Mann–Whitney U-test, as applicable, after checking normality using the Kolmogorov–Smirnov test. Test results with p values <0.05 were determined to be statistically significant.

RESULTS

In the study, 10810 digoxin orders of 4420 patients from all age groups were evaluated. While the median age of the patients was 72.6 (12.4-110 years), 2.44 orders were made per patient. The main content of our study was 8390 digoxin orders of 3502 patients aged 65 and over, and it was observed that 2.39 digoxin orders were made per patient in the elderly group. According to order-based evaluation the median age of all elderly patients was 77.3 years (72-82.2 years). Among all patients, 3307 were young-old (39.4%); 3797 were middle-old (45.3%); and 1286 were very-old (15.3%). The median age of the young-old patients was 70.7 years (68.2-73 years); that of the middle-old was 79.6 years (77.4-81.9 years); and that of the very-old was 87.8 years (86-90.8 years). The results included 5392 (64.3%) levels in women and 2998 (35.7%) levels in men. In men, the median digoxin level was 1.18 ng/mL (0.61-1.81 ng/mL), and the median age was 76.2 years (70.7-81.5 years). In women, the median digoxin level was 1.3 ng/mL (0.72-2.06 ng/mL), and the median age was 77.8 years (72.6-82.8 years). Both of these variables were statistically significant (p<0.001). Outpatient orders (4605, 54.9%) were higher than inpatient orders (3785, 45.1%). In outpatients, the median digoxin level was 1.08 ng/mL (0.53-1.74 ng/mL), and the median age was 77.3 years (71.9-82.6 years). In inpatients, the median digoxin level was 1.5 ng/mL (0.89-2.19 ng/mL), and the median age was 77.3 years (72.2-81.9 years). The difference in the median digoxin levels between outpatients and inpatients was statistically significant (p<0.001), but no significant difference was found for age or gender (p>0.05). While 6282 (74.9%) of all pre-diagnoses entered into the hospital information system were cardiac-related or digoxin-related, 2108 (25.1%) were non-cardiac, irrelevant diagnoses.

The median digoxin level for all patients was 1.26 ng/mL (0.68-1.98 ng/mL). In young-old, middle-old, and very-old patients, the median digoxin levels were 1.15 ng/mL (0.64-1.81 ng/mL), 1.33 ng/mL (0.71-2.06 ng/mL), and 1.4 ng/mL (0.7-2.17 ng/mL), respectively. According to age groups, there was a significant difference in the mean serum digoxin levels between the young-old groups and the other groups (p<0.001), but the difference between middle-old and very-old groups was not significant (p>0.05). Among the digoxin levels, 46.6% (3908) were therapeutic; 29.2% were subtherapeutic (2453); and 24.2% (2029) were toxic. Toxic levels were more frequent in women than in men (26.5% and 20%, respectively), and subtherapeutic levels were more frequent in men than in women (32.4% and 27.5%, respectively). The relationship between subtherapeutic and toxic levels and gender was statistically significant (p<0.001). Therapeutic levels were similar in men and women (46% and 47.6%, respectively). The distribution of therapeutic levels by gender is shown in Figure 1. The subtherapeutic level rate was higher in outpatients

Figure 1. The therapeutic level rates of digoxin by gender in elderly. Data are presented percentages (%). *p<0.001 between female and male.

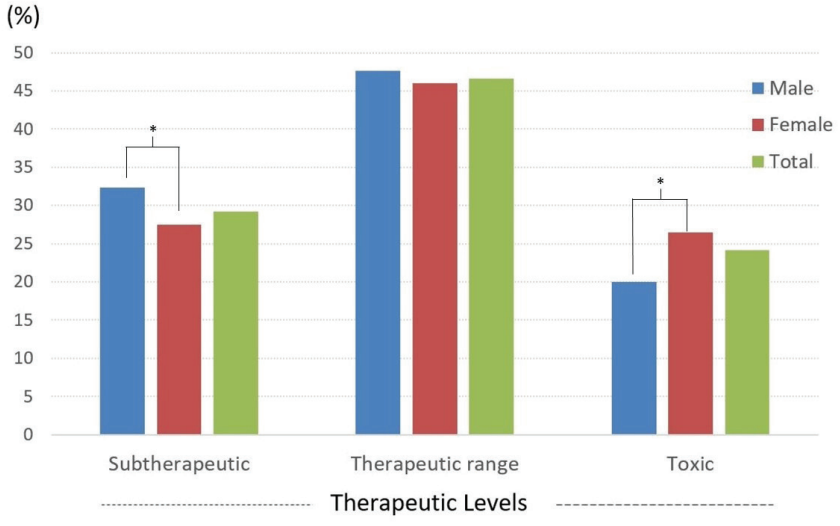
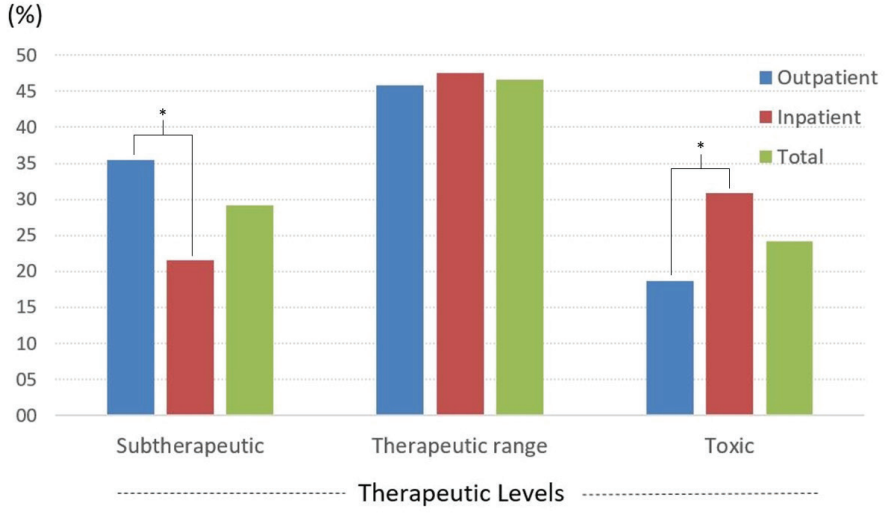


Figure 2. The therapeutic level rates of digoxin by outpatients and inpatients in elderly. Data are presented percentages (%). *p<0.001 between outpatients and inpatients.



than in inpatients (35.5% and 21.6%, respectively). In contrast, inpatients had higher therapeutic (47.6% vs. 45.3%) and toxic (30.8% vs. 18.7%) levels than outpatients. The relationship between inpatients and outpatients and therapeutic levels was significant (p<0.001). The distribution of all outpatient and inpatient orders according to therapeutic levels is shown in Figure 2.

When the age groups were examined according to therapeutic levels, results within the therapeutic range were more frequently observed in the young-old patients (48.7%), followed by the middle-old (45.6%) and very-old (44%) patients. Toxic levels were more frequently observed in the very-old patients (28.1%), followed by the middle-old (26.7%) and young-old (19.8%) patients. The rate of subtherapeutic levels was similar between the middle-old and very-old groups (27.7% and 27.9%, respectively), and the rate was 31.5% in young-old patients. There was a significant difference in the rate of therapeutic levels between the young-old group and the other groups ($p < 0.001$), but there was no significant difference in this variable between the middle-old and very-old groups ($p > 0.05$). Table 1 shows the distribution for the frequency of the young-old, middle-old, and very-old patients who had therapeutic levels.

When the elderly patients from units that ordered digoxin were examined, the first three were the emergency department with 3711 orders (44.2%), coronary intensive care unit with 1585 orders (18.9%), and the internal medicine inpatient unit with 1561 orders (18.6%). These units were followed by the internal medicine outpatient clinic, cardiology outpatient clinic, and other intensive care units. The patient distribution and rates of orders by unit are shown in Figure 3. Middle-old patients were the majority of patients in the three

Table 1. Distribution of young-old, middle-old and very-old patient orders according to therapeutic level.

Age(Year)	Subtherapeutic		Therapeutic range		Toxic		Total	
	n	%	n	%	n	%	n	%
Young-old	1042	31.5	1609	48.7*	656	19.8	3307	100
Middle-old	1052	27.7	1733	45.6	1012	26.7	3797	100
Very-old	359	27.9	566	44	361	28.1	1286	100

Data are presented as frequencies (n) and percentages (%). *$p < 0.001$ between young-old group and the other groups in the rate of therapeutic levels.

Figure 3. Digoxin orders according to clinics.

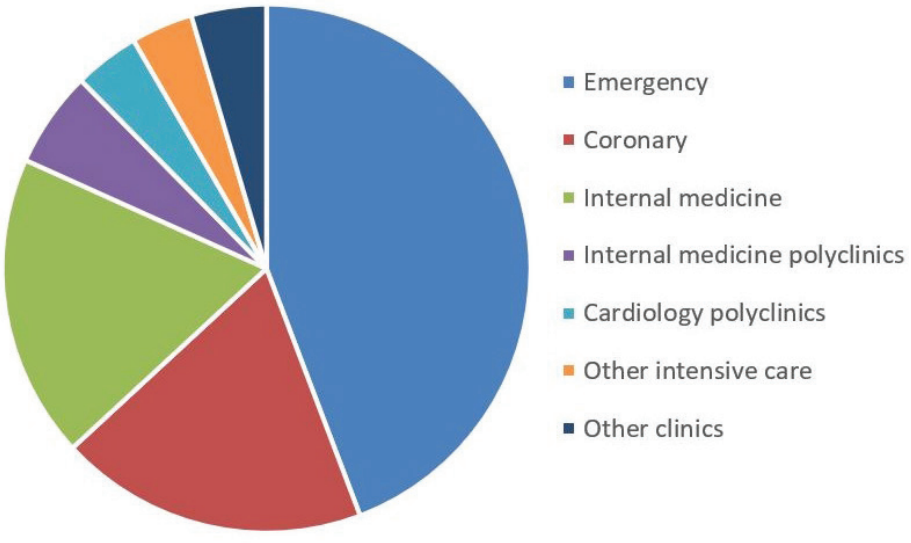
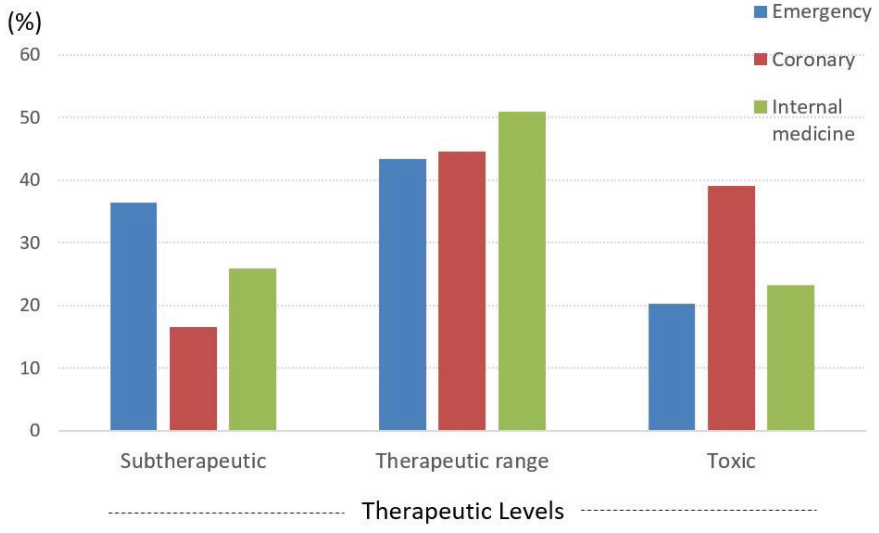


Table 2. Age distribution of emergency, coronary, internal medicine and other clinics.

Age(Year)	Emergency		Coronary		Internal medicine		Other clinics	
	n	%	n	%	n	%	n	%
Young-old	1327	35.8	590	37.2	616	39.5	774	50.5
Middle-old	1660	44.7	745	47	768	49.2	624	40.7
Very-old	724	19.5	250	15.8	177	11.3	135	8.8
Total	3711	100	1585	100	1561	100	1533	100

Data are presented as frequencies (n) and percentages (%).

Figure 4. The distribution of emergency, coronary intensive care and internal medicine service orders according to therapeutic level rates in elderly. Data are presented percentages (%).



units with the most orders (44.7%, 1660; 47%, 74; and 49.2%, 768, respectively). These patients were followed by young-old and very-old patients. The age distribution of all three units' orders is shown in Table 2. While the digoxin levels for emergency department orders were mostly in the therapeutic range (43.3%, 1608), subtherapeutic levels were also noted (36.4%, 1352). Of the coronary intensive care unit levels, 44.5% (706) were therapeutic, and 39% (618) were toxic. In the internal medicine unit, 50.9% (794) of all levels were therapeutic, while the rate of subtherapeutic and toxic levels were similar. The distribution of orders from the emergency department, coronary intensive care unit, and internal medicine unit according to therapeutic levels is shown in Figure 4.

DISCUSSION

Studies show that a significant proportion of patients with serum digoxin level orders is composed of patients aged 65 years or older (1, 12). Among the digoxin orders in all age groups, the orders in patients over 65 years were 77.6% in our study. Orders were especially made in the middle-old patients, followed by young-old patients at a similar rate. Similarly, Ozturk and Cuhadar stated that the number of orders in middle-aged patients was higher than in other elderly people, and mean digoxin levels were higher in the middle-aged group (12). In our study, however, the median digoxin levels were significantly higher in the very-old group than in the middle-old group.

The correlation between gender and heart failure is much stronger in women than in men. This correlation leads to increased heart failure and, therefore, more digoxin use in women (13). The fact that valve diseases and rhythm disorders are more common in women (14) and that mortality occurs at a later age compared to men may cause digoxin use to appear relatively higher in women. The 1.8-fold higher rate in older women observed in our study compared to older men supports this theory and is in accordance with the results of many studies in the literature (12, 14-18).

In our study, less than half of all digoxin levels were within therapeutic limits; one-third of elderly patients had subtherapeutic levels; and approximately one-fourth were exposed to toxic levels. A few studies involving only the elderly and most studies evaluating all age groups suggest that the number of patients with therapeutic levels was low in our study and there is both insufficient patient adherence and follow up (11, 15, 16, 18-20). In a study by Grzesk et al., in which 3037 digoxin orders in patients over 60 years of age were evaluated, the therapeutic level rates were similar to the subtherapeutic level rates, and the toxic level rates were 13% lower than ours (19). In the same study, the mean serum digoxin levels in women were significantly higher than in men. Limon et al. stated that there was no significant association between digoxin poisoning and gender in a study population composed of patients, mostly women, with digoxin poisoning (17), while Canas et al. claimed that the percentage of patients with high levels of digoxin was significantly greater among men than among women (4). In our study, the mean digoxin levels in older women were significantly higher than those in older men. Dalaklioglu also stated that toxic levels are higher in women than in men, which contrasts the results of Canas et al. (16). Women have an approximately 10% lower glomerular filtration rate than men when normalised for body surface area. This difference might explain the observed 12 to 14% lower digoxin clearance in women than in men, since digoxin is primarily renally eliminated. Differences in blood serum digoxin levels between men and women may be due to these pharmacokinetic properties. This difference may lead to an increased risk of toxicity in women and an increase in subtherapeutic levels in men, as was observed in our study.

Although a distinction in the number of orders in outpatients and inpatients has been made in few published studies, digoxin orders are predominantly made in inpatients in the elderly (15, 19). In our study, the higher rate of outpatient orders may be due to the fact that the emergency department orders comprised 44.2% of all the orders. The mean digoxin levels were significantly higher in inpatients than in outpatients. Also, the rate of toxic levels was particularly high in inpatients. Grzesk et al. described this result in their study with therapeutic levels similar to ours by using intravenous treatment in addition to oral treatment in inpatients (19). In our study, the rate of subtherapeutic levels was higher in outpatients. Bernard et al. reported that 41% of digoxin results were subtherapeutic in their outpatients with an average age of 64 years and attributed this finding to collecting samples prior to the complete distribution of digoxin in outpatients, which is a common issue in outpatient settings (11). Sampling time

errors before the drug has reached a stable state are important causes of subtherapeutic levels or inappropriate measurements in most developed countries (15, 21, 22). Unlike the studies of Oncu et al., it was not possible to question whether sample taking was performed after reaching the steady state concentration, due to the very wide time interval scanning and inadequacies in our hospital information management system (21, 22). This fact is one of the limitations of our study. However, it should be noted that our study includes not only patients who use oral medication but also those who are given intravenous digoxin. Our clinical observations indicate that, the issues related to steady state were not paid attention to inpatients adequately, which was similar to the Oncu et al.'s findings. We think that awareness trainings in inpatients departments will have positive effects, similar to this study (22). Adherence problems in older patients may also make it difficult to achieve therapeutic levels (7, 23). In our study, the subtherapeutic level rate in the young-old group was higher than that in the other groups.

The lowest rate of patients in the therapeutic range among all elderly patients was in the very-old group. These patients had the highest toxic level rate. Ozturk and Cuhadar stated that high serum digoxin results were observed more frequently in young-old, middle-old, and very-old patients than in other age groups, and the rate was especially high in the middle-old patients (12). Limon et al. demonstrated that the mean age of patients who experienced digoxin poisoning was significantly higher than that in patients who did not experience digoxin poisoning, and the average age of patients in the study was 76 years (17). Although there are few studies claiming that there is no relationship between age and inappropriate serum digoxin measurement (21), increased toxic values with increasing age are closely related to age-related changes in pharmacokinetics and pharmacodynamics of digoxin. Muscle mass and body mass decrease in the elderly, and as a consequence, the volume of distribution for digoxin decreases with age, which results in a relatively higher serum digoxin concentration. In addition, with the decline in renal function with advancing age, the half-life of digoxin may extend to 2-3 times longer than normal (1, 7, 22).

Similar to our study, other studies show that the number of digoxin orders among units in hospitals is the highest in the emergency departments (12, 16). In the elderly, emergency services are important because of more frequent drug intoxication and adverse effects of drugs in differential diagnosis and treatment follow-up (9, 10). In addition to toxicity, digoxin orders in the emergency department can be made to evaluate digoxin efficacy. Indeed, although most of our emergency department results were within the therapeutic range, unlike the results of Mundet et al., patients with levels in the subtherapeutic range comprised approximately one-third of emergency department patients, which was similar to the results of Mundet et al. (24). Interestingly, the proportion of patients with toxic levels was lower in the emergency department than in the coronary intensive care and internal medicine units, which were the other units that ordered levels most frequently. Similarly, in a study by Garcia-Iranzo et al., emergency department patients with subtherapeutic levels were more common than emergency department patients with toxic levels (14). In the coronary intensive care unit, where intravenous treatment is used extensively, it is expected that the proportion of toxic patients will be the highest (19).

In our study, approximately three-fourths of the pre-diagnoses of all orders consisted of cardiac or digoxin-related complaints. The rate of orders for appropriate indications did not differ substantially from the rates in the literature (15, 17, 19). Past studies show that serum digoxin measurements were performed with a wide range (32% to 88.4%) of inappropriate criteria (11, 18, 22, 25). It has been demonstrated that inappropriate requests can be significantly reduced through in-service therapeu-

tic drug monitoring training (22).

As a result, we evaluated serum digoxin orders in elderly patients for more than ten years. The changes in the pharmacokinetics and pharmacodynamics of digoxin in geriatric patients require physicians to be alert of subtherapeutic and toxic drug levels. Although serum digoxin concentrations may not always be a strong indicator of toxicity, they are the best available indicator and should be evaluated together with patients' clinic findings. It is appropriate to emphasize the importance of and raise awareness and plan periodic updated trainings for therapeutic digoxin levels in hospitals in order to promote individualized doses and optimized treatments in the elderly. There remains a great need for similar further clinical trials involving larger elderly populations.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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RESEARCH

EFFICACY OF A VIDEO-BASED PHYSICAL THERAPY AND REHABILITATION SYSTEM IN PATIENTS WITH POST-STROKE HEMIPLEGIA: A RANDOMIZED, CONTROLLED, PILOT STUDY

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Abstract

Introduction: The aim of this study was to evaluate the effects of video-based virtual reality exercises performed using the LeapMotion® device and Fizyosoft® software on the hand and upper extremity functions of patients with hemiplegia.

Materials and Method: The mean age of the patients in the study group was 63.6 ± 7.1 years and the duration of the disease was 13 ± 10.74 months. The mean age of the patients in the control group was 63.6 ± 9.2 years and the duration of the disease was 10 ± 9.89 months. This study was a randomized, controlled, single-blind study. The patients were randomly divided into two groups: an experimental group and a control group. Both groups were arranged to undergo a combination of a neurophysiological and a conventional exercise program and physical therapy. In addition, virtual reality training therapy was administered in the experimental group using the LeapMotion® device. The patients' range-of-motion (ROM) was measured using the Fizyosoft® software, which operates with the LeapMotion® device, and their upper extremity and general function status was evaluated using the Fugl-Meyer assessment of upper extremity motor impairment (FMA-UE) scale, the Brunnstrom recovery stage (BRS) scale, the Barthel Index (BI), and the Functional Ambulation Categories (FAC) scale at the beginning and end of treatment.

Results: Significant improvements were noted after treatment in the upper extremity range-of-motion values as well as in FMA-UE, BRS, BI, and FAC scores in the experimental and control groups. Additionally, there were significant differences in the ROM measurements of the hand and wrist joints between the groups. However, no significant differences in clinical test results were observed between the groups.

Conclusion: Virtual reality exercises have a positive effect on range-of-motion measurements in stroke patients. Studies with a larger number of participants are needed to demonstrate results more clearly using other scales.

Keywords: Hemiplegia; Stroke; Virtual reality; Rehabilitation.



INTRODUCTION

Cerebrovascular diseases (stroke) are central nervous system disorders that occur as a result of the blockage or hemorrhage of vessels caused by disorders that develop in cerebrovascular structures and/or in the properties of the blood passing through these vessels (1). After stroke, patients with hemiplegia continue to have major movement- and function-related problems in >50% of upper extremity functions (2). The limb affected by stroke is not used adequately; this tends to contribute to both reduced movement and dysfunction in daily living activities.

Neurodevelopmental treatment, proprioceptive neuromuscular facilitation, and Brunnstrom approach are among the conventional approaches for upper extremity rehabilitation following stroke, which aim to maximize upper extremity function (3).

With recent developments in computer systems, virtual reality (VR) applications are increasingly being used in the field of rehabilitation and have become well-established. Virtual/augmented reality applications enable users to move various objects in a virtual environment. The efficacy of this technology in treatment has been shown in various disorders, such as neurological diseases, diseases that cause acute/chronic pain, and fibromyalgia (4-6). However, it is not possible to adjust exercise parameters and inspect how accurately the patient performs the exercise in rehabilitation practices performed using game consoles. A unique system that allows these adjustments to be made, includes customized physical exercises, and uses depth sensors to follow developments and make necessary interventions, was developed and made available for use in the field of rehabilitation, and its effectiveness was demonstrated in some studies (7).

The aim of this study was to investigate the effect of VR applications developed specifically for the rehabilitation of patients with post-CVA hemiplegia on upper extremity functions and movements.

MATERIALS and METHODS

Participants

Twenty-four patients aged between 52 and 75 years who had a stroke for the first time and received inpatient treatment at the Physical Medicine and Rehabilitation Clinic between March 2016 and March 2018 were included in the study. All the recruited participants signed informed consent forms before participating in the study. The approval of the local Ethics Committee was obtained.

Patient with cognitive impairment, a Mini-Mental State Exam score <23, a disease other than stroke that would disrupt mobility, severe upper extremity spasticity (Modified Ashworth Scale score of 3 and above), a Brunnstrom motor staging score below 4 for the upper extremity, and patients who were unable to comprehend and perform instructions were excluded from the study.

Patients whose stroke diagnosis was verified by a neurologist through computerized tomography and/or magnetic resonance imaging techniques were randomized. However, the physician who conducted clinical evaluations in both groups were blinded to the patient group. Group 1 comprised patients who were given only a conventional rehabilitation program, and Group 2 comprised patients who were given both conventional and VR programs.

Intervention

1- Conventional rehabilitation treatment program

The treatment program of both the control and experimental group included physical therapy modalities and a combination of a neurophysiological and a conventional exercise program implemented 1 hour a day 5 days a week for a total of 6 weeks.

2- Virtual reality treatment program

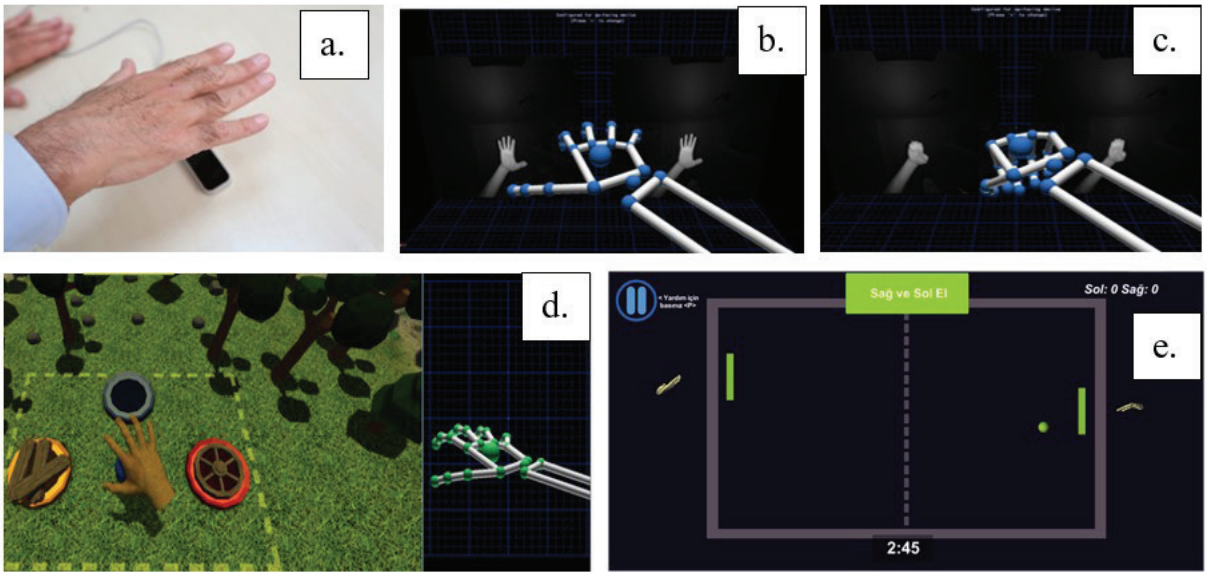
VR exercises for the upper extremity (speed, difficulty, duration, etc.) were implemented for the experimental group using a developed software. In recent years, it has become possible to track

hand movements in space using cameras with the LeapMotion® device. LeapMotion® is a motion detection device that uses infrared optics and cameras to capture and monitor current motion without the use of conventional interface devices such as mouse and keyboards (Figure 1-a). Unlike other motion sensors, its distinctive feature is its sensitivity to a change of 0.01 mm in the movement of fingers as well as hands, with a capture rate of 300 Hz. The LeapMotion® controller has a surface area of 24 cm2 and detects the hand in a three-dimensional space with a field view of approximately 150° (Figure 1b-c).

es multiple levels. It was designed for wrist flexion-extension, radial and ulnar deviations, forearm supination-pronation, and elbow flexion-extension movements (Figure 1e).

The LeapMotion® device and monitor were set up in a quiet room with sound insulation where patients would not be affected by external factors. Before the patients started the session, they were instructed how to play the game. Apart from their routine rehabilitation programs, the patients performed VR exercises twice a week for 6 weeks under the supervision of a therapist.

Figure 1. a. View of hand on LeapMotion® device, b-c. Close-up view of hand in computer environment, d-e. Leapball and pong game in computer environment.



The LeapBall game application is a rehabilitation game developed for wrist flexion-extension and finger flexion-extension movements. It was primarily developed for hand grasp movements, and the game comprised multiple levels (Figure 1d).

The Pong game application was developed for wrist and elbow movements, and also compris-

Assessment

In this study, the upper extremity subscale of the Fugl-Meyer assessment of upper extremity (FMA-UE) scale was used to evaluate the motor function of the upper extremity. The FMA-UE scale is an index developed to assess sensorimotor recovery following stroke (8).

Evaluation of the neurophysiological recovery



of the patients was conducted using the Brunnstrom recovery stages (BRS) developed by Brunnstrom for the hemiplegic upper extremity and hand (9). The Barthel Index (BI), for which a validity and reliability study was conducted on Turkish patients, was used in our study to evaluate the daily living activities of the patients (10). The ambulation status of all patients was evaluated using the Functional Ambulation Category (FAC) test (11).

FMA-UA, BRS, BI, and FAC scores of all patients were evaluated at the beginning of the treatment and 6 weeks after the beginning of treatment. In addition, the ROM results for joints were obtained using the LeapMotion® device before treatment and 6 weeks after treatment.

Statistical analysis

The IBM SPSS Statistics 22 software was used for statistical analysis. In the evaluation of study data, normal distribution of the parameters was evaluated using the Shapiro–Wilk test and descriptive statistical methods (mean, standard deviation, and frequency) were used. Because the quantitative data did not show a normal distribution, the Mann–Whitney U test was used as a non-parametric test for comparison between the two groups. The Wilcoxon signed-rank test was used for intra-group comparisons of parameters without normal distribution. The chi-square test or Fisher's Exact test were used to compare qualitative data. Parameters with a value of $p < 0.05$ were considered statistically significant.

RESULTS

Twelve experimental patients with a mean age of 63.6 ± 7.1 years and 12 control patients with a mean age of 63.6 ± 9.2 years were included in the study. Demographic characteristics were similar between the groups ($p > 0.05$). The descriptive characteristics of the groups are shown in Table 1. In Group 1, the patients' body mass index (BMI) was 29 ± 4.87, disease duration was 10 ± 9.89, and 92% of patients had an ischemic CVO. In Group 2, the pa-

Table 1. Demographic and clinical characteristics of the groups.

	Group 1 (n = 12)	Group 2 (n = 12)	p
	Mean±SD	Mean±SD	
Age, years (Mean±SD)	63.6±7.1	63.6±9.2	0.750
Gender, female, n (%)	8(67)	7(58)	1.000
Body mass index, Kg/m2, (Mean±SD)	29±4.87	27±2.24	0.299
Time since stroke, months, (Mean±SD)	10±9.89	13±10.74	0.175
Affected extremity, n (%)			
Right/left	4/8 (33/67)	5/7 (42/58)	1.000
Dominant	12(100)	12(100)	
Comorbidities, n (%)			0.311
no	0(0)	2(17)	
Hypertension	5(42)	5(42)	
Diabetes mellitus	7(58)	5(42)	

tients' BMI was 27 ± 2.24, disease duration was 13 ± 10.74, and 75% of patients had an ischemic CVO.

We compared the post-treatment clinical data of the groups that did and did not receive VR treatment. When the patients were evaluated in terms of clinical examination results, no statistically significant difference was found between the two groups in FAS scale, FM upper extremity, FM lower extremity, and FM total scores, as well as their BI change and Brunnstrom upper extremity, Brunnstrom hand, and Brunnstrom lower extremity scores at the end of the 6th week after treatment.

Intragroup evaluation revealed that the improvements in the clinical scales resulted in statistically significant improvement in all clinical tests in both groups before treatment and at 6th week after treatment (Table 2).

Using this software, it is possible to measure ROMs of all joints from the elbow onward. In this respect, we compared the ROMs of the patients between the groups before and after treatment. There was no significant difference in the elbow and wrist ROMs of the groups following treatment.

A statistically significant intragroup improvement was noted before and after treatment in the plantar-flexion of the wrist in Group 1 and in the plantar-flexion of the wrist, ulnar deviation of the wrist, and elbow pronation in Group 2. Although there was improvement in other elbow and wrist ROMs, they were not statistically significant (Table 3).

In the analysis of finger movements of the groups, the ROMs in group 1 and Group 2 did not show a statistically significant difference. In the intragroup evaluation, it was observed that before and after treatment, improvement was greater in finger movements in the VR group, especially in DIP joint movements. In Group 1, significant improvement was not achieved only in the 1st PIP joint flexion and the 3rd DIP joint flexion; however, a statistically significant improvement was

Table 2. Baseline and post-intervention comparisons in outcome measures within and between the groups.

	Group 1 (n=12)		p*	Group 1 (n=12)		p*	p§
	Baseline	Post-intervention		Baseline	Post-intervention		
	Mean±SD	Mean±SD		Mean±SD	Mean±SD		
FAC	1.92±1.08	3.75±1.14	0.002	2.42±1.16	3.83±0.94	0.003	0.976
Fugl-Meyer Assessment UE							
Total	55.08±7.37	62.08±3.23	0.003	48.75±14.48	53.58±13.13	0.003	0.105
Wrist	7.58±2.39	9.17±1.53	0.027	6.17±3.79	7.25±3.47	0.026	0.138
Hand	9.92±2.23	12.92±1.24	0.006	9.92±4.14	10.67±3.98	0.105	0.227
Barthel index	75.42±11.17	88.33±14.03	0.003	76.67±11.74	88.75±7.42	0.001	0.596
Brunnstrom Stages							
UE	5±0.74	5.83±0.39	0.004	5.25±0.62	5.55±0.69	0.046	0.261
Hand	5.42±0.51	6±0.38	0.008	5.25±0.75	5.55±0.82	0.046	0.058

Statistical analysis, *: Wilcoxon Signed Ranks test, §: Mann Whitney U test. FAC: Functional Ambulation Classification, UE: Upper Extremity.



Table 3. Comparison of elbow and wrist range-of-motion before and after treatment of hemiplegic patients.

	Group 1 (n=12)	Group 2 (n=12)	p
	Mean±SD	Mean±SD	
Elbow Pronation Pre	76±26.35	66±25.15	0.562
Elbow Pronation Post	78±23.58	82±18.82	0.603
p	0.893	0.012	
Elbow Supination Pre	27±27.71	14±20.45	0.198
Elbow Supination Post	34±34.48	32±33.52	0.707
p	0.386	0.173	
Wrist Flexion Pre	11±11.83	8±7.29	0.536
Wrist Flexion Post	32±23.65	25±19.3	0.339
p	0.01	0.008	
Wrist Extension Pre	51±16.06	42±18.95	0.797
Wrist Extension Post	55±12.62	53±14.3	0.666
p	0.508	0.11	
Wrist Ulnar deviation Pre	20±8.26	15±14.81	0.166
Wrist Ulnar deviation Post	23±8.98	26±5.95	0.774
p	0.445	0.038	
Wrist Radial deviation Pre	17±5.79	18±2.94	0.186
Wrist Radial deviation Post	18±4.76	17±6.98	0.678
p	0.463	0.779	

achieved in other finger joints. In Group 2, a statistically significant improvement was observed in all other finger joints expect the 1st PIP, 2nd PIP, 3rd PIP, 4th PIP, and 5th PIP joint flexions (Table 4).

DISCUSSION

In this study, the effect of VR applications, in addition to conventional treatments, on upper extremity functions and movements in patients with hemiplegia was investigated. A significant improvement was observed in the pre- and post-treatment clinical evaluation tests in both the group in which VR was implemented and the group that received only conventional rehabilitation therapy. While no significant difference was observed in elbow and wrist movements between the two groups, significant improvements were observed in some hand movements of the VR group.

It has been shown that because patients find VR to be more fun and exciting than other conventional rehabilitation programs, they put in more effort during VR-based treatment and therefore, more positive results are obtained due to positive reaction to this treatment and increased motivation (12). In addition, there are some arguments

Table 4. Comparison of hand range-of-motion of patients before and after treatment.

	Group 1 (n=12)	Group 2 (n=12)	p
	Mean±SD	Mean±SD	
MCP Flexion Thumb Pre	36±16.35	34±16.38	0.773
MCP Flexion Thumb Post	50±9.33	53±11.83	0.395
p	0.005	0.003	
MCP Flexion Index Pre	40±13.71	36±15.09	0.299
MCP Flexion Index Post	53±11.66	51±10.18	0.525
p	0.005	0.005	
MCP Flexion Middle Pre	38±13.86	29±15	0.083
MCP Flexion Middle Post	51±12.61	47±12.47	0.326
p	0.002	0.028	
MCP Flexion Ring Pre	32±12.13	28±12.95	0.236
MCP Flexion Ring Post	45±11.68	39±17.42	0.453
p	0.002	0.099	
MCP Flexion Little Pre	34±12.59	28±16.46	0.273
MCP Flexion Little Post	51±17.36	46±17.82	0.564
p	0.015	0.01	
PIP Flexion Thumb Pre	38±16.84	33±11.23	0.954
PIP Flexion Thumb Post	41±12.49	35±8.45	0.371
p	0.347	0.754	
PIP Flexion Index Pre	61±21.47	49±18.85	0.083
PIP Flexion Index Post	73±14.75	74±14.05	1
p	0.023	0.003	
PIP Flexion Middle Pre	58±23.94	40±22.45	0.073
PIP Flexion Middle Post	72±15.54	70±20.07	0.686
p	0.023	0.019	
PIP Flexion Ring Pre	50±24.48	38±17.57	0.225
PIP Flexion Ring Post	64±23.85	60±26	0.795
p	0.041	0.05	
PIP Flexion Little Pre	50±25.91	36±21.49	0.204
PIP Flexion Little Post	67±25.35	65±23.01	0.729



	Group 1 (n=12)	Group 2 (n=12)	p
	Mean±SD	Mean±SD	
p	0.019	0.008	
DIP Flexion Index Pre	37±18.25	56±16.8	0.013
DIP Flexion Index Post	58±21.74	63±16.95	0.544
p	0.034	0.213	
DIP Flexion Middle Pre	34±21.06	55±19.44	0.02
DIP Flexion Middle Post	53±22.59	58±17.34	0.653
p	0.062	0.594	
DIP Flexion Ring Pre	33±21.13	52±19.81	0.035
DIP Flexion Ring Post	54±19.25	58±16.92	0.477
p	0.041	0.241	
DIP Flexion Little Pre	34±23.27	57±19.62	0.011
DIP Flexion Little Post	56±21.8	65±14.36	0.374
p	0.041	0.185	

MCP: Metacarpophalangeal joints, PIP: proximal interphalangeal joints, DIP: distal interphalangeal joints

that the rehabilitation program implemented by mimicking the intended physical outcomes is more effective, and the VR program may be a solution for this treatment. In other studies conducted in this field, patients enjoyed performing in realistic environments and exhibited sufficient improvement in their physical abilities (13). In addition, activation in the corresponding neurological pathways of patients was demonstrated by functional magnetic resonance imaging during and after VR performed in a realistic setting (14).

However, there is little evidence in the literature showing the improvement of outcomes of rehabilitation in the physical environment. Although the authors have demonstrated that improvement can be achieved in rehabilitation results with the available realistic scenario and the rapidly implemented realistic application, research has not yet been able to show the main reason for the success of this program in the physical environment (15). This may be due to the fact that VR studies are difficult and expensive, and it is not possible to compare multiple VR programs with each other. Studies have shown that development has been achieved in upper extremity functions in patients diagnosed with hemiplegia through the game-based virtual reality application (16). It has been reported that the integration of an application used for gaming on Windows into the leapMotion® controller has been effective for the fine motor skills of the hand functions of patients followed up for hemiplegia and contributed to the evaluation of fine motor skills (17). Losa et al. reported that an increase in hand skills was achieved using the leapMotion® controlled video games that they developed for adult patients diagnosed with subacute stroke (18).

With the virtual reality program that we implemented, the ROMs of all joints can be measured

from the elbow onward, and the results can be monitored during patient follow-up. In addition, the exercises performed by patients at home can be recorded in the online system and followed up in a virtual environment.

In rehabilitation, the duration of the exercises and the number of repetitions of the movements are essential (19). The proposed virtual reality application provides patients with the ability to perform an unlimited number of repetitions while also ensuring the performance of a successful rehabilitation by drawing the patient's attention to the game environment on the screen. Patients will be able to be rehabilitated with a previously specified duration and number of repetitions in their homes in an environment where they feel comfortable and safe without having any fear. During the evaluation of results, patients' awareness of their clinical scores in the treatment process as well as discussion of the results and scores based on the knowledge and outlook of the patients' physiotherapist or physician will be more effective in motivating the patient (20).

While conventional treatment methods require minimal cognitive activity in the clinical environment during treatment, the patient may be unprepared for increased cognitive needs for the same performance outside of the clinic (such as listening and responding to someone while eating) (21, 22). VR may help in achieving the necessary cognitive attention with a set of adjusted scenarios, so that it can be ensured that instead of solely physical activity, patients' functions that require cognitive activity are also exercised. Researchers have already begun to write software designed to achieve this purpose. This software was developed for the recovery of impaired balance of patients against an unexpected stimulus (21, 22).

There are promising studies on the effectiveness of the VR program; however, studies on this treatment are still at the initial stages. Inability to obtain results from some studies may be due to the fact that researchers had limited time to develop and test their own VR programs. Nevertheless, the VR program is generally effective; in other words, it is a promising rehabilitation program that does not yield negative results. Whether or not the VR program would have been beneficial as an addition to conventional rehabilitation had been questioned until a few years ago; however, it has been recently included in rehabilitation research and practice. While there is no doubt regarding its benefit, it is recommended to perform a cost-benefit analysis before implementation (15, 23, 24).

Our study also had some limitations. We found that there was no difference between some objective tests between the group administered and the group not administered VR treatment. This may be attributed to the use of this device, which is still under trial, in limited durations under hospital conditions. More accurate results may have been obtained if more patients were included in the study and if the patients were administered the treatment five times a week instead of only twice a week.

The strength of our study is that it is possible to use VR technology initially in hand and upper extremity rehabilitation and later in rehabilitation programs that involve the whole body in the subsequent stages due to the features of the VR technology and program. One of the most important advantages of the VR program is its applicability to all patients who present to rehabilitation clinics. Another limitation of our study is that it may cause anxiety and distress in patients using VR because they are not familiar with the virtual reality environment and because they feel they cannot. In order to overcome this situation, we have given patients a period of familiarization and tried to encourage patients. We believe that this VR program will be widely used considering the fact that every household today possesses a computer.

CONCLUSION

VR technologies used in rehabilitation have cer-



tain advantages, such as the ability to implement the program at home, the elimination of time and space constraints, and the ability of the patient to use the time that needs to be allocated in a busy clinic in his/her own home or workplace. Rehabilitation programs customized for the patient should be developed using VR technologies together with conventional rehabilitation programs. Additionally, the target audience and exercise program of the virtual/augmented reality system that will be developed should be designed by experts, and studies should be planned with larger patient groups.

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RESEARCH

PARANASAL SINUS ANATOMICAL DIFFERENCES IN ELDERLY PATIENTS

Abstract

Introduction: Endonasal endoscopic sinus surgeries performed on elderly patients can be challenging due to anatomical variations, and can be studied using preoperative computed tomography. The aim of the present study was to evaluate paranasal sinus anatomical differences in elderly patients compared to a younger control group.

Materials and Methods: We retrospectively evaluated paranasal computed tomography scans of 47 elderly patients (>65 years old) (Elderly group) and 47 younger patients (Control group) for midfacial skeletal size (interzygomatic buttress distance, nasion-basion distance), anatomical variations, dimensions, and paranasal sinus volumes.

Results: The mean age of the Elderly group was 69.89 years (65- 81 years) and the mean age of the Control group was 33.15 years (20-49 years). There was no significant difference in midfacial size between the two groups. The prevalence of Keros Type III olfactory fossa was significantly higher in the Elderly group than in the Control group ($p<0.05$). The Elderly group had a significantly lower mean maxillary sinus volume ($p<0.01$) and mean anteroposterior diameter of the sphenoid sinus ($p<0.01$) compared to the Control group. Furthermore, there was no significant difference in the maxillary sinus volume between the elderly edentulous and dentulous patients($p>0.05$).

Conclusion: Elderly patients have more Keros Type III olfactory fossa, which confers a higher risk of iatrogenic cerebrospinal fluid leakage during endoscopic sinus surgery. The preoperative detailed evaluation of computed tomography scans of elderly patients should include, but not be limited to, the ethmoid roof for deep olfactory fossa, and the sphenoid sinus for its narrow anterioposterior dimention.

Keywords: Aged; Paranasal Sinuses; Endoscopy; Anatomy; Nose; Nasal Cavity; Computed Tomography.

INTRODUCTION

Paranal sinus development continues after birth, and changes during life. The maxillary sinus is the first to develop, and pneumatization of maxillary sinus continues after birth. The volume of the maxillary sinus increases until the age of 20 years, after which the volume decreases (1). The maxillary sinus volume is thought to be influenced by age, sex, tooth loss, height, and weight (2, 3). Although the paranasal sinus volume and skeletal size may change with these parameters, the midfacial skeletal size can be used as a reference of the skeletal size in studies assessing its volume (1, 4).

Sphenoid sinus aeration begins from birth, until the late 30's (5). After this, the volume of the sphenoid sinus begins to decrease (5). The frontal sinus can only be detected on radiologic images after the age of three, and is highly variable due to different pneumatization (6). Although individual frontal sinus anatomical variations exist, patients older than 60 years of age are suggested to have a higher frontal sinus volume due to osseous resorption (7). This process in elderly patients is accompanied by thinning of the cortical orbital plate, which can lead to orbital complications during endoscopic frontal surgery (6).

The ethmoid skull base consists of the fovea etmoidalis, an extension of the frontal bone, and the cribriform plate. These two structures converge at the lateral lamella of the cribriform plate, a fragile area known to be a common site for iatrogenic skull-base injury during endonasal endoscopic surgery (8). The Keros classification stages the depth of the cribriform fossa (Type I: 1–3.9 mm, Type II: 4–7.9 mm, Type III ≥8 mm), and suggests that a deeper cribriform fossa is more susceptible to iatrogenic cerebrospinal fluid (CSF) leakage during endoscopic sinus surgery (9, 10).

Elderly patients have a higher risk of complications than younger patients undergoing endoscopic sinus surgery (11). Thus, studying the anatomy of the paranasal sinus using computed tomography (CT) can promote endonasal endoscopic surgical safety. In addition to individual anatomical variations, analyzing the differences in a group of patients can increase our understanding of different susceptibilities in elderly patients during an endonasal surgery. Therefore, the aim of the present study was to evaluate paranasal sinus anatomical differences in elderly patients compared to a young control group.

MATERIALS AND METHODS

This study was carried out with the approval of the ethics committee. In this study, we retrospectively evaluated paranasal CT scans of 47 elderly patients (>65 years old) (Elderly group) from our radiology database. The control group included paranasal CT scans of 47 young patients (<50 years old). The CT scans for all patients were taken in the outpatient clinic for chronic nasal blockage. Patients with nasal polyposis, chronic sinusitis, previous paranasal sinus operations, tumors, fracture, and severe nasal septal deviations that could affect the paranasal anatomy were excluded from the study.

All patients were screened on a 16-detector spiral CT scanner (Toshiba Alexion, Tokyo, Japan) with 120 kV and 120 mA parameters. The coronal and sagittal reformat and reconstruction images were obtained from axial scans taken at 3 mm slice thickness from the patient in a supine position with their head on the scanning table. All images were analyzed by an expert radiologist using the OsiriX MD software (v8.0, Pixmeo, Geneva, Switzerland). In order to eliminate variability caused by patient orientation, the images were standardized in 3 orthogonal planes. Images of the two groups were examined for the following surgery-related anatomical variations;

1) Patients with at least one upper molar tooth were considered as dentulous, and patients with no teeth in the upper jaw were considered as edentulous.
2) Interzygomatic buttress distance (IBD) and nasi-

on-basion distance (NBD): IBD and NBD, modified from the method by Waitzman et al. (4), were adopted as an index for midfacial skeletal size. IBD was defined as the distance between the anterolateral corners of each zygomatic buttress in the axial CT scan. NBD was defined as the distance between the nasion and basion in the saggittal CT scan (Figure 1).

3) Keros classification: The depth of the cribriform plate was measured at the largest vertical height of the olfactory fossa in the coronal plane on both sides. Type I was 1–3.9 mm, type II was 4–7.9 mm, and type III was ≥8 mm (9). (Figure 2)

4) Ethmoid roof angle (ERA): We measured the ERA by measuring the angle between the midline corresponding with the crista galli, and the line drawn along the fovea ethmoidalis. This was measured at the coronal section that was posterior to the anterior most view of the superior turbinate on both sides (12).

5) Orbital floor angle (OFA): OFA was measured as the angle between the lamina papyracea and the orbital floor, measured in the coronal CT that depicted the hiatus semilunaris superioris (12).

6) Pneumatized middle turbinate: Pneumatization of the middle turbinate may include cells in the vertical lamella (an interlamellar cell) or in the inferior bulbous portion. It was evaluated on the coronal plane and classified as 0 (none), 1 (unilateral), and 2 (bilateral).

Figure 1. Midfacial dimensions. (a.) Interzygomatic buttress distance and (b.) nasion-basion distance.

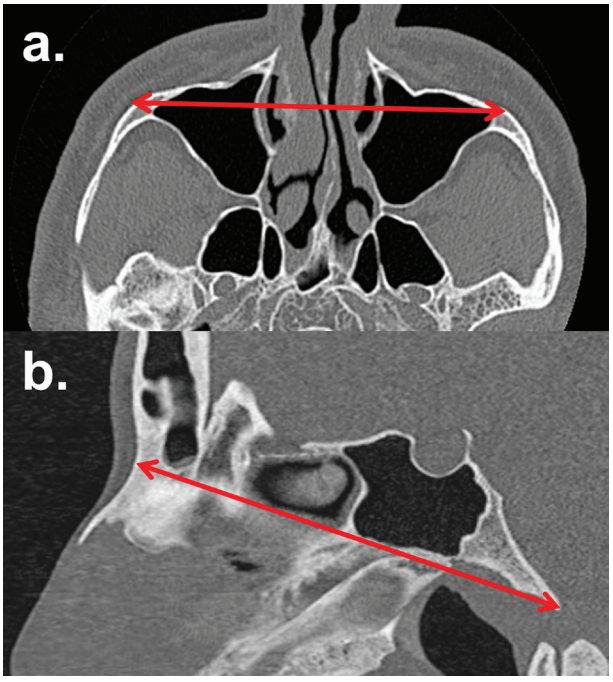
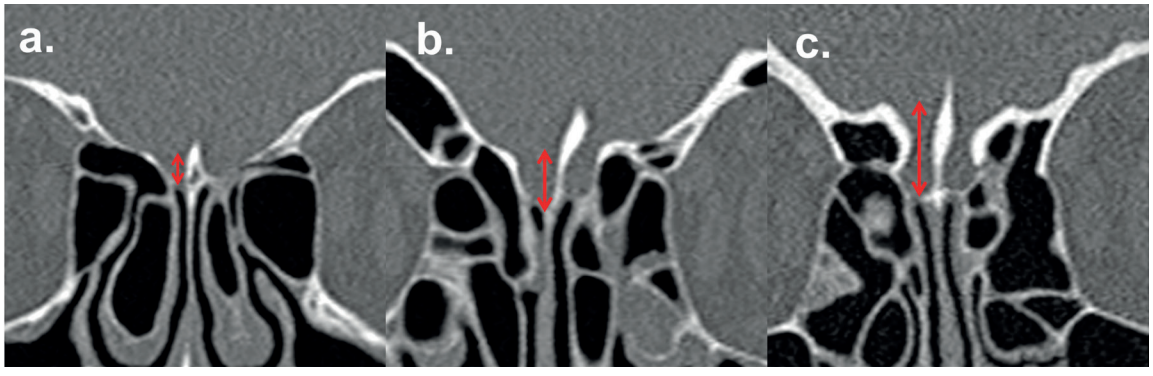


Figure 2. Keros classifications for the heigth of the olfactory fossa; a.Type I: 1–3.9 mm, b. Type II: 4–7.9 mm, c. Type III ≥8 mm



7) Pneumatized superior turbinate: This was evaluated on the coronal plane, and classified as 0 (none), 1 (unilateral), and 2 (bilateral).

8) Paradoxical middle turbinate: A curvature of the middle turbinate such that the convex surface was lateral rather than medial. This variation was considered to be present if paradoxical curvature was seen in at least two consecutive levels (13). It was evaluated on the coronal plane, and classified as 0 (none), 1 (unilateral), and 2 (bilateral).

9) Pneumatized crista galli: The crista galli sits anteriorly in the midline above the cribriform plates. Crista galli pneumatization was noted from either the left or right frontal sinuses on the coronal plane.

10) Pneumatized vomer: Pneumatization of the vomer was noted in sinuses on the coronal plane.

11) Agger nasi cell: Cells in an anterior ethmoid air chamber below the frontal sinus, which was intimately related to frontonasal recess, reaching the lacrimal fossa inferolaterally and anterolaterally arched by the nasal bones (13, 14) was evaluated on 3 planes, and classified as 0 (none), 1 (unilateral), and 2 (bilateral).

12) Haller cell: Any air cell located in the roof of the maxillary sinus or inferior portion of the lamina papyracea below the ethmoid bulla (14) was evaluated on 3 planes, and classified into 0 (none), 1 (unilateral), and 2 (bilateral).

13) Onodi cell: A posterior ethmoid air cell that pneumatized into the region normally occupied by the sphenoid sinus, this posterior ethmoid cell extends superior and lateral to the sphenoid sinus (15) was evaluated on 3 planes, and classified as0 (none), 1 (unilateral), and 2 (bilateral).

15) Accessory maxillary ostium: This was evaluated on the coronal plane and classified as0 (none), 1 (unilateral), and 2 (bilateral).

16) Maxillary floor-nasal floor distance: The parallel line drawn to the nasal floor and the maximum distance of the maxillary sinus floor to this line were measured on the coronal plane.

17) Dimensions and volumes of the paranasal sinuses: The maximum anteroposterior (AP), transverse (TRV) and craniocaudal (CC) diameters of the maxillary, ethmoid, and sphenoid sinuses were measured in 3 planes. The diameters were presented in millimeters (mm). The estimated volume of the paranasal sinus was calculated by the ellipsoid volume formula: $\pi/6 \times TRVdiameter \times APdiameter \times CCdiameter$. The estimated volumes were presented in cubic millimeters (mm^3).

Statistical analyses were performed using the SPSS 21.0 program (SPSS, Inc., Chicago, Illinois). For qualitative data analysis, Pearson chi-square test was used. For the quantitative data analysis, Kolmogorov-Smirnov test was used for compatibility with normal distribution. T-test and ANOVA test were used for independent groups for data that fit the normal distribution. Mann-Whitney U test and Kruskal-Wallis test were used for data that did not fit the normal distribution. In all statistical analyses, $p \leq 0.05$ was considered significant.

RESULTS

The mean age of the Elderly group was 69.89 (65-81 years) and the mean age of the Control group was 33.15 (20-49 years). There was no significant difference in the gender distribution between the Elderly group (26 males/ 21 females) and the Control group (21 males/ 26 females) ($p>0.05$). Paranasal anatomical variations are summarized in Table 1. There was no significant difference in paranasal anatomival variations between the two groups.

The Keros Classification results are summarized in Table 2. The prevalence of Keros Type III olfactory fossa was significantly higher in the Elderly group than in the Control group ($p<0.05$).



Table 1. Paranasal anatomical variations between the Elderly and Control groups.

		Elderly Group		Control Group		p
		n	%	n	%	
Pneumatized middle turbinate	absent	25	53,2	18	38,3	0.116
	unilateral	9	19,1	18	38,3	
	bilateral	13	27,7	11	23,4	
Pneumatized superior turbinate	absent	29	61,7	21	44,7	0.251
	unilateral	12	25,5	18	38,3	
	bilateral	6	12,8	8	17,0	
Paradoxical middle turbinate	absent	36	76,6	34	72,3	0.857
	unilateral	9	19,1	10	21,3	
	bilateral	2	4,3	3	6,4	
Pneumatized crista galli	absent	41	87,2	44	93,6	0.485
	present	6	12,8	3	6,4	
Pneumatized vomer	absent	30	63,8	27	57,4	0.527
	present	17	36,2	20	42,6	
Ager nasi cell	absent	8	17,0	2	4,3	0.099
	unilateral	11	23,4	9	19,1	
	bilateral	28	59,6	36	76,6	
Haller cell	absent	38	80,9	33	70,2	0.475
	unilateral	5	10,6	9	19,1	
	bilateral	4	8,5	5	10,6	
Onodi cell	absent	35	74,5	28	59,6	0.1342
	unilateral	8	17,0	8	17,0	
	bilateral	4	8,5	11	23,4	
Axessory maxillary ostium	absent	21	44,7	23	48,9	0.597
	unilateral	11	23,4	8	17,0	
	bilateral	15	31,9	16	34,0	

Midfacial dimensions, paranasal sinus volumes, and dimensions of the groups are summarized in Table 3. There was no significant difference in IBD and NBD between the two groups. The mean maxillary sinus volume was significantly lower in the Elderly group compared to the Control group. Three subjects in the Elderly group and one subject in the Control group had frontal sinus agenesis, and were excluded from the frontal sinus analysis. There were no significant differences in the

Table 2. Keros classifications of the Elderly and Control groups for the height of the olfactory fossa.

		Elderly Group		Control Group		p
		n	%	n	%	
Keros Type Left Side	I	8	17,0	14	29,8	0.004
	II	23	48,9	29	61,7	
	III	16	34,0	4	8,5	
Keros Type Right Side	I	10	21,3	17	36,2	0.045
	II	22	46,8	24	51,1	
	III	15	31,9	6	12,8	

Type I: 1–3.9 mm, Type II: 4–7.9 mm, Type III ≥8 mm

Table 3. Midfacial dimensions, paranasal sinus dimensions (mm) and volumes (mm^3) of the Elderly and Control groups.

		Elderly Group		Control Group		p
		Mean	Standart Deviation	Mean	Standart Deviation	
Midfacial Dimentions	IBD	106,7	5,93	105,74	5,61	0.232
	NBD	99,36	4,97	99,79	5,12	0.250
Maxillary Sinus Right	Volume	18,31	5,78	22,2	6,4	0.003
	AP	37,12	3,1	39,14	3,38	0.003
	TR	24,61	5,54	27,14	4,12	0.017
	CC	36,36	7,91	39,4	5,32	0.041
Maxillary Sinus Left	Volume	18,45	6,1	23,11	6,49	0.001
	AP	37,2	3,44	39,53	3,34	0.001
	TR	25,15	3,76	27,36	4,22	0.010
	CC	36,88	5,96	40,39	5,27	0.003
Frontal Sinus	Volume	16,21	4,56	13,38	5,25	0.070
	AP	17,41	10,14	14	5,25	0.050
	TR	56,69	18,64	54,23	17,8	0.532
	CC	27,84	9,39	29,23	8,39	0.459
Sphenoid Sinus	Volume	12,68	6,88	13,45	4,57	0.097
	AP	26,32	5,28	30,18	4,7	0.001
	TR	36,34	7,89	36,98	7,46	0.494
		23,69	4,91	22,61	3,22	0.501

IBD: Interzygomatic buttress distance, NBD: Nasion-basion distance, AP: Anterior-Posterior distance, TR: Transverse distance, CC: Craniocaudal distance



frontal sinus and sphenoid sinus volumes between the groups. The anteroposterior diameter of the sphenoid sinus was significantly lower in Elderly group compared to The Control group.

There was no significant difference in the maxillary floor-nasal floor distance between the Elderly group (6.9 ± 4.22) and the Control group (6.64 ± 3.38) ($p>0.05$). There was no significant difference in the ERA between the Elderly group (Right mean: 74.21 ± 11.41, Left mean: 79.78 ± 14.11) and the Control group (Right mean: 71.58 ± 8.64, Left mean: 75.43 ± 12.98) ($p>0.05$). Furthermore, there was no significant difference in the OFA between the Elderly group (Right mean: 114.21 ± 15.87, Left mean: 120.46 ± 7.16) and the Control group (Right mean: 117.10 ± 4.93, Left mean: 120.18 ± 5.44) ($p>0.05$).

The Elderly group was further divided into edentulous (n=23, 12 males/11 females) and dentulous (n=24, 14 males/10 females) groups. There was no significant difference in the maxillary sinus volumes between the edentulous and dentulous elderly group ($p>0.05$). All patients in the control group were dentulous.

DISCUSSION

As the life expectancy increases, the number of endonasal endoscopic surgeries performed on elderly patients increases (11, 16). Ramadan et al. reported that elderly patients undergoing endoscopic sinus surgeries had significantly more complications, such as CSF leakage (11). In this study, we found that the Keros classification for the olfactory fossa depth significantly differed between the Elderly group and Control patients. Elderly patients had more Keros Type III olfactory fossa comparing to young patients, which increases risk of iatrogenic skull base trauma during endonasal endoscopic surgery. Osseous resorption has been postulated to cause the higher frontal sinus volumes seen in elderly patients (6). Osseous resorption may not only affect ethmoid sinuses leading to a deeper olfactory fossa in elderly patients, but also lead to a fragile and vulnerable ethmoid skull base.

Yonetsu et al. studied the volume of the sphenoid sinus using CT images and found that the volume reduced after the age of 30 years (5). We found that the volume of the sphenoid sinus was lower in the Elderly group; however, this was not statistically significant. However, the mean anteroposterior diameter of the sphenoid sinus was significantly lower in the Elderly group. This was considered to be an important finding since a lower anteroposterior diameter can lead to iatrogenic trauma in the sphenoid sinus during endonasal endoscopic surgery. Iatrogenic sphenoid sinus injury may happen during endonasal sendoscopic surgeries performed on elderly patients. Emanuelli et al. reported cases of iatrogenic sphenoid sinus injury leading to CSF leakage in elderly patients (17).

Takahashi et al. studied maxillary sinus volumes in elderly cadavers and found that the maxillary sinus tends to be smaller when a greater number of molars are missing (3). Ariji et al. studied the maxillary sinus volume using CT scans and found that there was no difference between the dentate and edentulous group between the age 50 to 79 (1). In our study, we found no significant difference in the mean maxillary sinus volume between dentulous and edentulous elderly patients. Dedeoglu et al. studied maxillary sinus variations in elderly patients using cone-beam CTs and found that the accessory maxillary ostium was increased in elderly patients in than younger patients (18). We found no significant differences in the accessory maxillary ostium between the two groups.

Fatu et al. studied plain radiographs to evaluate the frontal sinus related to age and reported an increased frontal sinus area in elderly patients, which is thought to result from osseous resorption (6). This process in elderly patients is accompanied by thinning of the cortical orbital plate, which can lead to orbital complications during endoscopic frontal surgery (6). In our study, although not statistically significant, we found that the mean volume

of frontal sinus of elderly was higher.

Our study has some limitations worth mentioning. The volume of the paranasal sinuses may be influenced by height and weight, which we failed to assess (3). However, we measured the midfacial skeletal size as a reference and compared this between the groups (1, 4). We found no significant difference, which suggests that the changes observed in the elderly were not due to differences in skeletal sizes between the two groups. Second, we did not calculate the exact three-dimensional volumes, but instead calculated volumes using the dimensions of individual sinuses. Furthermore, we did not measure the left and right frontal sinus dimensions separately, which may lead to overestimation of the calculated volumes after using the formula.

Preventing complications during endoscopic endonasal surgeries requires an elaborate study of the anatomical variations observed on the preoperative CT scan. Preoperative CT evaluation of elderly patients should include, but not be limited to, the ethmoid roof for deep olfactory fossa, the sphenoid sinus for its narrow anterioposterior distance, and the frontal recess for orbital wall thinning. Endonasal endoscopic surgeons should be cautious at these vulnerable regions when operating on elderly patients.

CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

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RESEARCH

EFFECTS OF OUTDOOR NATURAL LIGHT EXPOSURE ON SLEEP QUALITY IN THE ELDERLY

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Abstract

Introduction: One of the serious outcomes associated with ageing is the high prevalence of age-related sleep disturbances detrimentally influencing general well-being in the elderly. Whilst underexposure to diurnal bright light appears to be a reason for disturbed sleep in old age, further empirical evidence is required to confirm such a relationship.

Materials and Method: In order to contribute to our current understanding of the subject, a study was conducted in a long-term care facility in Istanbul, Turkey. Participating elderly residents (N = 39) were exposed to natural light outdoors (> 10,000 lx) for 40 minutes in the morning on 17–21 June and 1–5 July 2019, and they were asked to report on their sleep quality by completing various questionnaires throughout the study.

Results: The results of the study demonstrated a significant difference ($p < 0.05$) between the pre- and post-treatment scores of the participants. Moreover, the participants reported significantly less ($p < 0.05$) disturbed sleep in the second period during which they were exposed to approximately 63% more natural light.

Conclusion: Based on our findings and those of other research groups, it is possible to conclude that light, or more specifically natural light, should be considered as an independent factor affecting sleep and, thus, general well-being in old age.

Keywords: Light; Sunlight; Sleep; Aged; Aging.



INTRODUCTION

In people aged 65 and above, a major change often accompanying the ageing process is the disruption of the daily sleep–wake cycle (1). There is ample evidence from epidemiological studies that sleep-related problems become more prevalent and severe as age advances. Approximately 50% of community-dwelling elderly and 67% of those residing in long-term care facilities have been reported to have considerable difficulties in initiating and maintaining sleep (2). There are serious consequences of disturbed sleep for the elderly such as increased risk of falling, decreased physical functioning, impaired memory and heightened mortality (3). Thus, improving sleep in older adults is key to a high quality life and good daytime functioning.

In humans, sleep and wakefulness are governed by the following two largely independent mechanisms: a) the homeostatic drive to sleep and b) the circadian system controlling diurnal oscillations (4). On one hand, the homeostatic sleep drive is determined by the time spent awake or the duration of previous sleep. The longer we stay awake, the more our sleep propensity increases. On the other hand, the circadian system synchronises the daily sleep–wake cycle and other biological rhythms with a number of exogenous temporal cues termed as zeitgebers. Whilst light is considered to be the principle zeitgeber in humans (5), its effectiveness differs with age. To elicit the same circadian response, a 65-year-old elderly adult needs roughly three times more light than a 25-year-old young adult due to crystalline lens yellowing and pupillary miosis (6).

Given the impact of ageing on the photic entrainment of our circadian rhythms, it can be postulated that there may be a close association between sleep disturbances and the amount of light exposure amongst the elderly, especially those living in long-term care facilities. According to the research on the subject, it should be noted that older adults spend only less than 1 hour at high illuminance levels exceeding 1,000 lx in a day (7). However, one should not leap to the conclusion that insufficient or limited exposure to an optimal light level is an independent risk factor for sleep disturbance. A review of the existing literature reveals that there are inconsistencies and discrepancies in the reported findings.

On one hand, some of the studies discredit the possible role of light, or more specifically diurnal bright light exposure. For example, Dowling and colleagues (8) observed that 1-hour exposure to light levels higher than 2,500 lx in the morning for 10 weeks could not influence sleep initiation and maintenance in a sample of institutionalised patients with Alzheimer's disease. On the other hand, a number of studies suggest the potency of natural light or illuminances is considerably higher than those commonly experienced indoors. The major problem with the latter studies is that the minimum amount and duration of light exposure necessary to improve and restore sleep cannot be specified. In one of these studies, Hood and colleagues (9) demonstrated that there was a significant relationship between the duration of exposure to illuminances over 3,000 lx and the nocturnal immobility amongst a sample of healthy aged participants. This finding is not in complete accord with the results obtained by Shochat and colleagues (7). Unlike the other research group, they were not able to identify a critical threshold. Higher light levels predicted fewer night-time awakenings in a nursing home population. Two other studies revealed that even a very brief exposure to outdoor illumination conditions may also be beneficial (10, 11). Exposing nursing home residents to natural light outdoors or extremely high levels more than 10,000 lx for 30–60 minutes generally in the morning was shown to be useful to ameliorate sleep disturbances.

Because of the above-mentioned discrepancies and methodological differences in the literature, it

is still not possible to state with certainty that the low daily light dose received by the elderly can detrimentally influence their sleep. Until we have a sound understanding of the effects of light on our sleep–wake rhythm, there is a compelling need to determine whether such a causal relationship exists. Therefore, in an attempt to build on the earlier work and contribute to our limited knowledge about the subject, this study was conducted in a long-term care facility over a 1-month period. The present paper reports the results of this investigation carried out to test the following hypotheses:

a) Elderly home residents have considerable difficulties in initiating and maintaining sleep and, as a direct consequence, have poor sleep quality.

b) Diurnal bright light exposure can alleviate sleep disturbances and, thus, improve sleep quality of the residents.

MATERIALS AND METHOD

2.1. Participants

A total of 43 (37 females and 6 males) elderly adults, who had been residing in an eldercare facility located in Istanbul for more than 6 months, voluntarily participated in the study. Of those participants, four females were excluded since they were experiencing difficulties in following the study protocol. All remaining participants were

a) older than 65 years (mean ± SD = 80.23 ± 5.19);

b) literate and had at least completed primary school education;

c) cognitively intact. Four weeks prior to the study, a general estimate of residents' cognitive status was obtained by administering a Turkish version of the Standardised Mini Mental State Examination (SMMSE) (12). This brief test comprises various questions and tasks that assess several domains of cognitive function. Whilst an SMMSE score of 30 indicates no impairment, scores between 26 and 30 are considered to be normal in the general population. Gungen and colleagues (13) translated the SMMSE into Turkish and recommended 23/24 as the cut-off score for reliably and validly diagnosing dementia with its Turkish version (SMMSE-T). Therefore, the residents who had scored less than 23 were screened out. The mean ± SD SMMSE-T score of the participants was 26.64 ± 2.75;

d) considered to be healthy on the basis of their medical records and scores on a general health profile. For profiling purposes, a Turkish version of the Short Form 36 (SF-36) (14) was self-administered by the residents to report on their physical and mental health status before the study. The SF-36 is a 36-item generic measure developed to determine perceived health transition and assess eight domains of health. For each domain evaluated, respective item scores are recoded, summed and transformed into a scale from zero, indicating an extreme disturbance, to 100, indicating no disturbance. Kocyigit and colleagues (15) translated the SF-36 into Turkish and reported that the psychometric properties of its Turkish version (SF-36T) were acceptable. Norms for SF-36T scores in the elderly (16) were compared with participants' scores. Whilst there were no significant differences between the role limitations because of physical health problems, bodily pain, general health perceptions, vitality and social functioning domain scores, it was observed that our participants had significantly better physical function [$t(152) = -2.74$; $p < 0.05$] and general mental health [$t(152) = -2.18$; $p < 0.05$]. The only dimension score that was found to be significantly lower in our sample was for the role limitations because of emotional problems domain [$t(152) = 2.09$; $p < 0.05$];

e) moderately morning-type, intermediate-type or moderately evening-type individuals. Apart from the above-mentioned measures, a Turk-



ish version of the Morningness–Eveningness Questionnaire (MEQ) (17) was also used to determine participants' chronotype. The MEQ is a self-administered questionnaire that consists of 19 items rated on a four-point Likert-type scale or a scale with various time intervals. An MEQ score, ranging from 16 to 86, is obtained by adding all item scores, and it is utilised to identify chronotypes. Agargun and colleagues (18) translated the MEQ into Turkish and demonstrated that its Turkish version (MEQ-T) was reliable and valid. To ensure compliance with the study protocol, evening-type residents who had scored between 16 and 30 were excluded from the study sample. The mean ± SD MEQ-T score of the participants was 57.97 ± 7.30.

In accordance with the Declaration of Helsinki and ethical clearance received from the Ethics Committee of our university, consent was obtained from each participant. Even though all participants were thoroughly informed about their rights and responsibilities, no information on possible study outcomes was given to minimise confounding effects of prior knowledge and expectations.

2.2. Sleep Assessment

2.2.1. Pittsburgh Sleep Quality Index

A Turkish version of the Pittsburgh Sleep Quality Index (PSQI) (19) was completed by the residents to assess their nocturnal sleep. The PSQI is a self-administered questionnaire developed to differentiate 'good' from 'poor' sleepers by evaluating sleep quality and disturbances in the preceding month. It consists of 19 self-report items and five additional items for the bed partner or roommate. Only the self-report items are used in the scoring of the PSQI. Responses to these items are grouped to obtain seven component scores. Each component score ranges from zero, indicating no difficulty, to three, indicating severe difficulty. A global PSQI score, varying from zero to 21, can also be obtained by adding the component scores. A global score greater than five was reported to provide a sensitive and specific measure of poor sleep quality. Agargun and colleagues (20) translated the PSQI into Turkish and reported that the psychometric properties of its Turkish version (PSQI-T) were satisfactory.

2.2.2. PROMIS Sleep Disturbance Short Form

Additionally, the participants filled in a Turkish version of the PROMIS Sleep Disturbance Short Form (PSDSF) (21). The PSDSF is a self-administered questionnaire devised to assess qualitative aspects of sleep over the last seven days. Eight items of the questionnaire are rated on a Likert-type scale ranging from one, not at all, to five, very much. A raw PSDSF score is obtained by adding all item scores, and it is used in order to estimate the corresponding t score. The t scores vary from 28.9 to 76.5, and they are interpreted as follows: less than 50, none to slight sleep disturbance; between 55.0 and 59.9, mild sleep disturbance; between 60.0 and 69.9, moderate sleep disturbance; 70 and over, severe sleep disturbance. Yuzeren and colleagues (22) translated the PSDSF into Turkish and provided evidence that its Turkish version (PSDSF-T) reliably and validly represents sleep disturbances in a sample of healthy and sleep-disturbed adults.

2.2.3. Richards–Campbell Sleep Questionnaire

Since there was a need for a measure to assess previous night's sleep, a Turkish version of the Richards–Campbell Sleep Questionnaire (RCSQ) (23) was also used. The RCSQ is a brief, five-item questionnaire developed to evaluate perceived sleep depth, latency, fragmentation, efficiency and quality in an acute care setting. For each item, respondents were asked to rate their sleep the previous night on a 100 mm visual analogue scale with two anchor points. An RCSQ score can be obtained by calculating the mean of all item scores ranging from zero to 100. Although there is no cut-off score for the questionnaire, a high mean score is indicative of subjective sleep satisfaction. Ozlu

and Ozer (24) translated the RCSQ into Turkish and demonstrated that its Turkish version (RCSQ-T) was reliable and valid.

2.3. Procedure

The study was conducted between 17 June and 15 July 2019. Over two five-day periods (Figure 1), during which the atmospheric and lighting conditions differed markedly, the participating residents were taken outside the nursing home at 9:00 AM. Whilst the participants were assessing their sleep, they were exposed to natural light in each morning for 40 minutes (see Table 1 for the tasks carried out throughout the study period). To gain insight of the pre-existing and post-treatment sleep quality of the study population, the PSQI-T was administered on the first and last days of the study. On 17–22 June and 1–6 July 2019, each participant filled in the RCSQ-T at 9:00 AM to report their previous night's sleep. Additionally, the participants evaluated their sleep through the PSDSF-T on 1 and 15 July 2019 to assess whether possible effects of the bright light exposure would carry over into the following weeks. It is important to note here that, instead of identifying trait sleep problems, the above-mentioned questionnaires had been devised to assess monthly, weekly or daily variations in sleep quality. Therefore, it was assumed that minimal or no habituation would be elicited from the participants repeatedly rating their sleep over the course of the study.

In each period, vertical illuminance levels at participants' sitting eye height (approximately at 120 cm) were also measured daily between 9:00 and 9:40 AM at 20-minute intervals in the cardinal compass directions (N, S, E and W). All measurements were carried out with a portable illuminance metre (model BF05; Trotec GmbH & Co., Heinsberg, Germany).

Figure 1. Dates and times for the two exposure periods.

Exposure Period 1														Exposure Period 2												
9:00–9:40 AM														9:00–9:40 AM												
17	18	19	20	21	22	23	24	25	26	27	28	29	30	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
June														July														
2019																												

Table 1. Tasks carried out throughout the study period.

Date	Task
17–21 June and 1–5 July 2019	40-minute morning bright light exposure
17 June and 15 July 2019	PSQI-T administration at 09:00 AM
17–22 June and 1–6 July 2019	RCSQ-T administration at 09:00 AM
1 and 15 July 2019	PSDSF-T administration at 09:00 AM

2.4. Statistical Analysis

Paired-samples (or dependent-samples) t-tests were performed in order to analyse the statistical differences between participants' PSQI-T, PSDSF-T and RCSQ-T scores. The rationale of comparison and comparison groups are presented in Table 2. It is evident from the table that four separate analyses were carried out for comparing: a) the total mean RCSQ-T scores for the two exposure periods; b) the mean RCSQ-T scores for the two nights before each exposure period; c) the mean PSDSF-T scores for the two weeks following the end of each exposure period; and d) the mean PSQI-T scores obtained on the first and last day of the whole study period. These statistical analyses were performed with the SPSS Statistical Software Package for Windows (version 20.0; SPSS Inc., Chicago, IL, USA). The statistical analyses to compare sample mean differences in the SF-36T scores were carried out with MedCalc for Windows (version 15.0; MedCalc Software, Ostend, Belgium). The level of significance was set at $p < 0.05$.

3. Results

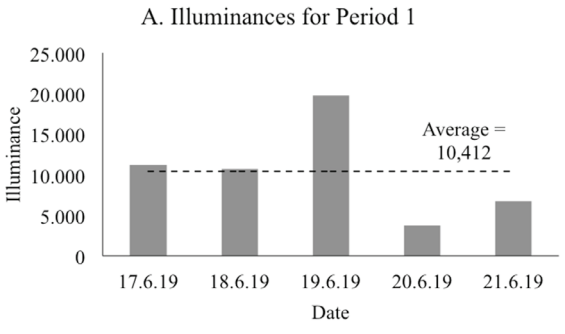
3.1. Light

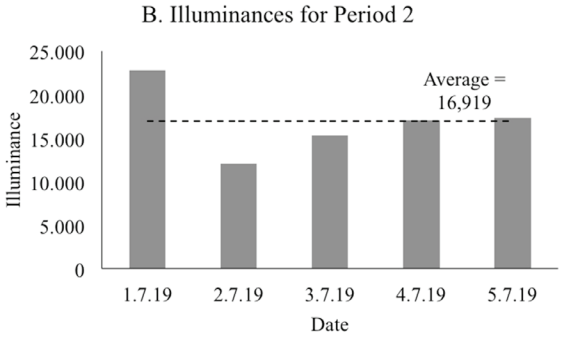
The calculated average illuminances to which the elderly were exposed during each exposure period are presented in Figures 2a and 2b. It can be seen from these figures that there are considerable differences. Due to the overcast sky and, as a

Table 2. TFour separate analyses performed for participants' PSQI-T, PSDSF-T and RCSQ-T scores.

Measure	Comparison Groups	Rationale
RCSQ-T	The total mean scores for the nights of 17–21 June and 1–5 July 2019	To check the effect of daylight exposure
RCSQ-T	The mean scores for the nights of 16 and 30 June 2019	To check whether the sleep quality levels were equivalent at the beginning of each exposure period
PSDSF-T	The mean scores obtained on 1 and 15 July 2019	To check whether there was a carry-over effect of daylight exposure
PSQI-T	The mean scores obtained on 17 June and 15 July 2019	To check pre-existing and post treatment sleep quality and assess the exposure effect

Figure 2a and 2b. Average vertical illuminances for each period.





direct consequence, relatively low illuminances on 20 and 21 June 2019, the elderly were exposed to an average illuminance of 10,412 lx in the first period. Since the sky was mostly clear between 1 and 5 July 2019, the average illuminance exposure over the second period was 16,919 lx and approximately 63% higher than that in the first period.

3.2. Sleep Quality

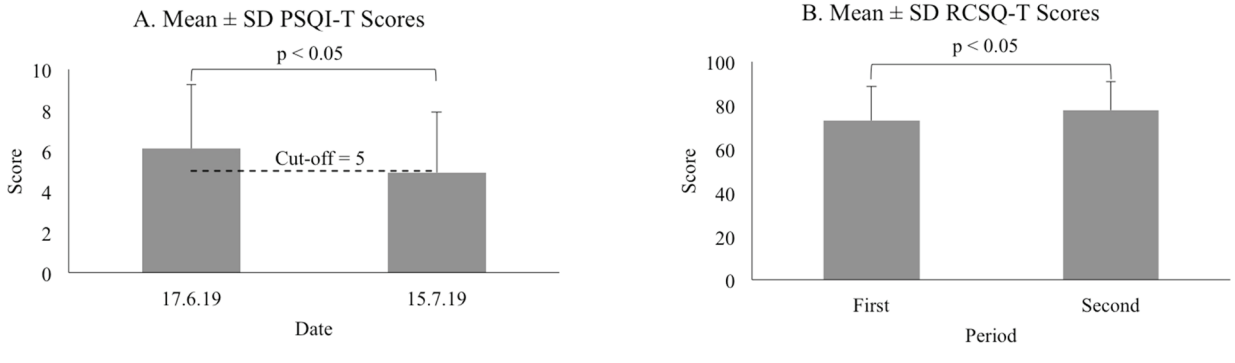
In order to assess the pre-existing and post-treatment sleep quality of the study population, a comparison between the mean scores obtained for the first and second PSQI-T administrations was done. The results obtained were in support of our first and second hypotheses. Participants' initial score (mean ± SD = 6.10 ± 3.13) was found to be above the cut-off for poor sleep quality and significantly higher [$t(38) = 2.93$; $p < 0.05$] than their score at the end of the study period (mean ± SD = 4.92 ± 2.99) (Figure 3a).

With the aim of understanding whether the observed improvement in sleep could be directly attributable to light, a further analysis was performed by comparing the mean RCSQ-T scores calculated for the five nights following the exposure to light outdoors. The analysis result was in favour with our second hypothesis. The score for the second period (mean ± SD = 77.79 ± 13.00) was significantly higher [$t(38) = -2.30$; $p < 0.05$] than the one for the first period (mean ± SD = 73.02 ± 15.59) (Figure 3b). To rule out the possibility that the effects of bright light exposure in the first period could carry over and account for this statistically significant difference, the initial mean RCSQ-T scores for the nights of 16 and 30 June 2019 were compared. Additionally, the mean PSDSF-T scores for the weeks after each exposure period were also compared with the same rationale. It was evident from the results that there were no statistically significant differences.

DISCUSSION

One of the questions that need to be answered by future research is whether sleep problems and light exposure in older adults are closely linked. Our findings suggest that light, or more specifically natural light, itself is a potent external stimulus for the daily sleep–wake cycle of the elderly. Even though our sample had less difficulty in initiating and maintaining sleep than those from other studies conducted at similar facilities in Turkey (25), there was a significant difference between pre- and post-treatment PSQI-T scores. This finding is in complete accord with the observations from some of the earlier research efforts. Like Alessi et al. (10) and another Turkish research group (11), it was demonstrated by the present study that ex-

Figure 3a and 3b. Participants' mean ± SD PSQI-T scores and their mean ± SD RCSQ-T scores for each period .





posure to natural light outdoors or very high illuminance levels for a brief period in the morning over five consecutive days could be beneficial to the sleep quality in older adults.

It should be noted here that on the basis of our findings, it would be erroneous to state an illuminance threshold or duration necessary to promote a healthy circadian response. Although exposing the participants to an average illuminance of approximately 17,000 lx for 40 minutes over a five-day period (Exposure Period 2) was observed to be more effective than the exposure to roughly 63% less daylight (~ 10,000 lx) for the same length (Exposure Period 1), it is not possible to state whether increasing exposure duration for much lower levels (< 10,000 lx) may yield similar results. For example, Hood and colleagues (9) reported that nocturnal immobility was positively correlated with the duration of exposure to levels over 3,000 lx. Moreover, it is not completely clear when the expected effects of natural or bright light exposure would wear off. Given the insignificant differences in the PSDSF-T and RCSQ-T scores obtained on the first day of each period, it is plausible to suppose that the exposure effects may last not more than a few days following light exposure and, thus, should only be expected for a short period in the elderly. However, it is unlikely to state with certainty what the exact effect duration can be.

There are a number of limitations that should be taken into account in interpreting the above-mentioned results and conducting future research. Firstly, possible gender effects on the study outcomes cannot be ruled out due to the scarcity of male residents in the facility and, as a direct consequence, relatively high number of females (33 females versus 6 males) in our sample. Secondly, the necessities of old age made it difficult to recruit participants who were not on medication. Despite being free from any prescribed sleep medication, the participants were taking medications, such as beta-blockers or diuretics, known to interfere with sleep. Thirdly, it is not clear to what extent the results obtained were influenced by the presence of depressed mood in our sample. In spite of the acknowledged association between depression and disturbed sleep in the elderly, participants' depression status could not be examined in the facility because of not being granted an official permission to use any measure diagnosing psychiatric illnesses. Therefore, the results of the present study should be considered accordingly.

Evidently, more interdisciplinary research in the fields of health care and architectural design is required to fully understand the non-visual effects of light. Nonetheless, it is already possible to draw some conclusions from the results discussed above. Firstly, given that diurnal bright light exposure can be a treatment or treatment adjunct for age-related sleep problems, a suitable approach to lighting design in long-term care facilities is to utilise the sun as the main source of daytime illumination. By adopting this approach, we may not only reduce our current dependency on electric light sources but also improve the well-being and overall life quality of elderly residents. Secondly, it seems reasonable to suggest that spending a substantial portion of a day in dimly lit environments virtually devoid of natural light is likely to be detrimental to sleep in older adults and, thus, should be avoided.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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CASE REPORT

ALKAPTONURIA DIAGNOSED IN A GERIATRIC PATIENT; A CASE REPORT

Abstract

Alkaptonuria is a hereditary and metabolic disease which is characterised by ocranosis, arthritis and aciduria. It is a rare clinical condition which has an estimated incidence varies from 1/ 250,000 to 1/1000000 live births. This autosomal recessive disorder occurs as a result of homogentisic acid dioxygenase enzyme deficiency which takes part in tyrosine metabolism. This case report aimed to present a geriatric patient who had diagnosed alkaptonuria. A 69 years old male was admitted to our department with knee-shoulder pain and range of motion (ROM) limitation. His medical history revealed that he had both mechanical and inflammatory joint pain for 22 years. The examination of his eyes were compatible with blue sclera and there was also bluish black discoloration on the ears. He had also hearing loss. Qualitative 24 hours collected urine examination showed dark black discoloration. The patient was diagnosed as alkaptonuria. A physical therapy programme were planned to the patient by our department. Clinicians should be aware of this pathology and the diagnosis should be confirmed by clinical, laboratory and radiological examinations.

Keywords: Alkaptonuria; Pain; Arthritis.

INTRODUCTION

Alkaptonuria is a hereditary and metabolic disease that is characterized by ochronosis, arthritis, and aciduria (1). The disease was described by Garrod in 1902 (2). It is a rare clinical condition with an estimated incidence that varies from 1/250,000 to 1/1,000,000 live births(3). This autosomal recessive disorder occurs as a result of the deficiency of homogentisic acid (HGA) dioxygenase enzyme, which takes part in tyrosine metabolism. The unexcreted HGA accumulates in various parts of the body, such as the skin, optic compartments, cardiovascular structures, and connective tissues of the musculoskeletal system with a bluish-black discoloration phenomenon termed as "ochronosis" (4). The diagnosis of alkaptonuriais based on clinical findings and urinary tests (5). Urine sample analysis that exhibits the presence of HGA is the gold standard for the confirmation of its diagnosis (5). Further, 24-hour urine collection and chromatographic techniques can be useful (5). Additionally, genetic tests could determine if an individualis homozygous or compound heterozygous (5). Although there is no treatment that could improve alkaptonuria, several studies reveal that nitisinone, which inhibits the tyrosine catabolic pathway, and dietary restriction of tyrosine and phenylalanine could be used as treatment options (6, 7). Here we present the case of a geriatric patient who was diagnosed with alkaptonuria.

CASE REPORT

A 69-year-old man was admitted to our department with knee and shoulder pain and range of motion (ROM) limitation. His medical history revealed that he had both mechanical and inflammatory knee and shoulder joint pain for 22 years. The level of his pain had been increased by moving and had a tendency to worsen at nights. He underwent total hip replacement operations bilaterally as a result of falls 6 and 14 years ago. His walking distance had decreased owing to the knee pain, and he could walk with a staff. The level of his pain was 100 mm based on a visual analog scale (VAS) from 0 to 100 mm. His pain was significant and caused functional impairments in his daily activities. Upon physical examination, ROM limitation on both knee and shoulder joints was detected. Moreover, effusion was detected on the knees bilaterally. He felt pain during the ROM examination. Upon examination of his eyes, it was compatible with a blue sclera, and there was a bluish-black discoloration on his ears. Laboratory findings revealed that serum C-reactive protein (CRP) level was 156.47 mg/L, erythrocyte sedimentation rate (ESR) was 93 mm/h, white blood cell count (WBC) was 6.97 × 109/L, and rheumatologic tests were negative. Urine examination showed multiple WBCs with a negative urine culture. Qualitative 24-hour-collected urine examination showed dark black discoloration. Symmetrical joint space loss, chondrocalcinosis and subchondral sclerosis were detected in both knee and shoulder X-ray graphics (Figures 1 and 2). Furthermore, there were multilevel intervertebral disk calcifications, disk space narrowing, and syndesmophytes in cervicothoracolumbar graphics (Figure 3). He was consulted in the cardiology department owing to the complaint of dyspnea. The degeneration in his aortic valve was detected by echocardiography. On the basis of the clinical, laboratory, and radiological findings, he was diagnosed with alkaptonuria presenting with ochronosis. A physical therapy program, including cold pack, transcutaneous electrical nerve stimulation, ROM, stretching, and progressive resistance exercises was planned for the patient by our department. In addition, he was treated with 50 mg diclofenac sodium (3 tablets/day) and 0.5 mg colchicum dyspert (2 tablets/day). After the physical therapy program, his VAS pain score decreased from 100 to 60 mm. The treatment helped to ameliorate his swelling. Furthermore, the serum levels of his CRP and ESR had decreased after the treatment.

Figure 1. Knee radiograph of knees shows narrowing in joint spaces, subchondral calcifications and degenerative changes of articular surfaces.

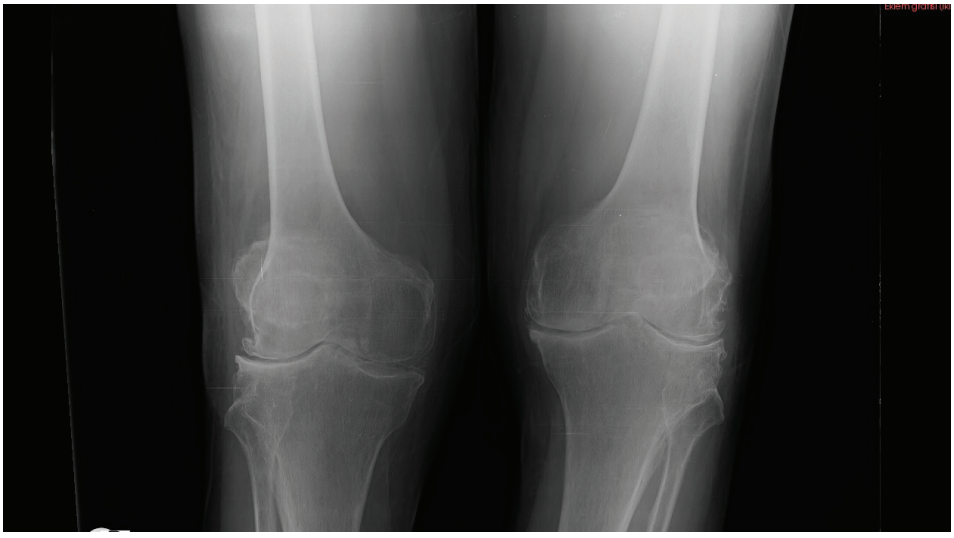


Figure 2. X-ray of shoulder shows significant calcifications, degenerative changes and narrowing of glenohumeral joint space.

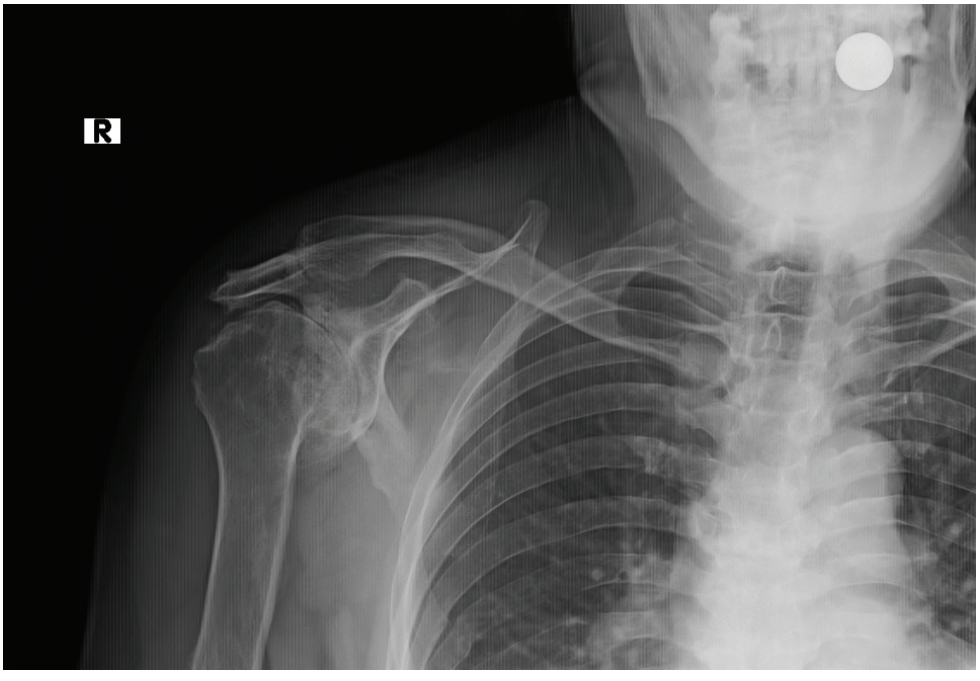
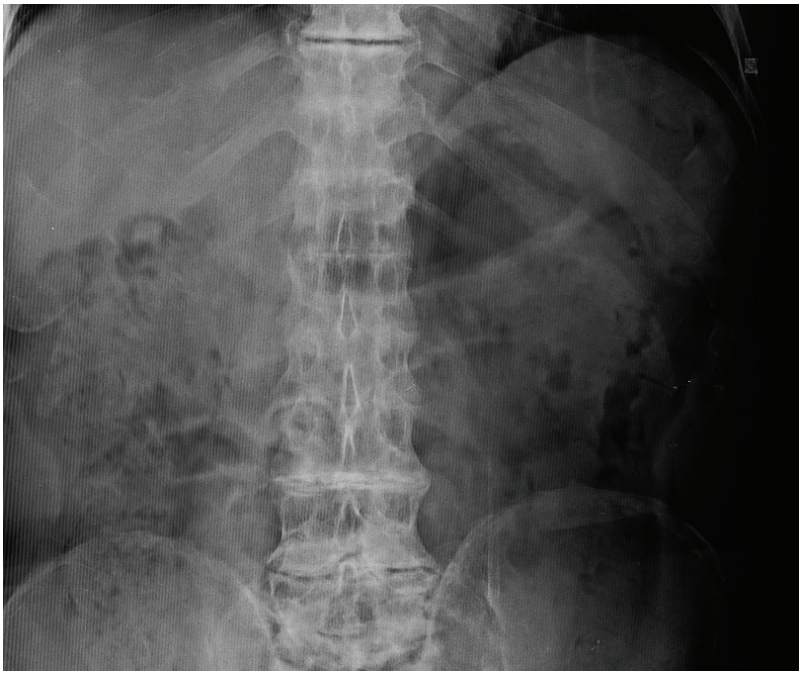


Figure 3. Radiograph of lumbar vertebral column shows narrowing in disc spaces and severe calcifications of intervertebral discs.



DISCUSSION

Alkaptonuria is a rare disorder of aromatic amino acid metabolism that has a Mendelian recessive inheritance pattern (1). The intracellular and extracellular accumulation of HGA, which plays an important role in phenylalanine and tyrosine metabolism, leads to this disorder (8). HGA is converted to maleylacetoacetic acid (MAA) by HGA dioxygenase enzyme in healthy individuals (5). The mutation in chromosome 3q21–q23 has been identified in alkaptonuria (6, 7). In this group of mutated patients, the conversion of HGA to MAA cannot be completed; therefore, HGA accumulates in various parts of the body and is excreted in the urine (5). As a result, HGA converts to benzoquinone acetate by oxidation and benzoquinone acetate monomers combine to generate melanin-like polymers in the tissues (8). Because of the polymerization and oxidation reactions of HGA, the color of the urine may turn into black or dark brown (9). Additionally, the polymerized HGA forms bluish-black discoloration called "ochronosis" that could exist in different parts of the body, such as the ear, sclera (Osler sign), joint capsules, cartilage, tendons, and ligaments (10, 11).Repeated dark brown or black discoloration of the urine during childhood is an important clue for the diagnosis; however, the prominent perspicuity of alkaptonuria in adults is a sign of arthritis (12). The symptoms of arthritis generally present in the third decade of life and ochronosis is formed after 30 years of age (13). Nevertheless, it is possible to diagnose the disease during infancy because of the darkening of the urine (12). To the best of our knowledge,



our patient is one of the oldest cases diagnosed with alkaptonuria in the literature. In this study, we reported the case of a 69-year-old patient with alkaptonuria who was previously undiagnosed. He had been living in a rural area and stated that he had rarely preferred to take medical consultation owing to the long distance to the hospital. We believe that this condition plays an important role in the delay of the diagnosis.

Alkaptonuric ochronosis can lead to more brittle cartilages and eventually, fractures may arise (11). Our patient had a history of total hip replacement operations bilaterally owing to acetabular and femoral neck fractures. Based on the studies in the literature, total joint replacement treatment in patients with ochronosis has successful results, similar to that in patients with osteoarthritis (14, 15).

The spinal involvement includes spondylosis, disc herniation, and vertebral osteophyte formations that conduce pain in the patients (11). It is possible to determine the evidence of the disease by radiographic examination (11). X-ray findings comprise calcifications, narrowing of joint spaces, bony spurs, ankylosis and kyphosis (9, 11).

Furthermore, ochronosis leads to the accumulation of HGA pigments in the sclera, cartilage of the ears, and dermis of the skin, which becomes blue–black in color (12). Renal stones, prostate pathologies, and coronary artery calcifications may also accompany the clinical features of the disease (3).Further, aortic involvement was also observed in our patient. The diagnosis in our patient was made on the basis of the ochronotic pigmentation of the sclera and ear cartilage, arthritis, cardiac calcifications, radiological findings, and urine color that turns black upon standing.

Since, the complaint of pain in geriatric patients is often due to the arthrosis; it is important to make the differential diagnosis of this clinical condition. A detailed examination of the patient and the detection of clinical signs such as color discoloration of urine and the formation of ochronosis in various parts of the body will benefit the clinician for the diagnosis. Due to the fact that alkaptonuria is a systemic involvement disease; the determination of urinary and cardiac pathologies besides radiological findings will also be able to support the diagnosis in clinical practice.

In conclusion, alkaptonuriais a rare metabolic disorder that can be difficult to distinguish from other pathologies, especially in patients with older ages. Hence, clinicians should be aware of this pathology and the diagnosis should be confirmed by clinical, laboratory and radiological examinations.

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