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ARAŞTIRMA MAKALESİ

RESEARCH ARTICLE

ASSOCIATIONS BETWEEN CLINICAL PRESENTATION, PCR-RT, LABORATORY PARAMETERS, AND CHEST CT FINDINGS IN SUSPECTED COVID-19 ADULTS

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ABSTRACT

Aim: This study compare the demographic, clinical, and laboratory characteristics of adult patients diagnosed with COVID-19 and to reveal the differences in laboratory parameters of symptomatic and asymptomatic patients. Material and Methods: Patients aged 18 years and older with a positive polymerase chain reaction-reverse transcriptase (PCR-RT) test and diagnosed with COVID-19 who presented to the Covid-19 emergency department of a Tertiary Education and Research Hospital between March 2020 and June 2020 were included. Demographic data, chronic diseases, clinical symptoms, and laboratory parameters of 4710 patients at the time of presentation to the emergency department were collected and analyzed retrospectively. Results: 4710 of 23268 patients who applied to the Covid-19 Emergency Department were included in our study. 50% of the patients were male. Patients were examined in 5 groups according to age groups. No difference was found between the groups according to age. ($p=0.067$) When the groups were examined according to age groups, the elevation of Mean Platelet Volume and D-Dimer levels was not found to be statistically significant. Assessment of the correlation between clinical presentation and laboratory parameters based on age groups revealed a weak but significant positive correlation between WBC, neutrophil, lymphocyte, monocyte, CRP, MPV and RDW parameters and symptomatic presentation ($p< 0.05$). Conclusions: There is a need to develop age-specific strategies for the diagnosis and treatment of COVID-19. The high rate of asymptomatic cases necessitates reconsidering the potential contribution of this group to the spread of the pandemic.

Keywords: COVID-19, Polymerase chain reaction- reverse transcriptase, Laboratory parameters

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INTRODUCTION

The process that began with reports coming from the Wuhan province of China of pneumonia patients with unknown etiology in December of 2019, turned into a global health crisis in a very short time. The genome sequencing studies by Lu¹ et al. reported that this new pathogen was a novel RNA virus of the beta- coronavirus family, named severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). This disease, named COVID-19 by the World Health Organization (WHO), was declared a pandemic in March of 2020 and has affected millions of people worldwide².

This disease caused by SARS-CoV-2 presents with a wide clinical spectrum, ranging from asymptomatic infections to acute respiratory distress syndrome³. In adults, the course of the disease is affected by factors such as age, presence of comorbidities and immune response capacity⁴. Huang⁵ et al.'s first case series in Wuhan reported fever in 98% of patients, cough in 76% and dyspnea in 55% of patients. In addition, it is remarked that asymptomatic cases represent a significant percentage of all cases, particularly in the elderly population. Understanding the role age plays in COVID-19 presentation is of critical importance in understanding the disease itself. It is established that in different age groups, the disease follows a heterogeneous course⁶. An interesting finding is the hypothesis that asymptomatic presentation might be prevalent than expected in the elderly population and that this may contribute significantly to the transmission of the disease.

Laboratory parameters play an important role in predicting the severity and prognosis of COVID-19 disease. Lymphopenia, elevated neutrophil/lymphocyte ratios, elevated CRP, D-dimer and ferritin levels are associated with poor prognosis^{7,8}. Tracking the dynamic changes of these parameters provides guidance for the assessment of these patients' clinical course. It has been reported that laboratory parameters vary between age groups⁹. However, how these parameters vary between age groups and their profile in asymptomatic patients have not been fully investigated.

Identifying clinical and laboratory characteristics of different age groups is of critical importance in managing patients in the COVID-19 pandemic. The aim of this study is to compare the demographic, clinical and laboratory characteristics of adult patients with a COVID-19 diagnosis, and present the differences in laboratory parameters of symptomatic and asymptomatic patients.

MATERIAL AND METHOD

1.1. Study design and participants

This study was conducted in COVID-19 Emergency Department (ED) of the Ankara Yenimahalle Training and Research Hospital between 30 March of 2020 and 01 June of 2020. Patients who presented to the COVID-19 Emergency Department of the Ankara Yenimahalle Training and Research Hospital, who received a COVID-19 diagnosis with a positive polymerase chain reaction-reverse transcriptase (PCR-RT) test and were 18 years of age or older were included in the study. Approval for our study was obtained from the Ethics Committee (Ethics Committee No: 2020-07/723 and date:22-07-2020). Demographic data, chronic diseases, clinical symptoms and laboratory parameters at presentation to the ED of patients were collected retrospectively and studied. Routine laboratory tests, including hemogram parameters, were obtained from the initial blood samples after patients were admitted to the ED. Patients were divided into two groups as symptomatic and asymptomatic. The presence of one the following symptoms; fever, dyspnea, sore throat, headache, cough, chest pain, abdominal pain, diarrhoea, joint pain, loss of taste or smell; was considered symptomatic, the lack of any of these was considered asymptomatic. Patients were divided into five groups based on age; 18-34 (Group 1), 35-44 (Group 2), 45-64 (Group 3), 65-84 (Group 4) and 85 and above (Group 5). Patients younger than 18 years of age, who did not have a positive PCR-RT test, and who had any of the studied laboratory parameters missing were excluded from the study. The study was conducted in accordance with the principles of the Helsinki Declaration. Due to the retrospective design, no consent was required from patients or relatives.

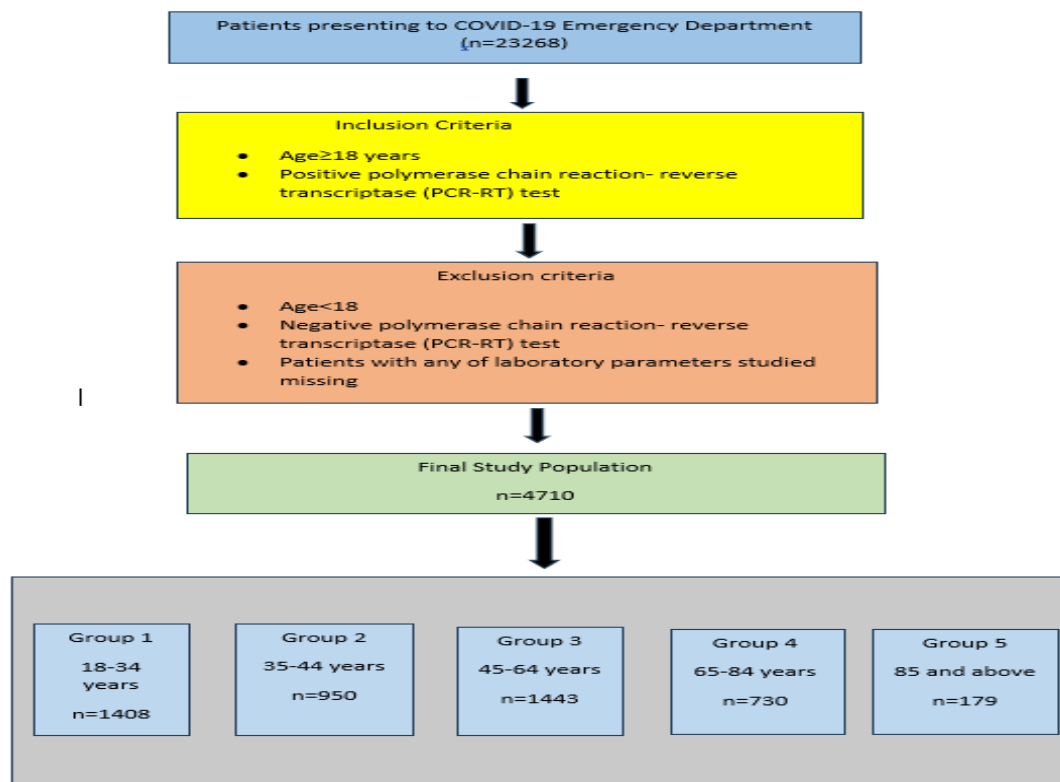


Figure 1. Study workflow

1.2. Statistical analysis

All statistical analysis was performed using SPSS 2.0 for Windows. Descriptive statistics were used in the demographic analysis of patients. Chi-square and Fisher's exact tests were used to compare the proportions of categorical variables. Numerical values in the study were expressed as $\pm$ standard deviation and minimum- maximum values. Kruskal- Wallis H test and Mann- Whitney U test were used for the statistical assessment of data obtained within the scope of the clinical study, depending on whether the nonparametric variables were categorical (nominal or ordinal) or numerical independent. Significant parameters were evaluated using the Spearman correlation. The results were evaluated at a significance level of $p < 0.05$.

FINDINGS

From among 23268 patients presenting to our COVID-19 Emergency Department (ED) between the dates of our study and were 18 years of age or above, 4710 patients were included in the study. Workflow of our study is shown in Figure 1. 50% (n= 2355) of patients were male, and 50% (n= 2355) were female. Mean age of patient groups were 26.7 ± 4.7 for Group 1 (n= 1408), 39.9 ± 2.8 for Group 2 (n= 950), 53.1 ± 5.7 for Group 3 (n= 1443), 73.3 ± 5.3 for Group 4 (n= 730) and 88.1 ± 2.9 for Group 5 (n=179). Gender distribution of patients based on age groups is summarised in Table 1.

Table 1. Demographic data of patients

Variables	18-34 age (mean $\pm$ sd)	35-44 age (mean $\pm$ sd)	45-64 age (mean $\pm$ sd)	65-84 age (mean $\pm$ sd)	>85 age (mean $\pm$ sd)	p value
Age mean/ year (mean $\pm$ sd)	26.7 ± 4.7	39.9 ± 2.8	53.1 ± 5.7	53.1 ± 5.7	88.1 ± 2.9	<0.05*
Gender						0.067
Male % (n)	%30.3 (712)	%20.9 (494)	%30.9 (725)	%15.1 (360)	%2.7 (64)	
Female % (n)	%29.7 (696)	%19.4 (456)	%30.7 (718)	%15.9 (370)	%4.7 (115)	
Clinical Findings						<0.05*
Asymptomatic	%13.1	%16.7	%13	%30	%57..3	
Fever	%21.6	%23.5	%22.2	%16.6	%13.4	
Dyspnea	%17.5	%17.5	%17.7	%12.6	%8.5	
Sore throat	%5	%7.3	%6.7	%4.5	%2.4	
Headache	%7.6	%7.6	%2.6	%5.3	%4.9	
Cough	%7.7	%7.3	%8.2	%5.8	%3.7	
Chest pain	%0.8	%1.9	%1.4	%1.1	%2.4	

Bulut B.

Abdominal pain	%15.3	%12.5	%5.3	%2.4	%2.4
Joint pain	%2	%3.3	%2.6	%3.8	%3.5
Pneumonia clinic	%8.5	%9.2	%7.3	%8.2	%3.7
Loss of taste- smell	%15	%20	%12	%21.2	%19

As statistical analysis, Kruskal Wallis test and Chi-square test was used. * = $p < 0.05$ was considered significant. SD: Standard Deviation

While Group 3 has more patients than the other groups, male dominance was evident in all groups. There was no statistical significance in gender distribution between groups based on age ($p=0.067$). Clinical presentation of patients is summarised in Table 1. While number of patients with asymptomatic presentation was large, there was significant difference between age groups; the rate of asymptomatic patients was particularly high in older ages ($p < 0.05$). Comparison of patient's laboratory parameters between age groups are shown in Table 2. There were significant differences in white blood cell (WBC), lymphocyte, platelet, red cell distribution width (RDW) and C- reactive protein (CRP) levels between groups (see table 2).

Table 2. Laboratory parameters of patients based on age groups

Laboratory parameters	18-34 age (mean $\pm$ sd)	35-44 age (mean $\pm$ sd)	45-64 age (mean $\pm$ sd)	65-84 age (mean $\pm$ sd)	>85 age (mean $\pm$ sd)	p value
WBC ($4.0-10.0 \times 10^9/L$)	4.5 $\pm$ 3.3	3.9 $\pm$ 3.4	3.9 $\pm$ 3.5	3 $\pm$ 4.6	1.9 $\pm$ 3.6	0.001*
Neutrophils ($2.0-6.0 \times 10^9/L$)	3.8 $\pm$ 2.5	3.5 $\pm$ 2.7	3.4 $\pm$ 2.8	2.6 $\pm$ 3.3	1.7 $\pm$ 2.9	0.265
Lymphocyte ($1.1-3.2 \times 10^9/L$)	1.3 $\pm$ 0.9	1.1 $\pm$ 1	1.1 $\pm$ 1.2	0.5 $\pm$ 1	0.3 $\pm$ 0.6	<0.05*
Monocyte $\times 10^9/L$	0.4 $\pm$ 0.3	0.3 $\pm$ 0.3	0.3 $\pm$ 0.2	0.2 $\pm$ 0.3	0.1 $\pm$ 0.2	0.098
Platelet	227 $\pm$ 67	226 $\pm$ 65	223 $\pm$ 78	243 $\pm$ 114	231 $\pm$ 93	<0.05*

Bulut B.

$\times 10^9/L$

Mean platelet volume fl	7.8 ± 4	7.1 ± 5.5	7.1 ± 6.8	7.7 ± 4.7	7.2 ± 3.4	0.135
Red blood cell distribution width-CV %	10.5 ± 5	9.3 ± 5.8	8.9 ± 5.9	8.5 ± 6.4	7.7 ± 5.7	0.005*
CRP	82.4 ± 20	157 ± 35	229 ± 41	275 ± 48	148 ± 41	<0.05*
D-dimer	257 ± 521	277 ± 651	295 ± 677	745 ± 1634	1067 ± 1913	0.065

As statistical analysis, Kruskal-Wallis test was used. * = $p < 0.05$ was considered significant. SD: Standard Deviation

Comparison of laboratory parameters based on clinical presentation revealed that D-dimer and mean platelet volume (MPV) levels were elevated regardless of clinical symptoms, but that this elevation was not statistically significant; and that elevation of other laboratory parameters were statistically significant in symptomatic patients ($p > 0.05$) (Table 3).

Table 3. laboratory parameters based on clinical findings

Laboratory parameters	Asymptomatic	Symptomatic	p value
WBC ($4.0-10.0 \times 10^9/L$)	3.8±3.9	4.4±3.7	<0.05*
Neutrophil ($2.0-6.0 \times 10^9/L$)	3.3±2.9	3.7±2.7	<0.05*
Lymphocyte ($1.1-3.2 \times 10^9/L$)	1±1.3	1.2±1.1	<0.05*
Monocyte $\times 10^9/L$	0.3±0.3	0.4±0.3	<0.05*
Platelet $\times 10^9/L$	228±84	229±81	0.628
Mean platelet volume fl	6.6±5.7	7.5±5.4	<0.05
Red blood cell distribution width-CV %	8.6±6	7.5±5.4	<0.05*
CRP	180±40	187±37	<0.05*
D-dimer	354±834	382±1001	0.079

As statistical analysis Mann-Whitney-U test was used. * = $p < 0.05$ was considered significant. SD: Standard Deviation

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Additionally, assessment of the correlation between clinical presentation and laboratory parameters based on age groups revealed a weak but significant positive correlation between WBC, neutrophil, lymphocyte, monocyte, CRP, MPV and RDW parameters and symptomatic presentation ($p < 0.05$, r_s : 0.08, r_s : 0.06, r_s : 0.10, r_s : 0.10, r_s : 0.09, r_s : 0.09, r_s : 0.06). Platelet and D-dimer levels had no statistically significant positive or negative relationship ($p > 0.05$, r : 0.628; p : 0.07, r : 0.033).

DISCUSSION

Clinical presentations and laboratory findings in COVID-19 varies based on the age of the patient^{8,9}. In our study, clinical and laboratory findings of 4710 patients were evaluated based on age groups, and it was established that the rate of asymptomatic cases were particularly high in older patients. Our most remarkable finding was that 57.3% of patients in Group 5 (85 years and older) were asymptomatic. We also found that WBC, lymphocyte, platelet, RDW and CRP levels varied between different age groups, and that D-dimer and MPV levels were higher in symptomatic patients than asymptomatic patients.

In their study evaluating 22445 cases with suspected COVID-19 in England, Goodacre¹⁰ et al. determined that hospitalization (67.1%) and mortality (15.5%) rates were high in adults and reported that as age advanced, symptoms decreased but mortality increased. Our findings suggest that the rate of asymptomatic cases in elderly patients is much higher than the 15-20% reported by Wang¹¹ et al. in their study with older COVID-19 patients. The up to 90% asymptomatic case rates in the paediatric population reported by Don¹² et al. supports that COVID-19 presentation follows a complex pattern based on age groups. Our study suggests that the rate of asymptomatic cases might be similar in the 85 and older age group to the paediatric population, thus provides significant contribution to the literature. Assessing the distribution of clinical symptoms in our study, we have seen that the number of patients presenting with fever and dyspnea reduces with age. In the study by She¹³ et al. evaluating the characteristics of COVID-19 in children, it was reported that typical symptoms were more pronounced as age decreased. Our findings support this observation by demonstrating that atypical presentation is more common in elderly patients. Loss of taste and smell being observed in similar rates in all age groups (12-21%) supports the hypothesis that this symptom is characteristic of COVID-19, independent of age.

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The number of patients being highest in the 45-64 age group (n= 1443) in our study population might be explained by this age group being active in work life and having high social mobilization. In the study by Wu⁷ et al. conducted in China, it was demonstrated that advanced age and male gender are independent risk factors for the development of ARDS and mortality. In our study, although male gender was more prevalent in all age groups, there was no statistical difference between age groups (p= 0.067). This finding suggests that COVID-19 can affect both genders with similar rates, however, the severity of the disease can vary depending on gender.

When evaluating laboratory parameters, there were significant differences in WBC, lymphocyte, RDW and CRP levels between age groups (p< 0.05). It was particularly remarkable that as age advances, the number of lymphocytes decreases progressively (from 1.3 ± 0.9 in Group 1 to 0.3 ± 0.6 in Group 5). In their study with 244 elderly patients, Sun¹⁴ et al. reported that low lymphocyte levels were related to poor prognosis. However, the high rate of asymptomatic cases observed in our study despite this decrease in lymphocyte numbers, suggest that lymphocytopenia may not always be correlated with disease severity. Although the meta-analysis by Biswas¹⁵ et al. emphasized that lymphocyte count might be an important prognostic factor in COVID-19, it must be considered that this relationship may vary depending on age groups. Huang¹⁶ et al. reported that in patients who require intensive care, all inflammatory markers, including CRP, were significantly elevated. In the prospective cohort study conducted in New York on 5279 COVID-19 patients, Petrilli¹⁷ et al. determined that just like age, elevated CRP and D-dimer levels were independent predictors for the development of critical disease. Ruan¹⁸ et al. reported that advanced age and elevated CRP are predictors of mortality in COVID-19. In our study, we also found that elevated CRP levels were more significant in older patients than younger patients.

In their study evaluating COVID-19 patients monitored in the intensive care unit, Kazancıoğlu¹⁹ et al. emphasized that changes occurring in D-dimer levels in the 72. hour is significant in terms of mortality. Similarly, Zhou²⁰ et al. have also reported that elevated D-dimer levels were an independent risk factor for mortality. The significant difference in D-dimer levels between age groups (p< 0.05) and particularly, the significant elevation in patients above 65 years of age that was observed in our study, suggest that the risk of thrombotic complications increase in advanced age.

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In our study, we also observed that D-dimer levels elevate as age advances (in the 85 and older group; 1067 ± 1913), however, paradoxically, the rate of asymptomatic cases are highest in this age group. This finding suggests that elevated D-dimer levels might be due to other age related comorbidities, and might not be specific to COVID-19. Additionally, the significant differences between symptomatic and asymptomatic patients in D-dimer and MPV levels demonstrates that these parameters are related to clinical presentation.

The strengths of our study are the high number of patients and the focus on different age groups. However, our study has its limitations. Firstly, our study was conducted with data obtained from a single centre and might not be generalised to the whole population. Secondly, due to the retrospective design, some clinical data and chronic diseases might not have been fully evaluated. Finally, patients follow-up data and clinical outcomes were not evaluated. Studies conducted on larger patient populations and with prospective design will strengthen the clinical use of age specific prognostic markers. Developing age specific treatment protocols with further studies will provide significant contributions to the management COVID-19.

CONCLUSION

The findings of our study emphasize the need for age specific approaches in the diagnosis and treatment of COVID-19. Particularly, the high rate of asymptomatic cases requires the need for re-evaluating the role this group may have played in the spread of the pandemic. We suggest that future studies focus on the long-term follow up of elderly patients and the viral spread dynamics in these patients.

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ARAŞTIRMA MAKALESİ

RESEARCH ARTICLE

THE ROLE OF SERUM HOMOARGININE LEVELS IN PATIENTS DIAGNOSED WITH ACUTE ISCHEMIC CEREBROVASCULAR DISEASE

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ABSTRACT

Objective: This study aimed to investigate the role of serum homoarginine levels in patients diagnosed with acute ischemic cerebrovascular disease (CVD) and to evaluate its potential as a biomarker. **Methods:** This prospective, single-center cross-sectional study included patients aged ≥ 18 years who presented to the Emergency Department of Ankara Numune Training and Research Hospital between February 1 and May 31, 2017, with suspected CVD and consented to participate. Patients with confirmed CVD by MRI ($n=43$) formed the study group, while 43 patients without CVD served as controls. Serum homoarginine levels were measured using ELISA. Clinical data, imaging findings, and NIHSS scores were analyzed statistically. **Results:** A total of 88 patients (56.8% male; mean age 60.1 ± 16.9 years) were included. Comorbidities were present in 70.5% of cases, with hypertension being the most common (60.2%). Serum homoarginine levels were similar between patients and controls ($1.54 \pm 0.64 \mu\text{mol/L}$ vs. $1.62 \pm 0.78 \mu\text{mol/L}$; $p=0.802$). Homoarginine levels were significantly lower in patients with comorbidities ($p=0.033$). No significant correlations were found between homoarginine levels and NIHSS score, ischemic area, or volume. **Conclusion:** In patients with acute ischemic CVD, serum homoarginine levels were not significantly associated with disease severity or prognosis. However, comorbidities may influence homoarginine concentrations. Larger, multicenter randomized controlled studies are needed to clarify the prognostic value of homoarginine in cerebrovascular disease and other high-mortality vascular conditions.

Keywords: Homoarginine; Acute Ischemic Stroke; Biomarker; Cerebrovascular Disease; Prognosis

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INTRODUCTION

Cerebrovascular diseases (CVDs) are of increasing global importance due to their high rates of mortality and morbidity, both worldwide and in our country. Thanks to the effectiveness of emerging treatment modalities, stroke—which was previously the third leading cause of death in the United States (USA)—now ranks fourth after heart disease, cancer, and chronic lower respiratory tract diseases [1,2]

An average of 795,000 people experience a first or recurrent stroke (ischemic or hemorrhagic) annually in the USA. Of these, approximately 610,000 are first-time strokes, while around 185,000 are recurrent events [3]. Strokes are the primary cause of long-term neurological disability; more than half of survivors remain dependent on others for daily activities [4]. Additionally, stroke is a major cause of depression, epilepsy, and falls [4]. Ischemic strokes account for 87% of all stroke cases [5]. Due to the rapidly aging global population, the burden of stroke is expected to rise significantly in the coming years [5].

Given the critical global health impact of stroke, numerous classification and scoring systems have been developed over the years. These tools aim to standardize the assessment of neurological deficits, lesion location, and prognosis in a language understandable to clinicians worldwide. Some commonly used scales include the National Institutes of Health Stroke Scale (NIHSS), the Pediatric NIHSS (pedNIHSS), the European Stroke Scale, the Canadian Neurologic Scale (CNS), and the Scandinavian Stroke Scale [6]. Among these, the NIHSS is the most widely utilized. In addition, the modified Rankin Scale (mRS) is commonly used to evaluate functional capacity and role loss [7].

With the discovery of neuronal nitric oxide synthase (nNOS) in the brain and cerebral arteries, nitric oxide (NO) has been recognized to play a critical role in cerebral perfusion [8]. Arginine serves as a substrate for NO synthesis [9]. Recent studies have shown that low levels of the endogenous amino acid homoarginine are associated with increased mortality in cardiovascular and cerebrovascular diseases [10–12].

In this study, we aimed to determine the role of serum homoarginine levels in patients diagnosed with ischemic cerebrovascular disease and to evaluate its potential utility as a biomarker in such cases.

According to the Global Burden of Disease Study, ischemic heart disease and stroke together accounted for approximately 15.2 million (15–15.6 million) deaths worldwide in 2015 [13]. Stroke incidence rates are reported to be 1.7–3.6 per 1000 persons in the 55–64 age group, 4.9–8.9 in the

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65–74 group, and 13.5–17.9 in those over 75. In men aged 55–64, incidence rates are reported to be 2–3 times higher than in women [14]. A multicenter study across eight European countries found that stroke risk increases annually by 9% in men and 10% in women [15]. The World Health Organization reported that stroke-related mortality between 1990 and 2006 was higher in women than in men [16].

Approximately 80% of cerebrovascular diseases are ischemic in nature, while 20% result from hemorrhagic causes [17]. Ischemic strokes can be categorized into thrombotic, embolic, and hypoperfusion-related subtypes. Hemorrhagic strokes are divided into intracerebral and non-traumatic subarachnoid hemorrhages. In both types of stroke, the fundamental problem lies in disruptions of neuronal perfusion [18].

Several classification systems are used to determine stroke etiology. Among the most frequently used are the Oxfordshire Community Stroke Project, the Causative Classification of Stroke System, and the Trial of ORG 10172 in Acute Stroke Treatment (TOAST). TOAST is not only widely applied for classifying ischemic stroke but also stratifies stroke subtypes based on neurological symptoms, imaging, and auxiliary test results [19]. The risks are shown in Table 1 [20].

Table 1. Risk factors for ischemic cerebrovascular disease

Non-modifiable Risk Factors	Modifiable Risk Factors	
	Confirmed	Unconfirmed
- Age - Race - Genetics - Gender	- Hypertension - Diabetes Mellitus - Heart Diseases - Dyslipidemia - Smoking -Asymptomatic Carotid Ste- nosis - Sickle Cell Anemia - Atrial Fibrillation	- Alcohol Consumption - Obesity - Dietary Habits - Physical Inactivity -Medication Use and Depen- dence - Hormone Therapy - Hypercoagulability - Inflammation - Hyperhomocysteinemia

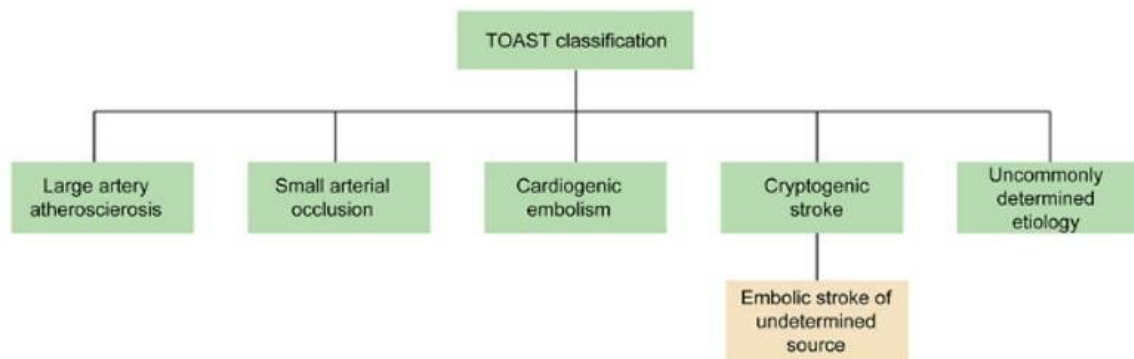


Figure 1. Cardiac risk groups according to the TOAST clasification [19]

1.1. Pathophysiology of Ischemic Cerebrovascular Disease

Ischemic changes, either reversible or irreversible, occur depending on the duration and severity of reduced blood flow to a specific brain region [21]. The pathophysiology of ischemic stroke involves three primary mechanisms: thrombosis, embolism, and systemic hypoperfusion [22]. Although not all aspects of the ischemic process are fully understood, several mechanisms are believed to play a role, including arterial wall injury, monocyte activity, oxidation of low-density lipoprotein (LDL) cholesterol, proliferation and migration of smooth muscle cells, platelet activation, plaque rupture, and thrombus formation [23].

The critical perfusion range that leads to brain dysfunction without causing permanent tissue damage is 12–20 mL/100 g/min [24]. Within this range, energy metabolism and membrane ion balance are preserved. However, due to the cessation of electrical activity in neurons, this area is referred to as the penumbra [25]. In these stress-affected zones, infarction has not yet occurred. When cerebral blood flow falls below the critical threshold of 10 mL/100 g/min, necrosis develops in the tissue, forming the ischemic core. Moving outward from the ischemic core, regions with varying levels of perfusion are observed. If ischemia is not promptly corrected, these areas may eventually progress to necrosis.

The penumbra, a potentially salvageable brain region where blood flow is reduced but permanent damage has not yet occurred, is the primary target in current treatment strategies for ischemic stroke [26].

1.2. Assessment of patients with acute cerebrovascular disease

Worldwide, one death occurs every 3-4 minutes due to stroke [27]. Approximately 785,000 new or recurrent strokes occur each year. Most of these cases are referred to hospitals by emergency departments [28]. Therefore, the diagnosis and management of stroke cases in emergency departments is very important.

1.3. Pre-hospital period

Public awareness is necessary for the early recognition of stroke patients. Time is the most critical factor in stroke patients. Therefore, educating the public about stroke symptoms and eliminating information gaps is important in preventing time loss in the pre-hospital period [29]. There are commonly used scales for assessing patients in the pre-hospital period. The most frequently used of these are the Cincinnati Prehospital Stroke Scale, the Los Angeles Prehospital Stroke Screen, and the Melbourne Ambulance Stroke Screen.

Emergency medical personnel encountering a stroke patient must quickly stabilise the patient. Since stroke patients may have a weak history, the emergency medical personnel should obtain the most accurate information about the time of the event from witnesses or family members at the scene and instruct them to come to the hospital as soon as possible. The emergency medical personnel should transport the patient to a centre where the most appropriate acute stroke treatment can be provided as soon as possible [29].

Although there is no strong evidence for the treatment of physiological parameters such as prehospital hypoxia, blood pressure, and hyperthermia, maintaining normoxia and treating hyperglycaemia and hypertension in stroke patients is not recommended unless it is extremely urgent [30].

1.4.Triage and primary care

The National Institutes of Neurological Disorders and Stroke (NINDS) has established evaluation times for stroke patients [31].

- Door – Physician evaluation ≤ 10 minutes
- Door – Stroke team activation ≤ 15 minutes
- Door – Computed tomography scan ≤ 25 minutes
- Door – Computed tomography interpretation ≤ 45 minutes
- Door – Medication ($\geq 80\%$ compliance) ≤ 60 minutes
- Door – Admission to stroke unit ≤ 3 hours

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The following should be assessed during the initial examination of the patient: evaluation of respiratory and pulmonary function, evaluation of accompanying cardiac diseases, evaluation of blood pressure and heart rate, evaluation of arterial oxygen saturation with a pulse oximeter, and early evaluation of dysphagia [31].

Neurological examination also helps determine the location of the lesion by assessing the patient's level of consciousness, vision, motor and sensory function, speech, and coordination. For this purpose, the National Institutes of Health Stroke Scale (NIHSS) is widely used worldwide. In addition, the mRS, developed to assess the long-term neurological status of stroke patients, is also used [7].

1.5. Homoarginine and the cerebrovascular system

Homoarginine (hArg) is an endogenous and exogenous amino acid with an additional methylene (CH₂) group added to the basic arginine structure. It has been shown that hArg can be produced from lysine in humans and is present in various body fluids and organs [32,33]. In humans, hArg synthesis is catalysed by the L-arginine glycineamide transaminase enzyme. This enzyme is also known as the rate-limiting enzyme for creatine synthesis [34].

Although the first reports on the biological importance of homoarginine have recently emerged, studies on hArg are rapidly increasing [35]. Homoarginine is a product necessary for nitric oxide (NO) synthesis [36]. Low levels of hArg have been demonstrated in many diseases. This condition has sometimes been shown to be a result and sometimes a causative factor of the disease [36]. The decrease in NO levels caused by low hArg concentrations in the blood appears to be the sole mechanism explaining the increased cardiovascular risk [37]. Various studies have shown that high plasma hArg levels are associated with BMI. This is because BMI is an indicator of metabolism and is associated with impaired glucose tolerance [38-41]. Another study showed that hArg is associated with metabolic syndrome [42].

A relationship between smoking and hArg concentrations is assumed. In the Hoorn and Dallas Heart Study, low hArg concentrations were found to be associated with current smoking [38]. In a study conducted on men with peripheral artery disease based on these studies, it was reported that age-adjusted hArg concentrations were reduced in smokers [45].

In the Hoorn study, which evaluated the relationship between homoarginine and blood pressure, a positive correlation was found between high systolic and diastolic blood pressure and hArg in 746 elderly individuals in the general population [46].

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Studies have indicated that hArg increases in atherosclerosis and that this condition leads to an increase in heart failure, stroke, and cardiovascular pathologies [47-48]. Analysis of related clinical phenotypes and experimental studies in mice has demonstrated a mechanical link between impaired hArg and cerebrovascular disease [48]. Several studies conducted over the past five years have reported that low concentrations of the naturally occurring amino acid hArg predict an increase in the risk of adverse cardiovascular and cerebrovascular outcomes and mortality [34,39].

2. MATERIALS AND METHODS

This study was conducted as a prospective cross-sectional single-centre study with the approval of the Ethics Committee of Ankara ***** Education and Research Hospital, Health Sciences University, Turkey, under number 1199/2017 and dated 08/02/2017.

The study included patients aged 18 years and older who presented to the emergency department of the Emergency Medicine Clinic at Ankara Numune Education and Research Hospital, Health Sciences University, Turkey, between 1 February 2017 and 31 May 2017 with suspected cerebrovascular disease and who voluntarily participated in the study. Blood was collected from patients who were initially suspected of having CVD based on clinical history and diagnostic evaluation to measure the level of homocysteine in the blood (1 gel-free biochemistry tube). Forty-three patients who were excluded from CVD after diffusion MRI were included in the control group. Forty-five patients diagnosed with CVD based on MRI results were included in the study. Two of the 45 patients diagnosed with CVD were excluded from the study because their blood was haemolysed. Patients under the age of 18, those who did not agree to participate in the study, those with anaemia (Hb < 10 g/dl), those with a history of trauma within the last 4 weeks, pregnant women, and those with intravenous drug abuse were excluded from the study.

The relationship between age, gender, complaints, duration of symptoms, comorbidities, treatment administered in the emergency department, CT scan results, MRI results, admission and discharge status, mortality status, and diffusion restrictions detected in the MRI scan was examined by calculating the area and volume using the Materialise Mimics Innovation Suite Medical v20.0 programme. The areas and volumes were calculated simultaneously and independently by the emergency medicine resident and the radiology resident.

For hArg measurement, 2 cc of blood was collected into standard gel-filled, anticoagulant-free tubes. Centrifugation was performed at 4000 rpm at (+4) degrees for 15 minutes. One millilitre of serum was transferred to an Eppendorf tube and stored at -80°C until the day of analysis. Eppendorf tubes were removed from -80°C 24 hours before hArg analysis and brought to +4°C. Serums that thawed slowly within 24 hours were brought to room temperature, and hArg levels were de-

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terminated using a competitive ELISA method (DLD Diagnostika GmbH, lot number: H113). Haemolysed and icteric serum samples were excluded in the study (expected normal values: 2.0 ± 0.7 micromoles/L; sensitivity (lower detection limit): 0.05 micromoles/L).

Our work has been conducted in accordance with the Helsinki Declaration.

3. STATISTICAL ANALYSIS

The data were analysed using SPSS for Windows version 23.0(Armonk, NY: IBM Corp.). Descriptive statistics for continuous variables included mean and standard deviation, while categorical variables were expressed as numbers and percentages. The significance of differences between groups for categorical variables was assessed using the Chi-square test. The Mann Whitney-U test was used for binary group comparisons, while the Kruskal-Wallis test and Bonferroni correction were used for multiple groups. The correlation of continuous variables was evaluated using the Spearman correlation test. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 88 patients, 50 of whom (56.8%) were male, were included in the study. The mean age of the patients was 60.1 ± 16.9 years. The homocysteine, troponin, creatinine, BUN, and NIHSS scores of all patients are shown in Table 2.

Table 2. Demographic characteristics and laboratory tests of patients

n (%) / Mean $\pm$ SD	
Sex	
Female	38 (%43,2)

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Male	50 (%56,8)
Age	60,1±16,9
Homoarginin (μmol/L)	1,58±0,71
Troponin (ng/mL)	15,49±73,98
Kreatinin (mg/dL)	1,03±0,52
BUN (mg (dL)	41,3±21
NIHSS skoru	5,7±3,3

NIHSS: National Institutes of Health Stroke Scale,BUN: Blood Urea Nitrogen

The distribution of comorbidities among patients is shown in Table 3. Comorbidities were present in 70.5% of all patients. Among those with comorbidities, hypertension was the most common (n=53; 60.2%).

Table 3. Distribution of patients' comorbidities

	n (%)
Comorbidity	62 (%70,5)
Hypertension (HT)	53 (%60,2)

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Diabetes mellitus (DM)	32 (%36,4)
Atrial fibrillation (AF)	11 (%12,5)
Congestive heart failure (CHF)	12 (%13,6)
Coronary artery disease (CAD)	24 (%27,3)
Cerebrovascular disease (CVD)	18 (%20,5)
Chronic obstructive pulmonary disease (COPD)	6 (%6,8)
Chronic renal failure (CRF)	8 (%9,1)

36.4% of patients visited the emergency department within the first hour, while 5.7% visited the emergency department more than 24 hours after onset. The most common symptoms were numbness (68.2%), weakness (56.8%), and nausea and vomiting (56.8%) (Table 4).

Table 4. Emergency department visit duration and distribution of symptoms at the time of presentation

	n (%)
Duration of Symptoms	

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First 1 hour	32 (%36,4)
2-4 hours	47 (%53,4)
5-8 hours	2 (%2,3)
9-24 hours	2 (%2,3)
>24 hours	5 (%5,7)
Symptoms	
Numbness	60 (%68,2)
Loss of strength	50 (%56,8)
Nausea and vomiting	50 (%56,8)
Altered consciousness	24 (%27,3)
Headache	19 (%21,6)
Dysarthria/Aphasia	18 (%20,5)
Dizziness	16 (%18,2)

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Facial asymmetry	7 (%8)
Syncope	7 (%8)
Other symptoms	14 (%15,9)

Troponin, creatinine levels, and NIHSS scores were similar in the patient and control groups (p=0.0826)(Table 5).

Table 5. Distribution of laboratory results and symptom duration in the patient and control groups

	Patients groups		
	Control	CVD	p
	n (%) / Mean ± SD		
Homoarginine (μmol/L)	1,62±0,78	1,54±0,64	0,802*
Troponin (ng/mL)	4,92±8,11	25,15±101,59	0,920*
Creatinine (mg/dL)	0,92±0,25	1,13±0,67	0,154*
BUN (mg (dL)	36,1±14,3	46±24,9	0,039*

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Symptom duration (hours)	2,9±7,2	5,8±11,1	0,027*
Symptom duration			
First 1 hour	21 (%50)	11 (%23,9)	
2–4 hours	19 (%45,2)	28 (%60,9)	
5–8 hours	1 (%2,4)	1 (%2,2)	0,075**
9–24 hours	-	2 (%4,3)	
>24 hours	1 (%2,4)	4 (%8,7)	

*Mann Whitney U testi, **Ki-kare testi (NIHSS: National Institutes of Health Stroke Scale) BUN: Blood Urea Nitrogen

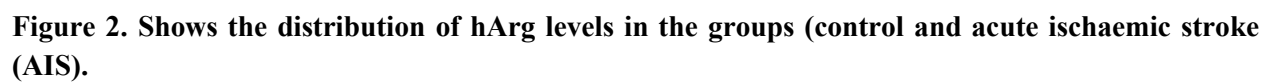


Table 6. Frequency of presenting symptoms in the patient and control groups

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Loss of strength	16 (%38,1)	34 (%73,9)	0,001
Nausea and vomiting	33 (%78,6)	17 (%37)	<0,001
Numbness	26 (%61,9)	34 (%73,9)	0,227
Headache	9 (%21,4)	10 (%21,7)	0,972
Dysarthria/Aphasia	-	18 (%39,1)	<0,001
Altered consciousness	11 (%26,2)	13 (%28,3)	0,828
Dizziness	15 (%35,7)	1 (%2,2)	<0,001
Facial asymmetry	3 (%7,1)	4 (%8,7)	0,788
Syncope	7 (%16,7)	-	0,004
Other symptoms**	6 (%14,3)	8 (%17,4)	0,691

* Chi-square test** Other symptoms: ataxia, fever, dyspnoea, vision loss, hemiparesis, convulsions and memory loss

There was no significant relationship between symptom duration and co-morbid disease and homoarginine levels ($p=0.939$). However, homoarginine levels were 1.44 ± 0.62 ($\mu\text{mol/L}$) lower in those with co-morbid disease ($p=0.033$). The correlation between NIHSS scores and serum homocysteine levels with ischemic area and volume measurements is shown in Table 7. (Spearman's rho)

Table 7. Correlation of NIHSS Score and Serum Homoarginine Levels with Ischemic Area and Volume Measurements (Spearman's rho)

Measurement Type	Evaluator	NIHSS Score ρ	p-value	Homoarginine ($\mu\text{mol/L}$) ρ	p-value
Ischemic area measurement	Radiology resident	0.179	0.250	– 0.186	0.221
	Emergency medicine resident	0.161	0.302	– 0.277	0.066
Ischemic volume measurement	Radiology resident	0.199	0.201	– 0.193	0.203
	Emergency medicine resident	0.174	0.265	– 0.276	0.067

Note: Spearman's rho correlation was used.

DISCUSSION

A total of 88 patients, 50 (56.8%) of whom were male, were included in our study. The age of the CVD group was 66.4 ± 12.2 , and 63% were male. When the study patients were divided into control and patient groups, the two groups were similar in terms of gender, but the average age was higher in the CVD group. Considering that age and gender-related factors may affect serum homoarginine levels, it was thought that the age difference might influence the study results. However, when examining the correlation between homoarginine levels and age, no correlation was found. Therefore, it was concluded that the age difference in the control group would not affect the study results.

With advancing age, the physiological process shifts from an anabolic process to a catabolic process, leading to an increase in pathologies at both the cellular and organ levels. These pathologies, which also affect vascular structures such as atherosclerosis, contribute to the increased incidence

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of conditions like CVD and MI, which are associated with ischaemic processes, in older age groups. In a study on thrombolytic therapy, it was noted that the average age of patients was 65 and 60% of patients were male [49].

In a community-based epidemiological study that classified patients according to TOAST criteria, 583 CVD patients were included in the study, and their average age was found to be 73.3. Again, in the same study, it was stated that 43% of the patients were male [50]. The age and gender ratio in our study is consistent with the literature.

In our study, 61.9% of the control group and 78.3% of the patient group had comorbidities. Hypertension was the most common comorbidity. It has long been known that comorbidities, particularly HT, DM, and AF, increase the incidence of CVD. A linear relationship has been found between high blood pressure and SVH. It has been reported that maintaining blood pressure within normal limits reduces the risk of stroke by up to 40% (51). A study on thrombolytic therapy emphasised that HT was the most common comorbidity in CVD patients (63%) and AF was the second most common (13%) (49). In our study, the prevalence of AF in the patient group was 15.2%, which was consistent with the literature.

In a study conducted in Hong Kong on low molecular weight heparin treatment in patients with CVD, it was noted that the most common comorbid condition accompanying the patients was HT [52].

Homoarginine is an amino acid involved in nitric oxide metabolism that inhibits the arginase enzyme, thereby increasing L-arginine levels and, consequently, nitric oxide production [53,54].

Homoarginine also acts as a substrate for nitric oxide production. Nitric oxide deficiency has been reported to cause endothelial and myocardial dysfunction [55,56].

In our study, the level of homoarginine, which is thought to be associated with vascular problems, was investigated in CVD, another vascular disease. In our study, the level of homoarginine was similar in the patient and control groups, and it was also similar in patients with good or poor outcomes according to mRS. A meta-analysis has indicated that homoarginine levels correlate with all causes of mortality (57). Since there was only one CVD patient who died in our study, the relationship between homoarginine and mortality could not be examined.

Recently, data from population studies have shown that low homocysteine levels predict morbidity independently of cardiovascular disease, including sudden cardiac death, heart failure, acute myocardial infarction, and fatal ischaemic stroke [40,58,59]. In a study aimed at determining the relationship between homoarginine and stroke, it was reported that low homoarginine levels in ischemic stroke patients were associated with poor prognosis [60]. Previous studies have reported that

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homoarginine levels are associated with vascular adhesion molecule-1 and intercellular adhesion molecule-1, and that homoarginine levels are inversely associated with CRP, beta-thromboglobulin, fibrinogen, and von Willebrand factor [40]. These findings suggest that homoarginine may play a role in the inflammatory and thrombotic processes in ischemic vascular diseases [60]

In our study, ischemic areas and volumes were measured and recorded simultaneously by an emergency medicine resident and a radiology resident. Interobserver agreement was high when examining interobserver agreement in ischemic area and volume measurements. Therefore, we believe that emergency medicine residents can effectively evaluate dMRG with the necessary radiological training.

CONCLUSION

Cerebrovascular disease is more common in men than in women, but there are modifiable risk factors in both sexes. Controlling these modifiable risk factors and regular follow-up and treatment significantly reduce the risk of CVD.

In our study, the similarity in homocysteine levels between patients with cerebrovascular disease and the control group, and the lack of association with admission to the ward, intensive care, or discharge, may be due to the small number of patients included in the study. The small number of patients and the short duration of the single-centre study are the most important limitations of our study.

The similarity in homocysteine levels between patients with good and poor outcomes at discharge and those with death or admission is due to the limited number of patients with a poor prognosis.

The ischemic area and volume were measured simultaneously by an emergency medicine resident and a radiology resident, and the high agreement between the two observers demonstrated that an emergency medicine resident with adequate training can interpret the results equivalently to a radiology resident. In our study, changes in basal homoarginine levels could not be examined due to the variability of comorbidities that could affect homoarginine in patients with CVD; however, we believe that examining changes relative to basal levels could yield meaningful results.

Our study may provide preliminary evidence for the use of homoarginine as a mortality predictor in diseases with high mortality rates, such as CVD and myocardial infarction.

Randomised controlled studies are needed in this area.

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ARAŞTIRMA MAKALESİ

RESEARCH ARTICLE

**COMPARISON OF THE NEUROMUSCULAR EFFECTS OF
CIS-ATRACURIUM AND ROCURONIUM IN YOUNG AND
ELDERLY PATIENTS**

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ABSTRACT

Objectives: The effects of neuromuscular blocking agents may vary between younger and older patients. The primary reason for this difference is decreased muscle perfusion secondary to decreased cardiac output in older patients. We aimed to compare the duration of action of Cis-atracurium and Rocuronium in normal and fast intubation doses on young and elderly patients. Materials and Methods: Our study is a prospective observational study. We included 120 adult patients (60 patients are 20-40 years, 60 patients are 60 years of age and above) who were scheduled for elective surgery and above ASA I-II group. Patients who used drugs that can affect muscle transmission, whose body weight was more than double their ideal body weight, who had a history of cardiac, pulmonary, renal, hepatic, neurological, psychiatric, muscular, inflammatory or endocrine diseases were excluded from the study. Patients were separated into 8 groups. The times to achieve single stimulus depression of %75, %95 and %100 blockade after the completion of muscle relaxant injection were recorded. SPSS for Windows Release 6.0 was used for the statistical analysis of the data. $p < 0.05$ value was accepted as significant. Key Findings: In the young patient group that was given cis-atracurium, time to achieve %75, %95 depression and maximum blockade of T1 were significantly shorter. The comparison of young and elderly patients given cis-atracurium at $2 \times ED_{95}$ dose revealed that the time to achieve %75, %95 depression and maximum blockade of T1 were longer in the elderly group. In elderly patients, time to achieve %75, %95 depression and maximum blockade of T1 were significantly shorter when given $3 \times ED_{95}$ dose, compared to $2 \times ED_{95}$. Duration of action was prolonged depending on dose. In the comparison of age groups using rocuronium dose, only duration of action was found to be significantly prolonged. The comparison of cis-atracurium and rocuronium at equivalent doses and same age groups revealed that time to achieve %75, %95 depression and maximum blockade of T1 were significantly shorter in all rocuronium groups than cis-atracurium groups. Implications: For both rocuronium and cis-atracurium, the onset time was longer in elderly patients. However, due to similar durations of action in both young and elderly patients, we have concluded that cis-atracurium is more advantageous for elderly patients.

Keywords: Cis-atracurium, Rocuronium, Neuromuscular blockade

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INTRODUCTION

Effects of muscle relaxants can be different in elderly patients compared to young patients. In older age, the decrease in cardiac output, body mass, total body fluids and protein binding can affect drug distribution in the body. Decrease in heart, liver and kidney functions can also prolong elimination times. However, the reason that is regarded as the most important among all of these, is reduced cardiac output and muscle perfusion. Decrease in these functions can double the onset time of the neuromuscular blocking effect of muscle relaxants [1].

Duration of action can be prolonged due to decreased clearance, for non-depolarising muscle relaxants (pancuronium, tubocurarine) that are eliminated by the renal route, or due to reduced liver mass for muscle relaxants that are eliminated by the hepatic route (rocuronium, vecuronium) [2,3]. It has been reported that the pharmacological profiles of non-depolarising muscle relaxants that are eliminated by routes other than renal or hepatic routes do not change with aging [4,5].

Cis-atracurium is the IR-cis, 1'r-cis isomer of atracurium. It has a similar neuromuscular effect potential to atracurium, and is 4 to 5 times more potent. Because of this, onset time is slower.

Rocuronium is an amino-steroid compound and has the shortest onset time among all current non-depolarising muscle relaxants[6]. Rocuronium and cis-atracurium are the novelist medium- acting non-depolarising muscle relaxants to enter clinical use in recent years. There are very few studies that compare the clinical effects of these two drugs in elderly patients.

In our study, we aimed to compare the duration of action of these two drugs in normal ($2 \times ED_{95}$) and fast intubation doses ($3 \times ED_{95}$) on young and elderly patients.

MATERIALS AND METHODS

This study was a prospective observational study that conducted on 120 adult patients [young group: 20-40 years of age (n=60); elderly group: 60 years of age and above (n=60)] who were scheduled for elective surgery and were above ASA I-II group. Patients were separated into 8 groups. Patients who were on drugs that can affect muscle transmission, whose body weight was more than double their ideal body weight, who had a history of cardiac, pulmonary, renal, hepatic,

neurological, psychiatric, muscular, inflammatory or endocrine diseases were excluded from the study.

30 minutes before anaesthesia induction, all patients were given 0,07 mg/kg of midazolam intramuscularly (IM) as premedication. When patients were in the operating theatre, standard monitoring, including ECG(electrocardiography), pulse oximeter and non-invasive blood pressure measurement was performed. Blood pressure and heart rate measurements were taken and recorded with one minute intervals in the first five minutes of anaesthesia, and with 5 minute intervals afterwards. An intravenous line was established in the back of the hand or forearm vein using an 18G cannula, and a 0.9% NaCl infusion was started at a rate of 5-7 ml/kg/hour.

Pre-oxygenation was performed for 3 minutes before induction, and induction was done with 6 mg/kg of thiopental. When loss of consciousness occurred, the ulnar nerve was stimulated supra-maximally via a surface electrode, using a TOF- Watch S (Organon- Teknika) neuromuscular monitor. Hand and forearm were stabilised using a splint. Contraction power of the adductor pollicis muscle under single simulation of 0.1 Hz frequency for 0.2 ms was observed with a TOF-Watch S monitor.

Once the calibration of the neuromuscular monitor was completed, patients were separated into the groups shown in Table 1, and the muscle relaxant drug was applied intravenously in bolus form.

Table 1. Neuromuscular Blockade Dosage of Groups

Group 1 (n=15)	20- 40 years of age, 0.1 mg/kg cis-atracurium (2×ED ₉₅)
Group 2 (n=15)	20- 40 years of age, 0.15 mg/kg cis-atracurium (3×ED ₉₅)
Group 3 (n=15)	60 years and older, 0.1 mg/kg cis-atracurium (2×ED ₉₅)
Group 4 (n=15)	60 years and older, 0.15 mg/kg cis-atracurium (3×ED ₉₅)
Group 5 (n=15)	20-40 years of age, 0.6 mg/kg rocuronium (2×ED ₉₅)
Group 6 (n=15)	20-40 years of age, 0.9 mg/kg rocuronium (3×ED ₉₅)
Group 7 (n=15)	60 years and older, 0.6 mg/kg rocuronium (2×ED ₉₅)
Group 8 (n=15)	60 years and older, 0.9 mg/kg rocuronium (3×ED ₉₅)

Following the administration of muscle relaxants, patients were given 1.5µg/kg of fentanyl. When %75 depression of the single stimulus occurred, endotracheal intubation was performed. Circumstances for endotracheal intubation were evaluated with a four-tier scale (Table 2).

Table 2. Circumstances of Endotracheal Intubation

Perfect	Laryngoscopy is easy, vocal cords are open, no straining
Good	Laryngoscopy is easy, vocal cords are open, slight straining with the tube
Poor	Laryngoscopy is easy, vocal cords are not fully open, moderate straining with the tube
Impossible	Laryngoscopy is difficult, vocal cords are completely closed

Anaesthesia was maintained with %66 nitrous oxide, %33 oxygen and sevoflurane at %1-2 end-tidal concentration. When analgesia was required, 50µg fentanyl was administered intravenously and the end-tidal concentration of sevoflurane was not increased above %2. The times to achieve single stimulus depression of %75, %95 and %100 (complete) blockade after the completion of muscle relaxant injection were recorded. The recovery time of the single stimulus to 25% after completion of the muscle relaxant injection was accepted as the duration of action.

Statistical Analysis

SPSS for Windows Release 6.0 was used for the statistical analysis of the data. Student's t test and two-way variant analysis was applied. $p < 0.05$ value was accepted as significant.

RESULTS

There were no significant differences between the weight, gender and ASA of patient groups. The mean age was significantly different between young and elderly patient groups ($p < 0.001$).

In the young patient group that was given cis-atracurium, time to achieve %75, %95 depression and maximum blockade of T1 were significantly shorter, depending on dose. Similarly, duration of action was longer in the group that was given $3 \times ED_{95}$ dose (Table 3).

Table 3. Comparison of Neuromuscular Blockade Durations of Group 1 and Group 2

	Group 1	Group 2
	(n=15) (20-40y)	(n=15) (20-40y)
	0.1 mg/kg cis-atracurium	0.15 mg/kg cis-atracurium
%75 depression of T1 (s)	178.4 $\pm$ 35.2	127.4 $\pm$ 36.2 [#]
%95 depression of T1 (s)	236.1 $\pm$ 35.6	189.6 $\pm$ 58.8 [°]
Duration to achieve maximum blockade (s)	268.3 $\pm$ 41.6	214.9 $\pm$ 56.3 ^π
Duration of action (min)	46.2 $\pm$ 5.3	53.6 $\pm$ 7.5 ^ψ

[#]: $p < 0.001$, [°]: $p < 0.05$, ^π: $p < 0.01$, ^ψ: $p < 0.01$

The comparison of young and elderly patients given cis-atracurium at $2 \times ED_{95}$ dose revealed that the time to achieve %75, %95 depression and maximum blockade of T1 were longer in the elderly group. The durations of action were similar in both groups (Table 4).

**Table 4. Comparison of Neuromuscular Blockade Durations of Group 1 and Group 3
(Mean $\pm$ SD)**

	Group 1	Group 3
	(n=15) (20-40y)	(n=15) (> 60y)
	0.1 mg/kg cis-atracurium	0.1 mg/kg cis-atracurium
%75 depression of T1 (s)	178.4 $\pm$ 35.2	236.1 $\pm$ 73.2 [#]
%95 depression of T1 (s)	236.1 $\pm$ 35.6	309.3 $\pm$ 82.2 [°]
Duration to achieve maximum blockade (s)	268.3 $\pm$ 41.6	358.6 $\pm$ 115.3 ^π
Duration of action (min)	46.2 $\pm$ 5.3	49.1 $\pm$ 4.4

[#]: $p < 0.05$, [°]: $p < 0.01$, ^π: $p < 0.01$

The findings of the comparison between young and elderly groups with $3 \times \text{ED}_{95}$ was similar to the finding obtained with $2 \times \text{ED}_{95}$ dose (Table 5).

**Table 5. Comparison of Neuromuscular Blockade Durations of Group 2 and Group 4
(Mean $\pm$ SD)**

	Group 2	Group 4
	(n=15) (20-40y)	(n=15) (> 60y)
	0.15 mg/kg cis-atracurium	0.15 mg/kg cis-atracurium
%75 depression of T1 (s)	127.4 $\pm$ 36.2	177.8 $\pm$ 45.7 [#]
%95 depression of T1 (s)	189.6 $\pm$ 58.8	241.3 $\pm$ 49.1 [°]
Duration to achieve maximum blockade (s)	214.9 $\pm$ 56.3	277.0 $\pm$ 66.2 ^π
Duration of action (min)	53.6 $\pm$ 7.5	62.1 $\pm$ 12.5

[#]: $p < 0.01$, [°]: $p < 0.05$, ^π: $p < 0.01$

In elderly patients, time to achieve %75, %95 depression and maximum blockade of T1 were significantly shorter when given 3×ED₉₅ dose, compared to 2×ED₉₅. Duration of action was prolonged depending on dose (Table 6).

Table 6. Comparison of Neuromuscular Blockade Durations of Group 3 and Group 4 (Mean ± SD)

	Group 3	Group 4
	(n=15) (> 60y)	(n=15) (>60y)
	0.1 mg/kg cis-atracurium	0.15 mg/kg cis-atracurium
%75 depression of T1 (s)	236.1 ± 73.2	177.8 ± 45.7 [#]
%95 depression of T1 (s)	309.3 ± 82.2	241,3 ± 49,1 [°]
Duration to achieve maximum blockade (s)	358.6 ± 115.3	277,0 ± 66.2 ^π
Duration of action (min)	49.1 ± 4.4	62.1 ± 12,5 ^ψ

[#]: $p < 0.05$, [°]: $p < 0.05$, ^π: $p < 0.05$, ^ψ: $p < 0.01$

In young patients given rocuronium, times to achieve %75, %95 depression and maximum blockade of T1 and durations of action were similar in the 2×ED₉₅ and 3×ED₉₅ dose groups (Table 7).

Table 7. Comparison of Neuromuscular Blockade Durations of Group 5 and Group 6 (Mean ± SD)

	Group 5	Group 6
	(n=15) (20-40y)	(n=15) (20-40y)
	0.6 mg/kg rocuronium	0.9 mg/kg rocuronium
%75 depression of T1 (s)	82.6 ± 46.5	85.9 ± 50.8
%95 depression of T1 (s)	119.5 ± 60.8	125.8 ± 77.0
Duration to achieve maximum blockade (s)	161.0 ± 109.9	146.7 ± 83.9
Duration of action (min)	43.7 ± 12.1	49.5 ± 11.7

When the young and elderly groups given rocuronium at $2 \times ED_{95}$ dose were compared, all parameters except the time to achieve %75 depression of T1 were significantly prolonged (Table 8).

Table 8. Comparison of Neuromuscular Blockade Durations of Group 5 and Group 7 (Mean $\pm$ SD)

	Group 5	Group 7
	(n=15) (20-40y)	(n=15) (> 60y)
	0.6 mg/kg rocuronium	0.6 mg/kg rocuronium
%75 depression of T1 (s)	82.6 $\pm$ 46.5	111.1 $\pm$ 39.9
%95 depression of T1 (s)	119.5 $\pm$ 60.8	186.1 $\pm$ 65.1*
Duration to achieve maximum blockade (s)	161.0 $\pm$ 109.9	246.2 $\pm$ 1042 ^{π}
Duration of action (min)	43.7 $\pm$ 12.1	57.5 $\pm$ 22.5 ^{ψ}

*: $p < 0.01$, π : $p < 0.05$, ψ : $p < 0.05$

In the comparison of age groups using rocuronium dose, only duration of action was found to be significantly prolonged (Table 9).

Table 9. Comparison of Neuromuscular Blockade Durations of Group 6 and Group 8 (Mean $\pm$ SD)

	Group 6	Group 8
	(n=15) (20-40y)	(n=15) (> 60y)
	0.9 mg/kg rocuronium	0.9 mg/kg rocuronium
%75 depression of T1 (s)	85.9 $\pm$ 50.8	94.7 $\pm$ 42.9
%95 depression of T1 (s)	125.8 $\pm$ 77.0	165.0 $\pm$ 124.3
Duration to achieve maximum blockade (s)	146.7 $\pm$ 83.9	222.1 $\pm$ 201.0
Duration of clinical effect (min)	49.5 $\pm$ 11.7	78.2 $\pm$ 19.4 ^{ψ}

ψ : $p < 0.001$

In elderly patients given rocuronium at $3 \times \text{ED}_{95}$ dose, only duration of action was significantly prolonged (Table 10).

**Table 10. Comparison of Neuromuscular Blockade Durations of Group 7 and Group 8
(Mean $\pm$ SD)**

	Group 7	Group 8
	(n=15) (> 60y)	(n=15) (>60y)
	0.6 mg/kg rocuronium	0.9 mg/kg rocuronium
%75 depression of T1 (s)	111.1 $\pm$ 39.9	94.7 $\pm$ 42.9
%95 depression of T1 (s)	186.1 $\pm$ 65.1	165.0 $\pm$ 124.3
Duration to achieve maximum blockade (s)	246.2 $\pm$ 104.2	222.1 $\pm$ 201.0
Duration of clinical effect (min)	57.5 $\pm$ 22.5	78.2 $\pm$ 19.41 ^ψ

ψ : $p < 0.05$

The comparison of cis-atracurium and rocuronium at equivalent doses ($2 \times \text{ED}_{95}$, $3 \times \text{ED}_{95}$) and same age groups revealed that time to achieve %75, %95 depression and maximum blockade of T1 were significantly shorter in all rocuronium groups than cis-atracurium groups. There was no significant difference between durations of action.

DISCUSSION

In this study, it was determined that the required time to reach maximum blockade with bolus administrations of cis-atracurium and rocuronium with $2 \times \text{ED}_{95}$ and $3 \times \text{ED}_{95}$ doses was prolonged with elderly patients compared to young patients. However, there was no statistically significant difference in duration of neuromuscular blockade in young and elderly patients. In equivalent doses of rocuronium administration, the time it takes to achieve maximum blockade was longer in elderly patients. Duration of neuromuscular blockade was also longer in this group.

In their study, Bluestein et al. compared the circumstances of intubation, duration to achieve blockade, duration of action and recovery indexes with cis-atracurium administration at $2 \times ED_{95}$ and $3 \times ED_{95}$ doses. They found that while duration to achieve maximum blockade was 4.6 minutes with $2 \times ED_{95}$, it was 3.4 minutes with $3 \times ED_{95}$. For the same doses, duration of action was 45.2 minutes and 54.5 minutes, respectively. They showed that with an increased initial dose of cis-atracurium (0.1 mg to 0.15), duration to achieve maximum blockade was shorter and duration of action was longer [7].

Caroll et al. compared cis-atracurium with other non-depolarising muscle relaxants and found that with the $2 \times ED_{95}$ dose used in the study, time to achieve maximum blockade was 3.4 minutes and duration of action was 41 minutes [8]. In another study, the duration of action was found to be 52 minutes with $3 \times ED_{95}$ dose of cis-atracurium [9]. In our study, we found the time to achieve maximum blockade was 3 minutes for $2 \times ED_{95}$, and 2.1 minutes for $3 \times ED_{95}$ doses of cis-atracurium ($p < 0.001$). Duration of action was found to be 46.2 and 53.6 minutes, respectively ($p < 0.01$). These findings are similar to the findings of previous studies conducted with cis-atracurium on young adult patients.

The onset time of action of cis-atracurium is shortened with increasing doses, as is the case with other non-depolarizing muscle relaxants [7]. The high doses administered in order to shorten onset time of action, causes to prolong the duration of action [8,10]. The shortened onset time of action and prolonged duration of action seen with increased doses of cis-atracurium administered to young and elderly patient groups in our study is consistent with these findings.

Administration of the same dose ($2 \times ED_{95}$) of cis-atracurium in different age groups revealed that the time to achieve maximum blockade was 1.5 minutes longer in the elderly patient group. Previous studies conducted with cis-atracurium have stated that onset of blockade was 1 minute longer in elderly patients. Study by Sorooshian et al. found that following the administration of 0.1 mg/kg cis-atracurium, duration to achieve maximum blockade was 3 minutes for the young patient group and 4 minutes for the elderly patient group [5]. Findings from the study by Ornstein et al. conducted with 0.1 mg/kg of cis-atracurium was similar to the findings of Sorooshian et al. [4]. Our findings are also similar to the findings of these two studies. The delayed time of onset for blockade seen in elderly patients could be due to the decreased cardiac output and slowed circulation.

Although time required to achieve maximum blockade is found to be longer, there was significant difference in young and elderly patient groups in terms of duration of action. Duration of action was 46.2 and 49.1 minutes for young and elderly patients, respectively. Like the studies by So-rooshian et al. and Ornstein et al., we also found that duration of action was similar, independent of age. Previous studies with pancuronium and d-tubocurarine showed that in elderly patients as the time to achieve maximum blockade was prolonged, so did the duration of action. This was explained by the decreased organ dependant clearance of non-depolarising muscle relaxants [4,5]. The absence of such prolongation in the duration of action of cis-atracurium could be explained by the elimination of this drug via the Hoffman pathway instead of organ dependant elimination.

Clinical findings that were obtained with the administration of cis-atracurium at $3 \times ED_{95}$ dose to similar to those of $2 \times ED_{95}$ dose. As expected, the time to achieve maximum blockade was approximately 1 minute shorter in both groups with this dose. With increased dose, duration of neuromuscular blockade was found to be 7 minutes longer in the young patient group, and 13 minutes longer in the elderly patient group

With our analysis conducted on the same age groups with equivalent doses of rocuronium, we established that this agent was a non-depolarising muscle relaxant with a rapid onset of action and moderate duration of action. With both doses, time to achieve blockade in elderly patients was approximately 1.5 minutes longer than in young patients.

A study researching the pharmacodynamics of rocuronium in geriatric patients (65-80y) found that the onset of blockade and recovery were slower in this population compared to younger patients. However, no difference was found in drug potency. Increasing rocuronium dose was found to prolong the time required to achieve maximum blockade. The study by DeMey et al. conducted on young patients reported that the onset time of neuromuscular blockade was 271 seconds with $2 \times ED_{95}$ dose and 135 seconds with $3 \times ED_{95}$ dose. Duration of action for the same doses were reported as 27.3 minutes and 53 minutes, respectively [11].

In our study, with increased rocuronium doses the time to achieve maximum blockade was shortened in both patient groups, but this shortening was not statistically significant. The times with 0.6 mg/kg and 0.9 mg/kg were 161 seconds and 146 seconds in young patients and 246 seconds and

222 seconds in elderly patients. The study by Matteo et al. researching the pharmacokinetics and pharmacodynamics of rocuronium on elderly patients reported that the duration of neuromuscular blockade was longer in elderly patients [12]. In elderly patients, elimination of drugs from the plasma via the hepatic route is reduced. This can be explained by reduced splanchnic blood flow, liver cell count and liver mass. The varied effects of rocuronium on young and elderly patients is due to the difference in distribution and elimination. In our study, duration of %25 recovery of T1 was 14 minutes longer with $2 \times \text{ED}_{95}$ dose in elderly patients than in young patients, and 29 minutes with $3 \times \text{ED}_{95}$ dose. The apparent prolonged duration of action in elderly patients could be because of the differences in pharmacokinetics that occur due to decrease in total body fluids and liver mass that comes with advanced age.

The fact that cis-atracurium and rocuronium have different pharmacodynamics have been shown with multiple studies. When rocuronium is compared to cis-atracurium based on the ED_{50} dose, the potency is reported as 1:4.2. Thus, it is reported that when administered in comparable doses, maximum blockade can be achieved much faster with rocuronium than cis-atracurium [13,14]. The time to achieve %75, %95 depression and maximum blockade of T1 in the same age groups were found to be much shorter with rocuronium in all groups, when compared to cis-atracurium. However, no statistically significant difference was found in the durations of action.

CONCLUSION

For both rocuronium and cis-atracurium, the time to achieve maximum blockade with $2 \times \text{ED}_{95}$ and $3 \times \text{ED}_{95}$ doses administered in bolus form, the onset time was longer in elderly patients. However, due to similar durations of action in both young and elderly patients, we have concluded that cis-atracurium is more advantageous for elderly patients.

Abbreviations

ASA	American Society of Anesthesiologists
ECG	Electrocardiography
ED	Effective Dose

G	Gauge
IM	Intramuscular
SPSS	Statistical Package for the Social Sciences
T	Time
TOF	Train of Four

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ARAŞTIRMA MAKALESİ

RESEARCH ARTICLE

**CLINICAL OUTCOMES AND SEPSIS PREDICTORS IN
EMERGENCY DECOMPRESSION OF URETERAL
STONES: A PROPENSITY-MATCHED STUDY OF PCN
VS. DJ STENT**

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ABSTRACT

Introduction: Obstructive uropathy due to ureteral calculi complicated by systemic infection represents a critical urological emergency. This study aimed to compare clinical outcomes and predictors of sepsis following emergency decompression with percutaneous nephrostomy (PCN) versus double-J (DJ) stent placement. Methods: We retrospectively analyzed 165 patients treated for obstructive ureteral stones with sepsis or systemic inflammatory response syndrome (SIRS) between September 2014 and April 2021 at two centers. After applying exclusion criteria, 100 patients (50 PCN, 50 DJ) were selected using 1:1 propensity score matching based on demographic, stone-related, and laboratory variables. Clinical outcomes and sepsis predictors were evaluated. Results: Baseline characteristics were comparable between the two groups. Hospital stay (7.2 ± 1.6 vs. 5.6 ± 1.3 days, $p = 0.012$) and procedure duration (32.5 ± 5.2 vs. 28.1 ± 4.6 minutes, $p = 0.037$) were significantly longer in the PCN group, while infection resolution, ICU admission, need for secondary intervention, and 30-day mortality showed no significant differences ($p > 0.05$). Sepsis developed in 19 patients (19%). Elevated serum procalcitonin (8.8 ± 2.7 vs. 6.3 ± 2.1 ng/mL, $p = 0.019$) and higher rates of positive urine (68.4% vs. 35.4%, $p = 0.041$) and blood cultures (63.2% vs. 21.5%, $p = 0.008$) were independent predictors of sepsis, whereas the decompression method was not associated with sepsis occurrence.

Conclusion: Both PCN and DJ stenting are effective emergency decompression techniques in septic obstructive uropathy. Although PCN is associated with longer hospitalization and operative time, neither method demonstrates superiority in preventing sepsis. Procalcitonin and culture positivity serve as valuable predictors of sepsis and should be incorporated into early clinical risk stratification.

Keywords: Obstructive uropathy, Sepsis, Procalcitonin, Nephrostomy, Ureteral stent

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INTRODUCTION

Obstructive uropathy due to ureteral calculi is a common urological emergency that can lead to severe complications such as pyelonephritis, sepsis, and multi-organ dysfunction if not promptly managed^{1, 2}. In the presence of systemic inflammatory response syndrome (SIRS) or sepsis, urgent urinary drainage is essential to relieve obstruction, eliminate the source of infection, and prevent further clinical deterioration³.

Two primary techniques are available for emergency decompression: percutaneous nephrostomy (PCN) and retrograde double-J (DJ) stent placement⁴⁻⁸. While both methods are endorsed by major urological guidelines such as those of the European Association of Urology (EAU), there remains a lack of consensus regarding the optimal approach, especially in the context of infection-related complications⁹. PCN offers the advantage of direct and complete renal drainage, which is often preferred in unstable or critically ill patients, while DJ stenting is less invasive and can be performed under regional anesthesia. However, comparative evidence on their clinical outcomes in septic patients is limited and often confounded by baseline differences in patient characteristics⁹.

To address these limitations, propensity score matching (PSM) has been increasingly employed in observational studies to reduce selection bias and provide more reliable comparisons. In the current study, we aimed to compare the clinical outcomes, including sepsis progression and infection resolution, of patients undergoing PCN versus DJ stenting for obstructive ureteral stones with systemic infection, using a PSM-based analysis.

MATERIALS AND METHODS

Patient enrollment

This retrospective study was conducted at two different centers and included patients who presented with obstructive ureteral stones complicated by sepsis or systemic inflammatory response syndrome (SIRS) between September 2014 and April 2021. This retrospective study was performed after obtaining approval from the ethics committee. The study was approved by the ethics committee of Karamanoglu Mehmetbey University Faculty of Medicine on 25/05/2021 with the

serial number No: 03/2021-12. A total of 165 patients underwent emergency urinary decompression either via percutaneous nephrostomy (PCN, n = 58) or retrograde double-J (DJ) stent insertion (n = 107). Of these, 50 patients from each group were selected and matched using propensity score matching (PSM) to minimize selection bias. The matched sample was created using 1:1 nearest-neighbor matching based on a logistic regression-derived propensity score calculated from the following covariates: age, sex, stone location (proximal or distal), stone size, presence of pyonephrosis, serum procalcitonin (PCT), white blood cell count (WBC), and serum creatinine levels. The final matched cohort included 100 patients (50 PCN and 50 DJ).

Inclusion and exclusion criteria

The inclusion criteria were patients aged 18 years or older with a diagnosis of proximal or distal ureteral stone confirmed by non-contrast-enhanced computed tomography (CT), and who met at least two SIRS criteria at the time of admission. Exclusion criteria included patients with bilateral ureteral stones, congenital or acquired urinary tract anomalies, coexisting infections from non-urological sources, patients under 18 years of age, and those with incomplete clinical follow-up data.

Therapeutic process

In the PCN group, patients underwent ultrasound-guided percutaneous nephrostomy placement under local anesthesia using a 10F nephrostomy catheter. After sterile preparation, the renal collecting system was punctured with an 18-gauge needle, followed by guidewire insertion and tract dilation. The nephrostomy tube was inserted and fixed after confirming proper placement.

In the DJ stent group, patients underwent cystoscopic placement of a 4.8F double-J ureteral stent measuring 26 or 28 cm in length, selected according to the patient's height. A guidewire was used to access the ureter, and the stent position was confirmed fluoroscopically or endoscopically.

All patients received empiric antibiotic therapy upon admission, adjusted according to urine and blood culture results. Supportive care, including intravenous fluids and antipyretics, was administered as needed.

Data collection and statistical analysis

Clinical variables collected included demographic data (age, sex), stone characteristics (location, size), laboratory findings (WBC, PCT, CRP, serum creatinine), presence of pyonephrosis, and radiologic findings. Outcomes such as the success rate of decompression, time to fever resolution, length of hospital stay, and need for ICU admission were also recorded.

Statistical analyses were conducted using SPSS version 2020 (IBM Corp., Armonk, NY). Continuous variables were compared using paired t-tests or Wilcoxon signed-rank tests, while categorical variables were analyzed using McNemar's test. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 165 patients who underwent emergency decompression due to ureteral stones accompanied by septic findings between September 2014 and April 2021 were retrospectively evaluated. After applying the exclusion criteria, 107 patients who underwent DJ stent placement and 58 patients who underwent percutaneous nephrostomy (PCN) were identified. Following 1:1 propensity score matching (PSM) based on age, gender, stone location, stone size, pyonephrosis, procalcitonin, white blood cell (WBC) count, and serum creatinine levels, 50 patients from each group were matched and included in the final analysis.

Baseline Characteristics

As shown in Table 1, there were no statistically significant differences between the PCN and DJ groups in terms of demographic variables (age, gender, BMI) and pre-intervention laboratory values (WBC, CRP, procalcitonin, creatinine, albumin). Stone characteristics, including size and density, were also comparable between the two groups ($p > 0.05$ for all). These findings confirm the adequacy of the PSM process in creating two clinically similar cohorts.

Clinical Outcomes

Clinical outcomes after decompression are summarized in Table 2. The mean hospital stay was significantly longer in the PCN group compared to the DJ group (7.2 ± 1.6 vs. 5.6 ± 1.3 days, $p = 0.012$). Similarly, procedure duration was significantly higher in the PCN group (32.5 ± 5.2 vs. 28.1 ± 4.6 minutes, $p = 0.037$). There were no statistically significant differences between the groups in terms of time to normalization of infection markers (WBC, CRP, body temperature), need for second intervention, ICU admission, or 30-day mortality ($p > 0.05$ for all).

Sepsis Analysis

Among the entire cohort of 100 matched patients, 19 patients (19%) developed sepsis, defined by the presence of ≥ 2 SIRS criteria within 48 hours after intervention. A comparison of patients with and without sepsis is shown in Table 3. No significant differences were observed between the two groups regarding age, sex, BMI, comorbidities (diabetes mellitus, hypertension), stone characteristics, or preoperative laboratory values (WBC, CRP, albumin, creatinine). However, procalcitonin levels were significantly higher in the sepsis group (8.8 ± 2.7 vs. 6.3 ± 2.1 ng/mL, $p = 0.019$). Moreover, positive urine cultures (68.4% vs. 35.4%, $p = 0.041$) and positive blood cultures (63.2% vs. 21.5%, $p = 0.008$) were more frequent among septic patients. Importantly, there was no statistically significant association between the type of decompression procedure (PCN vs. DJ) and the development of sepsis ($p = 0.318$).

Table 1. Baseline Characteristics of the Patients

Variable	PCN Group	DJ Group	p-value
Age (years)	55.0 ± 8.89	54.24 ± 8.54	0.654
Sex (male/female)	28/22	32/18	0.721
BMI (kg/m ²)	23.18 ± 1.98	23.03 ± 1.66	0.833
Diabetes mellitus (n)	13	10	0.478
Hypertension (n)	31	30	0.692

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Duration of symptoms (days)	3.16 ± 1.26	2.62 ± 1.11	0.774
Stone size (mm)	9.27 ± 2.2	9.55 ± 1.61	0.615
Stone density (HU)	880.69 ± 110.65	854.22 ± 93.43	0.589
Grade 1/2 hydronephrosis (n)	32	33	0.813
Grade 3/4 hydronephrosis (n)	18	17	0.667
WBC (×10 ⁹ /L)	12.94 ± 3.22	13.24 ± 3.0	0.493
Neutrophils (×10 ⁹ /L)	9.58 ± 3.26	10.61 ± 2.37	0.522
CRP (mg/L)	78.26 ± 31.85	86.57 ± 33.6	0.612
Albumin (g/L)	36.94 ± 4.05	37.11 ± 3.0	0.701
Procalcitonin (ng/mL)	6.78 ± 2.41	7.12 ± 2.58	0.641
Creatinine (mg/dl)	1.31 ± 0.4	1.5 ± 0.51	0.563
Urine leukocytes (/μL)	136.09 ± 115.28	146.23 ± 105.43	0.489
Positive urine culture (n)	22	23	0.738
Positive blood culture (n)	12	13	0.682

Data are presented as mean ± standard deviation or number (n).PCN: Percutaneous nephrostomy, DJ: Double-J stent, BMI: Body mass index, WBC: White blood cell, CRP: C-reactive protein, PCT: Procalcitonin. Continuous variables were compared using the paired t-test (for normally distributed data, Shapiro–Wilk test) or the Wilcoxon signed-rank test (for non-normal data). Categorical variables were analyzed using McNemar’s test. A two-sided p-value <0.05 was considered statistically significant.

Table 2. Comparison of Clinical Outcomes between Groups

Variable	PCN Group	DJ Group	p-value
Hospital stay (days)	7.2 ± 1.6	5.6 ± 1.3	0.012
Operation time (minutes)	32.5 ± 5.2	28.1 ± 4.6	0.037
Time to normalization of WBC (days)	2.1 ± 0.8	2.0 ± 0.7	0.681
Time to normalization of CRP (days)	3.3 ± 1.1	3.1 ± 1.2	0.512
Time to normalization of body temperature (days)	2.4 ± 0.9	2.3 ± 0.8	0.743
Duration of antibiotic treatment (days)	6.0 ± 1.4	5.8 ± 1.3	0.658
Fever after 48 hours (n)	6	5	0.812
Need for second intervention (n)	3	4	0.764
ICU admission (n)	2	1	0.445
Mortality (n)	0	0	1.000

Data are presented as mean ± standard deviation or number (n).CN: Percutaneous nephrostomy, DJ: Double-J stent, WBC: White blood cell, CRP: C-reactive protein. Continuous outcomes were analyzed using the paired t-test or Wilcoxon signed-rank test, as appropriate. Categorical outcomes were compared using McNemar's test. Effect sizes with 95% confidence intervals were additionally reported where applicable.

Table 3. Comparison of Clinical and Laboratory Parameters in Patients with and Without Sepsis

Variable	Sepsis (+)	Sepsis (–)	p-value
Age (years)	58.2 ± 9.1	55.1 ± 9.4	0.528
Sex (male/female)	12/7	48/33	0.645
BMI (kg/m ²)	23.0 ± 2.2	23.2 ± 1.9	0.702
Diabetes mellitus (n/N)	5/19	18/81	0.883
Hypertension (n/N)	10/19	51/81	0.791
Stone size (mm)	9.8 ± 3.2	9.3 ± 3.0	0.493
Stone density (HU)	880 ± 115	865 ± 105	0.621
WBC (×10 ⁹ /L)	14.0 ± 3.3	12.9 ± 3.1	0.312
Neutrophils (×10 ⁹ /L)	10.5 ± 2.8	9.8 ± 2.7	0.418
CRP (mg/L)	95 ± 32	80 ± 30	0.587
Procalcitonin (ng/mL)	8.8 ± 2.7	6.3 ± 2.1	0.019
Creatinine (mg/dL)	1.6 ± 0.3	1.3 ± 0.2	0.289
Albumin (g/L)	35.2 ± 3.9	36.0 ± 3.7	0.668
Urine leukocytes (/μL)	158 ± 110	150 ± 105	0.537
Urine culture (Positive/Negative)	13/6	32/49	0.041
Blood culture (Positive/Negative)	12/7	13/68	0.008
PCN/DJ placement (n)	11/8	39/42	0.318

Data are presented as mean ± standard deviation or number (n) or ratio (n/N).PCN: Percutaneous nephrostomy, DJ: Double-J stent, BMI: Body mass index, WBC: White blood cell, CRP: C-reactive protein, PCT: Procalcitonin, HU: Hounsfield unit.

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Continuous variables were analyzed using the independent t-test (for normally distributed data, Shapiro–Wilk test) or the Mann–Whitney U test (for non-normal data). Categorical variables were compared using the chi-square test or Fisher’s exact test when expected counts were <5. A two-sided p-value <0.05 was considered statistically significant.

DISCUSSION

This study compared two widely used emergency decompression methods—percutaneous nephrostomy (PCN) and double-J (DJ) ureteral stenting—in patients presenting with ureteral obstruction complicated by sepsis or systemic inflammatory response syndrome (SIRS). By employing propensity score matching (PSM), we aimed to mitigate the influence of confounding variables and establish more comparable cohorts for outcome assessment.

Following adjustment through PSM, no statistically significant difference in sepsis rates was observed between the PCN and DJ groups. This finding suggests that both interventions are equally effective in achieving initial infection control when decompression is performed promptly. Our results align with prior studies that demonstrated comparable outcomes between these techniques regarding infection resolution and short-term survival in obstructive uropathy complicated by infection^{10, 11}.

However, the PCN group was associated with significantly longer hospital stays and procedure times. These findings may reflect the more invasive nature of nephrostomy placement and the subsequent need for external drainage management and follow-up care. This logistical complexity should be taken into account when selecting a decompression strategy, especially in resource-limited settings.

One of the most clinically relevant observations in our study was the strong association between elevated procalcitonin levels and the development of sepsis. This corroborates previous research highlighting procalcitonin as a reliable early biomarker for severe bacterial infections and sepsis, particularly in urological emergencies¹². Moreover, the higher rates of positive urine and blood cultures in the sepsis subgroup emphasize the importance of early microbiological sampling to guide empirical antimicrobial therapy and stratify risk.

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Our study demonstrated that elevated serum procalcitonin (PCT) levels were significantly associated with the development of sepsis (8.8 ± 2.7 vs. 6.3 ± 2.1 ng/mL, $p = 0.019$). This finding is in line with previous studies indicating that PCT is a reliable biomarker for predicting sepsis in urological emergencies. Liu et al. reported a threshold PCT value of 6.5 ng/mL to predict post-interventional urosepsis with 82% sensitivity and 75% specificity following mini-percutaneous nephrolithotomy¹². Similarly, Hang et al. (2018) found that patients with PCT levels >5 ng/mL had a significantly higher incidence of bacteremia and septic shock in the context of obstructive uropathy¹³. These findings reinforce the clinical utility of PCT in early risk stratification.

In our cohort, hospital stay and procedure time were significantly longer in the PCN group, yet infection resolution and sepsis rates were comparable between PCN and DJ groups. Mokhmalji et al. conducted a prospective randomized trial comparing PCN and DJ stenting in patients with obstructive uropathy due to stones and found similar infection resolution rates (87.5% vs. 85.4%, $p > 0.05$), although PCN patients had prolonged hospitalization¹¹. Likewise, Pearle et al. (1998) reported no significant difference in septic complications between PCN and DJ stent groups, concluding that the timing and adequacy of decompression are more critical than the method itself¹⁰. These data corroborate our results and suggest that both techniques are valid options when performed promptly.

In our analysis, positive urine and blood cultures were significantly more frequent in patients who developed sepsis (urine: 68.4% vs. 35.4%, $p = 0.041$; blood: 63.2% vs. 21.5%, $p = 0.008$). Comparable findings were reported by Kitagawa et al., who found that bacteremia occurred in 60.5% of patients with obstructive pyelonephritis and was associated with a higher risk of septic shock and longer hospital stay¹⁴. Moreover, Mita et al. emphasized that early blood culture positivity was an independent predictor of sepsis in obstructive urolithiasis patients undergoing urgent drainage¹⁵. These findings emphasize the importance of early microbiological evaluation in guiding empiric antimicrobial therapy.

Interestingly, although PCN is frequently preferred in patients with advanced sepsis or pyonephrosis due to its capacity for direct and complete drainage, our findings did not demonstrate supe-

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riority over DJ stenting in sepsis prevention once baseline imbalances were adjusted for. This supports the growing consensus that the timing and adequacy of drainage may be more critical determinants of septic outcomes than the decompression modality itself⁹.

The strengths of our study include the application of PSM to reduce selection bias and the focus on a clinically significant population of patients with obstructive urolithiasis complicated by sepsis or SIRS. Nevertheless, certain limitations should be acknowledged. Its retrospective design carries a risk of bias despite propensity score matching. The relatively small number of septic patients may have reduced statistical power. In addition, unmeasured confounders such as antibiotic timing or operator experience could not be fully accounted for, and long-term outcomes such as renal function or stone clearance were not evaluated. Therefore, the findings should be interpreted with caution, and prospective studies are needed to confirm these results.

CONCLUSION

In patients presenting with septic obstructive uropathy due to ureteral calculi, both percutaneous nephrostomy (PCN) and double-J (DJ) stent placement are effective options for emergency decompression. When patient characteristics are appropriately matched, neither method shows superiority in preventing sepsis. Although PCN was associated with a longer hospital stay and procedure time, the rates of infection resolution and sepsis development were comparable between the groups. Additionally, elevated procalcitonin levels and positive urine and blood cultures were significant predictors of sepsis development, underscoring their importance in early risk stratification. These findings suggest that the choice of decompression technique should be guided by clinical feasibility and expertise, rather than an assumed advantage in infection control.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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ARAŞTIRMA MAKALESİ

RESEARCH ARTICLE

**ANALYSIS OF THE PATIENTS ADMITTED TO
EMERGENCY DEPARTMENT WITH SYNTHETIC
CANNABINOID (BONSAI) ABUSE**

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ABSTRACT

Objectives: Emergency departments frequently receive patients after substance abuse. The aim of this study was to determine the epidemiological and clinical characteristics of patients who directly referred to our emergency department with abuse of synthetic cannabinoid known as Bonzai. **Material and methods:** The study was carried out in Akdeniz University Hospital retrospectively by reviewing the files of the patients who applied to the emergency department after taking synthetic cannabinoids. Between 01.07.2015 - 31.07.2017, patients who applied directly to our emergency department after using synthetic cannabinoids, known as Bonzai, were identified in the hospital data processing program records. Descriptive statistics were performed by recording patients' age, gender, and presenting complaints. **Results:** A total of 47 patients were admitted to our emergency department between the specified dates. 45 patients were male, and 2 patients were female. The mean age of patients was 23.3 ± 6.8 . There were 33 patients in the 16-24 year age group, 12 patients in the 25-35 year age group and 2 patients in the over 35 age group. 30 patients had altered mental status. Cardiac side effects such as tachycardia (29 patients) and hypertension (24 patients) were found in most of the patients. Thirty-nine patients were evaluated in the emergency department and discharged from hospital. Four of the 5 patients who need inpatient treatment were admitted to intensive care units. 1 patient died during intensive care unit hospitalization. **Conclusion:** Synthetic cannabinoid intoxication is especially common in young males. Mostly, neurological and cardiac side effects occur. The level of knowledge of the physicians should be increased through relevant trainings and multi-centered studies should be carried out for more comprehensive epidemiological and clinical data.

Keywords: Synthetic cannabinoids, Bonzai, epidemiologic characteristics

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INTRODUCTION

Substance addiction is a serious disorder with genetic and neurobiological underpinnings that disrupts physical and mental health as well as family, social, and occupational functioning. (1). Intensive research continues worldwide to determine its prevalence and to develop new psychosocial and pharmacological treatment methods. Studies have screened the prevalence of substance use in various groups, such as students, healthcare professionals, and workers, and have reported results indicating substance dependence rates of up to 5% and risky alcohol and substance use of 10 to 30% (2) (3).

Emergency rooms are among the most common areas where substance abusers encounter problems. The violent behavior exhibited by substance abusers, as well as the intoxication and withdrawal symptoms that arise from different substances and require different clinical approaches, are all situations that physicians must be well aware of and able to manage.

Synthetic cannabinoids (SCs) are a subgroup of cannabinoids, and their use is quite popular and widespread due to their affordability, easy storage, and their undetectable nature in screening tests. (1) Commonly known as "K2" and "Spice" worldwide, SCs are known as Bonzai in our country. The use of these substances is increasing, especially among young people and young adults. Cases of poisoning are increasingly present in emergency departments, and fatal cases are being reported. This study aimed to investigate the demographic, epidemiological, and clinical effects of SC users, who are increasingly using them.

MATERIALS and METHODS

Between 01.07.2015 and 31.07.2017, 47 patients who presented to the Akdeniz University Medicine Faculty Hospital emergency department due to taking synthetic Cannabinoids were reviewed retrospectively. Patient data were obtained from patient files and electronic hospital records in the hospital archive. Data were collected, including age, gender, state of consciousness, vital signs, and discharge or admission status after emergency room evaluation. Major complications such as the need for intensive care, intubation, and death were also recorded. Statistical analyses of the obtained data were performed using SPSS 20.

RESULTS

During the study period, there were 1,294 emergency room visits related to substance use. 1229 Patients not identified as having taken synthetic cannabinoids or with incomplete information were excluded from the study. Of the 65 patients using Bonsai, 18 had repeated visits. Repeat visits were removed, and a total of 47 patients were included in the study. The study flowchart is shown in the figure 1.

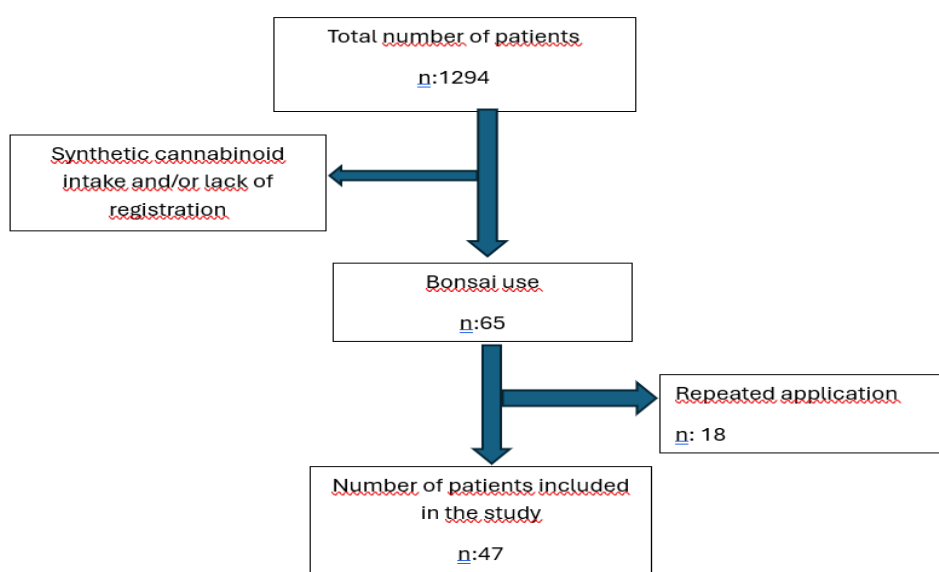


Figure 1. The study flowchart

The mean age of the patients was 23.3 ± 6.8 (16-53) years and 95.7% (n=45) were male. The age and gender distribution of the patients is shown in Table 1.

Thirteen of 27 patients who underwent a urine drug panel were positive for opioids, cocaine, cannabinoids, ecstasy, or benzodiazepines.

Tests capable of detecting five different synthetic cannabinoids yielded no positive results. Six patients had multiple substance use, and five patients were only positive for cannabinoids. Six patients (12.8%) had alcohol levels above the legal limit. At the time of admission, changes in

consciousness were detected in 30 patients (63.8%) and seizures were detected in 2 patients (4.3%). The patients' consciousness status and rates are shown in Table 2.

Table 1. The age and gender distribution of the patients

Average age	23.4±6.85
	Min 16, Max:53
<i>Distribution of age groups</i>	
16-24 year	%70,2 (n:33)
25-35 year	%25,5(n:12)
>35 year	%4,3(n:2)
Gender distribution	
Male	%95,7 (n:45)
Female	%4,3 (n:2)

Table 2: The patients' consciousness status and rates

State of consciousness	N:47	%
Conscious	17	36.2
Confused	17	36.2
Agitated	6	12.8
Unconscious	7	14.9

When vital signs were examined, 61.7% (n=29) had tachycardia, 53.3% (n=24) had hypertension, 6.6% (n=3) had hypotension, 21.7% (n=10) had tachypnea, and 6.5% (n=3) had bradypnea. No patients had bradycardia. Two patients (4.3%) were intubated.

Eighty-three percent (n=39) of the patients were discharged as outpatients, one patient (2.1%) was admitted to the regular clinic, four patients (8.5%) were admitted to the intensive care unit, and three patients (6.4%) refused treatment. One patient (2.1%) in the intensive care unit died, and

only opioid positivity was detected in this patient. The emergency department outcomes of the patients are shown in Table 3.

Table 3: The emergency department outcomes of the patients are

	N: 47	%
Discharge	39	83
Hospitalization	1	2.1
Intensive Care	4	8.5
Leaving the emergency without permission	3	6.4

It was determined that 40.4% of the patients applied to the Psychiatry or AMATEM (Alcohol and Drug Addiction Treatment and Education Center) outpatient clinic at least once after being discharged from the emergency department.

DISCUSSION

Synthetic cannabinoids (SCs) are substances with increasing global use, leading to unpredictable clinical effects and serious health risks, including poisoning. These compounds typically appear as white or yellowish odorless crystalline powders. They are dissolved in solvents such as acetone or ethanol and then sprayed onto herbal materials (e.g., thyme, sage, cannabis), paper, or other carriers.

SCs are most commonly consumed by smoking or sniffing. The preparation and administration methods make it difficult to determine or control the exact dosage. Due to their high binding affinity to cannabinoid (CB) receptors, synthetic cannabinoids can be 2 to 800 times more potent than THC (Δ^9 -tetrahydrocannabinol), the active compound in cannabis (2).

According to the European Drug Agency, SCs represent 227 out of more than 950 identified psychoactive substances (1). Their chemical structures and components are frequently modified, making them undetectable in standard rapid urine tests. Even reference laboratories face challenges in identifying them (3).

Despite these limitations, synthetic cannabinoid use can still be diagnosed clinically.

New types of products have been identified in the form of e-liquids for e-cigarettes and, in some European countries, in the form of candy. (1) The usage rate is 0.2-4%, but it is higher in young men (4).

The vast majority (95.7%) of the 47 bonzai users evaluated in the study were male. By age, the majority (70.2%) were between the ages of 16 and 24. In their study conducted in the emergency department, Küçük et al. (5) found that a total of 112 patients were admitted, 111 of whom were male and only 1 were female, and the mean age of the patients was 23.32 ± 6.14 years. Yılmaz et al. (6) reported that 69.1% of the 136 patients were male, and the majority of users (44.8%) were between the ages of 14 and 24.

Acute physical effects range from sweating, nausea, vomiting, appetite changes, hypertension/hypotension, chest pain, tachycardia/bradycardia, respiratory depression, confusion, psychomotor agitation, somnolence, and sedation. While some individuals experience sedation after SC use, others experience agitation, nausea, flushing, burning eyes, dry mouth, mydriasis, and tachycardia (7). In our study, the most common side effects were tachycardia and hypertension. While bradycardia was reported as a rare side effect in the study by Kane et al. (8), bradycardia was not observed in any patient in our study.

Serious clinical conditions such as seizures, rhabdomyolysis, and myocardial infarction (MI) can occur in some individuals due to SC use (9). The incidence of seizures associated with synthetic cannabinoid use was reported as 3.8% in the literature (10), but in our study, it was found to be 4.3%.

In their study conducted in the emergency department (5), 61 patients (54.4%) were evaluated and discharged in the emergency department, 27 patients (24.1%) were admitted to the intensive care unit, and 9 (8%) were admitted to the internal medicine unit. Advanced airway techniques were used in the emergency department for three of the patients. In our study, the rate of patients admitted to the intensive care unit was determined to be 8.5%, and two patients were intubated in the emergency department.

CONCLUSION

Bonzai use is more common among men, with the majority occurring in young adults. Cardiovascular and neurological side effects are common. The most common symptoms at presentation were tachycardia and impaired consciousness.

As synthetic cannabinoid use increases daily, it is understandable that it will become, and will continue to be, one of the most problematic drugs. Therefore, the need for examination, equipment, and experience to identify and report the chemicals contained in these substances will only increase daily.

It is believed that supporting the results obtained from the study with more comprehensive, prospective studies that include the entire country and improving recording will help in the fight against the use of this substance.

Nationwide, prospective, multicenter studies are needed to better understand the epidemiology and clinical effects of synthetic cannabinoid use

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ARAŞTIRMA MAKALESİ

RESEARCH ARTICLE

EVALUATION OF ELDERLY PATIENTS RECEIVING THROMBOLYTIC THERAPY FOR ISCHEMIC CEREBROVASCULAR STROKE IN THE EMERGENCY DEPARTMENT

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ABSTRACT

Objective: Acute cerebrovascular ischemic stroke is a significant disease in terms of mortality and morbidity. Advanced age is a considerable risk factor for stroke. Although intravenous thrombolytic therapy has proven effective in the acute phase of ischemic stroke, its use in patients over 80 years of age has been contentious. In this study, we aimed to evaluate the complications and prognosis of patients admitted to the emergency department with acute ischemic stroke and treated with intravenous thrombolytic therapy, as well as to assess mortality and morbidity about age. **Methods:** This retrospective study included 174 patients aged 18 years or older who presented to the emergency department between January 1, 2016 and April 30, 2021 and received intravenous thrombolytic therapy for acute ischemic stroke. Two groups, under 80 years of age (70.1%) and 80 years and older (29.9%), were formed and evaluated in terms of risk factors, clinical status, laboratory findings, mortality and morbidity. **Results:** The proportion of female patients in the 80 years and older age group was significantly higher than in the younger group ($p=0.007$). Among the risk factors, atrial fibrillation and hypertension were significantly higher in the 80 years and older group compared to the younger group ($p<0.001$). Hospitalization duration was significantly longer in the older group ($p=0.027$). Mortality rates were also significantly higher in this group ($p=0.004$). Based on NIHSS values at 1 week, stroke severity was significantly greater in patients aged 80 years and older ($p=0.024$). Based on 1-month Modified Rankin Score (mRS) averages, the elderly patient group had significantly higher scores ($p=0.002$). Post-treatment intracranial hemorrhage complication rates were not significantly different between the two groups ($p=0.808$). **Conclusion:** The mortality and morbidity rates of patients aged 80 years and older receiving thrombolytic therapy for acute ischemic stroke are higher than those of patients younger than 80 years. Since there is no significant difference between the two groups in terms of treatment complications, intravenous thrombolytic therapy can be safely administered in patients over 80 years of age.

Keywords : Ischemic Stroke, Emergency Department, Thrombolytic Therapy, Advanced Age, Hemorrhagic Complications

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INTRODUCTION

Acute ischemic stroke is a severe disease in terms of both mortality and morbidity and millions of people become disabled and die every year due to ischemic stroke (1,2). Early diagnosis, rapid treatment and close follow-up are critical for both survival and disability outcomes in this disease where even seconds matter for prognosis (3,4).

Since advanced age poses a risk in terms of complications of intravenous (IV) thrombolytic therapy in acute ischemic stroke patients, an age limit for treatment has been discussed in the past and no upper limit has been set for age in terms of treatment contraindications in the latest guidelines published after studies (5,6).

While previous guidelines contraindicated thrombolytic therapy in elderly (> 80) patients with acute ischemic stroke, the 2018 AHA guidelines emphasize that age is not a contraindication (In patients who presented within the first 3 hours after the onset of symptoms). However, the recommendation and level of evidence for thrombolytic therapy is lower in elderly patients who present within 3-4.5 hours (6).

Our study was planned in our tertiary care hospital, a stroke center in Istanbul. In this study, acute ischemic stroke patients who received IV thrombolytic therapy were retrospectively evaluated. Patients aged 80 years and older were compared with patients under 80 years of age to determine the differences in risk factors, clinical status, laboratory parameters, treatment complications, prognosis and mortality between the two groups.

MATERIALS AND METHODS

Our study was designed as a retrospective cross-sectional study comparing the demographic, clinical, laboratory findings, prognosis and treatment complications of patients who were admitted to Şişli Hamidiye Etfal Training and Research Hospital Emergency Department and diagnosed with acute ischemic stroke and received IV thrombolytic therapy (0.9 mg/kg alteplase 10% bolus and the rest 1 hour infusion). Approval was obtained from the ethics committee of our hospital on 22/02/2022 with decision number 3424.

A total of 174 patients with acute ischemic stroke admitted to the emergency department (ED) between January 1, 2016 and April 30, 2021 who underwent IV thrombolytic therapy were included in the study and divided into two groups under 80 years of age (70.1%) and 80 years and older (29.9%), and the groups were compared among themselves.

The patient groups listed below were not included in the study:

- Patients under 18 years of age,
- Pregnant patients,
- Patients with missing data

Risk factors, presence of comorbidities and history of drug use in both patient groups were recorded on the patient record form. Both groups were compared according to the results of laboratory tests performed in the ED. Hospital admission and treatment initiation times were calculated and compared. In patients who underwent mechanical thrombectomy, the outcome of the procedure was compared for both groups according to the mTICI (modified treatment in cerebral infarction) scale. The National Institute of Health Stroke Scale (NIHSS) was used to assess stroke severity. NIHSS score at admission, ED disposition, 1-week NIHSS score, need for mechanical ventilation, intracranial hemorrhage complication, duration of hospitalization, in-hospital mortality, and 1-month Modified Rankin Scale (mRS) were compared for both patient groups to evaluate prognosis, mortality and morbidity.

Statistical Analysis

In the evaluation of the data of our study, the conformity of the data to normal distribution was primarily evaluated by Kolmogorov-Smirnov and Shapiro-Wilk tests. Continuous variables were presented as mean $\pm$ standard deviation (SD) and categorical variables were presented as number (n) and percentage (%). For parameters that did not show normal distribution, the Mann-Whitney U test was used to compare two groups and the Kruskal-Wallis test was used to compare more than two groups. Intergroup comparisons of categorical (discrete) variables were analyzed using Chi-square (χ^2) and Fisher's exact tests. One Way ANOVA test was used for parametric variables in comparisons of more than two groups. SPSS (Statistical Package for Social Sciences;

IBM SPSS Statistics for Macintosh, Armonk, NY) Package program version 25.0 was used for statistical analysis of the data obtained. Hypotheses were two-way and $p < 0.05$ was considered statistically significant.

RESULTS

A total of 174 patients were included in our study, comprising 52 (29.9%) who were 80 years of age or older and 122 (70.1%) who were younger than 80 years of age. Of the participants, 83 were women and 91 were men, and it was determined that women were significantly more in the group aged 80 years and over with a rate of 63.5% ($p = 0.007$).

Patients included in our study were divided into two groups: patients aged 80 years and older and patients aged below 80 years. Patients in these two age groups were compared in terms of their medical history. Accordingly, no significant difference was found between these two groups in terms of the presence of general risk factors, smoking, history of previous stroke, presence of coronary artery disease, presence of congestive heart failure, hyperlipidemia, DM (Diabetes mellitus), antiaggregant and anticoagulant drug use. However, the presence of AF (Atrial fibrillation) was significantly higher in patients aged 80 years and older (55.80%) compared to those under 80 years (20.50%) ($p < 0.001$). Similarly, HT (hypertension) was found to be significantly higher in patients aged 80 years and older (80.80%) compared to patients aged <80 years (58.20%) ($p = 0.004$). The findings are shown in Table 1.

Table 1: Analysis of Risk Factors, Drug Use and Hematologic Parameters

	≥80 years (n=52)	<80 years (n=122)	
	n (%)	n (%)	p
Gender (Female)	33 (63.5)	50 (40.9)	0.007*
Presence of Risk Factors	50 (96.2)	106 (86.9)	0.066
Atrial fibrillation	29 (55.8)	25 (20.5)	<0.001*

Smoking	2 (3.8)	19 (15.6)	0.091
History of stroke	5 (9.6)	20 (16.4)	0.243
Coronary Artery Disease	13 (25.0)	37 (30.3)	0.477
Hypertension	42 (80.8)	71 (58.2)	0.004*
Congestive Heart Failure	10 (19.2)	11 (9.0)	0.058
Hyperlipidemia	15 (28.8)	39 (32.0)	0.684
Diabetes Mellitus	8 (15.4)	31 (25.4)	0.147
Antiaggregant use	21 (40.4)	51 (41.8)	0.862
Anticoagulant use	6 (11.5)	6 (4.9)	0.115
Laboratory Parameters:	Mean±SD (Median)	Mean±SD (Median)	p
Hemoglobin, g/L	12.39±1.37 (12.3)	13.46±1.88 (13.4)	0.003*
Platelet count, 10 ⁹ /L ⁹	221.40±76.18 (208.5)	236.47±86.02 (221.5)	0.116
Creatinine, mg/dL	1.07±0.49 (0.9)	0.97±0.43 (0.9)	0.150
Glucose, mg/dL	134.27±52.02 (125)	150.65±71.22 (127)	0.170
ALT, U/L	14.64±5.43 (14)	21.15±13.55 (18)	0.001*
Troponin T, ng/L	26.77±70.64 (13)	18.67±37.13 (8.3)	0.100
pH	7.40±0.04 (7.4)	7.40±0.04 (7.4)	0.363
Base Excess, mmol/L	0.60±2.72 (0.6)	0.38±1.91 (0.4)	0.589

HDL, mg/dL	46.14±12.17 (44)	42.71±10.47 (43)	0.143
Cholesterol, mg/dL	185.54±33.04 (189.5)	195.30±48.95 (193)	0.129

Abbreviations: n, number; SD, standard deviation; ALT, alanine aminotransferase; HDL, high-density lipoprotein.

In our study, we analyzed the time from symptom onset to emergency department admission and the time from admission to the initiation of thrombolytic therapy (injection). Accordingly, the mean time from the onset of the symptom to ED presentation was 76.74±40.61 minutes and the mean time from ED presentation until thrombolytic treatment was administered was 76.70±34.05 minutes. The mean time to visit the ED after symptom onset (symptom-door time) was longer in patients aged 80 years and older than in those under 80 years of age (79.19 minutes vs. 75.70 minutes), still there was no statistically significant difference between the two patient groups ($p=0.474$). The mean thrombolytic therapy initiation time (door-needle time) after ED presentation was shorter in patients aged 80 years and older (73.08 minutes vs. 78.24 minutes). However, the difference was not statistically significant ($p=0.265$). The mean time from symptom onset to the initiation of thrombolytic therapy (symptom-needle time) was 153.44±49.24 minutes. There was no significant difference ($p=0.862$) between the mean symptom-needle time (152.27±50.03) in the patient group aged 80 years and older and the patient group aged under 80 years (153.93±49.1). Details are shown in Table 2.

The patients included in our study were evaluated according to age groups and compared in terms of mean admission NIHSS score, ED toward or intensive care unit (ICU) intubation, need for mechanical ventilation, development of intracranial hemorrhage during follow-up, 1-month mRS, clinical outcome and mortality. Patients aged 80 years and older had a higher mean baseline NIHSS score 12.92±5.81, however, the difference did not reach statistical significance ($p=0.054$). Some parameters were determined as clinical outcome parameters for comparison in terms of treatment outcome. Since our patients were admitted to the ED, one of our primary outcome parameters was determined as the patient's transfer from the ED to the ward or ICU. In this context, no significant difference was found between the patient group aged 80 years and older and the patient group aged under 80 years ($p=0.426$). The need for mechanical ventilation was another outcome parameter, and in this context, there was no significant difference between patients under

80 years of age and patients aged 80 years or older ($p=0.191$). Regarding the clinical outcome, exitus was significantly higher in the group aged 80 years and older (30.8%) compared to the group under 80 years (12.3%) ($p=0.004$). Other outcome parameters were evaluated, including the 1-month mRS and duration of hospitalization, which is the time from admission to exitus or discharge. Patients aged 80 years and older had a significantly higher 1-month mRS (mean 3.63) compared to patients younger than 80 years (mean 2.56), in other words, the incidence of severe disability and/or death was significantly higher in patients aged 80 years and older ($p=0.002$). The mean duration of hospitalization was also significantly longer in patients aged 80 years and older (mean 22.96 days) than in patients younger than 80 years (mean 16.72 days) ($p=0.027$). Intracranial hemorrhagic complications after thrombolytic therapy was also evaluated. Intracranial hemorrhage was observed in 27.6% of all our patients ($n:174$); this rate was 28.8% in patients aged 80 years and older and 27.0% in patients younger than 80 years, which was similar ($p=0.808$). The prognosis and clinical outcome parameters and details are shown in table 2.

Table 2. Comparison of age groups according to symptom onset, clinical follow-up, prognosis and survival of patients

	≥ 80 years	< 80 years	P
	<i>mean$\pm$SD</i>	<i>mean$\pm$SD</i>	
Baseline NIHSS score	12.92 $\pm$ 5.81	11.03 $\pm$ 5.43	0.054
Symptom-to-door time, min	79.19 $\pm$ 41.22	75.70 $\pm$ 40.47	0.474
Door-to-needle time, min	73.08 $\pm$ 35.99	78.24 $\pm$ 33.22	0.265
Symptom-to-needle time, min	152.27 $\pm$ 50.03	153.93 $\pm$ 49.1	0.862
Duration of hospitalization	22.96 $\pm$ 24.36	16.72 $\pm$ 20.20	0.027*
mRS at 1 month	3.63 $\pm$ 2.12	2.56 $\pm$ 1.98	0.002*

	<i>n (%)</i>	<i>n (%)</i>	
Admitted to the ward from Emergency Department	26 (50.0)	69 (56.6)	0.426
Admitted to the ICU from Emergency Department	26 (50.0)	53 (43.4)	
Need for mechanical ventilation	22 (42.3)	39 (32.0)	0.191
Intracranial hemorrhage	15 (28.8)	33 (27.0)	0.808
Exitus	16 (30.8)	15 (12.3)	0.004*

Abbreviations: NIHSS, National Institutes of Health Stroke Scale; mRS, Modified Rankin Scale; ICU, intensive care unit; SD, standard deviation; min, minute.

The performance of thrombectomy in our patients was also evaluated. Accordingly, thrombectomy was performed in 34.5% (n=60) of all patients. Thrombectomy rates were similar for both age groups (p=0.17). Among the patients who underwent thrombectomy, 18.4% achieved complete recanalization (mTICI 3) (n=32). 10.3% achieved partial recanalization mTICI class 2B (n=18) and 3.4% achieved partial recanalization class 2A (n=6). Although thrombectomy was performed in 2.3% (n=4) of the patients, no recanalization (mTICI 1) was achieved. There was no significant difference between age groups according to recanalization rates (p=0.210). The findings are shown in Table 3.

Table 3. Comparison of age groups according to mechanical thrombectomy results

	≥80 years	<80 years	All Patients	p
mTICI score	<i>n (%)</i>	<i>n (%)</i>	<i>n (%)</i>	
No Thrombectomy	38 (73.1)	76 (62.3)	114 (65.5)	0.17
1	2 (3.8)	2 (1.6)	4 (2.3)	0.21

2A, 2B	7 (13.5)	17 (14.0)	24 (13.7)
3	5 (9.6)	27 (22.1)	32 (18.4)
Total	52 (100)	122 (100)	174 (100)

Abbreviations: mTICI, modified treatment in cerebral infarction; n, number.

Patients were evaluated using the modified Rankin score (mRS) to assess their prognosis according to age groups. Patients aged 80 years and older had a significant higher 1-month mRS score, indicating higher rates of severe disability and mortality compared to patients younger than 80, as shown in Table 4 (p=0.006).

Table 4. Comparison of 1-Month Modified Rankin Score by age groups

mRS	≥80 years	<80 years	All Patients	
	<i>n (%)</i>	<i>n (%)</i>	<i>n (%)</i>	p
0	4 (7.7)	18 (14.8)	22 (12.6)	
1	8 (15.4)	33 (27.0)	41 (23.6)	
2	7 (13.5)	15 (12.3)	22 (12.6)	
3	2 (3.8)	15 (12.3)	17 (9.8)	
4	11 (21.2)	15 (12.3)	26 (14.9)	
5	3 (5.8)	12 (9.8)	15 (8.6)	
6	17 (32.7)	14 (11.5)	31 (17.8)	
Total	52 (100)	122 (100)	174 (100)	0.006*

Abbreviations: n, number.

The patient's NIHSS scores at one week after treatment were also evaluated. Accordingly, analysis showed that patients under 80 years of age had lower clinical scores compared to older patients. While 25.0% of patients older than 80 years had high (>20) NIHSS scores, this rate was only 8.2% in patients younger than 80 years. The difference between the two groups was significant ($p=0.024$). Details are shown in Table 5.

Table 5. Comparison of 1-Week NIHSS by Age Groups

NIHSS score	≥ 80 years	< 80 years	p
	<i>n</i> (%)	<i>n</i> (%)	
< 5 (Mild)	17 (32.7)	55 (45.1)	
5-15 (Moderate)	19 (36.5)	47 (38.5)	
16-20 (Moderate-to-Severe)	3 (5.8)	10 (8.2)	
> 20 (Severe)	13 (25.0)	10 (8.2)	0.024**

Abbreviations: NIHSS, National Institutes of Health Stroke Scale; n, number.

Patients with intracranial hemorrhage after thrombolytic therapy were also evaluated according to the bleeding classification (ECASS-2). Hemorrhage occurred in a total of 48 patients (27.6%) after thrombolytic therapy. Of these, 37.5% were classified as hemorrhagic infarct type 1 (HI1), 22.9% as hemorrhagic infarct type 2 (HI2), 14.6% as parenchymal hemorrhage type 1 (PH1) and 25% as parenchymal hemorrhage type 2 (PH2). There was no significant difference in ECASS-2 classification according to age groups ($p=0.353$). The findings are shown in Table 6.

Table 6. Comparison of Post-Treatment Intracranial Hemorrhagic Complications by ECASS-2 Classification and Age Groups

	≥ 80 years	< 80 years	All Patients	p
ECASS-2 classification	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	0.353

HI1	4 (%26.7)	14 (%42.4)	18 (%37.5)
HI2	5 (%33.3)	6 (%18.2)	11 (%22.9)
PH1	1 (%6.7)	6 (%18.2)	7 (%14.6)
PH2	5 (%33.3)	7 (%21.2)	12 (%25.0)
Total	15 (%100)	33 (%100)	48 (%100)

Abbreviations: ECASS, European Cooperative Acute Stroke Study; n, number.

The association between the presence of intracranial hemorrhage and clinical outcome was also compared between age groups. Accordingly, 17 (54.8%) of the 33 patients who died had an intracranial hemorrhage, while 27.3% of the patients who were discharged had an intracranial hemorrhage. The presence of hemorrhage in deceased patients was similar between age groups ($p=0.870$). Similarly, the presence of intracranial hemorrhage in discharged patients did not differ significantly across age groups ($p=0.937$). Details are shown in Table 7.

Table 7. Association between mortality status and presence of intracranial hemorrhage by age groups

Outcome	Intracranial Hemorrhage status	p		
		≥80 years	<80 years	All Patients
		<i>n (%)</i>	<i>n (%)</i>	<i>n (%)</i>
Discharged, Alive	No Hemorrhage	26 (72.2)	78 (72.9)	104 (72.7)
	Hemorrhage present	10 (27.8)	29 (27.1)	39 (27.3)
	Total	36 (100)	107 (100)	143 (100)
Exitus	No Hemorrhage	7 (43.8)	7 (46.7)	14 (45.2)

Hemorrhage present	9 (56.3)	8 (53.3)	17 (54.8)	0.870
Total	16 (100)	15 (100)	33 (54.8)	

Abbreviations: n, number.

DISCUSSION

In our study, complications following thrombolytic therapy (intracranial hemorrhage, mortality) did not differ between older (≥ 80) and younger (< 80) groups among patients who presented to the ED with acute ischemic stroke and received IV thrombolytic therapy. The length of hospital stay in the elderly patient group was longer than in younger patients, and mRS scores were higher.

In the Canadian Alteplase for Stroke Effectiveness Study (CASES), a prospective analysis comparing alteplase treatment outcomes in ischemic stroke, 63% of patients aged 80 years and older were female, a significantly higher proportion than in the younger group (7). Similarly, in a study conducted by Berrouschot *et al.* That examined the complications and outcomes of thrombolytic therapy in patients with ischemic stroke by age groups, 60.5% of patients aged 80 years and older were female, a significantly higher proportion than in the younger group (8). In our study, females were significantly more prevalent in the group aged 80 years and older (63.5%), supporting previous studies.

In our study, when risk factors were compared between the elderly and young groups, it was observed that the prevalence of a history of HT was significantly higher in the group aged 80 years and older. In the CASES study, a significantly higher prevalence of history of HT was observed in the patient group aged 80 years and older compared to the younger group (7). In their study comparing IV thrombolytic therapy in acute stroke in elderly and young patients, Mouradian *et al.* observed a significantly higher prevalence of history of HT in the 80 years and older group (9). Our study supported these studies in the literature when the history of HT was compared in the elderly and young patient groups.

In the Engelter *et al.* study, when patients with acute ischemic stroke who underwent thrombolytic therapy were grouped and compared as 80 years of age or older and younger than 80 years of age,

a significantly higher proportion of patients had a history of AF was observed in the elderly group. In the CASES study, prevalence of AF history was also observed at a significantly higher rate in the elderly group. In a study conducted by Pego *et al.*, patients aged 80 years and younger who underwent thrombolytic therapy were compared with patients older than 80 years. In this study, AF was observed at a significantly higher rate in the elderly group compared to the younger group (7,10,11). In our study, AF was observed at a significantly higher rate in the group aged 80 years and older than in the younger group, which supports other studies.

Wang *et al.* compared the risk factors, in-hospital treatment and follow-up management and 1-year follow-up results in patients with acute ischemic stroke with the group aged 80 years and over and the group aged under 80 years and found that active smoking history was significantly higher in the younger group. Naess *et al.* found that smoking history was significantly higher in the younger group in their study comparing patients under and over 80 years of age with ischemic stroke. Similarly, in the CASES study and the study conducted by Pego *et al.*, smoking history was significantly higher in younger patient groups (7,11,12). In our study, although a higher rate of smoking history was observed in the younger patient group compared to the older group, the difference was not statistically significant. This difference may be explained by the relatively small sample size and the lack of complete data in the retrospectively analyzed patient files.

In the study by Engelter *et al.* compared a group aged 80 years and older who had acute ischemic stroke and received thrombolytic therapy with a group aged younger than 80 years, DM, hypercholesterolemia, coronary artery disease and history of previous stroke were not significantly different between the two groups in terms of risk factors (10). Similarly, in our study, the presence of these risk factors did not differ significantly between the older and younger groups.

In our study, it was found that the proportion of patients with congestive heart failure, one of the risk factors, was not significantly different in the elderly group compared to the young group. Similarly, no significant difference was observed between both groups in the study conducted by Pego *et al.* (11). However, the prevalence of congestive heart failure was significantly higher in the elderly group in the CASES study (7). This difference may be explained by the limited number of patients in the studies and demographic differences.

Immovilli *et al.* found that the prevalence of premorbid anticoagulant and antiaggregant use were not significantly different between the group under 80 years of age and the group aged 80 years and over in their stroke study (13). In our study, similarly, it was found that the prevalence of anticoagulant and antiaggregant use were not significantly different between both groups.

In the study conducted by Son *et al.* patients aged 80 years and older with acute ischemic stroke who underwent thrombectomy were compared with those under 80 years of age. Reperfusion status, assessed using the TICI scoring system, was not found to differ significantly between the older and younger groups (14). In a similar study conducted by Azkune Calle *et al.*, it was observed that recanalization rates were not significantly different between the older and younger groups (15). In our study, when the outcomes of mechanical thrombectomy performed in patients eligible for endovascular intervention were evaluated, no significant difference in recanalization was found between the older and younger groups, and the results were consistent with previous studies.

In the CASES study, patients aged 80 years and older who received thrombolytic therapy were compared with those under 80 years of age in terms of long-term outcomes, including mortality and mRS scores (7). As a result, MRS and mortality rates were significantly higher in the elderly group compared to the younger group. This was consistent with the results of previous studies, showing that advanced age increased the risk for mortality and morbidity in ischemic stroke. Similarly, in our study, 1-month MRS and mortality rates were higher in the elderly patient group compared to the younger patient group.

In the study by Pego *et al.*, baseline NIHSS scores at presentation to the ED were significantly higher in the elderly group compared to the younger group (11). Similarly, in the CASES study and the study by Immovilli *et al.*, baseline NIHSS scores at presentation to the ED were significantly higher in the elderly group (7,13). In our study, although the baseline NIHSS scores at presentation to the ED were higher in the patient group aged 80 years and older compared to the younger group, the result was not significant. However, the result was close to statistical significance. This may be explained by the small sample size of our study compared to other studies.

In the study by Mouradian *et al.* evaluating the prognosis of patients aged 80 years and over and patients aged less than 80 years who had ischemic stroke and received IV thrombolytic therapy,

in-hospital mortality was significantly higher in the elderly group (9). In a study conducted by Saposnik *et al.*, patients admitted to hospital due to acute ischemic stroke were evaluated in terms of prognosis according to age and in-hospital mortality was significantly higher in the group aged 80 years and older compared to the younger group (16). In our study, when both groups were compared in terms of in-hospital clinical outcome, it was observed that mortality was significantly higher in the older group compared to the younger group.

Saposnik *et al.* found significantly longer hospitalization times in the patient group aged 80 years and older compared to the younger group (16). In our study, similarly, hospitalization times were significantly longer in the elderly group compared to the younger group.

In the CASES study, complications following thrombolytic treatment were compared between age groups, and no significant difference was found in the rates of intracranial hemorrhage between the elderly and younger patients (7). In similar studies conducted by Engelter *et al*, Pego *et al*, Immovilli *et al*, no significant difference was observed between the elderly patient group and the young patient group in terms of intracranial hemorrhage complication rates (10,11,13). In our study, in accordance with the literature, intracranial hemorrhage rates were similar between patients aged 80 years and older and those younger than 80.

In the study by Costello *et al.* patients aged 80 years and older who received thrombolytics after ischemic stroke were compared with younger patients regarding intracranial hemorrhage complications. A total of 41 patients with intracranial hemorrhage were radiologically classified according to the ECASS II classification. When patients with intracranial hemorrhage, parenchymal hematoma and hemorrhagic transformation were compared across age groups, similar results were observed between the elderly and younger groups (7). In our study, when we grouped the patients who had intracranial hemorrhage after treatment as HI1, HI2, PH1, PH2 according to ECASS 2 classification, no significant difference was found between patients aged 80 years and older and those younger than 80 years.

In the Castello *et al.* study, no significant difference was observed between the elderly and younger groups in terms of mortality in patients with intracranial hemorrhage (17). In the CASES study,

rates of intracranial hemorrhage, symptomatic intracranial hemorrhage and fatal intracranial hemorrhage complications were similar between elderly and younger groups following thrombolytic therapy (7). In our study, the rates of intracranial hemorrhage following IV thrombolytic therapy were found to be similar between patients aged 80 years and older and those younger than 80 years, both among patients who died during hospitalization and those who were discharged, consistent with previous report in the literature.

In the study by Pego *et al.*, week 1 NIHSS scores after thrombolytic treatment were significantly higher in patients aged 80 years and older compared to those younger than 80 years (11). In our study, patients were classified as having mild, moderate, moderate-to-severe or severe stroke based on their NIHSS scores at week 1. When patients aged 80 years and older were compared with those younger 80 years, the older group was significantly more likely to be classified in the higher severity categories. Although our study employed a different methodology, the poorer prognosis observed in the elderly group, as assessed by NIHSS, was consistent with findings in the literature.

Limitations

There are some limitations in our study. One of them is that it was retrospective. Another limitation of the study is the limited number of patients. In addition, long-term (6 years, 1 year) follow-up of our patients could not be performed.

CONCLUSION

Although the prognosis of acute ischemic stroke patients was poorer in the elderly population compared to the younger population, the complication rates after IV thrombolytic therapy and the associated mortality rates were similar to the younger group. Therefore, patients eligible for treatment of acute ischemic stroke should be transferred to stroke centers regardless of age, and thrombolytic therapy should be administered.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available for sharing by the corresponding author upon request.

Author Contributions

AE, MA—provided the main framework, identified, and organized primary materials, and collaborated in writing the manuscript. AE, MA—identified appropriate references and collaborated on the writing of the manuscript. AE, MA—reviewed and contributed to drafting sections of the manuscript. All authors have read and agreed to the published version of the manuscript.

Ethics Approval and Consent to Participate

The study was performed after the approval of institutional ethics committee (University of Health Sciences Sisli Hamidiye Etfal Training and Research Hospital Health Application and Research Center Clinical Research Ethics Committee, decision no: 3424, dated: 22/02/2022) in accordance with the Declaration of Helsinki. Participation was voluntary and informed consent was obtained from all participants.

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Conflict of Interest

The authors declare no conflict of interest.

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ARAŞTIRMA MAKALESİ

RESEARCH ARTICLE

PROTECTIVE EQUIPMENT AND RISK FACTORS IN E-SCOOTER INJURIES: A RETROSPECTIVE STUDY

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ABSTRACT

Background: The increasing use of electric scooters (e-scooters) as an alternative transportation method has led to a significant increase in related injuries, especially in metropolitan areas. However, detailed analysis of injury patterns and clinical features of e-scooter accidents is still limited in the literature. Aim: This study aims to analyze the demographic characteristics, clinical features, and trauma patterns of e-scooter-related injuries presenting to the emergency department of a tertiary hospital. Materials and Methods: A retrospective analysis was conducted on 110 patients presenting to the emergency department with e-scooter-related injuries between January 2019 and December 2024. Patient demographics, accident characteristics, clinical findings, and outcomes were evaluated. Injury severity was assessed using the Injury Severity Score (ISS) and the Glasgow Coma Scale (GCS). Results: Most patients were young with a mean age of 19.3±12.0 years. The majority of accidents (68.3%) occurred without a collision and 86.4% of drivers were not wearing helmets. Head trauma (40%) and upper extremity injuries (31.8%) were the most common. The majority of patients (75.0%) were classified as minor trauma (ISS<9) and 86% were treated as outpatients. Most accidents occurred on weekdays (75.0%) and predominantly in the afternoon (51.7%) between 12:00 and 18:00. Advanced age, not wearing a helmet and using it in the evening pose a risk for serious trauma. Conclusion: Although e-scooter accidents predominantly result in minor trauma and soft tissue injuries, the implementation of strict protective equipment regulations and the development of appropriate infrastructure may help prevent these injuries.

Keywords: Electric scooter; emergency department; mode of injury; severity of trauma; protective equipment

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INTRODUCTION

Electric scooters (e-scooters) stand out among micromobility vehicles and are increasingly being used as an alternative transportation method, especially in metropolitan areas with heavy traffic. In cities with high population density, e-scooter sharing systems have been adopted as an integrated solution for public transportation and the number of users has increased to remarkable levels [1,2]. However, this rapid proliferation process has also raised significant security concerns. In recent years, injuries related to e-scooter use have been encountered with increasing frequency in emergency departments (ED). E-scooter accidents, especially in metropolitan areas, are a significant cause of morbidity in the young adult population and lead to a significant increase in ED visits [2,3]. Due to the increased use of e-scooters, such injuries pose a serious burden for emergency services and imaging requirements are significantly higher [3,5]. In recent years, it has been reported that inadequate use of protective equipment and inadequate infrastructure are the main factors that increase the risk of accidents in injuries related to e-scooter use [4,6]. Understanding the characteristics and risk factors for injuries related to e-scooter use is critical to developing effective prevention strategies. In this context, detailed analysis of injury patterns, demographic characteristics, and clinical outcomes is important for both optimizing ED management strategies and developing long-term preventive measures.

The aim of this study is to analyze the epidemiological features, clinical characteristics and trauma patterns of e-scooter injuries admitted to the ED of a tertiary hospital and to contribute to the development of preventive strategies in the light of the obtained data.

Material sand Methods

This retrospective cohort study was conducted in the Emergency Department of Aksaray Training and Research Hospital between January 1, 2019 and December 30, 2024. We received local ethics approval before the study (ethics committee number: 17.10.2023/227085176). The hospital where the study was conducted is a primary trauma center and serves an average of 3000 trauma patients per month. Patients who were admitted to the ED trauma center as a result of electric and/or non-electric scooter accidents were included in our study. Patients were divided into three groups: under 18 years of age, between 19-40 years of age, and over 40 years of age. Patients with a Glasgow Coma Score (GCS) of less than 15 or an Injury Severity Score (ISS) of 25 and above were considered to have Severe Trauma. These patients were divided into two groups: those with and without severe trauma. Patients were divided into 5 groups according to their injury sites: head trauma, spinal trauma, thoracic trauma, abdominal trauma and extremity trauma. If more than 2 systems were involved, it was defined as multiple system trauma. Patients with missing data in hospital records were excluded from the study. The study was conducted in accordance with the principles of the Declaration of Helsinki. Due to the retrospective design, patient consent was not required.

2.2. Study protocol and Data Collection

The study data were obtained from hospital electronic patient records. Demographic data of the patients, such as age, gender and time of accident, were recorded. Clinical findings such as vital signs, Glasgow Coma Score (GCS), Injury Severity Score (ISS), and injury sites were extracted from the database. In addition, variables such as the mechanism of the accident (collision with

motor vehicle/collision with scooter/hitting pedestrian/hitting bicycle/hitting stationary), driver/passenger status, use of protective equipment, accident site (pavement/main road/side road/other), alcohol and substance use were also obtained. Hospitalization, intensive care unit admission and mortality rates were evaluated.

2.3. Statistical Analysis

SPSS version 25.0 (IBM Corp., Armonk, NY, USA) was used for the statistical analysis of the data. When analyzing categorical variables, the Chi-Square Test or Fisher's Exact Test was used in comparisons between groups. In two-group comparisons of continuous variables, the Student's T-test was used for normal distribution, while the Mann-Whitney U test was used for non-normal distribution. In comparing three or more groups, One-Way Analysis of Variance (ANOVA) and post-hoc Tukey tests were used in normal distribution, while Kruskal-Wallis test and post-hoc Dunn tests were used in non-normal distribution.

Univariate and multivariate logistic regression analysis was applied to determine risk factors for severe trauma and mortality. Variables with a p value below 0.2 in univariate analysis were included in multivariate analysis. The statistical significance level was considered as a $p < 0.05$.

RESULTS

Of the 110 e-scooter accident cases included in the study, 64.5% (n=71) were male, while the mean age of the cases was 19.3 ± 64.5 years. The most common applicants are those under the age of 18. The characteristics of the patients in the study are given in Table 1.

Table 1. Demographic and Clinical Characteristics of E-Scooter Accidents (n=110)

Characteristics	n (%) or mean±SD
Demographics	
Age (years)	19.3±12.0
Age groups	
- <18	63 (57.3)
- 18-40	41 (37.3)
- >40	6 (5.4)
Gender	
- Male	71 (64.5)
- Female	39 (35.5)
Accident Characteristics	
Accident mechanism	
- Collision with motor vehicle	15 (13.6)
- Collision with fixed object	95 (86.4)
Protective equipment	
- Helmet use	25 (22.7)
- No helmet	85 (77.3)
Clinical Severity	
GCS (median, IQR)	15 (15-15)

Characteristics	n (%) or mean±SD
ISS (median, IQR)	4 (0-8)
Hospital Outcome	
Discharge from ED	105 (95.5)
Hospital admission	5 (4.5)

Considering the injury mechanism, 86.4% of the cases occurred by hitting a fixed object. Considering the injury location, head trauma (40.0%) was the most common, followed by extremity (31.8%) and pelvis (21.8%) injuries (figure 1). Additionally, accidents occurred most frequently (39.1%) in the evening hours (16:00-24:00) (figure 2).

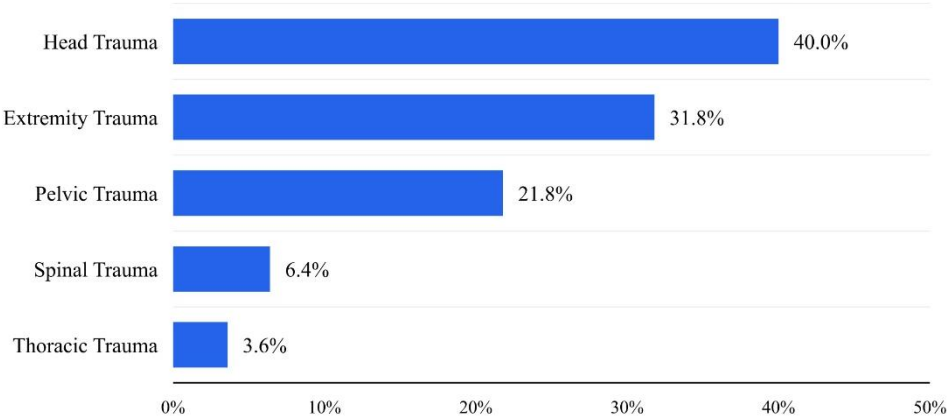


Figure 1. Distribution of Injury Locations in E-Scooter Accidents

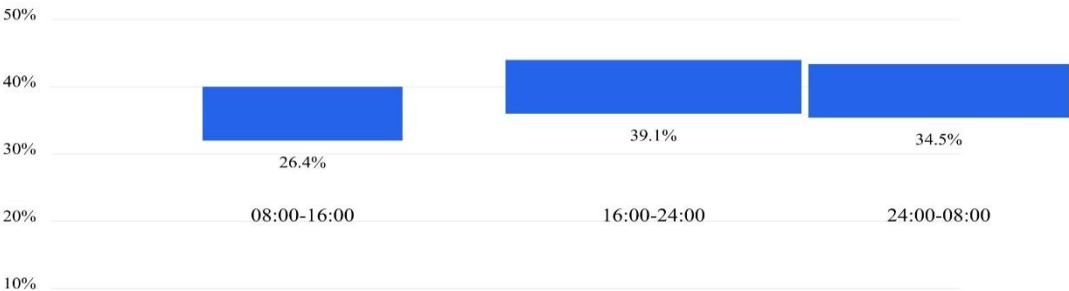
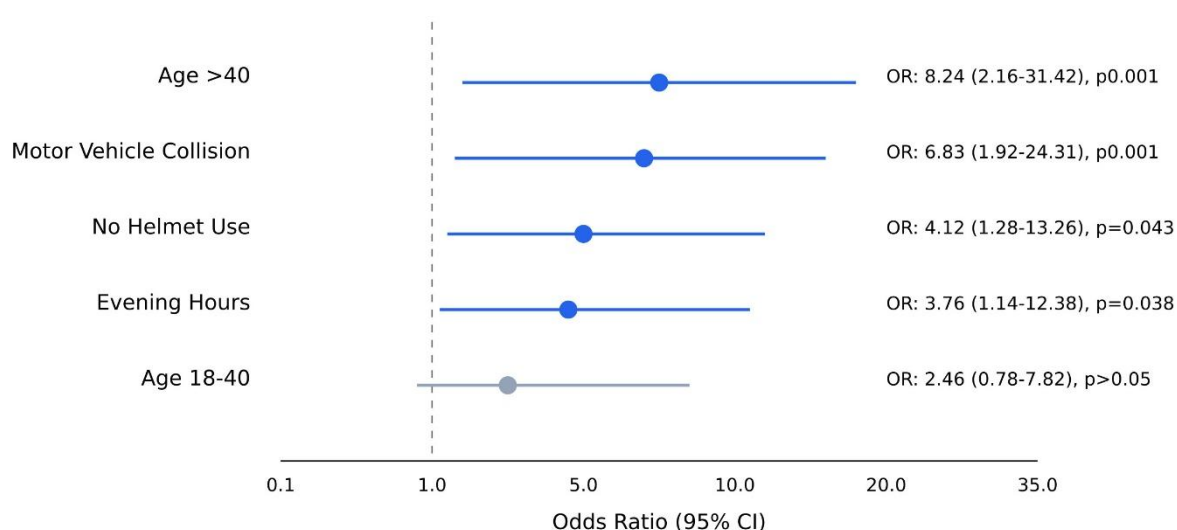


Figure 2. Temporal Distrubition of E-Scooter Accidents

Only 3 of the cases were identified as having serious trauma, and the patients of these 3 cases were not using protective equipment. In univariate logistic regression analysis, older age (OR: 8.24, 95% CI: 2.16-31.42, $p<0.001$), not using a helmet (OR: 4.12, 95% CI: 1.28-13.26, $p=0.043$) and accident in the evening hours (OR: 3.76, 95% CI: 1.14-12.38, $p=0.038$) were found to be significant risk factors for serious injury. Considering the age groups, 66.7% of serious injuries occurred in the over 40 age group. Risk factors associated with serious injury are given in figure 3.



Note: Horizontal lines represent 95% confidence intervals. Blue dots indicate statistically significant risk factors ($p<0.05$).

Figure 3. Risk for Severe Injury in E-Scooters Accidents

The effect of helmet use on head trauma is given in Table 2. The helmet use rate in the study population was 13.6%. The head trauma rate was 26.6% in helmet users, while this rate was 40.0% in those not using helmets ($p=0.043$). Considering the severity of head trauma, two serious head traumas (2.2%) and six skull fractures (6.3%) were found in the non-helmet group, while no serious head trauma or skull fractures were found in the helmet group ($p=0.029$). All five cases requiring hospitalization were in the non-helmet group ($p=0.040$).

Table 2. Analysis of Head Trauma Based on Protective Equipment Use

Variables	Helmet Use (n=15)	No Helmet (n=95)	p value
Head trauma presence	4 (26.6)	40 (42.1)	0.043
Head trauma severity			0.038
- No injury	11 (73.4)	55 (57.9)	
- Minor injury	4 (26.6)	38 (40.0)	
- Severe injury	0 (0.0)	2 (2.1)	
Type of head injury			0.029
- Facial injury	4 (26.6)	20 (21.1)	
- Epidural hemorrhage	0 (0.0)	1 (1.1)	
- Subdural hemorrhage	0 (0.0)	1 (1.1)	
- Skull fracture	0 (0.0)	6 (6.3)	
Associated factors			
- Evening accidents (16:00-24:00)	8 (53.3)	35 (36.8)	0.042
- Motor vehicle collision	2 (13.3)	13 (13.6)	0.034
Hospital admission	0 (0.0)	5 (5.3)	0.040

Data are presented as mean $\pm$ standard deviation Median and 25th–75th percentiles or n (%), *. p-value < 0.05

DISCUSSION

Electric scooters are now widely used as an alternative means of transport, especially in large cities[3,5]. A study by Badeau et al examining emergency department presentations reported a significant increase in the use of e-scooters in urban areas and a parallel increase in injuries [7]. Trivedi et al reported that the use of helmets and protective equipment by e-scooter users was very low and that head trauma consisted 40% of injuries, followed by extremity injuries at a rate of 31% [2]. A retrospective cohort study by Blomberg et al highlighted inadequate use of protective equipment and a significant association between injury severity and helmet use [8]. In our study, we found that the use of helmets and protective equipment was very low (13.6%) and that no helmet or protective equipment was used in those with severe trauma. We also found that older age and accidents occurring during the evening hours were risk factors for severe trauma.

A large series study by Kobayashi et al reported that minor trauma (ISS<9) was observed in 58% of e-scooter injuries and that the majority of cases were treated as outpatients [9]. In the comparative analysis by McGuinness et al, it was emphasised that single system injuries were more common in e-scooter accidents and this was particularly associated with low energy trauma [10]. In a study by Beck et al analysing emergency department visits following the launch of e-scooter sharing systems, they emphasised that minor severe injuries were most common, which may be related to the inexperienced user profile [1]. Similar to the literature, we found that 75% of the patients in our study were in the minor trauma group (ISS<9), predominantly had soft tissue injuries and the majority (86%) were treated as outpatients.

A study conducted by Amin et al in a level 1 trauma centre reported that a significant proportion of e-scooter injuries were observed in young adults and that cases requiring orthopaedic surgery were concentrated in this age group [11]. In similar studies, the proportion of e-scooter

injuries under the age of 18 years varies between 38-64% [3-8]. In our study, 57.3% of the cases were under 18 years of age and 13.7% were 15 years of age or younger, showing that the age limit for e-scooter use is not respected.

The study by Aizpuru et al, using the national electronic surveillance system, reported that extremity trauma was predominant in e-scooter injuries and this was closely related to the fall mechanism [5]. In the study by Mayhew et al examining emergency department imaging patterns, it was highlighted that a significant proportion of e-scooter injuries involved extremity trauma and required radiological assessment, which had a significant impact on emergency department resources [4]. The comparative analysis by McGuinness et al highlighted that single system injuries were more common in e-scooter accidents [10]. In the study by Namiri et al evaluating hospital admissions between 2014 and 2018, it was reported that e-scooter injuries were mostly treated as outpatients, with head and extremity trauma being the most common [12]. Similar to these studies, we found 40% head trauma and 31.4% extremity trauma in our study.

In our study, 75% of e-scooter accidents occurred on weekdays and it was observed that accidents occurred most frequently between 12:00-18:00 (51.7%). In a study by Vernon et al in a metropolitan area, it was emphasised that accidents were concentrated during rush hours and suggested that this may be related to traffic density [3]. McGuinness et al reported that 51.1% of scooter accidents occurred in the evening hours [11].

Although our study highlights important issues in e-scooter injuries, it also has some limitations. Firstly, the generalisability of our findings is limited due to it's the single centre design and relatively small cohort size. Secondly, not all data were available due to the retrospective design of the study.

CONCLUSION

In conclusion, we can say that injuries caused by e-scooters are traumas which mainly affect the young population, mostly affect the extremities and the head and neck, and tend to occur on working days and in the evenings. The low helmet use rate of 13.6% and the fact that there was never any helmet use reported in patients with severe trauma underlines the importance of safety measures. We found that advanced age and use in the evening hours were risk factors for severe trauma, just like lack of helmet use. These findings suggest that for safe e-scooter use, the use of protective equipment should be widespread and made a legal requirement, and that the use of e-scooters should be restricted after certain hours, especially in large cities. In addition, public awareness should be increased and infrastructure facilities should be improved. Future multicentre studies will be useful to evaluate the effectiveness of these recommendations.

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ARAŞTIRMA MAKALESİ

RESEARCH ARTICLE

**ENDOTHELIUM-DEPENDENT MODULATION OF
AGOMELATINE IN RAT THORACIC AORTA**

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ABSTRACT

Objective: This study aimed to investigate the vasomodulatory effects of agomelatine, a melatonergic antidepressant, on rat thoracic aorta tissue with and without endothelial integrity. **Methods:** Twelve male Wistar Albino rats (250–300 g) were divided into two groups: endothelium-intact and endothelium-denuded thoracic aorta rings. Isolated aortic rings were mounted in an organ bath system and precontracted with phenylephrine (10^{-6} M). Agomelatine was then applied cumulatively (10^{-8} – 10^{-4} M). Contractile responses were recorded, and endothelial damage was confirmed using acetylcholine (10^{-6} M). Data were analyzed using SPSS software, and statistical comparisons were made using one-way ANOVA followed by Tukey's post hoc test. A p-value of < 0.05 was considered statistically significant. **Results:** In the endothelium-intact group, agomelatine induced a statistically significant, dose-dependent vasodilation compared to baseline and phenylephrine-induced contraction ($p < 0.05$). In contrast, the endothelium-denuded group showed no significant vasodilatory response to agomelatine ($p > 0.05$), indicating the necessity of an intact endothelium for its effect. **Conclusion:** Agomelatine exerts a concentration-dependent vasodilatory effect that is dependent on endothelial integrity. These findings suggest a potential vascular benefit of agomelatine in patients with preserved endothelial function and support its cardiovascular safety profile, especially in those with comorbid depression and cardiovascular disease.

Keywords: Agomelatine; Endothelium; Vasodilation; Depression; Cardiovascular Disease; Aorta

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INTRODUCTION

Cardiovascular diseases (CVD), particularly in the elderly, place a significant burden on public health systems, mainly due to the high prevalence of multiple comorbidities in this population [1]. CVD broadly encompasses various alterations in cardiac function, such as systolic and diastolic dysfunctions, along with electrical disturbances of the heart manifested through different types of arrhythmias [2]. Depression often coexists with CVD. One in every five patients with coronary artery disease or heart failure suffers from depression. CVD and depression negatively impact overall quality of life, especially among patients with heart failure. Individuals with depression are at a higher risk of developing CVD over time and exhibit higher mortality rates compared to the general population. Furthermore, patients suffering from both CVD and depression tend to experience worse disease progression [3].

Behavioral and biological mechanisms have been investigated as potential pathways linking depression to increased cardiovascular disease (CVD) risk. In the context of hypertension, some studies suggest that depression may elevate cardiovascular risk by reducing the normal nocturnal drop in blood pressure [3]. The worsening of major depressive disorder or previous mood disorders is commonly observed as an adverse outcome in patients with coronary artery disease (CAD), heart failure, and those undergoing cardiac revascularization procedures [4]. Although the beneficial effects of antidepressant therapy in cardiac patients are well established, the use of certain antidepressants has been associated with adverse cardiac and extracardiac events, which may not only decrease survival but also increase morbidity and mortality [5]. Notably, several clinical cases emphasize the importance of individualized treatment strategies, particularly with newer antidepressant options, to minimize side effects [6].

Although various pharmacological and behavioral therapies are available for the treatment of depression, the most effective strategy for reducing mortality risk associated with coexisting depression and CVD remains unclear. In patients exhibiting both CVD and depressive symptoms, the identification of alternative therapies that directly target disrupted biological pathways is becoming increasingly important [7]. Depression is common in older adults and individuals with CVD. While selective serotonin reuptake inhibitors (SSRIs) are generally considered safe for treating depression in this population, identifying additional antidepressant options becomes essential when SSRIs prove ineffective. With careful administration and attention to each drug's potential adverse effects, such alternatives may offer safe and effective treatment options for elderly individuals and patients with cardiovascular comorbidities who do not respond to SSRIs [8]. Depression has been reported to be associated with reduced melatonin levels. Moreover, melatonin secreted during the night is believed to play a regulatory role in blood pressure control [9].

Agomelatine is known as a melatonin analogue among antidepressant agents [10]. It acts as a melatonergic receptor agonist and a serotonin (5-HT_{2C}) receptor antagonist. Its effects on mood

disorders and insomnia are mediated through melatonin type 1 and type 2 receptors (MT1 and MT2) [11].

Further research is needed to evaluate the safety and efficacy of antidepressants like agomelatine in this specific patient population. The aim of the present study is to investigate the endothelium-dependent effects of agomelatine on contractile force in rat thoracic aorta tissue.

MATERIAL AND METHODS

This study was approved by the Necmettin Erbakan University Experimental Medicine Application and Research Center Animal Ethics Committee (approval date: 20.02.2025; decision number: 2025-020). A total of 12 male Wistar Albino rats, aged 12 weeks and weighing 250–300 grams, were included in the study. The animals were housed under controlled conditions with a 12-hour light/12-hour dark cycle, at a constant room temperature of 24°C and a relative humidity of 55–60%. During the experimental period, they were provided with ad libitum access to standard rat chow and fresh water. After a 7-day acclimatization period, the experimental groups were formed.

For isolated organ bath experiments, the rats were anesthetized and sacrificed by decapitation, after which their thoracic aorta tissues were rapidly excised. The aorta segments were immediately placed in Krebs solution and transferred to the isolated organ bath system for functional analysis.

The isolated organ bath is a system that maintains the viability of excised tissues under in vitro conditions. The setup includes an amplifier, tissue chambers, isometric force transducers, a thermostatically controlled circulating pump, O₂–CO₂ gas mixture tubing, a recording unit, and fluid and gas delivery apparatus.

To preserve tissue viability within the isolated organ bath, Krebs solution is used, which mimics in vivo physiological conditions to a significant extent. The solution allows smooth muscle tissues to maintain their contractile properties under in vitro conditions. The composition of the Krebs–Henseleit solution used in the experiments includes: sodium chloride (NaCl), potassium chloride (KCl), potassium dihydrogen phosphate (KH₂PO₄), magnesium sulfate (MgSO₄), sodium bicarbonate (NaHCO₃), calcium chloride (CaCl₂), glucose (C₆H₁₂O₆), and ethylenediaminetetraacetic acid (EDTA).

After removal of tissue and blood residues in the Krebs solution, the thoracic aorta was cut into rings approximately 3–4 mm in length. These rings were mounted in the organ bath chambers in the transverse plane, which were filled with Krebs solution, maintained at 37°C, and continuously gassed with a mixture of 95% O₂ and 5% CO₂.

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To facilitate spontaneous contractions, the resting tension was set to 2 grams. Changes in isometric tension of the aortic rings were recorded using a four-channel isometric force transducer system. Following tissue mounting, the rings were washed every 15 minutes over a 45-minute period to minimize the effects of anesthetic agents.

Contractions were induced by adding phenylephrine (PE, 10^{-6} M) to the organ bath chambers. In half of the aortic segments from each group, endothelial injury was induced mechanically. Endothelial integrity was verified using acetylcholine (ACh, 10^{-6} M); lack of vasorelaxation confirmed successful endothelial denudation. These injured strips were then washed for 45 minutes to eliminate residual anesthetic effects, after which a second dose of PE was administered.

All contraction responses were recorded using the isolated organ bath system. Once a stable contraction plateau was achieved after PE administration, cumulative concentrations of agomelatine (10^{-8} to 10^{-4} M) were applied to both groups. Isometric contraction parameters were evaluated at three key points: 15 minutes before PE administration, 15 minutes after PE, and following each dose of agomelatine [12,13].

Experimental Design

Group 1 (Endothelium-Intact Aorta Group, n=6):

Maximum contractions were recorded following the administration of phenylephrine (PE, 10^{-6} M) into the organ bath chambers. Once a stable contraction plateau was achieved, cumulative concentrations of agomelatine (10^{-8} to 10^{-4} M) were applied. Isometric tension was measured at spontaneous contraction, after PE-induced contraction (15 min), and following each concentration of agomelatine.

Group 2 (Endothelium-Denuded Aorta Group, n=6):

Mechanical endothelial injury was induced in the aortic segments. PE (10^{-6} M) was applied to the organ bath chambers to record maximum contractions. Subsequently, acetylcholine (ACh, 10^{-6} M) was administered to confirm endothelial damage; the absence of relaxation verified successful denudation. After confirming damage, a second dose of PE was administered and contractions were again recorded. Once a contraction plateau was reached, cumulative doses of agomelatine (10^{-8} to 10^{-4} M) were applied. Isometric tension was measured at spontaneous contraction, after PE-induced contraction (15 min), and following each concentration of agomelatine.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics program. Data are expressed as mean $\pm$ standard error of the mean (SEM). Comparisons between multiple groups were conducted using one-way ANOVA followed by post hoc Tukey's test for normally distributed data. For non-

parametric data, the Kruskal–Wallis test was used. A p-value less than 0.05 ($p < 0.05$) was considered statistically significant.

RESULTS

In the endothelium-intact aorta group (Group 1), administration of phenylephrine (PE, 10^{-6} M) significantly increased the contractile tension compared to spontaneous contraction (SC) ($p < 0.05$). Following this, cumulative doses of agomelatine (10^{-8} to 10^{-4} M) were applied. A significant reduction in contraction force was observed at 10^{-5} and 10^{-4} M doses compared to the PE-induced contraction level ($p < 0.05$), indicating an endothelium-dependent vasodilatory effect of agomelatine at lower concentrations.

Furthermore, the highest dose of agomelatine (10^{-4} M) also showed a significant difference compared to both PE and agomelatine 10^{-8} M ($p < 0.05$), suggesting a dose-responsive vasorelaxant action. These findings support the notion that agomelatine, in the presence of intact endothelium, exerts a concentration-dependent vasodilation, likely mediated through endothelial signaling mechanisms (Fig. 1).

In the endothelium-denuded aorta group (Group 2), mechanical removal of the endothelium was confirmed by the absence of relaxation in response to acetylcholine (ACh, 10^{-6} M), indicating successful denudation. PE was re-administered to induce maximal contraction, followed by cumulative agomelatine dosing (Fig. 2).

In contrast to the intact group, agomelatine failed to induce significant relaxation or inhibition of contraction at any dose in the denuded group. Contraction levels remained statistically comparable to PE alone. These results suggest that agomelatine's vasodilatory effect is endothelium-dependent, and that its action is likely mediated via endothelial-derived relaxing factors (e.g., nitric oxide or prostacyclin).

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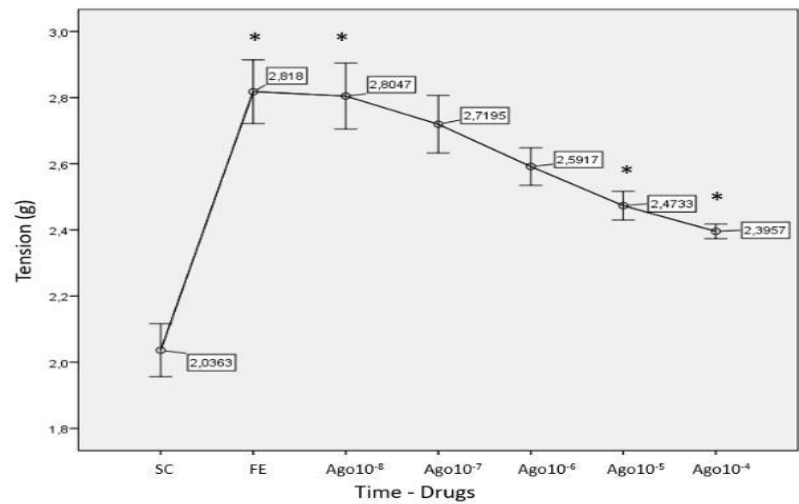


Figure 1. Vasodilatory effect of cumulative agomelatine doses on phenylephrine-induced contraction in endothelium-intact aortic rings (Group 1). Agomelatine induced a dose-dependent reduction in contractile tension following PE administration. *p < 0.05 vs. both spontaneous contraction (SC) and phenylephrine (PE) values.

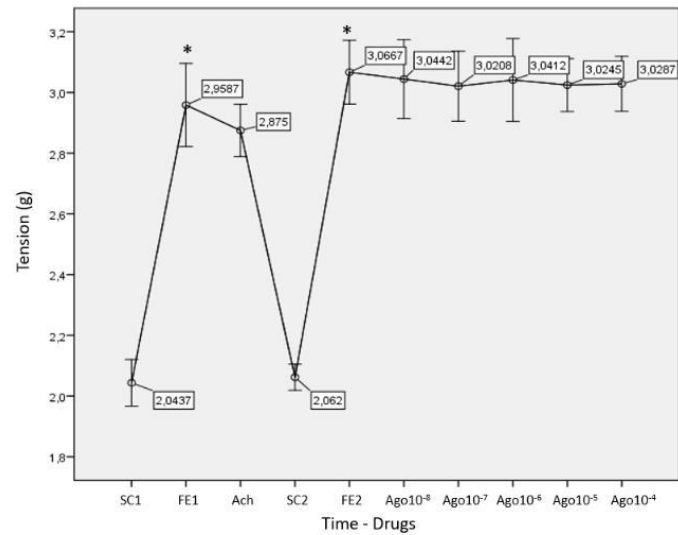


Figure 2. Effect of cumulative agomelatine doses on phenylephrine-induced contraction in endothelium-denuded rat aortic rings (Group 2). Following phenylephrine-induced contraction (FE2), cumulative doses of agomelatine (10⁻⁸ to 10⁻⁴ M) failed to reduce contractile tension, indicating the absence of an endothelium-independent effect. *p < 0.05 vs. spontaneous contraction (SC) and phenylephrine (FE) values.

DISCUSSION

Depression can influence the cardiovascular system through several mechanisms, including increased heart rate (positive chronotropic effect), elevated blood pressure, arrhythmias, platelet aggregation, and heightened systemic inflammation. Previous studies suggest that appropriate antidepressant therapy may contribute to a reduction in cardiovascular risk in depressive disorders [14].

The pathogenesis of psychiatric disorders has been linked to dysfunction of the pineal gland, often reflected in reduced melatonin levels. Many antidepressants, through increasing norepinephrine and serotonin levels, may indirectly elevate melatonin concentrations, thus supporting the proposed link between depression and melatonin deficiency. Importantly, melatonin has been shown to reduce both heart rate and blood pressure, indicating a potential role in modulating cardiovascular functions rather than directly treating cardiovascular disease [9].

Recent studies demonstrate that melatonin exerts cardiovascular effects via both receptor-mediated and non-receptor pathways. While it can induce vasoconstriction in cerebral arteries, it promotes vasodilation in peripheral vascular beds. Patients with coronary artery disease, particularly those at risk of myocardial infarction and sudden cardiac death, often exhibit low melatonin levels [15]. These observations are further supported by recent evidence highlighting melatonin's protective and regulatory role in cardiovascular pathophysiology, including its antioxidant and anti-inflammatory actions [16].

In the present study, we investigated the vascular effects of agomelatine, a melatonergic antidepressant, on rat thoracic aorta tissue with intact and denuded endothelium. Our findings show that agomelatine induces a dose-dependent vasodilatory effect in endothelium-intact aortic rings, whereas no such effect was observed in endothelium-denuded tissues. This highlights the critical role of endothelial integrity in mediating agomelatine's vascular actions. These results align with previous studies suggesting that agomelatine's cardiovascular effects are endothelium-dependent, likely involving nitric oxide or prostacyclin pathways.

In support of our results, a recent study demonstrated that agomelatine ameliorates lipopolysaccharide-induced endothelial and cardiac injury by modulating NF- κ B/p65 signaling, restoring SIRT1 levels, and reducing caspase-8 activity. These effects indicate the drug's antioxidant, anti-inflammatory, and anti-apoptotic properties [17]. Another investigation showed that agomelatine mitigated hypertension-induced cognitive deficits, endothelial dysfunction, nitrosative stress, mitochondrial impairment, and inflammation via MT1/MT2 and 5-HT_{2C} receptor pathways [18].

Although some reports have suggested a potential link between depression and hypotension, epidemiological evidence more consistently indicates a higher incidence of hypertension among individuals with depressive disorders compared to the general population. This paradox may be partially explained by the pharmacological actions of antidepressants on multiple neurotransmitter

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systems, including adrenergic, serotonergic, histaminergic, dopaminergic, and cholinergic pathways [19]. In addition, systemic inflammation has been identified as a shared pathophysiological mechanism in both depression and cardiovascular dysfunction, potentially exacerbating endothelial dysfunction and vascular damage [20]. Considering its unique pharmacodynamic and receptor profile, agomelatine appears to have a limited and indirect influence on blood pressure regulation [19]; however, this interpretation should be made cautiously given the *in vitro* nature of our study. Further investigations are necessary to determine whether these vascular effects have clinical relevance.

The present findings provide preliminary experimental evidence supporting an endothelium-dependent vasodilatory effect of agomelatine. These data should be interpreted within the limitations of an *in vitro* design and cannot be directly extrapolated to clinical outcomes. Future *in vivo* and clinical studies are needed to clarify whether the observed endothelial interactions may contribute to the overall vascular safety of agomelatine in patients with cardiovascular comorbidities.

Limitations

This study was conducted on isolated rat thoracic aorta tissues under *in vitro* conditions, which may not fully replicate *in vivo* vascular responses. Additionally, the sample size was limited, and only male rats were used, which may restrict the generalizability of the findings across sexes and species.

CONCLUSION

In summary, agomelatine produced a concentration-dependent vasodilatory effect in rat thoracic aorta only when the endothelium was intact, indicating that its vascular action relies on endothelial integrity. This endothelium-dependent relaxation suggests a possible role of endothelial mediators such as nitric oxide in agomelatine's mechanism of action. Overall, the results support the vascular safety of agomelatine and its potential relevance in patients with concomitant cardiovascular disease and depression. Further *in vivo* and clinical investigations are required to clarify the underlying mechanisms and confirm the translational value of these findings.

Conflicts of Interest

The authors declare no conflicts of interest related to this study.

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Author Contributions

Conceptualization: ROK, ZISG; methodology: ROK, ZISG; investigation: ROK, ZISG; resources: ROK, ZISG; data curation: ROK; formal analysis: ROK, ZISG; writing-original draft preparation: ROK; review & editing: ROK, ZISG

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VAKA TAKDİMİ

CASE REPORT

A CASE REPORT; LOW-ENERGY TRAUMA CAUSED TYPE 2 ODOTOİD FRACTURE

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ABSTRACT

*In most countries, the elderly are the most rapidly growing segment of society, and it is estimated that by 2025, almost a fifth of the population will be over the age of 65. These patients' group are vulnerable to cervical spine injuries with the upper cervical (C0-C2) spine being involved in more than 50% of the time. **Case:** A 63-year-old female patient applied to the emergency room at around 18:00 with complaints of falling from a height of 1 meter and neck pain. On physical examination, GCS: 15, conscious, cooperative, oriented, tenderness in the midline of the neck and abrasion in the left frontal. On lower extremity examination, there is abrasion on the left knee. Other System examinations are normal. Cervical CT revealed odontoid Type 2 Fracture. Since the neurosurgeon was on leave, the patient was contacted by 112 and referred to a center where there was a neurosurgeon. **Conclusion:** In case of traumatic falls in elderly patients, care should be taken in terms of cervical trauma and cervical vertebra stabilization should be done as soon as possible, and even if there is no clinical neurological deficit, it is important to be more careful, especially in terms of odontoid bone fracture.*

Keywords: Geriatrics, cervical trauma, odontoid, fracture, emergency service

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INTRODUCTION

In most countries, the elderly are the most rapidly growing segment of society, and it is estimated that by 2025, almost a fifth of the population will be over the age of 65. (1)These patiente's group are vulnerable to cervical spine injuries with the upper cervical (C0 C2) spine being involved in more than 50% of the time.(2,3,4,) There are a number of alternatives available in the treat ment of type II odontoid fractures, including external im mobilization using a halo orthosis or cervical collar, and surgical treatment, through an anterior or posterior appro ach. At present, there is no consensus on the optimal treatment. (5)In this article, we wanted to present a case in which we detected odontoid type two fractures following a fall that underwent surgery on the cervical ver-tebra and internal fixation.

CASE PRESENTATION

A 63-year-old female patient applied to the emergency room at around 18:00 with complaints of falling from a height of 1 meter and neck pain. On the same day, the patient stated that while going up the stairs, he fell from a height of approximately 1 meter and hit his head and neck. In the patient's history, it was learned that he had an operation on the brain and cervical vertebrae due to intraparenchymal bleeding in 2019. The patient's vitals were TA: 120/85 mmHg, saturation O2: 96, pulse: 95 beats/min. On physical examination, GCS: 15, conscious, cooperative, oriented, tenderness in the midline of the neck and abrasion in the left frontal. On lower extremity examination, there is abrasion on the left knee. Other System examinations are normal. A cervical collar was attached to the patient's neck. Hemogram and biochemistry blood tests were requested from the patient. No pathology was detected in blood tests. Brain computed tomography (CT), cervical CT, Thorax CT and left knee Xray were requested from the patient as imaging. There was an old operation scar on brain CT. Other than that, there was no feature. No pathology was detected in thorax CT and knee radiography. Cervical CT revealed odontoid Type 2 Fracture. (picture 1,2). Since the neurosurgeon was on leave, the patient was contacted by 112 and referred to a center where there was a neurosurgeon.



Figure 1. Type 2 Odontoid Fracture



Figure 2. Type 2 Odontoid Fracture

DISCUSSION

Although fractures of the odontoid occur in all age groups, younger patients often sustain these injuries after motor vehicle accidents while older patients present after low energy falls and are less likely to have severe neurological deficits [6, 7, 8, 9, 10]. In our case, it is compatible with the literature both in terms of age and the mechanism of trauma.

Fractures of the second cervical vertebrae are commonly seen in spine surgery. These fractures account for approximately one-third of all cervical spine fractures. The etiology for these fractures is either high-energy mechanisms in younger patients or low-energy trauma in the older population.(11) and our case had a low -energy trauma.

As is known, it is important to immobilize the cervical vertebrae in patients with cervical trauma. In this context, it is important to use a cervical collar in every patient with suspected cervical trauma. And we did this immediately with our patient.

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CONCLUSION

In case of traumatic falls in elderly patients, care should be taken in terms of cervical trauma and cervical vertebra stabilization should be done as soon as possible, and even if there is no clinical neurological deficit, it is important to be more careful, especially in terms of odontoid bone fracture.

Patient Consent

Written informed consent was obtained from the patient's parent for the publication of this case report and any accompanying images.

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CASE REPORT

**RISPERIDONE OVERDOSE–ASSOCIATED ACUTE
DYSTONIA COMPLICATED BY BILATERAL
TEMPOROMANDIBULAR JOINT DISLOCATION
IN AN ADOLESCENT: A CASE REPORT**

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ABSTRACT

Nowadays, the use of second-generation antipsychotics (SGAPs) is increasing in children and adults. This is accompanied by emergency room visits due to high doses or side effects of these medications. Acute dystonic side effects are treated with anticholinergics. A 16-year-old male patient presented with complaints of inability to speak and close his jaw following acute dystonic movements that began around the tongue and mouth at the 19th hour after taking high dose risperidone. After being unresponsive to anticholinergic treatment, bilateral temporomandibular joint (TMJ) dislocation was detected during his questioning and examination. After reduction, the patient was able to close his jaw and speak. It is important for clinicians to keep TMJ dislocation among the preliminary diagnoses in cases where the patient is unable to close their jaw and speech disorders occur together with acute dystonic reactions caused by antipsychotic side effects.

Keywords: Risperidone, Second-generation antipsychotics, Acute dystonia, Temporomandibular joint dislocation

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INTRODUCTION

Antipsychotics are not limited to the treatment of psychosis; they are also frequently used in acute agitation, bipolar mania and other psychotic conditions. (1) Side effects may occur when starting a new medication, changing daily doses, or taking too much.

Although second-generation antipsychotics have fewer extrapyramidal system (EPS) side effects than first-generation antipsychotics, in addition to the sedation, anticholinergic, metabolic, and cardiac side effects of these drugs, side effects such as akathisia, rigidity, bradykinesia, dysphagia, tremor, and acute dystonia, which are extrapyramidal system disorders, can also be observed. (1)

Oromandibular and facial dystonia, which are among the focal dystonias, are characterized by involuntary movements of the masticatory, lingual and pharyngeal muscles. (2) Following acute dystonia due to these drugs, bilateral jaw dislocations may be observed with excessive opening of the mouth and dislocation of the TMJ (3). Psychiatric conditions and acute dystonia findings may overshadow the recognition process of jaw dislocation and may delay the diagnosis of some cases for hours or days.

We present a case of an adolescent with bilateral temporomandibular joint dislocation following acute dystonia in the tongue and oral area caused by high-dose risperidone ingestion. Although numerous cases of jaw dislocation due to acute dystonia have been reported in the literature, no cases have been reported in adolescent age.

CASE PRESENTATION

A 16-year-old male patient was brought to the Emergency Department by his family approximately 17 hours after taking 19 tablets risperidone 1 mg for suicide. He was taking this medication regularly for a psychiatric disorder (anxiety). He was a student and weighed approximately 50 kg.

Upon initial evaluation, his vital signs were as follows: blood pressure (BP) 124/51 mmHg, pulse rate 79/min, oxygen saturation 98%, respiratory rate (RR) 18/min, and temperature 36.9°C.

On physical examination, his Glasgow Coma Scale (GCS) was 15. He was mildly drowsy; neurological and general examinations were otherwise normal. Complete blood count, biochemical tests, arterial blood gas, and an electrocardiogram (ECG) were performed, showing no abnormalities. After approximately 2.5 hours of observation in the Emergency Department (ED) the patient's family requested discharge against medical advice.

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While at home, the patient began experiencing outward tongue movements and repetitive jaw opening actions. Three hours after being discharged from the hospital, they returned to the emergency department with complaints of being unable to speak and close their jaw.

During the second examination, his GCS remained at 15, with vital signs recorded as BP 110/70 mmHg, pulse 71/min, RR 18/min, oxygen saturation 99%, and temperature 36.4°C. Apart from the inability to close his mouth, the physical and neurological examinations were otherwise normal. Initially, acute dystonia secondary to risperidone ingestion was suspected. Due to the unavailability of diphenhydramine or benztropine, 5 mg biperiden was administered. However, no clinical improvement was observed. Upon further detailed questioning, the patient recalled a similar complaint in the past; maxillofacial CT was obtained to support the diagnosis, which revealed bilateral temporomandibular joint dislocation. Sedation and analgesia were achieved using 2 mg intravenous midazolam, after which successful reduction of the mandibular dislocation was performed and bandage was applied. The patient was admitted to the pediatric inpatient clinic for further observation and management.

DISCUSSION

SGAPs are commonly used on psychosis, schizophrenia otherwise acute agitation, bipolar mania and other psychiatric conditions. Atypical antipsychotics (second-generation antipsychotics) cause dopamine D2 receptor blockade, but are considered safer than classical antipsychotics in terms of extrapyramidal side effects due to their higher affinity for serotonin 5-HT_{2A} receptors (4). However, especially with high doses or individual pharmacokinetic differences that increase sensitivity, serious motor side effects, such as acute dystonia, may develop. Risperidone, especially at doses above 4 mg per day, has the highest EPS side effect among second-generation antipsychotics in adults (5).

Dystonia is characterized by involuntary muscle contractions and abnormal postures that develop due to an imbalance between the dopaminergic and cholinergic systems. The face, neck, and extremities are the most commonly affected areas (6).

Diphenhydramine (25-50 mg IV) or benztropine (1-2 mg IV) is used in the treatment of acute dystonia due to their anticholinergic activity (1).

In this case, focal dystonia affecting the mouth and jaw muscles, which developed after risperidone overdose, caused bilateral TMJ dislocation, a rare but serious complication.

Following acute dystonia due to risperidone use, TMJ dislocation was reported in a 7-year-old male patient (7) who received daily 1 mg risperidone, in a 25-year-old male patient (8) 12 hours

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after the start of 2 mg risperidone treatment, and in a 30-year-old male patient (9) who received a 4 mg risperidone injection.

CONCLUSION

SGAPs used in psychosis, agitation, bipolar mania or other psychiatric conditions may cause side effects such as acute dystonia, although rare, at the beginning of treatment, with dose changes or excessive intake.

Following acute dystonia that begins with involuntary movements in the face and neck muscles, TMJ dislocation should be considered as a diagnosis in cases such as unresponsiveness to anticholinergic treatment, the jaw remaining fixed in the midline, inability to speak, and inability to close the jaw.

Patient Consent

Written informed consent was obtained from the patient's parent for the publication of this case report and any accompanying images.

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