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# Evaluation of the use and efficacy of prothrombin complex concentrates in patients presenting to the emergency department with warfarin-induced hemorrhage

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## ABSTRACT

**Aims:** Warfarin administration has been the standard treatment for many years to prevent thromboembolism in patients with prosthetic heart valves with atrial fibrillation. Because of warfarin's narrow therapeutic window, and life-threatening bleeding, it is generally considered that this requires rapid and complete warfarin reversal. Although there are treatments such as vitamin K and fresh frozen plasma (FFP) to reverse the effects of warfarin, the most effective method involves using prothrombin complex concentrates (PCC). This study aims to evaluate the use and efficacy of PCC in patients with warfarin-induced bleeding in the emergency department.

**Methods:** The patients receiving PCC for warfarin reversal in the emergency department between January 1, 2019 – April 1, 2021, were identified from the hospital's electronic database. Demographic data, reasons for warfarin use, PCC indications, international normalized ratio (INR) values before and after PCC, and mortality of the patients were evaluated. The four-factor PCC dose was determined according to the patient's weight, admission, and target INR level.

**Results:** The mean age of the patients was 69.3±15.5 years. The female/male ratio was 1/1.5. The most common PCC indications were gastrointestinal bleeding (32.9%), urogenital bleeding (23.3%), epistaxis (12.3%), and urgent surgical need (12.3%). The median INR values pre- and post-treatment were 9.2 (range 2.1-11.8) and 1.8 (range 1.0-4.6). The mean dose of PCC was 1500 IU (min-max 750-3250 IU). In addition to PCC, all patients received vitamin K; 17.8% of the patients received erythrocyte suspension, and 10.9% of the patients received FFP. There were no PCC-related complications in the emergency department. After visiting the emergency department, 56.2% of the patients were discharged following successful treatment, 38.4% were admitted to inpatient services, and 5.5% were referred to an external center. 26% of the patients were followed in the intensive care unit (ICU). It is important to note that there were no fatalities in the emergency department. However, the mortality rate during the hospital stay was 5.5%.

**Conclusion:** Four-factor prothrombin complex concentrate (PCC) has been proven to be a safe and effective treatment for reversing bleeding caused by warfarin.

**Keywords:** Warfarin-associated bleeding, prothrombin complex concentrates, emergency department

## INTRODUCTION

Warfarin is used as anticoagulant therapy in many thrombotic processes, such as pulmonary embolism, deep vein thromboembolism (DVT), and atrial fibrillation (AF). Warfarin-like vitamin K antagonists (VKA) inhibit vitamin K-dependent epoxide reductase, preventing the conversion of vitamin K-dependent clotting factors into their active forms.<sup>1</sup>

The most important side effect associated with warfarin is bleeding, and the risk of bleeding increases as a result of the increase in international normalized ratio (INR) values. Warfarin-induced bleeding is of concern due to the narrow therapeutic range and interindividual dose variability.<sup>2</sup> The first places of admission of patients with warfarin-associated

bleeding are to the emergency services. Therefore, the rapid diagnosis and treatment of warfarin-associated bleeding by emergency physicians are essential. It is recommended to discontinue the use of VKAs, vitamin K, Fresh Frozen Plasma (FFP), or Prothrombin complex concentrate (PCC) to treat bleeding associated with warfarin.<sup>3,4</sup> Several studies have compared the effectiveness of FFP and PCC in treating warfarin-induced bleeding.<sup>5,6</sup> Emergency departments are the most important places of admission for patients with warfarin-related bleeding. Therefore, rapid diagnosis and treatment of warfarin-related bleeding by emergency physicians are gaining importance.

This study aims to determine the acute bleeding conditions due to warfarin, the treatment protocols, and the treatment results applied to the emergency department.

## METHODS

The study was conducted with the approval of Samsun University Samsun Training and Research Hospital Clinical Researches Ethics Committee (Date:22.09.2021, Decision No:2021/6/8). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This retrospective and descriptive study included patients who applied to third level emergency department between January 2019 and April 2021, were older than 18 years of age, actively receiving warfarin treatment, had an INR level above 2, had active bleeding, or were using active warfarin but did not have active bleeding but required emergency surgical intervention and received PCC treatment. Patients under 18 years of age, patients who did not use warfarin, and patients with an INR level below were excluded from the study.

Sociodemographic data such as age and gender, indications for warfarin use, vital signs, comorbid diseases, bleeding characteristics (major bleeding characteristics are defined as GI bleeding, urogenital bleeding, urgent surgical need, and hemoptysis, intracranial bleeding), and laboratory data were analyzed from the patients in the study's electronic records. Bleeding parameters before and after the treatment were compared. All patients included in the study were followed up for 1 month for thromboembolic events. The outcome characteristics (mortality and adverse thromboembolic events) of the patients were also recorded. All patients included in the study received vitamin K. Other therapies (vitamin K, FFP) recommended to patients other than PCC were recorded in the emergency department. 20 minutes after PCC treatment, whether the patients reached target INR values was analyzed.

The online calculation table developed by the manufacturer was used so that the PCC doses were based on the patient's weight, the INR values at admission, and the target INR values, with the target INR<2.1.<sup>7</sup>

Statistical analyses were performed using the SPSS version 21.0 (Chicago, USA) software. The suitability of the variables for normal distribution was examined using visual (histogram and probability graphs) and analytical methods (*Kolmogorov Smirnov*, *Shapiro-Wilk test*). Descriptive statistics were

expressed as mean and standard deviation in normally distributed numerical data, median in non-normally distributed numerical data, and number and percentage in nominal data. Customarily distributed numerical variables between the two groups were analyzed using the "t-test in independent groups". Non-normally distributed numerical variables were analyzed using the "Mann Whitney U test" between two independent groups and the "Wilcoxon signed rank test" between two dependent groups. "Chi-square analysis" was used to compare the nominal data. "Spearman test" was used in correlation analysis. In the statistical analyses in the study, values below p<0.05 were considered statistically significant.

## RESULTS

73 patients were included in the study and 29 (39.3%) of these patients were female and 44 of the patients were male (60.7%). The mean age of the patients was 69.3±15.5 years. The most common indications for warfarin therapy were dysrhythmia (47.9%), heart valve prosthesis (32.9%), and embolism/thrombosis (8.2%). The most common reasons for presentation to the emergency department were GI bleeding (32.9%), followed by urogenital bleeding (23.3%), epistaxis (12.3%), and urgent surgical need (12.3%). The sociodemographic and clinical characteristics of the patients are shown in **Table 1**.

**Table 1.** Sociodemographic and clinical characteristics of the patients in the study

Characteristics	n (%)
<b>Age (year) (mean ± SD)</b>	69.3±15.5
<b>Gender</b>	
Female	29 (39.7)
Male	44 (60.3)
<b>Bleeding type</b>	
Major bleeding	32 (43.8)
Minor bleeding + Supratherapeutic INR	41 (56.2)
GI bleeding	24 (32.9)
Urogenital bleeding	17 (23.3)
Epistaxis	9 (12.3)
Urgent surgical need	9 (12.3)
<b>Presenting complaint</b>	
Subcutaneous hemorrhage	5 (6.8)
Hemoptysis	4 (5.5)
Intracranial hemorrhage	3 (4.1)
Hemarthrosis	1 (1.4)
Conjunctival hemorrhage	1 (1.4)
<b>Indication for the Warfarin usage</b>	
Dysrhythmia	35 (47.9)
Prosthetic heart valve	24 (32.9)
History of embolism/thrombosis	6 (8.2)
Peripheral arterial disease	5 (6.8)
Stroke	2 (2.7)
Pulmoner embolism	1 (1.4)

SD: Standard deviation, INR: International normalized ratio, GI: Gastrointestinal. After PCC treatment, 75.3% (n=55) of the patients had reached to target INR range, while 24.7% (n=18) were unable to reach to the target INR range. While 56.2% of the patients were discharged after treatment from the emergency department, 38.4% were hospitalized in the relevant wards. In addition, 26% of the patients were hospitalized in intensive care units. During the follow-up in the emergency department, no mortality occurred in

any patient, while mortality occurred in 5.5% (n=4) of the hospitalized patients. The length of stay in the emergency department was 4 (2-28) hours, and after PCC treatment there were observed no thromboembolic complications for one month.

INR, PT, aPTT, Hb, and Htc values of the patients at the admission to the emergency department and after PCC treatment are presented in Table 2. Accordingly, INR, PT and aPTT levels decreased significantly after PCC treatment (p<0.001).

**Table 2.** Analysis of laboratory parameters at the time of admission to the emergency department and after PCC treatment

Parameter	Admission Med (min-max)	After PCC Med (min-max)	p-value
INR	9.2 (2.1-11.8)	1.8 (1-4.6)	<0.001*
PT (sec)	96.5 (9.5-121)	20.4 (11.2-159)	<0.001*
APTT (sec)	72.6 (28.5-190)	32.8 (12-90)	<0.001*
Hb (g/dL)	11 (4.5-17.0)	10.5 (5.2-15)	0.011*

INR: International normalized ratio, PT: Prothrombin time, APTT: Activated partial thromboplastin time, Hb: Hemoglobin, PCC: Prothrombin Complex Concentrates  
\*Wilcoxon signed rank test was used in all analyzes.

Patients who achieved the target INR value with PCC treatment were compared to those who did not. It was found that patients who achieved the target INR value had shorter lengths of stay in the emergency department (p=0.035). Patients who did not achieve the target INR value had a higher prevalence of arrhythmia (p=0.027) and multiple comorbidities (p=0.022) Table 3.

**Table 3.** Comparison of patients, who reached and failed to reach the target INR level after PCC treatment

Characteristics		Target INR to the value of those who reach (n=55; %75.3)	Target INR to the value of those who can't reach (n=18; %24.7)	p value
Multiple comorbidity (+)	n (%)	17 (30.9)	11 (61.1)	0.022**
INR	Med (min-max)	8.7 (2.1-11.8)	9.9 (5.4-11.0)	0.072*
Pt (sec)	Med (min-max)	92.1 (9.5-121)	106 (59.3-120)	0.116*
Aptt (sec)	Med (min-max)	78.7 (28.5-190)	68.4 (39.3-190)	0.828*
Hb (g/dl)	Med (min-max)	11.2 (4.5-15)	10.5 (6.1-17)	0.217*
Plt (103/ $\mu$ L)	Med (min-max)	227 (98-662)	235 (82-479)	0.828*
Urea (mg/dL)	Med (min-max)	48 (19-290)	93 (29-291)	0.004*
Mortality (+)	n (%)	4 (7.3)	0	
Length of stay in the emergency department (hours)	mean $\pm$ SD	7.8 $\pm$ 8.6	12.3 $\pm$ 11.3	0.035*

INR: International normalized ratio, PT: Prothrombin time, APTT: Activated partial thromboplastin time, Hb: Hemoglobin, PCC: Prothrombin complex concentrates, Plt: Platelet  
\*Mann-Whitney U test, \*\*Chi-Square test

The analysis of patients admitted to the intensive care unit (ICU) and those not admitted is presented in Table 4. Patients received similar doses of PCC treatment in the emergency department (p=0.340). Patients hospitalized in the ICU had a higher frequency of major bleeding (p<0.001) and a longer length of stay in the emergency department (p=0.027). In addition, patients hospitalized in ICU had lower systolic blood pressure (p=0.049), Hb (<0.001), Htc (p<0.001) and higher urea values (p=0.008).

Correlation analyses of PCC dose and sociodemographic, clinical and laboratory outcomes are presented in Table 5. Accordingly, PCC dose was moderately positive correlated with INR (r=0.360; p=0.002), PT (r=0.310; p=0.008), aPTT (r=0.305; p=0.009) and PLT (r=0.323; p=0.005), while AST (r=0.249; p=0.035) and lower positive correlated with length of stay in the emergency department (r=-0.260; p=0.029).

**Table 4.** Comparison of laboratory parameters and PCC treatment doses in patients admitted to intensive care unit and non-admitted patients

		ICU (+) (n=19)	ICU (-) (n=54)	p-value	
Bleeding type	Major	Med (min-max)	16 (84.2)	16 (29.6)	<0.001**
	Minor+high INR value	Med (min-max)	3 (15.8)	38 (70.4)	
Vital parameters at the time of admission	SBP (mmHg)	mean $\pm$ SD	108 $\pm$ 30	124 $\pm$ 28	0.049***
	DBP (mmHg)	mean $\pm$ SD	67 $\pm$ 15	74 $\pm$ 14	0.061***
	Pulse	mean $\pm$ SD	100 $\pm$ 20	92 $\pm$ 19	0.129***
Laboratory	INR	Med (min-max)	9.6 (2.1-11)	9.2 (2.1-11.8)	0.915*
	Pt (sec)	Med (min-max)	102 (23-121)	96 (9-120)	0.469*
	Aptt (sec)	Med (min-max)	71 (32-190)	73 (28-190)	0.806*
	Hb (g/dL)	Med (min-max)	7.8 (4.5-14)	11.5 (5.5-17)	<0.001*
	Htc (%)	Med (min-max)	23 (13.1-42)	34.1 (16.5-46)	<0.001*
	Plt (103/ $\mu$ L)	Med (min-max)	230 (114-535)	227 (82-662)	0.980*
Urea (mg/dL)	Med (min-max)	74 (32-291)	45 (19-290)	0.008*	
Cr (mg/dL)	Med (min-max)	1.0 (0.7-4.5)	1.0 (0.5-6.4)	0.850*	
PCC (IU) Med (min-max)	Med (min-max)	1500 (750-3000)	1500 (750-3250)	0.340*	
Length of stay in the emergency department (hours)	mean $\pm$ SD	14.7 $\pm$ 14.0	6.8 $\pm$ 6.1	0.027*	

PCC: Prothrombin complex Concentrates, ICU: Intensive care unit, INR: International normalized ratio, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, PT: prothrombin time, APTT: Activated partial thromboplastin time, Hb: Hemoglobin, Htc: Hematocrit  
\*Mann-whitney u test, \*\* Chi-square test, \*\*\* Independent sample t test, Min: Minimum, Max: Maximum

**Table 5.** Correlation analyses of PCC dose and sociodemographic, clinical, and laboratory outcomes

	PCC dose	Correlation rate (r)	p-value
Age		0.005	0.968
Comorbidity numbers		0.043	0.719
Values at the time of admission	SBP	-0.049	0.682
	DBP	0.017	0.884
	Pulse	0.191	0.105
	INR	0.360	0.002
	PT	0.310	0.008
	aPTT	0.305	0.009
	Hb	-0.062	0.605
	Htc	-0.077	0.516
	PLT	0.323	0.005
AST	0.249	0.035	
ALT	0.128	0.283	
Length of stay in the emergency department		0.260	0.029
Length of stay in the ICU		0.425	0.070
Length of stay in the services		0.076	0.765

PCC: Prothrombin complex concentrates, ICU: Intensive care unit, INR: International normalized ratio, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, PT: Prothrombin time, APTT: Activated partial thromboplastin time, Hb: Hemoglobin, Htc: Hematocrit, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase  
\* Spearman rank correlation test was used in all analyzes.

## DISCUSSION

Warfarin is a vitamin K antagonist used for the primary and secondary prevention of arterial and venous thromboembolism in prosthetic heart valves, atrial fibrillation, peripheral arterial disease, antiphospholipid syndrome, and recurrent myocardial or cerebral infarcts. The critical challenge in warfarin therapy lies in maintaining a delicate balance between anticoagulation and the risk of bleeding. The narrow therapeutic range, high food-drug interactions, and different dose requirements according to the patient increase the risk of bleeding in patients using warfarin. In addition to methods such as vitamin K, FFP, and erythrocyte suspension replacement, PCC is significant among the treatment options for warfarin-related bleeding.<sup>8</sup> Especially compared with FFP, PCC has been reported to benefit patients more effectively in a shorter time frame, with less volume load and less risk of infection.<sup>5,6</sup> Perhaps the most crucial disadvantage of PCCs is that they are more expensive than other treatments.

In this study, in which we aimed to investigate the efficacy of PCC use in patients presenting to the emergency department with symptoms and signs of warfarin-induced bleeding, we found that PCC treatment significantly decreased INR levels. Similar to our study, Majeed et al.<sup>9</sup> evaluated patients who presented to the emergency department with warfarin-induced bleeding and received PCC treatment. In this study, the INR value of the patients was found to be 1.7 after PCC transfusion, and it was reported that target INR values were reached in 56.9% of the patients. It was also found that mortality developed in 10% of the patients. In our study, the target INR level was reached in 75.3% of the patients, and our mortality rate was 5.5%. The higher number of patients with intracranial hemorrhage in this study by Majeed et al.<sup>9</sup> compared to our study may explain the difference in mortality rates. Reactions developing after PCC transfusion may also contribute to this situation. Indeed, the analysis above reported that 3.8% of patients developed thromboembolic events after PCC. Still, no thromboembolic event was observed during the follow-up of the patients in our study.

Different results on reaching target INR levels after PCC treatment have been obtained from other studies. In the study by Appleby et al.<sup>10</sup>, the INR value was reduced below 1.5 in 88.2% of patients after PCC. The fact that the INR values of the patients at the time of presentation were lower (median 4.3) compared to our study and that only 17 patients were included in the study may have been effective in reporting a higher success rate. Pabinger et al.<sup>11</sup> said that target INR values were achieved in 93% of 43 patients after PCC treatment. Although considerably higher than our study, the median INR value at admission was 3.2 in this study, which may have led to high rates.

In our study, while no mortality was observed in the emergency department in patients who underwent PCC due to warfarin-related bleeding, the mortality rate in inpatient services (ward/intensive care unit) was found to be 5.5%. The reason for this may be the short follow-up time of the patients in the emergency department and transfer to inpatient services after initial treatment, early recognition of bleeding,

and rapid intervention. Studies are reporting similar and higher mortality rates to our study.<sup>12</sup> Karaca et al.<sup>13</sup> said that mortality developed in 5% of 20 patients treated with PCC. In this study, similar to our study, 40% of the patients were discharged after treatment in the emergency department, 40% were consulted at the relevant branch, and 15% were hospitalized in the ICU.

In our study, patients who failed to reach the target INR level in the emergency department had more than one comorbid disease, and their stay in the emergency department was longer. This may have been due to the prolonged consultation process in the emergency department. Our findings indicate that it is more challenging to return to the target INR level due to increased comorbidities. In addition, an increase in the number of comorbidities may have led to a rise in bleeding severity or difficulty in warfarin dose adjustment. In warfarin-related bleeding, the negative effect of the amount of bleeding on prognosis has been shown in previous studies.<sup>14</sup> It is thought that the rate of reaching the target INR range in treatment with PCC will be lower because coagulation factors will be lost more in patients with more bleeding. Therefore, early intervention in patients with significant bleeding may have a favorable effect on prognosis. In our study, the correlation between high admission INR levels and PCC doses indirectly supported this.

PCCs show both faster and safer efficacy compared to FFP in reversing the effects of VKAs.<sup>15</sup> In studies using PCCs in treating warfarin-induced bleeding, PCCs were reported to be very safe and effective.<sup>9,12,16</sup> In 2017, Brekelmans et al.<sup>17</sup> evaluated the efficacy and safety of PCCs in the reversal of vitamin K antagonist effects in a meta-analysis in which a total of 19 studies and 3000 patients were assessed, and it was stated that PCCs had a shorter time to reach the target INR and lower mortality rates and complications. In conclusion, the meta-analysis reported that PCCs were safer and more effective than FFP.

Although the efficacy of PCCs in reversing the effect of warfarin has been proven, they are used in combination with other treatment modalities.<sup>18</sup> In our study, vitamin K was administered to all patients in the emergency department. In addition, erythrocyte suspension (17.8%) was issued in patients with severe bleeding. FFP was administered to 3 patients (4.1%) with high control INR values. Other studies have reported that other treatment modalities were used at different rates. In the study by Majeed et al.<sup>9</sup>, vitamin K transfusion was administered in 74% of patients who underwent PCC, and FFP transfusion was administered in 34% of patients who underwent PCC. Access to PCC and other treatment modalities and different clinical presentations of the patients may have been adequate in the difference between the studies regarding other treatment frequencies.

Warfarin is an effective anticoagulant agent that is frequently preferred for the prevention of complications, including stroke, especially in atrial fibrillation.<sup>19</sup> In the study by Soyuncu et al.<sup>12</sup>, in which the effect of warfarin was reversed with PCC, the most common indications for warfarin were



atrial fibrillation (49.4%), heart valve replacement (21%), pulmonary embolism (12%) and deep vein thrombosis (12%). In our study, the most common indications for warfarin were similarly dysrhythmia (47.9%), heart valve replacement (32.9%) and embolism (8.2%).

In our study, we found that PCC treatment was administered due to GI bleeding (32.9%), urogenital bleeding (23.3%), epistaxis (12.3%) and surgical requirement (12.3%). In the literature, indications for PCC are reported similar to our study, but different indications and rates have also been reported. In the study by Majeed et al.<sup>9</sup>, the most common types of bleeding were reported as intracranial hemorrhage (37%), GI bleeding (13%) and intramuscular bleeding (4%), respectively. In the study by Soyuncu et al.<sup>12</sup>, the most common causes of bleeding in patients undergoing PCC were GI bleeding (32%), respiratory system bleeding (22.6%), muscular bleeding (12%) and urinary bleeding (12%), respectively. Toth et al.<sup>20</sup> reported that the most common indications for PCC were emergency surgery (29.8%), GI bleeding (27.5%) and intracranial hemorrhage (26.7%), respectively.

### Limitations

Our study had some limitations. The number of patients included in our study was relatively small. The effect of PCC was evaluated at 30 minutes in most studies. However, this period could not be standardized in our research because of the study's retrospective design. In addition, the effect of PCCs on mortality could not be evaluated clearly because of the small number of patients with mortality.

## CONCLUSION

PCC significantly reduces INR values for the reversal of warfarin-induced anticoagulation in the emergency department. However, treatment may be inadequate due to existing comorbidities.

## ETHICAL DECLARATIONS

### Ethics Committee Approval

The study was carried out with the permission of Samsun University Samsun Training and Research Hospital Clinical Researches Ethics Committee (Date:22.09.2021, Decision No:2021/6/8).

### Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

### Referee Evaluation Process

Externally peer-reviewed.

### Conflict of Interest Statement

The authors have no conflicts of interest to declare.

### Financial Disclosure

The authors declared that this study has received no financial support.

### Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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# The relationship between patient characteristics, laboratory findings and outcomes of the patients presenting with seizures to the emergency department

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## ABSTRACT

**Aims:** Most patients with epilepsy have recurrent admissions to the emergency department (ED) during the disease. Insufficient information about this patient population causes a mismatch between patients' needs and health care delivery. For this reason, there is a need for objective methods that can be used to monitor seizure patients in EDs and to determine the need for hospitalization. This study aimed to develop management recommendations for patients with active seizures or a history of seizures prior to admission and contribute to the determination of the criteria for the ED follow-up period. **Methods:** This study was designed as a single-center, prospective, and observational study and included patients over 18 who presented to the ED for seizures. After the patients were included in the study, demographic and laboratory findings were recorded, and patients were followed up for 30 days for mortality and recurrent seizures.

**Results:** Seventy-one patients were included in the study. The most known seizure causes were drug incompatibility (15.49%) and infection (9.86%). The most common comorbidities were Hypertension (16.90%), Diabetes Mellitus (12.68%), and cerebrovascular diseases (9.86%). The mortality rate was higher in patients who were hospitalized, had an active infection, and had a high CRP value.

**Conclusion:** The 30-day mortality is higher in patients presenting to the ED with epileptic seizures; in the advanced age group, patients with active infection have an elevated C-reactive protein in laboratory parameters.

**Keywords:** Emergency medicine, epilepsy, seizure

## INTRODUCTION

Epilepsy is defined as recurrent unprovoked seizures caused by a genetic predisposition or an acquired brain disorder. Approximately more than 10% of the population has a seizure at least once in their lifetime, and yet only 3% are diagnosed with epilepsy.<sup>1</sup> A small number of studies have shown that 15% to 35% of epilepsy patients present to the emergency department (ED) for seizures. Inadequate information regarding this patient population results in a mismatch between patients' needs and healthcare delivery. In particular, inadequate coordination between ED and clinical branches leads to unnecessary hospitalizations.<sup>2</sup> Additionally, significant differences were found in the care received by seizure patients in the hospital, both for those who were followed up in the ED and for those who were later admitted.<sup>3</sup>

Therefore, there is a need for objective methods that can be used to monitor epileptic patients in the ED and determine the need for hospitalization.

This study aimed to examine the relationship between clinical characteristics, laboratory findings, and patient outcomes who were admitted to the ED with seizures.

## METHODS

This study received approval from the Institutional Ethics Committee of the Kocaeli Derince Training and Research Hospital (Date: 01.09.2020, Decision No: 01.07.2021). This study was designed as single-center, prospective, and observational.



Pregnant women, patients under 18 years of age, presenting with their first seizure, seizure activity not longer than 5 minutes, status epilepticus, refractory status epilepticus, and seizures due to secondary causes (i.e., mass lesion, head trauma, graphic and clinical characteristic data, laboratory findings, and hospitalization information were recorded, and enrolled patients were followed up. Mortality information of the patients who were followed up and whether they had a seizure within 30 days were questioned by phone.

### Statistical Analysis

All analyses were performed in SPSS v21 (SPSS Inc., Chicago, IL, USA). Compliance of quantitative variables with normal distribution was checked with the Shapiro-Wilk test. Quantitative variables were summarized as mean ± standard deviation and median (minimum value - maximum value), while qualitative variables were summarized as frequency (percentage). Quantitative variables that assumed normal distribution were analyzed with t-test in independent samples. Quantitative variables that did not meet the assumption of normal distribution were analyzed with the Mann-Whitney U test or Kruskal Wallis test according to the number of groups. Qualitative variables were analyzed with the chi-square test or Fisher’s exact test. Spearman correlation coefficient was used to evaluate the relationships between quantitative and ordinal variables. P values <0.05 were considered statistically significant.

## RESULTS

Seventy-one patients who applied to the ED due to seizures within the study date range were included in our study. The average age of the patients included in the study was 42.66±18.22. Gender distribution was calculated as 46 males (64.78%) and 25 females (35.21%).

The seizure timeframe of 47.14% of the patients before admission to ED was between 10 and 30 minutes. There was a history of head trauma in 10 (14.08%) patients and aura in 19 (26.76%). The most common seizure type was generalized tonic-clonic seizures in 64 patients, 5 patients had complex partial seizures while 1 patient had absence and 1 patient had simple partial seizure. The most known causes of seizures were medication incompatibility (15.49%) and the patient’s infection (9.86%). The possible cause of seizures could not be determined in 47 patients (66.20%).

Sixty-four patients (90.14%) were using anti-epileptic drugs (AEDs). The most frequently used drugs were levetiracetam (54.93%), valproic acid (28.17%), and carbamazepine (16.90%). A total of 20 (28.17%) patients had additional chronic diseases. The most frequently observed additional diseases were determined as Hypertension (16.90%), Diabetes Mellitus (12.68%), and cerebrovascular diseases (9.86%). Except for lactate levels, the average ED admission parameters of the patients were within the normal range. ED admission laboratory parameters of the patients are summarized in Table 1.

Twenty patients (28.17%) had a seizure during ED follow-up. Levetiracetam (21.13%) and diazepam (19.72%) were most

frequently administered to these patients as treatment in the ED. The average follow-up time of the patients in ED was 367.77 minutes (70-1230, min-max). While 6 (8.45%) patients were admitted to the ward and 2 (2.82%) to the intensive care unit, 63 (88.73%) patients were discharged. 24 (33.80%) patients had a seizure again within 30 days, and 4 (5.63%) patients died.

**Table 1. Laboratory parameters of patients**

Laboratory parameters	Mean ± SD
WBC (x1000/mm <sup>3</sup> )	8.39±3.79
Lymphocyte (%)	31.05±11.96
Neutrophil (%)	59.49±13.58
pH	7.30±0.14
Lactate (mmol/L)	5.30±4.19
HCO <sub>3</sub> (mEq/L)	21.96±5.25
BE (mmol/L)	-4.36±6.97
Glucose (mg/dL)	126.85±48.53
CRP (mg/L)	7.31±12.91
Potassium (mmol/L)	4.20±0.50
Calcium (mg/dL)	8.82 ± 0.56
Sodium (mmol/L)	139.34±3.53

WBC: White blood cells, BE: Base excess, CRP: C reactive protein, SD: Standard deviation

No statistical difference was detected in terms of age, systolic and diastolic blood pressure and ED follow-up period between patients who were alive one month after discharge from the ED and those who died within one month Table 2.

**Table 2. Comparison of 30-day mortality and age, blood pressures and ED length of stay**

	30 day Mortality	Mean ± SD	p value
Age	Survivor	41.99 ± 17.89	0.312
	Non- survivor	54.00 ± 22.82	
SBP	Survivor	116.12 ± 20.52	0.494
	Non- survivor	120.00 ± 16.33	
DBP	Survivor	70.45 ± 10.93	0.927
	Non- survivor	70.00 ± 8.16	
LOS	Survivor	363.46 ± 183.14	0.162
	Non- survivor	440.00 ± 109.32	

ED: Emergency department, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, LOS: length of stay

While the most common cause of seizures was unknown in 46 (68.66%) patients who were alive after a month, the most common cause of seizures in patients who died within a month was infection (50.00%) (p=0.018). 30-day mortality and clinical characteristics have been compared and summarized in Table 3.

The mortality rate was higher in hospitalized patients than in others (p<0.001)—no statistical difference in seizure rates within one month between hospitalized and non-hospitalized patients Table 4.

No statistical difference was detected between patients who had a seizure again within 30 days in terms of laboratory findings; furthermore, CRP values were higher in patients with 30-day mortality (p=0.004), while no statistical difference was found in other laboratory values Table 5.

**Table 3.** Comparison of 30-day mortality and patients' characteristic and vital parameters

	30 day Mortality		p value
	Survivor	Non-survivor	
<b>Gender</b>			
Male	43 (%64.18)	3 (%75.00)	
Female	24 (%35.82)	1 (%25.00)	
<b>Body Temperature</b>			
Normal	64 (%95.52)	3 (%75.00)	0.211
>37,8	3 (%4.48)	1 (%25.00)	
<b>Time of seizure prior to the admission</b>			
<5 min	4 (%6.06)	1 (%25.00)	0.466
5-10 min	9 (%13.64)	0 (%0.00)	
10-20 min	20 (%30.3)	1 (%25.00)	
20-30 min	12 (%18.18)	0 (%0.00)	
>30 min	21 (%31.82)	2 (%50.00)	
<b>Aura</b>			
Not present	48 (%71.64)	4 (%100.00)	0.568
Present	19 (%28.36)	0 (%0.00)	
<b>Reason of seizure</b>			
Unknown	46 (%68.66)	1 (%25.00)	0.018
Drug incompatibility	11 (%16.42)	0 (%0.00)	
Infection	5 (%7.46)	2 (%50.00)	
Other	5 (%7.46)	1 (%25.00)	
<b>Comorbidities</b>			
Not present	58 (%86.57)	4 (%100.00)	0.065
Present	9 (%13.43)	0 (%0.00)	
<b>Prior admission within 30 days</b>			
Not present	58 (%86.57)	4 (%100.00)	1.000
Present	9 (%13.43)	0 (%0.00)	
<b>Seizure in the ED</b>			
Not present	47 (%70.15)	4 (%100.00)	0.571
Present	20 (%29.85)	0 (%0.00)	

Min: Minute, ED: Emergency department

## DISCUSSION

The average age of the patients included in our study was 42.66. Considering the incidence of seizures, which rises and plateaus in adulthood and increases even more in the group over 60 years of age, it was observed that 21.1% of the present study's patients were over 60 years of age, which was found to be similar to the literature.<sup>4</sup> Likewise, considering that epilepsy is more common in males in the literature, there was a similar gender distribution in our study.<sup>5</sup>

Although there was no statistically significant difference between the age factor and ED follow-up period, seizure recurrence, and mortality, the average age of the deceased patients was found to be higher in our study. In an observational study conducted by Quintana et al.,<sup>6</sup> a high age factor was found to be associated with higher mortality in the epileptic patient group.<sup>6</sup>

14.08% of the patients included in our study had a history of head trauma during the seizure. Due to loss of consciousness, which is the main feature of complex seizures seen in epilepsy patients, the head trauma history of the patients was obtained through the seizure-related anamnesis taken from their

**Table 4.** Comparison of re-seizure within 30 days, mortality and hospitalization

	Hospitalization		p
	No	Yes	
<b>Re-Seizure</b>			
Not present	37(%62.71)	1 (%33.33)	0.554
Present	22 (%37.29)	2 (%66.67)	
<b>Mortality</b>			
Survivor	63 (%100.00)	4 (%50.00)	<0.001
Non survivor	0 (%0.00)	4 (%50.00)	

**Table 5.** Comparison of laboratory parameters of 30-day mortality and re-seizures within 30 days

	Re-seizure	Mean ± SD	p	Mortality	Mean ± SD	p
<b>WBC (x1000)</b>	Notpresent	8.73 ± 3.92	0.248	Survivor	8.27 ± 3.58	0.636
	Present	7.64 ± 3.24		Non survivor	10.45 ± 6.78	
<b>Lymphocyte (%)</b>	Notpresent	30.66 ± 12.52	0.355	Survivor	31.60 ± 11.91	0.105
	Present	33.63 ± 11.74		Non survivor	21.85 ± 9.75	
<b>Neutrophil (%)</b>	Notpresent	60.56 ± 14.03	0.171	Survivor	58.81 ± 13.54	0.061
	Present	55.58 ± 13.37		Non survivor	70.93 ± 9.43	
<b>pH</b>	Notpresent	7.31 ± 0.11	0.414	Survivor	7.30 ± 0.14	0.186
	Present	7.26 ± 0.17		Non survivor	7.38 ± 0.06	
<b>Lactate (mmol/L)</b>	Notpresent	5.60 ± 4.42	0.573	Survivor	5.36 ± 4.28	0.871
	Present	5.18 ± 4.27		Non survivor	4.23 ± 2.31	
<b>HCO3 (mmol/L)</b>	Notpresent	21.32 ± 5.18	0.465	Survivor	21.81 ± 5.28	0.439
	Present	22.43 ± 5.59		Non survivor	24.53 ± 4.56	
<b>BE (mmol/L)</b>	Notpresent	-4.73 ± 6.79	0.707	Survivor	-4.60 ± 7.02	0.396
	Present	-4.71 ± 7.73		Non survivor	-0.37 ± 5.14	
<b>Glucose (mg/dl)</b>	Notpresent	125.66 ± 29.90	0.084	Survivor	123.27 ± 37.43	0.765
	Present	119.33 ± 49.00		Non survivor	186.75 ± 138.07	
<b>CRP (mg/L)</b>	Notpresent	5.82 ± 7.29	0.527	Survivor	5.25 ± 6.58	0.004
	Present	4.13 ± 5.48		Non survivor	41.78 ± 35.42	
<b>Potassium (mmol/L)</b>	Notpresent	4.17 ± 0.54	0.390	Survivor	4.19 ± 0.50	0.832
	Present	4.28 ± 0.42		Non survivor	4.30 ± 0.56	
<b>Calcium (mg/dl)</b>	Survivor	8.78 ± 0.56	0.564	Yok	8.82 ± 0.55	0.960
	Non survivor	8.86 ± 0.54		Var	8.85 ± 0.81	
<b>Sodium (m/mol)</b>	Survivor	139.24 ± 3.48	0.942	Yok	139.19 ± 3.38	0.304
	Non survivor	139.75 ± 3.18			141.75 ± 5.56	

WBC: White blood cells, BE: Base excess, CRP: C reactive protein, Min: Minute, ED: Emergency department

relatives and the patient's head trauma examination findings. Although there was no statistically significant difference in the hospitalization and re-seizure risk within 1 month of patients with a history of head trauma, the average ED follow-up time was observed to be higher.

When the seizure types of the patients were examined according to the epilepsy classification, the most common seizure type was generalized tonic-clonic (90.14%). In a retrospective, cross-sectional study conducted by Bozali et al.,<sup>7</sup> the characteristics of patients presenting to ED with seizures and the factors affecting the frequency of admission, generalized tonic-clonic seizures were found to be the most common seizure type.<sup>7</sup> In various prevalence studies, it has been observed that focal seizures vary between 33-65% and generalized tonic-clonic seizures vary between 17-60% .<sup>8</sup> The low number of focal seizures in our study may be because our study included only patients presenting with ED. Epilepsy patients with focal seizures may have fewer ED presentations. Although the correct classification of seizure types is important in terms of helping clinical communication

between the patient and the clinician and guiding the correct treatments, the high rate of 90.14% of generalized tonic-clonic seizures in our study in terms of ED admissions can be explained by several factors. These factors also explain the small number of patients in our study, with changes in patients' habits of using EDs due to the COVID-19 pandemic, which was during the study, and the fact that the study only included the adult age group.

The evaluation of non-epileptic chronic diseases of the patients included in our study revealed that the most common were HT DM. Similar to our study, a review study by Gasparini et al. stated that epilepsy and HT are both common chronic conditions with high prevalence in older age groups and that HT may have both a direct and indirect role in epileptogenesis.<sup>9</sup> In a study conducted by Shlobin et al.<sup>10</sup> examining the relationship between Type 2 DM and epilepsy, relationship and biological mechanisms found that mitochondrial dysfunction and adiponectin deficiency were common for epilepsy and Type 2 DM.

88.73% of the patients included in our study were discharged home after their ED follow-up period ended. 6 patients (8.45%) were admitted to the ward, and 2 patients (2.82%) were admitted to the intensive care unit. In a study conducted by Cordato et al.<sup>11</sup> on the number of patients presenting to ED with seizures, it was found that 58% of patients with seizures were discharged from ED.

The patients included in the study were called by phone 30 days after leaving the ED, and their health status and whether they had re-seizures were questioned. 24 (33.80%) patients had a seizure again within 30 days, and 4 (5.63%) patients died. Similar to the data we obtained in our study, in a study on epilepsy epidemiology in Europe conducted by Forsgren et al.,<sup>8</sup> approximately 20-30% of the epilepsy population may have more than one seizure per month. In the study conducted by Avilés et al.,<sup>12</sup> 16.2% of the patients had a seizure again within 30 days after ED discharge. The same study reported the mortality rate from any cause within 30 days as 1.4%.<sup>12</sup> Our study's relatively high mortality rate may be due to the small number of patients included in the study and the fact that the study was conducted during the COVID-19 pandemic.

In our study, CRP values were found to be higher in patients who died within the 30-day follow-up period after leaving ED than in other patients ( $p = 0.004$ ). Based on a review of the literature, CRP was previously considered an inflammatory marker but has subsequently been extensively studied in many non-inflammatory neurological conditions. However, studies on CRP in the context of seizures or epilepsy are limited. Alapirtti et al.<sup>13</sup> reported in their study that there was a significant increase in CRP levels in generalized tonic-clonic seizures. Fujii et al.<sup>14</sup> found that the CRP level did not increase significantly in acute encephalopathy seen with biphasic seizures and late reduced diffusion in the pre-seizure period. However, the increase in procalcitonin levels was significant. Since procalcitonin is not a routine test in patients with seizures, this parameter could not be evaluated in our study. Sohn et al.<sup>15</sup> investigated the frequency and severity of inflammation-like responses in patients presenting with ED with seizures, associated clinical

factors, and whether transient responses caused by seizures could be distinguished from responses caused by concurrent infection. In a meta-analysis in 2019, CRP levels in peripheral blood in epileptic patients increased significantly compared to healthy controls, and there was a significant relationship between inflammation and epilepsy. However, it was added that further studies should be conducted to evaluate the etiology of epilepsy, age of epilepsy onset, seizure frequency, and the effect of AED use on CRP levels in epilepsy. In our study, the fact that CRP levels were found to be higher in patients who died within the 30-day follow-up period than in other patients suggests that CRP levels should be carefully monitored in patients presenting to ED with seizures.

Finally, the data curation of this study conducted during COVID-19 pandemic which makes our data unique. Pandemic period resulted in fewer ED admissions for epileptic patients.<sup>16</sup> Delaying admissions in the fear of nosocomial cross-infection of COVID-19 might have changed outcomes, especially for the infected patients. Understanding the multifactorial concept of help-seeking behavior requires further studies with the data from the pandemic period.

### Limitations

This study was conducted in a single center; therefore, the results can not be generalized. The change in patients' ED admission habits due to the COVID-19 pandemic may have affected the number of patients applying to ED and their outcomes. Although the EEG could have been utilized for further re-seizure data due to its application to all patients in the ED, it is not feasible in our institution. Lastly in our institution we did not had the capacity to measure blood drug levels. Measuring the drug levels would have include more insight to the patients conditions.

### CONCLUSION

Among patients presenting to ED with epileptic seizures, the 30-day mortality is higher in patients who are elderly, have active infection, and have elevated CRP in their laboratory parameters. These patient groups should be followed up closely for a longer period.

### ETHICAL DECLARATIONS

#### Ethics Committee Approval

The study was carried out with the permission of Ethical Committee of Faculty of Kocaeli Derince Training and Research Hospital (Date:01.09.2020 , Decision No: 01.07.2021).

#### Informed Consent

All patients signed and free and informed consent form.

#### Referee Evaluation Process

Externally peer-reviewed.

#### Conflict of Interest Statement

The authors have no conflicts of interest to declare.

#### Financial Disclosure

The authors declared that this study has received no financial support.


## Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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# Trends and implications of ENT cases in emergency medicine: insights from a tertiary hospital study

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## ABSTRACT

**Aims:** This study aimed to investigate the epidemiological data of patients presenting to the emergency department of a tertiary care hospital with complaints of ear, nose, and throat diseases.

**Methods:** This retrospective study included patients who presented to the emergency department with complaints of ear, nose, and throat diseases between 01.04.2015 and 01.10.2015. Age, sex, presence of a diagnosed ear, nose, and throat disease, mode of presentation (referral/primary presentation), diagnosis in the emergency department, consultation status, forensic case status, examination status, and discharge status were analyzed. Descriptive statistics (frequency and percentage distribution) were used for statistical analysis. The results are presented as mean  $\pm$  SD or frequency (percentage).

**Results:** This study included 2425 patients. 51.5% of the patients were female. The mean age was 35.27 $\pm$ 15.6 years (0-88). The highest number of patient admissions was in the 21-30 age range (38.4%). 98.1% of the patients presented to the emergency department as outpatients. It was observed that 2.4% of the applicants had a known previous ear, nose and throat disease. Computed tomography (CT) was the most frequently requested test. The most common diagnoses were acute tonsillopharyngitis and vertigo (60.1%) and vertigo (25.1%, respectively). 3.5% of the patients were evaluated as forensic cases. 4.5% of the patients were consulted to the ear, nose and throat clinic and 3.6% to the plastic and reconstructive surgery clinic. The discharge rate was 97.5%.

**Conclusion:** The number of outpatient admissions to the emergency department (98.1%) was quite high; 95.5% of the patients did not consult the ear, nose, and throat clinic, and 97% were discharged with an outpatient prescription.

**Keywords:** Emergency department, otolaryngology, epidemiology

## INTRODUCTION

Ear, nose, and throat (ENT) emergencies encompass a range of conditions from mild to severe, necessitating prompt care in secondary or tertiary healthcare facilities. The most common reasons for presentation include ear pain, tinnitus, sudden hearing loss, ear infections, nasopharyngeal infections, vertigo, and maxillofacial traumas. Trauma-related cases, particularly those involving the ear, nose throat, head, and neck, are increasingly prevalent in emergency departments, a trend likely influenced by the rise in road traffic accidents and natural disasters.<sup>1</sup> It has been reported that foreign bodies seen in the external auditory canal, nasal cavity and airway are among the emergencies of the otorhinolaryngology clinic with a rate of 30%.<sup>2</sup>

It has been observed that approximately 10% of the patients consulted to the ENT clinic from the emergency department are really conditions requiring urgent intervention and the majority of them are diseases that can be resolved with

simple intervention.<sup>3</sup> In a study conducted in our country, it was found that there were 1 million 64 thousand 610 applications to the emergency department in a year, pathologies related to the ENT clinic were detected in 27795 (20.75%) of these applications, but more than 95% were treated by emergency physicians.<sup>4</sup> As stated in the studies, it is thought that the vast majority of especially outpatient applications to emergency departments do not need urgent treatment in terms of ENT clinic. Owing to the type of task, the crowding of non-urgent patients in the emergency department prevents patients in need of urgent treatment from receiving the attention they deserve. In many emergency departments, the subjectivity of the concept of emergency is detrimental to appropriate care.<sup>5</sup>

In this study, we aimed to examine the epidemiologic data of patients presenting to the emergency department of a tertiary care hospital with complaints of ENT diseases.





## METHODS

The study was carried out with the permission of the Bursa Uludag University Hospital Scientific Researchs Evaluation and Ethics Committee (Date:12.04.2016 Decision No: 2016-7/2). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.<sup>3</sup> Retrospective analysis was performed on patients who were hospitalized between April 15 and October 2015.

This retrospective study was conducted in the emergency department of a medical faculty hospital serving as a tertiary healthcare institution to provide a comprehensive overview of ENT-related presentations. In line with the study's objectives, patients who were admitted to the emergency room between April 1, 2015, and October 1, 2015, were assessed and given an ICD (International Classification of Disease) classification by the attending physician. Evaluations were conducted for H92 (otalgia), H93 (tinnitus), H91 (sudden hearing loss), R42 (vertigo), H60 (otitis externa), and H60. 21 (malignant otitis externa), H66 (otitis media), H73 (bullous myringitis), T16 (foreign body in the ear), T17 (foreign body in the nose), T18 (foreign body in the mouth), K11 (sialolithiasis), S03 (mandibular dislocation), R04 (epistaxis), J03 (acute tonsillitis), J36 (peritonsillar abscess), J05 (epiglottitis), J39 (retropharyngeal abscess), S02 (maxillofacial trauma), T78 (hereditary angioedema), Z93 (tracheostomy), and J95 (tracheostomy tube exchange). Patients who had the aforementioned ICD codes entered as the initial diagnosis by the emergency physician but who, upon file examination, were given a different diagnosis and course of treatment for a different condition, were not included in the study. Among patients under the age of 18, only patients with a diagnosis of maxillofacial fracture were included. Patients presenting with the same complaint on the same day were considered a single patient, and second visits were excluded from the study.

In this study, 63900 patients were screened, and 2425 patients were evaluated for ear, nose, and throat (ENT) emergencies and included in the study. Applications, protocol numbers, primary and referral applications, patient complaints upon admission to the emergency room, ENT or plastic and reconstructive surgery (PRC) consultation status, forensic case status, laboratory, X-ray, computed tomography (CT), magnetic resonance imaging (MRI), discharge status (discharge, hospitalization, refusal of treatment, leaving the emergency room without permission), and referrals to other healthcare facilities were all noted in the data form.

### Statistical Analysis

Statistical Package for Social Sciences for Windows 22.0 (SPSS 22.0) was used to analyze the data. Descriptive statistics (frequency and percentage distribution) were used for statistical analysis. The results are presented as mean  $\pm$  SD or frequency (percentage).

## RESULTS

Within the scope of this study, 2425 patients were evaluated. 51.5% (n=1248) of the patients were female. The mean age was 35.27 $\pm$ 15.6 years (0-88) (Table 1).

Table 1. Analysis of demographic data

Data	Mean/Number of Patients (n)	Rate (%)
Age	35.27 $\pm$ 15.6	
<b>Gender</b>		
Male	1177	48.5
Female	1248	51.5
<b>Application Form</b>		
Outpatient application	2350	98.1
Referral from another institution	75	1.9
<b>Pre-Existing Disease Status*</b>		
No	2368	97.6
Yes	57	2.4
<b>Investigation</b>		
No Examination	1795	74
Computerized Tomography	322	13.3
X-ray	155	6.4
Laboratory	153	6.3
Magnetic Resonance Imaging	61	2.5
<b>Diagnosis</b>		
Acute tonsillitis	1458	60.1
Vertigo	610	25.2
Maxillofacial trauma	182	7.5
Foreign body	86	3.5
Otitis externa	34	1.4
Peritonsillar abscess	10	0.4
Hereditary angioedema	6	0.2
Sudden hearing loss	6	0.2
Epistaxis	3	0.1
Tracheostomy tube exchange	2	0.1
Tracheostomy care	2	0.1
Tinnitus	2	0.1
Parotitis	2	0.1
Retropharyngeal abscess	1	0.0
Malignant otitis externa	1	0.0
<b>Forensic Case</b>		
No	2341	96.5
Yes	84	3.5
<b>Consultation</b>		
Ear Nose Throat	108	4.5
Plastic and Reconstructive Surgery	88	3.6
<b>Conclusion</b>		
Discharged	2364	97.5
Hospitalization	53	2.2
Treatment refusal	3	0.1
Leaving the emergency room without permission	4	0.2
Referral to another institution	1	0.0

\*Previously known ear, nose and throat disease status

The highest number of patient admissions was in the 21-30 age range (38.4%). The distribution of admissions according to the age range is shown in Figure 1.

A total of 98.1% of patients (n=2380) were admitted to the emergency department as outpatients. It was observed

that 2.4% (n=57) of the applicants had a known ENT disease. The most requested test was CT with a rate of 13.3% (n=322). The predominant diagnoses identified were acute tonsillopharyngitis, accounting for 60.1% (n=1458) of cases, followed by vertigo at 25.1% (n=610), highlighting the prevalence of these conditions in the emergency setting. A total of 3.5% (n=84) of patients were evaluated as forensic cases. A total of 4.5% (n=108) of the patients were referred to the ENT clinic, and 3.6% to the PRC clinic (n=88). The discharge rate was 97.5% (n=2364) (Table 1). Of the 53 inpatients, 12 (22.6%) were hospitalized in the ENT clinic. Among these patients were those with peritonsillar abscess (n=5), malignant otitis externa (n=1), tracheal stenosis (n=1), and vestibular neuritis (n=5). In our study, the rate of cranial MRI findings in patients presenting with dizziness was 2.5%. Four patients were found to have had ischemic stroke and were admitted to the neurology clinic.

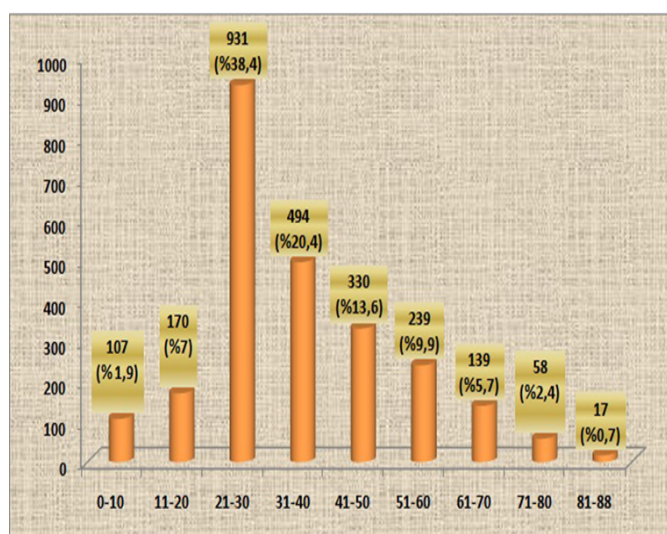


Figure 1. Distribution of patients according to age ranges

## DISCUSSION

While the number of home care patients, the widespread use of home ventilators, the extension of the average human life expectancy, and the rise in the number of immunosuppressed patients as a result of medical advances have increased the frequency of emergency department visits of non-traumatic ENT patients, the incidence of traffic and occupational accidents, along with disasters, have significantly contributed to an increase in trauma-related ENT emergencies. In this study, we conducted a detailed analysis of the demographic data of patients who presented with ENT in the emergency department.

In our study, 51.5% of the patients were female. When we look at the gender distribution in similar studies in the literature, Prestes et al. reported that 52% of the patients were female<sup>6</sup>, Symvoulakis et al.<sup>7</sup> reported that 51% were female, Lammens et al. reported that 57% were male and Yojana et al.<sup>8</sup> reported that 70% were male. Yojana et al.<sup>9</sup> evaluated that the 2.5-fold increase in the male rate in the study conducted in India can be explained by the cultural and social taboos of the country. The reason for this is that men have a higher working rate and therefore encounter traffic accidents more frequently,

while women live a life limited to the home.<sup>9</sup> As can be seen, gender distribution may vary according to regions and living conditions.

The age group of 21 to 30 years accounted for the largest percentage of admissions (38.4%) based on patient distribution by age range.

According to previous studies, the age range with the greatest number of applications was between 20 and 40 years (37%) according to Prestes et al.<sup>6</sup> and 15 to 34 years (Symvoulakis et al.<sup>7</sup>). Similar to other studies, we attributed the high rate of admission in patients aged 20-40 years to the fact that people in this age range are more active in daily life.

When we examined the distribution of diagnoses in patients, we found that tonsillopharyngitis was the most common (60.1%). In the study by Prestes et al. this rate was 53.6% and similarly constituted the first rank.<sup>6</sup> The rate of tonsillopharyngitis was 36% in the study of Furtado et al.<sup>10</sup> consisting of 26584 individuals. In the study by Symvoulakis et al.<sup>7</sup> this rate was 26.7% and ranked first. It was reported as 4.9% in the study by Lammens et al.<sup>8</sup> In our study, the second most common diagnosis was vertigo (25.1%). In the study by Prestes et al.<sup>6</sup>, no distinction was made between vertigo and dizziness, and the rate of vertigo was 3.93%; in a study by Symvoulakis et al.<sup>7</sup> this rate was found to be 3.5% for dizziness and 3.3% for vertigo. In a study including thirty thousand patients, the prevalence of vertigo was found to be around 17% and increased to 39% over the age of eighty.<sup>11</sup> One of the limitations of our study was that patients presented with complaints of dizziness in conditions such as motion sickness and dizziness; therefore, dizziness could not be differentiated, and all patients were evaluated as vertigo.

In our study, the rate of presentation to the emergency department due to maxillofacial trauma was 7.5%. This rate was found to be 6% in terms of nasal fracture secondary to trauma in a study conducted in Belgium.<sup>8</sup> In a study by Symvoulakis et al.<sup>7</sup> ear, nose and face traumas were found to be 5.4%. Similarly, the rate of maxillofacial trauma was found to be 7.9% in the study by Furtado et al.<sup>10</sup> As a different rate, the rate of maxillofacial trauma was found to be 84% in the study by Yojana et al.<sup>9</sup> The reason for this high rate may be related to the fact that only trauma cases were evaluated in the center where the study was conducted.

In our study, 3.5% of patients admitted to the emergency department had a foreign body in the ear, nose, or oropharyngeal region. In the study by Symvoulakis et al.,<sup>7</sup> the rate of foreign bodies was similar to that in our study (3.5%). In the study by Prestes et al.,<sup>6</sup> foreign bodies in the ear and nose were evaluated, and both had a rate of 0.56%. Yojana et al.<sup>9</sup> found this rate to be 5.8% in their study. In the study by Furtado et al.<sup>10</sup> the rate was 16.7%. When our study is evaluated proportionally with other studies, there are similar results in general.

An increasing demand for emergency rooms was suggested in a 2005 study by Rivero et al. when the frequency of visits to the emergency room was assessed. The most common causes of ENT emergencies were evaluated as nasal trauma, epistaxis, and otitis externa.<sup>11</sup>

In our study, the rate of patients diagnosed with external otitis was 1.4%. This rate was 2.8% in the study by Lammens et al.<sup>8</sup> Patients in the Yojana et al.<sup>9</sup> trial had an evaluation of ear discomfort with a rate of 0.9%, without making a distinction between otitis media and external otitis. These patients had otitis externa or acute otitis media of different etiologies. In a study by Prestes et al.<sup>6</sup> the rate of acute external otitis was 5.8%. In the study by Symvoulakis et al.<sup>7</sup> this rate was found to be 6%. The diagnosis of external otitis mediastinalis in patients admitted to our hospital's emergency department was comparatively lower than that in other studies. This may be related to the fact that there is no sea in the region where the study was conducted, pool facilities are limited, and the frequency of external otitis characterized as pool otitis is low.

In our study, uvular edema and angioedema were observed at rates of 0.3% and 0.2%, respectively, and uveal edema and angioedema were assessed together in the Symvoulakis et al.<sup>7</sup> study rather than separately, and a rate of 0.4% was observed. In a study of 1296 patients by Lammens et al.<sup>8</sup> the rate of angioedema was reported to be 0.8%.

In our study, patients presenting with isolated sudden hearing loss had a rate of 0.2%. Lammens et al.<sup>8</sup> reported the rate of patients presenting with hearing loss as 0.6% in their study. In the study by Symvoulakis et al.<sup>7</sup> the rate was found to be 0.4%. The rates observed in these results were similar.

In the present study, the rate of isolated epistaxis was 0.1%. In a study by Lammens et al.<sup>8</sup> the rate of patients admitted due to isolated epistaxis was reported to be 0.5%. The rate of isolated epistaxis was 12.98% in the study by Furtado et al.<sup>10</sup> In a study by Symvoulakis et al.<sup>7</sup> this rate was 3.4%. In a study by Prestes et al.<sup>6</sup> the rate of epistaxis was 4.9%. In a study by Yojana et al.<sup>9</sup> the rate of isolated epistaxis was 0.7%. While the results of our study and the Yojana et al.<sup>9</sup> study were similar, the other studies showed rates that were almost ten times higher. These rates were comparatively lower in the present study. This may be due to the fact that the physician entered diagnoses such as anticoagulant poisoning if the bleeding was due to warfarin overdose or hypertension if the bleeding was due to high blood pressure instead of epistaxis code as ICD diagnosis.

In our study, the admission rate due to tracheostomy and tracheostomy cannula exchange was 0.1%. However, studies conducted in Spain, Belgium, Brazil, Greece, Brazil, Greece, and India have shown that there were no admissions to the emergency department due to tracheostomy or tracheostomy cannula exchange.<sup>6-11</sup> This could mean that enhanced home care services in the research locations resolved planned and elective issues such as cannula exchange and tracheostomy care. We anticipate that this will solve the problems experienced during the transportation process of patients followed up with home mechanical ventilators to the hospital.

In our study, the proportion of patients with isolated tinnitus was 0.1%. This rate was 1.2% in the study by Prestes et al.<sup>6</sup> Symvoulakis et al.<sup>7</sup> evaluated tinnitus and decreased

hearing, together with a rate of 1.8%. In a study by Lammens et al.<sup>8</sup> the rate of patients presenting with tinnitus was 0.7%. In our study, the rate of diagnosis of parotitis was 0.1%. In the study by Yojana et al.<sup>9</sup> the rate of parotitis was 5.1%.

According to our analysis, situations requiring emergency intervention were assessed in the emergency department for 12.7% of patients associated with the ENT clinic. Similarly, Prestes et al.<sup>6</sup> evaluated 9.27% and Timsit et al.<sup>12</sup> evaluated 10% of patients admitted to the emergency department as emergency cases.

In our study, we observed that the number of outpatient applications related to ENT clinics (98.1%) was quite high in an institution serving as a tertiary health institution. It was observed that 95.5% of the patients were not asked for ENT consultation, and 97% were discharged with an outpatient prescription. Considering the results of our study, we think that the diagnosis and treatment of these patients can be organized especially in primary healthcare institutions.

### Limitations

Our study has several limitations. First, the experience of only one institution was included in our study, which was based on retrospective data. Outcomes may change in areas with distinct hospital characteristics and demographics.

It was not possible to ascertain patients' subsequent follow-up after being referred to an ENT physician. A prospective study design will allow the monitoring of this patient population.

## CONCLUSION

The results of this study indicate that most ENT emergencies seen in the emergency department may be managed as outpatient cases, which presents a significant opportunity for improving primary care pathways. Ensuring that only cases requiring immediate, specialized interventions obtain tertiary care will greatly expedite emergency care by formalizing a more stringent triage procedure supported by evidence-based protocols. Furthermore, the observed high discharge rates indicate the viability of this technique, which could have advantages, such as more efficient use of healthcare resources and less traffic in emergency rooms. It is essential to make more investments in the education and training of primary care physicians in order to provide them with the necessary skills to treat common ENT diseases. This calculated reorientation, underpinned by strong epidemiological insights, could improve the quality of treatment given, guarantee prudent use of emergency medical resources, and eventually promote a more sustainable healthcare environment.

## ETHICAL DECLARATIONS

### Ethics Committee Approval

The study was carried out with the permission of the Bursa Uludag University Hospital Scientific Researches Evaluation and Ethics Committee (Date:12.04.2016 Decision No: 2016-7/2 ).

### Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

### Referee Evaluation Process

Externally peer-reviewed.

### Conflict of Interest Statement

The authors have no conflicts of interest to declare.

### Financial Disclosure

The authors declared that this study has received no financial support.

### Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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# Aortic dissection in a renal transplant patient presenting with gastroenteritis: case report

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## ABSTRACT

Acute aortic dissection is a true cardiovascular emergency whose diagnosis and treatment process is very difficult for the patient and the physician, with a mortality rate of 50% in some cases if not intervened within the first 48 hours. Aortic dissection is classified according to the anatomical region of the aorta affected. Class 1 De Bakey dissection involves the ascending aorta, arcus aorta and descending aorta. Class 2 De Bakey is limited to the ascending aorta, while class 3 De Bakey starts from the descending aorta. According to the Stanford classification, dissection type is divided into A and B. The most common complaints at presentation are predatory chest pain in type A dissection and low back pain or abdominal pain in type B dissection.

## INTRODUCTION

Acute aortic dissection (AD) is a true cardiovascular emergency whose diagnosis and treatment process is very difficult for the patient and the physician, with a mortality rate of 50% in some cases if not intervened within the first 48 hours.<sup>1</sup> AD is often associated with genetic connective tissue disorders and hypertension.<sup>2</sup> AD is classified according to the anatomical region of the aorta affected. Class 1 De Bakey dissection involves the ascending aorta, arcus aorta and descending aorta. Class 2 De Bakey is limited to the ascending aorta, while class 3 De Bakey starts from the descending aorta. According to the Stanford classification, dissection type is divided into A and B (Figure 1).<sup>3</sup>

International Registry of Acute Aortic Dissection (IRAD) was established to evaluate aortic dissection cases with data from multiple centers. In the comprehensive study conducted by IRAD, 67% of patients were classified as type A.<sup>4</sup> The most common complaints at presentation are predatory chest pain in type A dissection and low back pain or abdominal pain in type B dissection. Patients presenting with atypical complaints other than the classical symptoms have a higher mortality and morbidity rate as the diagnosis becomes more difficult.<sup>5</sup> Multi-organw ischemia, cardiac tamponade, hemorrhage, shock and sudden death may occur undiagnosed in some patients.<sup>6</sup>

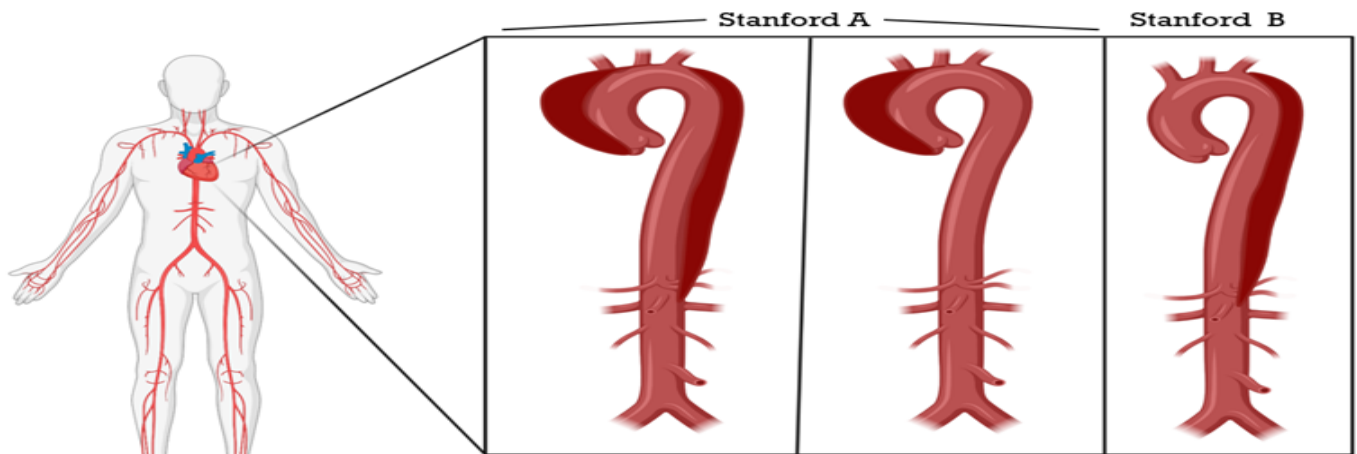
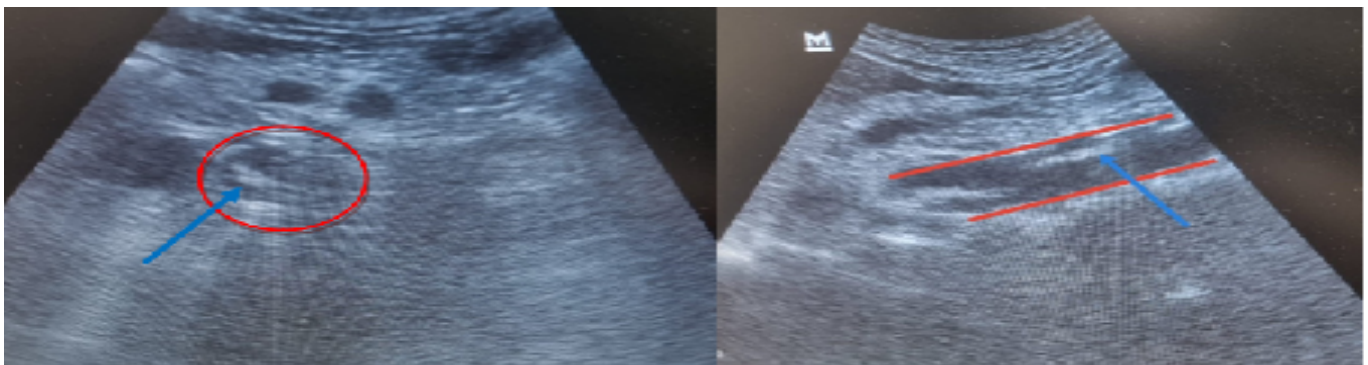


Figure 1. Classification of aortic dissection

## CASE

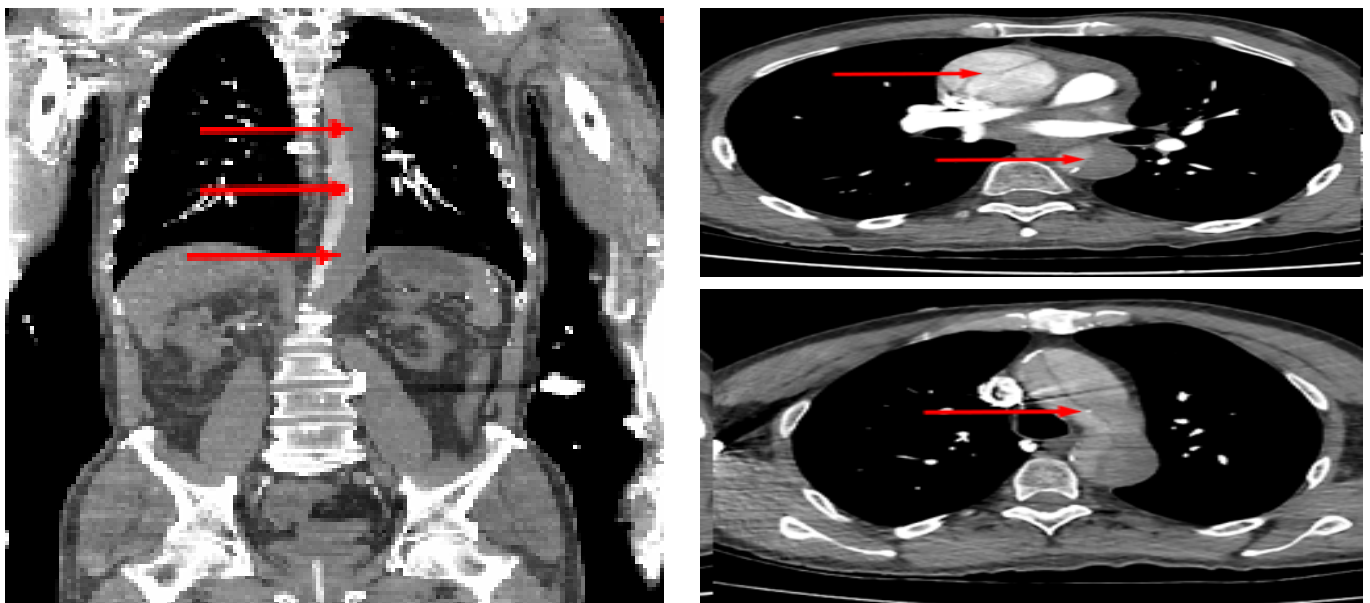
A 57-year-old man presented to the emergency department with sudden onset of nausea, vomiting and diarrhea. He reported colicky abdominal pain and no chest pain or back pain. His past medical history revealed hypertension and renal transplantation three years ago. In the vital signs checked; blood pressure: 100/60 mmHg, pulse rate: 78/min, temperature: 36.7°C, SpO<sub>2</sub> 94%. It was observed that the patient had a fistula in his left arm from the time he was on hemodialysis. On physical examination, general condition was moderate, consciousness was clear, oriented and coherent. His skin was moist, neurologic examination and respiratory system examination were normal. Diffuse abdominal tenderness and hyperactive bowel sounds were detected. It was learned that diarrhea was bloodless, watery and normal stool color. Electrocardiography (ECG) showed no acute ischemic changes. Symptomatic treatment and fluid replacement were initiated and the patient stated that his complaints regressed. In blood tests; WBC: 11900 /mm<sup>3</sup>, Hb: 14.6 g/dl, platelets: 256000/mm<sup>3</sup>, troponin: 16.7 ng/L

(normal range: 14-42.9), BUN: 15.5 (normal range:6-20), serum creatinine: 1.08 (normal range: 0.6-1.3). After fluid replacement, the patient's blood pressure improved, but it started to drop again during follow-up, the patient stated that he had cramp-like abdominal pain and left leg pain, which was not present at the first admission, started during follow-up. On examination for this complaint, equal pulsation was obtained in both femoral pulses. Blood pressure difference between extremities could not be monitored because of the fistula in the left arm. Contrast-enhanced imaging was planned to rule out possible cardiovascular pathology in a patient with a sweaty, toxic, agitated appearance that could not be explained by gastroenteritis only; however, considering that contrast may cause harm instead of benefit due to the fact that the patient had only one kidney, that kidney was "valuable" because it was a trans kidney, and the current creatinine value was at the upper limit, it was decided to evaluate the aorta with bedside ultrasonography (USG) first. USG showed a flap image in the abdominal aorta ([Figure 2](#)).



**Figure 2.** Red lines are aortic borders. Blue arrows are dissection flaps

The patient was consulted with cardiovascular surgery (CVS). Computed tomography (CT) angiography was recommended for preoperative classification and surgical technique planning. CT angiography revealed De Bakey type 1 aortic dissection ([Figure 3](#)) and the patient was transferred to the CVS clinic.



**Figure 3.** Arrows show flap views in the ascending aorta, descending aorta and arcus aorta

## DISCUSSION

Cardiovascular complications are the most common complications in renal transplant patients and are the most common cause of death. While hypertension is the most common disease, aortic dissection is a rare condition.<sup>7-8</sup> In the majority of AD cases, blood pressure is found to be elevated at presentation, while hypotensive patients are accompanied by clinical conditions such as neurological findings, altered consciousness, myocardial infarction, mesenteric ischemia, and limb ischemia.<sup>9</sup> In our case, hypotension was present at presentation but none of the mentioned symptoms were present. On follow-up, ischemic pain in the left leg started.

Routine laboratory tests are not very helpful in the diagnosis, and ECG changes may be seen in some cases. Magnetic resonance imaging (MRI) or contrast-enhanced CT can be used to confirm the diagnosis. MRI is disadvantageous in that it takes a long time, is not easily accessible and cannot be used in patients with metal implants. On the other hand, although CT angiography is highly effective in definitive diagnosis, caution should be exercised in patients with impaired renal function tests in terms of contrast nephropathy.<sup>10</sup> Transthoracic echocardiography or bedside ultrasonography is a practical diagnostic method that can be performed without additional contrast load on the patient.<sup>11</sup> In our case, since there were no classical symptoms suggestive of aortic dissection such as tearing chest pain, back pain, pulselessness, difference in blood pressure in both arms, the main presenting complaint was nausea, vomiting and diarrhea, the patient was a renal transplant recipient and the creatinine value was at the upper limit, we thought that performing contrast-enhanced tomography would mean exposing the trans kidney to the risk of contrast nephropathy. However, ischemic left leg pain developed during follow-up and bedside ultrasound was performed and a dissection flap was seen in the aorta at the level of the abdominal aorta. Contrast-enhanced tomography was then performed for dissection classification and surgical planning.

## CONCLUSION

Aortic dissection may present to emergency departments with very different complaints. Even in patients with classical symptoms, it takes a certain amount of time to make a differential diagnosis and to make a definitive diagnosis, and each passing hour increases the mortality rate of the patient. However, it is much more difficult for the patient and the physician to consider dissection and make a diagnosis in patients with atypical presentation as in this case. Moreover, administering contrast media in patients with impaired renal function or renal transplantation leads to serious dilemmas for physicians considering a possible negative diagnosis. Therefore, every emergency physician should have the ability to visualize the aorta with basic ultrasound techniques even if they cannot perform advanced echocardiography.

## ETHICAL DECLARATIONS

### Informed Consent

The patient signed and free and informed consent form.

### Referee Evaluation Process

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### Conflict of Interest Statement

The authors have no conflicts of interest to declare.

### Financial Disclosure

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### Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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# Bedside ultrasonography in diagnosing bilateral femoral arterial occlusion in an elderly patient with acute limb ischemia

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## ABSTRACT

**Aims:** Non-traumatic acute limb ischemia is a critical vascular emergency that can lead to limb loss or life-threatening complications. It is predominantly caused by arterial occlusions due to thrombi or emboli. Our report highlights the pivotal role of bedside ultrasonography in the emergency diagnosis of acute limb ischemia, exemplified by a case of bilateral femoral arterial occlusion.

**Case:** An 83-year-old woman with a medical history of atrial fibrillation, not on anticoagulation therapy, presented to the emergency department with increased right knee pain and dizziness. Initial examination revealed palpable peripheral pulses and sensitivity on knee palpation without overt signs of ischemia. However, subsequent systemic examination, prompted by the patient's worsening agitation and pain, revealed coldness, pallor, and weakened pulses in both lower extremities. Bedside ultrasonography confirmed the presence of thrombi in both femoral arteries. The patient underwent successful emergency thrombectomy and was discharged with full recovery after appropriate management of atrial fibrillation.

**Conclusion:** This case underscores the importance of vigilant systemic re-examination and the utility of bedside ultrasonography in the rapid diagnosis of acute arterial occlusion, particularly in patients with risk factors such as atrial fibrillation. Emergency physicians should consider acute limb ischemia in the differential diagnosis of patients presenting with non-specific symptoms like dizziness and localized pain, especially when coupled with a history of cardiovascular risk factors.

**Keywords:** Emergency medicine, bedside ultrasonography, acute arterial occlusion

## INTRODUCTION

Non-traumatic acute limb ischemia is a significant vascular emergency with potential consequences that can range from limb loss to life-threatening systemic complications.<sup>1</sup> It primarily results from impaired arterial blood flow due to a thrombus, which accounts for approximately 85% of cases, or an embolism, responsible for about 15% of instances. While acute limb ischemia is commonly associated with the middle-aged and elderly populations, it can also occur in younger patients under specific circumstances affecting arterial circulation, such as paradoxical embolism, intracardiac masses, endocarditis, or hypercoagulability syndromes.<sup>2-4</sup>

The most frequent source of an embolism causing acute limb ischemia is cardiac in origin. Conditions like apical thrombus formation and age-related atrial fibrillation, along with left ventricular dysfunction, are the predominant causes of cardioembolic events. This condition affects both male and female populations equally.<sup>2</sup>

The femoral artery is notably vulnerable to occlusions. Approximately two-thirds of non-cerebral emboli lead to blockages in the lower extremities, with a significant proportion involving the aorto-ilio-femoral arteries. Diagnosis of acute limb ischemia can be challenging due to its ability to induce sensory and motor deficits, which mimic the symptoms of a cerebrovascular accident.<sup>5</sup>

Our case illustrates the critical role of emergency physicians in the early recognition and diagnosis of acute arterial occlusion. We emphasize the utility of bedside ultrasonography as an integral part of the physical examination, aiding in the rapid diagnosis of this condition. The case of an 83-year-old woman with atrial fibrillation, who was not on anticoagulant therapy and presented with neurological symptoms, highlights the complexity of diagnosis in the emergency setting. Our case serves as a reminder of the importance of considering acute arterial occlusion in differential diagnosis, particularly in patients with known risk factors.



## CASE

Here, we present an 83-year-old female patient, known to have hypertension, heart failure, and hypothyroidism, and under medication with furosemide, ramipril, carvedilol, and levothyroxine whose medical history was obtained from accompanying relatives, due to her hearing and speech impairments.

She was admitted to the emergency department with complaints of increased pain in her right knee and dizziness, experienced after a nocturnal visit to the bathroom. Her medical history revealed a knee surgery performed two years prior, with subsequent chronic pain in the same area.

Upon initial examination, her vital signs were as follows: arterial pressure 117/87 mmHg, pulse rate 96/min, body temperature 36.6°C, and oxygen saturation 96% on room air. The right knee was tender on palpation, but there was no noticeable increase in temperature, hyperemia, or edema. Peripheral pulses were palpable, and a detailed neurological examination did not reveal any acute pathological findings. Knee radiography was performed, showing no acute abnormalities.

However, during subsequent observation, the patient exhibited signs of agitation and engaged in non-purposeful movements. Laboratory tests were ordered, and brain imaging was conducted to rule out a cerebrovascular accident, both of which reported without any acute pathological findings. The patient's ECG indicated atrial fibrillation. Given her chronic AF and lack of anticoagulant therapy, there was a heightened risk for embolic events. Cardiac biomarkers were within normal limits, excluding acute coronary syndrome.

As the patient's agitation persisted, a second systemic examination was performed. This time, we observed signs of acute arterial occlusion- notably, coldness, pallor, weakened pulses in both lower extremities, which were absent in the initial examination. Bedside ultrasonography revealed thrombi in both femoral arteries, leading to the diagnosis of bilateral femoral arterial occlusion (Figure).

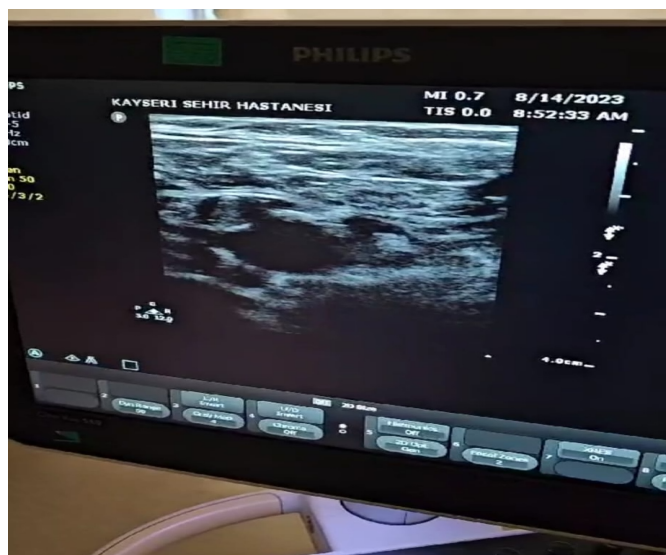


Figure. Thrombi in the patient's right and left femoral arteries (white arrows)

Emergency consultation with a cardiovascular surgeon resulted in an immediate thrombectomy. Post-surgery, the patient commenced appropriate treatment for atrial fibrillation and was discharged in approximately two weeks, fully recovered.

## DISCUSSION

The complexity of diagnosing acute limb ischemia (ALI) in elderly patients, particularly when they present with non-specific symptoms, is exemplified in the case of our 83-year-old patient. Acute limb ischemia, characterized by a sudden decrease in limb perfusion, can lead to severe outcomes, including limb loss if not promptly recognized and appropriately managed<sup>1</sup>. The diagnostic challenge is further compounded in elderly patients who often have multiple comorbidities and may present with atypical symptoms. In the context of ALI, the well-established clinical indicators, known as the 6P's (paresthesia, pain, pallor, pulselessness, poikilothermia, paralysis), should be rigorously sought in physical examinations.<sup>2</sup> However, these symptoms may not be immediately apparent, as demonstrated by our patient's initial presentation with knee pain and dizziness, masking the underlying vascular emergency. Atrial fibrillation (AF), a common arrhythmia in the elderly, significantly increases the risk of stroke and peripheral arterial thromboembolism.<sup>3</sup> The absence of anticoagulation therapy in patients with AF, as in our case, further elevates the risk for embolic events. Consequently, patients presenting with neurological symptoms and a history of AF, particularly those not on anticoagulation therapy, should be thoroughly evaluated for potential thromboembolic events, including ALI.<sup>5</sup> The use of bedside ultrasonography in the emergency department played a crucial role in diagnosing bilateral femoral arterial occlusion in our patient. This non-invasive, rapid, and reliable imaging modality is increasingly recognized as a valuable tool in emergency medicine for evaluating vascular emergencies.<sup>7,8</sup> In contrast, computed tomography (CT) angiography and magnetic resonance (MR) angiography, while effective, may not be suitable for all patients due to potential nephropathy from contrast agents and the time-consuming nature of these procedures.<sup>6</sup>

## CONCLUSION

It is imperative for emergency physicians to conduct comprehensive and iterative assessments in elderly patients, especially those presenting with non-specific symptoms. A heightened awareness of acute limb ischemia as a potential diagnosis is crucial, particularly in patients with known risk factors like atrial fibrillation. The application of bedside ultrasonography emerges as an invaluable diagnostic tool, facilitating prompt diagnosis and intervention. Such proactive and thorough approaches are key to enhancing patient outcomes in acute vascular emergencies.

## ETHICAL DECLARATIONS

### Informed Consent

The patient signed and free and informed consent form.

### Referee Evaluation Process

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### Conflict of Interest Statement

The authors have no conflicts of interest to declare.

### Financial Disclosure

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### Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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# A forgotten diagnosis in the emergency department: adult-onset still's disease

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## ABSTRACT

Adult-onset Still disease (AODS) is a rare condition that can be the cause behind high fever, rashes, and joint aches in adult patients. Being a rare condition, it is often overlooked as an improbable condition. Its prevalence is estimated to be 1 in 100,000. AODS generally presents itself in young adults, however in our case the patient was a lactating mother. Yamaguchi criteria remains as the diagnostic criteria for AODS. Our case report aims to demonstrate the diagnostic process and subsequent treatment of this rarely encountered condition.

**Keywords:** Fever, rash, Still's disease, arthralgia

## INTRODUCTION

Adult-onset Still's disease (AOSD), first described by Bywaters in 1971, is a systemic connective tissue disease of unknown etiology. It is characterized by fever, rash, and joint findings.<sup>1</sup> The disease may present with high fever alone, without typical skin rashes and joint findings.<sup>2-6</sup> Its prevalence is estimated to be 1 in 100,000, and the disease is thought to predominantly affect young adults. However, AOSD also presents itself in bimodal age groups, with the other affected group being 46–64-year-olds alongside young adults. This report aims to describe the symptoms and laboratory and imaging workups of a patient with adult Still's disease.

## CASE

A 33-year-old breastfeeding mother with no past medical history other than a C/S operation one month ago presented to the emergency department with intermittent fever, malaise, and a rash that started under the neck for the last two days. The patient's evanescent salmon-colored maculopapular rashes fluctuated in the presence of a fever. She had experienced widespread joint pain and difficulty in movement for the past 2 days. There were no prodromal or prior symptoms in the patient's medical history. She described the onset of the symptoms as an abrupt event. Vitals were within normal limits except 38°C of fever. On physical examination, the patient was conscious, oriented,

and cooperative, with no neck stiffness, and the oropharynx was hyperemic. Breath sounds were normal. Her wrists and right knee were swollen and her range of motion was restricted. Leukocyte count of 12,000/ $\mu$ L (normal range: 3,800-10,000/ $\mu$ L), neutrophil count of 9,850 / $\mu$ L (normal range: 1,560-6,130/ $\mu$ L) and eosinophil count of 440/ $\mu$ L (normal range: 40-3603/ $\mu$ L), CRP 224 mg/L (normal range: 0-5 mg/L), procalcitonin level of 3.57  $\mu$ g /L (normal range: <0.5  $\mu$ g /L), ferritin level of 579  $\mu$ g/L (normal range: 13-150  $\mu$ g/L) was detected in the blood results. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels were within normal limits, and lactate dehydrogenase (LDH) levels were 310 U/L (normal range: 135-214 U/L). Antinuclear antibody (ANA) and rheumatoid factor (RF) tests were negative. The leukocyte count was 1+ in the urine analysis. The peripheral blood smear results were negative. Brucella and viral serology tests were negative, and the blood and urine cultures yielded negative results. The tests were conducted at an inpatient clinic. No vegetation was observed on bedside echocardiography. Additional imaging revealed splenomegaly (present). The patient was evaluated using the Yamaguchi criteria with a potential diagnosis of Adult-Onset Still's disease. With the characteristic rashes, arthralgia, and leukocytosis of which 80% consisted of granulocytes, three major conditions were fulfilled. The patient also had a sore throat, negative test results for both RF and ANA,

and splenomegaly, fulfilling the three minor conditions for the Yamaguchi criteria. We also evaluated the patient using Yamaguchi exclusion criteria to clarify and confirm the potential diagnosis and to eliminate confounding conditions such as malignancy, infection, or other rheumatoid diseases. There were no prior symptoms older than two days, and the patient did not experience any weight loss or fatigue before the inception of the symptoms. This has pushed us away from a potential diagnosis of malignancy. Urine analysis and blood culture did not show positive results for potential infections. Alongside echocardiography, which showed no vegetation, these findings prompted us to search for an alternative diagnosis other than a potential infection. RF and ANA tests also had negative results, which is not a definitive exclusion criterion for other rheumatological diseases, but provided us with a direction towards the diagnosis of AOSD. After the initial treatment and evaluation, the patient was admitted to the internal medicine inpatient clinic with a preliminary diagnosis of adult-onset disease for further examination and treatment. In the internal medicine inpatient clinic, the patient was treated with anti-inflammatory therapy consisting of corticosteroids and non-steroidal anti-inflammatory drugs. Symptoms started to resolve after 48 h, and the clinical status of the patient did not deteriorate towards macrophage activation syndrome. The patient survived and was discharged from the internal medicine clinic a week after receiving a follow-up appointment.

## DISCUSSION

AOSD is a rare systemic inflammatory disorder of unknown etiology. The pathogenesis of AOSD relies on the activation of innate immune cells and involves the overproduction of pro-inflammatory cytokines, such as IL-1, IL-6, and IL-18. Treatments aim to neutralize these agents by using different ranges of available drugs. However, as the complete mechanisms behind AOSD remain unclear, treatment arrangements depend on the response and clinical outcome of the individual patient. Certain triggers are suggested to be responsible for the activation of the disease, such as infections or genetic background, but none has been definitively proven.<sup>7</sup>

AOSD shows no pathognomonic laboratory findings. It is important to exclude infections, neoplasms, and other systemic diseases with similar clinical findings. Although different criteria have been proposed for the evaluation and diagnosis of AOSD, the Yamaguchi criteria described by Yamaguchi et al.<sup>8</sup> in 1992 remain the most widely used and validated.

The Yamaguchi criteria contain major and minor elements. Persistent fever ( $>39^{\circ}\text{C}$  for over a week), arthralgia, rash, and neutrophil-dominant leukocytosis ( $>80\%$  neutrophils and  $>10 \times 10^3/\mu\text{L}$  white blood cells) were described as the major elements. To meet these criteria, the patient must fulfill five major or minor elements. Minor elements included sore throat, lymphadenopathy or splenomegaly, increased serum aminotransferase or lactate dehydrogenase levels, and negative IgM rheumatoid factor and antinuclear antibodies. As mentioned previously, our patient fulfilled three major and three minor criteria. There are also exclusion criteria

mentioned in the Yamaguchi criteria, which consist of infections, malignancies, and other rheumatoid diseases. We did not detect any exclusion criteria in our case.

According to literature, there are two different phenotypes of AOSD. The first phenotype is a more systemic manifestation involving fevers, rashes, and more severe symptoms. The second phenotype, however, is described as a more insidious disease with arthralgia and symptoms around joints forming the background and eventually turning into a chronic articular pattern.<sup>9</sup> In our case, we observed an example of the first phenotype with rashes, arthralgia, leukocytosis, and a more systematic manifestation of the disease.

In our case, the ferritin levels were significantly lower than those in most other cases ( $500 \mu\text{g/L}$  compared to  $1000 \mu\text{g/L}$  in most cases). Ferritin has been suggested as a potential biomarker for AOSD, with ferritin levels over the normal limit having high sensitivity for AOSD diagnosis. If the ferritin levels are found to be over 5 times the normal limit, sensitivity is detected at 40% and specificity is detected at 80%.<sup>7-10</sup> Our patient also presented with splenomegaly, which occurs in only 30% percent of the AOSD patients.<sup>11</sup> This is supported by the literature as well.

The treatment for AOSD remains empirical; however, the first-line therapy for AOSD is generally initiated with the use of non-steroidal anti-inflammatory drugs (NSAID), specifically indomethacin ( $150\text{--}200 \text{ mg}$ ). NSAID are considered ineffective in many patients; thus, the main therapy for the first-line treatment of AOSD is considered to be corticosteroids with doses of  $0,5 \text{ mg}$  from  $1 \text{ mg/kg}$ . If this treatment proves ineffective current treatment options suggest the usage of biologic disease-modifying antirheumatic drugs (DMARD) In this purpose; Canakinumab and Anakinra are widely employed in the treatment of AOSD.<sup>12</sup>

## CONCLUSION

AOSD is a rare systemic inflammatory disease. It is difficult to diagnose because the disease has no pathognomonic findings, presents with systemic findings, and is often confused with many other systemic diseases. The case in this report met two of the major and three minor Yamaguchi criteria. The patient was diagnosed with adult still disease in the emergency department and was transferred to an internal medicine inpatient service. This report reminds us that AOSD may be present in patients who have repeated admissions to the emergency department with fever and no obvious infectious or neoplastic pathology has been detected in their examinations and who have not received a specific diagnosis.

## ETHICAL DECLARATIONS

### Informed Consent

The patient signed the free and informed consent form.

### Referee Evaluation Process

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### Conflict of Interest Statement

The authors have no conflicts of interest to declare.

### Financial Disclosure

The authors declared that this study has received no financial support.

### Author Contributions

All of the authors declared that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

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