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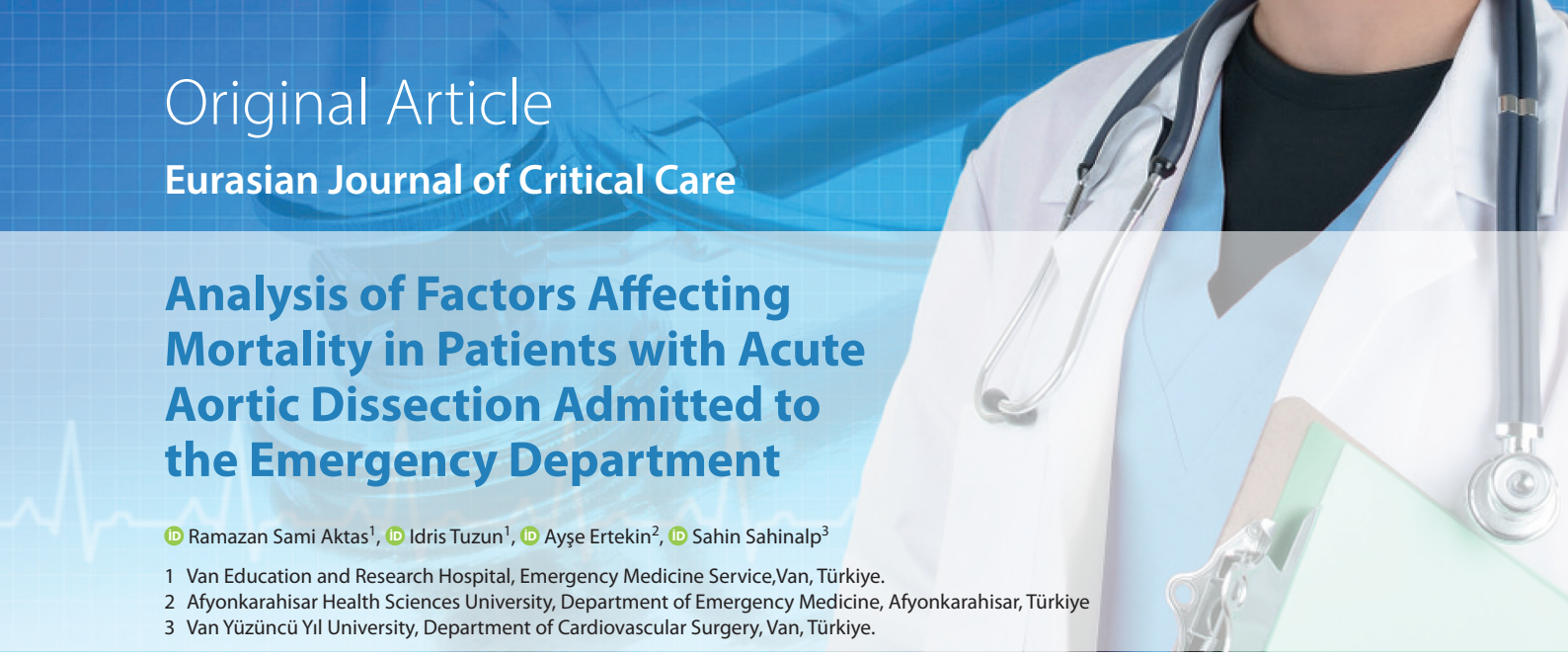

Analysis of Factors Affecting Mortality in Patients with Acute Aortic Dissection Admitted to the Emergency Department

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Abstract

Objective: Acute aortic dissection is a life-threatening cardiovascular emergency. The dissection may be admitted to the emergency department with different clinical pictures, depending on the place of involvement in the aorta. It is extremely important to know the factors affecting mortality, as delays in diagnosis and treatment can increase mortality rates. Our aim of this study is to evaluate the factors that may affect mortality rates.

Materials and Methods: One thousand two hundred and eighty-three patients were analyzed from the database. A definitive diagnosis of acute aortic dissection was identified in 48 patients. Two patients voluntarily refused treatment and left the emergency department. SPSS 27.0 program was used for data analysis. The p value was analyzed for the statistical significance of the data.

Results: The effects of patients' demographic data, age, gender, complaints on admission to the emergency department, onset time of complaints, duration of diagnosis, imaging and laboratory values on mortality were evaluated. We concluded that renal failure is associated with mortality at the time of first admission, especially in syncope and comorbid conditions.

Conclusion: It was evaluated that syncope, one complaint at admission, and renal failure, one of the accompanying diseases, increased mortality. Although our other data are not statistically significant, they contain significant differences. Bigger data analyzes will help identify risk factors.

Keywords: Aort dissection, emergency department, mortality

Introduction

Acute aortic dissection (AAD) is a life-threatening cardiovascular emergency due to rupture of the intima layer of the aorta from the outer layers (1,2). Aortic dissection is part of acute aortic syndromes and was described about 200 years ago (3).While it is seen 4-6 per 100 thousand in the general population, it peaks at 50-60 years (4). Especially in the 6th and 7th decades of life, this rate can reach up to 30 people per 100 thousand (2,4). AAD is an extremely fatal clinical situation (2). Quick and convenient diagnosis is crucial for successful management (5). For each hour of delay in treatment, the mortality rate increases by approximately 1-2% (6). It may cause delays in diagnosis because patients apply to the emergency department (ED) with different clinical presentations (5). The clinical condition is caused by the compression of the true lumen by the false lumen, resulting in various degrees of malperfusion depending on the involved aortic segment and the affected aortic branches (2).

In this study, we think that determining the factors affecting mortality will facilitate patient management. Therefore, we aimed to determine the factors affecting mortality before and after hospitalization of AAD patients.

Material and Methods

The study was initiated after obtaining approval from Van Yüzüncü Yıl University Hospital on 12/02/2021 with the local ethics committee number 2021/02-20. We reviewed

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the consultation notes, epicrisis and radiology reports of 1283 patients with suspicion of dissection, who applied to the ED between January 2010 and January 2021. We reached 48 patients diagnosed with AAD. Since two patients left the hospital voluntarily without treatment, we conducted a study with 46 patients who met the criteria. Although aortic dissection was suspected in the ED, patients with different or misdiagnosed patients were not included in the study.

Demographic data of the patients, such as age, gender, and comorbidities, were defined. Complaints records, blood parameters and treatment processes at the time of admission were examined from the hospital database. The imaging data used for diagnosis was re-evaluated by one specialist doctor, confirming dissection and measuring the aortic diameters. The ascending aorta was measured just above the valve, the arcus aorta was measured between the truncus brachiocephalic and the left carotid artery, and the descending aorta was measured at the level of the thoracic 4 vertebrae. From the database, the patients who died in the hospital were determined. The effects on mortality were evaluated by comparing these data. Patients who did not accept treatment or died after discharge were not included in the mortality.

Statistical Analysis: In the descriptive statistics of the data, the mean, standard deviation, median (minimum-maximum), frequency, and ratio values were used. The distribution of the variables was measured by the Kolmogorov-Smirnov test. Mann-Whitney u test was used in the analysis of quantitative independent data. The chi square test in the analysis of qualitative independent data, and the chi-square test conditions were not met, and the Fischer test was used. Statistical Package for the Social Sciences (SPSS) 27.0 program was used for analysis.

Results

Of the 46 patients included in the study, 30 (65.2%) were male. The mean age was 58.7±14.6 years. The median age was 58.5 (26-91) years. Age was found to have no effect on mortality (p=0.358). The most common comorbid condition is hypertension, and the other descriptive data are given in Table-1. The meantime between the first onset of the complaint and the admission to the ED was 8.5±25.5 hours. The most common symptom was chest pain, with 84.8%. Type A aortic dissection was seen 3 times more than Type B. The most used imaging method is direct chest X-ray. The in-hospital mortality rate was found to be 21.7% (Table 2). Statistically, syncope at first admission and renal failure in comorbid conditions were associated with mortality. The mean time from the onset of symptoms to diagnosis was 8.5 ± 25.5 hours, and the mean waiting time from ED presentation to diagnosis was 92.5 ± 56.5 minutes. No statistically significant difference was

Table 1. Effects of demographic data and comorbid conditions on mortality

		In-Hospital			
		Deaths n (%)	**Survivors n (%)**	**Total n (%)**	**p**
Gender	Male	6 (60%)	24(66.7%)	30 (65.2%)	0.695
	Female	4 (40%)	12(33.3%)	16 (34.8%)	
Smoking	yes	6 (60%)	20(55.6%)	26 (56.5%)	
	non-smoker	4 (40%)	16(44.4%)	20 (43.5%)	0.802
Co-morbidity					
Hypertension		6 (60%)	23 (63.9%)	29 (63.0%)	0.822
CAD		4 (40%)	17 (47.2%)	21 (45.7%)	0.685
DM		0 (0%)	1 (2.8%)	1 (2.2%)	1.000
COPD		0 (0%)	3 (8.3%)	3 (6.5%)	1.000
Stroke		0 (0%)	1 (2.8%)	1 (2.2%)	1.000
RF		**6 (60%)**	**1 (2.8%)**	**7 (15.2%)**	**<0.001**
BPH		1 (10%)	0 (0%)	1 (2.2%)	0.217
Asthma		0 (0%)	1 (2.8%)	1 (2.2%)	1.000
Cancer		0 (0%)	1 (2.8%)	1 (2.2%)	1.000
No		0 (0%)	3 (8.3%)	3 (6.5%)	1.000
CD/ID		0 (0%)	0 (0%)	0 (0%)	1.000
Unknown		1 (10%)	2 (5.6%)	3 (6.5%)	0.230

CAD: Coronary artery disease, DM: Diabetes mellitus, COPD: Chronic obstructive pulmonary disease
RF: Renal failure, BPH: Benign prostatic hypertrophy, CD/ID: Congenital disease/ Inflammatory diseases

Table 2. Effect of Clinical Features on Mortality

		In-Hospital			
		Deaths n (%)	**Survivors n (%)**	**Total n (%)**	**p**
***Admitted Complain*t**					
Chest pain		7 (70%)	32 (88.9%)	39 (84.8%)	0.163
Back pain		3 (30%)	15 (41.7%)	18 (39.1%)	0.504
Syncope		**4 (40%)**	**2 (5.6%)**	**6 (13%)**	**0.015**
Stomachache		4 (40%)	9 (25%)	13 (28.3%)	0.351
Dyspnea		1 (10%)	3 (8.3%)	4 (8.7%)	1.000
Hemoptysis		0 (0%)	1 (2.8%)	1 (2.2%)	1.000
Hematemesis		0 (0%)	0 (0%)	0 (0%)	1.000
Trauma		0 (0%)	4 (11.1%)	4 (8.7%)	0.562
Location of Pain					
Chest		7 (70%)	32 (88.9%)	39 (84.8%)	0.163
Back (interscapular)		5 (50%)	20 (55.6%)	25 (54.3%)	0.755
Abdomen		5 (50%)	13 (36.1%)	18 (39.1%)	0.426
Other		0 (0%)	2 (5.6%)	2 (4.3%)	1.000
Imaging					
Chest X-Ray		10 (100%)	32 (88.9%)	42 (91.3%)	0.562
Transthoracic Echocardiography		6 (60%)	23 (63.9%)	29 (63%)	0.822
Contrast-Enhanced CT		7 (70%)	24 (66.7%)	31 (67.4%)	0.842
Unknow		0 (0%)	1 (2.8%)	1 (2.2%)	1.000
Dissection type	A	6 (60%)	29 (80.6%)	35 (76.1%)	0.178
	B	4 (40%)	7 (19.4%)	11 (23.9%)	
Treatment					
Surgical		7 (70%)	26 (72.2%)	33 (71.7%)	0.795
Non-surgical		3 (30%)	9 (25%)	12 (26.1%)	0.929
Transfer to Outer Center		0 (0%)	1 (2.8%)	1 (2.2%)	1.000

AD: Aorta Diameter, CT: Computed Tomography

found between aortic diameter dimensions measured by echocardiography and the incidence of death and survival (p>0.05). Furthermore, no statistically significant difference was found between the patients' blood values and the incidence of death and survival (p>0.05) (Table 3).

Discussion

Acute aortic dissection is a rare but serious cardiovascular syndrome that can cause different clinical presentations (1,5). Although AAD can occur in any part of the aorta, it most commonly occurs in the right lateral wall of the ascending aorta. The most common clinical causes of AAD are malperfusion syndromes, aortic insufficiency, heart failure and stroke (2,7).

Although it is reported in the literature that AAD is seen at an early age in collagen tissue diseases, it is stated that the most common age range is 59-65 years (1,4,5,7). Some authors acknowledge age as a risk factor (2,7). Christoph et al. reported that mortality rates increase with increasing age (7). In our study, most of the patients were in the 6th decade and their mean age was 58 years. Although age did not affect mortality, the average age of those who died was higher. We believe this is due to the ease and frequency of access to emergency services in the region where the study was conducted. The frequency of visits gradually decreases with age. We have also observed AAD in younger patients. For this reason, AAD should be considered when there are clinically unexplained symptoms regardless of age group.

In studies, the male-female ratio is seen between 7/3 and 6/4 (1,5,7). Male gender is reported as a risk factor for AAD according to a study conducted in Switzerland (2). In the present study, the male-female ratio of AAD was 7.5/4. We evaluated gender did not affect mortality, since the female-male ratio was similar between the groups. Although the risk is higher in men, we believe that rapid diagnosis and treatment in the emergency department does not cause a difference in mortality rates between genders.

Although dissection because of trauma is extremely

Table 3. The Effects of Time, Aortic Diameter and Blood Values on Mortality

	In-Hospital		Total		
	Deaths	Survivors			
	Mean ± sd	Mean ± sd	Mean ± sd	Median (min-max)	p
CST (hour)	23.9 ± 52.6	4.2 ± 6.3	8.5 ± 25.5	2.0 (0.5-168)	0.351
WTED (minutes)	94.5 ± 77.1	91.9 ± 50.8	92.5 ± 56.5	60 (45-240)	0.558
Ascending AD (mm)	44.2 ± 12.3	42.3 ± 11	42.7 ±11.1	40.4 (25-87)	0.567
Arcus AD (mm)	31.7 ± 6.1	33.4 ± 4.7	33.1 ± 5	33.2 (25-45.7)	0.215
Descending AD (mm)	36.8 ± 8.2	34.9 ±8.1	35.3 ± 8.1	34 (24-62)	0.651
D-dimer (mg/L)	14.5 ± 12.7	9.6 ± 7.2	11.4 ± 9.4	9.6 (0.8-30)	0.386
Troponin (ng/ml)	0.3 ± 0.6	0.6 ± 2	0.5 ± 1.7	0 (0-9)	0.351
Hemoglobin (g/dl)	12.3 ± 3	13.3 ± 2.2	13.1 ± 2.4	13.7 (7.2-16.6)	0.077
Sodium (mmol/L)	140.2 ± 4.5	137.5 ± 3.5	138.1 ± 3.8	138.9 (129-147)	0.947
Potassium (mmol/L)	4.2 ± 0.8	4.1 ± 0.5	4.1 ± 0.6	4.1 (2.4-5.5)	0.593
Calcium (mg/dL)	8.8 ± 1	8.7 ± 0.7	8.8 ± 0.8	8.9 (7-10.4)	0.142
Magnesium (mg/dL)	2.5 ± 0.2	2.1 ± 0.5	2.2 ± 0.5	2 (1.7-3)	0.640
INR	1.7 ± 0.8	1.2 ± 0.2	1.3 ± 0.5	1.2 (0.9-3.2)	0.219

CST: Complaint Start Time, WTED: Waiting Time in the Emergency Department, INR: International normalized ratio

rare, according to the study of Eduardo et al., the mortality rate in traumatic aortic dissection is reported to be >80% (7,8). However, there were no deaths in 4 (8.7%) patients who developed AAD due to trauma. We think that this is because of the rapid diagnosis of trauma with advanced imaging.

In the present study, the most common complaints were chest, back and abdominal pain. Although only 6 (13%) of patients with AAD have syncope, it is the only symptom associated with mortality. We think that the reason for this situation is the sudden brain damage that occurs because of syncope.

The most common symptom is a sudden onset of tearing, typically in the chest and back (6). These symptoms can be confused with other diseases that can cause mortal chest pain, especially acute coronary syndrome (6,9). We found no correlation between the location of pain and mortality in this study.

Late diagnosis of AAD increases mortality(2,5). According to the study of Booher et al., if the onset of symptoms is in the first 24 hours, hyperacute, 2-7 days acute, 8-30 days subacute, and over 30 days are chronic aortic dissection (10). The time interval with the highest mortality is the first 48 hours after the onset of symptoms (7). In Zaschke's study, it was reported that early suspicion of AAD reduced the time from pain onset to surgery from 8.6 hours to 5.5 hours (6). Harris et al. reported that the diagnosis time would be shortened if the symptoms of admission to the ED were typical (chest, back and leg pain) (5). In a study conducted on 750 patients, the time from admission to the ED to the diagnosis of AAD was approximately 4.3 hours (5). In the presented study, the average time from the onset of the complaints to the diagnosis was 8.5 hours, and the time from admission to the ED to the diagnosis was approximately 92 minutes (~1.5 hours). We would like to state that only hyperacute and acute included patients in the study. Even though it is seen that this period does not have a statistically significant effect on in-hospital mortality, we saw that most of the deceased applied to the hospital almost 24 hours after the onset of their complaints. We think that by increasing the awareness of AAD, early diagnosis will decrease mortality.

Cigarette smoking is recognized as an independent risk factor in most studies (2,4,7). In this study, there were more smokers. However, we think that since we do not include the duration of smoking in the records as pack-years, its relationship with mortality cannot be determined.

The most common comorbid condition in AAD is hypertension (11). Congenital diseases such as Marfan syndrome, Loeys-Dietz syndrome, vascular Ehlers-Danlos syndrome, Turner's syndrome, aortic coarctation and bicuspid aortic valve are considered being risk factors for AAD (2,4,7). It is stated that hypertensive people increase the risk of AAD approximately 4 times compared to normotensives, and it is seen in 75% of patients (7,11). The most common comorbid conditions in the present study were hypertension and coronary artery disease. Its incidence was consistent with the literature, but the only comorbid condition affecting mortality among comorbid conditions was renal failure. According to the study of Chen et al., it is reported that there is a short and long-term mortality relationship between type-B dissection and renal failure (12). We found no connective tissue disease among the cases. We think that contrasting nephropathy developing after intravenous computed tomography for

the diagnosis of AAD aggravates the underlying renal failure and increases mortality.

Since chest and back pain are common, the first imaging method is direct chest X-ray (2,5). However, it should be known that the radiograph is normal in approximately 20% of Type A aortic dissections(5). Transthoracic echocardiography (TTE) or transesophageal echocardiography (TEE) may be performed where AAD is suspected and cannot be diagnosed (2,7). Echocardiography has the advantages of being rapid, reproducible and radiation-free in an unstable patient, but the possibility of false positives or negativity is known depending on the operator (7). The most widely used method is computed tomography with intravenous contrast, because of its rapid image acquisition and processing capability (2). Magnetic resonance imaging (MRI) is the most accurate diagnostic method for dissection, but it is not used very often due to the disadvantages of the imaging technique (5). The frequency of use of the triple CT protocol, which is used to show acute coronary syndrome, pulmonary embolism and AAD in a single session, is increasing (7). One disadvantage of CT is that it can cause renal failure due to ionizing radiation and contrast material (2). In our patients diagnosed with AAD, X-ray (91%), CT (67%) and echocardiography (63%) imaging methods were used, respectively. X-ray, echocardiography and CT were performed together in some patients, but MRI was not performed on any of the patients urgently. Images of a patient diagnosed in an external center could not be accessed from the database, only the reports of the images were accessed. Each method has its advantages and disadvantages. We think that with the widespread use of affordable MRI devices that can shoot quickly, they can be used instead of direct radiography, echocardiography and CT.

One of the most used classification methods in clinical practice is Stanford (12). If the first dissected segment is in the ascending aorta, it is called type A, and the other segment that is affected is called type B (2). According to Zaschke's study in 2020, the incidence of type AAD is 2.9-11.9/100000 persons annually (6). According to the Stanford classification, it is stated that Type A dissections can be seen at earlier ages than B (2). In the current study, it was seen that 76.1% of the patients were type A, 60% of those who died were type A and 40% were type B. we observed that Stanford classification did not affect mortality in AAD patients in the hyperacute and acute phases. We would like to point out that in-hospital and post-hospital mortality rates were not evaluated after hospitalization. We think that mortality rates may vary according to the type of dissection in long-term follow-ups.

The greater the aortic diameter, the greater the risk of dissection (2). According to Christoph, those with aortic diameter greater than 55 mm increase the mortality rate by 4 times compared to those with an aortic diameter less than 55 mm (7). In the study of Koechlin et al., the mean aortic diameter of the ascending aorta, aortic arch and thoracic aorta was reported as less than 45 mm in AAD (1). In the present study, the mean aortic diameter was measured as ascending/ arcus/ descending 42/ 33/ 35 mm, respectively. The aortic diameter was similar between both groups, but no statistically significant difference was detected. When evaluated according to the literature, we can say that the risk is less because the average of the measured aortic diameters is less than 55 mm.

It is stated that blood parameters contribute little to the diagnosis in AAD patients (2). There may be variability in blood values, depending on the affected organ (13). However, even if D-dimer is used more in the diagnosis of pulmonary embolism if it is <500 ng in the first 24 hours from the onset of symptoms, it is one parameter that can exclude dissection (2,7). It is stated that troponin is elevated in half of AAD patients (13). We think that the reason why troponin elevation had no effect on mortality in this study was that patients applied to the emergency room within an average of 2 hours after the symptoms began, thus preventing the development of heart failure and consequently, preventing hypoperfusion. Although the d-dimer value was high in the presented study, we did not evaluate it as a risk factor for mortality. Even though the use of blood parameters is helpful in rapid diagnosis and differential diagnosis, the diagnostic value is low in AAD. AAD should be considered if there is an unexplained blood parameter.

Medical treatment aims to reduce pain and complications by reducing blood pressure and heart rate and stopping its progression in the affected aortic segment (2,7). Initially, it is aimed to have a heart rate of 60-80/min and a blood pressure of 100-120 mmHg (7). Patients with malperfusion syndrome (clinically and radiologically) should have immediate surgical intervention (1). Surgical treatment aims to close the false lumen entrance and re-design the internal structure of the aorta to provide reperfusion (7). It has been reported that up to 90% of patients with type A dissection are treated surgically, even if they have comorbid conditions (1,2,4). If malperfusion syndromes are not revealed in patients with type B, conservative intervention can be performed (1,2). According to Bossone et al., surgical treatment has increased from 79% to 90%, and the mortality rate has been reported to have decreased from 31% to 22% 9. Trimarchi et al. report that the rate of surgical intervention decreases, and the rate of medical treatment increases in the treatment of patients with AAD as age progresses (11). In this study, 71.7% of the patients underwent surgery immediately after diagnosis. We decided on medical treatment depending on the clinical situation, advanced age, comorbid conditions, or the patient

and their relatives' refusal to have surgery. The effect of the patients' decision to undergo surgery immediately on mortality was not determined. We think it does not affect the mortality rates since the patients are followed closely in the intensive care unit and surgical treatment is available 24 hours if necessary.

There are many parameters affecting mortality in aortic dissection. Some external factors, such as hospital admission time, rapid diagnosis and treatment availability, change mortality rates (8). Some factors found to be associated with mortality may be recurrent chest and back pain and expanding refractory hypertension (2,4,7). The increase in troponin values after hospitalization was found to be associated with mortality (2). Therefore, close follow-up is very important. Mortality rates have decreased to 12% depending on the developing surgical methods (2). According to a study conducted at the University of Michigan, the hospital mortality rate was reported as 23.8% (11). In our study, 21.7% of patients with AAD died in the hospital shortly after admission. We think these rates will decrease with the patient's admission to the hospital before the development of malperfusion syndromes, rapid diagnosis and treatment.

Study Limitations: The limitations of this study are that the post-hospital and long-term results were not evaluated in the study, and that it was a retrospective and single-center study with a relatively low number of participants.

Conclusion

Despite the improvement in the rate of diagnosis and surgical techniques, the mortality rate of AAD is still very high. There are too many unknowns in parameters that affect mortality. In this study, which we conducted to reveal these unknowns, we found that renal failure is associated with increased mortality, especially in syncope and comorbid conditions, at the first admission. We believe that mortality-related factors will be determined in studies with more patients and more centers. In the light of these findings, we think that more effective health services will be provided.

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Ethical Statement: Ethical approval for this study was obtained from Van Yüzüncü Yıl University Hospital Ethics Committee (decision no: 2021/02-20, date:12.02.2021).

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