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The Relationship Between Blood Lactate Level and Mortality in Patients Diagnosed with Acute Aortic Dissection in the Emergency Department

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ABSTRACT

Objective: Acute aortic dissection is a time-sensitive and difficult-to-diagnose cardiovascular emergency. The aim of this study was to investigate the relation between blood lactate level and mortality in patients diagnosed with acute aortic dissection (AAD) in the emergency department.

Material and Methods: The study was conducted by retrospectively examining the electronic files of 32 patients who had been diagnosed with acute aortic dissection by computed tomography angiography in the emergency department and hospitalized between 01 January 2020 and 31 December 2020.

Results: Of the patients included in the study, 78.1% were males. Mean age of the patients was 60.9 ± 10.4 years. The most frequent complaints of the patients were chest pain (50%) and back pain (43.8%). When comorbidities were examined, hypertension was the most common (59.4%). Of the patients, 71.9% were treated surgically and 28.1% medically. According to the Stanford classification, 65.6% of the patients had Stanford type A and 34.4% had Stanford type B aortic dissection. Mortality was seen in 50% of the patients. When the relation between laboratory parameters and mortality was examined, mean serum lactate level was 1.6 ± 0.6 mmol/l in surviving patients and 3.5 ± 2.3 mmol/l in mortal patients (p= 0.004). When Reciever Operating Characteristic (ROC) analysis, which determines mortality predictive properties of laboratory parameters, was examined, the Area Under Curve (AUC) value of serum lactate level was determined as 0.875 (95% CI 0.738-1.0, p= 0.004). When the threshold value of serum lactate level determined to predict mortality was 2.1 mmol/l, its sensitivity was determined as 86.7% and specificity as 81.2%.

Conclusion: According to the study data, the threshold value of serum lactate level above 2.1 mmol/l in patients with acute aortic dissection may guide the clinician as a new and valuable marker in the evaluation of in-hospital mortality.

Keywords: Aortic dissection, emergency department, mortality, lactate

ÖZ

Acil Serviste Akut Aort Diseksiyonu Tanısı Alan Hastalarda Kan Laktat Düzeyinin Mortalite ile İlişkisi

Giriş: Akut aort diseksiyonu, zamana duyarlı ve teşhis edilmesi zor bir kardiyovasküler acildir. Bu çalışmanın amacı, acil serviste akut aort diseksiyonu (AAD) tanısı alan hastalarda kan laktat düzeyi ile mortalite arasındaki ilişkiyi araştırmaktır.

Gereç ve Yöntemler: Çalışma 01 Ocak 2020-31 Aralık 2020 tarihleri arasında acil serviste bilgisayarlı tomografi anjiyografi ile aort diseksiyonu tanısı alan ve hastaneye yatırılan 32 hastanın elektronik dosyalarının geriye dönük olarak incelenmesi ile yapıldı.

Bulgular: Çalışmaya alınan hastaların %78.1'i erkekti. Hastaların yaş ortalaması 60.9 ± 10.4 olarak saptandı. Hastaların en sık başvuru şikayeti göğüs ağrısı (%50) ve sırt ağrısı (%43.8) idi. Eşlik eden ek hastalıklar incelendiğinde ise en sık hipertansiyon izlendi (%59.4). Hastaların %71.9'u cerrahi, %28.1'i medikal yöntemle tedavi edildiler. Stanford sınıflamasına göre ise hastaların %65.6'sında Stanford Tip A, %34.4'un de ise Stanford Tip B aort diseksiyonu tespit edildi. Hastaların %50'si mortal seyretti. Ölen hastaların %87.5'inin Stanford Tip A aort diseksiyonu olduğu tespit edildi. Laboratuvar parametreleri ile mortalite arasındaki ilişki incelendiğinde, sağ kalan hastalarda serum laktat düzeyi ortalama 1.6 ± 0.6 mmol/l iken, ölen hastalarda ortalama 3.5 ± 2.3 mmol/l idi (p= 0.004). Laboratuvar parametrelerinin mortaliteyi öngörücü özelliklerini belirlemeyen ROC analizi incelendiğinde serum laktat seviyesinin AUC değeri 0.875 (%95 CI 0.738-1.0, p= 0.004) olarak belirlendi. Serum laktat düzeyinin mortaliteyi öngörmek için belirlenen eşik değeri 2.1 mmol/l alındığında duyarlılığı %86,7, özgüllüğü %81.2 olarak tespit edildi.

Sonuç: Çalışma verilerine göre akut aort diseksiyonu ile başvuran hastalarda serum laktat seviyesi eşik değerinin 2.1 mmol/l üzerinde olması hastane içi mortalitenin değerlendirilmesinde yeni ve değerli bir belirteç olarak klinisyene rehberlik edebilir.

Anahtar Kelimeler: Acil servis, aort diseksiyonu, mortalite, laktat

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INTRODUCTION

Acute aortic dissection (AAD) is a life-threatening cardiovascular emergency stemming from the rupture of the intima layer of the aorta and leakage of blood into the media layer (1). A 1-2 % increase has been observed in mortality per hour following the onset of the symptom in untreated ADD patients (2). Therefore, timely diagnosis and treatment planning are crucial for managing the condition successfully and increasing survival.

The most common complaint as regards AAD while applying to the emergency department is the onset of sharp and severe chest pain, followed by back and abdominal pain (3). In the initial evaluation of patients with acute chest pain and suspected chest pain, laboratory parameters may be required for differential diagnosis or detection of complications. However, there are no specific diagnostic laboratory parameters for AAD in clinical practice. Lactate is produced as the end product of glycolysis in anaerobic conditions and hypoperfusion states such as inadequate ventilation, hypovolemia, hypoxemia, end-organ hypoperfusion, and bleeding following trauma. There is a well-known relation between mortality and lactate in critically ill patients (4-8). Lactic acidosis with systemic hypoperfusion or malperfusion is increasingly recognized as a useful independent measure of disease severity and a predictor of mortality (9).

This study aimed to examine the relation between blood lactate level and mortality in patients with acute aortic dissection in the emergency department.

MATERIALS and METHODS

Study Design

The study was conducted with the inclusion of 32 patients hospitalized with AAD between 01/01/2020 and 31/12/2020 and as a retrospective observational case series. Ethics committee approval of the study was obtained on 21 April 2022 (Meeting no: 104, Ethics committee approval no: 1910).

Patients

Patients younger than 18 years of age and whose laboratory and file data could not be fully reached were excluded from the study. Symptoms during admission, demographic characteristics, symptoms during admission, laboratory parameters, dissection type, length of hospital stay, treatment methods, outcome data and complications of the patients included in the study were obtained from hospital electronic data. Hemogram and biochemical parameters of all patients obtained at the time of admission to the emergency department were recorded. Data analyzes were performed examining differences in demographic, clinical and laboratory data. The patients were classified according to Stanford classification (10) based on the results of the computed tomography angiography taken. In Stanford classification (10), dissection groups are made with the related aorta according to the descending and ascending parts. Stanford type A is defined as a dissection proximal to the brachiocephalic artery involving the ascending aorta, whatever the location of the primary intimal tear. Stanford type B is the type that arises from the distal left subclavian artery and only involves the descending aorta.

Statistical Analysis

Descriptive statistics of the data were given as standard deviation, mean, median lowest, median highest, ratio and frequency. Kolmogorov-Smirnov test was used analyzing the distribution of the variables. For quantitative and independent data, Mann-Whitney U test and independent sample t-test were used. In the analysis of qualitative independent data, Fisher's exact test was used when the Chi-square (χ^2) and/or Chi-square (χ^2) conditions could not be met. Receiver Operating Characteristic (ROC) analysis was performed to assign the power of all laboratory parameters to predict mortality. The Youden index was used to determine the cut-off value of the laboratory parameters. Analyses were performed through SPSS 25.0 software. For all analyses, p value of <0.05 was considered statistically significant.

RESULTS

Thirty-eight patients older than 18 years of age were diagnosed with acute aortic dissection throughout the course of the study. Thirty-two patients whose data were fully accessible were included in the study. Of the six patients who were excluded in the study, four did not accept hospitalization, one was referred to an external center, and the file data of one could not be reached completely. Of the patients included in the study, 78.1% (n= 25) were males. Mean age of the patients was 60.9 ± 10.4 years. The most common symptoms of the patients were chest pain (50%) and back pain (43.8%). No statistical difference was found among the complaints between non-surviving and surviving patients (Table 1). Mean arterial pressure (MAP) of the patients was 106.5 ± 30.5 mmHg. MAP was statistically significantly lower in patients with mortality (p= 0.003). While difference in blood pressure was detected between the extremities in 62.5% of the patients, it was low in the right arm (70%) most frequently. At least one comorbidity was present in 71.9% of the patients, and when the accompanying comorbidity was examined, hypertension was the most common one (59.4%) (Table 1).

Table 1. Comparison of demographic data between survivors and non-survivors

	Total	Survivor	Non-survivor	
	32 (100%)	16 (50%)	16 (50%)	p
Sex				
Male	25 (78.1%)	14 (87.5%)	11 (68.7%)	0.394
Female	7 (21.9%)	2 (12.5%)	5 (31.3%)	
Age (year)	60.9 ± 10.4	58.6 ± 11.3	63.31 ± 9.1	0.202
Pulse (min)	87 ± 19.9	80.8 ± 17.3	93.1 ± 20.9	0.079
SBP (mmHg)	150 ± 46.4	174.4 ± 37.1	125.9 ± 42.6	0.002
DBP (mmHg)	84.7 ± 23.2	95.3 ± 17.8	74.1 ± 23.6	0.007
MAP (mmHg)	106.5 ± 30.5	121.7 ± 23.8	91.4 ± 29.5	0.003
Presence of blood pressure difference	20 (62.5%)	10 (62.5%)	10 (62.5%)	1.000
Right arm	14 (43.8)	8 (50%)	6 (37.5%)	
Left arm	6 (18.8%)	2 (12.5%)	4 (25%)	0.621
Presence of concomitant comorbidity	23 (71.9%)	13 (81.3%)	10 (62.5%)	0.433
Hypertension	19 (59.4%)	11 (68.8%)	8 (50%)	0.473
Diabetes mellitus	8 (25%)	1 (6.3%)	7 (25%)	0.037
Coronary artery disease	7 (21.9%)	4 (25%)	3 (18.8%)	1.000
Chronic obstructive pulmonary disease	3 (9.4%)	2 (12.5%)	1 (6.3%)	1.000
Cerebrovascular disease	1 (3.1%)	1 (6.3%)	0 (0%)	1.000
Chronic renal failure	4 (12.5%)	3 (18.8%)	1 (6.3%)	0.600
Cancer	1 (3.1%)	0 (0%)	1 (6.3%)	1.000
Chest pain	16 (50 %)	9 (56.3%)	7 (43.8%)	0.724
Back pain	14 (43.8%)	6 (37.5%)	8 (50%)	0.722
Abdominal pain	7 (21.9%)	4 (25%)	3 (18.8%)	1.000
Syncope	4 (12.5%)	1 (6.3%)	3 (18.8%)	0.600
Dyspnea	3 (9.4%)	1 (6.3%)	2 (12.5%)	1.000
Cold sweating	3 (9.4%)	2 (12.5%)	1 (6.3%)	1.000
Weakness in legs	1 (3.1%)	1 (6.3%)	0 (0%)	1.000

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MAP: Mean arterial pressure.

According to the Stanford classification, 65.6% of the patients had type A and 34.4% had type B AAD (Table 2). Of the patients who died, 87.5% had type A AAD (p= 0.023). All (n= 23) patients with type A AAD and 18.2% (n= 2) of patients with type B AAD were taken to emergency surgery. Of the patients undergoing emergency surgery, 60.9% died and all were type A AAD. Of those treated surgically, 43.5% died during the operation and/or on the first postoperative day, and 17.4% died during the follow-up and treatment process. When the complications during treatment and follow-up were examined, it was observed that complications developed in 65.6% of the patients. Pneumonia (25%), bleeding diathesis (9.4%) and acute kidney injury (9.4%) were observed to develop commonly in the patients (Table 2).

When the relation between laboratory parameters and mortality was examined, it was seen that only serum lactate level had a statistically significant relationship with mortality (p= 0.004). While mean serum lactate level was 1.6 ± 0.6 mmol/l in surviving patients, it was 3.5 ± 2.3 mmol/l in non-surviving patients.

Figure 1 presents the ROC curve showing comparisons of laboratory parameters in predicting mortality. ROC analysis showing mortality predictive properties of laboratory parameters is presented in Table 4. In the study, the AUC value of the serum lactate level was 0.875 (0.875 95% CI 0.738-1.0, p= 0.004) and cut-off value for predicting mortality was 2.1 mmol/l, and specificity and sensitivity were 81.2% and 86.7%, respectively.

DISCUSSION

In this study, we examined the relationship between blood lactate level and mortality in patients with AAD. In the analytical evaluation for mortality, AUC value of blood lactate level was determined as 0.875. According to the study data, serum lactate level may be a mortality indicator in patients diagnosed with AAD.

AAD is one of the deadliest cardiovascular diseases encountered in the emergency department. In-hospital mortality of AAD is 26-58% for type A dissection and 11-31% for type B dissection (11). In this study, type A AAD was seen in

Table 2. Comparison of dissection type, treatment methods and complications between survivors and non-survivors

	Total	Survivor	Non-survivor	
	32 (100%)	16 (50%)	16 (50%)	p
Dissection Type				
Stanford type A	21 (65.6%)	7 (43.8%)	14 (87.5%)	
Stanford type B	11 (34.4%)	9 (56.3%)	2 (12.5%)	0.023
Treatment Methods				
Surgical	23 (71.9%)	9 (56.3%)	14 (87.5%)	0.113
Medical	9 (28.1%)	7 (43.8%)	2 (12.5%)	
Complications	21 (65.6%)	10 (62.5%)	11(68.8%)	1.000
Pneumonia	8 (25%)	2 (12.5%)	6 (37.5%)	1.000
Bleeding diathesis	3 (9.4%)	2 (12.5%)	1 (6.3%)	1.000
Acute kidney injury	3 (9.4%)	2 (12.5%)	1 (6.3%)	0.220
Cerebrovascular disease	2 (6.3%)	2 (6.3%)	2 (6.3%)	1.000
Length of hospital stay	10.3 ± 10.8	15.4 ± 9.1	5.1 ± 10.2	0.005

Table 3. Comparison of laboratory parameters of survivors and non-survivors

	Total 32 (100%)	Survivors 16 (50%)	Non-survivors 16 (50%)	p
ALT	50.5 ± 72.8	38.1 ± 33.8	62.9 ± 97.3	0.347
AST	63.6 ± 122.9	30.9 ± 20.9	96.4 ± 168.7	0.144
Urea	50.2 ± 30.4	47.5 ± 21	52.9 ± 38.1	0.621
Creatinine (0.51-0,95 mg/dl)	1.5 ± 1.2	1.5 ± 1.5	1.5 ± 1	0.906
Leukocytes (3.8-11.8 10^3/µl)	12.2 ± 3.8	13 ± 4.2	11.4 ± 3	0.251
Neutrophil (1.9-8.2 10^3/µl)	9.7 ± 3.8	13 ± 4.2	11.4 ± 3	0.442
Lymphocyte (1.1-3.1 10^3/µl)	1.4 ± 1.2	1.3 ± 0.5	1.5 ± 1.6	0.584
Hemoglobin	12.8 ± 1.7	13.3 ± 1.6	12.4 ± 1.7	0.099
Hematocrit	37.4 ± 4.2	38.4 ± 4	36.4 ± 4.3	0.191
INR	1.7 ± 2.1	2.1 ± 3	1.2 ± 0.4	0.254
Hs-Tn I (0-16 ng/l)	1005.4 ± 3728.2	25.9 ± 30.7	1984.9 ± 5165.1	0.150
CRP (0-5 mg/l)	57.5 ± 69.8	59.2 ± 65.7	55.9 ± 75.6	0.893
Albumin (35-55 g/l)	34.7 ± 6.2	35.4 ± 6.7	34.1 ± 5.8	0.556
CAR	1.9 ± 2.3	1.9 ± 2.1	1.9 ± 2.6	0.943
NLR	11.2 ± 9.5	9.2 ± 4.6	13.1 ± 12.5	0.251
Lactate (mmol/l)	2.6 ± 1.9	1.6 ± 0.6	3.5 ± 2.3	**0.004**

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, INR: International normalized ratio, Hs-Tn I: High-sensitivity troponin, CRP: C-Reactive protein, CAR: C-reactive protein/albumin ratio, NLR: Neutrophil/Lymphocyte ratio.

65.6% and type B AAD was seen in 34.4%. While the mortality rate of type A AAD patients was 66.6%, the mortality rate of type B AAD patients was 18.2%. Mortality of type A AAD is highly dependent on the patient's risk profile before surgery (12,13). Independent preoperative predictors of mortality are previous cardiac surgery, age>70 years, hypotension or shock during application to the hospital, cardiac tamponade, migrating pain, any lack of pulse, and ECG showing signs of myocardial ischemia or infarction (2). In type B AAD, hypotension/shock, absence of chest/back pain during application to the hospital, and branch vessel involvement are very important determinants of mortality (2). In a study, hypotension is emphasized to be the main determinant of risk for mortality in type A and B dissection (14). In the study, thirty

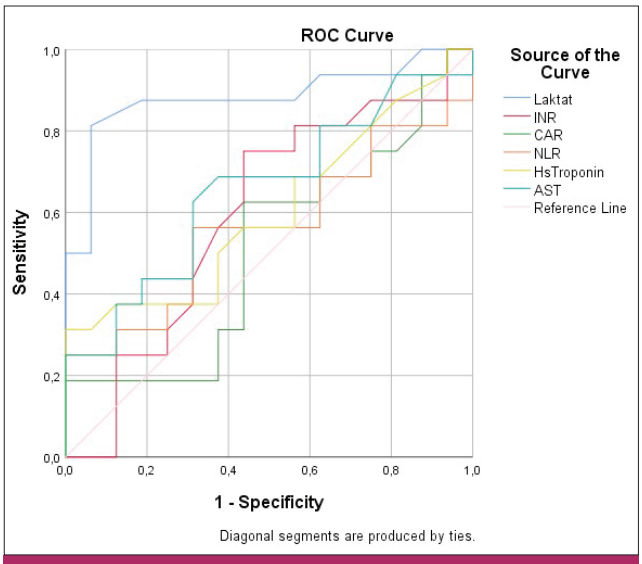

Figure 1. ROC curve showing comparisons of laboratory parameters in predicting mortality.

eight percent of the total patients had MAP≤ 100 mmHg, and low MAP was observed to be statistically related to mortality. Detection of hypotension with acute aortic dissection should guide the clinician to the diagnosis of serious complications such as shock, bleeding, and tamponade.

Lactate is formed by the transformation of pyruvate to lactic acid under anaerobic conditions by lactate dehydrogenase due to hypoperfusion of the tissues in conditions such as sepsis, trauma, hypovolemia, and hypoxemia. High lactate levels have been associated with a consistently increased mortality in sepsis and/or septic shock independent of hypotension (6,15). There are few studies in the literature demonstrating the relation between AAD and lactate (9,16-18). An important complication of type A AAD is malperfusion secondary to ischemia. Although the results of the surgical treatment of type A AAD have improved thanks to technical advances, mortality remains as high as 89% in the presence of visceral ischemia (19). The use of serum lactate level as a biomarker in mesenteric ischemia has been found to be potentially useful (20,21). In a study of type A AAD patients, it has been stated that preoperative high lactate levels as an indicator of malperfusion are useful in estimating short-term mortality (9). Demonstrating preoperative malperfusion/ischemia determines additional operations that patients need (9,22). Since the delay in diagnosis affects surgical management, high mortality rates may be observed. In the study, AUC value of the serum lactate level was 0.875 (p= 0.004) and cut-off value for predicting mortality was 2.1 mmol/l, and specificity and sensitivity were 81.2% and 86.7%, respectively. These data from the study suggest that high lactate levels may be a rapid and cost-effective alternative clinical marker for the severity of acute aortic dissection.

Degeneration of the media layer of the aortic wall is the main predisposing factor for aortic dissection (23). Induction of inflammatory cascade by vascular smooth muscle cells in the media layer as a result of mechanical or oxidative stress initiates the development of degeneration (24). Considering this pathophysiology caused by inflammation, the relation between inflammatory markers such as albumin, CRP, CRP/albumin ratio (CAR), Neutrophil/lymphocyte ratio (NLR) and mortality was investigated in the study. However, no statistically significant relationship with mortality was found.

As stated in the European Society of Cardiology (ESC) guidelines, data on the epidemiology of aortic dissection are scarce, and the true incidence is unknown (3). The incidence of AAD increases with age and is higher in men (2,25). The most common risk factor associated with AAD is poorly controlled hypertension (3,26). Several connective tissue diseases, Ehler-Danlos syndrome, Marfan syndrome, bicuspid aortic valve, family history of aortic disease, smoking, pregnancy, and cocaine use may be cited among the other risk factors (3,23). The most common complaint of AAD during admission to the emergency department is sudden onset

Table 4. ROC analysis to determine mortality predictive properties of laboratory parameters in patients with acute aortic dissection

	AUC (95% CI)	Cut-off	p	Sensitivity (%)	Specificity (%)
Lactate (mmol/l)	0.875 (0.738-1.000)	2.1	<0.001	86.7	81.2
AST	0.644 (0.444-0.843)	22.5	0.173	66.7	50
INR	0.617 (0.411-0.823)	1.07	0.268	66.7	56.2
Hs-Tn I	0.615 (0.410-0.819)	11.5	0.277	66.7	43.7
NLR	0.596 (0.388-0.804)	8.63	0.363	60	50
CAR	0.506 (0.295-0.717)	0.48	0.953	60	50

AUC: Area under the curve, CI: Confidence interval, AST: Aspartate aminotransferase, INR: International normalized ratio, Hs-Tn I: High-sensitivity troponin, CAR: C-reactive protein/albumin ratio, NLR: Neutrophil/lymphocyte ratio.

of sharp and severe chest and/or back pain. While patients with type A aortic dissection mostly complain of chest pain, those with type B dissection mostly complain of back pain (2,3). According to the study data, it was observed that aortic dissection was more frequently in male patients in their 60s who applied with chest and back pain and had a history of hypertension. Although it is known that a systolic blood pressure difference of >20 mmHg between both extremities usually predicts AAD, its diagnostic accuracy is not sufficient (27,28). Of the patients in the study, 62.5% had a blood pressure difference between the extremities. This data shows that double-arm blood pressure measurement is still important in the differential diagnosis of patients applying with chest and back pain.

The single-center and retrospective nature of the study may be a limitation. In addition, since this study was conducted with a small number of cases in a single hospital, generalizing to all patients diagnosed with aortic dissection may lead to misconceptions. Larger, prospective and multicenter studies are needed to support the use of blood lactate levels in predicting mortality in acute aortic dissection.

CONCLUSION

Aortic dissection is rarely observed in emergency departments but requires rapid diagnosis and treatment due to its high mortality rate. In patients presenting with AAD, blood lactate levels can be a rapid and cost-effective alternative clinical marker to estimate mortality. Early assessment of serum lactate level and risk of mortality may contribute to choosing the best treatment strategy for high-risk patients, allowing for a comprehensive preoperative evaluation. Thus, the risk of mortality and complications can be reduced.

Ethics Committee Approval: This study was approved by the Adana City Training and Research Hospital Clinical Research Ethics Commitee (Decision Number: 1910, Date: 21.04.2022).

Author Contributions: Concept/Design: All of authors; Analysis/Interpretation: SA, MG; Data Acquisition: SA, SS, MG; Writting: All of authors; Critical Revision: All of authors; Final Approval: All of authors.

Conflict of Interest: There is no conflict of interest.

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