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ORIGINAL RESEARCH

Rh-positive blood type is associated with improved in-hospital mortality in patients with surgically treated acute type A aortic dissection

Oya Güven[1,]*, Abdulrahman Naser[2], Uğur Arslantaş[3], Tanıl Özer[4]

[1]Department of Emergency Medicine, Kırklareli Training and Research Hospital, Kırklareli University Faculty of Medicine, 39000 Kırklareli, Turkey
[2]Department of Cardiology, Kırklareli Training and Research Hospital, 39010 Kırklareli, Turkey
[3]Department of Cardiology, Koşuyolu Training and Research Hospital, 34865 İstanbul, Turkey
[4]Department of Cardiovascular Surgery, Koşuyolu Training and Research Hospital, 34865 İstanbul, Turkey

***Correspondence**
oyaguven@klu.edu.tr
(Oya Güven)

Abstract

Background: Acute type A aortic dissection (ATAAD) is a severe cardiovascular emergency with high mortality. Shock, pericardial tamponade, malperfusion of coronary or peripheral arteries, and stroke are important predictive factors for in-hospital mortality in the setting of ATAAD. In this study, we aimed to evaluate the distribution of ABO blood groups and their effects on in-hospital mortality in ATAAD patients. **Methods**: The retrospective study included demographic and clinical data of 204 (surviving group: 154, non-surviving group: 50) patients diagnosed with ATAAD were collected from January 2013 to March 2016. The association between in-hospital mortality of ATAAD patients and ABO blood groups was analyzed using Binary logistic regression analysis. p value of < 0.05 was considered statistically significant. **Results**: There was a significant difference in terms of height, weight, cigarette smoking, hypertension, diabetes, ABO and Rh blood groups, systolic blood pressure, diastolic blood pressure (DBP), heart rate (HR), creatinine, glucose, white blood cells and fresh frozen plasma (FFP) transfusion between the surviving and non-surviving groups. Hight, Rh blood group, DBP, HR and admission blood glucose were independent predictors of in-hospital mortality. **Conclusions**: Our results show that Rh-positive blood type is an independent predictor of improved in-hospital mortality in patients with surgically treated acute type A aortic dissection. However, further studies involving large samples are needed to confirm the existence and strength of this relationship.

Keywords

ABO blood groups; In-hospital mortality; Acute type A aortic dissection

1. Introduction

Acute aortic dissection (AAD) is a life-threatening condition that occurs when the inner layer of the aorta tears, allowing blood to flow between the layers and weaken the vessel wall. AAD affects about 6 out of 100,000 people per year and has a worse prognosis in women than in men [1]. Surgery is the main treatment option for acute type A aortic dissection (ATAAD), as it can reduce the mortality rate from 90% to 30% within one month, and from 31% to 22% during hospitalization [1–3]. However, even with surgery and medical care, the risk of death remains high (25%) for patients with AAD [1]. Several clinical factors have been identified as predictors of in-hospital mortality for patients with ATAAD, such as aortic valve replacement, chest pain, shock, cardiac tamponade, limb ischemia and hypotension [2, 4].

In order to improve the outcomes and survival rates of patients with ATAAD, more parameters need to be explored beyond the conventional clinical factors. One of the potential parameters is blood type, which has been suggested to influence the risk and prognosis of AAD [5]. ABO blood groups are known to affect the thrombotic and inflammatory processes in the body and have been associated with various cardiovascular diseases, such as atherosclerosis and coronary heart disease [6]. Previous studies have reported conflicting results on the relationship between blood groups and in-hospital mortality in patients with AAD [3, 7, 8]. Some studies have found that AB and A blood groups are associated with higher mortality than O blood groups [7], while others have reported that non-O blood type is associated with lower mortality, especially in patients who do not undergo surgery [5]. Another study found no significant association between blood groups and short-term mortality in patients with ATAAD [8]. These discrepancies may be due to the genetic variation of ABO blood groups in different populations or samples.

The effect of blood groups on in-hospital mortality in ATAAD patients has not been sufficiently investigated in general, and there are no publications on this topic from Turkey. Therefore, our study aimed to evaluate whether blood groups are linked with in-hospital mortality of ATAAD patients in a sample from the Turkish population.

2. Material and methods

2.1 Study design

We conducted a retrospective study of 204 Caucasian patients who underwent emergency surgery for ATAAD at a single center between January 2013 and March 2016. Inclusion criteria for this study were age $\geq$18 years, having complete data on in-hospital survival and clinical characteristics, and being surgically treated. Patients who died before surgery and out of the hospital and patients with missing data were excluded from the study. One hundred eleven patients were excluded due to missing data.

2.2 Data collection

We obtained the data from the hospital records and the national death registry. We collected information on the patients' demographic, clinical and laboratory variables, as well as their surgical details and outcomes. The primary endpoints of the study were the proportions of blood groups in the study sample and their association with in-hospital mortality. We defined ATAAD as cases with an intimal tear involving the ascending aorta, diagnosed and treated surgically within 14 days of symptom onset. We defined in-hospital mortality as all-cause death during the index admission.

2.3 Echocardiographic evaluation

Upon arrival at the emergency department, patients underwent bedside transthoracic echocardiography evaluation, and long-axis, short-axis, two-, three- and four-chamber images were recorded. Left ventricular ejection fraction, aortic valve structure and function, presence of pericardial effusion, ascending aortic diameter, and presence of dissection flap were carefully examined.

2.4 Surgical procedure

Median sternotomy, cardiopulmonary bypass, and intermittent cardioplegic arrest were performed sequentially. The cannulation site was variable according to the operator and the characteristics of the patient. In complicated cases and in cases where the aorta was attached to the sternum, sternotomy was performed after peripheral (femoral artery and vein) cannulation under heparinization. In most cases, open distal surgical repair involving resection and inspection of the aortic arch was performed under profound (18 °C) hypothermic total circulatory arrest, with or without the use of selective cerebral perfusion. The extent of dissection and location of the intimal tear were determinants of the extent of distal repair. Reimplantation of the supra-aortic branch was performed when necessary. In cases of high suspicion of dissection in the aortic arch and, therefore, intervention to the arch vessels, cannulation was performed from the right subclavian artery or innominate artery. A cross-clamp was placed distal to this cannulation, and antegrade cerebral perfusion was applied from here while the patient was in complete circulatory arrest. Meanwhile, the arch branches were separated, and a graft was placed on them. The arch vessels were placed on the graft, the total circulatory arrest (TCA) was ended, and supracoronary aortic replacement was performed. The two grafts were stitched together, or the procedure was completed with a single graft. Aortic valve replacement or total root replacement was performed when necessary, and aortic valve competence was achieved with sub-commissural plication, commissural resuspension, or valvuloplasty when possible. In addition, concomitant procedures such as coronary artery bypass was performed when required. Any endovascular treatment was not performed in the index admission.

2.5 Total surgery time

The time between the initiation of general anesthesia and the completion of the surgical procedure and closure of the skin layers.

2.6 Aortic cross-clamp time

The time between the first application of the clamp before performing cardioplegia and the time when the clamp is removed after the anastomoses are completed.

2.7 Data analysis

We used SPSS version 27.0 (IBM Corp. IBM SPSS Statistics for Windows, Armonk, NY, USA) for statistical analysis. We considered the p value < 0.05 as statistically significant in all tests. We classified the patients based on their in-hospital mortality into surviving and non-surviving groups. We assessed the distribution of the quantitative data by the Kolmogorov-Smirnov test of normality. We expressed categorical data as numbers and percentages and continuous data with normal distribution as mean $\pm$ standard deviation and continuous data that did not have a normal distribution as median (minimum–maximum). We compared the baseline characteristics between the two groups using independent-samples T test for normally distributed continuous variables and Mann-Whitney U test for non-normally distributed continuous variables. We used Chi-square (Yates-Continuity Correction) test for the comparison of categorical variables between the two groups. We performed univariable and multivariable logistic regression (forward method) analyses to evaluate the independent predictors of in-hospital mortality. The ROC curve (receiver operating characteristic curve) was used to determine the cutoff, sensitivity, and specificity of admission blood glucose regarding in-hospital mortality. Artificial intelligence-supported technologies were not used in the production of this study.

3. Results

The mean age of the patients was 54.88 $\pm$ 11.57 years, and 148 (72.5%) of them were male. The distribution of blood groups was as follows: A 92 (45.1%), B 32 (15.7%), AB 12 (5.9%), and O 68 (33.3%). Table 1 shows the general characteristics of the study population and the comparison between the survivor and nonsurvivor groups. Height, weight, heart rate (HR), creatinine, plasma glucose, White blood cell (WBC), smoking, diabetes and negative Rh blood groups were

TABLE 1. General characterized of the patients.

Variables	Entire sample	Surviving group n = 154	Non-surviving group n = 50	*p*
Age (yr), Mean ± SD	54.88 ± 11.57	54.41 ± 11.91	56.34 ± 10.44	0.306
Gender, F/M, n (%)	56 (27.5)/148 (72.5)	47 (30.5)/107 (69.5)	9 (18.0)/41 (82.0)	0.085
Height (cm)	170.77 ± 7.19	169.55 ± 6.94	173.39 ± 5.63	**0.010**
Weight (kg)	80.97 ± 13.13	79.33 ± 11.72	84.74 ± 15.40	**0.028**
BMI (kg/m^2)	27.55 (15.76–43.34)	27.44 (17.93–443.34)	27.92 (15.76–34.60)	0.138
Cigarette, n (%)	107 (52.5)	74 (48.1)	33 (66.0)	**0.027**
Hypertension, n (%)	176 (86.3)	138 (89.6)	38 (76.0)	**0.015**
Diabetes, n (%)	79 (38.7)	53 (34.4)	26 (52.0)	**0.027**
Hyperlipidemia, n (%)	130 (63.1)	101 (65.6)	29 (58.0)	0.332
ARF, n (%)	76 (37.2)	52 (33.8)	24 (48.0)	0.070
AVR, n (%)	38 (18.6)	32 (20.8)	6 (12.0)	0.239
BAV, n (%)	13 (6.4)	8 (5.2)	5 (10.0)	0.314
Pericardial effusion, n (%)	58 (28.4)	43 (27.9)	15 (30.0)	0.918
Ejection fraction (%)	60 (25–65)	65 (25–65)	60 (45–65)	0.903
Coronary involvement, n (%)	24 (11.8)	15 (9.7)	9 (18.0)	0.168
Blood group, n (%)				
• A	92 (45.1)	67 (43.5)	25 (50.0)	**0.045**
• B	32 (15.7)	22 (14.3)	10 (20.0)	
• AB	12 (5.9)	12 (7.8)	0 (0.0)	
• O	68 (33.3)	53 (34.4)	15 (30.0)	
Rh group, n (%)				
• Positive	154 (75.5)	125 (81.2)	29 (42.0)	**0.001**
• Negative	50 (24.5)	29 (18.8)	21 (58.0)	
SBP mmHg	148 (80–208)	150 (84–191)	137 (80–208)	**<0.001**
DBP mmHg	82.5 (30–110)	84.0 (54–110)	73.0 (30–105)	**<0.001**
Heart rate (beat/min)	89 (68–119)	89 (68–119)	95 (73–109)	**<0.001**
Creatinine (mg/dL)	0.92 (0.43–6.50)	0.89 (0.43–6.50)	1.12 (0.60–2.70)	**<0.001**
Glucose (mg/dL)	118.5 (65–304)	115.0 (65–297)	159.5 (89–304)	**<0.001**
WBC (10^9/L)	10.30 (4.15–23.90)	10.05 (4.15–23.25)	11.40 (7–23.90)	**0.036**
Hemoglobin (g/dL)	12.50 (6.3–17.2)	12.50 (6.9–17.2)	12.55 (6.3–16.55)	0.278
CRP (mg/dL)	2.67 (0.34–43)	2.56 (0.34–41)	5.15 (0.34–43)	0.206
AAD (cm)	5.20 (4.1–7.3)	5.20 (4.1–7.3)	5.15 (4.38–6.35)	0.133
ACCT (min)	85.5 (23–289)	89.0 (23–289)	81.5 (43–275)	0.993
TST (min)	275 (155–515)	280 (155–515)	270 (180–469)	0.360
Heparin infusion	350 (0–900)	360 (0–490)	325 (0–900)	0.155
PLT transfusion	148 (72.5)	116 (75.3)	32 (64.0)	0.169
FFP transfusion	167 (81.9)	135 (87.7)	32 (64.0)	**<0.001**

AAD: ascending aortic diameter; ACCT: aortic cross-clamp time; ARF: acute renal failure; AVR: aortic valve replacement; BAV: Bicuspid aortic valve; BMI: body mass index; CRP: C-reactive protein; DBP: diastolic blood pressure; FFP: fresh frozen plasma; PLT: platelet; SBP: systolic blood pressure; SD: Standard deviation; TST: total surgery time; WBC: White blood cell; F/M: Female/male.
Significant values ($p < 0.05$) are marked in bold.

significantly higher in the nonsurvivor group than in the survivor group. On the other hand, the frequency of hypertension and FFP transfusion, as well as systolic blood pressure (SBP) and diastolic blood pressure (DBP) values, were significantly lower in the nonsurvivor group than in the survivor group.

We performed univariate and multivariate logistic regression analyses to identify the factors associated with in-hospital mortality. Table 2 presents the results of the logistic regression analysis, which revealed that height, weight, Rh group, diabetes, smoking, SBP, DBP, HR, creatinine, plasma glucose and white blood cell (WBC) count were significantly related with in-hospital mortality according to the results of univariate logisitc regression. In addition, height, Rh group, DBP, heart rate and plasma glucose were independently associated with in-hospital mortality. The multivariate model was statistically significant (Chi-square (6, n = 204) = 77.178, $p < 0.001$) and had a good fit to the data (Hosmer and Lemeshow Test, $p = 0.219$). The model also had a high prediction accuracy (sensitivity = 54, specificity = 96.1, overall accuracy = 85.5%) and explained 31.5% (Cox and Snell R square) and 46.9% (Nagelkerke R square) of the variance in survival.

4. Discussion

We conducted a retrospective study to evaluate the association between blood groups and in-hospital mortality in patients with ATAAD. We found that the type AB blood group was significantly lower than other blood groups. In addition, height, weight, Rh group, diabetes, smoking, SBP, DBP, HR, creatinine, plasma glucose, and white blood cell (WBC) count variables were significantly related to in-hospital mortality. Furthermore, height, Rh group, DBP, heart rate, and plasma glucose were independently associated with in-hospital mortality.

A patient's Rhesus status is defined by the presence of the Rh factor, an inherited transmembrane protein found on the surface of red blood cells [9]. Previous studies have shown an association between Rhesus state and coronary artery disease; this suggests a genetic link between the Rhesus factor and cardiovascular disease [9]. In addition, Rh-negative state was associated with a worse prognosis in patients with ischemic cardiomyopathy [10]. To our knowledge, our analysis is the first to investigate the Rhesus status in the context of in-hospital mortality in ATAAD cases. We demonstrated that, Rh-positive blood type is associated with improved in-hospital mortality in patients with surgically treated acute type A aortic dissection. Causal studies are needed to elucidate the relationship between Rhesus status and in-hospital mortality in ATAAD cases.

Our finding that blood type did not affect survival is in contrast with some previous studies that reported a lower risk of intraoperative mortality for blood group O in surgical ATAAD patients, and a reduced risk of in-hospital mortality for non-O blood type in non-surgically managed type A aortic dissection patients [5, 8]. However, it is consistent with other studies that failed to demonstrate a connection between ABO blood groups and the development or rupture of abdominal aortic aneurysm (AAA) [11]. Moreover, we observed that there was no AB blood group in the non-surviving group, which may suggest a protective effect of this blood type. However, this finding should be interpreted with caution, as the sample size of AB blood group was small (n = 12). The possible mechanisms underlying the relationship between ABO blood groups and ATAAD are not fully understood, but they may involve the role of blood group antigens in cell membrane integrity, cell adhesion, and glycosylation of the vascular endothelium [12–15]. The heterogeneity of ABO antigens among different populations and their specific predisposition to increased risk of cardiovascular and thromboembolic disease may also explain the conflicting results in the literature [8, 16].

Hypertension is among the independent risk factors for aortic dissection. It is associated with AAD, and a history of

TABLE 2. Factors affecting in-hospital mortality.

	Univariate			Multivariate		
	OR	95% CI	*p*	OR	95% CI	*p*
Height	1.063	1.014–1.115	**0.011**	1.071	1.009–1.137	**0.025**
Weight	1.028	1.003–1.054	**0.030**			
Rh group	3.121	1.563–6.234	**0.001**	2.807	1.148–6.862	**0.024**
Diabetes Mellitus	2.064	1.081–3.942	**0.028**			
Smoking	2.099	1.079–4.081	**0.029**			
Systolic blood pressure	0.972	0.954–0.991	**0.004**			
Diastolic blood pressure	0.929	0.898–0.960	**<0.001**	0.927	0.890–0.964	**<0.001**
Heart rate	1.095	1.053–1.140	**<0.001**	1.093	1.042–1.147	**<0.001**
Creatinine	1.575	1.024–2.421	**0.039**			
Plasma glucose	1.019	1.011–1.027	**<0.001**	1.020	1.011–1.029	**<0.001**
WBC	1.125	1.033–1.227	**0.007**			
O *vs.* non-O blood groups	1.224	0.614–2.442	0.565	1.874	0.765–4.593	0.170

Significant values (p < 0.05) are marked in bold.
WBC: White blood cell; OR: Odds ratio; CI: confidence interval.

hypertension is the most common predisposing factor for AAD [13]. On the other hand, decreased diastolic blood pressure and increased heart rate are indicators of hemodynamic instability, which is a common complication and a poor prognostic factor in ATAAD patients [17–19]. Hypotension may result from cardiac tamponade, aortic rupture, or severe aortic regurgitation, and it may lead to end-organ ischemia and multiorgan failure [17]. Increased HR may increase the aortic wall stress and the propagation of the dissection, and it may also reflect the presence of pain, anxiety, or inflammation [19]. Therefore, blood pressure and heart rate control are essential components of the management of ATAAD patients [17, 19]. We found that each unit decrease in DBP increased the odds of in-hospital mortality by 0.066, and that the cut-off value of DBP 65 mmHg predicted the in-hospital mortality with 80% sensitivity and 55% specificity. These results are in line with those of Sari S. *et al*. [17], who also reported an inverse association between DBP and survival in ATAAD patients. We also found that each unit increase in HR increased the odds of in-hospital mortality by 0.032, and that the cut-off value of HR 90 bpm predicted the in-hospital mortality with 70% sensitivity and 65% specificity. These results are similar to those of Zhou Y *et al*. [19], who also found a positive association between HR and mortality in acute aortic dissection patients.

Glucose is another factor that may influence the outcome of ATAAD patients, as hyperglycemia is associated with increased oxidative stress, inflammation, and endothelial dysfunction [20, 21]. Acute and serious diseases can affect glucose metabolism and cause stress-induced hyperglycemia (SIH) or admission hyperglycemia. This condition can worsen the prognosis of cardiovascular diseases such as acute myocardial infarction and acute aortic dissection (AAD). A recent paper reported that about 40% of patients with acute type A aortic dissection (ATAAD) had SIH, which was associated with high-risk clinical features and increased mortality risk [21]. The paper also suggested that severely elevated blood glucose could be a biomarker of disease severity in ATAAD patients [21]. However, another study did not find admission hyperglycemia to be a predictor of in-hospital mortality in ATAAD patients [20]. Hyperglycemia may also impair the healing process of the aortic wall and increase the risk of infection [21]. We found that each unit increase in glucose increased the odds of in-hospital mortality by 0.005, and that the cut-off value of glucose 128.5 mg/dL predicted the in-hospital mortality with 74% sensitivity and 66.9% specificity. These results are consistent with those of Liu S *et al*. [21], who also reported a positive association between glucose and mortality in acute aortic dissection patients. In our study, we found a significant association between high glucose level at admission and in-hospital mortality.

Body size has recently been associated with the occurrence of various cardiovascular diseases (CVDs) in different populations [22]. Although the exact mechanisms leading to aortic disease remain unclear; biomechanical wall stress, which exceeds the mechanical strength of the arterial wall, has been identified as the final common pathway. Taller height is one of the factors that can increase aortic peak wall stress [23]. In addition, in a large, community-based, prospective cohort study, the researchers observed generally positive associations between height and mortality risk from AAA [23]. In the same work the authors, reported a non-significant and non-linear positive trend between height and mortality from total aortic disease and aortic dissection [23]. In this context, our study showed a positive association between the body height and in-hospital mortality in ATAAD.

Our study has some limitations that should be acknowledged. First, the sample size was relatively small, and the study was conducted in a single center, which may limit the generalizability of the results. Second, the study was retrospective, and there may be selection bias, information bias, or confounding bias in the data collection and analysis. Third, we did not have data on some potential predictors of in-hospital mortality, such as the extent and location of the dissection, the presence and severity of aortic regurgitation, the occurrence and management of complications, and the long-term outcomes. Therefore, future studies with larger and more diverse samples, prospective and randomized designs, and more comprehensive and standardized data are needed to validate and extend our findings.

5. Conclusions

Factors contributing to vascular pathology can significantly increase the risk and, therefore, outcomes of ATAAD. There are controversial results regarding the relationship between blood groups and the outcome of acute aortic dissection. This study could not reveal a significant relationship between ABO blood groups and ATAAD in-hospital mortality. However, our results show that the Rh antigen, in particular, has a protective role in this context. We found that individuals with Rh-positive blood groups have a significantly lower in-hospital mortality rate. This compelling evidence underscores the need for further research to enhance our understanding of the underlying mechanisms. The insights gained could be vital in improving patient care and outcomes.

AVAILABILITY OF DATA AND MATERIALS

Data is available from the corresponding author upon reasonable request.

AUTHOR CONTRIBUTIONS

AN, TÖ, UA—conception; literature review. AN, TÖ—design–supervision; material. AN, OG—data collection. AN, TÖ, OG—analysis. AN, TÖ, UA, OG—writer; critical review.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was conducted in accordance with the Declaration of Helsinki. The study protocol was approved by Kartal Dr. Lütfi Kırdar Training and Research Hospital Clinical Research Ethics Committee (No: 2016/514/79/11, date: 10 March 2016). The ethics committee waived informed consent to participate. However, we ensured the privacy and confidentiality of the patient's data.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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