

## The effect of referral and transfer of patients with acute type A aortic dissection on treatment outcomes

Ersin Kadiroğulları<sup>1</sup>, Onur Şen<sup>2</sup>, Safa Göde<sup>3</sup>, Muhammed Bayram<sup>4</sup>, Abdülkerim Buğra<sup>5</sup>, Barış Timur<sup>6</sup>, Erhan Kutluk<sup>7</sup>, Ünal Aydın<sup>8</sup>, Burak Onan<sup>9</sup>

Department of Cardiovascular Surgery, University of Health Sciences, Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital, Istanbul, Turkey

### ABSTRACT

**Objectives:** This study aims to evaluate the effect of referral and transfer of patients with acute type A aortic dissection (AAAD) and treatment outcomes in the emergency setting.

**Patients and methods:** A total of 131 patients (75 males, 56 females; mean age 52.2±13.1 years; range, 18 to 80 years) who underwent surgery due to AAAD in the emergency setting in our center between January 2010 and December 2017 were included in the study. The patients were divided into two groups as those who were diagnosed with AAAD in another health care facility and transferred to our hospital (Group A, n=65) and those who were diagnosed in our emergency room (Group B, n=66).

**Results:** The rate of postoperative neurological complications was 24.6% in Group A and 12.1% in Group B (p=0.74). The postoperative persistent neurological deficit rate was 10.5% in Group A and 9% in Group B (p=0.456). The overall hospital mortality rate was 23.2% (p=0.310). Hemodynamic instability, age, and cardiopulmonary bypass time were independent risk factors for overall hospital mortality.

**Conclusion:** Although the patients diagnosed with AAAD in another healthcare facility were hemodynamically unstable compared to those diagnosed in our center, the mortality and morbidity rates did not significantly differ. Based on our study results, we recommend transferring such patients to a reference hospital.

**Keywords:** Mortality, referral, transfer, type A aortic dissection.

Acute type A aortic dissection (AAAD) is a disease in which approximately 50% of patients die within 48 h, if not treated surgically.<sup>[1]</sup> Despite the development of surgical experience and hospital infrastructure in recent years, the early postoperative mortality rate ranges between 9 and 36%.<sup>[2-4]</sup> The international Registry of Acute Aortic Dissection revealed a hospital mortality of 26% in multicenter studies.<sup>[5]</sup> Although there are several factors which affect hospital mortality, the main factor is that the patients should undergo surgery, when they are hemodynamically stable.<sup>[6]</sup> The number of patients who are diagnosed with AAAD and transferred to a reference hospital is quite high, as AAAD surgery is unable to be performed in every cardiac center. It is also critical that these patients should be hemodynamically stable during the transfer

to the reference hospital. In cardiac centers where algorithms for the effective transfer of patients with AAAD have been implemented, hospital mortality rates are lower.<sup>[7]</sup>

In the present study, we aimed to evaluate the effect of referral and transfer of patients with AAAD and treatment outcomes in the emergency setting.

### PATIENTS AND METHODS

A total of 139 patients underwent surgery with the diagnosis of AAAD in our center between January 2010 and December 2017. Of these patients, eight who were operated due to the development of dissection during an invasive procedure in the coronary

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**Correspondence:** Ersin Kadiroğulları, MD, SBÜ Mehmet Akif Ersoy Göğüs Kalp Damar Cerrahisi Eğitim Araştırma Hastanesi Kalp ve Damar Cerrahisi Kliniği, 34303 Küçükçekmece, İstanbul, Türkiye. e-mail: ersinkadirogullari@gmail.com

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angiography laboratory were excluded from the study. Finally, a total of 131 patients (75 males, 56 females; mean age  $52.2 \pm 13.1$  years; range, 18 to 80 years) who underwent surgery due to AAAD in our center were included in the study. The patients were divided into two groups as those who were diagnosed with AAAD in another health care facility and transferred to our hospital (Group A, n=65) and those who were diagnosed in our emergency room (Group B, n=66). The diagnoses of all patients were made based on thoracoabdominal computed tomography (CT) and transthoracic echocardiography. The clinical condition, preoperative status, and health condition at the time of admission to the emergency room of the patients who were transferred from other centers were recorded. Medical data of the patients were obtained from the recording system of the hospital and from the patient files. We contacted patients who did not attend to their scheduled follow-up visits in our hospital through telephone calls. Follow-up data were also recorded. A written informed consent was obtained from each patient. The study protocol was approved by the Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.

The diagnosis of AAAD was made according to the Stanford classification.<sup>[8]</sup> The patients who underwent surgery within 14 days of symptom onset were defined as having AAAD (those with previously known atherosclerotic heart disease, valvular diseases, and ascending aortic aneurysms were defined as heart disease). Hospital mortality was defined as mortality within the first 30 days and during the initial hospitalization. The conditions associated with preoperative hemodynamic instability included undergoing cardiopulmonary resuscitation (CPR), hypotension (i.e., systolic arterial blood pressure below 80 mmHg), and neurologic instability (i.e., confusion, hemiplegia, and hemiparesis). Patients presenting with these clinical findings were immediately taken to the operation room and operated. The major morbidities were defined as reoperation, prolonged ventilation, neurological complications, kidney failure, and deep sternal injury infections. Postoperative neurological complications were defined as permanent neurological deficit (PND), hemiplegia-hemiparesis, and transient ischemic attack. Patients with permanent neurological damage during discharge were defined as PND.

### Surgical technique

All patients underwent aortic surgery within 24 h of symptom onset. All procedures were performed under

**Table 1. Demographic and clinical data of patients**

	Total				Group A				Group B				p
	n	%	Mean±SD	Min-Max	n	%	Mean±SD	Min-Max	n	%	Mean±SD	Min-Max	
Patients	131				65	49.6			66	50.4			
Control time (months)			24.8±20.4	1-80			22.7±18.4	1-80			26.7±21.9	1-80	0.330
Age (year)			52.2±13.1	18-80			54±1.1	24-78			50.5±2	18-80	0.129
Gender													
Male	99	75.6			48	73.8			51	77.3			0.688
Hypertension	111	84.7			59	90.8			52	78.8			0.087
Diabetes mellitus	25	19.1			16	24.6			9	13.6			0.124
COPD	33	25.2			20	30.8			13	19.7			0.163
CKD	15	11.5			10	15.4			5	7.6			0.181
Cardiac disease	41	31.3			18	27.7			23	34.8			0.452
Previous cardiac surgery	9	6.9			4	6.1			5	7.6			0.373
Preoperative status													
HD instable patient													
Arrest-with CPR	7	5.3			5	7.7			2	3.3			0.274
Neurological instability	5	3.8			4	6.2			1	1.5			0.208
Hypotension	29	22.1			20	30.8			9	13.6			0.021
HD stable patient	90	68.7			36	55.4			54	81.8			0.001
Echocardiography													
Ejection fraction			56.6±3.8	30-65			56.4±3.7	30-65			56.8±4.3	45-65	0.743
AVI (moderate-severe)	50	38.5			19	29.9			31	47			0.042
Bicuspid aortic valve	12	9.2			4	6.2			8	12.1			0.365

SD: Standard deviation; Min: Minimum; Max: Maximum; COPD: Chronic obstructive pulmonary disease; CKD: Chronic kidney disease; CPR: Cardiopulmonary resuscitation; HD: Hemodynamically; AVI: Aortic valve insufficiency.

general anesthesia with single-lumen intubation. The surgical procedure consisted of a median sternotomy with standard cardiopulmonary bypass (CPB) via axillary artery (AxA) or femoral artery cannulation. The right atrium was cannulated with a double-stage cannula for venous drainage and the left ventricle was vented through the right upper pulmonary vein. After CPB was established, systemic cooling was started immediately. Following gradual cooling and deep hypothermic circulatory arrest (18°C), the distal anastomosis was performed in the open technique.

Over the last five years, AxA has been preferentially used in our center as the route for systemic perfusion, except for patients presenting with shock (i.e., systolic blood pressure <50 mmHg) and requiring immediate CPB via femoral arterial cannulation. Before the antegrade cerebral perfusion, vascular clamps were placed on the brachiocephalic trunk, left common carotid artery, and left subclavian artery and cerebral perfusion was initiated via AxA

with a flow rate of 10 mL/kg/min with oxygenated blood at a temperature of 26°C. After aortotomy, the distal anastomosis was performed in the open technique in which the entry tear was removed completely in all patients. Subsequent to distal anastomosis termination, we clamped the graft and systemic heating was initiated. Selective antegrade blood cardioplegia was used for myocardial protection. During the evaluation of the aortic root, root replacement was performed in cases of tear involving the coronary ostia. Supracoronary graft replacement was performed in patients with an intact root. The decision for hemiarch replacement, total arch replacement or elephant trunk was made intraoperatively. When the dissection involved the coronary arteries, coronary artery bypass grafting was performed. Aortic valve resuspension was performed in suitable patients with aortic insufficiency. The Dacron tube graft (Vascutek, Terumo Inc., Glasgow, Scotland, UK) was used for ascending aorta repairs.

**Table 2. Intraoperative data of patients**

	Total				Group A				Group B				p
	n	%	Mean±SD	Min-Max	n	%	Mean±SD	Min-Max	n	%	Mean±SD	Min-Max	
Patients	131				65	49.6			66	50.4			
Aortic rupture	31	23.7			19	29.2			12	18.2			0.154
Cardiac tamponade	20	15.3			12	18.5			8	12.1			0.341
Arterial cannulation													
Femoral cannulation	70	53.4			36	55.6			34	51.5			0.727
Axillary cannulation	40	30.5			18	27.7			22	33.3			0.570
Femoral + axillary cannulation	12	9.2			6	9.2			6	9.1			1.000
Truncus brachiocephalicus	6	4.6			3	4.6			3	4.5			1.000
Aortic arch	3	2.3			2	3.1			1	1.5			0.619
Perfusion method													
CPB	24	18.3			9	13.8			15	22.7			0.259
CPB + ACP	20	15.3			9	13.8			11	16.7			0.809
CPB + TCA	69	52.7			38	53.5			31	47			0.222
CPB + ACP + TCA	18	13.7			9	13.8			9	13.6			1.000
Operation procedure													
Supracoronary graft	75	57.3			42	64.6			33	50			0.113
Hemiarch replacement	23	17.6			14	21.5			9	13.6			0.259
Total arch replacement	11	8.4			5	7.7			6	9.1			1.000
Frozen elephant trunk	2	1.5			2	3.1			0	0			0.244
Bentall procedure	56	42.7			23	35.4			33	50			0.113
Aortic valve replacement	2	1.5			0	0			2	3			0.496
Additional procedure													
Coronary artery bypass grafting	16	12.2			7	10.8			9	13.6			0.791
Aortic valve resuspension	12	9.2			6	9.2			6	9.1			1.000
Cross-clamp time (min)			98.6±46.2	27-262			94.2±49.4	27-262			102.9±46.8	33-209	0.281
CPB time (min)			195.8±80	66-531			195.2±79.7	83-463			194.5±84.9	36-531	0.05
Antegrade cerebral perfusion													
Mean time (min)			32.6±16.9	15-98			29.1±10.3	15-53			35.9±21	18-98	0.223
Total circulatory arrest													
Mean time (min)			20.3±13	1-78			20.4±11.9	1-52			21.5±3.9	1-78	0.053

SD: Standard deviation; Min: Minimum; Max: Maximum; CPB: Cardiopulmonary bypass; ACP: Antegrade cerebral perfusion; TCA: Total circulatory arrest.

The BioGlue (Cryolife Inc., Kennesaw, GA, USA) was used in selected patients. The dissected aortic layers were strengthened using a Teflon strip.

### Statistical analysis

Statistical analysis was performed using the IBM SPSS for Windows version 22.0 software (IBM Corp., Armonk, NY, USA). Continuous variables were expressed in mean  $\pm$  standard deviation (SD) and median (min-max), while categorical variables were expressed in number and frequency. Comparisons of continuous and categorical variables between the groups were done using the Student's unpaired t and chi-square ( $\chi^2$ ) test, respectively. Univariate and multivariate analyses were used to identify significant factors related to the hospital mortality. A two-tailed *p* value of  $<0.05$  was considered statistically significant.

## RESULTS

Baseline demographic and clinical data of the patients are shown in Table 1. There was no statistically significant difference between the groups in terms of age, sex, preoperative diseases, reoperation rates, and echocardiography findings. However, there was a statistically significant difference in type of surgery in hemodynamically stable patients between Group A and Group B ( $n=36$ , 55.4% vs.  $n=54$ , 81.8%, respectively) ( $p=0.001$ ). A total of 12 patients (5.3%) underwent

surgery under CPB, five (3.8%) with neurological instability, and 29 (22.1%) with hypotension.

Intraoperative data of the patients are shown in Table 2. There was no statistically significant difference between the two groups in terms of aortic rupture, cardiac tamponade, place of arterial cannulation, perfusion method, and operation procedure. The mean CPB time was  $195.8\pm 80$  min, the mean cross-clamp time was  $98.6\pm 46.2$  min, the mean selective antegrade cerebral perfusion time was  $32.6\pm 16.9$  min, and the mean total circulatory time was  $20.3\pm 13$  min in all patients, indicating no statistically significant difference between the groups.

Postoperative data of the patients are shown in Table 3. There was no statistically significant difference between the groups in terms of postoperative inotrope use, length of stay in the intensive care unit and hospital, and mechanical ventilation duration. A total of 39 patients (29.8%) in both groups underwent redo surgery due to bleeding and pericardial tamponade. There was no statistically significant difference in the rate of the development of postoperative cerebrovascular accidents between the groups, and 16 patients (24.6%) in Group A and eight patients (12.1%) in Group B developed a postoperative cerebrovascular accident ( $p=0.074$ ). Permanent neurological deficit developed in 13 patients (9.9%) in both groups. There

**Table 3. Postoperative data of patients**

	Total				Group A				Group B				<i>p</i>
	n	%	Mean $\pm$ SD	Min-Max	n	%	Mean $\pm$ SD	Min-Max	n	%	Mean $\pm$ SD	Min-Max	
Patients	131				65	49.6			66	50.4			
Early mortality	31	23.2			18	27.7			13	19.7			0.310
Inotrope use	87	66.4			48	73.8			39	59.1			0.054
IABP/ECMO	3	2.3			3	4.6			0	0			0.562
Intensive Care Unit time (day)			5.0 $\pm$ 8.3	1-60			5.7 $\pm$ 10	1-60			4.4 $\pm$ 6.1	1-45	0.379
Duration of hospital stay (day)			10.4 $\pm$ 11.3	1-85			11.2 $\pm$ 9.6	1-85			13.1 $\pm$ 9.1	1-60	0.427
Ventilation time (hour)			71.5 $\pm$ 99.3	1-540			110 $\pm$ 13.6	1-540			87.5 $\pm$ 10.9	1-500	0.429
Early revision													0.479
Bleeding	30	22.9			18	27.6			12	18.2			
Tamponade	9	6.9			4	6.2			5	7.6			
Late revision													0.600
Tamponade	5	3.8			2	3.1			3	4.5			
Sternum repair	6	4.6			4	6.2			2	3			
Postoperative neurological complication	24	18.3			16	24.6			8	12.1			0.074
Permanent neurological deficit	13	9.9			7	10.5			6	9			0.456
Postoperative CKD	21	16			17	26.2			4	6.1			0.001
Postoperative infection	17	13			12	18.5			5	7.6			0.074
Postoperative pleurisy	13	9.9			9	13.8			4	6.1			0.156

SD: Standard deviation; Min: Minimum; Max: Maximum; IABP: Intra aortic balloon pump; ECMO: Extracorporeal membrane oxygenators; CKD: Chronic kidney disease.

**Table 4. Causes of hospital mortality**

	Total		Group A		Group B	
	n	%	n	%	n	%
Bleeding	5	3.8	2	3.1	3	4.5
Low cardiac output syndrome	18	13.7	11	16.9	7	10.6
Multiple organ failure-sepsis	5	3.8	4	6.1	1	1.5
Cerebrovascular accident	1	0.8	0	0	1	1.5
Acute respiratory distress syndrome	1	0.8	1	1.5	0	0
Resistant arrhythmia	1	0.8	0	0	1	1.5

**Table 5. Causes of hospital mortality**

	Univariate analysis			Multivariate analysis		
	Odd ratio	95% CI	p	Odd ratio	95% CI	p
Age	1.061	1.022-1.102	0.002	1.073	1.023-1.126	0.004
Hypertension	1.286	0.396-4.177	0.676			
Diabetes mellitus	1.698	0.651-4.430	0.279			
Cardiac disease	3.200	1.385-7.392	0.006	1.535	0.538-4.380	0.423
Hemodynamic instability	3.845	1.655-8.935	0.002	3.792	1.339-10.740	0.012
Rupture	1.450	0.585-3.598	0.422			
Tamponade	2.551	0.933-6.972	0.068			
Arch surgery	1.227	0.500-3.012	0.655			
Cardiopulmonary bypass time	1.013	1.007-1.020	0.000	1.011	1.004-1.018	0.001

CI: Confidence interval.

was a statistically significant difference in the rate of development of postoperative kidney failure with 17 patients (26.2%) in Group A and four patients (6.1%) in Group B ( $p=0.001$ ).

The overall hospital mortality was 23.2% ( $n=31$ ). The hospital mortality rate was 27.7% ( $n=18$ ) in Group A and 19.7% ( $n=13$ ) in Group B, indicating no statistically significant difference ( $p=0.310$ ). The causes of mortality in both groups are summarized in Table 4. The causes of mortality were identified as low cardiac output syndrome in 18, sepsis-induced multiple organ failure in five, bleeding in five, neurological complications in one, acute respiratory distress syndrome in one, and resistant arrhythmia in one patient. The univariate analysis revealed that age, hemodynamic instability, heart disease, and CPB time were the risk factors for hospital mortality. The multivariate analysis revealed that hemodynamic instability, age, and CPB time were independent risk factors for hospital mortality (Table 5).

## DISCUSSION

The referral and transfer of a patient diagnosed with AAAD in a non-cardiac center are of utmost

importance. The transfer of the patient to the surgical center under hemodynamically stable conditions during transfer is associated with improved mortality and morbidity rates.

Acute type A aortic dissection is a complex disease and hospital mortality has been reported to be 25% in studies of aortic dissection registries.<sup>[7]</sup> However, some authors have shown a decline to 10 to 20% in surgically-equipped centers in developed countries.<sup>[9]</sup> In the aforementioned study, the study period was 24 years and was mainly divided into three equal periods. The mortality rates in the first, middle, and final periods were found to be 33%, 16%, and 11%, respectively. The authors concluded that the mortality rate of the surgical center decreased with increasing surgical experience.

In another study, surgical mortality rates were compared between high-volume aortic surgery centers with low-volume centers.<sup>[10]</sup> Hospitals performing more than 100 AAAD surgeries within seven years were accepted as high-volume centers in the study. The mortality rates were found significantly lower in high-volume centers (24.1% vs. 14.1%). Although our hospital is a newly established medical center, the number of patients undergoing surgery due to AAAD

has increased over the years which makes our center a high-volume center. However, we found no significant difference in terms of surgical mortality throughout the years.

Some authors have reported the possibility of the development of postoperative neurological complications after AAAD surgery as about 15%.<sup>[11]</sup> The total rate of neurological complications in all patients in our study was 18.3%. Another study found the rate of PND to be 10.9% in all patients.<sup>[8]</sup> In our study, 13 patients (9.9%) developed PND and no significant difference was found between the two groups. However, the rate of postoperative acute kidney failure was significantly higher in the patients referred from external centers (16% vs. 6.1%,  $p=0.001$ ).

Although there are many factors which affect mortality, preoperative hemodynamic instability is one of the main factors.<sup>[12]</sup> Hemodynamic instability often develops due to the development of malperfusion, rupture, and tamponade. It is critical to transfer the patient quickly to the center where cardiac procedures are to be performed before this condition develops. In our study, we operated 65 patients (49.6%) who were diagnosed with AAAD in another center as a high-volume reference hospital. Twenty-nine (44.7%) of these patients were hemodynamically unstable at the time of admission to the emergency room. Although we found no statistically significant difference in the hospital mortality rates between two groups, we found the most important risk factor to be hemodynamic instability for all patients in the multivariate analysis. We, therefore, suggest that hemodynamically unstable presentation of patients to our hospital may be due to the absence of an algorithm during the transfer. Previously, it was shown that the mortality rates were lower in high-volume centers implementing an established protocol for the transfer of patients with AAAD from centers where no aortic surgery was available.<sup>[7]</sup> This study also showed that even the use

of beta blockers during the transfer of patients with AAAD had a positive effect on mortality. In addition, the time taken for the operation of the patient can be shortened by the communication between the team that transfers the patient to the center of the aortic surgery and the staff of the surgery center.

Surgical treatment of AAAD is life-saving, and surgeons aim to decrease hospital mortality and avoid cardiac and neurological complications.<sup>[13]</sup> Aortic surgery centers in developed countries provide a high-quality service, offering preoperative evaluation, operative management, and good postoperative follow-up.<sup>[14]</sup> The fact the infrastructure of these centers is up-to-grade and non-surgical personnel are experienced and skillful, low surgical mortality rates can be obtained.<sup>[15]</sup> In Turkey, there are also aortic surgery centers which have undertaken treatment with a separate multidisciplinary approach. Referral and transfer of hemodynamically stable patients from external centers would also decrease the hospital mortality.

Furthermore, the surgical technique which should be used in AAAD patients is critical. The decision to perform aortic root and arch surgery during the operation affects the mortality and morbidity rates. In our study, there was no significant difference between the two groups in terms of the cannulation and surgical techniques performed during the operation.

There are several AAAD studies conducted in Turkey. These studies showed a mortality rate of 17% in patients operated with a frozen elephant trunk repair at Kartal Koşuyolu Yüksek İhtisas Training and Research Hospital which is the first aortic surgery center of our country.<sup>[16]</sup> Another center reported that, with the selection of the AxA for the arterial cannulation, the mortality rate was 12%, indicating that the AxA should be performed routinely.<sup>[17]</sup> In another publication of the same center, brain imaging

**Table 6. Causes of hospital mortality**

	Diagnostic center	Transfer team	Operation team
Definitive diagnosis	+++		+++
Blood pressure control ---Beta blockers	+++	+++	
Pain control ---Morphine?	++	++	
Blood group detection	+++		
Blood products preparation			+++
Usage of transesophageal echocardiography			+++

methods were found to be useful for AAAD patients during operation.<sup>[18]</sup>

During transfer of patients with AAAD to the center where surgery is to be performed, communication and treatment strategies play a key role. Two centers and transfer team should arrange what to do in this direction (Table 6). The most important step is the communication among the three separate teams.

### Limitations

As our center is newly established heart center, we were unable to perform randomization. In addition, surgeries were performed by more than one surgical team. Although the patients who were transferred to our hospital due to AAAD from other centers were promptly prepared for the surgery, we had missing information about how long the patients waited in the other center. Finally, we were unable to recognize the reason for hemodynamic instability at the time of admission (whether it resulted from the intervention of the emergency team of the external center or whether paramedic interventions were inadequate during the transfer).

In conclusion, morbidity and mortality rates would decrease with the establishment of aortic dissection teams for prompt treatment of patients with AAAD. Education on aortic dissection for emergency staff and health teams who are responsible for the transfer of the patients would also improve hemodynamic stability of the patients, thereby decreasing hospital mortality rates of reference hospitals.

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The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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