Risk Factors for Mortality in Acute Aortic Dissection Type A: A Centre Experience Over 15 Years

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Abstract Introduction Acute aortic dissection Type A (AADA) is still associated with a							
	mortality rate and frequent postoperative complications. This study was designed to						
	evaluate the risk factors for mortality in AADA patients.						
	Patients and Methods This retrospective analysis included 344 consecutive patients						
	who underwent surgery for AADA in moderate hypothermic circulatory arrest (20–24°						
	C nasopharyngeal) between 2001 and 2016.						
	Results The 30-day mortality rate was 18%. Nonsurvivors were significantly older (65.7 \pm						
	12.0 years vs. 62.0 ± 12.5 years; $p = 0.034$) with significantly higher Euro-score II [15.4%						
	(6.6; 23.0) vs. 4.63% (2.78; 9.88); $p < 0.001$)]. Intraoperatively, survivors had statistically						
	shorter cardiopulmonary bypass times [163 (134; 206) vs. 198 min (150; 245); $p = 0.001$].						
	However, the hypothermic circulatory arrest time was similar between both groups.						
	Postoperatively, the incidence of acute kidney injury (AKI) (55.9 vs. 15.2%; $p < 0.001$),						
	stroke (27.9 vs. 12.1%; $p = 0.002$) and sepsis (18.0 vs. 2.1%; $p < 0.001$) were significantly						
Keywords	higher among nonsurvivors. The multi-variable logistic regression confirmed that older age,						
 aorta/aortic 	previous cardiac surgery, preoperative cardiopulmonary resuscitation (CPR), blood transfu-						
 aortic valve and root 	sion and postoperative acute kidney injury (AKI) were independent risk factors for mortality.						
 cardiopulmonary 	Conclusion Our analysis suggested that the reason for mortality was multifactorial,						
bypass	especially age, previous cardiac surgery, CPR, transfusion, as well as postoperative AKI						
► CPB	were considered risk factors for mortality.						

Introduction

Acute Type A aortic dissection (AADA) is a fatal disease, associated with a high mortality rate, if not treated urgently. The mortality rate of untreated AAD increases 1 to 2% every hour after its onset, and it reaches up to 50% in the first 48 hours.¹⁻⁶

The incidence of AAD increased nowadays due to increasing mean age of the population.⁷ Hospital mortality remains high in spite of the improved outcomes after emergency surgery; it reaches up to 30%.⁸ However, the chances of survival could be significantly improved with early involvement and management.

received September 2, 2019 accepted after revision March 4, 2020 The aim of surgical repair of acute Type A aortic dissection is to avoid sudden death due to aortic rupture and to maintaining the blood flow for organs that have been affected by the dissected membrane, as well as to correct the associated aortic valve regurgitation, if the dissection extends proximally till it reaches the aortic valve. Prosthetic replacement of the supracoronary ascending aorta is the most frequent approach after refixation of the dissected wall of the aorta.

In our study, we have reported our 15-year experience of surgical repair of AADA using hypothermic circulatory arrest. The aim of this study is to analyze the perioperative risk factors for death in patient who underwent surgical repair of AADA.

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Patients and Methods

Patient Population

In this retrospective analysis, 344 consecutive patients who underwent surgery for AADA in moderate hypothermic circulatory arrest (MHCA)(20–24°C, nasopharyngeal) between 2001 and 2016 were included. According to our center strategy, we used the Stanford classification of aortic dissection, where all patients with Type A were included. In terms of 30-day mortality, patients were divided into two groups: 82% survived the 30 days postoperative, and 18% died within this period. All patients who died before the operation are excluded from the study.

The primary endpoint was 30-day mortality. Secondary endpoints were pre- and intraoperative variables, as well as the postoperative courses such as blood loss and transfusion of blood products, redo-surgery, acute renal failure, mechanical ventilation time, and postoperative neurologic complications.

Data were supplied from the institution's database and medical records. The study protocol was approved by the local Ethics Committee.

Patient Management

Patients with AADA were operated on an emergency basis after confirmation of the diagnosis with an emergency contrast computed tomography (CT-scan) and then transported directly with life threatening indication to the operating room. The exact timing between the diagnosis and the operation do not exceed 30-60 minutes and are based on a life threating condition with presence of an emergency team including anesthesia team for the preparation of surgery. The time between the onset of symptoms and operation could not be exact due to the life-threatening condition of the patient, who are in many cases not responsive, as well as the lack of time to collect a detailed anamnesis. The exact location and extension of the dissection membrane were detected preoperatively by the tomography (CT-scan). If possible, patients were investigated for neurological symptoms and questioned at hospital admission for any positive history of neurological events.

Postoperative neurological outcomes were consulted directly by a neurologist and categorized according to neurological assessment. The neurological findings will be documented in patient's file from the attended neurologist, followed by head and neck computer tomography as well as, in many cases, CT-angiography for the carotid arteries to estimate the extent of stroke and brain ischemia. After CT control, a neurologist will be consulted again for further plan.

Transesophageal echocardiography (TEE) was performed intraoperatively under general anesthesia.

Surgical Procedure

All patients underwent a corrective surgery performed by the senior surgeons. A standard median sternotomy followed by longitudinal pericardiotomy was performed under general anesthesia. The cardiopulmonary bypass (CPB) was performed with direct cannulation of the distal ascending aorta or retrograde femoral artery cannulation for arterial cannulation. Since 2010, we use the transatrial cannulation of the left ventricle via the right upper pulmonary vein as an alternative for arterial cannulation under moderate hypothermic circulatory arrest with core temperature between 20 and 24°C. This cannulation position is ideal for the antegrade flow of the blood and to avoid any kind of manipulation of ascending aorta as well as to avoid extra incision during preparation of the axillary or the subclavian artery.⁹ Venous drainage was performed either through direct cannulation of the right atrium or through the femoral vein with a cannula that extends to the right atrium. A standard retrograde injection of cold blood cardioplegic solution for myocardial protection was performed. An antegrade cerebral perfusion with oxygenated cold blood (18°C) was introduced through a balloon catheter inserted in the left common carotid artery and the brachiocephalic artery with flow pressure of 50-60 mm Hg and flow rate of 40-60 mL/kg/min, without perfusion of the subclavian artery, which remain open during the time of perfusion. The distal extent of aortic repair depends on the extent of the dissected intimal tear. The aortic repair was limited to the ascending aorta just proximal to the innominate artery if the intimal tear did not extend or originated from the aortic arch, otherwise, the aortic repair extended to hemiarch or total arch replacement in cases where the intimal tear extended to the aortic arch, with re-implantation of head and neck arteries. In several cases, an elephant trunk was also introduced in the proximal descending aorta. After insertion of the perfusion cannula directly into the graft, CPB restarted again slowly. The proximal aortic repair was performed either through isolated supra-coronary ascending aorta replacement or either through Bentall-Op, David-Op or with extra isolated aortic valve replacement with preservation of aortic root in case of associated isolated aortic valve disease. After the establishment of the proximal anastomosis, residual air was removed by restarting retrograde perfusion via the venous cannula. Continuous CO2 insufflation was used as a standard for the cardiac de-airing. Transesophageal echocardiography was performed to control the presence of residual air in the left side of the heart. During rewarming, other procedures, if required, such as coronary artery bypass graft (CABG) were performed.

Statistical Analysis

Statistical analysis was performed using the SPSS Statistics software (Version 18.0) and Stata 10 SE (StataCorp., College Station, Texas, United States). Normality of continuous variables was assessed by Kolmogorov-Smirnow Test. Normally distributed data are presented as the mean \pm standard deviation and not normally distributed data as median with range or interquartile range when appropriate. Categorical variables are displayed as frequency distributions (*n*) and simple percentages (%). Univariate comparison between the groups for categorical variables was made using the χ^2 and the Fisher's exact test as appropriate. A *p*-value of < 0.05 was considered as significant. Logistic regression analysis was used to determine the odds ratio (OR) of risk factors upon the 30-days survival time.

Results

The preoperative analysis reported the risk factors for AADA as shown in **- Table 1**.

	Total	30-day survivors	30-day deceased	p Value
No. of surgical procedures	344 (100%)	282 (82%)	62 (18%)	
Age, y	62.7 ± 12.4 63.1 (54.1; 72.1)	62.0 ± 12.5 62.6 (54.2;70.9)	65.7 ± 12.0 68.9 (53.7; 75.3)	0.034
Age \geq 75 y	63 (18.3%)	44 (15.6%)	19 (30.6%)	0.006
Female	117 (34.0%)	93 (33.0%)	24 (38.7%)	0.388
EuroSCORE II (%)	5.49 (3.06; 12.99)	4.63 (2.78; 9.88)	15.4 (6.6; 23.0)	< 0.001
Body mass index, kg/m ²	26.3 (24.0; 28.6)	26.3 (24.1; 28.6)	26.3 (23.8; 28.6)	0.934
Arterial hypertension	244 (72.4%)	210 (75.0%)	34 (59.6%)	0.018
Diabetes mellitus type 2	20 (6.1%)	14 (5.1%)	6 (10.9%)	0.118
Hyperlipoproteinaemia	47 (14.4%)	38 (13.9%)	9 (16.7%)	0.599
Chronic renal failure/insufficiency	45 (13.6%)	37 (13.5%)	8 (14.5%)	0.830
Renal replacement therapy	7 (2.1%)	6 (2.2%)	1 (1.8%)	1.000
COPD	20 (6.0%)	14 (5.0%)	6 (10.7%)	0.119
Coronary heart disease	60 (18.3%)	41 (14.9%)	19 (35.8%)	< 0.001
Previous PCI	23 (6.9%)	14 (5.0%)	9 (16.4%)	0.006
Previous cardiac surgery	12 (3.6%)	6 (2.1%)	6 (10.9%)	0.006
Marfan syndrome	9 (2.7%)	6 (2.2%)	3 (5.0%)	0.202
Aortic aneurysm	108 (31.5%)	93 (33.1%)	15 (24.2%)	0.172
Bicuspid aortic valve	9 (2.4%)	8 (2.6%)	1 (1.6%)	1.000
Aortic valve insufficiency	121 (40.5%)	108 (43.9%)	13 (24.5%)	0.609
Neurological deficits	69 (20.5%)	53 (19.0%)	16 (27.6%)	0.140
Cardiogenic shock	27 (7.9%)	19 (6.8%)	8 (13.3%)	0.111
CPR (48 h)	30 (8.8%)	11 (3.9%)	19 (31.1%)	<0.001
Intubated	37 (10.9%)	19 (6.8%)	18 (29.5%)	<0.001

Tal	ble	1	Preoperative	risk-factors	for AADA
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Arterial hypertension was the most common risk factor for AADA presented in 72.4% of the study population, followed by the presence of aortic valve insufficiency in 40.5%. Preoperative cardiopulmonary resuscitation (CPR) was conducted in 8.8% in all patients (3.9% in survivors vs. 31.1% in nonsurvivors; p < 0.001). Incidence of intubation and mechanically ventilation before hospital admission represented 10.9% of the total study population with high significance in nonsurvivors (6.8 vs. 29.5%; p < 0.001). Cardiogenic shock was diagnosed in 7.9% of patients. Presence of previous cardiac surgery was associated with higher mortality (2.1% in survivors vs. 10.9% in nonsurvivors; p < 0.006). Furthermore, nonsurvivors suffered form more incidence of preoperative myocardial ischemia than survivors (35.8 vs.14.9%; p < 0.001). Intraoperatively, the length of surgery was significantly shorter in survivors [275 min (227; 331) vs. 319 min (239; 410); *p* = 0.004]. Survivors had statistically shorter cardiopulmonary bypass times $[163 \min(134; 206) \text{ vs. } 198 \min(150; 245); p = 0.001]$. However, the hypothermic circulatory arrest time was similar between both groups [33 min(25; 45) vs. 33 min (27; 49); p = 0.368]. Moreover, survivors received a significantly fewer number of transfused packed red blood cells than nonsurvivors [3 (0; 6) vs. 5 units (2; 10); p = < 0.001]. The surgical procedure was extended to include coronary artery bypass

surgery more frequently in nonsurvivors (25.0 vs. 6.4%; p = < 0.001) (**-Table 2**).

Postoperatively, the incidence of AKI (55.9 vs. 15.2%; p < 0.001), stroke (27.9 vs. 12.1%; p = 0.002) and sepsis (18.0 vs. 2.1%; p < 0.001) were significantly higher among non-survivors. The 30-day mortality rate for all patients was 18%. Patients who did not survive were significantly older (65.7 ± 12.0 vs. 62.0 ± 12.5 years; p = 0.034) with significantly higher Euro-score II [15.4% (6.6; 23.0) vs. 4.63% (2.78; 9.88); p < 0.001)]. Moreover, patients older than 75 years had a higher mortality rate up to 30.6%. 56.6% of deaths were due to cardiac causes, and 32.3% were due to multi-organ failure.

The multivariate logistic regression confirmed that older age, previous cardiac surgery, preoperative CPR, intraoperative transfusion and postoperative acute kidney injury (AKI) were statistically significant independent risk factors for death (p < 0.05) (**~Table 3**).

We found out that the percentage of 30-day-mortality in proportion to the rate of operation showed no significant differences between patients operated between 2001 and 2009 (mid-point of the study) and between 2010 and 2016. However, a slightly increase in the percentage of 30-daysmortality could be contributed to the huge increase in the number of patients operated in the last decade in comparison



Fig. 1 Proportion between the rate of operation and the 30- day mortality per each year.

to the decade before. **Fig. 1** represents the course of the 30-day-mortality annually.

Discussion

In the recent decades, there was a huge improvement in the diagnosis of AADA, its emergency transport and perioperative management. Advanced cerebral protection,^{10–12} and antegrade arterial perfusion is used nowadays to achieve organ perfusion.¹³ However, its hospital mortality rate is still high; it ranges between 20 and 30%.^{8,14–17} A nationwide inpatient survey in the USA with a cohort of 3,013 patients with aortic dissection who underwent aortic resection between 1995 and 2003 showed a hospital mortality rate of 26%.¹⁸ The German Registry for Acute Aortic Dissection Type A (GERAADA) reported overall 30-day mortality of 16.9% in a cohort of 2,137 patients who underwent surgical repair of AADA between 2006 and 2010.¹⁹

The current study analyzed the independent risk factors for mortality in patients with AADA, evaluated by univariable or multivariable analysis. The study was in line with previous studies which showed that old age, preoperative shock conditions, the extent of aortic repair, length of operation, organ malperfusion as well as associated CABG are considered risk factors for mortality.^{14,15,20–22}

Our study showed that mortality within 30 days postoperative was higher in patients older than 75 years (30.6%). The majority of studies showed that increased age is associated with increased short- and long-term mortality rates after surgical repair of AADA, while other studies demonstrated that patients with old age could undergo surgery with acceptable mortality rates. Trimarchi et al in a study belonged to the International Registry of Acute Aortic Dissection (IRAD) analyzing the role of age in AADA confirmed that increased age (70 years or more) is an independent predictor of in-hospital mortality in comparison to younger patients (38.2 vs. 26.0%).²³ McKneally et al delivered a further concept in avoiding that type of surgery. Under this message - "We don't do that here" - he stated that surgery for AADA in patients older than 80 years should not be performed at alldue to the tragical experience they encountered with operative treatment of AADA.²⁴

On the contrary, Zheng and Stamou et al demonstrated that patients older than 70 years could safely undergo surgery of AADA with acceptable rates of mortality and neurological adverse outcomes.^{3,25} An overall conclusion from GERAADA suggests that surgical management of AADA was still associated with significantly lower in-hospital mortality than medical management until the age of 80 years. Rylski B et al in a study belonged to GERAADA showed a mortality rate of 15.8% in patients between 70 and 80 and 34.9% in patients older than 80 years. The high mortality rate in the older group of patients was attributed to the octogenarians' poorer preoperative condition.¹⁹

According to the affected aortic branch vessels, one of the major complications of AADA is the malperfusion of various organs. Preoperative malperfusion is known as a risk factor for mortality after surgical repair of AADA.²⁶ Myocardial ischemia is considered one of the major concerns after AADA due to obstruction of coronary blood flow and usually the right coronary artery is involved.²⁶ Kawahito K et al reported an overall incidence of coronary malperfusion with acute aortic dissection reached up to 6.1% in a total of 196 patients. The study reported that preoperative ST elevation identified

on the ECG is a significant independent risk factor for hospital mortality after surgery for AADA. The incidence of hospital mortality was 33.3% among those patients affected by coronary malperfusion. The mortality rate was higher than that in patients without coronary malperfusion (33.3 vs. 8.2%), and the degree of associated myocardial damage caused by coronary dissection with concomitant CABG was considered in the study as one of the leading predictors of hospital death.²⁶ Our experience showed that patients with coronary malperfusion who underwent an additional CABG with surgical repair of AADA were associated with high mortality rate than those without preoperative signs of acute myocardial ischemia or infarction (25.0 vs. 6.4). Those findings confirm that coronary malperfusion is considered a risk factor for mortality after AADA.

Acute kidney injury (AKI) is frequent in patients with AADA. The extension of the dissected membrane distally until it reaches the renal vessels facilitates organ malperfusion. We report a significantly higher incidence of AKI among non-survivors than survivors (55.9 vs. 15.2%; p < 0.001). Moreover, cerebral malperfusion was an indicator of high postoperative mortality. The incidence of cerebral ischemia or infarct confirmed by computed tomography were higher in nonsurvivors than survivors (27.9 vs. 12.1%; p = 0.002). A study from the International Registry of Acute Dissection (IRAD) showed worse results in a larger study population of 1873 patients with AADA. The overall hospital mortality in patients without brain injury was 22.7%; 40.2% in patients with cerebrovascular accident, and 63.0% in patients with coma (p < 0 0.001). However, the mortality rate varied according to the treatment strategy (76.2% medical vs. 27.0% surgical in cases with cerebrovascular accident; p < 0.001 and 100% medical vs 44.4% surgical in cases with coma; *p* < 0.001).²⁷

Mesenteric malperfusion syndrome was reported as an uncommon complication in patients with AADA in the

literature. However, this is the most lethal form of associated malperfusion with more than 60% hospital mortality according to the International Registry of Acute Dissection (IRAD). Only 3.8% from a total number of 1,809 of patients were presented with mesenteric malperfusion. It was reported that patient with previous cardiac operation as well as with chronic kidney failure are more prone to develop those kinds of malperfusion. Moreover, presence of mesenteric malperfusion was associated with greater incidence of cerebral and spinal cord injuries. The in-hospital mortality of those patients with mesenteric malperfusion was significantly high in patient receiving medical treatment in comparison to those with endovascular intervention or surgical/hybrid therapy (95.2, 72.7, and 41.7%, respectively) (p < 0.001).²⁸

The current study showed that the extension of surgical repair of AADA distally involving total arch replacement (22.0% in nonsurvivors vs. 12.9% in survivors) is associated with a higher mortality rate in comparison with those patients who underwent only replacement of ascending aorta or even limited only to the partial replacement of aortic arch. As shown in **- Table 2**, there were no significant differences between both survival and nonsurvivor group regarding each individual technique. However, the higher mortality associated with more extended surgery toward aortic arch was attributed to the elongated surgical duration. In our analysis, we found out that the length of surgery and cardiopulmonary bypass time was significantly shorter in the survivor group than those of nonsurvivors. Lansmann et al stated that the extension of intimal tear either in aortic arch or more distally increased the in-hospital mortality rate due to associated more aggressive surgery.²⁹

On the other hand, Kautzi et al reported in a study of over 70 patients that extended total arch replacement for AADA could be justified in properly selected patients. The early mortality rate was 16% which was similar to those mortalities of recent studies recommending less aggressive surgical

	Total	30-day survivors	30-day deceased	p Value
Length of surgery, min	280 (227; 346)	275 (227; 331)	319 (239; 410)	0.004
Cardiopulmonary bypass time, min	168 (136; 214)	163 (134; 206)	198 (150; 245)	0.001
Cross-clamp time, min	91 (70; 127)	89 (68; 126)	101 (77; 135)	0.114
Circulatory arrest, min	33 (26; 46)	33 (25; 45)	33 (27; 49)	0.368
Number of packed red blood cells	3.5 (0; 6)	3 (0; 6)	5 (2;1 0)	< 0.001
Surgical procedure				
Supracoro. aorta ascending replacement	171 (49.7%)	138 (48.9%)	33 (53.2%)	0.541
Partial arch replacement	70 (20.3%)	62 (22.0%)	8 (12.9%)	0.108
Total arch replacement	48 (14.0%)	36 (12.8%)	12 (19.4%)	0.175
Conduit/Bentall operation	61 (17.7%)	51 (18.1%)	10 (16.1%)	0.715
David operation	21 (6.1%)	18 (6.4%)	3 (4.8%)	0.778
Elephant-trunk	7 (2.0%)	7 (2.5%)	0 (0.0%)	0.359
Additional CABG	33 (9.7%)	18 (6.4%)	15 (25.0%)	< 0.001
Additional aortic valve replacement	55 (16.0%)	44 (15.6%)	11 (18.0%)	0.639

 Table 2
 Intraoperative data

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	Total	30-day survivors	30-day deceased	p Value
New onset of Hemodialysis	76 (22.3%)	43 (15.2%)	33 (55.9%)	<0.001
48-hour drainage loss, mL	825 (488; 1250)	750 (450; 1200)	1010 (600; 1775)	0.040
Total number of packed red blood cells	2 (0; 7)	2 (0; 6)	4 (0; 12)	0.074
Total number of fresh frozen plasma	0 (0; 4)	0 (0; 4)	4 (0; 12)	0.001
Total number of platelets concentrate	0 (0; 1)	0 (0; 1)	0.5 (0; 3)	0.001
Postoperative myocardial infarction	3 (0.9%)	0 (0.0%)	3 (4.9%)	0.005
TIA/Stroke (CT-proofed)	51 (14.9%)	34 (12.1%)	17 (27.9%)	0.002
CPR	28 (8.2%)	17 (6.1%)	11 (18.0%)	0.002
7-day Mortality	47 (13.7%)	0 (0.0%)	47 (75.8%)	< 0.001
Hospital Mortality	61 (17.8%)	2 (0.7%)	59 (95.2%)	< 0.001
Cardiac death	36 (56.3%)	1 (50.0%)	35 (56.5%)	
Cerebral death	4 (6.3%)	0 (0.0%)	4 (6.5%)	
MOF	21 (32.8%)	1 (50.0%)	20 (32.3%)	

Table 3 Postoperative data

repair.³⁰ Piccardo et al found that the less aggressive surgical approach is a key factor in reducing operative time and mortality.³¹ We recommend, if possible, a less aggressive surgical repair in old patients, which is considered safer and shorter in time than those operations with surgical repairs extending distally toward total arch replacement.

We figured out in our analysis an experience over 15 years on the risk factors that lead to AADA and the hospital mortality. We also found out that the major determinants for postoperative mortality in AADA are the associated preoperative complications and comorbidities. Patients admitted for surgery with an unstable condition such as shock, cardiopulmonary resuscitation, severe neurologic damage, aortic rupture, and malperfusion of various organs have a higher mortality rate than those with a more stable condition. The decision making should be taken individually according to the general condition of each patient and the presence of the above comorbidities and risk factors. Young patients with a stable condition can undergo more aggressive surgical repair, if necessary, to avoid postoperative complication and to improve the prognosis.

Conclusion

The current study suggested that AADA remains associated with a high mortality rate. The reason for mortality and complications in patients undergoing surgical repair of AADA were multifactorial. Especially older age, previous cardiac surgery, preoperative CPR, transfusion of blood products, as well as postoperative AKI were considered risk factors for mortality.

Limitations

This is a retrospective single-center study and based on a non-randomized analysis of data. Another limitation is the inability to define the exact time of onset of symptoms in all cases due to the emergency nature of AAD and inability to collect a detailed anamnesis from the study population.

Conflict of Interest None declared.

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