# Acute type A aortic dissection: significance of multiorgan malperfusion

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#### Abstract

**OBJECTIVES**: Acute type A aortic dissection (AAAD) remains one of the most challenging diseases in cardiothoracic surgery, and despite numerous innovations, early mortality still remains high. The aim of this study was to review the Emilia-Romagna experience in the treatment of AAAD and to evaluate the effect of malperfusion on mortality and morbidity.

**METHODS**: We examined data of 502 patients between January 2000 and December 2008, from the Emilia-Romagna Regional Registry of AAAD. The mean age was 62.4 ± 13 years and 66.5% were male. At presentation, various types of malperfusion syndromes (cerebral, cardiac, ileo-femoral, renal, mesenteric and spinal cord) were present in 103 patients (20.5%; malperfusion [MPS] group). Three hundred ninety-nine patients (No-MPS group) did not have pre-operative malperfusion. Arterial access for cardiopulmonary bypass was usually via the femoral artery (81.9%), while the axillary artery was used only in 14.7%. The aortic repair was performed using the 'open technique' in 348 patients (69.3%) and with aortic cross-clamping without circulatory arrest in 154 patients (30.7%).

**RESULTS**: Overall in-hospital mortality was 20.9%: 43.7% in the MPS group vs 15% in the No-MPS group (P = 0.001). The operative technique and the cannulation site did not influence post-operative outcomes. Multivariate regression analysis identified mesenteric (odds ratio [OR] 9.5, confidence interval [CI] 2.4–37.4; P = 0.0012), cardiac malperfusion (OR 3.7, CI 1.7–8.0; P < 0.0001) and shock (OR 2.1, CI 1.2–3.5; P = 0.007) as significant risk factors for in-hospital mortality after surgery for type A dissection. Patients who presented singleorgan malperfusion had a mortality rate of 34.7%, which increased to 61.9% and to 85.7% if two or more than two organ systems were involved, respectively.

**CONCLUSIONS**: The results of the surgical treatment of AAAD are acceptable and mainly influenced by patient's status at presentation. Malperfusion of more organ systems makes the prognosis unfavourable and immediate proximal aortic repair may be sub-optimal. In these situations, alternative management strategies should be considered.

Keywords: Aorta · Aortic dissection · Surgery · Malperfusion

## INTRODUCTION

Acute type A aortic dissection (AAAD) remains one of the most challenging diseases in cardiothoracic surgery, and despite numerous innovations in medical and surgical management, early mortality still remains high [1–6]. Various techniques of aortic repair with similar results have been proposed [1], but the preoperative status of the patient represents the most important risk factor for hospital mortality. Approximately one-third of AAAD patients manifest pre-operative malperfusion syndrome [1, 7-9] of various organ systems, and end-organ malperfusion can dramatically reduce the chance of successful outcome.

The aim of this study was to review the Emilia-Romagna experience in the treatment of AAAD and to evaluate the incidence of malperfusion syndrome in these patients. Moreover, we sought to examine the effect of malperfusion on mortality and morbidity.

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#### MATERIALS AND METHODS

#### Patients

We reviewed the data of 502 patients listed in the Emilia-Romagna Registry of AAAD between January 2000 and December 2008. This registry is part of the RERIC (Registro Emilia-Romagna Interventi Cardiochirurgici), a clinical registry that includes all the cardiac surgical procedures performed in the six Cardiac Surgery Departments of the Emilia-Romagna region. Additional information relevant to the study was retrieved through record linkage procedures between the Emilia-Romagna Registry of AAAD and the administrative databases available at the regional level, in particular, with the regional database of hospital admissions and the regional mortality registry to identify the patients who died in or out of the hospital.

All patients underwent surgery on an emergency basis in the six regional hospitals, and in three of them, more than 100 operations (range 20-151) were performed.

The clinical characteristics of these patients are reported in Table 1. There were 334 males (66.5%) having a mean age of 62.4  $\pm$  13 years. Hypertension was present in 403 patients (80.3%), 6 (1.2%) had Marfan syndrome and 9 (1.8%) had a bicuspid aortic valve.

On admission, 96 patients (19.1%) were in a state of clinical shock or cardiac tamponade. Clinical shock was defined as systolic blood pressure <80 mmHg or cardiac index <1.8 l/min/m<sup>2</sup>. One hundred and sixty-eight patients (33.5%) had moderate or severe aortic valve regurgitation diagnosed by transthoracic and/or transesophageal echocardiography. Thirty patients (6%) had undergone previous cardiac surgery.

At presentation, various types of malperfusion syndromes were present in 103 patients (20.5%; malperfusion [MPS] group).

Table 1: Demographic patient characteristics

Malperfusion syndrome was defined as the presence of signs and symptoms due to altered blood flow in an organ system with clinical evidence of a lack of blood flow, resulting in ischaemia with organ dysfunction. Depending on the organ system, the malperfusion syndromes were classified as cerebral (stroke or transient ischaemic attack), cardiac (electrocardiographic changes, creatine kinase or troponin elevation with myocardial dysfunction), limb (loss of pulse, sensory or motor function with clinical signs of limb malperfusion), mesenteric (abdominal tenderness, bowel paralysis, lactate acidosis with elevation of liver and pancreatic function tests) and renal (creatinine elevation, lack of urine output) malperfusion.

Malperfusion syndrome was also confirmed by radiographic or intra-operative evidence of dissection involving the aortic branch vessels concerned. A dissection flap in the branch vessels was not considered to be a malperfusion syndrome where there was an absence of clinical findings. Cerebral malperfusion occurred in 39 patients (7.8%), coronary malperfusion in 32 (6.4%), limb malperfusion in 32 (6.4%), renal malperfusion in 14 (2.8%), mesenteric in 12 (2.4%) and spinal cord malperfusion in 5 (1%). Seventy-five patients (14.9%) had malperfusion in one organ system, 21 (4.2%) had malperfusion in two, and 7 (1.4%) had malperfusion in three or more organ systems.

Three hundred and ninety-nine patients (79.5%; No-MPS group) did not present pre-operative signs and symptoms of malperfusion.

#### Operative technique

The Emilia-Romagna Regional Registry of AAAD includes patients from different cardiothoracic regional centres as previously described [10]. Differences in patient management and operative

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	All patients (n = 502)	MPS group ( <i>n</i> = 103)	No-MPS group ( <i>n</i> = 399)	P-value
Age, mean ± standard deviation (SD)	62.4 ± 13.0	61.9 ± 12.0	62.6 ± 13.2	0.6368
Male sex, N (%)	334(66.5)	72(69.9)	262(65.7)	0.4174
Risk factors				
Hypertension, N (%)	403(80.3)	81(78.6)	322(80.7)	0.6401
Bicuspid aortic valve, N (%)	9(1.8)	3(2.9)	6(1.5)	0.3377
Marfan, N (%)	6(1.2)	1(1.0)	5(1.3)	0.8146
Shock/cardiac tamponade, N (%)	96(19.1)	40(38.8)	56(14.0)	< 0.0001
Aortic valve insufficiency				
Moderate, N (%)	56(11.2)	15(14.6)	41(10.3)	0.2187
Severe, N (%)	112(22.3)	18(17.5)	94(23.6)	0.1869
Previous cardiac surgery				
Aortic valve replacement, N (%)	10(2.0)	2(1.9)	8(2.0)	0.9674
Thoracic aorta, N (%)	5(1.0)	1(1.0)	4(1.0)	0.9771
CABG, N (%)	6(1.2)	1(1.0)	5(1.3)	0.8146
Mitral, N (%)	3(0.6)	0(0.0)	3(0.8)	0.3784
Others, N (%)	6(1.2)	4(3.9)	2(0.5)	0.0048
Site of primary intimal tear				
Aortic root, N (%)	55(11.0)	20(19.4)	35(8.8)	0.0020
Ascending aorta, N (%)	346(68.9)	65(63.1)	281(70.4)	0.1530
Aortic arch, N (%)	68(13.5)	12(11.7)	56(14.0)	0.5293
Descending aorta, N (%)	11(2.2)	2(1.9)	9(2.3)	0.8466
Unknown, N (%)	22(4.4)	4(3.9)	18(4.5)	0.7819

MPS group: malperfusion group; No-MPS group: no malperfusion group; CABG: coronary artery bypass grafting.

**AORTIC SURGERY** 

Intraoperative characteristics	All patients (n = 502)	MPS group ( <i>n</i> = 103)	No-MPS group ( <i>n</i> = 399)	P-value
Operative procedures				
DHCA, N (%)	83(16.5)	34(33.0)	49(12.3)	0.0018
ASCP, N (%)	265(52.8)	57(55.3)	208(52.1)	0.5617
Blood cardioplegia, N (%)	226(45)	49(47.6)	177(44.4)	0.2360
Crystalloid cardioplegia, N (%)	276(55)	60(58.3)	216(54.1)	0.6242
Femoral cannulation, N (%)	411(81.9)	85(82.5)	326(81.7)	0.8477
Axillary cannulation, N (%)	74(14.7)	15(14.6)	59(14.8)	0.9546
Extension of replacement				
Ascending aorta, N (%)	265(52.8)	58(56.3)	207(51.8)	0.930
Hemiarch, N (%)	156(31.1)	27(26.2)	129(32.3)	0.2325
Total arch, N (%)	81(16.1)	18(17.5)	63(15.8)	0.6790
Supra-aortic vessel reimplantation, N (%)	82(16.3)	21(20.4)	61(15.3)	0.2127
Associated procedures				
Bentall procedure, N (%)	110(21.9)	22(21.4)	88(22.1)	0.8793
David procedure, N (%)	8(1.6)	1(1.0)	7(1.8)	0.5722
CABG, N (%)	24(4.8)	12(11.7)	12(3.0)	0.0002
Mitral valve, N (%)	5(1.0)	2(1.9)	3(0.8)	0.2792
Circulation time				
CPB time (min), mean ± SD	171.3 ± 80.6	185.2 ± 91.0	167.6 ± 77.4	0.0513
Myocardial ischaemia time (min), mean ± SD	105.7 ± 105.4	99.0 ± 43.5	107.4 ± 116.0	0.5019
ASCP time (min), mean ± SD	50.0 ± 33.6	50.4 ± 42.2	49.8 ± 30.8	0.9036
Visceral ischaemia time (min), mean ± SD	47.3 ± 34.6	47.5 ± 44.4	47.2 ± 31.0	0.9556

#### Table 2: Intraoperative patient characteristics

MPS group: malperfusion group; No-MPS group: no malperfusion group; DHCA: deep hypothermic circulatory arrest; ASCP: antegrade selective cerebral perfusion; CABG: coronary artery bypass grafting; CPB: cardiopulmonary bypass.

techniques are present. Standard median sternotomy was performed in all patients. Arterial access for cardiopulmonary bypass (CPB) was usually via the femoral artery (411 patients, 81.9%), while the axillary artery was used only in 74 patients (14.7%).

Three hundred forty-eight patients (69.3%) underwent aortic repair using the 'open technique': in 88 of them (25.3%), the proximal repair was done with aortic cross-clamping before the distal anastomosis, while in the remaining 260 patients (74.7%), the aorta was not clamped at all.

In 154 patients (30.7%), the aortic repair was performed without circulatory arrest. Myocardial protection was achieved by crystalloid cardioplegia in 276 patients (55%), while blood cardioplegia was used in 226 (45%).

Cerebral protection was achieved with deep hypothermic circulatory arrest (DHCA) with a nasopharyngeal temperature of 18–20°C in 83 patients (16.5%), while antegrade selective cerebral perfusion (ASCP) was used with mild hypothermia (25–26° C) in 265 (52.8%).

The extension of aortic repair and associated procedures is reported in Table 2. After careful inspection, the decision for replacement or for conservative treatment of the aortic root with reconstruction techniques depended on the individual morphology and on the extent of the dissection. In the case of a dilated root (exceeding 45 mm) or in Marfan patients, the aortic root was always replaced. Replacement of the aortic arch was performed when the arch was aneurysmal, ruptured or extensively involved by the intimal tear.

The mean times for CPB, myocardial ischaemia, ASCP and visceral ischaemia were  $171 \pm 81$ ,  $106 \pm 105$ ,  $50 \pm 34$  and  $47 \pm 35$  min, respectively.

The intra-operative data for both groups are shown in Table 2. There were no significant differences between the groups except for the use of DHCA and coronary artery bypass grafting (CABG) as associated with procedures and the duration of CPB.

#### Follow-up

All hospital survivors were available for follow-up and every patient had at least one computed tomography scan performed within 1 year from the operation. Follow-up information was obtained by direct examination or by correspondence with the patient.

#### Statistical analysis

Characteristics of the patients with and without malperfusion syndrome were compared with  $\chi^2$  and Mann-Whitney *U*-tests. The association between pre-operative characteristics and in-hospital mortality was expressed as odds ratio and the statistical significance assessed through the Mantel-Haenszel  $\chi^2$  test.

The variables significantly associated (P < 0.05) with mortality onset were subsequently included into two logistic regression models. In one model, malperfusion was considered as a dichotomous variable. In the second model, to better evaluate the effect of the various types of organ malperfusion, the malperfused organ systems were inserted as separate variables. The goodness of fit of the logistic models was assessed with the Hosmer-Lemeshow test and the C-statistic [11]. The incidence of post-operative complications in both groups of patients (excluding intraoperative deaths) was assessed using the Mantel-Haenszel  $\chi^2$  test.

Kaplan-Meier crude estimates of the cumulative incidence of mortality at 5 years in both study groups were compared

through the log-rank test [12]. All statistical analyses were carried out using SAS software, version 9.1 (SAS Institute, Cary, NC, USA).

# RESULTS

Overall, in-hospital mortality was 20.9% (105 patients); it was lower in the three centres in which more than 100 operations were performed (19.1 vs 27.2%; P = 0.058).

The in-hospital mortality rate was 43.7% (45 of 103) in the MPS group and 15% (60 of 399) in the No-MPS group; the difference was statistically significant at univariate analysis (P = 0.001). Intra-operative mortality was significantly higher in the MPS group (16.5 vs 3.8%, P < 0.001).

Univariate analysis showed that age, coronary, intestinal and renal malperfusion, limb ischaemia, re-operation and preoperative cardiogenic shock were also significantly associated with in-hospital mortality. At multivariate analysis, malperfusion syndrome (OR = 2.4, P = 0.0006), previous cardiac operation (OR = 6.7, P = 0.0347) and pre-operative shock (OR = 0.2.3, P = 0.0018) were found to be independent risk factors for in-hospital mortality (C-statistic = 0.74; Hosmer-Lemeshow test, P = 0.38). When malperfusion of a specific organ system was inserted into the logistic model, coronary and mesenteric malperfusion and preoperative shock resulted as risk factors for in-hospital mortality (C-statistic = 0.74; Hosmer-Lemeshow test, P = 0.65; Table 3).

The mean time of hospitalization was  $17.7 \pm 26.5$  days without significant differences between the groups.

Post-operative complications are reported in Table 4. Seventy-seven patients (15.3%) required prolonged mechanical ventilation. Post-operative stroke occurred in 44 patients (8.8%): 9 of them had pre-operative brain malperfusion, while it was a new cerebral event in 35. Sixty-two patients (12.3%) had transient neurological deficits (TND): in 8 of them, pre-operative brain malperfusion was present. Post-operative myocardial infarction occurred in 12 patients (2.4%). Post-operative renal failure was found in 65 patients (12.9%), while 72 (14.3%) underwent re-exploration for bleeding.

Post-operative complications occurred more frequently in patients with pre-operative malperfusion. The incidences of post-operative stroke (16.5 vs 6.7%; P < 0.001), post-operative acute myocardial infarction (6.8 vs 1.2%; P = 0.008) and renal insufficiency (24.2 vs 10%; P < 0.001) were significantly higher in the MPS group (Table 4). There were no differences in the incidences of TND and bleeding between the groups.

During a mean follow-up time of 41.4 months, there were 59 deaths. The actuarial survival rate of the overall population was 72.3 ± 2.1% and 65.3 ± 2.4% at 1 and 5 years, respectively. At 5 years, long-term survival was significantly lower in patients with organ malperfusion syndrome than in patients without organ malperfusion (45.4 vs 70.2%; P < 0.001; Fig. 1). Late survival was also influenced by the type of pre-operative organ system malperfusion. Patients with mesenteric malperfusion had the worst long-term prognosis, with a survival rate of 10% at 5 years. Five-year survivals of patients with renal and cardiac malperfusion were 15.4 and 28.2%, respectively. Patients who had cerebral malperfusion had a 5-year survival of 57.1%.

Variable	Univariate analysis		Multivariate analysis			
			First model		Second model	
	OR	P-value	OR	P-value	OR	P-value
Age	1.02	0.083				
Previous cardiac surgery	7.8	0.0057	6.7	0.0347		
Shock	2.7	< 0.0001	2.3	0.0018	2.1	0.007
Malperfusion	3.6	0.001	2.4	0.006		
Coronary malperfusion	4.3	< 0.001			3.7	< 0.0001
Renal malperfusion	7.3	0.0001				
Mesenteric malperfusion	12.3	< 0.0001			9.5	0.0012
Limb ischaemia	2.4	0.0179				

#### Table 3: Univariate and multivariate analyses of in-hospital mortality

#### Table 4: Post-operative complications

	All patients (n = 502)	MPS group ( <i>n</i> = 103)	No-MPS group ( <i>n</i> = 399)	OR (MPS vs No MPS)	P-value
Stroke, N (%)	44(8.8)	17(16.5)	27(6.7)	3.5	<0.001
Transient neurological deficit, N (%)	62(12.3)	11(10.6)	51(12.7)	0.98	0.9637
AMI, N (%)	12(2.4)	7(6.8)	5(1.2)	4.8	0.008
Renal insufficiency, N (%)	65(12.9)	25(24.2)	40(10)	3.9	< 0.001
Prolonged ventilation >144 h, N (%)	77(15.3)	21(20.3)	56(14)	1.9	0.0198
Bleeding, N (%)	72(14.3)	15(14.5)	57(14.3)	1.24	0.4885

MPS group: malperfusion group; No-MPS group: no malperfusion group; AMI: acute myocardial infarction.

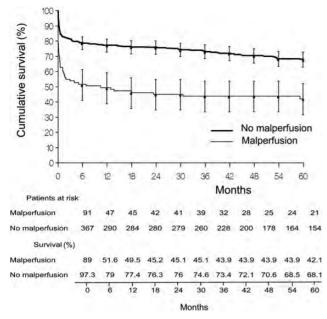


Figure 1: Kaplan-Meier survival curves for patients with or without organ system malperfusion.

During follow-up, 14 patients (3.5%) underwent re-operation on the thoracic or thoraco-abdominal aorta. Freedoms from re-operation were  $98.6 \pm 2.3$  and  $96.6 \pm 2.9\%$  at 1 and 5 years, respectively.

## DISCUSSION

In recent decades, the outcome of patients after surgical repair for AAAD has improved considerably, but the mortality rate is still high [1–6]. These improvements are mainly related to improvements in technology and strategies for CPB and organ protection (myocardial and brain), such as improvement in intensive care management.

The first objective of our study was to evaluate the experience in our region regarding the treatment of acute aortic dissection. It was found that, even if the period was limited to a few years, the approaches to this pathology are extremely different in each centre, mainly depending on surgeon preference.

The main cannulation site was the femoral artery (81.9%), while axillary artery cannulation was used in only 14.7% of the patients. Even today, due to ease of access, size and ability to achieve adequate flow, the femoral artery remains one of the main preferred cannulation sites [1]. However, even if the superiority of specific cannulation techniques has not been clearly demonstrated, antegrade systemic perfusion should be preferred, because intra-operative malperfusion may occur anytime during retrograde perfusion through the femoral artery.

Regarding the technique of aortic replacement, current consensus favours open distal anastomosis [1], but some surgeons, when they find the intimal tear in the ascending aorta, still prefer the cross-clamping technique disregarding secondary tears that are frequently located in the aortic arch. In our experience, one-third of the patients (30.7%) underwent aortic repair using the cross-clamping technique.

The presence of malperfusion did not influence the operative management (cannulation site, aortic cross-clamping, extension

of aortic replacement, etc.) except for the use of DHCA, which was more frequently used in malperfused patients (33 vs 12.3%, P = 0.0018). Moreover, no significant differences were found in the operative management even between the various centres.

Those different surgical approaches were not associated with significant differences in early mortality and morbidity. Furthermore, it could not be demonstrated that a more conservative approach (closed distal anastomosis) was associated with a higher re-operation rate during the follow-up. This was probably related to the limited follow-up time; in a short period of time, dilatation of the false lumen may not have required further aortic repair.

The rate of Marfan patients treated for AAAD was very low (1.2%), compared with a recently published series in which the incidence ranges from 4.5 to 5.3% [2, 5, 8, 13], even if the prevalence of Marfan syndrome in the Emila-Romagna (0.4 per 10 000 people) is comparable with that reported in the literature [14]. This may probably be due to a more aggressive surgical policy for those patients in the centres of our region. Usually, in these patients, aortic repair is performed at an earlier stage of aortic dilatation (ascending aortic diameter of 4.5 cm).

Another purpose of the study was to analyse the impact of organ malperfusion (and each category) on hospital morbidity and mortality in patients affected by AAAD. Several studies demonstrated that the patients' status at presentation is the main factor affecting post-operative outcome [2, 7–9].

The International Registry of Acute Aortic Dissection [2] showed predictors of hospital mortality following repair of type A acute aortic dissection to be pulse deficit, aortic rupture with pre-operative hypotension, shock or cardiac tamponade and signs of acute myocardial ischaemia.

The pre-operative characteristics of our patients with and without organ malperfusion were similar except for shock or cardiac tamponade, which was significantly higher in patients with pre-operative organ malperfusion than in patients without (38.8 vs 14%; P < 0.001).

The location of the primary intimal tear seems to play a role in the genesis of malperfusion, above all, in the coronary and cerebral systems. In fact, patients with malperfusion syndrome had a primary intimal tear more frequently located at the level of the aortic root (19.4 vs 8.8%: P = 0.002), probably because, in these cases, the coronary arteries and supra-aortic vessels were more likely to be involved by the dissection. Contrary to other reports [1, 15], we were not able to demonstrate any correlation between the location of the intimal tear in the arch or in the descending aorta and distal malperfusion (mesenteric, renal, etc.). However, although the extension of aortic replacement was similar in MPS and no-MPS groups, total arch replacement was more frequently performed in patients with mesenteric (41.7 vs 15.5%, P = 0.015) and renal (35.7 vs 15.6%, P = 0.044) malperfusion. We can assume that in these patients, although the tear was more often located in the ascending aorta, the arch such as the proximal descending aorta were involved by intimal rupture predisposing the development of malperfusion.

Another feature was that patients with malperfusion required CABG more frequently than the others (11.7 vs 3%; P = 0.0002) in order to resolve myocardial ischaemia.

In our region, the results of surgical treatment of AAAD are comparable with those reported in the literature [1–6, 13, 16, 17]; we had an overall in-hospital mortality rate of 21% with slightly better results in high-volume centres (19.1 vs 27.2%, P = 0.058). We also clearly confirmed that mortality is mainly related to pre-operative organ malperfusion; it was significantly higher in

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the MPS group than in the No-MPS group (43.7 vs 15%; P < 0.001).

Furthermore, not only the presence of malperfusion, but also the type and number of system organs malperfused influenced post-operative mortality. Patients who presented single-organ malperfusion had a mortality rate of 34.7% (26 of 75 patients), which increased to 61.9% (13 of 21 patients) if two organ systems were involved. Patients with malperfusion of three or more organ systems had a mortality rate that reached 85.7% (6 of 7 patients).

According to the literature [9], long-term survival was found to be influenced by the type of pre-operative malperfusion. Intestinal, renal and cardiac malperfusion were associated with the worst long-term survival (10, 15.4 and 28.2%, respectively at 5 years).

#### SYSTEM ORGAN MALPERFUSION

Brain malperfusion is not a rare finding in acute aortic dissection and its incidence ranges from 7.2 to 14% [1, 2, 7-9]. It has been reported to be an important risk factor for in-hospital mortality, with associated mortality reaching 50% [8]. In our study, cerebral malperfusion occurred in 7.8% of the patients, and it was the most frequently involved organ system. We were not able to demonstrate that cerebral malperfusion was an independent risk factor for mortality, even if these patients had a higher in-hospital mortality rate than the other patients (28.2 vs 20.4%; P = 0.250) and, certainly, it has to be considered as a severe risk factor. The cerebral protection method can influence the neurological outcome of patients with pre-operative brain malperfusion limiting the progression of cerebral damage. ASCP, that represents the best method of cerebral protection during open arch surgery [18], was used in all our cases with pre-operative brain malperfusion and it may have played a role in limiting the cerebral damage.

DHCA with the aid of retrograde cerebral perfusion [8] may not offer the same sufficient cerebral protection in this kind of patients.

Patients with pre-operative brain malperfusion have a higher risk of post-operative stroke which, in the present study, was found to be 23% (9 of 39 patients) in patients with brain malperfusion, significantly higher than in the remaining 463 patients without brain malperfusion (7.6%). Moreover, in comparing the MPS and the No-MPS group, the incidence of stroke in the post-operative course was significantly higher in the first group (16.5 vs 6.7%; P < 0.001). However, the duration and the extension of cerebral malperfusion before surgery are the most important influencing factors for the neurological outcome and post-operative course of the patient.

Coronary malperfusion occurred in 6.4% of our overall population (32 of 502 patients), with a similar incidence to that reported in the literature. This group of patients had a post-operative acute myocardial infarction rate of 15.6% with an in-hospital mortality of 50%. On the other hand, post-operative acute myocardial infarction occurred in only 1.5% of patients without pre-operative coronary malperfusion (7 of 470 patients). Moreover, comparing the MPS and the No-MPS groups, the incidence of post-operative myocardial infarction was significantly higher in the MPS group (6.8 vs 1.2%; P = 0.008). Multivariate analysis confirmed coronary malperfusion as a risk factor for hospital mortality (OR% 3.7, CI 1.7–8.0; P < 0.001). We believe that, in patients with myocardial malperfusion, prompt surgical

intervention is recommended in order to achieve early myocardial perfusion restoration. Moreover, as it has been well reported in the literature [19], these patients more often require a root replacement with coronary ostia reimplantation, associated either with CABG or not.

In our population, CABG was more frequent in patients with coronary malperfusion; however, none underwent the Bentall procedure.

Mesenteric malperfusion with ischaemia is one of the sneakiest and devastating complications in patients with type A aortic dissection. Fortunately, mesenteric ischaemia is a rare complication of type A aortic dissection, occurring in <2.5% of patients [1, 2, 7–9]. Clinical presentation is not uniform and patients may or may not have abdominal pain.

The lack of immediate symptoms can delay diagnosis and management. In our population, the incidence of mesenteric malperfusion was 2.4% and it was associated with a postoperative hospital mortality rate of 70%. Multivariate analysis also demonstrated that mesenteric malperfusion was an independent risk factor for mortality.

Although a lack of consensus exists, mesenteric malperfusion may be addressed prior to definitive aortic repair, above all, when it is clinically evident.

Improvement in results has been reported when the malperfusion was initially addressed with intensive medical management associated or not with revascularization procedures and staged aortic repair [20]. Various revascularization procedures have been demonstrated to be effective in resolving malperfusion. In the case of dynamic mesenteric malperfusion, stenting of the descending thoracic aorta can be effective [21, 22]. We successfully treated 3 patients, who had persistent mesenteric malperfusion after surgical repair, with thoracic endografting. In other cases of visceral malperfusion with a dynamic/static mechanism, percutaneous or surgical fenestration can be used with good results [23, 24]. We have very limited experience with this technique, and it was used in only 1 case in the current series.

Renal malperfusion occurred in 2.8% of our overall population; 46.2% of them developed post-operative renal insufficiency and the mortality rate was extremely high, reaching 64.3%. At univariate analysis, renal malperfusion was a risk factor for hospital mortality (OR% 9.5, CI 2.4–37.4; P = 0.0001).

As reported by other authors [2, 7–9], it is difficult to define preoperative renal insufficiency; in fact, a variety of causes can lead to it, such as involvement of the renal artery by the dissection or not.

Spinal cord malperfusion has always resulted in permanent neurological damage. Due to the small number of cases in our population (5 patients), it was difficult to draw a definite conclusion regarding the reversibility of paraplegia and its clinical relevance.

In our opinion, the Emilia-Romagna Registry can be considered a good source for studying and analysing a large group of patients with type A acute aortic dissection. However, it presents several limitations. Data were collected retrospectively, and some clinical features were excluded from analysis because of incompleteness. Moreover, different operative protocols among surgeons and centres and the absence of patient randomization can be considered to be further limitations.

# CONCLUSIONS

The results of AAAD surgical treatment can be considered acceptable in terms of hospital mortality and morbidity and in line with the experience of other authors but, despite major progress in surgical treatment during the last decade and earlier and more accurate diagnoses, it still remains doubtful.

Patient status at presentation represents an important predictive factor for post-operative outcome, and the presence of pre-operative mesenteric malperfusion is the most devastating condition. Furthermore, malperfusion of more organ systems makes the prognosis really unfavourable, and immediate proximal aortic repair may be sub-optimal. In these situations, in addition to immediate aortic repair, alternative management strategies should be considered.

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#### REFERENCES

- Bonser RS, Ranasinghe AM, Loubani M, Evans JD, Thalji NM, Bachet JE et al. Evidence, lack of evidence, controversy, and debate in the provision and performance of the surgery of acute type A aortic dissection. J Am Coll Cardiol 2011;58:2455–74.
- [2] Rampoldi V, Trimarchi S, Eagle KA, Nienaber CA, Oh JK, Bossone E et al. Simple risk models to predict surgical mortality in acute type A aortic dissection: the International Registry of Acute Aortic Dissection score. Ann Thorac Surg 2007;83:55–61.
- [3] Hagan PG, Nienaber CA, Isselbacher EM, Bruckman D, Karavite DJ, Russman PL *et al*. The international registry of acute aortic dissection (IRAD): new insights into an old disease. JAMA 2000;283:897-903.
- [4] Ehrlich M, Fang WC, Grabenwöger M, Cartes-Zumelzu F, Wolner E, Havel M. Perioperative risk factors for mortality in patients with acute type A aortic dissection. Circulation 1998;98(19 Suppl.):11294–8.
- [5] Chiappini B, Schepens M, Tan E, Dell'Amore A, Morshuis W, Dossche K et al. Early and late outcomes of acute type A aortic dissection:

analysis of risk factors in 487 consecutive patients. Eur Heart J 2005;26: 180-6.

- [6] Krüger T, Weigang E, Hoffmann I, Blettner M, Aebert H, GERAADA Investigators. Cerebral protection during surgery for acute aortic dissection type A: results of the German Registry for Acute Aortic Dissection Type A (GERAADA). Circulation 2011;124:434-43.
- [7] Immer FF, Grobety V, Lauten A, Carrel TP. Does malperfusion syndrome affect early and mid-term outcome in patients suffering from acute type A aortic dissection? Interact CardioVasc Thorac Surg 2006;5:187–90.
- [8] Geirsson A, Szeto WY, Pochettino A, McGarvey ML, Keane MG, Woo YJ et al. Significance of malperfusion syndromes prior to contemporary surgical repair for acute type A dissection: outcomes and need for additional revascularizations. Eur J Cardiothorac Surg 2007;32:255-62.
- [9] Girdauskas E, Kuntze T, Borger MA, Falk V, Mohr FW. Surgical risk of preoperative malperfusion in acute type A aortic dissection. J Thorac Cardiovasc Surg 2009;138:1363–9.
- [10] Fortuna D, Vizioli M, Contini A, Ghidoni I, Biagi B, Pacini D et al. Interact assessing clinical performance in cardiac surgery. Does a specialised clinical database make a difference? Interact CardioVasc Thorac Surg 2006; 5:123-7.
- [11] Hosmer DW, Lemeshow S. Applied Logistic Regression. New York: John Wiley & Sons, 2000.
- [12] Kleinbaum DG, Klein M. Survival Analysis a Self Learning Text. New York: Springer, 2005.
- [13] Trimarchi S, Nienaber CA, Rampoldi V, Myrmel T, Suzuki T, Mehta RH et al. Contemporary results of surgery in acute type A aortic dissection: the International Registry of Acute Aortic Dissection experience. J Thorac Cardiovasc Surg 2005;129:112–22.
- [14] Dietz HC, Loeys B, Carta L, Ramirez F. Recent progress towards a molecular understanding of Marfan syndrome. Am J Med Genet C Semin Med Genet 2005;139C:4–9.
- [15] Lansman SL, McCullough JN, Nguyen KH, Spielvogel D, Klein JJ, Galla JD et al. Subtypes of acute aortic dissection. Ann Thorac Surg 1999;67: 1975–8.
- [16] Bachet J. Acute type A aortic dissection: can we dramatically reduce the surgical mortality? Ann Thorac Surg 2002;73:701–3.
- [17] Kazui T, Washiyama N, Bashar AH, Terada H, Suzuki K, Yamashita K et al. Surgical outcome of acute type A aortic dissection: analysis of risk factors. Ann Thorac Surg 2002;74:75–82.
- [18] Pacini D, Leone A, Di Marco L, Marsilli D, Sobaih F, Turci S et al. Antegrade selective cerebral perfusion in thoracic aorta surgery: safety of moderate hypothermia. Eur J Cardiothorac Surg 2007;31:618–22.
- [19] Neri E, Toscano T, Papalia U, Frati G, Massetti M, Capannini G et al. Proximal aortic dissection with coronary malperfusion: presentation, management, and outcome. J Thorac Cardiovasc Surg 2001;121:552-60.
- [20] Deeb GM, Patel HJ, Williams DM. Treatment for malperfusion syndrome in acute type A and B aortic dissection: a long-term analysis. J Thorac Cardiovasc Surg 2010;140:S98-100.
- [21] Dake MD, Kato N, Mitchell RS, Semba CP, Razavi MK, Shimono T et al. Endovascular stent-graft placement for the treatment of acute aortic dissection. N Engl J Med 1999;340:1546-52.
- [22] Fattori R, Nienaber CA, Rousseau H, Beregi J-P, Heijmen R, Grabenwoger M et al. Talent thoracic retrospective registry: results of endovascular repair of the thoracic aorta with the Talent Thoracic stent graft—the Talent Thoracic Retrospective Registry. J Thorac Cardiovasc Surg 2006; 132:332–9.
- [23] Slonim SM, Miller DC, Mitchell RS, Semba CP, Razavi MK, Dake MD. Percutaneous balloon fenestration and stenting for life-threatening ischemic complications in patients with acute aortic dissection. J Thorac Cardiovasc Surg 1999;117:1118-27.
- [24] Fabre O, Vincentelli A, Willoteaux S, Beregi J-P, Prat A. Preoperative fenestration for type A acute aortic dissection with mesenteric malperfusion. Ann Thorac Surg 2002;73:950–1.