ORIGINAL ARTICLE

Outcome of acute type A aortic dissection: single-center experience from 1998 to 2007

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Summary

Introduction. *Acute aortic dissection (AAD) is a serious disease of the aorta with high mortality and morbidity, which requires emergency surgical treatment in order to close the site of the dissection and direct blood flow into the true lumen. Improvements in surgical technique have led to better management of patients with reduced operative mortality, although it still remains high. The aim of this study is to evaluate early and late outcomes of the surgical treatment of acute type A aortic dissection at the hospital of Lecce between 1998 and 2007. We also aim to establish a correlation between these outcomes and pre-operative conditions, surgical procedures and location of the site of the tear.*

Methods. *From 1998 to 2007, 100 patients (69 males and 31 females, average age 62.2 ± 12.3 years, range 22-85 years) underwent surgery for acute AAD at the center. Surgical techniques included replacement of the ascending aorta (Asc Ao) with or without valve replacement (including five patients who underwent the Bentall/De Bono procedure) and replacement of the Asc Ao with or without arch or hemiarch replacement.*

Results. *In-hospital mortality was 22%, with different results between surgery for replacement of the aorta and for aorta with valve replacement (respectively, 16% and 23%). Different mortality rates were found between the distal surgical treatments, with rates of 20.8% and 18.2% respectively between replacements of the Asc Ao and of Asc Ao with arch/hemiarch, although they were not statistically significant. A different mortality rate that was subject to the patient's preoperative condition has also been found (33.3% of mortality in patients in unstable or high-risk condition vs 13.8% in patients in stable condition). The peak reached 43.5% mortality in patients taken to the operating room while in shock or cardiac tamponade. The location of the site of the tear is another factor that distinguishes mortality rates, which are 17.8% if localized at the proximal ascending aorta and 22.2% in the aortic arch. Assessment of the outcome (10 years after surgery), has shown that four patients died several years later but for reasons unrelated to the surgery.*

Conclusions. *The surgery of dissection is still an intervention with a relatively high in-hospital mortality risk, and whose outcome, which has been steady in the last 20 years, can be predicted according to the preoperative condition of the patient. This underlines the need to reduce the time of diagnosis indicating immediate surgical treatment.*

Introduction

Acute aortic dissection (AAD) is a disease that affects the aorta, characterized by separation of the layers within the aortic wall. Blood under the influence of hydrodynamic forces enters the intima-media space in an antegrade and/or retrograde sense by creating a false lumen (dissecant channel) parallel to the true lumen [1].

AAD is a severe disease with low incidence (about 2.9 in 100,000/year) [2] but with a high in-hospital mortality rate (about 27.4%) [3]; mortality for this disease, if left untreated or only treated medically, is estimated to be 80 to 90% in the first 15 days after onset of symptoms [4, 5].

Recent estimates show that over 20% of patients with AAD die before arriving at the hospital or before diagnosis [2]. The percentage of mortality in untreated patients has been reported to increase by 1-3% per hour after presentation, and is about 25% in the next 24 h, 70% during the first week and 80% after two weeks [6].

In patients undergoing operations for type A AD in tertiary care centers, data from the International Registry of Aortic Dissection (IRAD) show an in-hospital mortality rate of 25.1% [7], while in other centers the observed mortality varies from 7 to 30% [3, 5, 8-10].

A correct diagnosis of dissection from clinical suspicion, to confirm diagnosis and localize the affected aortic segment, is essential in order to perform a repair and to select the most appropriate surgical access. However, delayed diagnosis, different surgical techniques, and surgeons' different degrees of experience can greatly affect surgical outcome. Choosing the most appropriate treatment is closely linked not only to the type of dissection, but also to the site of entry and its extent, involvement of the coronary arteries, the arch and the aortic valve, the presence of false lumen open or closed and the possible presence of thrombi [11].

Current surgical techniques mainly replace the ascending aorta tear site in order to restore flow in the true lumen by replacing or repairing the root and aortic valve [12]. In particular, proper management of the

valve and root are the main factors to consider in order to achieve a safer and stable surgical procedure. Recent data underline the need, where possible, to carry out a conservative "tear-oriented" procedure preserving the aortic valve and directing the action toward the repair of the root or re-suspension of the valve [13, 14]. Interventions that require the replacement of both the ascending aorta and the arch have not been proven to riskier than simple replacement of the aorta. Similarly, operative mortality in the short term does not seem to be influenced by concomitant aortic valve replacement [15].

The intervention of aortic dissection can often be complicated by bleeding, which may require another intervention after a few hours [16, 17].

After the surgical repair, the patient requires continuous medical monitoring and the percentage of survival at 5 and 10 years by staying on values seems to be quite high – 80% and 65% respectively [10, 18, 19]. The relationship between the pre-operative characteristics, location of the tear and outcome of surgery, assessed only recently and in few studies, needs to be analyzed [7, 9, 20].

Therefore, the purpose of this study was to assess short- and long-term mortality in patients with AAD who undergo surgical repair, correlating it with patient characteristics, pre-operative conditions, site of tear, surgical methods and number of days in hospital.

Methods

From October 1998 to March 2007, 100 patients with acute type A AD were referred for surgery to the Operative Unit (O.U.) of Cardiosurgery at the "Vito Fazzi" Hospital of Lecce.

The O.U. of Cardiosurgery, opened in 1998 and the only Public Department of Cardiosurgery in Salento, is a peripheral Health Unit in Puglia, covering a population of 1,764,658 residents [21].

Patients were stratified by age and sex and by transferral from a referral hospital, having a clinical condition on arrival at our hospital, and site of origin of dissection. Surgical procedures were divided between proximal surgical strategies (with replacement of the ascending aorta and replacement or re-suspension of aortic valve) and distal surgical strategies (with replacement of ascending aorta and partial or total aortic arch replacement). All patients studied are still under observation; therefore it is possible to assess the rates of both intra-operative mortality and death at the hospital, until patients are given the all-clear and a follow-up is carried out for 10 years.

Intra-hospital and long-term survival were estimated by Kaplan-Meier analysis. In addition, surgical outcome was assessed in terms of operative mortality, hospital survival and need for further operations due to bleeding. According to their pre-operative condition, patients were defined as "patients in critical condition" (Group I) presenting symptoms of shock, cardiac tamponade and coma and "stable patients and/or with moderate risk" (Group II) in stable hemodynamic condition. It was

therefore estimated that the mortality rate correlates with the characteristics of each patient, risk profile before surgery and site of the tear. Hospital mortality was also assessed for different types of intervention, time of circulatory arrest, deep hypothermia (when applied) and number of days in hospital. Finally, the relationship between the type of intervention and re-operation for bleeding was taken into account.

All data were obtained from a retrospective view of medical records and follow-up information came from verbal communication with patients in subsequent visits or by telephone contact. The study was approved by the Local Ethics committee.

DIAGNOSTIC IMAGING

The diagnosis of acute type A AD was made using at least one imaging method, including transesophageal echocardiography (TEE), computed tomography (TC), nuclear magnetic resonance (NMR) or thoraco-abdominal preoperative angiography and TEE in the operating room.

SURGICAL PROCEDURES

A standard median sternotomy was performed in all patients. After systemic heparinization, the extracorporeal circuit was established introducing a two-stage venous cannula via right atrium and an arterial cannula via femoral artery, which had shown the best pulse. Alternative arterial pathway was the subclavian artery. A vent was inserted into the upper right pulmonary vein to provide drainage of the left heart. Cardiac protection was obtained by infusion of cardioplegic solution via antegrade or retrograde. After establishment of the extracorporeal circuit, patients were cooled to a nasopharyngeal temperature of 18°C to 26°C. Once the target core temperature was achieved, the extracorporal circuit was stopped and the aorta opened. In cases in which antegrade brain perfusion was used, the patient was positioned in Trendelenburg and two cannulae were inserted into the anonymous trunk and into the left common carotid artery. The left subclavian artery was clamped or closed with a Fogarty catheter (Baxter Health Care, Irvine CA; IFM, Clearwater, FL). Cerebral perfusion was started at a flow of 10 ml/kg per min and adjusted to keep arterial pressure between 40 and 70 mmHg. During distal anastomosis, the extracorporeal circuit in the lower part of the body was stopped. After the anastomosis, a clamp was placed on the prosthesis and the circulation was restored in antegrade through the side branch of the prosthesis. The site of the tear of the dissection was resected if localized in the ascending aorta or in the aortic arch. The layers of the aorta were reinforced with gelatine-resorcine-formol (GRF) glue (GRF-glue, fii, Sain-Just-MALMONT, France) or fibrinous glue (Tissue-col, Immuno AG, Vienna, Austria).

If needed, re-suspension of the aortic valve was performed. Replacement was needed in 25 patients with structural abnormalities of the valve. In five patients the Bentall/De Bono intervention was performed to replace the aortic valve, Valsalva sinuses and ascending aorta

with a composite tube graft containing an aortic valve prosthesis. Consequently the coronary ostia had to be re-implanted on the prosthetic tube.

STATISTICAL ANALYSIS

The relationship between pre-operative conditions, the site of the tear of the dissection, different surgical procedures and disease outcome (such as mortality, number of days in hospital and reoperation due to bleeding) was assessed by the Chi-Square test (χ^2) for comparison of rates and Student's unpaired t-test for comparison of means.

A value of $p < 0.05$ was considered statistically significant. Actuarial survival estimates were calculated using the Kaplan-Meier method (GRAPH PAD Prism 5).

Results

The main characteristics of patients who underwent surgery for AAD are summarized in Table I. A total of 100 patients (69.0% male) with Type A AAD were referred for surgery in the O.U. of Lecce between October 1998 and March 2007. Average age was 62.2 ± 12.3 years, (range, 22-85 years) with 53.0% ($p = 0.04$) older than

65 years of age. Type A Dissection was due to Marfan's syndrome in only two cases (one patient 26 years old and one 43 years old). Of all patients, 61 (61.0%) had been transferred to our center from a referral hospital for definitive treatment. Mortality rates among patients who arrived directly at the hospital and those transferred from another hospital did not show any statistically significant difference ($p = 0.44$). Of all patients, 42.0% presented with high-risk conditions (Group I) and 23.0% of these were in shock or cardiac tamponade. The 63.6% of patients who died in hospital of AAD had arrived in the operating room in critical condition and were strongly affected, showing a mortality of 33.3% in Group I compared to 13.8% in Group II ($p = 0.02$).

The primary site of the tear was located in the proximal ascending aorta in 73.0% of patients and in 18.0% in the aortic arch, and the mortality rate shown was respectively 17.8% and 22.2% ($p = 0.67$). Overall in-hospital mortality was 22.0% with differences between the surgical procedures (Tab. II). The aortic valve was replaced in 25 patients and a repair was needed in 74 patients. In addition to replacement of the aorta the total or partial aortic arch replacement was included in 22 patients (Tab. II). The mortality rates in replacement of the ascending aorta with aortic valve preserved or

Tab. I. Demographic and preoperative parameters of surgical acute Type A Aortic Dissection patients and correlated hospital mortality.

Variable	Overall N (%)	Survived N (%)	Dead N (%)	p value [***]
N	100 (100.0)	78 (78.0)	22 (22.0)	–
Age (years) mean (± SD)	62.2 ± 12.3	60.7 ± 12.5	67.4 ± 10.3	0.02
Age ≥ 65 years	53 (53.0)	37 (47.4)	16 (72.7)	0.04
Male gender	68 (68.0)	58 (74.4)	11 (50.0)	0.03
Transferred patients	61 (61.0)	53 (67.9)	13 (59.1)	0.44
Severe hemodynamic problems (Group I)	42 (42.0)	28 (35.9)	14 (63.6)	0.02
Presenting shock or tamponade	23 (23.0)	13 (16.7)	10 (45.5)	0.01
Moderate hemodynamic problems (Group II)	58 (58.0)	50 (64.1)	8 (36.4)	0.02
Site of tear in ascending aorta	73 [*] (73.0)	60 (76.9)	13 (59.1)	0.67
Site of tear in aortic arch	18 [**] (18.0)	14 (17.9)	4 (18.2)	0.67

[*] 73 patients with site of tear in ascending aorta, four of them with more sites of tear and five of them between ascending aorta and aortic arch. [**] 18 patients with site of tear in the aortic arch, four of them with site also in the ascending aorta. [***] p-value tested by χ^2 test with 1DF.

Tab. II. Hospital mortality related to operative procedures.

Variable	Overall N (%)	Hospital mortality N (%)	p-value [*]
All patients	100 (100.0)	22 (22.0)	–
Surgical strategies proximal			
Valve replacement [**]	25 (25.0)	4 (18.2)	0.55
Valve preservation or valve repair	74 (74.0)	17 (77.3)	0.55
Dead before surgery	1 (1.0)	1 (4.5)	–
Surgical strategies distal			
Ascending aorta	77 (77.0)	17 (77.3)	0.75
Ascending + hemiarch/arch	22 (22.0)	4 (18.2)	0.75
Dead before surgery	1 (1.0)	1 (4.5)	–

[*] p-value tested by χ^2 test with 1DF. [**] Bentall operation (five patients).

repaired vs replacement with valvular prosthesis (including patients subjected to Bentall/De Bono method) were 23.0% and 16.0% (p = 0.46) respectively. The in-hospital mortality from sample replacement of the ascending aorta and with hemiarch/arch was 22.1% and 18.2% (p = 0.69) respectively. Circulation arrest in deep hypothermia (14-18°C) was used in 65 patients, (mean time: 23.4 ± 11.8 min). In the remaining patients the intervention was performed in moderate systemic hypothermia (24-27°C).

Deep hypothermia in the replacement of the ascending aorta was applied in 59.7% of patients and in 86.4% of patients with replacement of ascending aorta and arch/hemiarch (p = 0.02). Of all patients 46.0% had profuse bleeding after surgery and 36% were reoperated. A smaller percentage of patients undergoing intervention with valve replacement had problems with bleeding (n = 36) and of these 20% were reoperated for this reason rather than for conservation or repair of the valve itself, with rates of 50.0% (p = 0.22) and 41.9% (p < 0.05) respectively. Any statistical difference for bleeding and subsequent reoperation through patients operated to replace of the ascending aorta and ascending aorta plus arch or hemiarch. Average number of days spent in hospital was 22.7 ± 22.2 with a longer period for patients undergoing aortic valve replacement compared to those having undergone repair or preservation of the aortic valve (31.7 ± 27.0 vs 21.5 ± 19.8 days).

The number of days spent in hospital for replacement of the ascending aorta and replacement of arch or semi-arch was 23.3 ± 22.9 and 30.5 ± 19.2 respectively (Tab. III). According to the Kaplan-Meier method, Figure 1 shows that during the first 3 days the mortality rate was 50% (11/22) of all hospital patients deceased. The hospital survival curve in the first and second week show a survival rate of 85. 9% and 82% respectively. The duration of the study was 10 years; during this period the 77 patients who survived the operation and were discharged from the hospital were followed up (average follow-up 36 months). Figure 2 shows the actuarial survival curves. Overall, 94.8% of patients who managed to survive for 5 years after the operation lived for another 10 years. Four patients died during this period. Causes of death

Tab. III. Deep hypothermia, circulatory arrest, bleeding and days in hospital in different surgical procedures.

Variable	Overall N (%)	Deep Hypothermia N (%)	p*	Circolatory arrest (min)	p**	Bleeding N (%)	p*	Reop. for bleeding N (%)	p*	Days in hospital (Days ± DS)	p**
All patients	100 (100.0)	65(65.0)	–	23.4 ± 11.8	–	46 (46.0)	–	36 (36.0)	–	22.7 ± 22.2	-
Surgical strategies proximal											
Valve replacement	25 (25.0)	14 (56.0)	0.24	20.1 ± 5.2	0.07	9 (36.0)	0.22	5 (20.0)	< 0.05	31.7 ± 27.0	0.09
Valve preservation	74 (74.0)	51 (69.0)		27.2 ± 13.2		37 (50.0)		31 (41.9)	< 0.05	21.5 ± 19.8	
Surgical strategies distal											
Ascending aorta	77 (77.0)	46 (59.7)	0.02	23.7 ± 12.4	0.16	35 (45.5)	0.71	28 (36.4)	> 0.99	23.3 ± 22.9	0.21
Ascending + Hemiarch/arch	22 (22.0)	19 (86.4)		28.6 ± 10.7		11 (50.0)		8 (36.4)	> 0.99	30.5 ± 19.2	
Dead before surgery	1 (1.0)	–	–	–	–	–	–	–	–	–	-

*p-value tested by χ^2 test with 1DF. **Unpaired Student's *t*-test with 97 DF.

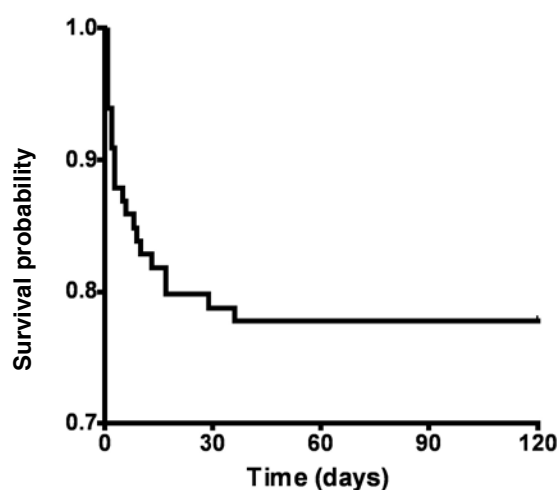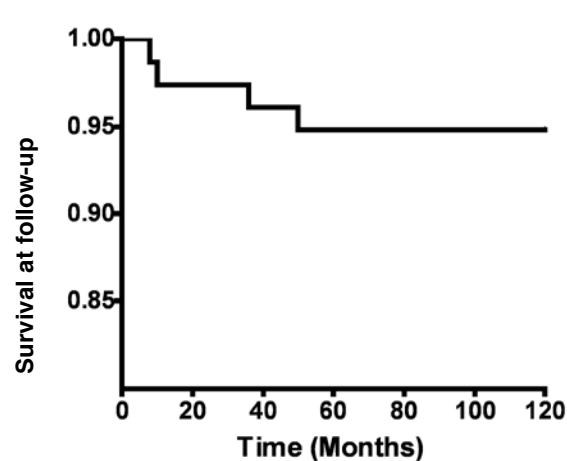Fig. 1. Hospital survival curve for acute Type A Aortic Dissection.

Fig. 2. Actuarial survival curve for patients after surgery for acute Type A Aortic Dissection.

were stroke in one patient, heart failure in two patients and sepsis in one patient.

Discussion

Aortic dissection is a catastrophic event, with incidence estimated at 5-30 per 1 million people per year [3]. Despite considerable progress in recent years both in the medical and surgical treatment of DAA, the mortality rate is still significant. In patients subjected to medical management alone, the mortality rate increases by 1-3% for every hour after the event and reaches about 20% after 24 h, 30% at 48 h, 40% at 7 days and 50% after 1 month [22]. Some studies have shown that among those not receiving surgery (typically due to advanced age and co-morbidity), in-hospital mortality was greater than 50% [3, 20, 23]. The rate of mortality between patients undergoing surgical treatment, however, varies between 15% and 30% [3, 17, 23]. Some authors have also described single-center series with markedly lower mortality, even as low as 6.3% [13].

Rather low rates of mortality were found in highly specialized hospitals with well-trained doctors and good facilities for treating such patients, while mortality remained high in local hospitals or in hospitals with small patient volume. In patients with DAA the elective treatment is immediate surgical procedure, which can save the lives of many patients. However, recent data suggest that optimized medical treatment may be considered acceptable in certain high-risk groups. In recent years, improvement in diagnostic imaging, development of better prosthetic materials, improved cardiac and brain protection and the increasing experience of surgeons have resulted in reduced complications [24]. Hagan and colleagues report that in the IRAD survey 28% of patients with AAD did not undergo surgery, and that 42% of these patients were subsequently discharged after intensive medical treatment [3].

Our hospital is located in southern Italy, generally known to have a lower level of specialization than northern Italy. Hence, current analysis might reflect the real-world experience of a newly established hospital with a small patient volume.

In our study we analyzed all patients undergoing surgery for AAD in this health care center and the rate of in-hospital mortality observed (22%) reflects the contemporary "real world" literature [3, 23, 25]. The existing literature regarding follow-up outcomes in patients after discharge from the hospital is less established. In our study, the 5- and 10-year survival in the cohort surviving to hospital discharge is 94.8%. These numbers are excellent and reflect the successful and timely repair of the aorta. Comparison to the existing research is difficult because the most of the research begins their survival analysis on hospital day 1, thereby including in-hospital deaths [26-29]. In contrast, few published reports such as ours begin their survival analysis on the day of discharge. A recent report by Tsai and co-workers reported on post-discharge survival rates of 96.1 ± 2.4 at 3 years and 90.5 ± 3.9 at 5 years [30], while Chiappini et al. reported on post-discharge survival rates of 94.8 ± 1.2 and 88.1 ± 2.6 at 5 and 10 years in 487 patients enrolled at two centers over 27 years [29]. By extrapolation, findings corroborated the excellent results in Lecce Hospital reported here.

Age is a variable independently associated with an adverse outcome in all patients with AD. The longer life expectancy of the population results in an increasing number of elderly patients suffering from this disease, so the decision to operate or not on an elderly patient cannot be ethically correct if not based on precise clinical evidence. The hospital mortality rate we observed in patients > 65 years old was 30.2% vs 13.0% in patients aged < 65 years. Metha et al. showed an in-hospital mortality rate of 45.5% in patients 80-84 years of age and a rate of 50% in patients older than 85 years [31]. Despite the above, advanced age cannot be an exclusion criterion for surgical treatment, which is a valuable aid to physicians in choosing the most appropriate treatment. As expected, the disease affects mainly men but in women there is a higher mortality rate (34.4% vs 16.2% in men). This has also been observed in other studies [7, 20, 30] and it is believed to be related to the different diameters of arteries in the two sexes, which influences a different surgical outcome.

No statistical difference has been found between the mortality rate in the first 5 years of the study (1998-2002) and in the last 5 years (2003-2007), despite improved surgical techniques, the development of optimal standards and a highly specialized and dedicated working team. These results may depend on the preoperative clinical condition of patients and inadequate medical and surgical procedures. Indeed, patient preoperative condition is often the primary cause of post-surgical death [7, 9, 32].

Mortality rates among patients transferred from another center and those who came directly to our center did not show any significant difference, and this is probably due to the network of fast connection and communication between local hospitals. The geographic area studied is relatively small, so the maximum distance from one hospital to another is never more than 45 min. Furthermore, transferred patients have similar results to patients who come directly to our hospital (Tab. I). Diagnostic imaging is essential in order to identify and classify aortic dissection, regardless of the clinical context. The most important techniques for diagnosing AAD and identifying the origin site of dissection are Computerized Tomography (CT), Nuclear Magnetic Resonance (NMR) and Transesophageal Echocardiography (TEE) [33, 34]. Diagnostic sensitivity is equally high for all diagnostic modalities. Currently however, the initial imaging modality of choice for acute aortic dissection is TEE followed by CT. Aortic dissection is an emergency, and the most readily available technique that can be performed near the emergency department or the patient's bed is usually requested as the initial diagnostic imaging test. CT and TEE satisfy these criteria, being noninvasive and readily available. Despite

having the highest sensitivity, NMR is used as the first imaging modality for a very small number of patients with AAD, because it is less available and is harder to carry out with critically ill patients.

In this study, the diagnosis of AAD was performed in almost all patients by CT and intra-operative TEE. In association with technical problems, the operating result is also known to be largely related to the patient's preoperative condition. Preoperative condition is often the primary cause of post-surgical death, which might even be predicted from pre-surgical assessment of individual risk conditions [20, 32]. Differentiation between stable and unstable patients showed a significantly higher surgical mortality in unstable than in stable patients (Group I: 33.3 vs Group II: 13.8%, p = 0.02). Similar results were obtained by Trimarchi and colleagues in the IRAD, who report that mortality in unstable patients is significantly higher compared to stable patients (31.4% vs 16.7%) [7]. In particular, patients who arrive in shock or cardiac tamponade have a higher risk of mortality post-surgery (45.5%). As noted by Chiappini and associates, among other things this represents a risk factor predicted for reoperation for bleeding. Other risk factors are pre-operative cardiac disease, aortic arch dissection, age > 70 years and cardiopulmonary resuscitation [29]. Postoperative bleeding is one of the most common reasons for high morbidity and mortality rates [35].

The various surgical procedures used do not affect patient outcome; no significant differences have been emphasized in mortality among patients undergoing replacement or repair of the aortic valve (23.0% vs 16.0%) or subject to replacement of the ascending aorta compared to replacement also of the arch or hemiarch aortic (20.8% vs 18.2%).

Usually a partial or hemiarch replacement is sufficient in most patients, and extended total arch replacement is advocated for selected patients, such as young patients or those with Marfan's syndrome or a markedly dilated aortic arch [16]. A limited ascending replacement did not increase the risk of mortality and would not compromise surgical results.

Among other variables considered (deep hypothermia, time of cardiac arrest, bleeding and re–operation for bleeding), there was more frequent use of deep hypothermia in subjects who required replacement of the ascending aorta and the arch or hemiarch with a time of cardiac arrest on higher average (28.6 ± 10.7 vs 23.7 ± 12.4) with a consequent increased risk of neurological complications.

Bleeding and subsequent re-operation for bleeding are more common among those who do not undergo intervention for valve replacement, although this is not supported by an increased number of days in hospital, which are on average higher, although without statistically significant differences between those who are undergoing valve replacement. Early recognition of the disease and earlier referral to surgical units would improve the outcome of emergency surgery for this lethal disease. Emergency aortic surgery is a major challenge due to the severity of the injures, hypothermia, circulatory arrest and long Cardiopulmonary Bypass (CPB) time, conditioning postoperative bleeding and producing high morbidity and mortality.

In order to improve the outcome for these patients, an early diagnosis certainly would produce a drastic reduction in mortality. Initial results of studies on possible biomarkers for early diagnosis of dissection are currently being published and the initial results are very encouraging. Promising biomarkers of aortic dissections such as calponin [36] and plasma fibrin D-dimers have been tested in a recent study [37].

In conclusion, the surgical treatment of AAD that patients undergo in Lecce hospital indicates an acceptable mortality rate although it still high (22%) and shows excellent survival rates in patients who survive to hospital discharge. Also, the year in which it was carried out did not appear to influence the high mortality rate, which indicates that a lower mortality rate and improved survival rate of patients with AAD can be achieved only through early diagnosis and accurate assessment of factors predictive of the disease and its complications, which can determine the best therapeutic choice and/or surgery.

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