FACULDADE DE MEDICINA
UNIVERSIDADE D
COIMBRA

MESTRADO INTEGRADO EM MEDICINA – TRABALHO FINAL

DANIELA MOREIRA TAVARES

Perioperative and long-term results of ascending aorta replacement: 432 case series

ARTIGO CIENTÍFICO

ÁREA CIENTÍFICA DE CIRURGIA CARDIOTORÁCICA

Trabalho realizado sob a orientação de:
PROFESSOR DOUTOR GONÇALO FREITAS COUTINHO
DRA. JOANA COUTINHO SARAIVA

MARÇO DE 2021

“Perioperative and long-term results of ascending aorta replacement: 432 case series”

Resultados peri-operatórios e a longo prazo da substituição da aorta ascendente: série de 432 casos

ARTIGO CIENTÍFICO ORIGINAL

Authors: Daniela Moreira Tavares[1], Joana Coutinho Saraiva[1,2], Gonçalo Freitas Coutinho[1,2]

Affiliations:

[1]Faculdade de Medicina da Universidade de Coimbra, Portugal

[2]Centro Hospitalar e Universitário de Coimbra, E.P.E. – Serviço de Cirurgia Cardiotorácica, Coimbra, Portugal

EMAIL: DANIEETAVARES@GMAIL.COM

INDEX

LIST OF FIGURES

LIST OF TABLES

ABBREVIATIONS

∆P	Pressure gradient
ACP	Antegrade cerebral perfusion
AV	Atrioventricular
AVA	Aortic valve area
BAV	Biscuspid aortic valve
BMI	Body mass index
BSA	Body surface area
CABG	Coronary artery bypass grafting
COPD	Chronic obstructive pulmonary disease
CPB	Cardiopulmonary bypass
CT	Computed tomography
DHCA	Deep hypothermic circulatory arrest
ECC	Extracorporeal circulation
EOA	Effective orifice area
EF	Ejection fraction
FS	Fractional shortening
HR	Hazard ratio
iEOA	Indexed effective orifice area
LA	Left atrium
LVEDd	Left ventricle end-diastolic diameter
LVESd	Left ventricle end-systolic diameter
MHCA	Moderate hypothermic circulatory arrest
PASP	Pulmonary artery systolic pressure
PPM	Prosthesis-patient mismatch
TIA	Transient ischemic attack

ABSTRACT

Introduction: Ascending aortic aneurysm is a condition associated with potentially life-threatening complications. The best treatment approach, when indicated, consists of surgical replacement of ascending aorta. The aim of this study is to analyze the perioperative and long-term results after surgery for ascending aortic aneurysm and identify potential risk factors that affect long-term survival.

Methods: From January 2010 to December 2019, 432 consecutive patients with ascending aortic aneurysm who underwent elective surgical replacement of the ascending aorta constituted our study population. Data were collected retrospectively from patient records and the mortality records were retrieved from the national patient registry. To compare long-term survival with the general population, data from the National Institute of Statistics (2011 census) were consulted. Histopathological analysis was performed in 248 patients (57,4%).

Results: There were no cases of in-hospital mortality. In the 30 postoperative days, there was 1 death (0.2%). Long-term survival at 1, 5 and 10 years of follow-up was 98.8%, 91.9% and 80.1%, respectively. There was no difference in overall survival between patients who underwent ascending aortic replacement and the general population matched by age and gender. The most common in-hospital complication was new-onset transient atrial fibrillation (15.3%). There were no cases of myocardial infarction and the prevalence of postoperative stroke and transient ischemic attack was 0.5% and 0.2%, respectively. Regarding histopathological results, 13 patients (5.2%) had histological criteria for connective tissue diseases, 11 of whom had Marfan syndrome (4.4%) and 2 patients (0.8%) had Ehlers-Danlos syndrome. In 15 patients (6.0%), the presence of aortitis was recorded, with syphilitic aortitis being the cause of 10 of these cases (4.0%). On the multivariable analysis, age ($p<0.001$), preoperative creatinine values ($p=0.017$), preoperative left atrium size ($p=0.015$) and circulatory arrest time ($p=0.018$) were identified as independent risk factors for late mortality.

Conclusions: This study showed that patients who underwent elective surgical treatment restored their life expectancy and this procedure had a very low early mortality and in-hospital complications. Longer circulatory arrest times had a negative impact on long-term survival.

KEYWORDS: Aortic Aneurysm, Thoracic; Ascending Aorta; Cardiac Surgery; Perioperative Period; Survival Analysis.

RESUMO

Introdução: O aneurisma da aorta ascendente é uma condição associada a complicações potencialmente fatais. A melhor abordagem terapêutica, quando indicada, consiste na substituição cirúrgica da aorta ascendente. O objetivo deste estudo é analisar os resultados perioperatórios e a longo prazo após a intervenção cirúrgica e identificar potenciais fatores de risco que afetem a sobrevivência tardia.

Métodos: A nossa população em estudo inclui 432 doentes com aneurisma da aorta ascendente que foram submetidos a cirurgia eletiva de substituição da aorta ascendente de janeiro de 2010 a dezembro de 2019. Os dados foram recolhidos retrospetivamente a partir dos processos clínicos dos doentes e os registos de mortalidade foram retirados do registo nacional de utentes. Para comparar a sobrevivência a longo prazo com a população em geral, foram consultados dados do Instituto Nacional de Estatística (censos de 2011). Foram analisados os resultados histopatológicos em 248 doentes (57,4%).

Resultados: Não existiram casos de mortalidade intra-hospitalar. Nos primeiros 30 dias pós-operatórios, ocorreu 1 óbito (0,2%). A sobrevivência a longo prazo em 1, 5 e 10 anos de *follow-up* foi de 98,8%, 91,9% e 80,1%, respetivamente. Não existiram diferenças na sobrevivência global entre os doentes submetidos a substituição da aorta ascendente e a população em geral, de acordo com a idade e sexo. A complicação hospitalar mais comum foi fibrilhação auricular de novo (15,3%). Não houve casos de enfarte agudo do miocárdio e a prevalência de AVC pós-operatório e acidente isquémico transitório foi de 0,5% e 0,2%, respetivamente. Em relação aos resultados histopatológicos, 13 doentes (5,2%) apresentaram critérios histológicos para doenças do tecido conjuntivo, sendo que 11 destes tinham síndrome de Marfan (4,4%) e 2 (0,8%) apresentavam síndrome de Ehlers-Danlos. Em 15 doentes (6,0%), foi registada a presença de aortite, sendo a aortite sifilítica a causa em 10 desses casos (4,0%). Na análise multivariada, a idade ($p<0.001$), os valores de creatinina pré-operatória ($p=0.017$), o diâmetro da aurícula esquerda pré-operatório ($p=0.015$) e o tempo de paragem circulatória total ($p=0.018$) foram identificados como fatores de risco independentes para a mortalidade tardia.

Conclusões: Este estudo mostrou que os doentes submetidos a cirurgia eletiva de substituição da aorta ascendente recuperaram a esperança de vida. A mortalidade precoce foi muito baixa e complicações intra-hospitalares foram mínimas. Períodos mais longos de paragem circulatória total tiveram um impacto negativo na sobrevivência a longo prazo.

PALAVRAS-CHAVE: Aneurisma da Aorta Torácica; Aorta Ascendente; Cirurgia Cardíaca; Período perioperatório; Análise de sobrevivência.

INTRODUCTION

One of the main indications for ascending aortic replacement surgery is aneurysmal disease. The annual incidence of thoracic aortic aneurysms varies between 7,6 and 10,4 cases per 100.000 habitants.[1,2] Ascending aortic aneurysm is the most common form of thoracic aneurysms.

There are several well-known risk factors associated with ascending aortic aneurysm such as advanced age, male gender, smoking, hypertension, aortic valve malformations, such as bicuspid aortic valve (BAV), connective tissue disorders (Marfan's syndrome, Loeys-Deitz syndrome, and Ehlers-Danlos syndrome), and other genetic causes.[3,4]

The main complications of this condition are acute dissection and rupture of the aorta. As it is a condition with potentially life-threatening complications, it is necessary to consider the indication and timing for intervention. The rate of rupture and dissection increases significantly with the increase of the maximum diameter of the aorta and it is known that, without treatment, survival at 5 years of patients with aneurysms with diameters greater than 6 cm is only 56%.[5] According to the most recent guidelines, surgical treatment should be considered in patients whose diameter of the ascending aorta is ≥55 mm. For patients with Marfan syndrome, who have BAV and associated risk factors, or indication for aortic valve surgery, replacement of the ascending aorta in smaller diameters may be considered. [6]

Since elective surgical intervention is often performed in previously asymptomatic patients, it is important to know the main perioperative complications, their frequency, and the late survival of this procedure.

The aim of this study is to present the experience of our surgical center, analyze the perioperative and long-term results and identify potential risk factors that affect late survival in patients with ascending aortic aneurysms undergoing surgery for replacement of the ascending aorta.

METHODS

Patient selection and data collection

From January 2010 to December 2019, 432 patients underwent elective ascending aortic replacement surgery for aneurysm in Coimbra Hospital and University Centre, Portugal. Patients undergoing emergency surgeries, with aortic dissection or with concomitant prosthetic endocarditis, and patients who underwent aortic replacement in the context of aortic valve surgery, where the ascending aorta was not dilated, were excluded from our study.

Preoperative characteristics, such as demographic records, relevant clinical information, including echocardiographic results and other diagnostic tests were retrospectively collected. The severity of aortic insufficiency was classified into four categories (I - minimal; II - mild; III - moderate; IV - severe). We considered aortic valve disease (mixed lesion) whenever there was concomitant aortic insufficiency (≥ grade III) and aortic stenosis (mean gradient ≥ 20mmHg).

The aortic ratio was obtained by dividing the measured diameter of the aorta by the predicted diameter for a certain age and body surface area (BSA). [7]

Prosthesis-patient mismatch (PPM) was characterized according to the indexed effective orifice area (iEOA) which is calculated as effective orifice area (EOA) divided by BSA. The EOA was obtained from prosthetic aortic valve charts. When iEOA is equal to or below 0,85 cm^2/m^2, PPM is considered to be present. Moderate PPM is defined by an iEOA between 0.65 and 0.85cm^2/m^2, while severe PPM means an iEOA equal to or below 0.65 cm^2/m^2. [8]

Details regarding surgery and postoperative results, namely records of in-hospital morbidity (before medical discharge), early (up to 30 days) and late mortality, and long-term survival were also included. All data were collected retrospectively from patients' medical records and mortality records were taken from the national patient registry.

Other definitions were based on EuroScore II [9] and can be consulted in Appendix I.

This study received a favorable opinion from the Health Ethics Committee of Coimbra Hospital and University Centre on December 17, 2020.

Surgical Technique

The surgical procedure was standard in all patients. Median sternotomy was performed and cardiopulmonary bypass (CPB) was initiated by cannulating the proximal aortic arch and the right atrium while establishing hypothermia (temperatures between 25ºC and 27ºC). Cardioplegia was administered via the ascending aorta or the coronary ostia.

In most patients, supracoronary replacement of the ascending aorta by a Dacron graft was performed, with the proximal anastomosis at the level of the sinotubular junction. In cases with aortic root dilation, a Bentall procedure was most commonly performed. If the aortic valve was normal and competent, a valve-sparing aortic root replacement was conducted (David or Yacoub Surgery). The distal anastomosis was performed in the majority of cases during a brief period of moderate hypothermic circulatory arrest (6-10 minutes), therefore in an open fashion.

Statistical Analysis

Categorical variables are presented with absolute and relative frequencies. Continuous variables with normal distribution were characterized using the mean and standard deviation and parametric tests were conducted; variables with non-normal distribution are presented with the median and the interquartile range.

The normality of continuous variables was assessed with the Shapiro-Wilk and Kolmogorov – Smirmov tests.

To identify potential risk factors for late mortality, a multivariable analysis was performed using a Cox regression study with the hazard ratio (HR) and a 95% confidence interval. All variables with a $p < 0.2$ in the univariate analysis were included.

For long-term survival studies, Kaplan-Meier analyzes were used and compared with the general Portuguese population with corresponding age and gender. This data was obtained from the National Institute of Statistics, 2011 census.

Statistical analysis was performed on IBM® SPSS® Statistics version 26.

RESULTS

Our study population included 113 (26.2%) females and the median age was 64 years (interquartile range 25 - 75 = 56.0 – 72.0) with a minimum age of 20 and a maximum age of 91 years.

As for the associated comorbidities, we highlight the presence of established coronary disease in 62 patients (14.4%), hypertension in 297 patients (68.8%), dyslipidemia in 222 patients (51.4%), obesity, defined as a body mass index (BMI) ≥ 30, in 84 patients (19.4%) and diabetes mellitus in 41 patients (9.5%).

In 56.9% of patients, the aortic valve was bicuspid. The most prevalent aortic valve pathology was isolated aortic insufficiency in 216 patients (51.2%), followed by aortic disease in 100 patients (23.7%) and aortic stenosis in 103 patients (24.4%). All preoperative characteristics of our sample are shown in table 1.

Table 1. Preoperative characteristics

Variables	N (%) or mean ± *standard deviation* or median (interquartile range 25 to 75)
Female	113 (26.2)
Age (years)	64.0 (56.0– 72.0)
BMI (kg/m^2)	26.9 ± 3.6
BSA (m^2)	1.8 ± 0.2
Aortic valve pathology	
Stenosis	103 (24.4)
Insufficiency	216 (51.2)
Disease (mixed lesion)	100 (23.7)
BAV	240 (56.9)
Previous Aortic Prosthesis	10 (2.3)
Previous cardiac surgery	13 (3.0)
NYHA III-IV	96 (22.2)
Preoperative creatinine (mg/dL)	0.9 (0.8-1.0)
Creatinine clearance (mL/min) [a]	85.0 (65.0– 106.8)
Comorbidities	
Obesity (BMI≥30)	84 (19.4)
Overweight (25≤BMI<30)	217 (50.2)
Established coronary disease	62 (14.4)
Diabetes mellitus	41 (9.5)
Arterial hypertension	297 (68.8)
Dyslipidemia	222 (51.4)
Smoking	
Active smoker	19 (4.4)
Former smoker	103 (23.8)

COPD	16 (3.7)
Stroke or TIA	20 (4.6)
Peripheral artery disease	2 (0.5)
Previous endocarditis	5 (1.2)
Chronic kidney disease	13 (3.0)
Atrial fibrillation	
Permanent	51 (11.8)
Paroxysmal	13 (3.0)

BMI= Body Mass Index; BSA= Body Surface Area; COPD= Chronic Obstructive Pulmonary Disease; TIA= Transient Ischemic Attack.

[a] Calculated from *Cockcroft-Gault* formula

In the preoperative assessment of the maximum diameter of the aorta, the echocardiographic results showed a median of 51.0 mm (interquartile range 25 - 75 = 47.0 - 56.0 mm). The maximum value among all patients was 89 mm and the minimum was 35 mm. Results of computed tomography (CT) show a median of 55.0 mm (interquartile range 25 - 75 = 51.0 - 60.0 mm). The remaining echocardiographic and CT scan data are shown in Table 2.

Table 2. Preoperative imaging data (echocardiographic and CT scan data)

Variables	N (%) or mean ± *standard deviation* or median (interquartile range 25 to 75)
Preoperative echocardiogram	
Maximum aortic diameter	51.0 (47.0 – 56.0)
Maximum aortic root diameter	41.5 ± 7.6
LA (mm)	40.0 (35.0 – 45.0)
LVEDd (mm)	57.0 (31.0 – 63.0)
LVESd (mm)	36.0 (31.0 – 43.0)
Aortic valve gradients (mmHg)	
Maximum	70.5 (39.0 – 86.8)
Mean	44.0 (29.5 – 56.0)
AVA, if aortic stenosis (cm^2)	0.7 (0.6 – 1.0)
EF (%)	60.0 (55.0 – 64.0)
FS (%)	35.22 ± 8.65
PASP (mmHg)	33.0 (27.0 – 40.0)
Aortic Ratio	1.6 (1.5 – 1.8)
PPM	
Moderate	52 (16.1)
Severe	4 (1.2)
Preoperative CT	

Maximum aortic diameter	55.0 (51.0 – 60.0)
Maximum aortic root diameter	48.81 ± 9.57

LA= Left Atrium; LVEDd= Left ventricle end-diastolic diameter; LVESd= Left ventricle end-systolic diameter; AVA= aortic valve area; EF= ejection fraction; FS= fractional shortening; PASP= pulmonary artery systolic pressure; CT= computed tomography

Of the 432 patients, only 29 (6.7%) underwent isolated ascending aorta replacement. Among those who had concomitant surgical interventions, 195 patients received a mechanical aortic prosthesis (45.1%), 152 a biological aortic prosthesis (35.2%), and 36 underwent aortic valvuloplasty (8.3%). The size of the *Dacron* tube graft was 26 mm in 19 patients (4.4%), 28mm in 115 patients (26.6%), 30mm in 220 patients (50.9%), and 32 mm in 78 patients (18.1%). The remaining interventions are summarized in Table 3.

The surgical technique was supracoronary replacement in 399 patients (92.4%), Bentall procedure in 26 patients (6.0%), and Yacoub or David procedure in 7 patients (1.6%).

Table 3. Surgical Procedures

Variable	N (%) or median (interquartile range 25 to 75)
Surgical Technique	
Supracoronary replacement	399 (92.4)
Bentall procedure	26 (6.0)
Yacoub or David procedure	7 (1.6)
Aortic valve intervention	
Aortic valvuloplasty	36 (8.3)
Mechanical prosthesis implantation	195 (45.1)
Biological prosthesis implantation	152 (35.2)
Concomitant procedures	
CABG	34 (7.9)
Mitral valve surgery	19 (4.4)
Tricuspid valve surgery	9 (2.1)
Other procedure	46 (10.6)
Operative times	
ECC time (min)	93.0 (79.0 – 107.0)
Aortic cross-clamp time (min)	50.0 (41.0 – 59.0)
Circulatory arrest time (min)	7.0 (6.0 – 8.0)

CABG= *Coronary Artery Bypass Grafting*; ECC= extracorporeal circulation

Histopathological analysis was performed in 248 patients (57,4%). Thirteen patients (5.2%) had histological criteria for connective tissue diseases, 11 of whom had

Marfan syndrome (4.4%) and 2 patients (0.8%) had Ehlers-Danlos syndrome. In 15 patients (6.0%), the presence of aortitis was recorded, with syphilitic aortitis being the cause of 10 of these cases (4.0%). The remaining histopathological findings are shown in Table 4.

Table 4. Histopathological findings

Findings	N=248
Atherosclerotic aneurysm	89 (35.9%)
Nonspecific changes in the media	83 (33.5%)
Ageing related changes	23 (9.3%)
Aortitis	15 (6.0%)
Connective tissue diseases	13 (5.2%)
Dissecting aneurysm	6 (2.4%)
No changes	19 (7.7%)

Echocardiography results

Postoperative echocardiographic findings are shown in Table 5. The ejection fraction had a median of 60.0% (interquartile range 25 to 75: 55.0 - 65.0%). No moderate or severe periprosthetic leaks were identified and only 49 patients (11.3%) had minimal/mild periprosthetic leaks.

Table 5. Postoperative data

Variables	N (%) or median (interquartile range 25 to 75)
Echocardiographic findings	
EF (%)	60.0 (55.0 – 65.0)
LVEDd (mm)	50.0 (46.5 – 55.0)
LVESd (mm)	32.0 (28.8 – 37.0)
∆P transprosthetic, maximum (mmHg)	18.0 (13.0 – 24.0)
∆P transprosthetic, mean (mmHg)	10.0 (8.0 – 13.0)
Pericardial effusion	131 (31.4)
Periprosthetic leaks	
No leak	383 (88.7)
Minimal/mild	49 (11.3)
Moderate/severe	0
In-hospital complications	
New-onset transient atrial fibrillation	66 (15.3)
Anemia	27 (6.3)
Acute kidney injury	20 (4.6)
Respiratory complications	15 (3.5)
Need of inotropic support	12 (2.8)
Complete AV block with the need for a pacemaker	8 (1.9)

Bleeding	8 (1.9)
Cardiac tamponade	3 (0.7)
Prolonged mechanical ventilation	2 (0.5)
Stroke	2 (0.5)
TIA	1 (0.2)
Other	42 (9.7)

EF= Ejection Fraction; ∆P= Pressure gradient; LVEDd= Left ventricle end-diastolic diameter; LVESd= Left ventricle end-systolic diameter. AV= Atrioventricular; TIA= Transient Ischemic Attack

Early morbidity and mortality and long-term survival

There were no cases of in-hospital mortality. In the first 30 postoperative days, there was 1 death (0.2%) of unknown cause. During the period of clinical follow-up, there were 43 deaths (10.0%), 5 (1.2%) of non-cardiac cause, 2 (0.5%) of cardiac cause, and 36 (8.3%) of unknown cause.

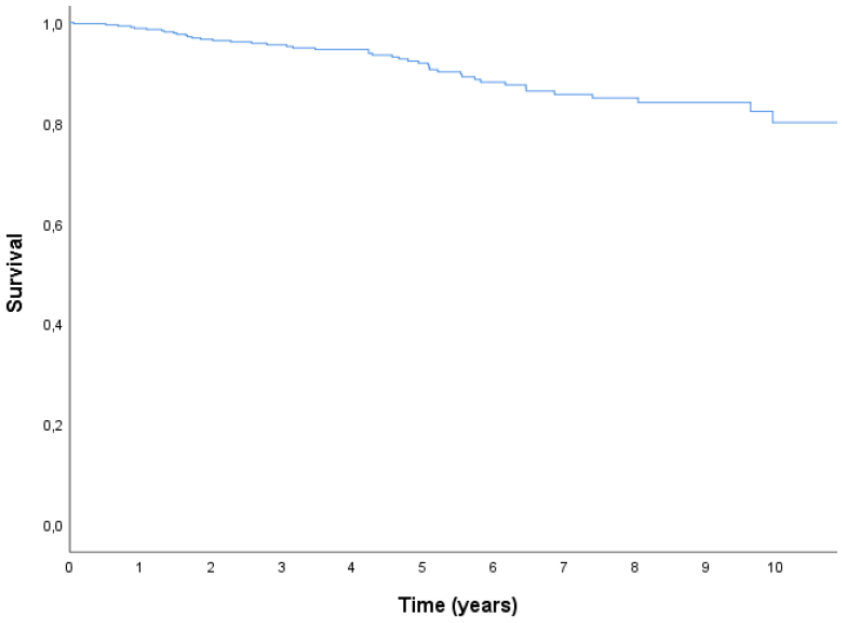
The length of hospital stay had a median of 7.0 days (interquartile range 25 to 75: 7.0 - 9.0 days).

The most common complications after surgery were new-onset transient atrial fibrillation in 66 patients (15,3%), anemia in 27 patients (6,3%), and acute kidney injury in 20 patients (4,6%). Other complications are summarized in Table 5. There were no patients needing extracorporeal membrane oxygenation or with acute myocardial infarction. During hospitalization, 8 patients (1.9%) required reoperation for bleeding, 3 of which had cardiac tamponade.

The median follow-up time was 5.0 years (interquartile range 25 to 75: 7.7 – 2.8 years) and 100% complete. Survival at 1 year was 98.8%, at 5 years was 91.9% and at 10 years was 80.1%. The Kaplan-Meier survival curve is shown in Figure 1A. There was no difference in overall survival between patients who underwent ascending aortic replacement for aneurysm in comparison to the general population matched by age and gender (Figure 1B).

Regarding the impact of the type of intervention on the aortic valve, patients who did not need intervention on the aortic valve or those who received a mechanical prosthesis had better late survival results. There was no difference in long-term survival between patients who underwent aortic valve repair or patients who received a bioprosthetic valve (Fig. 2)

A)



Years	1	2	3	4	5	6	7	8	9	10
Patients at risk	427	374	314	270	217	164	128	96	66	35

B)

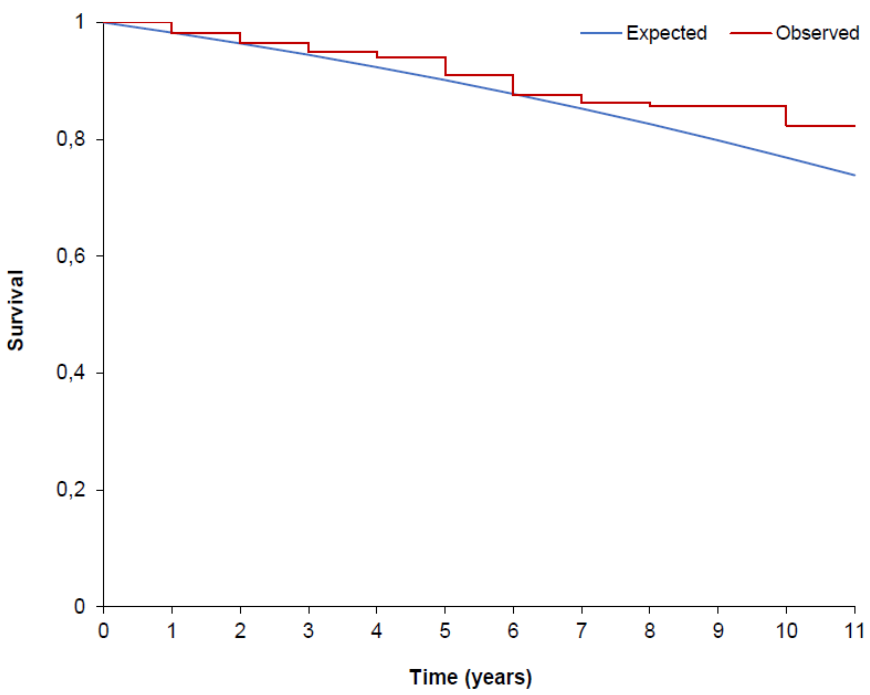
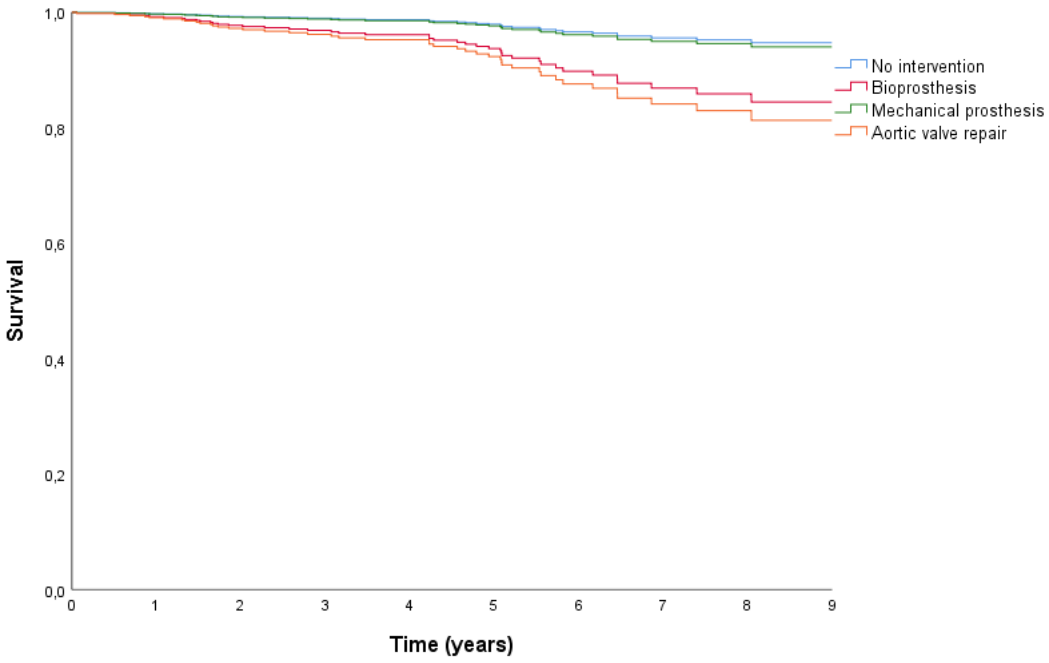


Figure 1. Overall survival curves. **A)** Kaplan-Meier curve with long-term survival in patients who underwent ascending aortic replacement. **B)** Comparison between who underwent ascending aortic replacement with the age and sex matched general population.



Years	1	2	3	4	5	6	7	8	9
Patients at risk									
No intervention	47	43	40	36	29	23	18	14	11
Bioprosthesis	140	108	82	66	46	30	18	10	4
Mechanical prosthesis	186	170	150	129	109	87	70	52	35
Aortic valve repair	32	26	22	17	12	9	8	6	3

Figure 2. Comparison of long-term survival according to aortic valve intervention, adjusted for age.

Risk factors for late mortality

In the univariable analysis, we identified the following statistically significant variables (p-value <0.05): age, chronic obstructive pulmonary disease (COPD), previous stroke or transient ischemic attack (TIA), pre-operative atrial fibrillation, pre-operative creatinine clearance, pre-operative left atrium diameter, pre-operative pulmonary artery systolic pressure (PASP), mechanical prosthetic aortic valve implantation, prosthetic patient mismatch, concomitant mitral or tricuspid procedure, post-operative creatinine clearance, length of hospital stay, post-operative ejection fraction and post-operative maximum transprosthetic pressure gradient.

In the multivariable analysis (Table 6), through the analysis of a Cox regression, it was possible to identify age, preoperative creatinine values, preoperative LA size (mm) and circulatory arrest time as risk factors for late mortality.

Table 6. Multivariable Analysis – Cox regression model

Variables	HR	95% CI	*P-value*
Age	1.098	1.043 – 1.157	<0,001
Preoperative creatinine (mg/dL)	2.562	1.166 – 4.846	0.017
Circulatory arrest time (min)	1.069	1.012 – 1.130	0.018
Preoperative LA (mm)	1.049	1.007 – 1.071	0.015

LA = Left atrium

DISCUSSION

Contemporaneous ascending aorta replacement carries a very low risk of mortality (30-day mortality of 0.2%) and also a low risk of morbidity. Longer circulatory arrest times had a negative impact in late survival, therefore other techniques of cerebral protection should be pursued. Our study shows no difference in the overall survival of patients submitted to ascending aortic replacement comparing to the general population, matched by age and sex. Therefore, patients submitted to ascending aortic aneurysm replacement restore their life expectancy, as reported in some studies in the literature.[5,10]

Previous studies have analyzed late mortality in patients who underwent ascending aortic replacement but had some limitations such as small sample sizes[11,12] and short follow-up times[13,14]. In the most recent study to our knowledge by Hernandez-Vaquero et al, long-term survival was 93.17%, 84.86% and 76.53% at 1, 5 and 8 years, respectively.[10] We report a long-term survival of 98.8% at 1 year of follow-up, 91.9% at 5 years and 80.1% at 10 years. In our study population, there were no in-hospital deaths and there was only one death in the first 30 postoperative days (0.2%) which was lower than what was reported in other studies (1.9 % - 5.5 %).[15–18] We have also reported a difference in long-term survival depending on which procedure was performed on the aortic valve. Patients who underwent aortic valve repair or implantation of a bioprosthesis had lower long-term survival in comparison to patients who received a mechanical prosthesis or didn't need any intervention on the aortic valve.

Our most common early postoperative complication was new-onset transient atrial fibrillation (15.3%) which was similar to what was found in other studies.[18,19] There were only 2 patients (0.5%) with stroke and one patient with TIA (0.2%) which was lower than what was reported in previous studies (3.2% - 7.8%).[17–19] There were no cases of myocardial infarction.

The need for early reoperation was reported as 3.0 - 6.5% in some studies. [10,15,20] In our sample, only 8 patients (1.9%) required early reoperation for bleeding, 3 of which had cardiac tamponade.

One of the causes that may justify variation in early mortality, long-term survival and long-term morbidity results between previous studies is the fact that some of them combine patients who underwent elective surgery with patients with acute aortic syndromes.[15] Nevertheless, Pan and colleagues reported no difference in long-term survival for 30-day survivors regardless of whether they had aortic replacement surgery for aneurysm or dissection.[16]

There are several well-known techniques to achieve appropriate cerebral protection. Few studies show no difference between cerebral perfusion techniques such as anterograde cerebral perfusion (ACP), retrograde cerebral perfusion (RCP), and deep hypothermic circulatory arrest (DHCA).[21–23] Nevertheless, those studies included an heterogeneous group of patients who underwent aortic arch surgery and patients with aortic dissection. Ziganshin and Elefteriades[24] suggest in their work that DHCA is equal or even superior to other cerebral perfusion techniques concerning mortality and stroke rates. Studies comparing DHCA with moderate hypothermic circulatory arrest (MHCA) show better overall results in the latter group, namely lower mortality and neurologic events.[25–27] Nevertheless, in those studies, MHCA is always associated with an ACP strategy. In our surgical center, MHCA alone was the adopted standard technique. We obtained excellent results concerning early and long-term mortality and a very low postoperative of neurologic deficits (0.7%), which indicates that MHCA alone may be an effective method for cerebral perfusion.

In our center, distal anastomosis was performed in an open fashion with a brief MHCA. This procedure offers the possibility of an extended resection of the aorta with a more effective anastomosis, and it also lowers the risk of clamp injury. This procedure is frequently performed[25,28] and it is the preferred method for acute type A aortic dissection.[29]

Previous studies have identified age, left ventricle ejection fraction inferior to 20%, preoperative stroke and/or TIA, COPD, diabetes mellitus, chronic renal failure, and peripheral artery disease as risk factors for late mortality.[10,16,30,31] Our results showed two similar risk factors such as increasing age and preoperative creatinine values. Besides that, we also identified higher LA diameters and higher circulatory arrest times to be independent risk factors for late mortality. Surprisingly, even though most of our patients required total circulatory arrest, and higher circulatory arrest times were associated with worse long-survival outcomes, the rate of postoperative neurologic events and early deaths was still very low.

Hence, moderate hypothermia alone associated with optimal circulatory arrest times can be recommended in ascending aortic replacement surgery, with excellent outcomes regarding post-operative complications and mortality. However, since longer circulatory arrest times were associated with poorer outcomes in terms of survival, alternative cerebral protection techniques should be evaluated.

One of the strengths of this study is the inclusion of histopathology results. Idrees et al. reported a prevalence of aortitis of 5.8% which was similar to our findings (6.0%). They also had 10% of patients with a documented connective tissue disorder and 36% with bicuspid aortic valve.[14] In our study population, there was a lower

prevalence of documented connective tissue disorder (5.2%) and a higher prevalence of bicuspid aortic valve (56.9%).

The major limitation of this study is its retrospective nature. Although all data was collected from patients' records, there is also a possibility of incomplete information. Even though we did not find differences in long-term survival between our patients and the general population, there is also missing information regarding the cause of death. Since long-term follow-up information was not available, it was not possible to determine long-term morbidity. Further studies are needed to identify long-term complications associated with this procedure.

This study comprises the largest series of patients who underwent elective surgery for ascending aortic aneurysm in Portugal. It provides useful data on perioperative and long-term results for this procedure. Ascending aortic aneurysm remains a life-threatening condition if left untreated. This study showed that patients who underwent elective surgical treatment restored their life expectancy and this procedure had a very low early mortality and in-hospital complications.

CONCLUSION

Long-term survival for patients with ascending aortic aneurysm undergoing surgical replacement of the ascending aorta is similar to general population. Early mortality and in-hospital complications associated with this procedure were very low. Longer circulatory arrest times was considered an independent risk factor for long-term survival,

ACKNOWLEDGEMENTS

First and foremost, I would like to express my sincere gratitude to my supervisor, Prof. Gonçalo Freitas Coutinho for his time, priceless support, and guidance at every stage of this project.

I would also like to thank my co-supervisor, Dr. Joana Coutinho Saraiva, for her support and advice throughout the construction of this master thesis.

And finally, I would like to extend my special thanks to my family and closest friends for the unconditional support, patience, and encouragement, especially during difficult times.

REFERENCES

1. Clouse WD, Hallett, Jr JW, Schaff H V., Gayari MM, Ilstrup DM, Melton III LJ. Improved Prognosis of Thoracic Aortic Aneurysms. Jama. 1998;280(22):1926.
2. McClure RS, Brogly SB, Lajkosz K, Payne D, Hall SF, Johnson AP. Epidemiology and management of thoracic aortic dissections and thoracic aortic aneurysms in Ontario, Canada: A population-based study. J Thorac Cardiovasc Surg [Internet]. 2018;155(6):2254-2264.e4. Available from: https://doi.org/10.1016/j.jtcvs.2017.11.105
3. Lavall D, Schäfers HJ, Böhm M, Laufs U. Aneurysmen der Aorta ascendens. Dtsch Arztebl Int. 2012;109(13):227–33.
4. Ahmad MM, Kiani IA, Ammar KA, Ahmad MN, Khandheria BK, Paterick TE, et al. Ascending Aortic Aneurysm Is an Inherited Disease: A Contemporary Literature Review Based on Hill's Criteria of Specificity, Strength of Association, and Biological Coherence. Cardiol Rev. 2017;25(6):268–78.
5. Davies RR, Goldstein LJ, Coady MA, Tittle SL, Rizzo JA, Kopf GS, et al. Yearly rupture or dissection rates for thoracic aortic aneurysms: Simple prediction based on size. Ann Thorac Surg. 2002;73(1):17–28.
6. Erbel R, Aboyans V, Boileau C, Bossone E, Di Bartolomeo R, Eggebrecht H, et al. 2014 ESC guidelines on the diagnosis and treatment of aortic diseases. Eur Heart J. 2014;35(41):2873–926.
7. Henry WL, Gardin JM, Ware JH. Echocardiographic measurements in normal subjects from infancy to old age. Circulation. 1980;62(5):1054–61.
8. Pibarot P, Dumesnil JG. Prosthesis-patient mismatch: Definition, clinical impact, and prevention. Heart. 2006;92(8):1022–9.
9. Nashef SAM, Roques F, Sharples LD, Nilsson J, Smith C, Goldstone AR, et al. Euroscore II. Eur J Cardio-thoracic Surg. 2012;41(4):734–45.
10. Hernandez-Vaquero D, Silva J, Escalera A, Álvarez-Cabo R, Morales C, Díaz R, et al. Life Expectancy after Surgery for Ascending Aortic Aneurysm. J Clin Med. 2020;9(3):615.
11. Peterss S, Mansour AM, Zafar MA, Thombre K, Rizzo JA, Ziganshin BA, et al. Elective surgery for ascending aortic aneurysm in the elderly: Should there be an age cut-off? Eur J Cardio-thoracic Surg. 2017;51(5):965–70.
12. Van Duffel D, Van Gemert R, Starinieri P, Pauwels J-L, Natukunda A, Rakhmawati TW, et al. Elective reconstruction of the ascending aorta for aneurysmal disease restores normal life expectancy. An analysis of risk factors

for early and late mortality. Acta Cardiol. 2013;68(4):349–53.

13. Narayan P, Caputo M, Rogers CA, Alwair H, Mahesh B, Angelini GD, et al. Early and mid-term outcomes of surgery of the ascending aorta/arch: Is there a relationship with caseload? Eur J Cardio-thoracic Surg. 2004;25(5):676–82.

14. Idrees JJ, Roselli EE, Lowry AM, Reside JM, Javadikasgari H, Johnson DJ, et al. Outcomes after Elective Proximal Aortic Replacement: A Matched Comparison of Isolated Versus Multicomponent Operations. Ann Thorac Surg. 2016;101(6):2185–92.

15. Meharwal ZS, Khanna SN, Choudhary A, Misha M, Mehta Y, Trehan N. Ascending aortic aneurysm resection: 15 year's experience. Asian Cardiovasc Thorac Ann. 2006;14(4):300–5.

16. Pan E, Kytö V, Savunen T, Gunn J. Early and late outcomes after open ascending aortic surgery: 47-year experience in a single centre. Heart Vessels. 2018;33(4):427–33.

17. Lohse F, Lang N, Schiller W, Roell W, Dewald O, Preusse CJ, Welz A SC. Quality of life after replacement of the ascending aorta in patients with true aneurysms. Tex Hear Inst J [Internet]. 2009;36(2):104–10. Available from: https://pubmed.ncbi.nlm.nih.gov/19436802/

18. Bekkers JA, Te Riele RJLM, Takkenberg JJM, Bol Raap G, Hofland J, Roos-Hesselink JW, et al. Thoracic aortic surgery: An overview of 40 years clinical practice. J Thorac Cardiovasc Surg [Internet]. 2014;147(1):332–43. Available from: http://dx.doi.org/10.1016/j.jtcvs.2012.11.036

19. Dunne B, Marr T, Andrews D, Larbalestier R, Edwards M, Merry C. Aortic root replacement for ascending aortic disease: A 10 year review. Hear Lung Circ [Internet]. 2013;22(2):81–7. Available from: http://dx.doi.org/10.1016/j.hlc.2012.08.050

20. Cohn LH, Rizzo RJ, Adams DH, Aranki SF, Couper GS, Beckel N, et al. Reduced mortality and morbidity for ascending aortic aneurysm resection regardless of cause. Ann Thorac Surg. 1996;62(2):463–8.

21. Matalanis G, Hata M, Buxton BF. A retrospective comparative study of deep hypothermic circulatory arrest, retrograde, and antegrade cerebral perfusion in aortic arch surgery. Ann Thorac Cardiovasc Surg. 2003;9(3):174–9.

22. Apaydin AZ, Islamoglu F, Askar FZ, Engin C, Posacioglu H, Yagdi T, et al. Immediate clinical outcome after prolonged periods of brain protection: Retrospective comparison of hypothermic circulatory arrest, retrograde, and antegrade perfusion. J Card Surg. 2009;24(5):486–9.

23. Forteza A, Martín C, Centeno J, López MJ, Pérez E, De Diego J, et al. Acute type a aortic dissection: 18 Years of experience in one center (Hospital 12 de Octubre). Interact Cardiovasc Thorac Surg. 2009;9(3):426–30.

24. Ziganshin BA, Elefteriades JA. Deep hypothermic circulatory arrest. Ann Cardiothorac Surg. 2013;2(3):303–15.

25. Abdelgawad A, Arafat H. Moderate versus deep hypothermic circulatory arrest for ascending aorta and aortic arch surgeries using open distal anastomosis technique. J Egypt Soc Cardio-Thoracic Surg [Internet]. 2017;25(4):323–30. Available from: https://doi.org/10.1016/j.jescts.2017.11.006

26. Tian DH, Wan B, Bannon PG, Misfeld M, LeMaire SA, Kazui T, et al. A meta-analysis of deep hypothermic circulatory arrest versus moderate hypothermic circulatory arrest with selective antegrade cerebral perfusion. Ann Cardiothorac Surg [Internet]. 2013;2(2):148–58. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23977575%0Ahttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC3741839

27. Tsai JY, Pan W, Lemaire SA, Pisklak P, Lee VV, Bracey AW, et al. Moderate hypothermia during aortic arch surgery is associated with reduced risk of early mortality. J Thorac Cardiovasc Surg [Internet]. 2013;146(3):662–7. Available from: http://dx.doi.org/10.1016/j.jtcvs.2013.03.004

28. Livesay JJ, Cooley DA, Duncan JM, Ott DA, Walker WE RG. Open aortic anastomosis: improved results in the treatment of aneurysms of the aortic arch. Circulation [Internet]. 1982;66(2 Pt 2):I122-7. Available from: https://pubmed.ncbi.nlm.nih.gov/6211297/

29. Bonser RS, Ranasinghe AM, Loubani M, Evans JD, Thalji NMA, 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 [Internet]. 2011;58(24):2455–74. Available from: http://dx.doi.org/10.1016/j.jacc.2011.06.067

30. Higgins J, Lee MK, Co C, Janusz MT. Long-term outcomes after thoracic aortic surgery: A population-based study. J Thorac Cardiovasc Surg [Internet]. 2014;148(1):47–52. Available from: http://dx.doi.org/10.1016/j.jtcvs.2013.07.028

31. Son SA, Jung H, Cho JY. Long-term outcomes of intervention between open repair and endovascular aortic repair for descending aortic pathologies: a propensity-matched analysis. BMC Surg [Internet]. 2020;20(1):1–13. Available from: https://doi.org/10.1186/s12893-020-00923-4

APPENDIX I

Table A. Definitions

BSA (m2)	Du Bois formula: BSA = 0.007184 × W0.425 × H0.725 (W: weight; H: height)
Previous Aortic Prosthesis	Previous surgery with aortic prosthesis implantation
Previous cardiac surgery	One or more previous major cardiac operation involving opening the pericardium
Established coronary disease	History of previous CABG or coronary angioplasty; previous myocardial infarction or coronary lesions ≥50%;
Diabetes mellitus	History of Diabetes treated with oral medication or insulin
Arterial hypertension	History of arterial hypertension with antihypertensive treatment
Dyslipidemia	History of dyslipidemia with pharmacological treatment
COPD	Long-term use of bronchodilators or steroids for lung disease
Stroke or TIA	Documented previous episode of stroke or TIA
Peripheral artery disease	Intermittent claudication or ≥ 50% lesions of femoral arteries
Chronic kidney disease	Creatinine ≥ 2.0 mg/dL or history of CKD
NYHA classification	I: no symptoms on moderate exertion; II: symptoms on moderate exertion; III: symptoms on light exertion; IV: symptoms at rest.