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Aortic Center: specialized care improves outcomes and decreases mortality

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Aortic Center: specialized care improves outcomes and decreases mortality

Centro de Tratamento da Aorta: a especialização reduz complicações e mortalidade

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Abstract

Objective: **To compare in-hospital outcomes in aortic surgery in our cardiac surgery unit, before and after foundation of our Center for Aortic Surgery (CTA).**

Methods: **Prospective cohort with non-concurrent control. Foundation of CTA required specialized training of surgical, anesthetic and intensive care unit teams, routine neurological monitoring, endovascular and hybrid facilities, training of the support personnel, improvement of the registry and adoption of specific protocols. We included 332 patients operated on between: January/2003 to December/2007 (before-CTA, n=157, 47.3%); and January/2008 to December/2010 (CTA, n=175, 52.7%). Baseline clinical and demographic data, operative variables, complications and in-hospital mortality were compared between both groups.**

Results: **Mean age was 58±14 years, with 65% male. Group CTA was older, had higher rate of diabetes, lower rates of COPD and HF, more non-urgent surgeries, endovascular procedures, and aneurysms. In the univariate analysis, CTA had lower mortality (9.7 vs. 23.0%, *P*=0.008), which occurred consistently across different diseases and procedures. Other outcomes which were reduced in CTA included lower rates of reinterventions (5.7 vs 11%, *P*=0.046), major complications (20.6 vs. 33.1%, *P*=0.007), stroke (4.6 vs. 10.9%, *P*=0.045) and sepsis (1.7 vs. 9.6%, *P*=0.001), as compared to before-CTA. Multivariable analysis adjusted for potential counfounders revealed that CTA was independently associated with mortality reduction (OR=0.23, IC 95% 0.08 – 0.67, *P*=0.007). CTA independent mortality reduction was consistent in the multivariable analysis stratified by disease (aneurysm, OR=0.18, CI 95% 0.03 – 0.98, *P*=0.048; dissection, OR=0.31, CI 95% 0.09 – 0.99, *P*=0.049) and by procedure (hybrid, OR=0.07, CI 95% 0.007 – 0.72, *P*=0.026; Bentall, OR=0.18, CI 95% 0.038 – 0.904, *P*=0.037). Additional multivariable predictors of in-hospital mortality included creatinine (OR=1.7 [1.1-2.6], *P*=0.008), urgent surgery (OR=5.0 [1.5-16.7], *P*=0.008) and thoracoabdominal aneurysm (OR=24.6 [3.1-194.1], *P*=0.002).**

Conclusions: **Thoracic aorta surgery in specialized center was associated with lower incidence of complications and all-cause mortality as compared to usual care.**

Descriptors: **Aortic surgery. Specialized care. Surgical outcomes. Inpatient mortality.**

Resumo

Objetivo: **Comparar desfechos intrahospitalares em pacientes submetidos a cirurgia da aorta torácica e toracoabdominal, antes e após a constituição do Centro Especializado de Tratamento da Aorta (CTA).**

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Abbreviations, acronyms & symbols	
AAA	Abdominal aortic aneurysms
AMI	Acute myocardial infarction
ARF	Acute renal failure
CABG	Coronary artery bypass grafting
CAD	Coronary artery disease
COPD	Chronic obstructive pulmonary disease
CPB	Circulatory bypass
CRF	Chronic renal failure
CTA	Center for Aortic Surgery
CVA	Cerebrovascular accident
DM	Diabetes mellitus
ICU	Intensive Care Unit

Métodos: **Coorte prospectiva com controle não contemporâneo. A criação do CTA envolveu treinamento cirúrgico especializado, sala híbrida, monitorização neurológica, capacitação de pessoal de apoio, aperfeiçoamento dos registros e uso de protocolos específicos. Foram incluídos 332 pacientes operados em 2 períodos: janeiro/2003 a dezembro/2007 (pré-CTA, n=157, 47,3%); e janeiro/2008 a dezembro/2010 (CTA, n=175, 52,7%). As características demográficas, clínicas, dados cirúrgicos, complicações e mortalidade hospitalar foram comparados nos 2 grupos.**

Resultados: **A idade média foi 58±14 anos, com 65% sexo masculino. O grupo CTA teve idade, prevalência de diabete (DM) e glicemia maiores; menor prevalência de doença pulmonar obstrutiva crônica e insuficiência cardíaca; maior proporção de aneurismas e cirurgias eletivas; e mais procedimentos endovasculares que o pré-CTA. Na análise univariada, o grupo CTA mostrou redução de mortalidade (9,7% x 23,0%, *P*=0,008), que foi consistente nos diferentes subgrupos estratificados por patologia e por procedimento. O grupo CTA teve também redução de reoperações (5,7% x 11%, *P*=0,046), complicações maiores (20,6% x 33,1%, *P*=0,007), acidente vascular cerebral (4,6% x 10,9%, *P*=0,045) e sepse (1,7% x 9,6%, *P*=0,001), comparado ao pré-CTA. Na análise multivariada, o CTA se associou de forma independente a redução de mortalidade hospitalar (OR=0,23, IC 95% 0,08 - 0,67, *P*=0,007). A redução de mortalidade do CTA também ocorreu na análise estratificada por patologia (cirurgias de aneurisma, OR=0,18, IC 95% 0,03 - 0,98, *P*=0,048; cirurgias de dissecção, OR=0,31, IC 95% 0,09 - 0,99, *P*=0,049) e por procedimento (híbridos, OR=0,07, IC 95% 0,007 - 0,72, *P*=0,026; Bentall, OR=0,18, IC 95% 0,038 – 0,904, *P*=0,037). Também foram preditores independentes de mortalidade a creatinina pré-operatória (OR=1,7, IC 95% 1,1-2,6, *P*=0,008), a cirurgia de urgência (OR=5,0, IC 95% 1,5-16,7, *P*=0,008) e o aneurisma toracoabdominal (OR=24,6, IC 95% 3,1-194,1, *P*=0,002).**

Conclusão: **O tratamento cirúrgico de patologias da aorta torácica e toracoabdominal em centro especializado, em comparação ao tratamento usual, se associou a menor incidência de complicações e mortalidade global.**

Descritores: **Cirurgia de aorta. Centro especializado. Desfechos cirúrgicos. Mortalidade hospitalar.**

INTRODUCTION

The assessment and management of aortic pathologies impose multiple challenges. Aneurysms are usually asymptomatic, with slow growth and may develop distal thromboembolism, rapid expansion and rupture, with catastrophic evolution. Dissections have high early mortality, with mortality rate up to 1-2% per hour[1]. The diagnosis is complex, requiring integration with multiple clinical imaging studies (echocardiography, CT angiography, MRI and aortography). The initial clinical management is critical for limiting the spread of disease, and surgical planning is complex, including endovascular and hybrid procedures and new forms of neurological monitoring and protection[2,3].

Evidence has supported the concept that complex surgery should be performed in high-volume centers of care to improve outcomes in these patients[4]. Accordingly, there is evidence that highly complex surgeries such as esophagectomies[5], resection of lung neoplasms[6], duodenopancreatectomies[7], and endarterectomy[8], performed in centers with high surgical volume, result in reduction of morbidity and mortality.

The challenges and complexities presented by aortic surgery have stimulated the creation of multicenter registries, such as the International Registry of Acute Aortic Dissections (IRAD), a consortium of specialized centers in 12 countries that aims to study the etiology, clinical findings, treatment and hospital outcomes of patients with aortic dissection[9]. Specialized aortic centers have also been created, aiming to systematize the medical and surgical treatment by the best evidence, taking into account parameters such as the extent of aortic involvement, the underlying pathology, the need for anticoagulation and life expectancy[10]. These centers have multiplied, serving patients with complex pathologies that require sophisticated surgical techniques and high-tech prostheses[11].

In the management of abdominal aortic aneurysms (AAA), strategies of regionalization of care have been implemented, directing patients to specialized centers with high volume (> 50 cases per year). Surgical outcomes in these centers have been better than low-volume centers, with 20-30% reduction in complications and in-hospital mortality[12]. In thoracic aortic pathologies in general, however, there is no studies evaluating the outcomes, complications and mortality of surgery in specialized centers, compared to non-specialized centers[13,14]. Therefore, the aim of this study is to evaluate the impact of surgical treatment of the thoracic and thoracoabdominal aortic diseases in specialized center (CTA) on hospital outcomes, complications and mortality compared to treatment in a non-specialized center.

METHODS

Patients

Between January/2003 and December/2010, 332 adults consecutively underwent thoracic/thoracoabdominal aortic surgery and were divided into two periods: pre-CTA (January/2003 to December/2007) and CTA (January/2008 to December/2010). The mean age was 58±14 years; 65% male.

CTA

The constitution of the CTA involved: 1. surgical training in specialized centers (national and international); 2. improvements in infrastructure (hybrid room, C-arc, intraoperative echocardiography, neurological monitoring, reform of the Intensive Care Unit (ICU), new postoperative protocols of care); 3. Training of personnel (anesthetists, diagnostic services, perfusionists); 4. Research activities (improvement of records and databases, publication of results); 5. standardization of care and use of evidence-based guidelines[15,16]. These procedures take place between November/2007 and January/2008.

Design

Prospective observational study with a non-contemporaneous control (historical), comparing in-hospital outcomes in patients undergoing thoracic and thoracoabdominal aortic surgery before and after the creation of the CTA.

Patient evaluation and surgical treatment

Preoperative imaging studies included CT angiography using multidetector scanner (Model Aquilion, Toshiba, New York, USA). The images were post-processed with three-dimensional reconstruction, allowing surgical planning and measurement of aortic diameters. Magnetic resonance angiography or contrast angiography were rarely used. Preoperative transesophageal echocardiography was used in emergency situations. All patients were assessed by a group of surgeons who analyzed the surgical options and planned the surgery. The surgical procedures performed included the Bentall surgery, replacement of the aortic root with interposition of a Dacron graft, aortoplasty, implantation of endovascular prosthesis (stent) and hybrid procedures, using standard techniques[10,11,17]. After surgery, patients were transferred to the ICU in mechanical ventilation.

Variables

Demographic, clinical, laboratory and preoperative echocardiographic variables, the location of the aneurysm, the type of dissection, the operative data and the procedure performed were prospectively collected. The primary outcome was in-hospital mortality. Secondary outcomes included major complications, reoperation rate and ICU stay. Major complication included cerebrovascular accident (CVA), acute renal failure (ARF), acute myocardial infarction (AMI), reoperation for bleeding, acute visceral or lower limb ischemia, or paraplegia).

Statistical analysis

Continuous variables with normal distribution were described using mean ± SD and compared using Student's t test. The non-normal continuous variables underwent log transformation or have been described using the median and interquartile range, and compared with the Mann-Whitney test. Categorical variables were described as proportions (%) and compared with the chi-square test. In univariate analysis, the outcomes were compared between groups using chi-square test with Yates correction. A stratified analysis was performed by subgroups, trying to detect heterogeneity of effect in subgroups of interest (mortality by pathology and by procedure), using a test-variable interaction effect, using the P value of <0.05. To exclude confounding (variability of mortality by other factors over time, unrelated to CTA), a sensitivity analysis was performed by evaluating separately the evolution of the annual mortality in the pre-CTA period, followed by the CTA period; then the mortality between the two periods was compared using chi-square with correction for multiple comparisons.

Univariate analysis of factors associated with mortality was performed using chi-square test for categorical variables and t test or Mann-Whitney test for continuous variables. Using multivariate analysis (logistic regression), the adjusted comparison of mortality was performed in the two groups, and the independent effect of predictor variables - covariates associated with outcome (P<0.1) in univariate analysis - on hospital outcomes was evaluated[18]. The discrimination ability of the logistic model was assessed using the area under the ROC curve (receiver operating characteristics curve); calibration was assessed using the Hosmer-Lemeshow test. The model was tested for the presence of multicollinearity and its predictive value was determined. All analyzes were performed using SPSS 17.0 (Statistical Package for Social Science, Chicago, IL) software. Statistical significance was confirmed when P<0.05.

The project was approved by the Research Ethics Committee (No. N2094/09), and all patients signed a written informed consent.

RESULTS

332 patients who had undergone surgery for diseases of the thoracic and thoracoabdominal aorta between January/2003 and December/2010 were included (pre-CTA, January 2003-December 2007, n=157, 47.3%; CTA, January 2008-December 2010, n=175, 52.7%). Cases included 175 aneurysms (52.7%), and 150 dissections (45.2%).

Approximately 85% of patients were hypertensive, 41.6% were smokers, 31% had CHF, 20.6% chronic obstructive pulmonary disease (COPD), 21% coronary artery disease (CAD), 17% chronic renal failure (CRF) and 7,3% had diabetes mellitus (DM) (Table 1).

Regarding aneurysms, the most common location was the ascending aorta, with a similar rate in both groups (46 patients (68.0%) in the pre-CTA group and 68 (62.1%) in CTA - *P*>0.05). We also found, with a similar percentage between groups, aneurysms of the descending aorta, with 10 patients (14.9%) in the pre-CTA group and 11 patients (10.1%) on CTA, and thoracoabdominal aortic aneurysms with 6 patients (9.0%) in pre-CTA group and 13 patients (11.8%) of the CTA group (*P*>0.05 for all comparisons).

Regarding dissections, there was also similar distribution between the two groups: the acute type A dissections amounted 83% (74 patients) of the pre-CTA group and 73% (45 patients) of the CTA group; type B acute aortic dissection amounted 17% (15 patients) of pre-CTA group and 24% (16 patients) of CTA group (*P*>0.05 for both comparisons).

Patients from CTA group (Table 1) were older (*P*=0.01), with a higher prevalence of DM (*P*=0.005), higher blood glucose (*P*=0.001) lower prevalence of COPD (*P*=0.037) and HF (*P*=0.005) and higher proportion of aneurysms than dissections (*P*=0.001), shorter circulatory arrest (*P*<0.001), less urgent surgeries (*P*<0.001), more hybrid (*P*=0.023) and endovascular (*P*=0.024) procedures. The proportion of Bentall surgeries and aortoplasties was similar in the 2 groups.

Table 1. Baseline clinical characteristics and operative variables according to the group.

	Overall	Before-CTA	CTA	*P*
N (%)	332	157 (47.3%)	175 (52.7%)	
Age (years)	58±14	56±13	60±15	0.013
Male gender n (%)	214 (64%)	105 (49%)	109 (51%)	0.224
Disease				
Aneurysm	175 (52.7%)	65 (41.4%)	110 (62.9%)	
Dissection	150 (45.2%)	91 (58.0%)	59 (33.7%)	<0.001
Coarctation	3 (0.9%)	1 (0.6%)	2 (1.1%)	
Penetrating ulcer	3 (0.9%)	0 (0%)	3 (1.7%)	
Previous CV surgery	54 (23.2%)	12 (19.7%)	42 (24.4%)	0.285
High blood pressure	197 (84.5%)	48 (78.7%)	149 (86.6%)	0.104
Diabetes	17 (7.3%)	0 (0%)	17 (9.9%)	0.005
Chronic kidney disease	40 (17.2%)	13 (21.3%)	27 (15.7%)	0.209
Myocardial infarction	16 (6.9%)	6 (9.8%)	10 (5.8%)	0.215
Cerebrovascular disease	23 (9.9%)	8 (13.1%)	15 (8.7%)	0.226
Smoking	97 (41.6%)	31 (50.8%)	66 (38.4%)	0.062
COPD	48 (20.6%)	18 (29.5%)	30 (17.4%)	0.037
Carotid disease	8 (3.4%)	0 (0%)	8 (4.7%)	0.084
Heart failure	71 (31.7%)	28 (45.9%)	43 (26.4%)	0.005
Hemoglobin (mg/dl)	12.6±2.0	12.5±2.1	12.6±1.9	0.636
Creatinine (mg/dl)	1.44±1.14	1.42±1.22	1.44±1.1	0.938
Glucose (mg/dl)	104±29	94±20	110±31	<0.001
Body mass index (kg/m^2)	25.7±4.6	25.5±3.5	25.7±4.8	0.777
Aortic size (mm)	60.5±16.1	66.9±14.2	58.6±16.2	0.006
Urgent surgery	85 (25.6%)	56 (35.7%)	29 (16.6%)	<0.001
Bypass time (min)	147±56	144±51	148±62	0.532
Ischemia time (min)	82±36	78±37	85±35	0.110
Circulatory arrest (min)	29±17.5	38±14	18±14	<0.001
Procedure				
Aortic root replacement	105 (31.6%)	53 (33.8%)	52(29.7%)	
Bentall	96 (28.9%)	48 (30.6%)	48(27.4%)	
Endovascular	50 (15.1%)	13 (8.3%)	37(21.1%)	0.024
Hybrid	71 (21.4%)	38 (24.2%)	33(18.9%)	
Aortoplasty	8(2.6%)	5 (3.2%)	3(1.7%)	
Concomitant procedures				
None	279 (84%)	135 (86%)	144 (82.3%)	
CABG	30 (9.0%)	14 (8.9%)	16 (9.1%)	0.772
Valve surgery	14 (4.2%)	6 (3.8%)	8 (4.5%)	
CABG + valve surgery	5 (1.5%)	2 (1.3%)	3 (1.7%)	

CABG=coronary artery bypass graft; COPD=chronic obstructive pulmonary disease; CTA=Center for the Treatment of Aorta

Procedures

Primary procedures included aortic root replacement with Dacron graft (105 patients, 31.6%), Bentall surgery (96 patients, 28.9%), endovascular repair (50 patients, 15.1%), hybrid procedure (71 patients, 21.4%), and direct aortoplasty (8 patients, 2.4%). Tirone surgery was performed in 1 patient. Concomitant procedures were performed in 16% of patients, with similar distribution between the groups; CABG (9.0%), valve surgery (4.2%), and combined surgery (coronary artery bypass and valve surgery, 1.5%) predominated. There was no difference between groups in the rate of associated procedures. The surgeries were performed urgently in 25.6% of patients, and were more common in the pre-CTA group (35.7%) than in the CTA group (16.6%, *P*<0.001).

Univariate analysis

In-hospital morbidity and mortality

The overall unadjusted mortality was 16.3% (54 patients). Major complications occurred in 88 patients (26.5%), and 27 patients suffered reoperation (8.2%). The average length of ICU stay was 5.2 days; the average hospital stay was 14.7 days. The most common complications are postoperative bleeding (17.2%), arrhythmias (11.1%), pneumonia (7.2%), stroke (7.5%) and sepsis (5.4 %). The CTA group had lower in-hospital mortality in univariate analysis compared to the pre-CTA (9.7% vs. 23%, *P*=0.002) (Figure 1). The CTA also had a lower incidence of complications (38.9% vs 56.7%, *P*=0.001) and major complications (20.6% vs 33.1%, *P*=0.007) (Figure 1 and Table 2). There was also a reduction in length of stay in the ICU in CTA group (4.8±8.4 days vs. 6.4±7.2 days, *P*=0.001).

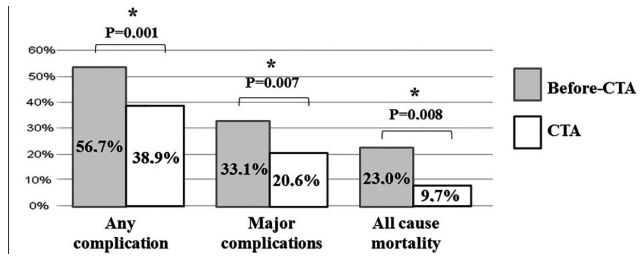

Fig. 1 - Complications and mortality in groups Before-CTA and CTA.

In subgroup analyzes stratified by timing of surgery (urgent vs. non-urgent surgery) (Figure 2), the CTA group showed a numerical reduction of mortality in urgent surgery (27.6% vs. 35.7%), without reaching statistical significance (*P*=0.158). There was also a significant reduction in mortality in elective procedures (6.9% vs. 15.8%, *P*=0.034).

In subgroup analyzes stratified by disease (Figure 2 and 3A), CTA group had reduced mortality in aneurysms in general (6.9% vs. 16.7%, *P*=0.043), in aneurysms of the ascending aorta (1.4% vs. 6.5%, *P*=0.048) and associations of ≥ 2 aneurysms (20.0% vs. 100%, *P*=0.04).

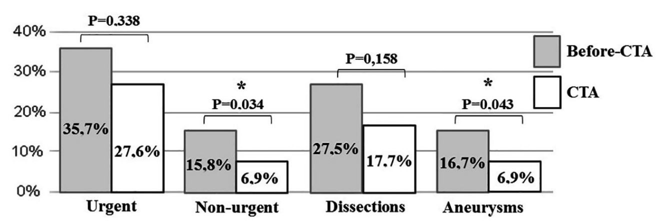

Fig. 2 - Mortality according to urgency and to disease subgroups.

Table 2. Postoperative outcomes according to the group.

	Overall	Before-CTA	CTA	*P*
Reintervention	27 (8.2%)	17 (10.9%)	10 (5.7%)	0.046
Complications	157 (47.3%)	89 (56.7%)	68 (38.9%)	0.001
Major complications	88 (26.5%)	52 (33.1%)	36 (20.6%)	0.007
ICU LOS (days)	5.2±8.2	6.4±7.2	4.8±8.4	0.001
Hospital time (days)	14.7±13.9	14.4±12.8	14.8±14.2	0.651
Stroke	25 (7.5%)	17 (10.9%)	8 (4.6%)	0.045
Myocardial infarction	6 (1.8%)	3 (1.9%)	3 (1.7%)	0.605
PO bleeding	57 (17.2%)	32 (20.4%)	25 (14.3%)	0.083
Acute kidney injury	7 (2.1%)	3 (1.9%)	4 (2.3%)	0.560
Mediastinitis	6 (1.8%)	3 (1.9%)	3 (1.7%)	0.605
AV block	8 (2.4%)	2 (1.3%)	6 (3.4%)	0.180
Arrhytmia	37 (11.1%)	15 (9.6%)	22 (12.6%)	0.243
Pneumonia	24 (7.2%)	15 (9.6%)	9 (5.1%)	0.090
Sepses	18 (5.4%)	15 (9.6%)	3 (1.7%)	0.001
Low cardiac output	17 (5.1%)	8 (5.1%)	9 (5.1%)	0.592
Pleural effusion	13 (3.9%)	5 (3.2%)	8 (4.6%)	0.359
Myocardial ischemia	2 (0.6%)	0 (0%)	2 (1.1%)	0.277

ICU=intensive care unit; CTA=Center for the treatment of aorta; AV=atrioventricular; LOS=lenght of stay; PO=postoperative

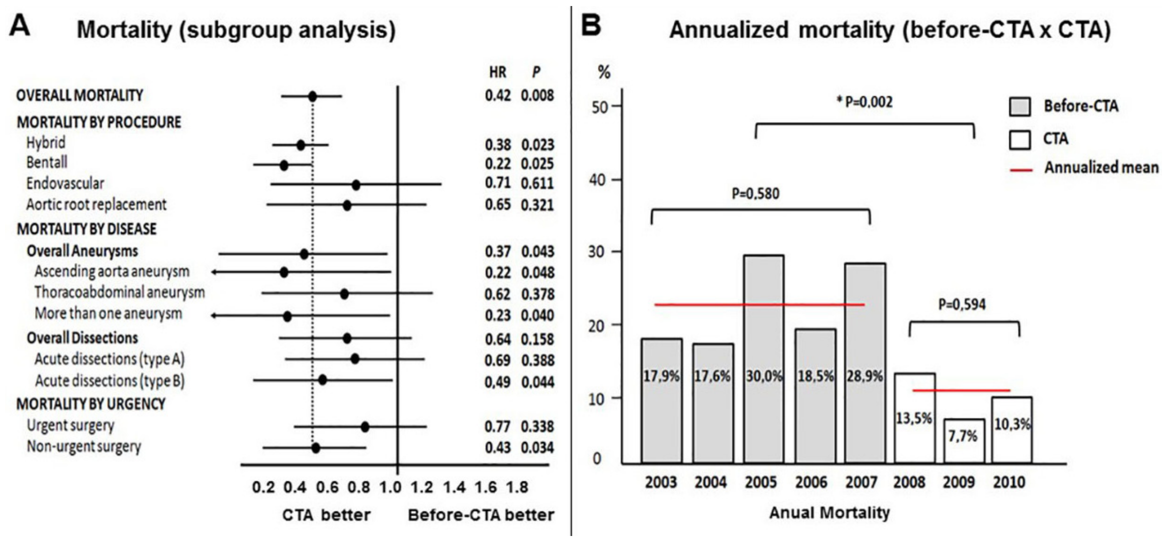

Fig. 3 - A) Subgroup analysis showing overall, procedure- disease-, and urgency-stratified mortality; B) Sensitivity analysis, comparing mortality by year in Before-CTA group, in CTA group, and mean annualized mortality between the 2 groups.

In the repair of thoracoabdominal aneurysms, there was a reduction in mortality, without reaching statistical significance (30.8% *vs*. 50.0%, *P*=0.378). In aneurysms of arch and descending aorta, the number of surgical cases was low and there were no deaths, precluding comparison between groups.

In patients undergoing surgery for acute type A aortic dissection, there was no significant reduction in mortality in the CTA group (17.7% *vs*. 25.7%, *P*=0.238), and the analysis stratified by the involvement of the aortic arch did not change this outcome. In acute type B dissections, however, there was a reduction of mortality in the CTA group compared to pre-CTA (18.7% *vs*. 37.5%, *P*=0.038).

In stratified analysis by procedure (Figure 3A) the CTA group showed reduced mortality in hybrid procedures (15.2% vs 39.5%, *P*=0.023) and in the Bentall surgery (4.2% vs 18.8%, *P*=0.025). In urgent/emergency surgeries and in the aortic root replacement surgeries, the CTA group showed reduced mortality, without reaching statistical significance (27.6% vs 35.7%, *P*=0.338, and 13.5 vs 20%, 8%, *P*=0.321, respectively). In the endovascular treatment, mortality was similar in the 2 groups (10.8% vs 7.7%, *P*=0.611).

In the sensitivity analysis to assess the evolution of annual mortality (Figure 3B), mortality within the pre-CTA (2003-2007) period remained between 17.6% and 30% (annualized average 23%), with no significant variation in the period (*P*=0.580). In CTA period (2008-2010), the annual mortality was between 7.7% and 13.5% (annualized average 9.7%), also with no variation within the period (*P*=0.594). However, comparing the annualized mortality between the two periods, a statistically significant reduction in the CTA group (*P*=0.002) appeared, suggesting that the reduction in mortality has not occurred by seasonal variation, gradual decrease over time, or improvements in other factors not related to the CTA, but by the direct effect of the creation of the CTA.

In the specific complications (Table 2), the CTA group had lower incidence of reoperation (*P*=0.046), stroke (*P*=0.045) and sepsis (*P*=0.001). The increased incidence of postoperative bleeding (14.3% vs. 20.4%) and pneumonia (5.1% vs. 9.6%) also had a reduced number without reaching statistical significance.

Factors associated with mortality

The baseline and operative risk factors associated with in-hospital death in the univariate analysis were: CTA, group (dissections), location of the aneurysm (thoracoabdominal and aneurysms associations), urgent surgery, reoperation, age, hemoglobin, creatinine, increased aortic diameter and CPB time (Table 3).

Multivariable Analysis

Independent predictors of mortality

Multivariate logistic regression (Table 4) was performed to evaluate whether specialized treatment in CTA was an independent predictor of mortality reduction. Logistic regression allows defining which variables are independently related to the outcome after simultaneous adjustment for all potential confounders[18]. The multivariate model included covariates associated with mortality in univariate analysis; thus, any association between the CTA and the primary outcome have occurred regardless of baseline differences between groups[19]. The prevalence of diabetes mellitus, COPD and heart failure; ejection fraction, and the rate of endovascular procedures were not associated with outcome in the univariate analysis, so they were not included in the multivariate model.

Table 3. Univariate analysis of baseline characteristics and operative variables associated with in-hospital mortality after aortic surgery.

	Survivals	Deaths	*P*
Group			0.008
Before-CTA	121 (77.1%)	36 (22.9%)	
CTA	157 (89.7%)	17 (9.7%)	
Disease Group			0.002
I (Aneurysms/coarctation)	161 (89.9%)	16 (8.9%)	
II (Dissection/ulcer)	117 (76.5%)	35 (22.9%)	
Aneurysm location			<0.001
Ascending aorta	110 (96.5%)	4 (3.5%)	
Aortic arch	4 (100%)	0 (0%)	
Descending aorta	20 (95.2%)	1 (4.8%)	
Thoracoabdominal	12 (63.2%)	5 (26.3%)	
Aneurysm association	4 (44.4%)	5 (55.6%)	
Abdominal aorta	11 (91.7%)	5 (8.3%)	
Type of dissection			0.160
A	91 (67.1%)	27 (22.9%)	
B	24 (72.7%)	8 (24.2%)	
Urgent	57 (20.5%)	28 (52.8%)	<0.001
Reintervention	16 (5.7%)	11 (20.7%)	0.001
Age (years)	58±14	62±11	0.032
Hemoglobin (mg/dL)	12.7±1.9	11.9±2.4	0.065
Creatinine (mg/dL)	1.3±0.8	2.2±2.2	0.053
Aortic size	59.1±15.2	73.3±19.4	0.002
Bypass time (min)	138±47	180±58	<0.001

In the univariate analysis, there was no association of the following variables with death: gender, disease, previous cardiac surgery, high blood pressure, diabetes, chronic kidney failure, myocardial infarction, previous stroke, coronary artery disease, smoking, COPD, carotid disease, liver disease, heart failure, type of procedure, concomitant procedure, glucose, body mass index, left atrial volume, left ventricular diastolic diameter, ejection fraction

The logistic regression model showed that the surgery in specialized center (CTA) led to a 77% reduction of in-hospital mortality compared to the pre-CTA period, with an odds ratio = 0.23 (95% CI 0.07 to 0.67, *P*=0.007). Other independent predictors of death were thoracoabdominal aneurysm surgery, with an odds ratio = 24.6 (95% CI 3,1 to 194, *P*=0.002); urgent surgery, with an odds ratio = 5.0 (95% CI 1.5 to 16.7, *P*=0.008); and preoperative creatinine, with an odds ratio = 1.7 (95% CI 1.1-2.6, *P*=0.008); for each 0.1mg/dL increase in preoperative creatinine, the risk of death increased by 7.3%. These factors are independently associated with hospital mortality, even after adjustment for possible confounding factors.

The predictive characteristics of the multivariate model were as follow: overall accuracy of 90% for predicting hospital mortality; explains 40% of the variability in the outcome of hospital death (Nagelgerke R *square*=0.391); very good discriminatory power (area under the ROC curve=0.824); have a good fit (Hosmer-Lemeshow test for goodness-of-fit: *P*=0.184), and shows stability and absence of significant multicollinearity.

Table 4. Multivariable analysis showing predictors of in-hospital mortality after aortic surgery.

	N	(%)	Adjusted OR	95% CI	*P*
Period					0.007
Before-CTA	65	(34.5)	1.0	Reference	
CTA	123	(65.5)	0.23	0.08-0.67	
Aneurysm location					
Ascending aorta	66	(58.9)	1.0	Reference	
Thoracoabdominal	15	(13.4)	24.59	3.11 - 194.1	0.002
Descending aorta	6	(5.3)	5.83	0.89 - 37.9	0.065
Urgent surgery	33	(17.5)	5.04	1.52 - 16.75	0.008
Age	188	(100)	1.04	0.99 - 1.09	0.079
Creatinine	188	(100)	1.73	1.15 - 2.60	0.008

Independent predictors of in-hospital death in multivariable analysis are marked in bold letters. Logistic regression model was adjusted for the following covariates: period (CTA), aneurysm location, disease, type of dissection, reintervention, hemoglobin, aortic size and bypass time. OR=odds ratio; 95%CI=95% confidence interval.

A multivariate analysis was also performed to assess the impact of the CTA (compared to pre-CTA) on hospital mortality stratified by pathology (aneurysms and dissections) and procedure (Table 5). This analysis showed that the CTA group had reduced mortality in both aortic aneurysms (odds ratio=0.18, 95% CI 0.034 to 0.983, *P*=0.048) and in the dissection (odds ratio=0.31, 95% CI 0.094 - 0.99, *P*=0.049), even after multivariate adjustment; similarly, reduced mortality occurred in hybrid procedures (odds ratio=0.07, 95% CI 0.007 to 0.726, *P*=0.026) and in the Bentall surgery (odds ratio=0.18, 95% CI 0.038 to 0.904, *P*=0.037) after multivariate adjustment.

Table 5. Multivariable analysis showing independent association of CTA with reduction of in-hospital mortality. stratified according to group (aneurysms and dissections) and by procedure.

Disease/Procedure	Adjusted OR	IC 95%	*P*
Aneurysms	0.18	0.034 – 0.983	0.048 [a]
Dissections	0.31	0.094 – 0.99	0.049 [b]
Hybrid procedure	0.07	0.007 – 0.726	0.026 [c]
Bentall procedure	0.18	0.038 – 0.904	0.037 [d]

a. Model adjusted for: previous cardiac surgery, urgency, age, chronic kidney disease, aortic size. b. Model adjusted for: diabetes, smoking, urgency, previous cardiac surgery. c. Adjusted for: disease, urgency, creatinine, age; d. Model adjusted for: disease, urgency, age, creatinine, heart failure. OR=odds ratio; 95%CI=95% confidence interval

DISCUSSION

In the present study, the thoracic aortic surgery in a specialized center (CTA) decreased the rate of complications (stroke, sepsis, bleeding) and was independently associated with lower in-hospital mortality after thoracic and thoracoabdominal aortic surgeries (reduction ~77%). There was a reduction of in-hospital mortality in CTA in subgroups stratified by disease (in aneurysms, especially of the ascending aorta and in more than one segment; in acute dissections, especially type B) and by procedure (hybrid procedures, Bentall). In addition to surgery in non-specialized center, baseline creatinine, urgent surgery and thoracoabdominal aneurysms were also independent predictors of in-hospital death.

Aortic surgeries are complex, have high morbidity and mortality, and require great care and preparation to ensure favorable outcomes[20-22]. In the most complex diseases the effect of specialized interventions on clinical outcomes is more relevant[23]. Therefore, it is expected that specialized centers in thoracic aortic surgeries may obtain the best results. There is already evidence of efficacy of this strategy in the pathologies of the infrarenal aorta[12,24].

Specialized centers in aortic surgery with high surgical volume have reported good results in thoracic aortic surgery. However, these results do not reflect the reality of all centers. Thus, multicenter registries including non-specialized centers have reported increased morbidity and mortality, especially for high-risk cases. Indirectly, this suggests that patients with high surgical risk patients present better outcomes in specialized centers[25,26]. This study objectively confirms this notion, showing a reduction of clinically relevant outcomes after thoracic aortic surgery (in-hospital mortality, complications, reoperations, stroke and sepsis).

The outcomes described herein for the CTA group are comparable to those described in reports of case series undergoing surgery in large centers specialized in aortic surgery. In a series of 597 patients undergoing the Bentall surgery, overall mortality was 3.8%[27], similar to what was reported in our study (4.2%), and consistent with recommendations to specialized centers (mortality 1-5%)[14]. Regarding endovascular treatment, in a report of 400 cases, the mortality rate was 6.5%[28], comparable to our group (7.7%).

On the other hand, the outcomes reported for pre-CTA group are similar to those described in multicenter registries that include non-specialized centers. In a cohort study of 12,573 patients with thoracic aortic aneurysms[29], the authors reported mortality for urgent surgery of 46%, even higher than that reported by us in the pre-CTA group (35.7%). The mortality rate for endovascular repair was 6.1% (elective), similar to reported in our pre-CTA group (10.3%); in urgent surgery, the mortality was 28%, comparable to our data (25%).

An important finding was revealed by the sensitivity analysis that evaluated the evolution of annual mortality. During the period 2003-2010, there was a significant reduction in mortality (P=0.008). This reduction did not occurred in 2003-2007 period, where mortality was stable (annualized average: 23%). This reduction also didn´t occur in the period 2008-2010, where the mortality remained stable (annualized average: 9.7%). This analysis confirms that there was no reduction of outcomes only by gradual improvement in care or progressive incorporation of new techniques. Finally, comparing mortality among pre-CTA vs. CTA period, there was a significant reduction (P=0.002), showing clearly that the improvement in outcomes occurred exactly at the transition between the two periods. Considering that our service has performed aortic surgery for over 15 years, one can say that the improvement in outcomes was not due to the impact of the learning curve or increased surgical volume, but due to the specialization[21,22].

The improved outcomes reported herein repeated consistently in different subgroups of patients, in multivariate analysis adjusted for baseline differences and comorbidities. The CTA group had independent mortality reduction in aneurysms, dissections and also in hybrids procedures and Bentall surgeries. Thus, we can confirm that the lowest mortality occurred by the beneficial effect of specialization of the center, and not by the differences in the baseline clinical variables between pre-CTA and CTA patients.

There is only one study in the literature directly comparing outcomes in thoracic aortic surgery at high-volume centers (> 80 surgeries in 3 years) with lower volume centers (<80 surgeries in three years); this study retrospectively evaluates the data from the Virginia Cardiac Surgery Quality Initiative (VCSQI)[30]. However, unlike the present study, the authors evaluate only the thoracic aortic aneurysms and exclude emergency surgeries. More than 500 elective aortic aneurysm surgeries were performed in high-volume centers and 216 surgeries in low-volume centers. In-hospital mortality was 3.8% for high-volume centers compared with 8.3% in low-volume centers (P=0.01). This difference demonstrated in the univariate analysis was tested after multivariate adjustment. For this, the authors performed the same multivariable logistic regression that we did, and they showed that elective surgery for thoracic aortic aneurysm in high-volume centers was an independent predictor of reduced mortality, with an odds ratio=0.41 (95% CI 0.18 to 0.92, P=0.03, 59% reduction). In our study, unselected thoracic aortic surgery at the CTA also reduced in-hospital mortality (odds ratio=0.23 (95% CI 0.08 to 0.67, P=0.007, 77% reduction). It is noteworthy the fact that hospital mortality for elective thoracic aortic aneurysms of our CTA group (n=84, mortality 3.8%) was equal to the mortality of high-volume centers of the aforementioned study (3.8%), and mortality for aneurysms of our pre-CTA group (n=54, mortality 7.4%) was slightly better than the mortality of low-volume centers (8.3%).

A more recent study[31] aimed to compare surgical outcomes in patients with type A acute aortic dissection, before and after installation of a multidisciplinary program in thoracic aortic surgery ("TASP"). In this study, the post-TASP group also had several baseline differences when compared to the pre-TASP group: it had a lower rate of infarction, fewer emergency surgeries, less concomitant procedures, shorter CPB and circulatory arrest, a higher percentage of patients undergoing selective cerebral perfusion, and more use of VIIa factor postoperatively. The results showed a very important reduction in mortality in the post-TASP group compared to pre-TASP group (from 33.9% to 2.8%, *P*=0.002). The authors didn´t perform any kind of multivariate analysis to adjust the results for differences in baseline characteristics; they only compared the pre-TASP and post-TASP mortalities with their predicted mortality by Rampaldi Score, which is a score that still lacks external validation. In contrast, in the present study, we performed a rigorous multivariate adjustment to avoid confounding caused by differences in baseline characteristics between the groups; in addition, we assessed the effect of CTA in a broader group of patients including dissections, aneurysms and different types of procedures.

Multiple aspects may explain the improved outcomes in specialized centers in aortic surgery. It has been shown that performing highly specialized procedures with high surgical volumes generates expertise by repetition[32]. Specific technology used by trained staff creates operational efficiency, economy in scale and greater cost-effectiveness[33]. In addition, trained and specialized teams can quickly add new technologies and scientific advances to patient care with improved outcomes[34].

Our study has limitations. Our patients were not randomized for allocation in the pre-CTA or CTA groups. Therefore, unmeasured baseline differences between groups may be present, with a potential impact on the estimate of the effect of the intervention. However, it seems inappropriate to randomize patients to surgery in non-specialized center, precluding the use of treatment strategies which are part of the best current therapy (and included here as part of the CTA strategy), because it would be unethical and could add risk to patients. Therefore, our study used a non-contemporaneous (historical) control group. This strategy has been questioned for possible selection bias (differences in baseline characteristics or disease severity) and bias by variation of other factors associated with outcome[35,36]. More recently, however, it has been shown that studies with historical controls, conducted carefully and accurately, can provide important evidence about benefits and harms of interventions, especially when there is effect plausibility, poor prognosis with usual treatment or risk of worse outcomes in patients not treated with the intervention under test[37,38].

Quality criteria and requirements for using historical controls have been proposed[39,40]. They include: collecting data in a blinded way (our data collection was prospective and blind); including patients with the same eligibility during the entire period (all treated patients with aortic disease in our hospital were eligible to allocation, and conditions of referral from other facilities were stable over the period); maintaining stable strategies of treatment over time (surgical techniques and perioperative care were similar throughout the study); using similar diagnostic methods (CT angiography of the aorta, aortography and transesophageal echocardiography were available for the whole period); indicating surgery at the same stage of evolution (we met surgical indications of relevant guidelines and avoided comparing outcomes between groups undergoing surgery in different stages of disease progression); and rigorous multivariate adjustment (we used multivariate logistic regression with adjustment for all covariates associated with outcome)[39,40]. If performed with such care, studies with historical controls have enabled major advances in relevant diseases[41-45], also having influenced health policies of several countries[41-43].

The implications of the reported findings are potentially relevant. It is essential that new studies confirm our findings, and enable additional analyzes, by determining the cost-effectiveness of CTA strategy. It is also important to determine if there is a positive impact on long-term outcomes. Nevertheless, these data may be an important stimulus for new surgical groups to create specialized centers, offering patients positive results as demonstrated herein. The allocation of public resources supporting the creation of new centers may be needed to ensure the availability of aortic centers in many hospitals and cities, expanding this strategy and reducing adverse outcomes.

In conclusion, surgical treatment of thoracic and thoracoabdominal aortic diseases in specialized center (aortic center) was associated with lower rates of complications and in-hospital mortality. Further studies will be required to confirm these data and to assess the cost-effectiveness and long-term outcomes.

Authors' roles & responsibilities	
MCS	Author
JDFF	Coauthor
CA	Coauthor
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