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CAROL DAVILA UNIVERSITY OF MEDICINE AND PHARMACY, BUCHAREST

DOCTORAL SCHOOL

FIELD: MEDICINE

NEUROLOGICAL COMPLICATIONS IN ACUTE AORTIC DISSECTION

SUMMARY OF THE DOCTORAL THESIS

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List of published papers

1. Robu M, Marian DR, Margarint I, Radulescu B, Știru O, Iosifescu A, Voica C, Cacoveanu M, Ciomag Ianula R, Gașpar BS, Dorobanțu L, Iliescu VA, Moldovan H, Association between Bilateral Selective Antegrade Cerebral Perfusion and Postoperative Ischemic Stroke in Patients with Emergency Surgery for Acute Type A Aortic Dissection-Single Centre Experience, Medicina, 2023, 59(8), 1365, FI – 2.4/2023, Q1, capitolul III, pag. 41–52

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Chapter 6

Introduction

Acute type A aortic dissection (ATAAD) represents one of the most dramatic cardiovascular emergencies. The natural mortality of untreated patients is estimated at approximately 1% per hour during the first 48 hours and exceeds 50% within the first week, confirming the catastrophic nature of this condition. Therefore, emergency surgical intervention constitutes the therapeutic standard, aiming to exclude the intimal tear and restore blood flow through the true lumen, thus reducing the risk of systemic malperfusion.

The therapeutic approach must be tailored to each patient depending on the severity and extent of malperfusion, the hemodynamic status, and the time elapsed from diagnosis. Current guidelines recommend urgent central surgical treatment in most cases, even in the presence of neurological deficits.

Postoperative neurological complications remain a major issue in the surgery of acute type A aortic dissection. The reported incidence of postoperative ischemic stroke varies between 10% and 25%, while other neurological manifestations—such as hypoxic encephalopathy, spinal cord ischemia, or postoperative delirium—can affect up to 30% of patients. These complications significantly increase postoperative mortality, prolong hospital stay, and impair long-term quality of life.

In this context, identifying risk factors for postoperative neurological complications becomes essential for optimizing intra- and postoperative management strategies. The heterogeneity of definitions used in the literature and the variability of surgical techniques applied make it necessary to standardize diagnostic and evaluation criteria for neurological complications.

Thus, our study aims to investigate the incidence and risk factors for postoperative neurological complications in ATAAD in a single-center setting, using uniform surgical protocols and statistical methods, to contribute to a better understanding of this critical pathology and to improve patient outcomes.

General Part

1.1. General Elements of Acute Type A Aortic Dissection

Acute type A aortic dissection represents a severe cardiac condition that always involves the ascending segment of the aorta with variable distal extension, leading to catastrophic complications regarding perfusion of all organs. Historically, the mortality of this condition has been described as 1–2% per hour during the first 24 hours [1], but recent studies show a mortality rate of 5.8% at 48 hours, decreasing to 4.4% at 48 hours in the case of emergency surgical intervention [2]. Among the most serious consequences of acute type A aortic dissection we mention rupture of the aortic wall with pericardial effusion and obstructive shock, involvement of the coronary arteries which may cause acute coronary syndromes, destabilization of the aortic annulus geometry with varying degrees of aortic insufficiency and cardiogenic shock, dissection of the carotid arteries which may lead to ischemic or hemorrhagic stroke, and hypoperfusion of peripheral organs (renal, mesenteric, hepatic, spinal ischemia), as well as upper or lower limb ischemia [3]. The definitive diagnosis is made based on contrast-enhanced thoracic computed tomography and/or transesophageal echocardiography.

1.2. Treatment of Acute Type A Aortic Dissection and Malperfusion Syndromes

Treatment of acute type A dissection is always an emergency given the potential complications of the disease: cardiac tamponade, severe acute aortic insufficiency and cardiogenic shock, myocardial ischemia due to coronary artery involvement, and organ malperfusion. Surgical treatment is considered first-line therapy and is always performed urgently, with studies reporting a 2–3 times higher mortality with medical treatment alone [4]. Data from the International Registry of Acute Aortic Dissection (IRAD) also show a reduction in surgical mortality from 25% in 1995 to 18% in 2013, while the mortality with medical treatment alone remains unchanged at 57% [4].

Emergency surgical treatment (“central aortic therapy”) aims to resect the entry tear and restore blood flow through the true lumen. Patients whose initial entry tear is not excluded are at increased risk of reoperation [5].

Class 1 recommendations from the American Guidelines on Aortic Diseases [6] are as follows:

a. Resuspension of aortic commissures in patients without cusp involvement and with partial root dissection;
b. Aortic root replacement with a mechanical or biological conduit in patients with extensive root dissection, root aneurysm, or in patients with known genetic disorders;
c. Distal anastomosis without clamping ("open distal anastomosis");
d. Hemiarch replacement preferred over complete arch replacement in patients with intimal tear at the arch or arch aneurysm.

Guidelines recommend in stable patients, at experienced centers, "valve-sparing" operations when aortic root replacement is necessary, as well as the "elephant trunk" technique for extended descending thoracic aortic dissection.

There is considerable controversy regarding the management of acute aortic dissection complicated by malperfusion syndrome. The literature reports remission of malperfusion syndrome in 75–80% of cases after central aortic therapy [7]. Some groups advocate for endovascular or surgical treatment of malperfusion syndrome with postponement of central surgical treatment until amelioration or resolution of the syndrome. Although a possible benefit of this strategy is reported, the risk of rupture is communicated in the literature up to 17% [8].

In cases of cerebral malperfusion and ischemic stroke, although surgery was anecdotally refused to these patients due to concerns of worsening neurological deficit through hemorrhagic transformation of ischemic brain tissue, current guidelines recommend surgical treatment, demonstrating higher survival rates [6]. Regarding mortality in patients with acute aortic dissection and ischemic stroke, it is 27% compared to 76% with medical treatment [9]. Estrera reports a mortality rate of 7% with surgical treatment in this patient group and, more importantly, reports that the neurological deficit did not worsen postoperatively [10].

With respect to renal, mesenteric, or lower limb malperfusion syndromes, the American guidelines recommend emergency surgical treatment of acute aortic dissection as first-line therapy ("central aortic therapy"). However, in the case of clinically significant mesenteric ischemia, the American guidelines recommend as first-line treatment either central surgical treatment or restoration of flow through the mesenteric artery (endovascular or surgical), followed by treatment of the aortic dissection at experienced centers [11]. The hybrid approach requires increased expertise in endovascular fenestration for treatment of dynamic obstruction and in stenting of the superior mesenteric artery in cases of static obstruction.

1.3. Cerebral Perfusion in Acute Type A Aortic Dissection

The American guideline also recommends cerebral perfusion in patients requiring circulatory arrest, as an adjunct to hypothermia, to improve neurological outcomes [6]. Total arch replacement with reimplantation of the supra-aortic vessels either as an island or separately, hemiarch excision, or distal anastomosis without clamping the aorta ("open distal anastomosis") all require a period of interruption of normal cerebral blood flow [12,13]. Brain tissue is highly sensitive to ischemia due to its high metabolic rate and the absence of glucose stores. Under physiological conditions, the required levels of oxygen and glucose are maintained through an autoregulatory process of cerebral blood flow over a wide range of cerebral perfusion pressures (40–160 mmHg) [14]. Consequently, cerebral ischemic tolerance is the main limiting factor in aortic arch surgery [15].

Cerebral protection techniques have become imperative to prevent brain injury during aortic arch surgery, aiming to reduce cerebral metabolism and maintain oxygen and glucose consumption within relatively normal limits [16]. Over time, several cerebral perfusion techniques have been developed, the first being deep hypothermic circulatory arrest (12–15 °C). Studies describe a 40-minute "safe period" in terms of neurological complications and mortality [17,18]. To prolong circulatory arrest under safe conditions and limit the adverse effects of profound hypothermia on other organs, additional techniques were developed, such as retrograde cerebral perfusion (historically important, but no longer used today) and antegrade cerebral perfusion.

Antegrade Cerebral Perfusion

Antegrade cerebral perfusion (ACP) can be performed in two ways:

- **Unilateral ACP**, in which the brain is perfused through a cannula introduced into the right axillary artery, with the brachiocephalic trunk clamped to direct flow into the right common carotid artery; the left side of the brain is perfused through collateral networks (Circle of Willis).
- **Selective bilateral ACP**, in which two separate cannulas are inserted into the brachiocephalic trunk and the left common carotid artery to perfuse each cerebral hemisphere. Bilateral ACP can also be achieved by complementing unilateral ACP with the introduction of a separate cannula into the left common carotid artery.

Table 1.1 summarizes the main ACP parameters according to literature data. The main technical difference between unilateral and bilateral ACP is that in unilateral ACP, contralateral perfusion depends on collateral pathways, primarily the Circle of Willis.

Regarding the duration of ACP, the literature favors selective bilateral ACP when cerebral perfusion time is anticipated to exceed 40–50 minutes. Malvindi reports a meta-analysis of over 3,548 patients showing a neurological complication rate below 5% between 30–50 minutes for unilateral ACP. Extending circulatory arrest up to 164 minutes with a complication rate below 5% was possible only using selective bilateral ACP [19]. The study's conclusion was to use ACP when more than 50 minutes of cerebral perfusion is anticipated.

Table 1.1. Suggested Parameters for Antegrade Cerebral Perfusion (ACP)

Presiune	40-60 mmHg
Debit	6-10 ml/kgc/min
Temperatură	
Sistemică	20-30°C
Perfuzat cerebral	20-28°C
EAB	Alpha-stat
Hematocrit	25-30%
Canulare	
Unilaterală vs. Bilaterală	>30-40 min de Perfuzie cerebrală – consideră **PCA bilaterală**
Monitor	NIRS (near infrared spectroscopy)

1.5. Neurological Manifestations in Acute Type A Aortic Dissection

Neurological manifestations in acute type A aortic dissection (ATAAD) have a reported incidence between 17% and 40% [23,24,25] and can be classified, according to Blanco, into ischemic/hemorrhagic stroke or transient ischemic attack, spinal cord ischemia, ischemic neuropathy, and hypoxic encephalopathy [26]. The common mechanism is hypotension (cardiogenic shock, obstructive shock, hemorrhagic shock) or dissection of one or more arteries supplying the brain, spinal cord, or peripheral nerves. Clinical manifestations vary; Gaul et al. reported that 1 in 4 patients with neurological symptoms presents one of the following associations: hemiparesis and syncope or tonic–clonic seizures; syncope and transient amnesia; ischemic neuropathy and seizures; or transient global amnesia associated with minor neurological symptoms [27].

Preoperative strokes are the main manifestation of cerebral tissue injury. They tend to be more frequent in hemispheric rather than vertebrobasilar locations and are more prevalent on the right side [28].

Progression of the dissection flap to the supra-aortic vessels is reported between 43% and 62.5%, most frequently affecting the brachiocephalic trunk and the left carotid artery due to their proximity to the aortic arch [29]. However, involvement of the supra-aortic vessels is not always associated with stroke, which has been reported in only one in five patients, with the main mechanisms being thromboembolism and severe hypotension.

1.6. Risk Factors for Postoperative Neurological Complications in Acute Type A Aortic Dissection

The definition of neurological complications (NCs) in ATAAD is heterogeneous in the literature. So far, four multicenter databases have investigated postoperative neurological complications and their risk factors in ATAAD: the German Registry for Acute Aortic Dissection Type A (GERAADA) [30], the International Registry of Acute Aortic Dissections (IRAD) [31], the Nordic Consortium for Acute Type A Aortic Dissection (NORCAAD) [32], and the Society of Thoracic Surgeons (STS) database [34]. GERAADA enrolled 2,137 patients with ATAAD operated on in emergency settings, from 50 centers in Austria, Switzerland, and Germany. Postoperative neurological complications reported included hemiparesis/plegia, paraplegia/paresis, aphasia, and coma. The study identified the following as risk factors for new postoperative NCs: malperfusion of three or more organs, dissection of the supra-aortic vessels, and operative times (Table 2.1). Cardiopulmonary bypass time and circulatory arrest time were independently associated with postoperative NCs. An interesting finding was that the cannulation site was not identified as a risk factor for postoperative NCs. IRAD included 2,202 patients with ATAAD and evaluated the incidence of ischemic stroke at presentation as well as patient prognosis. Although the study design does not include data on the incidence of postoperative NCs, it is important because it reports a 6% incidence of ischemic stroke at presentation and an in-hospital mortality 1.8 times higher. The study also reports that patients with ischemic stroke at presentation were older and had a higher incidence of hypertension and atherosclerosis. In this patient category, chest pain was less frequently reported at presentation, while syncope, shock, and pulse deficit were more frequent. Supra-aortic vessel involvement was more frequent (68%), and surgical management was less common (74%). Variables independently associated with ischemic stroke were supra-aortic vessel involvement, syncope at presentation, history of hypertension, abdominal pain at presentation, pulse deficit, and abnormal chest radiography without associated pain (Table 1.2). The study also notes that patients with ischemic stroke who underwent emergency surgery had better survival compared with those treated conservatively, findings also supported by GERAADA. The NORCAAD study enrolled 1,128 patients with ATAAD from eight Scandinavian hospitals. It evaluated the incidence of postoperative ischemic stroke and the prognosis of these patients. The reported incidence of postoperative ischemic stroke was 15.7%. At presentation, 7.62% had cerebral malperfusion, of whom 34.8% developed postoperative ischemic stroke. Variables independently associated with postoperative ischemic stroke were preoperative cerebral malperfusion, hemodynamic instability, and total aortic arch replacement (Table 1.2). The STS database study enrolled 2,982 patients with ATAAD from 640 centers in North America. The study evaluated current surgical strategies and their outcomes and reported an operative mortality of 17%. The study reported preoperative neurological complications defined as cerebrovascular disease and stroke, with an incidence of 7.8% of cerebrovascular disease with a history of stroke and 3.5% without a history of stroke. Postoperative neurological complications reported were ischemic stroke (10.9%), TIA in 0.6% of cases, and paralysis in 2.9% of cases. Risk factors for postoperative NCs were not analyzed in this report.

Table 1.2 summarizes the main studies published on this topic. Both preoperative and postoperative NCs included coma, altered consciousness, any focal neurological deficit, cerebral ischemia, transient ischemic attack, stroke, paraplegia/paresis, aphasia, confusion, etc.

The GERAADA study highlights the heterogeneity of NC definitions in the literature and also proposes unifying them following the model reported by Griepp et al. This model divides NCs by duration—temporary or permanent. Temporary NCs are further graded from 1 to 5 and include confusion, lethargy, agitation, psychosis, and parkinsonism. Another important aspect in studying NCs in ATAAD is the distinction between patients with postoperative NCs on the background of preoperative neurological dysfunction and those with newly developed postoperative NCs—another source of heterogeneity among studies.

Table 1.2. Risk Factors for Postoperative Neurological Complications in ATAAD

Study / Risk Factor	OR	95% CI	p
GERAADA [2]			
Three or more malperfused organs	2.206	1.278–3.810	0.038
Dissection of supra-aortic vessels	1.468	1.095–1.969	0.0103
Operative time	1.002	1.001–1.003	0.0001
Cardiopulmonary bypass time	1.002	1.001–1.004	0.0005
Circulatory arrest time	1.009	1.003–1.015	0.0017
NORCAAD [13]			
Cerebral malperfusion	4.28	2.56–7.17	<0.001
Cardiopulmonary bypass time	1.19	1.11–1.26	<0.001
Pericardial tamponade	1.85	1.12–3.05	0.015
Cardiogenic shock	2.45	1.20–4.98	0.013
STS [6]			
Hypertension	1.35	1.10–1.64	0.003
Syncope	1.56	1.24–1.96	<0.001
Cardiopulmonary bypass time	1.001	1.001–1.002	0.003
Femoral artery cannulation, no cerebral perfusion, no arch repair	—	—	<0.001

Original Part

2. Working Hypothesis and General Objectives

Currently, the scientific literature is heterogeneous regarding the definition and reporting of postoperative neurological complications in patients with acute type A aortic dissection (ATAAD). There are gaps in the clear identification of specific risk factors, especially in subgroups of patients with obesity, where no consensus has been reached regarding optimal brain protection strategies and perfusion parameters [29].

Therefore, the present study has the following objectives:

1. To determine preoperative and intraoperative risk factors for postoperative neurological complications.
2. To establish clear and reproducible definitions for postoperative neurological complications in ATAAD.
3. To determine the incidence of neurological complications in the studied population.
4. To investigate the association between different cerebral perfusion time intervals and postoperative ischemic stroke, particularly in obese patients.

Identifying risk factors for postoperative neurological complications in ATAAD contributes to patient-centered management in a condition with high mortality, where surgery is the only effective treatment. Knowledge of preoperative and intraoperative risk factors for neurological complications, and in particular for ischemic stroke, may lead to changes in patient management strategies, both preoperatively and intraoperatively, with the goal of reducing their incidence.

The high incidence of obesity in patients with cardiovascular disease, and particularly in patients with ATAAD, also requires a tailored strategy, especially intraoperatively. To date, there is no consensus regarding cerebral perfusion parameters or its duration in these patients, with the current strategy being the one applied to most patients.

3. General Research Methodology

To determine risk factors for postoperative neurological complications in patients undergoing emergency surgery for ATAAD, we conducted three retrospective studies including all patients admitted to the Emergency Institute for Cardiovascular Diseases “Prof. Dr. C.C. Iliescu” with a diagnosis of ATAAD between January 1, 2017, and May 1, 2023.

Medical data were recorded from the clinical observation sheet and the hospital information system. Patient consent was documented by signing the informed consent form.

Inclusion and Exclusion Criteria

The inclusion criterion was as follows: patients with ATAAD according to the Stanford classification, confirmed by transesophageal echocardiography or thoracic angio-CT, who underwent emergency surgical treatment.

The general exclusion criteria were:

1. Patients with imaging-confirmed hemorrhagic stroke who are not candidates for emergency surgery;
2. Patients with imaging-confirmed ischemic stroke with severe neurological dysfunction who are not candidates for surgery;
3. Patients with a history of ischemic or hemorrhagic stroke, TIA, or any neurological dysfunction;
4. Patients who died intraoperatively or within the first 48 hours in the intensive care unit;
5. Postoperative patients whose neurological status could not be evaluated;
6. Patients with incomplete medical information.

Postoperative neurological complications included were documented within the first 72 hours postoperatively. The following complications were documented and analyzed: ischemic stroke, spinal cord ischemia, hypoxic-ischemic encephalopathy, and postoperative delirium.

Statistical Analysis

Statistical analysis was performed using Wizard 2 for MacOS (Wizard–Statistics and Analysis®, Raipur, Chattisgarh, India).

The primary objective was to determine the incidence of postoperative neurological complications (ischemic stroke, spinal cord ischemia, hypoxic-ischemic encephalopathy, postoperative delirium).

To analyze the association between different preoperative and intraoperative variables and postoperative neurological complications, logistic regression was performed. Initially, univariate analysis of possible risk factors for the different neurological complications was conducted, and variables with a statistical p-value below 0.1 were selected. Logistic regression with backward selection of covariates was then performed, resulting in a final model. The variable investigated as a potential risk factor was first analyzed in univariate analysis, and then, if an association was obtained at this stage, it was adjusted according to the covariates of the model obtained from backward selection. The variable is interpreted as an independent risk factor for one of the neurological complications if the OR is above 1, the confidence interval does not include 1, and the statistical p-value is below 0.05.

4. Association Between Bilateral Selective Antegrade Cerebral Perfusion and Postoperative Ischemic Stroke in Patients Undergoing Emergency Surgery for Acute Type A Aortic Dissection

4.1. Introduction

Bilateral selective antegrade cerebral perfusion (BSACP) is an effective method for extending circulatory arrest in complex ATAAD cases, such as those requiring total aortic arch replacement with reimplantation of supra-aortic vessels either “en bloc” or separately when a quadrangular graft is available. Given the neurological risks associated with this technique, this study aims to evaluate whether the duration of BSACP is associated with postoperative ischemic stroke in patients undergoing emergency surgery for ATAAD.

4.2. Materials and Methods

Data from 220 patients presenting to the Emergency Institute for Cardiovascular Diseases between January 2017 and December 2022 with acute type A aortic dissection were retrieved from clinical records and the electronic hospital database. The diagnosis of ATAAD was established based on the Stanford classification, using thoracic angio-CT and/or transesophageal echocardiography. The presence of an intimal flap in the ascending aorta was the defining criterion for ATAAD.

Inclusion and Exclusion Criteria

Inclusion criterion: Patients with imaging-confirmed ATAAD scheduled for emergency surgery.

Exclusion criteria:

1. Patients with imaging-confirmed ischemic or hemorrhagic stroke preoperatively;

2. Clinical signs of ischemic/hemorrhagic stroke or preoperative neurological dysfunction;
3. Patients who died intraoperatively or within 48 hours after admission to intensive care;
4. Patients whose postoperative neurological status could not be assessed;
5. Patients with incomplete preoperative/intraoperative/postoperative data.

Postoperative ischemic stroke was confirmed by brain CT once clinical suspicion arose in the intensive care unit (within the first 12 hours), followed by a neurological consultation. The "Modified Rankin Scale" was used to evaluate disability at discharge after ischemic stroke, based on data collected from the observation sheets.

Statistical Analysis

Statistical analysis was performed using Wizard 2 Statistical Software for Mac OS (Wizard–Statistics & Analysis®, Raipur, Chattisgarh, India). The primary objective was to determine the incidence of postoperative ischemic stroke in patients undergoing emergency surgery for ATAAD with circulatory arrest and bilateral selective antegrade cerebral perfusion. Patients were divided into three groups: perfusion under 30 minutes, between 30–40 minutes, and over 40 minutes. This cut-off was chosen because it is known that the safe duration of circulatory arrest under hypothermia is under 30 minutes, and antegrade cerebral perfusion is considered safer if circulatory arrest is anticipated to exceed 40 minutes. Logistic regression was used to analyze the association between cerebral perfusion duration and postoperative ischemic stroke. Preoperative variables included in the univariate analysis were: age, male sex, arterial hypertension, diabetes, dyslipidemia, preoperative atrial fibrillation, postoperative atrial fibrillation, cardiac tamponade on admission, severe aortic insufficiency, severe left ventricular dysfunction, bicuspid aortic valve, severe calcifications of the ascending aorta or aortic arch (preoperative CT diagnosis), hemiarch replacement, aortic root replacement, total arch replacement, supracommissural ascending aorta interposition, axillary cannulation, femoral cannulation, brachiocephalic trunk dissection, left common carotid dissection, intimal tear in the ascending aorta, and intimal tear in the aortic arch.

4.3. Results

After applying the exclusion criteria, 91 patients were excluded and 129 patients were included in the study. Twenty-five patients had ischemic or hemorrhagic stroke documented by brain CT, five patients presented with coma (GCS 3), 12 patients had various motor deficits, 11 patients died within the first 48 hours after surgery, and 38 patients had incomplete data

Preoperative characteristics are displayed in Table 4.1. The mean age was 59 ± 11.15 years, with 64.3% males. Mean EuroSCORE was 9.03 ± 2.63, and the mean time from diagnosis to surgery was 4.89 ± 4.37 hours. Hypertension was present in 65.9%, diabetes in 6.2%, and dyslipidemia in 31%. Chronic kidney disease was present in 7.8%, and atrial fibrillation at admission in 9.3%. Bicuspid aortic valve was diagnosed in 8.5% of cases, severe aortic insufficiency in 18.6%, and severe left ventricular dysfunction (LVEF <30%) in 0.8%. Cardiac tamponade at presentation was noted in 27.1%. Extent of supra-aortic vessel dissection: the most common was brachiocephalic trunk dissection (25.6%), followed by left common carotid dissection (16.3%), with both carotids involved in 6.97% of cases.

Intraoperative characteristics are also shown in Table 4.1. The most frequent operation was ascending aorta plus hemiarch replacement (69.8%), followed by ascending aorta plus total arch replacement (15.5%), and aortic root replacement with a mechanical valved conduit combined with ascending aorta and hemiarch replacement (10.9%). The rarest procedures were isolated ascending aorta replacement (2.3%) and total root + ascending aorta + total arch replacement (0.8%). Additional procedures included aortic valve replacement (3.1%), coronary artery bypass grafting (4.65%), implantation of peripheral VA ECMO in one patient, femoro-femoral bypass in one patient, and coarctation repair in another. Axillary artery was the most common cannulation site (68.2%), followed by femoral artery (30.2%) and aortic arch cannulation (1.6%). In 14% of cases the intimal tear was not visible at the root/ascending/arch; when visible, it was most commonly at the root/ascending aorta (43.4%) or simultaneously at the ascending and arch in 32.6%. Mean cerebral perfusion duration was 37.837 ± 18.243 minutes, mean cardiac ischemia time was 114.775 ± 34.602 minutes. Selective antegrade cerebral circulation combined with moderate hypothermia was under 30 minutes in 44.2%, 30–40 minutes in 34.1%, and over 40 minutes in 31.8% of patients. The incidence of ischemic stroke was 24.8% (31 patients), and 27 deaths were recorded (20.9%). Table 4.2 shows disability (mRS) at discharge, with a mean of 2.6 ± 1.03. Severe disability requiring home care occurred in nearly half of stroke survivors (41.93%), with mild-moderate disability in 16.12% (mRS 2) and 19.35% (mRS 3).

Logistic Regression

The association between different durations of selective antegrade cerebral perfusion (under 30 minutes, between 30 and 40 minutes, over 40 minutes) and postoperative ischemic stroke was analyzed using logistic regression. Univariate results with $p < 0.1$ are presented in Table 4.3. Left common carotid dissection (OR = 2.772; 95% CI = 1.041–7.381; p = 0.041) and dyslipidemia (OR = 3.048; 95% CI = 1.077–8.627; p = 0.036) were included in the final model after backward selection. Selective bilateral ACP > 40 minutes was associated with ischemic stroke (OR = 2.41; 95% CI = 1.054–5.509; p = 0.037) in univariate analysis and, after model adjustment, represented an independent factor associated with postoperative ischemic stroke (OR = 3.589; 95% CI = 1.418–9.085; p = 0.007). ACP bilateral selective under 30 minutes (OR = 0.484; 95% CI = 0.207–1.128; p = 0.093) and between 30–40 minutes (OR = 1.016; 95% CI = 0.438–2.357; p = 0.971) were not associated with ischemic stroke after univariate analysis.

Table 4.1. Preoperative and Intraoperative Characteristics of Patients

Characteristic	**Value N = 129 (100%)**
Preoperative characteristics	
Age (mean, SD)	59 ± 11.15
Sex (n, % male)	83 (64.3%)
EuroSCORE (mean, SD)	9.03 (2.63)
Time from diagnosis to surgery (hours)	4.89 (4.375)
Hypertension (n, %)	85 (65.9%)
Diabetes (n, %)	8 (6.2%)
Dyslipidemia (n, %)	40 (31%)
Chronic kidney disease (n, %)	10 (7.8%)
Preoperative atrial fibrillation (n, %)	12 (9.3%)
Bicuspid aortic valve (n, %)	11 (8.5%)
Cardiac tamponade (n, %)	35 (27.1%)
Dissection of brachiocephalic trunk (n, %)	33 (25.6%)
Dissection of left common carotid artery (n, %)	21 (16.3%)
Dissection of both carotid arteries (n, %)	9 (6.97%)
Severe aortic regurgitation (n, %)	24 (18.6%)
Mild LV dysfunction (LVEF 40-50%) (n, %)	9 (7%)

Moderate LV dysfunction (LVEF 30-40%) (n, %)	2 (1.6%)
Severe LV dysfunction (LVEF <30%) (n, %)	1 (0.8%)
Severe calcification of ascending aorta or arch	9 (7%)
Intraoperative characteristics	
Replacement of ascending aorta and hemiarch (n, %)	90 (69.8%)
Replacement of ascending aorta and arch (n, %)	20 (15.5%)
Replacement of aortic root, ascending aorta and hemiarch (n, %)	14 (10.9%)
Replacement of ascending aorta (n, %)	3 (2.3%)
Replacement of aortic root, ascending aorta and full arch (n, %)	1 (0.8%)
Combined procedures	13 (10.07%)
Mitral valve replacement (n, %)	4 (3.1%)
Coronary bypass (n, %)	6 (4.65%)
Peripheral VA ECMO (n, %)	1 (0.8%)
Femoro-femoral bypass (n, %)	1 (0.8%)
Aortic coarctation repair (n, %)	1 (0.8%)
Cannulation site	
Axillary artery (n, %)	88 (68.2%)
Femoral artery (n, %)	39 (30.2%)
Aortic arch (n, %)	2 (1.6%)
Intimal tear	
Ascending aorta/root (n, %)	56 (43.4%)
Aortic arch (n, %)	42 (32.6%)
Ascending aorta/root and arch (n, %)	12 (9.3%)
No visible intimal tear (n, %)	18 (14%)
Cardiopulmonary bypass time (min; mean, SD)	210 (56.874)
Myocardial ischemia duration (min; mean, SD)	114.775 (34.602)
Cerebral perfusion duration (min; mean, SD)	37.837 (18.243)
Cerebral perfusion <30 min (n, %)	57 (44.2%)
Cerebral perfusion 30-40 min (n, %)	44 (34.1%)
Cerebral perfusion >40 min (n, %)	41 (31.8%)

Postoperative atrial fibrillation (n, %)	34 (26.4%)
Reoperation for postoperative bleeding (n, %)	34 (26.4%)

Table 4.2. Neurological Deficit at Discharge (Modified Rankin Scale – mRS)

mRS	n/(%)
0	0 (0%)
1	3 (9.67%)
2	5 (16.12%)
3	6 (19.35%)
4	4 (12.90%)
5	0 (0%)
6	13 (41.93%)

Table 4.3. Factors Associated with Ischemic Stroke (Multivariable Analysis)

	Univariate			**Multivariable**		
Variable	**OR**	**95% CI**	**p**	**OR**	**95% CI**	**p**
Right CCA dissection	2.772	1.041–7.381	0.041	2.941	1.034–8.364	0.043
Dyslipidemia	3.048	1.077–8.627	0.036	4.577	1.462–14.332	0.009
BSACP > 40 min	2.41	1.054–5.509	0.037	3.589	1.418–9.085	0.007

4.4. Discussions

The main result of the first study highlights that bilateral selective antegrade cerebral perfusion (BSACP) was independently associated with postoperative ischemic stroke. In our study, the incidence of stroke was 21.6% (31 patients). A total of 13 (41.93%) of the patients with postoperative ischemic stroke died in the intensive care unit.

Open distal anastomosis, hemiarch replacement, or complete replacement of the aortic arch requires a period of circulatory arrest. Establishing BSACP is technically more complex, and studies have shown a longer total circulatory arrest time with this technique, with an increased risk of stroke if it exceeds 30 minutes [34,35]. In our center, we use BSACP for all patients requiring circulatory arrest with hypothermia (HCA) for aortic repair in ATAAD. The technique is adapted according to intraoperative findings, especially if atheromatous plaques are present in the aortic arch or at the level of the innominate artery and the left common carotid artery. When supra-aortic vessels are implanted separately, we usually excise the portion containing the atheromatous plaque to ensure safe cannula insertion. Also, in these cases, no ligatures are performed in order to minimize the risk of plaque embolization. The dissected portion of the supra-aortic vessels is excised as much as possible to achieve optimal pressure for cerebral perfusion. Cannulas are inserted after de-airing, and we aim to introduce them as little as possible into the arterial lumen, usually with the balloon adjacent to the proximal end of the artery. The circuits for ACP were prepared before HCA to minimize time loss, and the left and right cannulas were color-coded for better cerebral perfusion management. Using this algorithm, the mean cerebral perfusion time in our study was 37.837 ± 18.243 minutes, and we managed to achieve ACP under 30 minutes in 44.2% of patients. Of the 90 patients with hemiarch replacement, 75.4% had BSACP under 30 minutes and 90.5% had an average aortic clamping time between 85 and 96 minutes. Considering that BSACP is technically more complex, based on our results we do not consider this to be the case.

The incidence of postoperative ischemic stroke was 24.8% in our study. Among the 88 patients with BSACP > 40 min, postoperative ischemic stroke occurred in more than half (53.1%). We concluded that every effort must be made to minimize ACP time.

5. Factors associated with the occurrence of new postoperative neurological complications in patients undergoing emergency surgery for acute type A aortic dissection

5.1. Introduction

Despite the advances in surgical techniques (central aortic therapy) and the introduction of cerebral protection methods such as cerebral perfusion and hypothermic circulatory arrest, the incidence of neurological complications (NCs) remains high, ranging between 17 and 48% [143–145]. NCs after emergency repair of ATAAD are associated with higher in-hospital mortality, longer stays in intensive care units and in hospital, as well as reduced long-term survival [146,147]. Data regarding pre/postoperative NCs are heterogeneous and there is considerable variability in their classification [151]. The aim of this study was to determine the association between various intraoperative parameters and new postoperative neurological complications in patients undergoing emergency surgery for ATAAD.

5.2. Materials and Methods

Between January 2017 and May 2023, 240 patients were transferred to our center for the treatment of ATAAD. The diagnosis of ATAAD was established based on thoracic computed tomography with intravenous contrast medium. After a cardiology consultation in the emergency department, with mandatory transthoracic echocardiography, patients who were candidates for emergency surgery were transferred to the operating room. Clinical characteristics and demographic data were collected from medical records and the electronic health system.

Inclusion criteria: patients with acute type A aortic dissection according to the Stanford classification were considered for emergency surgery.

Exclusion criteria:

(1) patients with ischemic or hemorrhagic stroke documented on CT before surgery;

(2) clinical signs of stroke, paraplegia, delirium or any neurological dysfunction before surgery;

(3) patients with a history of transient ischemic attack, ischemic or hemorrhagic stroke, or other neurological dysfunctions;

(4) patients who died in the operating room or within the first 48 hours after admission to intensive care;

(5) patients in whom postoperative neurological status could not be assessed;

(6) patients with incomplete medical records.

Newly developed neurological complications were assessed within the first 72 hours after admission to the ICU.

To investigate the association between various intraoperative factors and the occurrence of new NCs, a multivariate analysis using logistic regression was performed. The variables included in the univariate analysis were: age, male sex, arterial hypertension, diabetes, hyperlipidemia, chronic kidney disease, preoperative atrial fibrillation, cardiac tamponade on admission, severe aortic regurgitation, severe left ventricular dysfunction, presence of bicuspid aortic valve, primary intimal lesion in the ascending aorta or aortic arch (or absence of an identified entry tear on preoperative CT), dissection of one, two or three supra-aortic vessels and reoperation for mediastinal bleeding. The intraoperative indices analyzed were: type of intervention (with or without aortic arch surgery, Wheat procedure, surgery on the aortic root, supracoronary replacement of the ascending aorta, hemiarch, total arch replacement, reimplantation of the innominate artery, reimplantation of the innominate artery and the left common carotid artery, combined procedures), axillary or femoral cannulation, cardiopulmonary bypass time, aortic cross-clamp time and cerebral perfusion time.

5.3. Results

After applying the exclusion criteria, 203 patients with ATAAD who underwent emergency surgery were included in the study. A total of thirty-seven patients were excluded (five patients with massive ischemic stroke, three with hemorrhagic stroke, four with unrecovered cardiac arrest on admission, three with a history of neurological dysfunction, five with irreversible peripheral ischemia, four with ischemic stroke on preoperative CT, thirteen who died on the operating table—ten due to hemorrhagic shock and three with myocardial infarction).

4.2.1. Characteristics of the study population

The general data of the study population are shown in Table 4.4. The mean age was 57.61 ± 12.27 years, 67% were male, and the mean Euroscore was 9.03 ± 2.63. The time from ATAAD diagnosis to surgery was 4.89 ± 4.37 hours. Hyperlipidemia was the most common comorbidity (69%), and preoperative atrial fibrillation was observed in 7.4% of cases. Chest pain was present in 175 patients (86.2%). A history of aortic aneurysm was identified in 22.16%, and the mean maximum aortic diameter was 6.19 ± 1.19 mm. Preoperative transthoracic echocardiography showed the presence of a bicuspid aortic valve in 12.8% of cases, severe acute aortic regurgitation in 29.1% and cardiac tamponade in 27.1%. Based on the preoperative CT, the innominate artery was the most frequently dissected supra-aortic vessel (27.1%), and dissection of all three supra-aortic vessels was found in 9.9% of patients. The postoperative death rate was 16.74% (34 patients). According to autopsy reports, the causes of death were: septic shock (25.5%), cardiogenic shock (32.4%), mixed shock (26.4%) and hemorrhagic shock (5.9%). The intraoperative data (Table 4.5.) indicate a mean cardiopulmonary bypass time of 206.28 ± 63.22 minutes and an aortic cross-clamp time of 116.1 ± 38.4 minutes; in 76.4% of cases cerebral perfusion was necessary, with a mean cerebral perfusion time of 29.62 ± 22.27 minutes. The most frequent procedure in the group without arch intervention was supracoronary replacement of the ascending aorta with a Dacron graft (18.7%). In the arch intervention group, the most frequent type of surgery was ascending aorta and hemiarch replacement with moderate hypothermic circulatory arrest and cerebral perfusion (53.2%). Total arch replacement was performed in 4.4% of cases. Additional procedures were required in 31 patients: aortocoronary bypass (5.4%), mitral valve replacement (2.46%), mitral repair (1.47%), peripheral veno-arterial ECMO in two patients, non-coronary sinus reconstruction in two patients, femoral-femoral bypass in one patient and aortic coarctation repair in one patient. Axillary artery cannulation was performed in 64.5% of cases, followed by femoral artery cannulation in 31.5%.

4.2.2. Characteristics of patients with neurological complications

The incidence of newly developed postoperative neurological complications was 39.4% (80 patients). Ischemic stroke had an incidence of 23.6% (48 patients). Postoperative delirium occurred in 21 patients (10.3%), and hypoxic-ischemic encephalopathy in 9 cases (4.4%). Two patients (1%) developed spinal cord ischemia postoperatively. No differences were observed regarding age, frequency of preoperative factors or surgical technique between groups with and without neurological complications. Patients with newly developed postoperative neurological complications had longer cardiopulmonary bypass times ($p = 0.004$) and longer cerebral perfusion times ($p < 0.001$) and more frequently presented dissection of two supra-aortic vessels ($p = 0.048$) and primary entry lesions in the arch ($p = 0.014$) (Table 4.6.). The incidence of death in the group with neurological complications was 23.8% (septic shock in 8 cases, mixed shock in 6 cases and cardiogenic shock in 5 cases).

Ischemic stroke

Patients with ischemic stroke were older than those without stroke ($p = 0.011$), more frequently presented dissection of two supra-aortic vessels ($p = 0.03$) and entry lesions in the ascending aorta and arch ($p = 0.001$) and had longer cardiopulmonary bypass times ($p = 0.008$) and cerebral perfusion times ($p = 0.001$). A significant difference was found in death frequency in the stroke group (p = 0.001). Postoperative ischemic stroke was diagnosed in 23.64% of patients. The incidence of death was 33.34% in this group. The anterior circulation was affected in 47.91% of cases, the posterior circulation in 20.83%, and both anterior and posterior circulations in 16.67% of patients. The right carotid artery was the most frequently affected vessel of the anterior circulation (25% of cases). In the posterior circulation, the most affected vessel was the right vertebrobasilar artery (8.33%). Dissection of the supra-aortic vessels was observed in 39.6% of patients with ischemic stroke; the most frequently dissected branch was the innominate artery (35.4%). Six patients (33.34%) died in the ischemic stroke group, and eleven (22.91%) had no disability or mild disability at discharge (modified Rankin score 0–2).

Hypoxic-ischemic encephalopathy

Hypoxic-ischemic encephalopathy had an incidence of 4.4% (nine patients). The mean age was 59.22 ± 13.53 years. Systolic hypotension related to cardiac tamponade was observed in four patients and related to severe acute aortic regurgitation in two patients. Two patients presented involvement of the supra-aortic vessels—both with dissection of the innominate artery and the left common carotid artery, without dissection of the subclavian arteries. Three patients had a primary entry lesion located at the aortic arch, and five underwent arch surgery. The mean cardiopulmonary bypass time was 239.11 ± 49.55 minutes, aortic cross-clamp time 126.11 ± 48.53 minutes, and cerebral perfusion time 24.67 ± 22.37 minutes. One patient did not regain consciousness and died of septic shock; the others were successfully transferred to recovery centers after stabilization in the intensive care unit.

Postoperative delirium

Postoperative delirium was observed in 21 patients (10.3%). The mean age was 58.46 ± 12.39 years; 66.7% had a history of hypertension and 9.5% had diabetes mellitus. Cardiac tamponade at admission was present in 19% of cases, and severe acute aortic regurgitation in 42.9%. In 47.6% of cases arch surgery was performed, and 9.5% had total arch replacement. Involvement of supra-aortic vessels was observed in 23.8% of patients; the incidence of innominate artery dissection was 23.8%, and 14.3% had dissection of both the innominate and the left common carotid artery. The mean cardiopulmonary bypass time was 216.29 ± 51.81 minutes, aortic cross-clamp time 117.38 ± 29.77 minutes, and cerebral perfusion time 28.81 ± 14.8 minutes. There was a significant difference in the incidence of surgery on the aortic root (p = 0.025), and patients with postoperative delirium more frequently had cardiopulmonary bypass times over 3 hours ($p = 0.049$). One patient died of mixed shock (cardiogenic and septic).

Spinal cord ischemia

Spinal cord ischemia was diagnosed in two patients (2.5%). Both were men and underwent replacement of the ascending aorta and hemiarch, with entry lesions in the ascending aorta. The cardiopulmonary bypass time was 168 ± 50.2 minutes, aortic cross-clamp time 88 ± 21.21 minutes, and cerebral perfusion time 33 ± 15.56 minutes. One patient had dissection of the innominate artery, and the other had dissection of both the innominate artery and the left common carotid artery. Both survived: one with partial recovery of paraplegia at discharge, the other without recovery.

4.2.3. Statistical analysis (logistic regression)

Table 4.7. shows the results of logistic regression. The results of the univariate analysis (for variables with $p < 0.1$) and multivariate analysis by logistic regression show that, after backward selection, only age (OR = 1.03; 95% CI = 1.01–1.06; $p = 0.013$) and hyperlipidemia (OR = 2.08; 95% CI = 1.05–4.12; $p = 0.035$) remained in the final model. Cardiopulmonary bypass time was associated with newly developed postoperative neurological complications in the univariate analysis (OR = 1.01; 95% CI = 1.003–1.02; $p = 0.001$) and, after model adjustment, was an independent risk factor (OR = 1.01; 95% CI = 1.01–1.02; $p < 0.001$). Aortic cross-clamp time was not associated in the univariate analysis ($p = 0.06$); however, an aortic cross-clamp time over 3 hours was associated both in the univariate analysis (OR = 2.2; 95% CI = 1.2–4.04; $p = 0.011$) and, after adjustment, as an independent risk factor (OR = 2.71; 95% CI = 1.43–5.14; $p = 0.002$). Cerebral perfusion time was associated in the univariate analysis (OR = 1.01; 95% CI = 1.001–1.03; $p = 0.042$) and, after adjustment for age and hyperlipidemia, remained an independent risk factor for newly developed postoperative neurological complications (OR = 1.02; 95% CI = 1.002–1.03; $p = 0.027$).

Table 4.4. General characteristics of patients undergoing emergency surgery for ATAAD

Parameter (Unit)	**n = 203 (100%)**
Age (years)	57.61 ± 12.27
Sex (male)	136 (67%)

EuroSCORE	9.03 ± 2.63
Time from diagnosis to surgery (hours)	4.89 ± 4.37
Arterial hypertension	130 (64%)
Diabetes mellitus	13 (6.4%)
Hyperlipidemia	140 (69%)
Chronic kidney disease	14 (6.9%)
Hemodynamically stable patients	149 (73.4%)
Preoperative atrial fibrillation	15 (7.4%)
Cardiogenic shock	22 (9.56%)
ST-elevation acute myocardial infarction	7 (3.44%)
Mesenteric ischemia	5 (2.46%)
Lower limb ischemia	32 (15.76%)
Aortic root aneurysm	11 (5.41%)
Chest pain	175 (86.2%)
Abdominal pain	32 (15.76%)
History of aortic aneurysm	45 (22.16%)
Acute heart failure	31 (15.27%)
Bicuspid aortic valve	26 (12.8%)
Maximum diameter (mm)	6.19 ± 1.19
Severe acute aortic regurgitation	59 (29.1%)
Severe left ventricular dysfunction (LVEF < 30%)	4 (1.97%)
Moderate left ventricular dysfunction (LVEF 30–40%)	5 (2.5%)
Mild left ventricular dysfunction (LVEF 40–50%)	111 (54.67%)
Cardiac tamponade at admission	49 (24.1%)
Innominate (brachiocephalic) artery dissection	55 (27.1%)
Brachiocephalic and left common carotid artery dissection	32 (15.8%)
Dissection of all supra-aortic vessels	20 (9.9%)
Primary entry tear in the ascending aorta	132 (65%)
Ascending aorta and aortic arch	17 (8.4%)
Aortic arch	66 (32.5%)
No entry tear identified	23 (11.3%)

Table 4.5. Intraoperative data; mean ± SD; n (%)

Operative data	**n = 203 (100%)**
No aortic arch intervention	76 (37.4%)
Supracoronary ascending aorta replacement	38 (18.7%)
Wheat procedure	6 (3%)
Aortic root and ascending aorta replacement	11 (5.4%)
Aortic arch intervention	127 (62.6%)
Ascending aorta and hemiarch replacement	108 (53.2%)
Ascending aorta and total arch replacement	9 (4.4%)
Aortic root, ascending aorta and hemiarch replacement	21 (10.3%)
Innominate artery reimplantation	6 (3%)
Innominate and left common carotid artery reimplantation	8 (3.9%)
Combined procedures	31 (15.3%)
Coronary artery bypass grafting (CABG)	11 (5.4%)
Mitral valve prosthesis	5 (2.46%)
Mitral valve repair	3 (1.47%)
Peripheral veno-arterial ECMO	2 (0.98%)
Non-coronary sinus reconstruction	2 (0.98%)
Femoral–femoral bypass	1 (0.5%)
Aortic coarctation repair	1 (0.5%)
Cannulation site	
Axillary artery	131 (64.5%)
Femoral artery	64 (31.5%)
Dissected ascending aorta	7 (3.4%)
Aortic arch	1 (0.5%)
Cardiopulmonary bypass time (min)	206.28 ± 63.22
Aortic cross-clamp time (min)	116.1 ± 38.4
Selective bilateral antegrade cerebral perfusion (min)	29.62 ± 22.27

Cerebral perfusion and deep hypothermic circulatory arrest	155 (76.4%)
Reoperation for mediastinal bleeding	50 (24.6%)

Table 4.6. Comparison between patients with type A dissection with and without neurological complications: mean ± SD; n (%)

Variable	**NC (+) n=80**	**NC (–) n=123**	**p**
Age	60.02 ± 10.71	56.04 ± 12.99	0.098
Male sex	54 (67.5%)	82 (66.7%)	0.902
Arterial hypertension	49 (61.3%)	81 (65.9%)	0.504
Diabetes mellitus	4 (5%)	9 (7.3%)	0.51
Hyperlipidemia	61 (76.2%)	79 (64.2%)	0.07
Chronic kidney disease	6 (7.5%)	8 (6.5%)	0.784
Cardiac tamponade	22 (27.5%)	27 (22%)	0.367
Severe aortic regurgitation	22 (27.5%)	37 (30.1%)	0.692
Preoperative atrial fibrillation	8 (10%)	7 (5.7%)	0.251
Dissection of supra-aortic vessels	26 (32.5%)	39 (31.7%)	0.906
One vessel	10 (12.5%)	22 (17.9%)	0.303
Two vessels	11 (13.8%)	7 (5.7%)	0.048
Three vessels	9 (11.2%)	11 (9%)	0.603
Bicuspid aortic valve	9 (11.2%)	17 (13.8%)	0.592
LVEF < 30%	3 (3.8%)	2 (1.6%)	0.34
LVEF 30–40%	2 (2.5%)	4 (3.3%)	0.757
LVEF 40–50%	32 (40%)	37 (30.1%)	0.145
No arch surgery	29 (36.2%)	47 (38.2%)	0.778
Wheat procedure	1 (1.2%)	5 (4.1%)	0.247

Aortic root surgery	15 (18.8%)	18 (14.6%)	0.437
Supracoronary ascending aorta replacement	12 (15%)	26 (21.1%)	0.273
Arch surgery	51 (63.7%)	76 (61.8%)	0.778
Innominate artery reimplantation	3 (3.8%)	3 (2.4%)	0.59
Innominate + left common carotid reimplantation	4 (5%)	4 (3.3%)	0.532
Total arch replacement	5 (6.2%)	4 (3.3%)	0.311
Hemiarch replacement	42 (52.5%)	66 (53.7%)	0.872
Combined procedures	9 (11.2%)	22 (17.9%)	0.199
Axillary artery cannulation	56 (70%)	49 (61%)	0.189
Femoral artery cannulation	24 (30%)	42 (34.1%)	0.583
Ascending aorta entry tear	48 (60%)	84 (68.3%)	0.226
Aortic arch entry tear	34 (42.5%)	32 (26%)	0.014
Ascending aorta and arch entry tear	12 (15.2%)	5 (4.1%)	0.005
No entry tear	10 (12.5%)	13 (10.6%)	0.671
Cardiopulmonary bypass time	224.8 ± 66.62	194.24 ± 58.07	0.004
Aortic cross-clamp time	122.47 ± 41.71	111.96 ± 35.66	0.12
Cerebral perfusion time	33.6 ± 22.25	27.02 ± 21.98	<0.001

Cerebral perfusion used	65 (81.2%)	90 (73.2%)	0.186
Death	19 (23.8%)	17 (13.8%)	0.07

Table 4.7. Logistic regression

	Univariate			**Univariate**		
Variable	**OR**	**95% CI**	**p**	**OR**	**95% CI**	**p**
Age (years)	1.02	1.01–1.05	0.025			
Aortic arch entry tear	2.36	1.29–4.35	0.015			
Ascending aorta and arch entry tear	5.25	1.77–15.61	0.009			
Dissection of two supra-aortic vessels	2.64	0.98–7.13	0.055			
Hyperlipidemia	1.79	0.95–3.37	0.072			
Cardiopulmonary bypass time	1.01	1.003–1.02	0.001	1.011	1.01–1.02	<0.001
Aortic cross-clamp time	1.007	1.003–1.015	0.060			
Aortic cross-clamp over 3 hours	2.20	1.20–4.04	0.011	2.71	1.43–5.14	0.002
Cerebral perfusion time	1.01	1.001–1.03	0.040	1.02	1.002–1.03	0.027

5.4. Discussions

The main results of the second study were: cardiopulmonary bypass time (OR = 1.011; 95% CI = 1.01–1.02; p < 0.001), aortic clamping time over three hours (OR = 2.71; 95% CI = 1.43–5.14; p = 0.002) and cerebral perfusion time (OR = 1.02; 95% CI = 1.002–1.03; p = 0.027) were independent risk factors associated with new postoperative NCs in the present study. This is in line with the GERAADA study, where increased operative times were associated with NC. In our study, the incidence of newly developed postoperative neurological complications (NC) was 39.4%. The high variability in reported NC incidence may be due to the difficulty of recording them in critically ill patients [36]. Data on pre- and postoperative NC are heterogeneous and there is considerable variability in their classification [37,38,39]. The incidence of ischemic stroke in this study was 23.6%, being the most frequent NC (60%), consistent with previous reports [40,41,42]. Ischemic stroke tends to occur more frequently in the anterior circulation (47.91%) than in the posterior circulation (20.83%) and is predominantly on the right side in both cases (25% right anterior carotid artery, 8.33% right vertebrobasilar artery). Involvement of supra-aortic vessels was observed in 39.6% of patients with ischemic stroke, and the frequency of involvement of two vessels was significantly higher in the NC group (16.7% vs. 6.5%; p = 0.03). One reason for the dominance of right-sided lesions may be the greater hydraulic stress on the right lateral wall of the ascending aorta [43]. However, 60.4% of patients with ischemic stroke had no involvement of supra-aortic vessels, suggesting that other mechanisms such as thromboembolism, microembolism, or hypotension are involved in the pathogenesis of ischemic stroke. Patients with ischemic stroke were significantly older (61.12 ± 9.27 vs. 56.52 ± 12.9; p = 0.011), which can be explained by the worsening of atherosclerosis with advancing age [18]. Sixteen patients (33.34%) with ischemic stroke died in the intensive care unit, and 43.75% had an mRS between 3 and 5, confirming the high mortality and morbidity of this postoperative complication. Hypoxic-ischemic encephalopathy is a severe complication of global ischemia, with a disability spectrum ranging from full recovery after coma to death, and data on long-term outcomes are scarce [44,45,46]. The incidence of hypoxic-ischemic encephalopathy in ATAAD is also rare. A retrospective study of 278 patients with type A and B aortic dissection found a preoperative incidence of 3.2% [47]. Blanco et al. reported 5 patients with preoperative hypoxic-ischemic encephalopathy out of 24 patients with ATAAD [41]. In our study, the incidence was 4.4% (nine patients). Systolic hypotension associated with cardiac tamponade was observed in four patients (44.4%) and with severe acute aortic regurgitation in two patients. Two patients had involvement of supra-aortic vessels, both with dissection of the brachiocephalic artery and the left common carotid artery, without involvement of the subclavian arteries. Spinal cord ischemia in ATAAD is also a rare condition and data on its incidence are limited [48]. It presents as an anterior spinal artery syndrome in 87.2% of cases, while SCI in the posterior spinal artery territory is very rare [164]. Two patients developed SCI in our study and both were discharged, one without recovery and the other with partial recovery from paraplegia. Postoperative delirium is a severe brain disorder characterized by inattention, disturbed thinking, and altered levels of consciousness [49,50]. A meta-analysis of 12 studies from 2016–2022 found that low oxygen level, prolonged mechanical ventilation, renal dysfunction, low hemoglobin level, and prolonged intensive care unit stay are risk factors for delirium in ATAAD [51]. Its incidence in cardiac surgery is high (32.5–52%) and it involves between 12 and 37% of patients with ATAAD [52,53]. In our study, 21 (10.3%) patients developed this

NC. Only one patient died in our study (mixed cardiogenic and septic shock). While preoperative risk factors for NC in ATAAD may be considered endogenous, patient-dependent, and non-modifiable, intraoperative factors largely depend on the surgical team and strategy.

6. Investigation of the association between bilateral selective antegrade cerebral perfusion and postoperative ischemic stroke in obese patients undergoing emergency surgery for acute type A aortic dissection.

6.1. Introduction

The incidence of obesity is increasing in all industrialized countries, and common comorbidities such as diabetes mellitus, hypertension, hyperlipidemia, and obesity-induced systemic inflammation pose a challenge in cardiac surgery, especially in cases requiring cardiopulmonary bypass [182]. Obese patients are more likely to develop ATAAD [12]. Moreover, obese patients undergoing emergency surgery for ATAAD have shown higher operative mortality and an increased risk of low cardiac output syndrome and pulmonary complications [183,184].

The relationship between obesity and postoperative neurological complications in patients undergoing surgery for ATAAD is not well defined. This study investigated the association between obesity and postoperative ischemic stroke in patients undergoing emergency surgery for ATAAD with HCA and selective antegrade cerebral perfusion.

6.2. Materials and Methods

Between January 2015 and May 2023, 319 patients were transferred to our center for ATAAD management. Diagnosis was based on thoracic computed tomography (CT) with intravenous contrast performed before admission. After cardiology consultation in the emergency department, with mandatory transthoracic echocardiography, patients eligible for emergency surgery were transferred to the operating room. Clinical characteristics and demographic data were collected from medical records and the electronic system.

Inclusion criteria: patients with acute type A aortic dissection according to the Stanford classification considered for emergency surgery.

Exclusion criteria:

(1) patients with hemorrhagic stroke documented on CT prior to admission who were not surgical candidates;

(2) patients with ischemic stroke documented on CT prior to admission and with severe neurological dysfunction who were not surgical candidates;
(3) patients who died in the operating room or within the first 48 hours after admission to intensive care;
(4) patients whose postoperative neurological status could not be assessed;
(5) patients with incomplete medical records.

Obesity was defined as a BMI over 30 kg/m². Neurological examination and brain CT were the methods used to diagnose a new postoperative ischemic stroke.

The incidence of newly developed postoperative ischemic stroke was investigated in patients undergoing emergency surgery for ATAAD. Patients with BMI over 30 kg/m² were divided into two groups: patients with selective ACP under 40 minutes and patients with selective ACP over 40 minutes, considering that literature data suggest that ACP is safer when DHCA exceeds 40 minutes [6]. To investigate the association between the duration of selective ACP in obese patients undergoing emergency surgery for ATAAD and the development of a new postoperative ischemic stroke, a multivariate analysis using logistic regression was performed.

6.3. Results

A total of 292 patients with ATAAD and emergency surgery were included in the study. Of these (Figure 7.3), 27 patients were excluded (3 patients with hemorrhagic stroke and 2 patients with massive ischemic stroke who were not surgical candidates, 4 patients with unrecovered cardiac arrest at admission, 5 patients with irreversible peripheral ischemia, 13 patients who died on the operating table, 10 due to hemorrhagic shock and 3 patients with myocardial infarction). Preoperative data are summarized in Table 4.8. The mean age was 59.42 ± 10.68 years, and the mean EuroSCORE was 9.12 ± 1.63. The mean time from ATAAD diagnosis to surgery was 3.89 ± 2.37 hours. Obesity was present in 76.4% of cases. The most common symptom at admission was chest pain, present in 92.1% of patients, followed by abdominal pain in 12.3% and syncope in 11% of cases. Preoperative ischemic stroke was documented by cranial CT in 7 patients (2.4%), 30 patients presented with lower limb ischemia, and mesenteric ischemia was documented clinically and by abdominal CT with contrast in 5 patients (2%). A bicuspid aortic valve was present in 9.24% of cases, acute severe aortic regurgitation in 25.3% of patients, and cardiac tamponade in 12.7% of cases. The brachiocephalic artery was the most frequently dissected supra-aortic artery, in 19.2% of cases, followed by the left common carotid artery in 12.9% of cases. The right common carotid artery was dissected in 7.7% of cases. In 48.6% of patients, the primary intimal tear was located in the ascending aorta. Intramural hematoma was diagnosed in 8.6% of cases, and penetrating aortic ulcers were present in 2.1% of patients. Postoperative death occurred in 26.7% of patients (78 cases). The causes of death were as follows: septic shock in 36 patients (46.15%) and cardiogenic shock in 12 patients.

Intraoperative and postoperative data

Table 4.9 summarizes intraoperative and postoperative data. The incidence of a new postoperative ischemic stroke was 27.5% (81 patients). The incidence of in-hospital death in patients with ischemic stroke was 31.8% (28 patients), and 81.8% (73 patients) were obese. The mean cardiopulmonary bypass time was 206.81 ± 75.48 minutes, and the mean aortic clamp time was 118.2 ± 46.42 minutes. In 90% of cases, cerebral perfusion was applied with a mean duration of 30.8 ± 24.41 minutes. The supracoronary ascending aorta was replaced in 96.9% of cases. At the level of the aortic arch, hemiarch replacement was performed in 45.9% of patients, and total arch replacement was selected in 5.5% of cases. Aortic root replacement was necessary in 23.3% of patients. Concomitant procedures were required in 72 patients: coronary bypass in 5.5% of cases, mitral valve repair in 1% of cases, aortic valve replacement in 16.8% of cases, peripheral VA ECMO in two patients, one patient required femoro-femoral bypass, and one patient had aortic coarctation repair. Axillary artery cannulation was performed in 64.5% of cases, followed by femoral artery cannulation in 31.5% of patients. Early reoperation for mediastinal bleeding was necessary in 24.1% of patients. The mean intensive care stay was 11.2 ± 13.6 days, prolonged mechanical ventilation over 24 hours was required in 74% of patients, and dialysis was required in 51% of cases. Postoperative mesenteric ischemia was observed in 22 patients (7.5%), while 6 patients (2.1%) developed deep sternal wound infections. The treatment of mesenteric ischemia was open abdominal surgery with resection of the affected intestine in 21 patients, and one patient received interventional treatment with stenting of the superior mesenteric artery.

Characteristics of obese patients

Table 4.10 shows the comparison between patients with and without obesity. Regarding preoperative characteristics, obese patients had a higher frequency of in-hospital death ($p = 0.009$), hyperlipidemia ($p = 0.03$), smoking ($p = 0.036$), hypertension ($p = 0.023$), dissection of the left common carotid artery ($p < 0.001$) and dissection of the right common carotid artery ($p = 0.029$). A higher frequency of femoral artery cannulation ($p = 0.026$), aortic root replacement ($p = 0.009$), aortic valve replacement ($p = 0.005$) and early reoperation for bleeding ($p = 0.004$) was observed in obese patients. No differences were observed between the two groups regarding characteristics.

7.3.5. Logistic regression

The variables included in the univariate analysis were: age, smoking, hypertension, female sex, diabetes, chronic obstructive pulmonary disease, family history of aortic dissection, anemia, renal dysfunction, liver dysfunction, lactic acidosis, BMI, at admission: chest pain, abdominal pain, syncope, lower limb ischemia, mesenteric ischemia, cardiac tamponade, severe aortic regurgitation, severe ventricular dysfunction, intimal tear in the ascending aorta, intimal tear in the aortic arch, dissection of the brachiocephalic artery, dissection of the right common carotid artery, dissection of the right subclavian artery, dissection of the left common carotid artery, dissection of the left subclavian artery, cardiopulmonary bypass time, aortic clamp time, cerebral perfusion time, femoral artery cannulation, axillary artery cannulation, aortic root replacement, supracoronary ascending aorta replacement, hemiarch replacement, total arch replacement, coronary bypass, aortic valve replacement, mitral valve repair, and early reoperation for bleeding. The results of the univariate analysis of variables associated with a new postoperative ischemic stroke with p value < 0.5 are presented in Table 4.11. Cardiac tamponade at admission (OR = 6.27; 95% CI = 2.57–15.25; $p < 0.01$) and dissection of the brachiocephalic artery (OR = 0.21; 95% CI = 0.06–0.72; $p = 0.013$) were included in the final model after backward selection. Selective antegrade cerebral perfusion over 40 minutes in obese patients was associated with a new postoperative ischemic stroke (OR = 2.18; 95% CI = 1.12–4.22; $p = 0.021$) in the univariate analysis and, after model adjustment, was independently associated with a new postoperative ischemic stroke (OR = 2.35; 95% CI = 1.14–4.86; $p = 0.021$).

Table 4.8. Preoperative characteristics of patients included in the study

Variable	**N = 292**
Preoperative variables	
Age (years)	59.42 ± 10.68

EuroSCORE	9.12 ± 1.63
Time from diagnosis to surgery (hours)	3.89 ± 2.37
Obesity (BMI > 30 kg/m²)	223 (76.4%)
Hyperlipidemia	202 (69.5%)
Smokers	85 (29.1%)
Female sex	92 (31.5%)
Hypertensive	269 (92.1%)
Diabetes	23 (7.9%)
COPD	14 (4.8%)
Aortic diameter (mm)	6.36 ± 1.29
Family history of aortic dissection	7 (2.4%)
Chest pain	269 (92.1%)
Abdominal pain	36 (12.3%)
Syncope	32 (11%)
Lower limb ischemia	30 (10.3%)
Mesenteric ischemia	5 (2%)
Preoperative ischemic stroke	7 (2.4%)
Cardiac tamponade	37 (12.7%)
Cardiogenic shock	17 (5.8%)
ST-segment depression	32 (11%)
ST-segment elevation	25 (8.6%)
Bicuspid aortic valve	27 (9.24%)
Severe aortic regurgitation	74 (25.3%)
Severe left ventricular dysfunction	14 (4.8%)
Pericardial effusion	158 (54.1%)
Intramural hematoma	25 (8.6%)
Penetrating aortic ulcers	6 (2.1%)
Intimal tear in the ascending aorta	142 (48.6%)
Intimal tear in the aortic arch	13 (4.5%)
Dissection of the brachiocephalic artery	55 (19.2%)
Dissection of the right common carotid artery	22 (7.7%)
Dissection of the left common carotid artery	37 (12.9%)

Dissection of the right subclavian artery	13 (4.5%)
Dissection of the left subclavian artery	24 (8.4%)

Table 4.9. Intraoperative and Postoperative Data

Intraoperative and Postoperative Data	**Values**
Cardiopulmonary bypass time (minutes)	206.81 ± 75.48
Aortic cross-clamp time (minutes)	118.2 ± 46.42
Cerebral perfusion time (minutes)	30.8 ± 24.41
Hypothermic circulatory arrest and cerebral perfusion	262 (90%)
Axillary artery cannulation	144 (49.3%)
Femoral artery cannulation	140 (47.9%)
Ascending aorta cannulation	8 (2.74%)
Aortic root replacement	68 (23.3%)
Supracoronary ascending aorta replacement	283 (96.9%)
Hemiarch replacement	134 (45.9%)
Total aortic arch replacement	16 (5.5%)
Combined procedures	68 (23.28%)
Aortic valve replacement	49 (16.8%)
Coronary artery bypass grafting (CABG)	16 (5.5%)
Mitral valve repair	3 (1%)
Femoro-femoral bypass	1 (0.34%)
Aortic coarctation repair	1 (0.34%)
Peripheral VA ECMO	2 (0.68%)
Postoperative	
Early reoperation for bleeding	70 (24.1%)
Mean ICU stay (days)	11.2 ± 13.6
Mechanical ventilation >24 h	216 (74%)
Dialysis	149 (51%)
Ischemic stroke	81 (27.5%)
Hemiplegia	63 (21.57%)

Coma	11 (3.76%)
Aphasia	5 (2.6%)
Visual field deficits	2 (0.68%)
Mesenteric ischemia	22 (7.5%)
Deep sternal wound infection	6 (2.1%)

Table 4.10. Comparison between patients with and without obesity

Variable	BMI < 30 kg/m² (n=69)	BMI > 30 kg/m² (n=223)	p
Age (years)	59.46 ± 8.16	59.41 ± 11.36	0.828
Smokers	27 (39.1%)	56 (26%)	0.036
Female sex	27 (39.1%)	65 (29.1%)	0.119
Hypertension	68 (98.6%)	201 (90.1%)	0.023
Hyperlipidemia	26 (37.7%)	176 (79%)	0.03
Diabetes	4 (5.8%)	19 (8.5%)	0.463
COPD	2 (2.9%)	12 (5.4%)	0.399
Family history of aortic dissection	2 (2.9%)	5 (2.2%)	0.755
Chest pain	65 (94.2%)	204 (91.5%)	0.463
Abdominal pain	8 (11.6%)	28 (12.6%)	0.832
Syncope	12 (17.4%)	20 (9%)	0.05
Lower limb ischemia	6 (8.7%)	24 (10.8%)	0.621
Mesenteric ischemia	1 (1.7%)	5 (2.1%)	0.825
Ischemic stroke	1 (1.4%)	6 (2.7%)	0.556
Cardiac tamponade	9 (13%)	28 (12.6%)	0.915
Cardiogenic shock	3 (4.3%)	14 (6.3%)	0.550
ST-segment depression	10 (14.5%)	22 (9.9%)	0.282
ST-segment elevation	7 (10.1%)	18 (8.1%)	0.591
Aortic regurgitation (TTE)	65 (94.2%)	190 (85.2%)	0.05
Pericardial effusion (TTE)	32 (46.4%)	126 (56.5%)	0.14
Severe LV dysfunction (TTE)	1 (1.4%)	13 (5.8%)	0.137
Intimal tear ascending aorta (TEE)	8 (11.9%)	50 (22.4%)	0.06
Intramural hematoma (TEE)	4 (6%)	21 (9.4%)	0.378
Aortic plaque (TEE)	2 (3%)	4 (1.8%)	0.536

Brachiocephalic artery dissection	34 (25%)	39 (17.5%)	0.178
Right common carotid artery dissection	10 (14.1%)	13 (5.8%)	0.029
Left common carotid artery dissection	18 (26.6%)	20 (9%)	<0.001
Right subclavian artery dissection	4 (6.2%)	9 (4%)	0.453
Left subclavian artery dissection	9 (12.5%)	16 (7.2%)	0.175
CPB time (minutes)	192.02 ± 73.18	211.39 ± 75.76	0.558
Aortic cross-clamp time (minutes)	113.53 ± 48.23	119.65 ± 45.86	0.392
Cerebral perfusion time (minutes)	31.58 ± 23.54	30.53 ± 24.78	0.38
Femoral artery cannulation	25 (36.2%)	115 (51.6%)	0.026
Axillary artery cannulation	41 (59.4%)	103 (46.2%)	0.055
Cerebral perfusion	45 (65.2%)	145 (64.9%)	0.957
Aortic root replacement	8 (11.6%)	154 (26.9%)	0.009
Ascending aorta replacement	64 (92.8%)	219 (98.2%)	0.022
Hemiarch replacement	32 (46.4%)	102 (45.7%)	0.926
Total arch replacement	2 (2.9%)	14 (6.3%)	0.281
Aortic valve replacement	4 (5.8%)	45 (20.2%)	0.005
Coronary bypass	5 (7.2%)	11 (4.9%)	0.461
Mitral valve repair	0 (0%)	3 (1.3%)	0.333
Early reoperation for bleeding	26 (37.3%)	45 (20.2%)	0.004
ICU days	13.18 ± 14.41	10.62 ± 13.37	0.859
In-hospital mortality	10 (14.5%)	68 (30.5%)	0.009
Mechanical ventilation >24 h	56 (81.2%)	160 (71.7%)	0.12
Dialysis	30 (43.5%)	119 (53.4%)	0.151
Multiple organ failure	17 (24.6%)	81 (36.3%)	0.072
Ischemic stroke	15 (21.7%)	66 (29.6%)	0.203
Mesenteric ischemia	6 (8.7%)	16 (7.2%)	0.676
Mediastinitis	1 (1.4%)	5 (2.2%)	0.685

Table 4.11. Logistic Regression

	Univariate			**Multivariable**		
Variable	**OR**	**95% CI**	**p**	**OR**	**95% CI**	**p**

Family history of aortic dissection	6.87	1.31–36.18	0.023			
Lower limb ischemia	0.07	0.01–0.58	0.013			
Cardiac tamponade on admission	4.87	2.37–9.96	<0.001	6.27	2.57–15.25	<0.001
Primary intimal tear in ascending aorta	0.17	0.05–0.56	0.004			
Dissection of brachiocephalic artery	0.26	0.11–0.65	0.004	0.21	0.06–0.72	0.013
Dissection of left subclavian artery	0.20	0.06–0.68	0.01			
Cardiopulmonary bypass time	1.004	1.001–1.007	0.028			
Cerebral perfusion time	0.01	0.005–0.031	0.008			
Aortic root replacement	0.42	0.21–0.85	0.017			
Hemiarch replacement	3.038	1.78–5.18	<0.001			
Reoperation for bleeding	1.93	1.09–3.41	<0.001			
BMI >30 kg/m² and BSACP >40 min	2.18	1.12–4.22	0.021	2.35	1.36–4.86	0.021

6.4. Discussions

The main result of the third study is that selective ACP over 40 minutes is associated with newly developed postoperative ischemic stroke in obese patients (BMI > 30 kg/m²) undergoing emergency surgery for acute type A aortic dissection with HCA. This result is consistent with data from the literature on risk factors for neurological complications (GERAAD, NORCAD). Obese patients had a higher frequency of in-hospital death, femoral artery cannulation, dissection of the left and right carotid arteries, aortic root replacement, aortic valve replacement, and early reintervention for bleeding. The incidence of ischemic stroke in this study was 27.5%. This is consistent with previous studies reporting an incidence of up to 32.8% in NC [54–58]. Of the 223 patients with a BMI over 30 kg/m², 75.7% had selective ACP, and 66 (29.6%) patients developed ischemic stroke. Literature data suggest an increased risk of air or atheromatous embolism when arch vessels are manipulated during surgery [59]. This could explain the high incidence of ischemic stroke in our study, given the association between obesity and atherosclerosis. Inflammation is the link between the two and is explained by the fact that adipose tissue releases adipokines, which in turn induce insulin resistance, endothelial dysfunction, and hypercoagulability, all of which promote atherosclerosis [60]. There are reports stating that operative times are longer in obese patients [61,62], and combined with the technical difficulties of establishing selective ACP, could increase the rate of ischemic stroke. Operative time was not significantly higher in obese patients in our study (CPB time: 192.02 ± 73.18 vs. 211.39 ± 75.76; p = 0.558; aortic clamp time: 113.53 ± 48.23 vs. 119.65 ± 45.86; p = 0.392; cerebral perfusion time: 31.58 ± 23.54 vs. 30.53 ± 24.78; p = 0.38). The mean cerebral perfusion time in our study was 30.8 ± 24.41 min and 30.53 ± 24.78 min in obese patients. Given this, our data do not support the claim that BSACP is technically more complex.

Obese patients undergoing emergency surgery for acute type A aortic dissection had significantly higher in-hospital mortality (14.5% vs. 30.5%; p = 0.009). This finding is supported by data from several studies [63,64,65]. The high mortality rate could be explained by the increased risk of low cardiac output syndrome and pulmonary complications in obese patients [66]. Inflammatory mechanisms seem to be involved in the process of lung injury in obese patients [67]. Obesity may play a protective role regarding perioperative bleeding and transfusion requirements [68]. Studies report this "obesity paradox" in patients undergoing myocardial revascularization [207,226]. In our study, this does not seem to be the case, as obese patients had higher rates of early reintervention for bleeding (37.3% vs. 20.2%; p = 0.004). This could be explained by a higher incidence of coagulopathy, given the complexity of surgery for acute type A aortic dissection with HCA and longer CPB times, compared to myocardial revascularization alone or combined with valve procedures.

7. Conclusions and Personal Contributions

The doctoral thesis consists of three retrospective studies including patients who underwent emergency surgical reintervention for a diagnosis of acute type A aortic dissection according to the Stanford classification.

There is increasing interest in identifying risk factors for neurological complications in these patients, given their significant impact. In the literature, there is heterogeneity in the risk factors identified for neurological complications. These differences can be explained by several reasons:

1. Patients operated for acute type A aortic dissection have heterogeneous demographic profiles and comorbidities that influence vulnerability to ischemia, especially during extracorporeal circulation.
2. There are differences between patient inclusion and exclusion criteria. While some studies include only patients operated in absolute emergencies, others also include chronic or subacute patients. Furthermore, excluding patients with severe hemodynamic instability or severe neurological dysfunction may alter the identified risk factors.
3. The lack of a standardized definition of neurological complications. While some studies analyze only stroke, others include postoperative encephalopathy, delirium, seizures, transient strokes, spinal cord ischemia, peripheral neuropathy, cognitive dysfunction, etc.
4. Different surgical and anesthetic strategies. Neurological risk is influenced by the cannulation method, type of cerebral perfusion, duration of circulatory arrest, degree of hypothermia, duration of extracorporeal circulation, and myocardial ischemia time.
5. Center experience and surgical volume, as well as technological evolution and changing cerebral protection protocols. Thus, high-volume centers with specialized multidisciplinary teams have shorter operative times and more advanced cerebral monitoring protocols (NIRS, color Doppler transcranial ultrasound, Diffuse Correlation Spectroscopy, and Frequency-Domain near-Infrared Spectroscopy), which may influence the identification of risk factors.

6. Individual anatomical factors such as variability of the circle of Willis or pre-existing stenoses at the level of supra-aortic or intracerebral vessels, rarely evaluated preoperatively, may lead to heterogeneous identification of risk factors.

The purpose of the doctoral thesis was to establish clear definitions for postoperative neurological complications in patients undergoing emergency surgery for acute type A aortic dissection and to identify risk factors both particularly for ischemic stroke and more generally for neurological complications.

To standardize this study as much as possible and to avoid the above reasons regarding the identification of risk factors, patients included were operated in a single center, surgical interventions were standardized, the same technique was used for cerebral perfusion (selective antegrade cerebral perfusion), for the temperature at which circulatory arrest was performed, and for the cerebral monitoring technique, all known to have a direct impact on neurological prognosis.

The neurological complications investigated included: ischemic stroke, spinal cord ischemia, postoperative delirium, and hypoxic encephalopathy. In this work, the definitions and diagnostic criteria established by current international guidelines were used. Ischemic stroke is defined according to the American Heart Association and American Stroke Association Guidelines for the Early Management of Acute Ischemic Stroke (2021). Post-hypoxic ischemic encephalopathy is described based on the recommendations of the European Resuscitation Council and the American Heart Association on post-resuscitation care (2021). Postoperative delirium is defined and classified according to the Society of Critical Care Medicine and anesthesia societies guidelines, which establish diagnostic, prevention, and treatment criteria (2022). Spinal cord ischemia is defined according to the recommendations of the Society of Thoracic Surgeons and the European Society of Cardio-Thoracic Surgery for thoracic aortic surgery and spinal cord protection (2022). These references allow the standardization of diagnosis and analysis, minimizing heterogeneity of results.

Statistical analysis for risk factor identification was the same in all three studies, using the logistic regression method. Determining the incidence of neurological complications was the primary objective, followed by risk factor analysis through univariate and then multivariate analysis.

First study (Association between Bilateral Selective Antegrade Cerebral Perfusion and Postoperative Ischemic Stroke in Patients with Emergency Surgery for Acute Type A Aortic Dissection—Single Centre Experience), published in the journal Medicina MDPI (Q1, IF 2.4) on July 26, 2023, and included 129 patients who underwent emergency surgery for acute type A aortic dissection. This study investigates the association between different intervals of cerebral perfusion—under 30 min, between 30 and 40 min, and over 40 min—and postoperative ischemic stroke. The incidence of this postoperative complication was 24.8%, namely 31 patients. Of these, 41.93% of patients were discharged with severe disability (mRS of 6). Selective antegrade cerebral perfusion over 40 minutes was independently associated with the occurrence of postoperative ischemic stroke (OR = 3.589, 95% CI = 1.418–9.085, p = 0.007). The intervals under 30 min and between 30–40 min were not associated in univariate analysis with the occurrence of this complication. Given the high incidence of postoperative stroke in our study population (24.8%), we concluded that selective bilateral ACP should be used with caution, especially in patients with severely calcified ascending aorta or aortic arch and supra-aortic vessels. Careful handling of these vessels at the time of introducing and securing the balloon cannulas and deairing the vessels upon completion of the distal anastomosis are mandatory. Perfusion parameters must be carefully adapted for each patient according to NIRS values. Every effort must be made to minimize the duration of circulatory arrest when using selective bilateral ACP, with a target of under 30–40 minutes at a body temperature of 25–28 °C.

Second study (Factors Associated with Newly Developed Postoperative Neurological Complications in Patients with Emergency Surgery for Acute Type A Aortic Dissection), published in the journal Medicina MDPI (Q1, IF 2.4) on December 23, 2023, included 203 patients. This study investigates risk factors associated with postoperative neurological complications in patients undergoing emergency surgery for acute type A aortic dissection. Neurological complications occurred in 39.4% of patients. The incidence of neurological complications was as follows: 23.6% for ischemic stroke, 10.3% for postoperative delirium, 4.4% for hypoxic encephalopathy, and 1% for postoperative spinal ischemia. The risk factors associated with neurological complications were cardiopulmonary bypass time (OR = 1.01; 95% CI = 1.01–1.02; p < 0.001), aortic clamping time exceeding 3 hours (OR = 2.71; 95% CI = 1.43–5.14; p = 0.002), and cerebral perfusion time (OR = 1.02; 95% CI = 1.002–1.03; p = 0.027). These results underline that perioperative management, the technical facilities of each center, and surgical strategies are important in the prognosis of these patients. Every effort must be made to minimize operative times, given that the study results prove that longer operative times are associated with an increased risk of NC.

Third study (Investigation of the Association between Bilateral Selective Anterograde Cerebral Perfusion and Postoperative Ischemic Stroke in Obese Patients with Emergency Surgery for Acute Type A Aortic Dissection), published on April 19, 2024 in the journal Medicina MDPI (Q1, IF 2.4), analyzed data from 292 patients. This study specifically aimed to investigate the association between selective cerebral perfusion and obese patients undergoing emergency surgery. This study was justified by the high incidence of obesity in the study population and by the difficulties related to the surgical technique and management of these patients (special anticoagulation and hemostasis regimen, cerebral perfusion monitoring and different cerebral perfusion parameters, systemic inflammatory syndrome, particular sternal reinforcement). The incidence of postoperative ischemic stroke was 27.5%, of which 81.8% were obese (BMI > 30 kg/m^2). The incidence of obese patients in the study population was 76.4% of cases. Selective cerebral perfusion over 40 min was again independently associated with postoperative ischemic stroke (OR = 2.35; 95% CI = 1.14–4.86; $p = 0.021$). In addition to the conclusions from the first study, this result could be explained by the increased atheromatous burden, more frequent in obese patients, at the level of the supra-aortic vessels, together with the risk of atheromatous embolism when selective bilateral ACP is used.

Regarding the personal contributions, they are as follows:

1. Use of standard definitions for neurological complications — I studied risk factors using standardized definitions for neurological complications according to current guidelines. This approach reduced diagnostic variability and allowed correlated analysis of clinical data.
2. Standardization of the surgical technique and protocols — The analysis of risk factors was carried out based on a uniform surgical technique and a standardized protocol of circulatory arrest and cerebral perfusion. Thus, methodological variables that can influence the incidence of neurological complications were eliminated.
3. Exclusively selective antegrade cerebral perfusion — In all included cases, cerebral protection was achieved by selective antegrade cerebral perfusion, without the use of retrograde perfusion. This uniformity allowed a clear assessment of the relationship between perfusion duration and postoperative neurological risk.

4. Single-center cohort — The analysis was performed on patients treated in a single cardiovascular surgery center. This ensures consistency of demographic data, perioperative protocols, and monitoring criteria.
5. Uniform statistical methodology — All analyses were performed using multivariate logistic regression, allowing the identification of independent risk factors for neurological complications.
6. Creation of a unified database for patients with acute type A aortic dissection — The prospective database integrated clinical, intraoperative, and postoperative information, enabling accurate correlation between risk factors and neurological outcomes.
7. Direct correlation of intraoperative parameters with neurological outcome — In addition to classical variables (duration of cerebral perfusion, aortic clamping duration, extracorporeal circulation duration), I included markers such as temperature at the initiation of circulatory arrest and the flow of selective antegrade perfusion. This level of detail is rarely reported in similar studies.
8. Differentiated subgroup analysis, including obese patients — I performed stratified analyses by weight status, demonstrating for the first time the independent association between selective antegrade cerebral perfusion duration and postoperative ischemic stroke in obese patients. This contribution has prognostic value and potential clinical application.
9. Standardization of inclusion/exclusion criteria — I used strict criteria to exclude patients with preexisting neurological deficit or major neurological comorbidities. This approach eliminated confounding factors and allowed a “cleaner” evaluation of intraoperative risks.
10. Integration of preoperative imaging data into risk analysis — For the first time, neurological risk assessment included the uniform interpretation of preoperative imaging (brain CT, aortic CT angiography), which allowed correlation of the dissection location or cerebral malperfusion with postoperative complications.
11. Comparative evaluation of circulatory arrest duration and cerebral perfusion duration — I identified pragmatic thresholds (for example, >40 minutes selective antegrade cerebral perfusion) for increased risk of neurological complications, useful for guiding intraoperative decisions.
12. Reporting of a single-center cohort with a uniform operative strategy — All patients benefited from the same operative strategy, eliminating interinstitutional variability.

13. Use of a robust statistical method to validate results — I applied multivariate logistic regression with adjustment for confounding factors, internally validated (goodness-of-fit, ROC curves), conferring robustness to the conclusions.
14. Identification of a combined risk profile — I proposed a risk model based on operational parameters (aortic clamping duration, CPB duration, cerebral perfusion duration) integrated with patient factors (obesity), usable as a risk stratification tool for patients with acute type A aortic dissection.
15. Generation of hypotheses for future studies — The results suggest research directions for improving cerebral protection, including personalized algorithms based on hemodynamic status, BMI, anatomical peculiarities of the circle of Willis, and biological markers of cerebral ischemia.
16. Identified results:

    • Selective antegrade cerebral perfusion longer than 40 minutes was independently associated with postoperative ischemic stroke.

    • The major risk factors for postoperative neurological complications were extracorporeal circulation time, cerebral perfusion duration, and aortic clamping time over 3 hours.

    • In obese patients, selective antegrade cerebral perfusion longer than 40 minutes was independently associated with ischemic stroke.

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