ORIGINAL ARTICLE

HEMODYNAMIC PREDICTORS AND CHANGES DURING CAROTID ENDARTERECTOMY UNDER REGIONAL ANESTHESIA

Vera A. Silva[1]*, Luís D. Gamas[2,3]*, A.; Juliana Pereira-Macedo[1,4]; Mariana Carreira[5]; Piotr Myrcha[6,7], José P. Andrade[8,9], André L. Moreira M[2,10]; João Rocha-Neves[8,9]

[1] Faculty of Medicine, University of Porto, Portugal
[2] Department of Physiology and Surgery, Faculty of Medicine, University of Porto, Portugal
[3] Department of Angiology and Vascular Surgery, Centro Hospitalar Universitário de São João, Porto, Portugal
[4] Department of General Surgery, Centro Hospitalar do Médio-Ave, Vila Nova de Famalicão, Portugal
[5] Centro Hospitalar de Leiria
[6] 1st Chair and Department of General and Vascular Surgery, Faculty of Medicine, Medical University of Warsaw, 02-091 Warsaw, Poland
[7] Department of General, Vascular and Oncological Surgery, Masovian Brodnowski Hospital, 03-242 Warsaw, Poland
[8] CINTESIS@RISE, RISE@Health, Faculty of Medicine, University of Porto, Portugal
[9] Department of Biomedicine – Unity of Anatomy, Faculty of Medicine of the University of Porto, Portugal
[10] Cardiovascular R&D Centre – UnIC@RISE, Department of Surgery and Physiology, Faculty of Medicine of the University of Porto, Porto, Portugal

* Corresponding author: ju.p.macedo18@gmail.com

Abstract

Objectives: *Carotid endarterectomy (CEA) is the standard treatment for carotid stenosis, but it can lead to cerebral hypoperfusion and hemodynamic stroke. Regional anesthesia (RA) and light sedation allow continuous monitoring of intraoperative neurological function. However, the relationship between perioperative hemodynamic management and neurological dysfunction has yet to be thoroughly investigated. This study aims to identify hemodynamic patterns that are associated with intraoperative cerebral ischemia in CEA under RA.*

Material and Methods: *Patients who underwent CEA at an academic tertiary referral center between January 2012 and December 2019 were included. Cases were individuals who developed intraoperative neurological deficits (ND). Consecutive controls without ND were sampled in 1:1 ratio.*

Results: *154 patients were included, 78.6% male, and mean age was 70.1±9.1 years. Cases were on average older than controls (72.0 ± 9.90 vs 68.3 ± 8.3 years, p=0.012). Baseline systolic blood pressure (SBP) values were higher in the ND group (154.6 ± 31.8 vs 141.8 ± 41.2 mmHg, p=0.035), alongside pulse pressure (98.1 ± 24.0 vs. 87.4 ± 32 mmHg, p=0.023). The ND group also had a statistically significant higher mean arterial pressure at the 3rd-minute post-clamp (108.3 ± 19.7 vs 101.1 ± 20.2 mmHg, p=0.028) and a smaller drop in SBP between the pre-clamp and the 1st and 3rd minutes post-clamp (11.95±16.19 vs. 19.79±24.01 mmHg, p=0.021 and 11.12±21.83 vs 19.42±26.78 mmHg, p=0.039, respectively).*

Conclusions: *Intraoperative ND showed no characteristic predictive pattern, besides higher SBP. Hemodynamic management could be key for preventing unwanted deficits.*

Keywords: *Carotid stenosis; neurologic exam; hemodynamic monitoring; awake test; locoregional anesthesia.*

INTRODUCTION

Carotid endarterectomy (CEA) is an established and beneficial procedure for treating and preventing cerebral ischemic events in patients with severe symptomatic carotid stenosis. Its efficacy has been demonstrated through randomized clinical trials [1]. CEA is routinely performed as a standard procedure for eligible patients. [2, 3]. This procedure is recommended for symptomatic patients or patients with a high degree of stenosis (>70%), which in turn results in an increased risk of stroke [4]. However, the procedure carries a risk of clamp-associated intraoperative cerebral ischemia [5], whose currently recommended method of detection is the clinical assessment of neurologic deficits (ND) under regional anesthesia (RA) [6]. It is important to note that patients who develop ND during the procedure are at a higher risk of

postoperative morbidity [7-9], including an increased risk of stroke. These factors raise concerns regarding the risk-benefit profile of surgical intervention in such cases.

Lately, pre-CEA morbidity factors have been associated with worse outcomes. These factors include advanced age, body mass index (BMI) >30kg/m^2, an ipsilateral low-grade carotid stenosis, contralateral high-grade stenosis, and increased red blood cell distribution width [10]. These factors are associated with an increased risk of complications and poorer outcomes following CEA [9, 10]. Thus, risk calculators are under development to highlight which patient variables have the greatest discriminatory power for risk and predict which patients will benefit the most from CEA [11].

To mitigate the risk of ischemia during carotid cross-clamping (CACC), current prevention measures emphasize the importance of avoiding intraoperative hypotension and implementing strategies to increase mean arterial pressure (MAP) by approximately 20% [8, 12]. In patients undergoing CEA, it is common to observe hypotension, hypertension, and bradycardia episodes during the perioperative period. These hemodynamic changes can be attributed to various factors such as the underlying disease, administration of vasoactive drugs, surgical manipulation of the carotid sinus, and other related factors [13]. However, there are a few studies, yet not conclusive, that hypothesize that severe preoperative hypertension should predispose the patient to future cardiovascular and/or neurological complications [8, 12].

This study investigates the relationship between the hemodynamic profile during CEA under RA and the occurrence of intraoperative ND.

METHODS

Study Population

The present work follows the Strengthening the Reporting of Cohort Studies in Surgery (STROCSS) criteria [14]. The study protocol respects the Declaration of Helsinki and follows the European Union General Data Protection Regulation (GDPR). The local Ethics Committee approved the study protocol (protocol 248 -18).

This study is based on a previously conducted nested case-control database. A secondary analysis was performed on 154 patients who underwent carotid endarterectomy (CEA) under regional anesthesia (RA) as a sole procedure. The study period ranged from January 2012 and December 2019, and the procedures were performed at an academic tertiary referral center.

Cases were defined as patients who developed de novo intraoperative neurological deficits (ND), detected through neurologic examination. A total of 77 cases were identified. Control patients (n=77) were selected in a concurrent 1:1 fashion, meaning one immediately consecutive control patient was chosen for each case. The control patients underwent the same surgical and anesthetic technique but did not develop ND (Fig.1). Patients who received an anesthetic modality other than RA or underwent concomitant cardiac surgery were excluded from the study.

Data on comorbidities and demographics of study participants were collected. Information regarding medications administered during the intraoperative period and blood pressure measurements at various time points during the CEA procedure was also recorded. One month after the procedure, patients were reevaluated in an outpatient setting. Subsequently, yearly follow-up assessments were conducted for a total of two years. After the two-year mark, patients were advised to continue their follow-up with their respective family physicians.

Database of the present study sample is registered and available at clinicaltrials.gov (NCT04347785).

CEA protocol

The degree and extent of atherosclerotic lesions were measured using Doppler ultrasound or computed angiography tomography, as indicated by clinical guidelines [15]. Pre-procedure consultations with both the angiology and anesthesiology teams were carried out to evaluate the patients' overall health condition, assess potential risks, and determine the appropriate indications for the procedure. Following established clinical guidelines, patients were prescribed antiplatelet therapy and a statin for a minimum duration of two days before the CEA procedure [16]. Pharmacological or mechanical thrombolysis was not administered to patients in the present study. An ipsilateral ultrasound guided "intermediate" cervical plexus block was performed on all patients for anesthesia by injecting 12-15mL of ropivacaine 0.75% posterior to the plane of the sternocleidomastoid muscle. Conscious sedation was achieved using continuous infusion of dexmedetomidine, at a maximum rate of 0.7 μg/kg/h. Benzodiazepines were optionally added to the sedation regimen based on the anesthesiologist's preference.

Hemodynamic status monitoring

During the intraoperative period, BP was continuously monitored by arterial catheterization of the upper limb contralateral to the carotid artery being operated on. The target mean BP range was set between 100 and 120% of baseline BP. Several time points were analyzed, including at admission by the nursing team, after arterial catheterization, after the regional block, pre-clamping of the carotid artery, and at 1, 3, and 10 minutes after clamping. The latest time point analyzed was set at 10 minutes to avoid potential confounders such as surgical technique (carotid sinus denervation in eversion CEA vs. preservation in patched CEA) and shunt insertion, which usually occurred beyond that time mark. The zenith (highest) and nadir (lowest) pressures after clamping were also recorded.

In addition to blood pressure, other hemodynamic parameters, such as pulse pressure (PP), heart rate (HR), and oxygen saturation, were also simultaneously analyzed and documented for each patient.

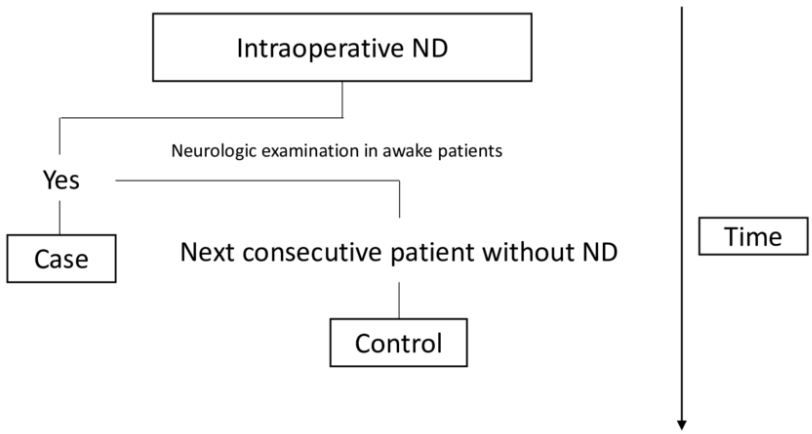

Figure 1

Summary of the study design
ND - Alterations on the neurologic examination during carotid clamping.

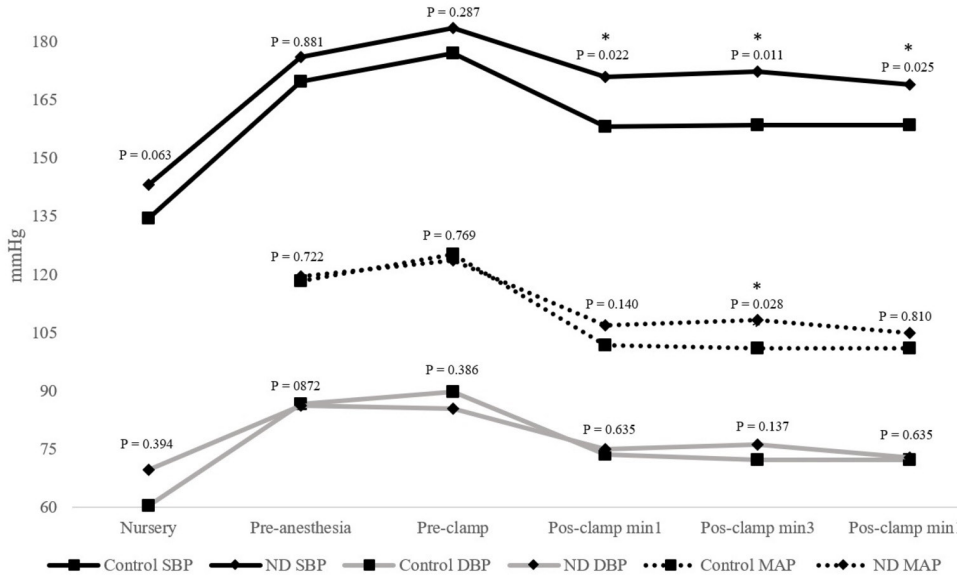

Figure 2

Graphical representation of blood pressure values in all time points
■ Control; DBP ····· Diastolic blood pressure; MAP •••• Mean Arterial Pressure; ND ◆ Alterations on the neurologic examination during carotid clamping; Nursery – first blood pressure measurement in the nursery; Pos Clamp min 1 – blood pressure 60 seconds after carotid clamping; Pos Clamp min 3 - blood pressure 180 seconds after carotid clamping; Pos Clamp min 10 - blood pressure 600 seconds after carotid clamping; Pre-anesthesia – first blood pressure measurement after arterial catheterization and before anesthetic administration; Pre clamp – blood pressure measurement 3 minutes before carotid clamping; SBP ····· Systolic Blood pressure.

Intraoperative Neurologic Examination

Both groups of patients underwent CEA under RA, and their neurologic status was assessed using a comprehensive neurologic examination. This examination included evaluating consciousness (response to direct commands by the anesthesiologist, simple questions) and subsequent surveillance at 5-minute intervals and continuous cerebral oximetry monitoring (INVOS, Medtronic) [6]. However, neurological testing was used as the sole criterion for adjudication of diagnosis [17-19].

Surgical Technique

Depending on the surgeon's preference, the surgical technique employed for CEA included options such as patch angioplasty, eversion, or direct suture. The decision to shunt during the procedure was also at the surgeon's discretion. Carotid sinus block, as a rule, is not performed in the study center.

The stroke rate observed at the center falls within the recommended range in clinical guidelines [20]. The ND rate at the present center is 8% per year. Additionally, over 98% of CEA at this referral center are performed under RA. The involved

Table 1 **Demographics and comorbidities of the patients**

	Control N (%) 77 (50)	ND N (%) 77 (50)	p-value
Age (years) (mean ± SD)	68.3 ± 8.3	72.0 ± 9.61	0.012
Side (Right)	41 (53.9)	39 (47)	0.381
Sex (Male)	63 (81.8)	58 (75.3)	0.326
Hypertension	67 (87.0)	72 (93.5)	0.174
Smoking history	44 (57.9)	35 (45.5)	0.124
Diabetes	30 (39.5)	31 (40.3)	0.921
Dyslipidemia	64 (84.2)	63 (81.8)	0.694
CKD	8 (10.5)	10 (13.0)	0.637
BMI > 30 kg /m2	7 (9.3)	17 (22.1)	0.029
PAD	19 (25.3)	17 (22.1)	0.637
CAD	25 (33.3)	29 (37.7)	0.577
AF	4 (5.3)	6 (7.8)	0.541
COPD	10 (13.3)	8 (10.4)	0.574
CHF	6 (8)	9 (11.7)	0.446
ASA:			0.685
II	12 (17.1)	12 (16.4)	
III	54 (77.1)	54 (74.0)	
IV	4(5.7)	7 (9.6)	
Asymptomatic	42 (55.3)	41 (53.2)	0.691
Symptomatic			
TIA	8 (10.5)	8 (10.4)	
Stroke	26 (34.2)	28 (36.4)	
ICA stenosis- ipsilateral (%)	84.9±9.4	81.4±10.6	0.953
ICA stenosis- contralateral (%)	59.7±16.1	65.5±20.7	0.05
Contralateral ICA stenosis ≥80%	6 (7.8)	13 (16.9)	0.104
Anti-hypertensive agents (numbers)	2.0±1.15	2.0±1.33	0.948
ACEI/ARB	56 (75.7)	52 (70.3)	0.459
Beta-Blocker	25 (33.8)	23 (31.1)	0.725
CCB	27 (36.5)	31 (41.9)	0.500
Thiazide diuretic	34 (45.9)	32 (43.2)	0.741
Nitrate	7 (9.5)	7 (9.5)	1

Legend: ACEI – Angiotensin-converting enzyme inhibitor/Angiotensin receptor blocker; AF – Atrial fibrillation; ASA – American Society of Anesthesiologists Physical Status Classification System; CAD – Coronary artery disease; CCB - Calcium Channel Blocker; CHF – Chronic heart failure; CKD: Chronic kidney disease (creatinine = 1.5 mg/dl); COPD – Chronic obstructive pulmonary disease; ND – Alterations on the neurologic examination during carotid clamping; PAD – Peripheral artery disease; Obesity – Body Mass Index >30kg/m2; TIA – Transient ischemic attack; ICA – internal carotid

vascular department has reported rates of stroke and death after CEA that list 1.10% and 0.6% in symptomatic patients, respectively [21, 22].

Patients were followed up for 30-90 days in the postoperative period through medical examinations and Doppler ultrasonography (DUS). These evaluations aimed to detect any potential complications, including early restenosis.

Definitions

The European Vascular Surgery Society clinical practice guidelines were the basis for classifying carotid stenosis as symptomatic [23]. Furthermore, the first event was the first stroke identified as the first ischemic neurologic event six months before CEA.

The criteria used to define ND in this study involved any refractory alteration observed during the clinical neurologic examination (description above) that did not respond to hemodynamic adjustments during CACC (e.g., hemiparesis, aphasia, etc).

Outcomes

The primary outcome was the presence of intraoperative ND.

Statistical analysis

The sample size that was needed for a case-control study was calculated on http://sample-size.net, based on means, and the aim was to accomplish a statistical power (1-ß) of 90%, an effect size of 0.6 and a type I error rate (∂) inferior to 0.05. The sample was calculated at 118, with the least difference between groups at 17% [24].

Statistical analysis was run on SPSS 28.0 (IBM Corp., released 2017. IBM SPSS Statistics for Windows, version 28.0, Armonk, NY, USA)

Univariable analysis was evaluated through A^2 or Fisher's tests regarding categorical data and Student's t-test analysis for continuous data. Continuous variables following a normal distribution are presented with mean ± standard deviation, median, and interquartile range for non-normally distributed variables. Categorical variables are presented as percentages.

RESULTS

Demographics and baseline characteristics of patients

The study sample consisted of 154 patients, 121 (78.6%) of whom were male, and only 33 were female. The mean age of the participants was 70.1 ± 9.1 years. There was a similar distribution of men in both the control group (81.8%) and the ND group (75.3%), and no statistically significant differences were observed in this regard (Table 1).

Patients with ND had a mean age of approximately 72.0 ± 9.90 years. In contrast, control patients had a significantly lower mean age of 68.3 ± 8.3 years (p=0.012). Approximately 50.5% of the procedures were performed on the right side. CEA was performed on the right side in 53.9% and 47% of patients in the control and ND groups, respectively (p= 0.381).

Regarding comorbidities, obesity was more prevalent in the ND population (22.1 vs. 9.3%, p=0.029). However, no statistically significant differences were observed in the two groups' other comorbidities and cardiovascular (CV) risk factors (Table 1).

The average degree of ipsilateral stenosis was similar in the ND population compared to the control group (85 ± 9.4% vs. 81 ± 10.6%, p=0.953). However, the degree of contralateral carotid artery stenosis was higher in the ND group (65.5 ± 20.7% vs. 59.7 ± 16.1%, p=0.05). The prevalence of contralateral stenosis ≥80% was higher in ND patients, although the difference was not statistically significant (16.9% vs. 7.8%, p=0.104). Less than half of the patients in the study (46.1%) had symptomatic carotid stenosis. Among these, the majority presented with a stroke (35.3%), followed by a smaller number of cases with a transient ischemic attack (10.45%) (Table 1).

No significant differences between the two groups were observed in the number or pharmacological classes of anti-hypertensive agents used in the preoperative period.

Hemodynamic evaluation

The surgical duration of the control group tended to be longer than that of the group with ND (123.9±49.5 vs 110.0±32.7 min, p=0.059). There was no significant difference in clamping duration between groups (46.1±23.3 vs. 49.1±23.25 min, p=0.558) (Table 2).

Pre-clamping SBP was significantly higher in patients with ND than controls (154.6±31.8 vs. 141.8±41.2 mmHg, p=0.035). The ND group also maintained significantly higher PP values (98.1±24.0 vs. 87.4±32 mmHg, p=0.023) (Table 3).

In the first minute after carotid clamping, the ND group maintained significantly higher SBP compared to the control group (171.0±29.7 vs. 158.3±40.0 mmHg, p=0.022) and likewise PP values (96.0±23.1 vs. 84.7±27.3 mmHg, p=0.007). This difference continued until the 3rd and 10th post-clamping minutes, retaining significance for SBP and PP. Additionally, at the 3rd post-clamping minute, the MAP obtained in the ND group (108.3±19.7 mmHg) was higher than in the control group (101.1±20.2mmHg), p=0.028 (Table 2).

Both the post-clamping SBP nadir (153.4±29.2 vs. 142.6±33.7 mmHg, p=0.042) and zenith (188.8±34.1 vs. 173.0±33.7 mmHg, p=0.006), along with their respective PP (105.5±23.1 vs. 90.3±26.0 mmHg, p=0.001), were significantly higher in the ND group (Table 2). The ND group also exhibited a statistically higher MAP at the 3rd post-clamping minute (108.3±19.7 vs. 101.1±20.2 mmHg, p=0.028). The ND group also showed a significantly smaller drop in diastolic blood pressure (DBP) at the 3rd post-clamping minute than the control group (9.3±20.4 vs. 18.0±28.8 mmHg, p=0.035), indicating that it maintained higher DBP.

Table 2 **Hemodynamic status during carotid endarterectomy procedure**

Positive awake test	Control n=77 mmHg (50%)	ND n=77 mmHg (50%)	p-value
Positive awake test	123.9±49.5	111.0±32.7	0.059
Surgery duration (min)	49.1±39.1	46.05±23.25	0.558
Clamping duration (min)			
Nursery			
Diastolic	60.5±24.7	69.8±14.3	0.394
Systolic	134.6±25.5	143.2±29.0	0.063
Before anesthetic induction			
SBP min	153,6±37.2	158.0±36.4	0.469
DBP min	73.6±18.7	74.9±19.7	0.661
MAP min	106.2±24.7	106.8±25.5	0.881
SBP max	169.8±36.7	176.2±33.2	0.262
DBP max	86.7±22.1	86.2±17.8	0.872
MAP max	118.3±23.7	119.6±21.7	0.722
HR max (bpm)	73.4±18,6	77.0±21.6	0.273
HR min (bpm)	63.8±12.2	65.0±13.3	0.589
SatO2 min (%)	93.9±10.5	93.9±5.5	0.940
Pre-clamping			
SBP max	177.2±40.7	183.6±32.3	0.287
DBP max	89.8±32.2	85.5±24.0	0.355
MAP max	125.3±34.2	123.8±26.0	0.769
SBP min	141.8±41.2	154.6±31.8	0.035
DBP min	65.4±18.5	67.7±13.5	0.386
MAP min	94.8±26.5	100.8±20.5	0.124
Pulse pressure	87.4±32.5	98.1±24.0	0.023
HR max (bpm)	75.7±17.4	74.7±16.1	0.719
HR min (bpm)	63.3±14.0	64.3±13.1	0.678
SatO2 min (%)	95.1±7.3	95.6±4.6	0.616
Post-clamping minute 1			
SBP	158.3±40.0	171.0±29.7	0.022
MAP	101.8±23.7	107.0±18.8	0.140
DBP	73.6±20.3	75.0±16.3	0.635
Pulse pressure	84.7±27.3	96.0±23.1	0.007
HR (bpm)	70.7±16.4	70.6±16.0	0.965
SatO2 (%)	97.63±2.8	97.6±2.8	0.957
Post-clamping minute 3			
SBP	158.6±34.2	172.5±31.4	0.011
MAP	101.1±20.2	108.3±19.7	0.028
DBP	72.3±15.6	76.2±16.3	0.137
Pulse Pressure	86.3±25.6	96.3±23.1	0.014
HR (bpm)	70.3±15.0	71.1±15.8	0.762
SatO2 (%)	97.4±3.2	97.7±2.6	0.469

Positive awake test	Control n=77 mmHg (50%)	ND n=77 mmHg (50%)	p-value
Post-clamping minute 10			
SBP	158.6±34.2	169.0±33.6	0.025
MAP	101.1±20.2	105.0±19.4	0.131
DBP	72.3±15.6	72.9±14.6	0.635
Pulse pressure	84.8±24.9	96.1±25.4	0.007
HR (bpm)	70.3±15.0	70.0±15.6	0.861
SatO2 (%)	97.4±3.2	97.6±1.8	0.576
Post-clamping nadir			
SBP min	142.6±33.7	153.4±29.2	0.042
MAP min	94.1±21.1	98.5±20.3	0.810
DBP min	65.1±14.9	65.7±13.7	0.810
Pulse pressure	77.5±25.4	87.7±21.0	0.001
HR min (bpm)	63.7±14.0	63.5±15.1	0.923
SatO2 min (%)	95.5±5.4	94.3±11.4	0.400
Post-clamping Zenith			
SBP max	173.0±33.7	188.8±34.1	0.006
MAP max	116.8±25.0	123.3±22.9	0.103
DBP max	82.7±22.6	83.3±17.6	0.850
Pulse pressure	90.3±26.0	105.5±23.1	0.001
HR max	78.6±26.0	77.3±19.1	0.731

ND – Alterations on the neurologic examination during carotid clamping SBP – Systolic blood pressure; DBP – Diastolic blood pressure; HR – Heart rate; MAP – Mean arterial pressure; ND: - intraoperative neurologic deficit; Nursery – first blood pressure measurement in the nursery; Pos Clamp min 1 – blood pressure 60 seconds after carotid clamping; Pos Clamp min 3 - blood pressure 180 seconds after carotid clamping; Pos Clamp min 10 - blood pressure 600 seconds after carotid clamping; Pre-anesthesia – first blood pressure measurement after arterial catheterization and before anesthetic administration; Pre clamp – blood pressure measurement 3 minutes before carotid clamping; SBP - Systolic Blood pressure; SatO2 – Peripheral Oxygen Saturation

Table 3 **BP variation between pre-clamping and different post-clamping times**

Positive awake test	Control n=77 mmHg (50%)	ND n=77 mmHg (50%)	p-value
Systolic			
Δ pre-clamp _ post-clamp min1	19.79±24.01	11.947±16.19	0.021
Δ pre-clamp _ post-clamp min3	19.42±26.78	11.12±21.83	0.039
Δ pre-clamp _ post-clamp min10	21.55±31.97	14.62±30.48	0.178
Δ pre-clamp _ post-clamp zenith	5.6±23.6	-5.7±23.9	0.005
Diastolic			
Δ pre-clamp _ post-clamp min1	16.72±28.2	10.3±20.8	0.119
Δ pre-clamp _ post-clamp min3	18.0±28.8	9.3±20.4	0.035
Δ pre-clamp _ post-clamp min10	18.6±28.8	12.6±23.0	0.160
Δ pre-clamp _ post-clamp zenith	7.9±25.7	1.4±22.3	0.106
Shunt	0	17 (22.1)	0.001

BP – Blood pressure; ND – Alterations on the neurologic examination during carotid clamping; Pos Clamp min 1 – blood pressure 60 seconds after carotid clamping; Pos Clamp min 3 - blood pressure 180 seconds after carotid clamping; Pos Clamp min 10 - blood pressure 600 seconds after carotid clamping; Pre clamp – blood pressure measurement 3 minutes before carotid clamping.

Additionally, the ND group showed a significant change in SBP, which together affected the MAP. These factors may explain this difference between groups (Fig. 2).

No statistically significant differences were observed for DBP and HR values between both groups before induction of anesthesia, before carotid cross-clamping, or at any of the analyzed time points (Table 2).

Blood pressure variation and complications after carotid clamping

Table 3 shows the pre-clamp and post-clamp BP variation for minutes 1, 3, and 10. The drop in SBP values registered at the 1st post-clamping minute relative to pre-clamping values was significantly smaller in the ND group compared to controls (11.95±16.19 vs. 19.79±24.01 mmHg, p=0.021), and this difference was observed up to the 3rd post-clamping minute (11.12±21.83 vs. 19.42±26.78 mmHg, p=0.039). When observing the variation between post-clamping zenith and pre-clamping SBP values, controls group exhibited a drop in SBP of 5.6±23.6 mmHg whereas ND patients showed an increase of 5.7±23.9 mmHg (p=0.005).

Regarding the DBP variations obtained, no statistical difference was found between the groups, except for the variation between pre-clamp and post-clamp at the 3rd minute. In the ND group, the variation was 9.3±20.4 mmHg, significantly lower than the difference observed in the control group (p=0.035).

The correlation between variation in pressure and INVOS values was studied in a subset of 55 patients where INVOS data was available. The Δ between the pre-clamp maximum and post-clamp minimum systolic pressure at 3 minutes demonstrated a weak negative correlation (c = -0.246, p = 0.070, 95% CI: -0.249 to 0.010) with Δ INVOS. At 1 minute, this correlation was slightly more substantial but remained non-significant (c = -0.261, p = 0.054, 95% CI: -0.270 to 0.003). At 10 minutes, a statistically significant negative correlation emerged (c = -0.274, p = 0.043, 95% CI: -0.243 to -0.004), while the nadir pressure within the first 10 minutes showed the strongest and most significant correlation (c = -0.358, p = 0.007, 95% CI: -0.296 to -0.048). No linear relationship was observed for diastolic pressure.

The analysis of the diastolic pressure delta (Δ) between the pre-clamp and post-clamp measurements at 1, 3, and 10 minutes in the contralateral stenosis group demonstrated a trend toward statistical significance. However, it Δ was consistently lower in the IND group. Saturation was significantly lower in the IND group with contralateral stenosis) (p=0.019).

In the sample of patients who presented ND during clamping, approximately 17 (22.1%) underwent a carotid vascular shunt. In contrast, none of the patients in the control group underwent this additional procedure.

DISCUSSION

This study highlights the significance of hemodynamic values, especially SBP and pulse pressure, in determining the occurrence of clamping-associated neurologic deficits. Another finding was that patients in the ND group demonstrated a smaller drop in SBP from pre-clamping to various post-clamping time points. Moreover, the limited variation in BP exhibited by this group during the procedure suggests cerebral autoregulation might have been less effective in these patients. Secondly, PP before clamping and post-clamping was always significantly higher in the ND group. Additionally, this group had a higher prevalence of obesity and a greater degree of contralateral stenosis.

Pathophysiologically, induced hypertension seems to be a reasonable measure to ensure sufficient cerebral perfusion in the presence of a high-grade ICA stenosis. The anesthesiology intervention after the establishment of ND, might probably explain the smaller drop in SBP from pre-clamping to post-clamping time points [25]. Patients with pre-existing hypertension who are said to be more dependent on a high normal pressure level had a significantly higher ND rate [25]. Hypertension is an important risk factor for recurrent stroke both in the acute phase and the long-term. Moreover, hypertension is an important risk factor for complications of CEA [26]. An increased pulse pressure is also associated with an increased risk of hyperperfusion syndrome [27]. It might also indicate that the brain is already experiencing increased arterial stiffness or adaptation to the compromised blood flow due to the carotid artery blockade [28].

Some predictors associated with neurological deficits and a greater likelihood of post-surgical complications have already been studied [1, 29]. Previous evidence has already established the relationship between obesity and a higher incidence of focal neurological deficits, which aligns with the findings of this study [9]. Therefore, it would be valuable to explore how obesity interacts with BP values during CEA, considering that individuals with higher body mass index (BMI) tend to have elevated BP profiles [30]. Furthermore, other risk factors, such as ipsilateral and contralateral stenosis, have also been identified [9, 31].

Research indicates cerebral autoregulation (CA) and arterial baroreflex (BR) are crucial to maintaining stable cerebral perfusion during stress events such as carotid endarterectomy [32, 33]. This mechanism becomes especially important in patients with severe carotid stenosis and older individuals at risk of reduced CA effectiveness [34-37]. The ND group, with a significant proportion of older patients and severe stenosis, is likely to be particularly vulnerable to perioperative blood pressure fluctuations and related neurological damage [38].

Additionally, the ND group's persistently higher systolic and pulse pressure values from pre-clamping to post-clamping stages suggest the influence of anesthetic blockade and contralateral atherosclerotic stenosis. Another

study from the same database demonstrated that a higher degree of contralateral stenosis was associated with the occurrence of ND[9]. Thrasher et al. demonstrated the importance of BR function reserve on the contralateral side of the operated carotid artery and the baroreceptors of the aortic arch [39,40]. Specifically, severe contralateral stenosis could reduce BR sensitivity on the affected side, potentially limiting compensatory capacity during anesthesia induction. As a result, even minor interactions with the ipsilateral carotid sinus might trigger significant hemodynamic variations in the ND group compared to the control group.

Although the duration of carotid clamping did not show a statistical difference between the groups, the total duration of the surgery was shorter for the ND group. The authors suggest that upon detecting neurological alterations, surgeons probably expedite surgical procedures to minimize patients' exposure to ischemia and potentially reduce any hemodynamic exacerbation of these changes. Another contributing factor for the lower duration of surgery in the ND group is the higher prevalence of endarterectomy with direct closure, as shown in another publication from the same database [41]. This proposition is supported by previous studies showing an increased risk of postoperative complications with longer surgical times in CEA[7, 42]. Therefore, there is probably a bias in the reverse causality relationship and a link between the shorter surgical time and the clinical outcome.

The ND group had a higher prevalence of obesity, associated with excessive fibrosis in smooth muscle cells, increased media layer thickness, and subsequent endothelial dysfunction [43]. These factors contribute to arterial stiffness and thickening, which likely justifies that this group's PP is more elevated. The difference in PP is statistically significant both before and after clamping, as these are the moments when most major hemodynamic changes occur, accentuating the differences in PP between the groups.

On par with the hemodynamic differences between groups, a more considerable post-clamp drop in INVOS values correlated with a smaller drop in SBP values. However, it was only seen after 10 minutes. The correlation was weak (c= -0.274), which could be explained by the diagnostic accuracy of INVOS in detecting clamp-associated cerebral ischemia. INVOS has a relatively low sensitivity in detecting clamp-associated cerebral ischemia in CEA under RA, according to a systematic review and meta-analysis [44]. While it monitors superficial and cortical oxygen saturation, it may not detect desaturation in deeper tissues, such as basal ganglia, which have been shown to be a predictor of post-clamping ND 45.

However, it is essential to acknowledge the limitations of this study. The sample consisted of 154 individuals, predominantly male, and from a single tertiary referral center. Therefore, it is necessary to conduct multicenter studies with a larger sample size to confirm and validate the present results. Additionally, patients admitted to a tertiary referral center often have more significant comorbidities compared to those of peripheral centers, which may introduce bias when interpreting the results. Furthermore, the study did not assess differences among surgical teams due to the low incidence of events. Considering the low incidence and the limited number of events studied, potential confounders were intentionally not adjusted for, and as a result, confounding may be present in the findings.

CONCLUSION

This study highlights the significance of thorough perioperative assessment and the importance of perioperative and intraoperative blood pressure management in determining the outcome of CEA. The study specifically found that higher systolic blood pressure and pulse pressure are predictive of the occurrence of clamp-associated cerebral ischemia, probably related to the patient's own failing hemodynamic control. These findings could prove useful in determining surgical risk and customizing strategies such as using strict and evidence-based blood pressure management protocols. However, careful interpretation of the results is advised due to the low sample size. Furthermore, large studies and multicenter cohorts are needed to validate these findings.

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