INFLUENCE OF COLLATERAL CIRCULATION AND CLAMPING DURATION ON NEUROLOGICAL OUTCOMES IN ASYMPTOMATIC PATIENTS AFTER CAROTID ENDARTERECTOMY

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ABSTRACT

Asymptomatic carotid artery stenosis (ACS) is prevalent in approximately 2% of the general population and increases with age. Identifying high-risk patients for neurological complications during elective carotid endarterectomy (eCEA) is critical for improving surgical outcomes. This retrospective cohort study included 70 asymptomatic patients with carotid artery stenosis >70%, treated with eCEA between January and July 2023. Patients were classified based on the morphology of the Circle of Willis (CoW) into complete and incomplete groups. Primary outcomes were postoperative stroke, transient ischemic attack (TIA), and neurological mortality. Additional variables included risk factors and clamping duration. The frequency of incomplete CoW was significantly higher in men (p=0.004). Neurological complications were observed in 2 patients (2.9%). There was no significant association between risk factors and postoperative complications. However, longer clamping duration was significantly associated with neurological complications (p=0.034). Interestingly, the absence of anatomical CoW variations did not correlate with postoperative complications, suggesting effective compensatory collateral flow. Neurological complications in eCEA are low and more closely related to clamping duration than CoW morphology. Effective preoperative assessment and surgical technique are essential for minimising risks.

Keywords: *Circle of Willis, Reperfusion, Asymptomatic Carotid Stenosis, Collateral Circulation, Carotid Surgery.*

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INTRODUCTION

Asymptomatic carotid artery stenosis (ACS) refers to stenosis in persons without a history of ischemic stroke, transient ischemic attack, or other neurologic symptoms referable to the carotid arteries [1]. The prevalence of asymptomatic carotid artery stenosis is around 2% in the general population but increases with age [2]. Silent brain infarcts larger than 3 mm were registered in 20-30% of asymptomatic patients [3]. The European Society for Vascular Surgery (ESVS) has recently updated its guidelines on the management of atherosclerotic carotid artery disease, emphasizing the importance of best medical treatment for patients with significant asymptomatic carotid stenosis. The guidelines recommend considering carotid endarterectomy (CEA) or carotid artery stenting for patients with significant stenosis who also present one or more clinical or imaging features indicating a higher risk of future stroke despite BMT [2].

The cerebral arteries on the side of extracranial carotid stenosis experience maximal dilation as a compensatory mechanism to uphold adequate brain perfusion, thereby diminishing the functional reserve of circulation [4]. Prior investigations in individuals with extracranial carotid disease suggest a notable increase in postoperative complications when there is a disruption in the continuity of the anterior or posterior segment of the Circle of Willis (CoW) [5]. Recent studies indicate that the completeness and functionality of the CoW are crucial in determining the risk of ischemic events during carotid interventions. Studies by Czinege et al. and Magyar-Stang et al. have shown that CoW integrity significantly affects cerebrovascular reserve and perioperative risk in carotid artery disease patients [6,7]. Furthermore, data suggest that incomplete CoW configurations are present in over 50% of individuals, with significant variability influencing collateral blood flow capacity [8].

Given the importance of cerebrovascular collateralization in preserving neurological function, evaluating the role of CoW morphology and clamping duration during CEA is essential. This study aims to assess the impact of CoW integrity and duration of carotid clamping on postoperative neurological outcomes in asymptomatic patients undergoing elective CEA. Understanding these factors may contribute to refining patient selection and optimizing surgical techniques to reduce perioperative risks.

METHODS

This retrospective cohort study enrolled 70 asymptomatic patients between January 2023 and July 2023 who underwent elective carotid endarterectomy (eCEA). Inclusion criteria comprised asymptomatic patients with carotid artery stenosis >70% (including those with unilateral stenosis >70% and contralateral occlusion). Symptomatic patients presenting typical carotid symptoms such as transient ischemic attack (TIA), amaurosis fugax, or a history of stroke were excluded. Anamnestic data on risk factors were collected, including hypertension (diagnosed or under chronic antihypertensive therapy), diabetes (diagnosed or under chronic therapy), hyperlipoproteinemia (LDL cholesterol >3.5 mmol/L, total cholesterol >5.2 mmol/L, or chronic hypolipemic therapy), smoking history within the past two years, and diagnosed heart diseases based on cardiologist findings. Variables included the presence of coronary disease, angina pectoris, previous myocardial infarction, myocardial revascularization, left ventricular hypertrophy, heart rhythm disorders, and peripheral arterial disease. Additionally, 8 patients had simultaneous coronary artery bypass grafting (CABG) performed with eCEA due to extensive coronary artery disease. The decision for simultaneous operation was reached by Heart and Vascular Team.

The decision for eCEA was made following duplex ultrasonography and multidetector computed tomography (MDCT) angiography, with carotid stenosis assessed based on established criteria. Patients were categorised into two groups based on CoW morphology: those with complete CoW and those with incomplete CoW, characterized by anterior segment disruption (ACA1, AcomA), ipsilateral posterior collateral segment disruption (ACP1, AcomP), hypoplasia of both anterior and posterior collateral segments on the side of significant carotid stenosis, or the presence of foetal ACP.

All patients underwent eCEA under general anaesthesia, utilizing the eversion technique. Intraoperatively, the duration of carotid artery clamping was recorded for each patient. Postoperatively, patients were closely monitored by a neurologist and discharged home after an average of 3 days in the absence of complications. Primary outcomes included postoperative stroke, TIA, and neurological mortality.

The research has been conducted in full compliance with the Helsinki Declaration on ethical conduct and in accordance with the principles of Good Clinical Practice (GCP), national regulations and institutional policies and has been approved by the authors' institutional Ethics committee (No29/22).

Statistical analysis

Data were analyzed using parametric or nonparametric methods. Observed characteristics were expressed as mean values, standard deviation, median, and interquartile range (IQR). The normality of the distribution for each variable was assessed using both graphical methods and the Shapiro-Wilk test. Student's t-test was used for continuous parametric data. For non-parametric data, the Chi-square test, Fisher's test and Wilcoxon rank statistic were used. Significance was set at 2-sided $p<0.05$. IBM SPSS Statistics 26 (Armonk, New York, USA) was used for the analysis.

RESULTS

Risk factors in the group of patients with and without insufficiency of the ring of Willis are given in Table 1. There was no statistically significant difference in age between patients with complete and incomplete CoW ($p>0.05$). There is

a significant difference in the frequency of CoW insufficiency in men compared to women (p=0.004). Twenty patients (28.6%) reported vertigo on admission. There is a statistically significant difference in the frequency of vertebrobasilar basin insufficiency in these patients compared to those without vertigo symptoms (p<0.05).

Postoperative neurological complications were recorded in 2 patients (2.9%). Both had ischemic stroke. None of the examined risk factors was associated with the occurrence of postoperative neurological complications in asymptomatic patients (Table 2). All patients with postoperative neurological complications had a preserved polygon of Willis.

The average duration of the clamp was 20 minutes (range 9-30 minutes). There is a statistically significant difference in the duration of the clamp in patients with postoperative neurological complications compared to patients without complications (p=0.034). In univariate logistic regression analysis, the length of clamping proved to be a significant predictor of neurological complications (OR: 1.191; 95% CI: 0.999-1.419; p=0.049).

In 8 (11.4%) patients, CABG was performed simultaneously with the operative treatment of carotid disease. No postoperative neurological complication was recorded in this group of patients.

In-hospital mortality was recorded in one patient (1.4%) who died as a result of stroke. In this patient, CoW inefficiency was not described, and the clamp lasted 30 minutes.

The average length of hospitalization was 5 days (range 4-92 days). Length of hospitalization was not significantly different in patients with and without neurological complications. Hospitalization was significantly longer in patients who underwent myocardial revascularization in addition to carotid surgery (22 vs 4.5 days; p<0.001).

Table 1. Risk factors in the group of patients with and without Circle of Willis insufficiency

Risk factors	CoW-C n=34	CoW-IC n=36	p
Male sex (%)	76.5	41.7	0.004
Age (median, min-max)	73 (40-80)	71 (54-84)	0.701
DM (%)	47.8	25	0.135
HTA (%)	100	87.5	0.234
Dyslipidaemia (%)	87	87.5	0.955
Smoking (%)	63.6	71.4	0.547
Previous MI (%)	34.8	16.7	0.193
Previous PCI/CABG (%)	34.7	29.2	0.688
CHF (%)	17.4	0	0.050
AF (%)	13	12.5	0.955
PAD (%)	8.7	16.7	0.666
COPD (%)	8.7	16.7	0.666
CKD (%)	0	4.2	1

CoW-C - complete circle of Willis, CoW-IC - incomplete circle of Willis, DM - diabetes mellitus, HTA - hypertension, MI - myocardial infarction, PCI - percutanes coronary intervention, CABG - coronary artery bypass grafting, CHF - congestive heart failure, AF - atrial fibrillation, PAD - peripheral arterial disease, COPD - chronic obstructive pulmonary disease, CKD - chronic kidney disease

Table 2. Predictors of adverse neurological events

Factor	OR	95% CI	p
Male sex	0.150	0.016-1.422	0.098
Duration of clamping	1.191	0.999-1.419	0.049
Age	0.997	0.877-1.133	0.958
DM	0.833	0.125-5.556	0.851
Smoking	6.667	0.641-69.344	0.112
Previous MI	1.419	0.143-14.111	0.765
COPD	0.541	0.050-5.852	0.613

DM – diabetes mellitus, MI – myocardial infarction, COPD – chronic obstructive pulmonary disease

DISCUSSION

While prior research has emphasized anatomical variations in the CoW, our findings suggest that functional insufficiency-the inability of existing collaterals to compensate for hypoperfusion-is a more critical determinant of perioperative risk. Patients with an incomplete CoW do not necessarily experience neurological deficits if functional collateral flow is adequate.

The CoW serves as the primary source of contralateral blood supply in patients who undergo carotid artery cross-clamping (CC) for CEA. Its anatomical variations influence outcomes, with fully developed collaterals present in 35-50% of the population. [9,10]. In these individuals, hemodynamic disturbances are minimal, reducing the risk of neurological deficits [11]. However, collateral remodelling in response to carotid stenosis suggests that many CEA candidates have adapted over time, preventing preoperative neurological deficits.

Incomplete CoW has been linked to watershed infarcts and ischemic lesions, with anterior collateral disruption considered an independent risk factor for cerebral ischemia [12-14]. According to some authors, the interruption of continuity in the anterior collateralization represents an isolated risk factor for the occurrence of cerebral ischemia even without the presence of extracranial carotid disease [12,15,16]. These results led to the hypothesis that asymptomatic patients with incomplete CoW have an increased risk of developing a neurological deficit, and that such patients would benefit the most from surgical treatment. Surgical treatment performed in asymptomatic patients represents primary prevention before the onset of neurological deficit [2,17]. On the other hand, in the same patients due to incomplete CoW, there is an assumption that there will be a higher risk of perioperative neurological complications. Prior studies report an 87.3% frequency of incomplete CoW in symptomatic patients, with Göksu et al. noting a 72.6% prevalence in those with atherosclerotic carotid disease [18]. The study by Myrcha et al. examined the role of cerebral collateral circulation, particularly the CoW, in carotid artery cross-clamping tolerance during CEA [9]. Their findings showed that contralateral carotid stenosis >70% or occlusion significantly increased the risk of intraoperative neurological deficits ($p<0.001$), while an incomplete CoW alone was not a predictor. However, data were insufficient to assess its impact on early postoperative outcomes. Similarly, Banga et al. observed a tenfold increase in neurological risk with incomplete anterior or posterior collateralization during CEA without shunting, reinforcing the importance of routine shunt placement in high-risk patients [19]. Conversely, evidence suggests that CEA significantly improves functional reserve and normalizes cerebrovascular reactivity in both asymptomatic and symptomatic patients.

In high-volume institutions, performing more than 150 carotid surgeries annually, perioperative complications in asymptomatic patients are rare, occurring in less than 2% of cases [20]. Our sample did not record any instances of reversible cranial nerve damage, indicating an adequate surgical approach.

Hyperperfusion syndrome was observed in one patient who fully recovered and was discharged for home treatment. The reported incidence of cerebral hyperperfusion after CEA is about 20% [21]. Previous analyses have shown that cerebral hyperperfusion is dependent on the completeness of collateralization within the CoW, poorly controlled arterial tension, and the duration of the clamp. There are currently a few papers discussing the use of ischemic postconditioning (IPCT) in the prevention of hyperperfusion syndrome [22,23].

In patients with disruptions in both anterior and posterior collaterals, a selective shunt was required in 80% of operated patients, compared to only 7% in those with at least one collateral pathway [21]. Hendrikse et al. found that collateral diameter decreases post-CEA, indicating a dynamic CoW capable of flow adaptation [24]. While operative treatment enhances circulatory reserve, particularly in patients with incomplete CoW, the extent to which this influences preoperative and postoperative stroke risk remains unclear. This underscores the need to differentiate between anatomical insufficiency and functional collateral compensation, as functional adaptation may mitigate ischemic risk despite an incomplete CoW.

Patients with a complete CoW have greater tolerance to clamping duration and fewer perioperative neurological complications. Our research showed that the prevalence of CoW variation in asymptomatic patients is 51.4%. There is a significant difference in the frequency of CoW insufficiency between men and women, and a significant association between preoperative dizziness and incomplete CoW in the posterior circulation, likely due to VB insufficiency [25,26].

The absence of anatomical variations of the CoW in asymptomatic patients with postoperative neurological complications may be explained by the development of functional collateral flow over time, which compensates for chronic hypoperfusion and keeps these patients asymptomatic despite significant stenosis [27]. This compensatory mechanism may protect them from neurological complications during surgery. In our study, neurological complications were more dependent on clamping duration, supporting recent research that suggests perioperative risk assessment should consider both the anatomy and functionality of the CoW. Other factors such as inadequately regulated hypertension, anaesthesia type, cardiac instability, and comorbidities also influence outcomes.

In our study, neurological complications correlated more with CC duration than CoW anatomy, emphasizing the need for functional assessments beyond anatomical variations. Our low postoperative stroke rate (2.9%) highlights the protective role of CEA, optimized by surgical expertise and

techniques such as IPCT. Notably, patients with functional collateral insufficiency preoperatively exhibited improved hemodynamic stability postoperatively, suggesting that CEA enhances cerebrovascular reserve over time.

Limitations

This study is limited by its small sample size (70 patients, 2 index events) and retrospective design, which introduces selection bias. Additionally, we focused on anatomical variations without directly assessing functional collateral circulation using advanced imaging like perfusion MRI. Larger prospective studies are needed to validate these findings and further explore CoW functionality in surgical risk stratification.

CONCLUSION

Half of the patients with asymptomatic extracranial carotid disease exhibit CoW discontinuity, yet operative treatment effectively restores perfusion with a low complication rate. CoW remodelling and functional collateral adaptation likely compensate for hypoperfusion, explaining the lack of association between CoW insufficiency and neurologic complications. Other compensatory mechanisms, including collateral recruitment and autoregulation, further support cerebral circulation. However, extended clamping duration remains a key risk factor, highlighting the need for careful intraoperative management.

REFERENCES

1. Krist AH, Davidson KW, Mangione CM, Barry MJ, Cabana M, Caughey AB, et al. Screening for Asymptomatic Carotid Artery Stenosis: US Preventive Services Task Force Recommendation Statement. JAMA 2021;325:476-81.
2. Naylor A, Rantner B, Ancetti S, de Borst G, De Carlo M, Halliday A, et al. Editor's Choice - European Society for Vascular Surgery (ESVS) 2023 Clinical Practice Guidelines on the Management of Atherosclerotic Carotid and Vertebral Artery Disease. European Journal of Vascular & Endovascular Surgery 2023;65:7-111.
3. Fanning JP, Wong AA, Fraser JF. The epidemiology of silent brain infarction: a systematic review of population-based cohorts. BMC Med 2014;12.
4. [4] Zarrinkoob L, Wåhlin A, Ambarki K, Birgander R, Eklund A, Malm J. Blood Flow Lateralization and Collateral Compensatory Mechanisms in Patients With Carotid Artery Stenosis. Stroke 2019;50:1081.
5. Westphal LP, Lohaus N, Winklhofer S, Manzolini C, Held U, Steigmiller K, et al. Circle of Willis variants and their association with outcome in patients with middle cerebral artery-M1-occlusion stroke. Eur J Neurol 2021;28:3682.
6. Czinege Z, Sándor ÁD, Gyürki D, Varga A, Csípő T, Székely A, et al. Understanding perioperative risk determinants in carotid endarterectomy: the impact of compromised circle of Willis morphology on inter-hemispheric blood flow indices based on intraoperative internal carotid artery stump pulse pressure and backflow patterns. Geroscience 2024.
7. Magyar-Stang R, Pál H, Csányi B, Gaál A, Mihály Z, Czinege Z, et al. Assessment of cerebral autoregulatory function and inter-hemispheric blood flow in older adults with internal carotid artery stenosis using transcranial Doppler sonography-based measurement of transient hyperemic response after carotid artery compression. Geroscience 2023;45:3333-57.
8. Feng L, Zhai FF, Li ML, Zhou LX, Ni J, Yao M, et al. Association between Anatomical Variations of the Circle of Willis and Covert Vascular Brain Injury in the General Population. Cerebrovasc Dis 2022;52:480.
9. Myrcha P, Pinheiro F, Rocha-Neves J, Myrcha J, Gloviczki P. The effect of the collateral cerebrovascular circulation on tolerance to carotid artery cross-clamping and on early outcome after carotid endarterectomy. J Vasc Surg 2024;0.
10. Manojlovic V, Popovic V, Nikoloc D, Milosevic D, Pasternak J, Budakov N. Completeness of Circle of Willis in asymptomatic and symptomatic extracranial carotid disease. Med Pregl 2016;69:351-5.
11. Marshall RS, Festa JR, Cheung YK, Chen R, Pavol MA, Derdeyn CP, et al. Cerebral hemodynamics and cognitive impairment: Baseline data from the RECON trial. Neurology 2012;78:250.
12. Chuang YM, Liu CY, Pan PJ, Lin CP. Anterior cerebral artery A1 segment hypoplasia may contribute to A1 hypoplasia syndrome. Eur Neurol 2007;57:208-11.
13. Hoksbergen AWJ, Legemate DA, Csiba L, Csáti G, Síró P, Fülesdi B. Absent collateral function of the circle of Willis as risk factor for ischemic stroke. Cerebrovasc Dis 2003;16:191-8.
14. Henderson RD, Eliasziw M, Fox AJ, Rothwell PM, Barnett HJM. Angiographically defined collateral circulation and risk of stroke in patients with severe carotid artery stenosis. North American Symptomatic Carotid Endarterectomy Trial (NASCET) Group. Stroke 2000;31:128-32.
15. Spacek M, Tesar D, Veselka J. The Paramount Role of the Anterior Communicating Artery in the Collateral Cerebral Circulation. Int J Angiol 2015;24:236.
16. Romero JR, Pikula A, Nguyen TN, Nien YL, Norbash A, Babikian VL. Cerebral Collateral Circulation in Carotid Artery Disease. Curr Cardiol Rev 2009;5:279.
17. AbuRahma AF, Avgerinos ED, Chang RW, Darling RC, Duncan AA, Forbes TL, et al. Society for Vascular Surgery clinical practice guidelines for management of extracranial cerebrovascular disease. J Vasc Surg 2022;75:4S-22S.
18. Zhou C, Yuan C, Li R, Wang W, Li C, Zhao X. Association Between Incomplete Circle of Willis and Carotid Vulnerable Atherosclerotic Plaques. Arterioscler Thromb Vasc Biol 2018;38:2744-9.
19. Banga PV, Varga A, Csobay-Novák C, Kolossváry M, Szántó E, Oderich GS, et al. Incomplete circle of Willis is associated with a higher incidence of neurologic events during carotid eversion endarterectomy without shunting. J Vasc Surg 2018;68:1764-71.

20. Radak D. Carotid endarterectomy should be performed early after a cerebral ischemic event in order to be most effective. Vojnosanit Pregl 2011;68:166-9.
21. De Rango P. Cerebral hyperperfusion syndrome: The dark side of carotid endarterectomy. European Journal of Vascular and Endovascular Surgery 2012;43:377.
22. Wu L, Wei M, Zhang B, Zhang B, Chen J, Wang S, et al. Safety and Tolerability of Direct Ischemic Postconditioning Following Thrombectomy for Acute Ischemic Stroke. Stroke 2023;54:2442-5.
23. Ilijevski N, Atanasijević I, Lozuk B, Gajin P, Matić P, Babić S, et al. Direct Ischemic Postconditioning After Carotid Endarterectomy in the Prevention of Postoperative Cerebral Ischemic Complications-Observational Case-Control Study. J Cardiovasc Pharmacol Ther 2022;27.
24. Hendrikse J, Rutgers DR, Klijn CJM, Eikelboom BC, Van der Grond J. Effect of carotid endarterectomy on primary collateral blood flow in patients with severe carotid artery lesions. Stroke 2003;34:1650-4.
25. De Silva KRD, Silva R, Gunasekera WSL, Jayesekera RW. Prevalence of typical circle of Willis and the variation in the anterior communicating artery: A study of a Sri Lankan population. Ann Indian Acad Neurol 2009;12:157-61.
26. Jones JD, Castanho P, Bazira P, Sanders K. Anatomical variations of the circle of Willis and their prevalence, with a focus on the posterior communicating artery: A literature review and meta-analysis. Clin Anat 2021;34:978-90.
27. Khan AA, Patel J, Desikan S, Chrencik M, Martinez-Delcid J, Caraballo B, et al. Asymptomatic carotid artery stenosis is associated with cerebral hypoperfusion. J Vasc Surg 2021;73:1611.