Predicting Hemodynamic Changes of Cerebral Blood Flow during Temporal Carotid Occlusion: A Review of Current Knowledge with Implication for Carotid Artery Stenting

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Abstract

Keywords

- cerebrovascular reserve
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- carotid stenting
- carotid endarterectomy
- transcranial Doppler
- cerebral collateral circulation

Carotid artery disease (CAD) plays an important role in the stroke development and its prevalence increases with aging of the population. Its wide variability of clinical manifestation ranges from incidental asymptomatic finding to devastating or fatal stroke, although cerebral collateral circulation is considered one of the major modifying factors. Over time, carotid artery stenting (CAS) has evolved into a reputable method for the treatment of patients with severe CAD. With expanding use of proximal protection systems resembling surgical clamp, there is an increasing demand to understand collateral cerebral circulation to protect patients from periprocedural hypoperfusion, which increases the risk of cerebral events. Transcranial Doppler ultrasound (TCD) is a useful tool allowing monitoring in real time during procedure patients cerebral hemodynamic status providing the operator with valuable information. Its role in predicting periprocedural hypoperfusion is, however, less well established. In this article, we discuss the role of cerebral collateral circulation, summarize the current knowledge regarding its evaluation with TCD and suggest future implications for CAS.

Stroke has become the second most common cause of death worldwide and a major cause of disability in industrialized nations.¹ Stenosis of the internal carotid artery (ICA) was found to be responsible for up to 15 to 20% of all strokes or transient ischemic attacks.² To decrease the stroke burden, carotid endarterectomy (CEA) has been used extensively to eliminate both hemodynamically significant stenosis as well as a source of cerebral atheroemboli. Over time, carotid artery stenting (CAS) has evolved into a reputable treatment alternative that might be considered even preferential to CEA in selected patients.³ The long-term benefit of CAS may, however, be offset by the risk of periprocedural stroke, which has mostly been related to the thromboembolism released during endovascular manipulation. To minimize embolic load, several types of emboli protection devices have been developed,

with distal filters being most commonly used so far. Nevertheless, its major limitation is the need for lesion crossing and the inability to capture small particles. This is why proximal protection devices have been invented and are increasingly used in daily praxis. These systems essentially reproduce the hemodynamic condition brought about by surgical clamp–balloon inflation in both external and common carotid artery provides stagnation (or reversal) of flow in the ICA throughout the procedure. Despite being proven effective in reducing the amount of emboli particles released during the procedure, the tradeoff is that the ipsilateral hemisphere is totally dependent on collateral cerebral circulation and may suffer from “silent hypoperfusion.”⁴ This may partly explain why inconsistent results have been reported regarding the superior safety of these systems.^{5,6} Provided that there is no

possibility to “shunt” the lesion, the ability to assess in advance the risk of hypoperfusion induced by carotid clamping might help in identifying those for whom flow arrest/reversal would be inappropriate, thus potentially increasing the safety of the procedure.

Anatomy and Variations of Collateral Cerebral Circulation

The backbone of the collateral cerebral circulation includes intracranial as well as extracranial sources of blood flow which have more commonly been categorized as primary and secondary collateral pathways (►Fig. 1). The circle of Willis constitutes the main/primary collateral cerebral network which is immediately (within seconds) able to support or restore flow in the middle cerebral artery (MCA) following ICA occlusion.⁷ It is formed by anterior communicating artery, which provides interhemispheric blood flow and is considered to be the most potent collateral, and posterior communicating arteries that may supply blood flow in either direction between the anterior and posterior circulations.^{8–10} Other collateral pathways such as the leptomeningeal anastomoses or reversible ophthalmic artery flow are considered secondary networks, which need time for proper functioning and are presumed to be recruited once the primary collaterals have failed.^{11,12} Notably, Okudaira et al showed close relationship between ICA mean stump pressure during balloon occlusion (as a function of the circle of Willis) and the vasomotor reactivity suggesting that collateral circulation in acute ICA occlusion is predominantly determined by the circle of Willis.¹³ Conversely, besides the proposed role in penumbra outcome during acute stroke, leptomeningeal anastomoses adapt very slowly and their meaningful contri-

bution is expected in gradually developing ischemic states such as in patients with moya-moya disease.¹⁴

A considerable heterogeneity of reports can be found in the literature regarding the prevalence of the typical “normal polygon” circle of Willis—bilaterally symmetrical and complete ring of vessels. Despite a likely explanation is the diversity of nomenclature and the criteria used to define hypoplastic vessels, most of the authors agree that the normal polygon is present in less than 50% of the individuals.^{15–17} Interestingly, it has been observed that the posterior portion of the circle of Willis is more likely to be hypoplastic while the anterior portion tends to include duplicate vessels. Thus, the most common anomaly of the circle of Willis is hypoplasia of one or both posterior communicating arteries, which can be found in almost every fourth normal brain. The proximal portion of the posterior cerebral artery segment is the next to be hypoplastic, while hypoplasia in anterior segments can be found in up to 10% of the patients (far more commonly being detected in proximal anterior cerebral artery (ACA) segment (A-1) compared with anterior communicating artery).^{15,16} Therefore, it is not surprising, that the capacity of collateral circulation has large interindividual variation and influences the outcomes of carotid artery disease.^{18–21}

Hemodynamic Consequence of Abrupt Internal/Common Carotid Artery Occlusion in Lesion-Naïve Patients

An invaluable insight into the capability of collateral circulation and its relationship to neurological outcomes in case of acute ICA occlusion can be derived from patients undergoing therapeutic ICA sacrifice. This procedure may sometimes be necessary in case of the treatment of certain tumors of neck or cranial base, cerebral aneurysms, and carotidocavernous fistulae. Because nonselective, abrupt sacrifice of the ICA carries a high risk of morbidity and mortality from hemodynamic stroke, preoperative occlusion test should be performed to assess the adequacy of collateral circulation.^{22,23} While some operators rely on clinical tolerance combined with angiographic techniques such as examination of delayed arterial and/or venous filling (from contralateral or vertebral angiography), others use transcranial Doppler ultrasound (TCD) to measure residual mean blood flow velocity (MBFV) in MCA during balloon test occlusion, which has been shown highly accurate in predicting the collateral capacity. Indeed, several authors attempted to define optimal cut off values beyond which collateral circulation is inadequate and neurological adverse events may be expected.

Most importantly, in the prospective study of Eckert et al, a 20-minute balloon test occlusion with TCD monitoring was performed before therapeutic sacrifice, which was performed in all patients who clinically tolerated the test irrespective of the results of TCD monitoring.²⁴ The authors reported that MBFV drop in MCA of more than 50% was critical for the occurrence of neurological symptoms developing within hours following therapeutic occlusion of the ICA suggesting that these patients were exposed to “silent” ischemia regardless of previous clinical tolerance. Accordingly, using short-

Fig. 1 A schematic illustration of cerebral collateral flow through the circle of Willis and ophthalmic arteries.

lasting (60–90 seconds) balloon occlusion, Sorteberg et al suggested that patients with an immediate drop in MCA velocity to no less than 65% of baseline value tolerated ICA sacrifice well, whereas hemodynamic infarction was likely in those with a corresponding velocity drop below 54% of baseline values.²² Hetzel et al used a manual carotid artery compression and concluded that a threshold of maximal decrease in MBFV of the MCA of 60% would best predict ischemic intolerance.⁷ The compression time of at least 10 seconds was proposed to be mandatory to estimate the collateral capacity of the circle of Willis, however, delayed improvement of flow was occasionally reported.^{7,24}

Thus, albeit different in intended duration of occlusion compared with CAS or CEA (usually lasting no longer than 15 or 40 minutes, respectively), these observations suggest that an abrupt MBFV drop in MCA of more than 50 to 60% exposes the patient to the risk of ischemic complication.

Experience in Carotid Endarterectomy

During CEA, a similar condition to balloon test occlusion is induced by surgical clamping with the addition that the flow in the external carotid artery is interrupted as well. Interestingly, in more than 50 years that CEA has been performed, there has been considerable variation in the approach to the type of anesthesia used during the procedure, without any clear recommendation to date.²⁵ While some surgeons prefer local anesthesia permitting observation of the patient's level of consciousness and motor function, others perform the procedure under general anesthesia using mostly electroencephalography or TCD to identify the development of ischemia. A key reason to monitor cerebral function is to select patients who may benefit from shunt placement during the period of clamp, while arguments for selective as opposed to routine shunting were related to complications that occasionally occur during shunt insertion (such as mechanical injury to the distal ICA) in addition to the greater length of the procedure.

Notably, in the general anesthesia group, it was recommended that shunting be performed in case of TCD-detected MBFV fall below 50% of preclamp value.²⁶ On the other hand, shunt placement based on clinically observed intolerance was traditionally considered the most relevant parameter (due to its high risk of ischemic complication) in the local anesthesia group and, therefore, thoroughly investigated including the potential of TCD to predict this situation in advance.^{27–29} In this regard, Anzola et al found in their large multicenter retrospective analysis that significantly higher flow drops (in most cases > 85% decrease of MCA baseline MBFV) are needed to clinically compromise patients.²⁹ They also suggested that TCD assessment of recruitable collaterals (such as reversal of ipsilateral A-1 segment of ACA) and maximal decrement in MCA flow velocity after carotid compression are useful preoperative predictors of clamping intolerance.

Nevertheless, because the carotid compression test in CAD patient population carries a risk of plaque mobilization potentially resulting in stroke, other means of predicting clamping intolerance were evaluated as well. While most of the usual static parameters such as the asymmetry in pulsa-

tility indexes or in absolute values of MCA or ACA flow velocity were proved to be worthless, ambiguous reports can be found regarding the use of cerebrovascular reserve induced by vasodilatory stimulus. This inconsistency is probably caused by the heterogeneity of patient population in most of the trials.^{27,30–33} Indeed, one of the well-known factor that makes the search for predictors of future shunting difficult is contralateral stenosis or occlusion, which is by itself considered a risk factor.^{27,28} Keeping that in mind, Telman et al used acetazolamide as a vasodilatory stimulus and evaluated the cerebrovascular reserve in 76 patients with isolated unilateral stenosis undergoing CEA.²⁷ Based on their experience, they concluded that the accuracy of predicting the need for shunt was 81%. However, one of the drawbacks of the study was that flow in the ophthalmic artery was not systematically assessed, which in case of reversal may significantly contribute to MCA flow and, as a collateral of last resort, may signify per se exhausted cerebrovascular reserve.³⁴

Implications for Carotid Stenting

Proximal protection systems that impose flow arrest or reversal as a protection against distal embolization significantly reduce the embolic burden of CAS.⁴ Because of its inherent inability to perform a shunt, these systems rely on collateralization to the ipsilateral hemisphere with the risk of insufficient perfusion if collateral pathways are not ready to come into play. Although these systems seem appealing, the rates of clinical adverse events as well as the amount of ischemic brain lesions detected by magnetic resonance imaging have not significantly decreased compared with filter type protections and most of the concerns arise from the risk of silent hypoperfusion during the procedure proposing more careful patient selection.^{5,6} Notably, in a large register of 1,300 patients, Stabile et al reported that clinical intolerance was observed in almost every fifth patient during the period of blood aspiration suggesting that a large proportion of procedures were performed susceptible to complications related to hypoperfusion.³⁵ Indeed, during hypoperfusion, the capacity to clear emboli is impaired, which may be critical during the period of clamp termination and balloon deflation, where emboli showers might still occur.^{36–38}

Similarly as in CEA, angiographic markers of good clinical tolerance (such as size of communicating arteries of > 1 mm or, particularly, marked cross-filling through the anterior communicating artery^{39,40}) are commonly applied in CAS. Nevertheless, these estimates do not provide information about the real-time hemodynamics during CAS procedure. On the other hand, TCD provides the operator with continuous evaluation of cerebral flow, which is mostly beneficial during blood aspiration to avoid further compromising the flow.⁴¹ Although the use of TCD seemed promising in helping to predict clamp tolerance in CEA procedures, there are, however, specific differences related to proximally protected CAS requiring further investigation.

First of all, because the procedure cannot be performed with shunting, patients demonstrating clinical intolerance

during clamp induction are quickly converted to distally protected procedure. Immediate clamp intolerance is, therefore, a less relevant endpoint for preprocedural testing, and thus, based on the available data, it seems more logical to focus on and test for a cut off of limit of 50 to 60% decrease of MCA MBFV during clamp. Accordingly, inability to perform a shunt precludes majority of patients with significantly reduced or absent contralateral flow to undergo balloon clamp without clinical intolerance and therefore further investigation should primarily focus on patients with unilateral CAD. Finally, there is a paucity of knowledge regarding the evaluation of the ophthalmic artery flow as a predictor of collateral reserve, which may, in case of longstanding hypoperfusion, significantly add to the cerebral circulation.

Conclusion

CAS has become a valuable treatment method for selected patients with significant CAD in the risk of stroke or its recurrence. Its most promising innovation is the use of proximal protection systems which, resembling surgical clamp, offer the opportunity to further improve the safety of the procedure. However, the risk of hemodynamic stroke during “silent” hypoperfusion, albeit considered less frequent compared with embolic, may disqualify its potential and further studies should focus on selecting patients with sufficient collateral reserve, who would benefit most from this type of procedure. Transcranial Doppler is an excellent method providing important insight into real-time cerebral hemodynamics. Despite promising data suggest its ability to help predict patients with compromised cerebrovascular reserve, its use in CAS for prediction of silent ischemia should further be tested.

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References

- Donnan GA, Fisher M, Macleod M, Davis SM. Stroke. *Lancet* 2008; 371(9624):1612–1623
- Sacco RL, Kargman DE, Gu Q, Zamanillo MC. Race-ethnicity and determinants of intracranial atherosclerotic cerebral infarction. The Northern Manhattan Stroke Study. *Stroke* 1995;26(1): 14–20
- Spacek M, Veselka J. Carotid artery stenting - current status of the procedure. *Arch Med Sci* 2013;9(6):1028–1034
- Montorsi P, Caputi L, Galli S, et al. Microembolization during carotid artery stenting in patients with high-risk, lipid-rich plaque. A randomized trial of proximal versus distal cerebral protection. *J Am Coll Cardiol* 2011;58(16):1656–1663
- Bijuklic K, Wandler A, Hazizi F, Schofer J. The PROFI study (Prevention of Cerebral Embolization by Proximal Balloon Occlusion Compared to Filter Protection During Carotid Artery Stenting): a prospective randomized trial. *J Am Coll Cardiol* 2012;59(15): 1383–1389
- Castro-Afonso LH, Abud LG, Rolo JG, et al. Flow reversal versus filter protection: a pilot carotid artery stenting randomized trial. *Circ Cardiovasc Interv* 2013;6(5):552–559
- Hetzel A, von Reutern G, Wernz MG, Droste DW, Schumacher M. The carotid compression test for therapeutic occlusion of the internal carotid artery. Comparison of angiography with transcranial Doppler sonography. *Cerebrovasc Dis* 2000;10(3):194–199
- Spacek M, Tesar D, Veselka J. The Paramount Role of the Anterior Communicating Artery in the Collateral Cerebral Circulation. *Int J Angiol* 2014 (e-pub ahead of print). doi: 10.1055/s-0034-1370889
- Miralles M, Dolz JL, Cotillas J, et al. The role of the circle of Willis in carotid occlusion: assessment with phase contrast MR angiography and transcranial duplex. *Eur J Vasc Endovasc Surg* 1995;10(4): 424–430
- Liebeskind DS. Collateral circulation. *Stroke* 2003;34(9): 2279–2284
- Romero JR, Pikula A, Nguyen TN, Nien YL, Norbash A, Babikian VL. Cerebral collateral circulation in carotid artery disease. *Curr Cardiol Rev* 2009;5(4):279–288
- Hofmeijer J, Klijn CJ, Kappelle LJ, Van Huffelen AC, Van Gijn J. Collateral circulation via the ophthalmic artery or leptomeningeal vessels is associated with impaired cerebral vasoreactivity in patients with symptomatic carotid artery occlusion. *Cerebrovasc Dis* 2002;14(1):22–26
- Okudaira Y, Arai H, Sato K. Cerebral blood flow alteration by acetazolamide during carotid balloon occlusion: parameters reflecting cerebral perfusion pressure in the acetazolamide test. *Stroke* 1996;27(4):617–621
- Brozici M, van der Zwan A, Hillen B. Anatomy and functionality of leptomeningeal anastomoses: a review. *Stroke* 2003;34(11): 2750–2762
- Hoksbergen AW, Fülesdi B, Legemate DA, Csiba L. Collateral configuration of the circle of Willis: transcranial color-coded duplex ultrasonography and comparison with postmortem anatomy. *Stroke* 2000;31(6):1346–1351
- Iqbal S. A comprehensive study of the anatomical variations of the circle of willis in adult human brains. *J Clin Diagn Res* 2013;7(11): 2423–2427
- Alpers BJ, Berry RG, Paddison RM. Anatomical studies of the circle of Willis in normal brain. *AMA Arch Neurol Psychiatry* 1959;81(4): 409–418
- Henderson RD, Eliasziw M, Fox AJ, Rothwell PM, Barnett HJM; North American Symptomatic Carotid Endarterectomy Trial (NAS-CET) Group. Angiographically defined collateral circulation and risk of stroke in patients with severe carotid artery stenosis. *Stroke* 2000;31(1):128–132
- Telman G, Kouperberg E, Sprecher E, Gruberg L, Beyar R, Yarnitsky D. TCD evaluation before and after stenting in patients with severe primary carotid artery stenosis versus restenosis. *J Endovasc Ther* 2007;14(4):483–488
- Sánchez-Arjona MB, Sanz-Fernández G, Franco-Macías E, Gil-Peralta A. Cerebral hemodynamic changes after carotid angioplasty and stenting. *AJNR Am J Neuroradiol* 2007;28(4): 640–644
- Silvestrini M, Troisi E, Matteis M, Cupini LM, Caltagirone C. Transcranial Doppler assessment of cerebrovascular reactivity in symptomatic and asymptomatic severe carotid stenosis. *Stroke* 1996; 27(11):1970–1973
- Sorteberg A, Bakke SJ, Boysen M, Sorteberg W. Angiographic balloon test occlusion and therapeutic sacrifice of major arteries to the brain. *Neurosurgery* 2008;63(4):651–660, 660–661
- Mathis JM, Barr JD, Jungreis CA, et al. Temporary balloon test occlusion of the internal carotid artery: experience in 500 cases. *AJNR Am J Neuroradiol* 1995;16(4):749–754
- Eckert B, Thie A, Carvajal M, Groden C, Zeumer H. Predicting hemodynamic ischemia by transcranial Doppler monitoring during therapeutic balloon occlusion of the internal carotid artery. *AJNR Am J Neuroradiol* 1998;19(3):577–582

- 25 Brott TG, Halperin JL, Abbara S, et al. 2011 ASA/ACCF/AHA/AANN/AANS/ACR/ASNR/CNS/SAIP/SCAI/SIR/SNIS/SVM/SVS guideline on the management of patients with extracranial carotid and vertebral artery disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, and the American Stroke Association, American Association of Neuroscience Nurses, American Association of Neurological Surgeons, American College of Radiology, American Society of Neuroradiology, Congress of Neurological Surgeons, Society of Atherosclerosis Imaging and Prevention, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of NeuroInterventional Surgery, Society for Vascular Medicine, and Society for Vascular Surgery. *J Am Coll Cardiol* 2011;57(8):e16–e94
- 26 Garami Z, Lumsden AB. Intra-operative TCD monitoring. In: Alexandrov AV, ed. *Cerebrovascular Ultrasound in Stroke Prevention and Treatment*. 2nd ed. Oxford, United Kingdom: Wiley-Blackwell Publishing; 2011:214–227
- 27 Telman G, Kouperberg E, Nitecki S, et al. Preoperative cerebral hemodynamics and shunting during carotid endarterectomy in patients with severe unilateral carotid stenosis. *J Clin Ultrasound* 2007;35(9):498–503
- 28 Visser GH, Wieneke GH, van Huffelen AC, Eikelboom BC. The use of preoperative transcranial Doppler variables to predict which patients do not need a shunt during carotid endarterectomy. *Eur J Vasc Endovasc Surg* 2000;19(3):226–232
- 29 Anzola GP, Limoni P, Cavrini G. Predictors of carotid clamping intolerance during endarterectomy that would be wise to apply to stenting procedures. *Cerebrovasc Dis* 2008;26(5):494–501
- 30 Thiel A, Zickmann B, Stertmann WA, Wyderka T, Hempelmann G. Cerebrovascular carbon dioxide reactivity in carotid artery disease. Relation to intraoperative cerebral monitoring results in 100 carotid endarterectomies. *Anesthesiology* 1995;82(3):655–661
- 31 Lucertini G, Cariati P, Ermirio D, et al. Can cerebral vasoreactivity predict cerebral tolerance to carotid clamping during carotid endarterectomy? *Cardiovasc Surg* 2002;10(2):123–127
- 32 Belardi P, Lucertini G. Cerebral vasoreactivity does not predict cerebral ischaemia during carotid endarterectomy. *J Cardiovasc Surg (Torino)* 2003;44(6):731–735
- 33 Lam JM, Smielewski P, al-Rawi P, et al. Prediction of cerebral ischaemia during carotid endarterectomy with preoperative CO₂-reactivity studies and angiography. *Br J Neurosurg* 2000;14(5):441–448
- 34 Fearn SJ, Picton AJ, Mortimer AJ, Parry AD, McCollum CN. The contribution of the external carotid artery to cerebral perfusion in carotid disease. *J Vasc Surg* 2000;31(5):989–993
- 35 Stabile E, Salemm L, Sorropago G, et al. Proximal endovascular occlusion for carotid artery stenting: results from a prospective registry of 1,300 patients. *J Am Coll Cardiol* 2010;55(16):1661–1667
- 36 Caplan LR, Hennerici M. Impaired clearance of emboli (washout) is an important link between hypoperfusion, embolism, and ischemic stroke. *Arch Neurol* 1998;55(11):1475–1482
- 37 Orlandi G, Fanucchi S, Gallerini S, et al. Impaired clearance of microemboli and cerebrovascular symptoms during carotid stenting procedures. *Arch Neurol* 2005;62(8):1208–1211
- 38 Spacek M, Veselka J. Microembolization following balloon deflation during proximally protected carotid artery stenting—a potential focus of procedure improvement? *Catheter Cardiovasc Interv* 2014;83(7):1185–1186
- 39 Wain RA, Veith FJ, Berkowitz BA, et al. Angiographic criteria reliably predict when carotid endarterectomy can be safely performed without a shunt. *J Am Coll Surg* 1999;189(1):93–100, discussion 100–101
- 40 Schomer DF, Marks MP, Steinberg GK, et al. The anatomy of the posterior communicating artery as a risk factor for ischemic cerebral infarction. *N Engl J Med* 1994;330(22):1565–1570
- 41 Spacek M, Sorrell VL, Veselka J. Transcranial doppler ultrasound in the current era of carotid artery stenting. *Ultraschall Med* 2014; (e-pub ahead of print)