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Plasticity of Circle of Willis: A Longitudinal Observation of Flow Patterns in the Circle of Willis One Week after Stenting for Severe Internal Carotid Artery Stenosis

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Key Words

Carotid artery stenting · Circle of Willis · A1 hypoplasia · P1 hypoplasia · Posterior communicating artery hypoplasia · Magnetic resonance angiography

Abstract

Background and Purpose: The purpose of the present study was to assess whether the direction of flow via the circle of Willis (CoW) changed after stenting for severe internal carotid artery (ICA) stenosis. ***Methods:*** 65 patients (38 men, mean age 63.2 ± 8.4 years, range 44–82) with a symptomatic ICA occlusion were investigated. Magnetic resonance angiography was performed prior to and 1 week after carotid artery stenting (CAS). The pattern in the CoW was assessed. ***Results:*** One third of the subjects (35.38%) had a significantly altered flow pattern in the CoW after unilateral CAS, including blocked ipsilateral A1 segment collateral (n = 4), blocked contralateral A1 segment collateral (n = 5), blocked ipsilateral posterior communicating artery (PCoA) segment collateral (n = 4), blocked ipsilateral A1 segment and P1 segment collateral (n = 1), opening of ipsilateral A1 segment collateral (n = 5), opening of ipsilateral PCoA segment collateral (n = 3) and opening of ipsilateral P1 segment collateral (n = 1). ***Conclusions:*** CoW segmental hypoplasia is not a static feature. Willisian collateralization with recruitment of the CoW segment (A1, P1 and PCoA) may be blocked after CAS. CAS also leads to the opening of new willisian collateralization, either for relief of reperfusion pressure or for other hypoperfused areas.

Background and Purpose

Klijn et al. [1] stated that the reason why patients with severe carotid artery stenosis (CAS) may show no evidence of intracranial hemodynamic compromise is because collateral circulation compensates for the decrease in cerebral blood flow. The circle of Willis (CoW) is considered the primary collateral pathway. Hoksbergen et al. [2] explained that among the general population, only approximately 50% have a complete CoW; for others a multitude of possible anatomical variations are present, with absent or hypoplastic vessels being quite common. Schomer et al. [3] and Chuang et al. [4] described that the

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anatomical variations in the CoW [including the posterior communicating artery (PCoA) hypoplasia and A1 hypoplasia] may preclude collateral compensation, which is regarded as a risk factor for ischemic cerebral infarction. Accordingly, early recognition of such anatomical risk factors has been suggested. However, Liebeskind and Sansing [5] depict the dynamic transformation of the CoW. Recruitment of a right hypoplastic PCoA was demonstrated in a progressive right middle cerebral-artery stenosis. Kablak-Ziembicka et al. [6] described the hemodynamic transformation of a ceased anterior communicating artery collateral flow after CAS.

Therefore, before validation of the pathologic significance of a PCoA and A1 hypoplasia, it is necessary to determine if the assumed anatomical risk factors are a static feature or a variable parameter. More recently, the hypoplastic segments of the CoW could easily be defined by using magnetic resonance angiography (MRA; diameter, <1 mm on MRA) [3]. Thus, we conducted a longitudinal study of the MRA pattern of the CoW in patients with a severe symptomatic stenosis of the internal carotid artery (ICA) after CAS. We hypothesized that the hypoplastic segment of the CoW may not be a static feature and that an altered flow pattern of the CoW after CAS may indicate a hemodynamic adaptation after CAS.

Subjects and Methods

Patients

There were 71 CAS procedures conducted in our hospital from 2005 to 2007. Forty-one men (mean age 62.8 ± 8.6 years, range 44–82) with a ≥70% ICA stenosis, diagnosed by Doppler ultrasound and MRA, were referred to the Department of Neurology of our hospital. The decision to perform CAS was reached by an independent neurologist and interventionist. Conventional invasive angiography was performed immediately prior to CAS in all patients. The grade of stenosis, as well as the anatomy of other extracranial and cerebral arteries, was assessed with quantitative angiography (Coroscop, Siemens, Erlangen, Germany; Quantcor QCA V2.0 software). A neuroprotection system (proximal or distal) was used in all patients. All patients had transient (lasting <24 h) or minor disabling (Rankin Score 15 ± 3) deficits in the supply territory of a stenosed ICA within a period of 6 months before the first MRA investigation. Sixty-two patients had clinical features caused by hemispheric ischemia (hemispheric transient ischemic attack n = 9, minor disabling ischemic stroke n = 41). Two patients had symptoms of retinal ischemia only (transient monocular blindness n = 1, chronic ocular ischemic syndrome n = 1). The degree of stenosis of the contralateral ICA was assessed according to the criteria of the North American Symptomatic Carotid Endarterectomy Trial. All patients received the best medical treatment available at the time of treatment.

We reviewed all the records of CAS patients retrospectively. Our inclusion criteria required that all subjects were: (1) studied repeatedly with MRA prior to and 1 week after CAS, and (2) not treated by means of a contralateral CAS or a contralateral carotid endarterectomy with an ipsilateral extracranial-intracranial bypass procedure. Afterwards, 6 subjects were excluded due to either incomplete MRA records (n = 3, all were intolerant to the postoperative MRI examination) or having had a contralateral CAS (n = 2) or a contralateral carotid endarterectomy (n = 1).

Therefore, 65 patients were selected for our study and morphologies of serial cerebral MRA studies were analyzed (38 men; mean age 63.2 ± 8.4 years, range 44–82). Each patient provided informed consent to participate in the study. The Human Research Committee of our hospital approved the study protocol.

MRA Study

The MR investigations were performed with a 1.5-tesla whole-body system (ACS-NT 15 model; Philips Medical Systems). The CoW was visualized with a 3-dimensional time-of-flight MRA sequence (TR 31 ms, TE 6.9 ms, flip angle 20°, 2 signals acquired, 50 slices, slice thickness 1.2 mm with a slice overlap of 0.6 mm, field-of-view 100 × 100 mm, matrix size 128 × 128), after which a reconstruction (256 × 256 matrix) was made in 3 orthogonal directions with a maximum intensity projection algorithm.

The images of the CoW were evaluated independently by 2 investigators (Wen-Chuin Hsu, Ho-Fai Wong) to assess the magnetic resonance angiographic morphology of the CoW. Any discrepancy between the 2 investigators was reevaluated in a consensus meeting. The diagnosis of the A1, PCoA and P1 segment hypoplasia was based on the MR angiogram (if <1 mm in diameter including segments not visible on MRA).

Statistical Analysis

The χ^2 test was used to compare the case number differences between patient subgroups with different CoW morphology changes after CAS. Incidences of a complete CoW in preoperative MRA were compared with that of postoperative MRA (table 1). The case number of the subgroup with a blocked CoW segment after CAS was compared with the case number of the subgroup with an openCoW segment after CAS. The case number of the subgroup with a redistribution of the anterior circulation was compared with the case number of the subgroup with a redistribution of the posterior circulation (table 2).

Results

The baseline characteristics of the 65 patients, and the time intervals between the ischemic events and the various investigations, are shown in table 1. An overview of the baseline and postoperative cerebral MRA morphologies are presented in table 1. Baseline MRA tested only 11 subjects (16.9%) with a complete CoW configuration; the majority (n = 54) had an incomplete CoW configuration (83.1%), which included 50 hypoplastic PCoA segments, 23 hypoplastic A1 segments and 4 hypoplastic P1 segments. Postoperative MRA tested 20 subjects (30.7%)

with a complete CoW configuration; the remaining patients (n = 45) had an incomplete CoW configuration (69.3%), which included 45 hypoplastic PCoA segments, 20 hypoplastic A1 segments and 3 hypoplastic P1 segments. Accordingly, the probability of a complete CoW is statistically higher in the postoperative setting (p = 0.03), which indicates a normalization effect from CAS on the CoW.

In individual CoW morphology registration, one third of the subjects (35.38%) had a significantly altered flow pattern in the CoW after unilateral CAS, including morphologies which could be categorized in 7 different patterns (table 2 and fig. 1A–G). The rest (64.62%) remained the same. The probability of a blocked recruitment segment in the CoW after CAS was statistically higher than an opening of a hypoplastic segment in the CoW (p = 0.021). This indicated a normalization effect from CAS, which mainly shut down the previously provoked primary collaterals of the ICA occlusion.

The probability of recruitment of an open/blocked hypoplastic A1 occupied 60% of morphology alterations occurring after CAS, which was statistically higher than the total number of PCoA and P1 (p = 0.025; one subject with a simultaneous redistribution of ant. and post. circulation was excluded). Accordingly, redistribution of anterior circulation served as a predominant major cushion after CAS.

Blocked Recruitment Segment of CoW after CAS (n = 14)

Blocked recruitment of ipsilateral and contralateral A1 segments (n = 9) was the most common feature after CAS. There were 4 subjects who developed ceased recruitment of the ipsilateral A1 (fig. 1A) and 5 subjects who developed ceased recruitment of the contralateral A1 segment (fig. 1B). Accordingly, ipsilateral or contralateral A1 hypoplasia appeared after CAS. The A1 segment of the anterior cerebral artery was the horizontal precommunicating part of the anterior cerebral artery. The A1 segment of the anterior cerebral artery connected with the anterior communicating artery, and served as a collateral pathway for anterior circulation. The frequency of A1 hypoplasia was 1–13%, as derived from angiograms and autopsy reports. To the best of our knowledge, no reports have mentioned the probability of dynamic transformation in A1 segments [4].

Blocked recruitment of an ipsilateral PCoA (n = 4) was the third most common feature after CAS (fig. 1C). Accordingly, an ipsilateral PCoA hypoplasia appeared after CAS. The PCoA communicated with the ICA and posterior cerebral artery (PCA), and served as a collateral pathway between anterior and posterior circulation. The frequency of PCoA hypoplasia was 6–21%, as derived from angiograms and autopsy reports. Our observation of dynamic transformation of the PCoA supported the hypothesis of Liebeskind and Sansing [5].

Table 1. Baseline characteristics, time from ischemic event to investigation, and time between consecutive investigations

Demographic characteristics	
Age, years	63.2 ± 8.4
M/F, n	51/11
Degree of contralateral ICA obstruction, n	
0–69%	55
70–99%	6
100%	4
Time from ischemic event to investigation	
1st MRA, days	93 ± 48
Complete CoW, n	11 (16.9%)
Incomplete CoW, n	54 (83.1%)
1st–2nd MRA, days	7
Complete CoW, n	20 (30.7%)*
Incomplete CoW, n	45 (69.3%)

* p = 0.03.

Table 2. Patterns of CoW morphology alteration after CAS of 23 subjects

No alteration of CoW after CAS	62
Altered flow pattern of CoW after CAS	23
Blocked recruitment segment of CoW after CAS (n = 14)	
(A) Blocked ipsilateral A1 segment	4
(B) Blocked contralateral A1 segment	5
(C) Blocked ipsilateral PCoA segment	4
(D) Blocked ipsilateral A1 segment and P1 segment	1
Opening of hypoplastic segment of CoW after CAS (n = 9)	
(E) Opening of ipsilateral A1 segment	5
(F) Opening of ipsilateral PCoA segment	3
(G) Opening of ipsilateral P1 segment	1
Number of blocked versus open CoW segment	14/9 p = 0.021
Number of redistribution of ant. versus post. circulation	14/8 p = 0.025

Simultaneous redistribution of ant. and post. circulation was excluded (n = 1).

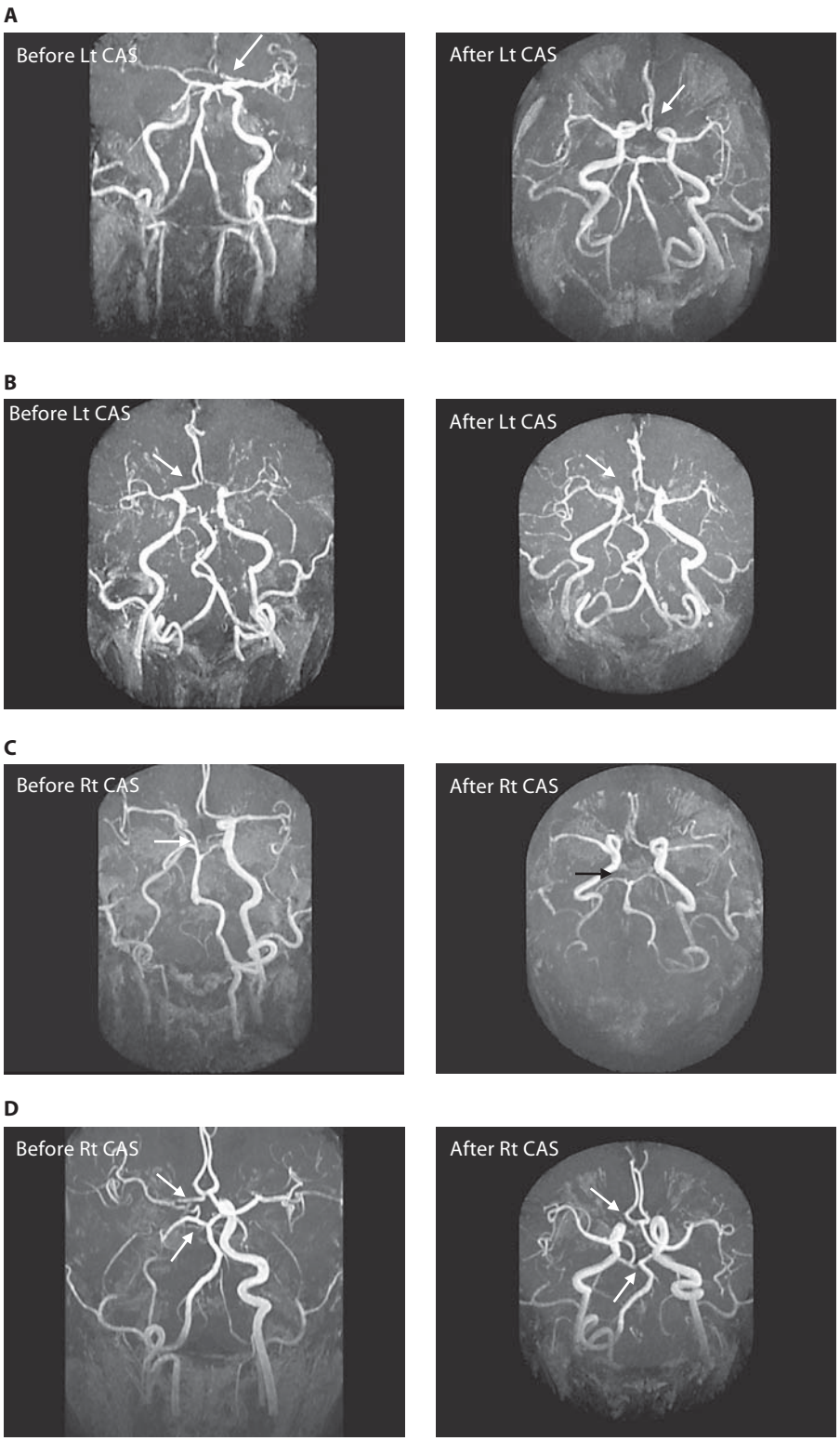

Fig. 1. A comparison of baseline and postoperative MRA morphology of the CoW. There were 7 patterns of CoW alterations after CAS, categorized according to the type of classification shown in table 2. Lt = Left; Rt = right. **A** Blocked ipsilateral A1 segment after CAS (n = 4). **B** Blocked contralateral A1 segment after CAS (n = 5). **C** Blocked ipsilateral PCoA segment after CAS (n = 4). **D** Blocked ipsilateral A1 segment and P1 segment after CAS (n = 1).

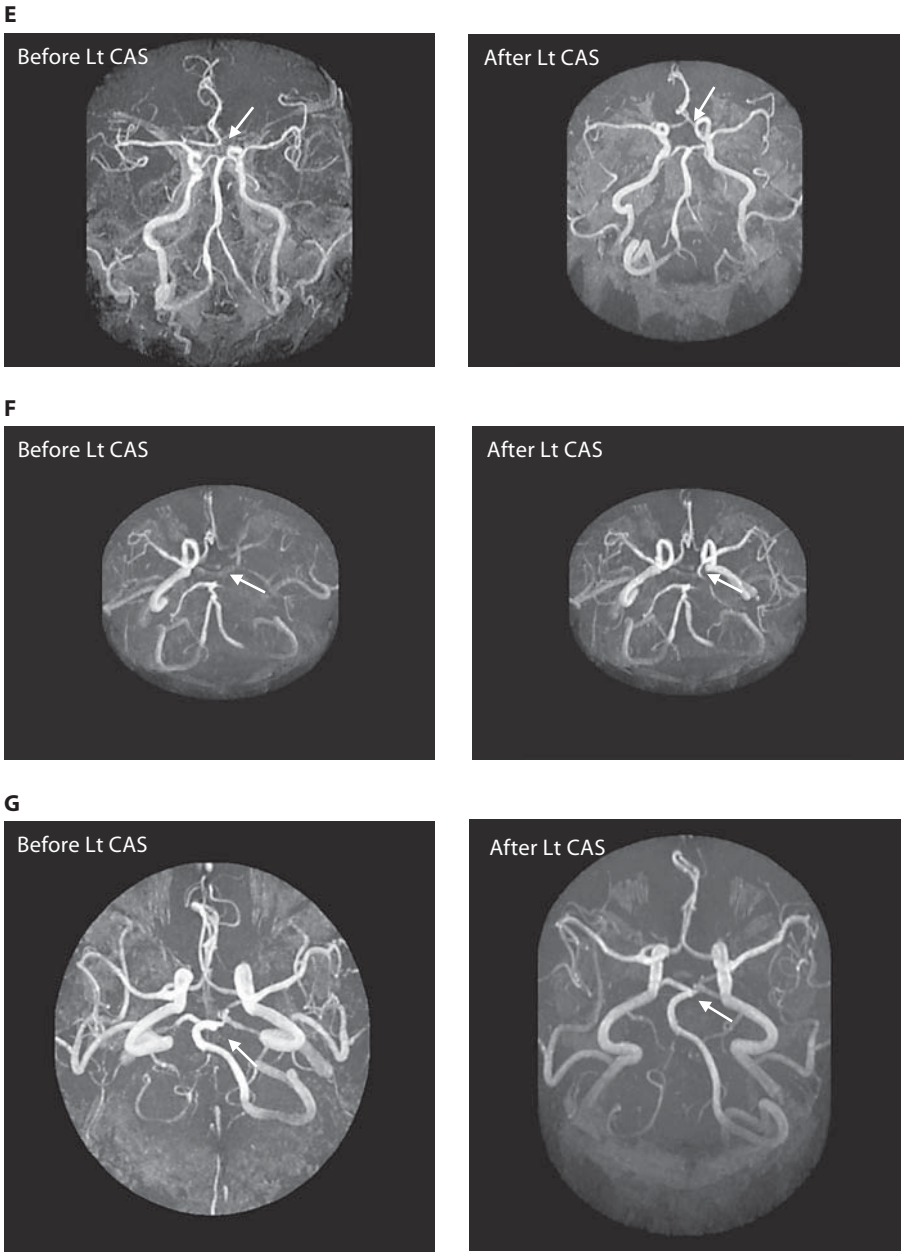

Fig. 1. A comparison of baseline and postoperative MRA morphology of the CoW. There were 7 patterns of CoW alterations after CAS, categorized according to the type of classification shown in table 2. Lt = Left; Rt = right. **E** Opening of ipsilateral A1 segment after CAS (n = 5). **F** Opening of ipsilateral PCoA segment after CAS (n = 3). **G** Opening of ipsilateral P1 segment after CAS (n = 1).

A simultaneous shutdown of the ipsilateral A1 and P1 segments of the PCA after CAS was noted in 1 subject, indicating the simultaneous blocked collaterals of the anterior and posterior circulation after CAS (fig. 1D). Accordingly, an ipsilateral P1 hypoplasia appeared after CAS. The P1 segment of the PCA was the precommunicating segment of the PCA. The incidence of P1 hypoplasia measured 3% in an autopsy study of Voljevica et al. [7]. To the best of our knowledge, no reports have mentioned the probability of dynamic transformation in a P1 segment.

Opening of Hypoplastic Segments in the CoW after CAS (n = 9)

The opening of ipsilateral A1 hypoplastic segments (n = 5) was the second most common feature after CAS. Five subjects developed an opening of an ipsilateral hypoplastic A1 segment after CAS (fig. 1E). Accordingly, the ipsilateral A1 hypoplasia disappeared after CAS. In sum, open (n = 5) and blocked recruitment (n = 9) of the hypoplastic A1 accounted for 60% of morphological alterations after CAS, which indicated that the redistribution of anterior circulation served as a major buffer after CAS.

The opening of an ipsilateral hypoplastic PCoA (n = 2) was also noted after CAS (fig. 1F). Accordingly, the ipsilateral PCoA hypoplasia disappeared after CAS. As we traced back the raw data, there were co-morbid PCA occlusions in these 2 subjects. CAS may lead to new willisian collateralization for other hypoperfused areas. There was 1 subject that developed an opening of the ipsilateral hypoplastic P1 after CAS (fig. 1G). With the absence of co-morbid occlusions in the vertebrobasilar artery, the reason why CAS leads to recanalization of the hypoplastic P1 segment was not clear.

Separate Analyses for Those with Retinal versus Hemispheric Ischemia

Only 2 subjects with retinal ischemia and carotid artery stenosis underwent CAS. There were no morphological alterations of the CoW after CAS. The sample size was too small. Statistical analysis was not attempted.

Discussion

As time-of-flight rather than phase contrast MRA was used, direction of flow cannot be ascertained per se. We emphasize that despite the critiques of time-of-flight MRA in the literature, the modality is of interest precisely because of these flow effects [7, 8].

Based on the results of our small-scale, longitudinal study, we interpreted the fact that the change in the functional anatomy of the CoW after CAS might be caused by false-positive or false-negative findings in part of the circle. Willisian collateralization with recruitment of a substantial hypoplastic segment contributes to a false-negative MRA diagnosis. Carotid revascularization reduced the collateralization demand which shut down the recruitment and led to a false-positive MRA diagnosis of CoW vascular hypoplasia. CoW segmental hypoplasia is not only a variable feature, but also mimics an adaptive electric capacitance. CoW segmental hypoplasia was enrolled as a part of an autoregulation mechanism [8]. In the preoperative 'hypoperfusion' state, a reactive dilatation of a CoW hypoplastic segment was perfused for carotid stenosis. In contrast, a dilated CoW hypoplastic segment was drained and returned to its original caliber in the postoperative setting.

The number of blocked recruitment segments in the CoW was statistically higher than that of the opening of hypoplastic segments in the CoW ($p = 0.021$). We would like to emphasize the critical point that blocked recruitment is more important than the opening of hypoplastic vessel segments. Flow in the brain depends on demand and downstream resistance, not simply upstream pressure that may open hypoplastic segments [9].

A simultaneous shutdown of ipsilateral A1 and P1 segments of the PCA after CAS was noted in 1 subject, indicating the simultaneous blocked collaterals of anterior and posterior circulation after CAS. We would like to stress that it is the total pattern of blood flow to an area that is important, not individual feeding vessels. In other words, once one starts to consider collaterals, one has to consider all potential collateral sources [2]. However, among them, redistribution of anterior circulation was a predominant phenomenon. The probability of open/blocked recruitment of a hypoplastic A1 made up 60% of morphological alterations after CAS. Redistribution of anterior circulation served as a predominant phenomenon. Our explanation was a difference of autoregulation efficiency between the anterior and posterior circulation. Henninger and Fisher [10] described that the sphenopalatine ganglion mainly modulates the vasomotor activity in the anterior two thirds of the CoW. Thus, cerebral autoregulation in the anterior circulation precedes that of the posterior circulation by means of quick neurovascular interaction [11].

Our observation that CoW segmental hypoplasia is not a static feature challenges the position of Schomer et al. [3] and Chuang et al. [4]. Their study's design and diagnosis of CoW segmental hypoplasia was solely based on a single MRA study. After acknowledging that CoW segmental hypoplasia is a variable parameter, the pathologic significance of PCoA and A1 hypoplasia was debated from a static observation. It is necessary to refine those assumed anatomical risk factors. The claims of Schomer et al. [3] should be revised to say that autoregulation failure to recruit a hypoplastic PCoA is a risk factor. In fact, our paper focusing on the hemodynamic aspects of ischemia is refreshing, as the current stroke literature has been focused on arterial anatomy, seemingly isolated from the pathophysiology of blood flow in the brain.

Our conclusion is not straightforward. In fact, the majority of our subjects did not have any alterations of the CoW configuration after CAS. Clearly, a bias against small sample sizes exists. For example, separate analyses for those with retinal versus hemispheric ischemia should be performed due to the different pathophysiologies. However, there were only 2 subjects enrolled with retinal ischemia, who had no morphological alterations of the CoW after CAS. Thus, the sample size was too small for statistical analysis.

In hemodynamic physics, the optimal range of the CoW segmental caliber, 0.4–1.6 mm, was sensitive enough for cerebral autoregulation [11]. Within this range, a competent neurovascular autoregulation can be achieved. Out of this range (<0.4 or >1.6 mm) the CoW segment may fail to regulate upper-stream hemodynamic catastrophes [11, 12]. Thus, evidence-based size criteria of hypoplastic segments <0.4 mm in diameter seemed more appropriate than the widely accepted range of 0.8–1.0 mm [3, 13]. We contradict ourselves by noting that size criteria should be used. Pathophysiology is more relevant than strict adherence to anatomical criteria.

Finally, we plotted the MRA in the CoW 1 week after CAS to determine how carotid artery reconstruction affects the distribution of blood flow. We chose this period because we expected the postoperative hemodynamic chaos would initially become stabilized [14]. Nevertheless, a large-scale study utilizing adequate MRA criteria for hypoplastic CoW segment with a longer time interval MRA registration and a follow-up will be needed to test the reproducibility of our findings. Despite these limitations, we believe that the plasticity of the CoW is a real entity and its pathophysiology deserves greater attention.

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