Aneurysmal Remodeling in the Circle of Willis Following Carotid Occlusion

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Introduction

Carotid occlusion could be caused by carotid pathologies (stenosis), trauma, or surgical ligation as a defensive treatment option for preventing potential rupture of complex intracranial aneurysms (IA). Regardless of etiology, carotid occlusion has lesser-known repercussions including pathological remodeling of the neurovasculature due to compensatory contralateral flow increase. More and more reports have described de novo IA formation contralateral to carotid occlusion,1 but this phenomenon is seldom studied and thus not well understood.

Our previous research using bilateral common carotid artery ligation in rabbits has demonstrated that compensatory flow increase through the basilar artery (BA) after ligation causes aneurysm formation at the basilar terminus (BT).2 The goal of this study2 was to quantitatively investigate the characteristics and extent of flow-induced vascular remodeling in the entire Circle of Willis (CoW) caused by carotid occlusion using the same rabbit model.

Methods

Bilateral Carotid Artery Ligation

We ligated the carotid arteries of rabbits (n=9) to emulate carotid occlusion in clinical scenarios. This manipulation stopped flow through the carotid arteries and increased it through the BA, rerouting it through the CoW.3 For control, a sham surgery was performed where vessels were accessed but not ligated. Three ligated rabbits and 3 sham rabbits were euthanized 5 days after surgery, and the remaining ligated rabbits (n=6) were euthanized after 6 months.

Vascular Corrosion Casting & Scanning Electron Microscopy

We created vascular corrosion casts of the CoW after euthanasia. These casts were imaged with scanning electron microscope at 50 X magnification. Mosaic images of the entire CoW were created.

Quantification of Gross Morphological Properties

Vessel diameters and lengths were measured on mosaic images. For available arteries, vascular tortuosity was assessed with a tortuosity index, TI=(L-C)/C, where L is vessel arc length and C is the straight-line chord distance.

Quantification of Macro- and Microscopic Vascular Damage

In 9 regions, we assessed 5 different types of damage, and stratified them based on increasing severity:

- Endothelial cell (EC) irregularities: deviations from typical EC morphology.
- Internal elastic lamina (IEL) fenestrations: focal luminal indentations due to IEL weakening or matrix damage.
- Smooth muscle cell (SMC) imprints: striations perpendicular to flow that indicate massive IEL loss that places the EC layer directly on top of SMCs.
- Segmental dilations: circumferential arterial expansions of a vessel segment.
- Pre-aneurysmal bulges: localized outpouchings of the artery.

Damage in each region was evaluated with a progressive graded scoring method called the Vascular Damage Score (0-no damage to 30-maximum damage), which combined the contribution of each type of damage into one value.5

![Diagram](image1)

![Diagram](image2)

![Graph](image3)

![Graph](image4)

![Diagram](image5)

![Graph](image6)

4. Vascular damage was progressive with time.

Damage occurred in the CoW at 5 days and was increased at 6 months. Aneurysmal damage occurred most prominently at the BT, OA origin, and PCom.

5. Segmental dilations correlated with elevated tortuosity

Segmental dilations only developed on PComs that were sufficiently tortuous.

Conclusions

Although carotid occlusions have been associated with de novo IA formation in clinical case reports, the phenomenon has not been widely studied. In this study, we used a blood flow manipulation (bilateral common carotid artery ligation) to simulate carotid occlusion in rabbits, and vascular corrosion casting and scanning electron microscopy to evaluate its effects on the CoW.

Flow increase after ligation elicits both early compensatory adaptive arterial enlargement and progressive pathological remodeling, including tortuosity and aneurysm formation, in the CoW. Early vessel diameter increase is an adaptive response to increased flow through the posterior CoW. Pathological remodeling, specifically pre-aneurysmal bulge and segmental dilation formation and PCom tortuosity increase are likely the result of flow-induced IEL damage (fenestrations and SMC imprints). Carotid occlusions are frequently diagnosed. The lesser-known consequences of occlusion – progressive pathological remodeling such as tortuosity and saccular/fusiform aneurysm – are rarely taken into account in current clinical management algorithms. Potential complications from this pathological remodeling should be considered when managing patients with carotid artery disease and when contemplating carotid ligation as a treatment option.

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References


Data is presented as mean ± standard error. * p<0.05 vs. sham. † p<0.05 vs. 5-day.