

IMAGING CASE

Evaluating Vascular Hemodynamics in Cerebral Proliferative Angiopathy Using Advanced Arterial Spin Labeling MRI

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Cerebral proliferative angiopathy (CPA) is a rare vascular disorder that affects normal blood circulation in the brain. Although the structural changes in CPA can be characterized using standard radiologic modalities, assessing the vascular hemodynamics in patients with CPA remains challenging due to inadequate imaging technologies. Arterial spin labeling (ASL) is a noninvasive magnetic resonance technique that allows quantitative assessments of cerebral blood flow. ASL with multiple labeling delays (multidelay ASL) also enables the quantification of arterial transit time. Here, we report the first application of multidelay ASL in a patient with CPA before and after bypass surgery. Our study demonstrated that ASL can be effectively applied to evaluating hemodynamic changes in patients with CPA. Our quantitative results indicated that, in regions affected by CPA, cerebral blood flow increased by at least 14% and arterial transit time decreased by 9.4% after bypass surgery.

A 4-year-old male with no pertinent past medical or surgical history presented after a left hemisphere transient ischemic attack characterized by acute onset right-sided transient weakness on his upper and lower extremities. There were subsequent stroke-like episodes lasting for 1 to 2 hours of right-sided weakness, right facial droop, slurred speech, and word-finding difficulty about once a week over the course of 1 month. On exam, the patient was noted to be neurologically normal. The patient did not have any port wine stains or other cutaneous marks suggestive of a neurocutaneous syndrome.

DIAGNOSTIC WORKUP

After the initial head computed tomography (CT) with CT angiogram scan, a left hemisphere arteriovenous malformation was suspected (Figure 1). A digital subtraction angiography was performed and showed dif-

fuse capillary ectasia in the left basal ganglia/thalamus, with additional foci in the posterior frontal lobe, parietal lobe, temporo-parieto-occipital junction, and parahippocampal regions, without associated large vessel stenosis and early venous drainage without a dominant shunt (Figure 2). These findings were compatible with cerebral proliferative angiopathy (CPA).¹ The patient was submitted to a magnetic resonance (MR) imaging session with the aims of confirming the diagnosis and contributing to characterization of the hemodynamics of the lesion, on a 3T MR imaging system (Discovery MR 750, GE Healthcare, Waukesha, WI, USA). Key MR sequences include 3-dimensional time-of-flight MR angiography, diffusion weighted imaging, T1-weighted, and T2-weighted fluid-attenuated inversion recovery structural images. Two arterial spin labeling (ASL) sequences were performed: the standard single-delay ASL (labeling duration = 1450 ms; postlabeling delay = 2025 ms) and the advanced multidelay ASL (labeling duration = 2000 ms; postlabeling delay = 700, 1325,

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1950, 2575, 3200 ms).² For single-delay ASL data, cerebral blood flow (CBF) was calculated using the approach in the ASL white paper.³ For multidelay ASL data, CBF and arterial transit time (ATT) were calculated by fitting the ASL difference data to the general kinetic model using the FMRIB Software Library tool Bayesian Inference for Arterial Spin Labeling MR imaging.⁴ CBF and ATT maps were transferred to Montreal Neurological Institute Standard Space to facilitate visualization using both linear and nonlinear registration. The mean±SD of CBF and ATT were calculated within the regions affected by CPA (left middle cerebral artery territories). The regions of interest were delineated based on the Harvard–Oxford cortical and subcortical structural atlases.⁵

The main findings on conventional MR sequences are shown in Figure 3, demonstrating some volume loss in the left cerebral hemisphere as well as some T2/fluid-attenuated inversion recovery hyperintense signals in the white matter and nonspecific punctate hyperintense T2/fluid-attenuated inversion recovery signals in the bilateral frontal and parietal lobes.

MANAGEMENT/INTERVENTIONS

It was considered the patient could benefit from a left indirect bypass to restore normal hemodynamics in the affected regions and reduce the likelihood of additional transient ischemic attacks or full-blown ischemic events. Three days after the presurgery MR scan, an indirect left encephalo-duro-arterio-synangiosis revascularization procedure was performed using the patient's parietal superficial temporal artery (STA) as the donor, widely opening the arachnoid and placing the dura STA above on the pial surface of the brain surface such that, over time, new blood vessels would grow into the brain, improving blood flow to the affected area. Specifically, the parietal branch of the STA was identified as the donor blood vessel. After isolating this artery, the arachnoid membrane was opened, and the was placed in direct contact with the brain's pial surface. Additionally, the dura was positioned to hold the STA in place. This positioning promotes angiogenesis, whereby new blood vessels naturally grow from the STA into the surrounding brain tissue over time. As these vessels develop, they enhance blood supply to the affected brain regions. By gradually restoring circulation, encephalo-duro-arterio-synangiosis reduces the risk of future ischemic events and improves overall neurological health, supporting better long-term outcomes for patients.⁶ The patient tolerated the procedure well

Nonstandard Abbreviations and Acronyms

ASL	arterial spin labeling
ATT	arterial transit time
CBF	cerebral blood flow
CPA	cerebral proliferative angiopathy
MR	magnetic resonance
STA	superficial temporal artery
VRT	volume rendering technique

and was discharged home 3 days later with a stable neurological examination.

FOLLOW-UP

After the extracranial–intracranial bypass, the patient's episodes initially resolved, but resumed around 4 months later, albeit less frequent, less severe, and usually shorter than prior episodes. The patient started kindergarten, which is going well, with no concerns regarding all his developmental milestones. The patient was submitted to a control digital subtraction angiography 6 months after surgery, showing a widely patent indirect bypass on the left with extensive extracranial to intracranial revascularization, and otherwise stable findings of CPA (Figure 4).

Postsurgical MR images were acquired following the same protocol described previously. Figure 5 shows the MR angiography, CBF, and ATT maps of this patient before and after bypass surgery. Before the surgery, both single-delay and multidelay ASL showed high CBF values in both middle cerebral artery territories. Additionally, multidelay ASL also revealed delayed ATT mostly in the left hemisphere. After the bypass surgery, ATT measured by multidelay ASL decreased, implying improved hemodynamics. Table 1 shows the mean±SD of CBF and ATT in both middle cerebral artery territories. Overall, CBF measured by both ASL techniques increased and ATT measured by multidelay ASL decreased in the left hemisphere after surgery.

BRIEF DISCUSSION

CPA is a rare vascular disease characterized by a diffuse network of abnormally dilated capillaries within the brain, with a lack of dominant venous drainage and with normal brain parenchyma in between the abnormal vessels, presenting significant challenges

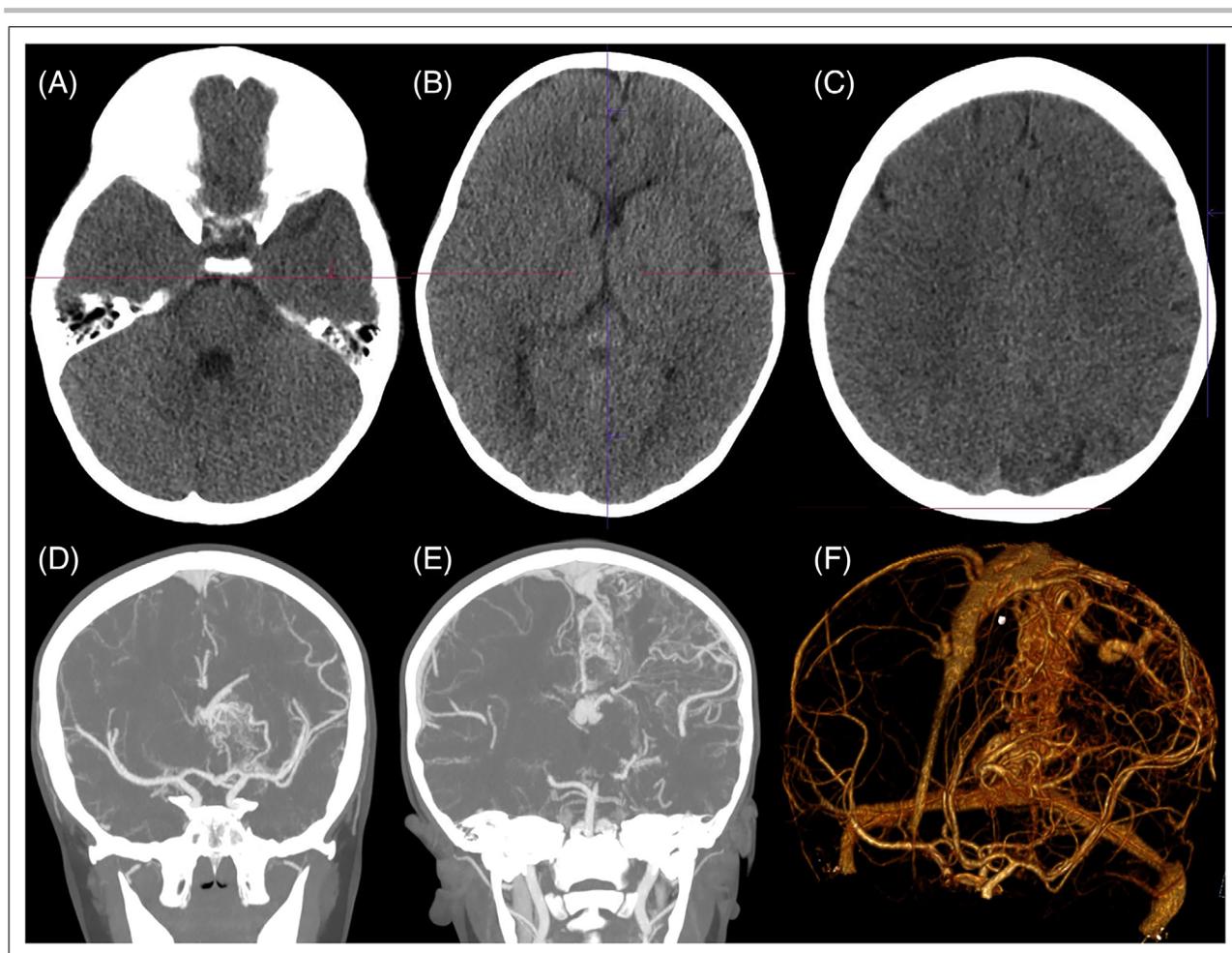


Figure 1. Initial head CT scan. Noncontrast head CT axial images (Subplots **A**, **B**, and **C**) at the posterior fossa, ganglionic, and supraganglionic levels, respectively, excluding signs recent intracranial hemorrhage, a territorial infarction or a space-occupying lesion. CT angiography coronal MIP (Subplots **D** and **E**) and VRT (Subplot **F**) images showed diffuse vascular dilation mainly involving distal branches of the left MCA without a clearly defined nidus, and associated ectasia of numerous superficial and deep venous structures in the region. CT indicates computed tomography; MCA, middle cerebral artery; MIP, maximum intensity projection; and VRT, volume rendering technique.

Table. Mean±SD of CBF and ATT Measurements in the MCA Territories Before and After Surgery

		Before surgery	After surgery
Left hemisphere	Single-delay ASL CBF (mL/100 g/min)	44.3±26.9	58.1±38.7
	Multidelay ASL CBF (mL/100 g/min)	52.1±29.1	59.6±32.6
	Multidelay ASL ATT (seconds)	1.59±0.44	1.44±0.40
Right hemisphere	Single-delay ASL CBF (mL/100 g/min)	22.6±10.7	20.8±9.33
	Multidelay ASL CBF (mL/100 g/min)	76.3±22.7	65.0±26.1
	Multidelay ASL ATT (seconds)	1.20±0.95	1.18±0.65

ASL indicates arterial spin labeling; ATT, arterial transit time; CBF, cerebral blood flow; and MCA, middle cerebral artery.

for diagnosis and management.^{1,7} Whereas the diagnosis of CPA relies on cerebral digital subtraction angiography, assessing the vascular hemodynamics in patients with CPA requires other imaging modalities. For instance, Saito et al, demonstrated changes in hemodynamics using single-photon emission computed tomography.⁸ The advent of advanced imaging

technologies has enhanced neurovascular diagnostics, allowing quantitative and noninvasive assessments of vascular hemodynamics.

ASL is a noninvasive and quantitative MR imaging technique that can measure CBF. Multipostlabeling delay pseudocontinuous ASL is an advanced ASL technique that not only enables more accurate CBF but can

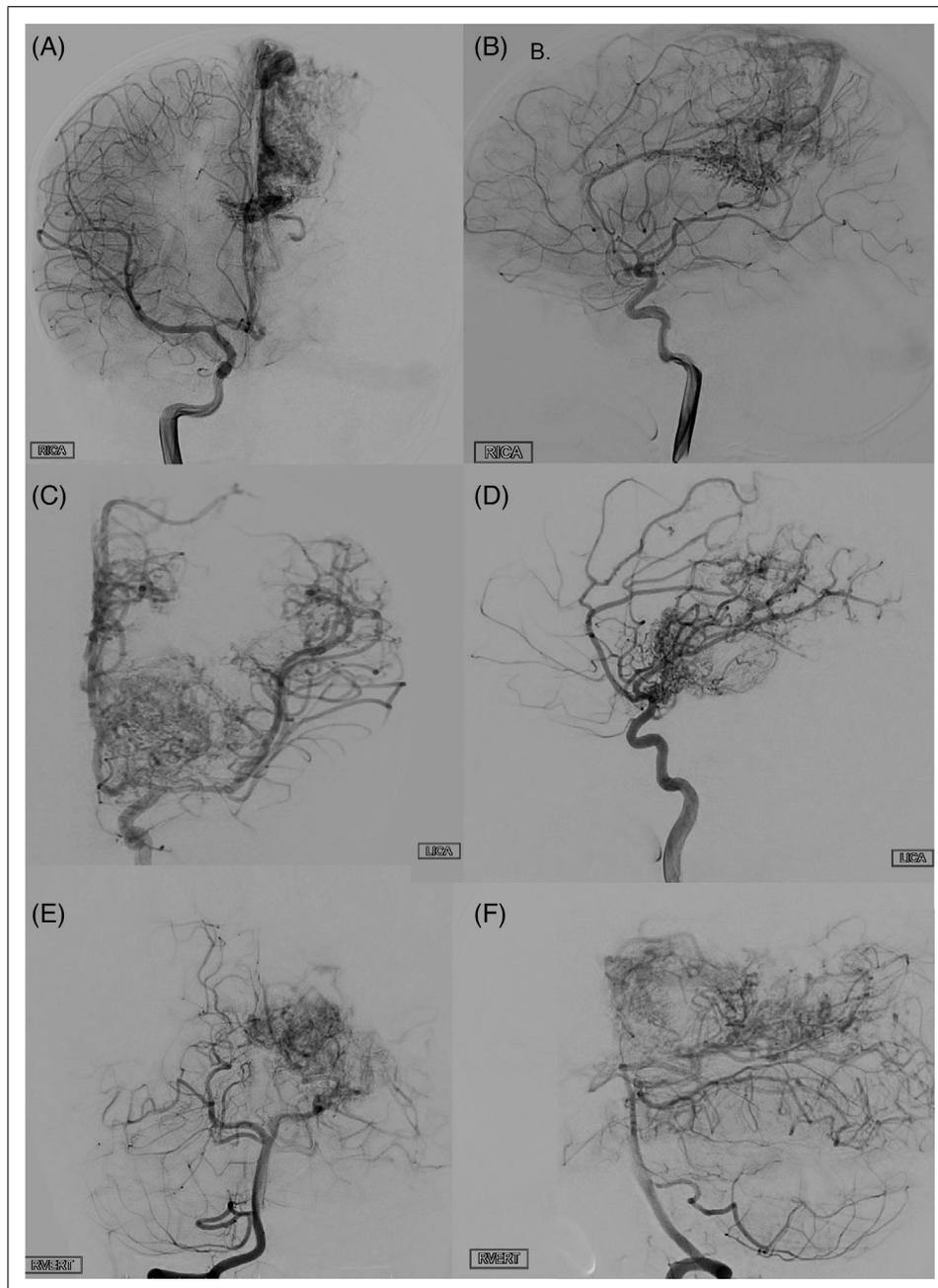


Figure 2. Presurgical conventional angiography. Digital subtraction angiography images following selective catheterization of the right internal carotid artery (Subplots **A** and **B**), left internal carotid artery (Subplots **C** and **D**) and right vertebral artery (Subplots **E** and **F**) showing a diffuse capillary ectasia in the left basal ganglia/thalamus, with additional foci in the posterior frontal lobe, parietal lobe, temporo-parieto-occipital junction, and para-hippocampal regions. Arterial supply arising from the left anterior, middle, and posterior cerebral arteries as well as the anterior choroidal artery and medial and lateral lenticulostrate branches, without associated large vessel stenosis. Early venous drainage mainly into multiple parietal and occipital cortical veins (Subplot **B**).

also derive ATT, a quantitative metric representing the time for the labeled blood to travel from the labeling plane to brain tissues.⁹

This is the first report demonstrating changes in CBF and ATT measured by ASL, before and after revascularization surgery in a pediatric patient with CPA. Given

the rarity of CPA, studies have focused on structural progression of the impaired arteries of the disease and evaluating vascular hemodynamics in patients with CPA has been challenging especially due to the absence of a validated noninvasive and noncontrast dependent method.

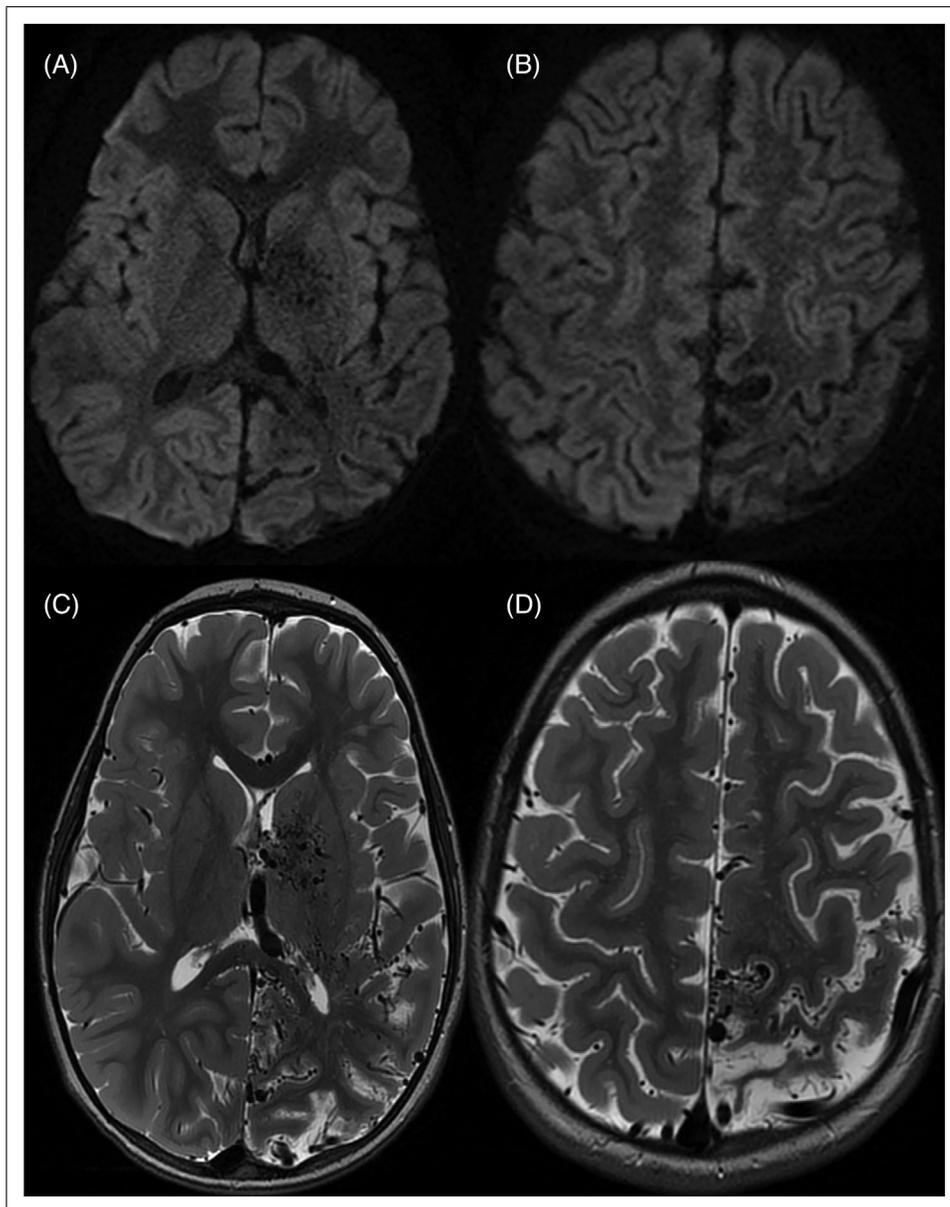


Figure 3. Main findings on conventional MR scan. Conventional brain MR sequences (Subplots **A** and **B**: DWI, ganglionic and supra-ganglionic levels respectively; Subplots **C** and **D**: axial T2 images at the same levels) on the preoperative study showing mild left hemispheric atrophy, predominantly involving the left parietal lobe, a few small T2 hyperintense lesions in the white matter of both cerebral hemispheres without evidence of acute ischemic lesions on DWI. Prominent ipsilateral flow-voids suggestive of a diffuse vascular malformation, without a clear nidus, and with an apparently normal intervening parenchyma at both levels. DWI indicates diffusion weighted imaging; and MR, magnetic resonance.

In this work, we have demonstrated that both single-delay and multidelay ASL are effective in evaluating vascular hemodynamics in patients with CPA. In our quantitative data, we have shown that in brain regions affected by CPA CBF increased by 32% and ATT decreased by 9.4% after bypass surgery. These results imply improved hemodynamics in the cerebral circulation. One limitation of this study is that the measurements provided were calculated in regions affected by CPA, with possible influence of the hyperperfusion

of the abnormal vessels in the quantitative results presented.

In conclusion, we have presented changes in vascular hemodynamics in a patient with CPA. Our imaging study revealed that, in regions affected by CPA, CBF increased and ATT decreased over a 6-month period. This is the first documented evidence of the impact of bypass surgery on vascular hemodynamics assessed using advanced MR imaging in patients with CPA.

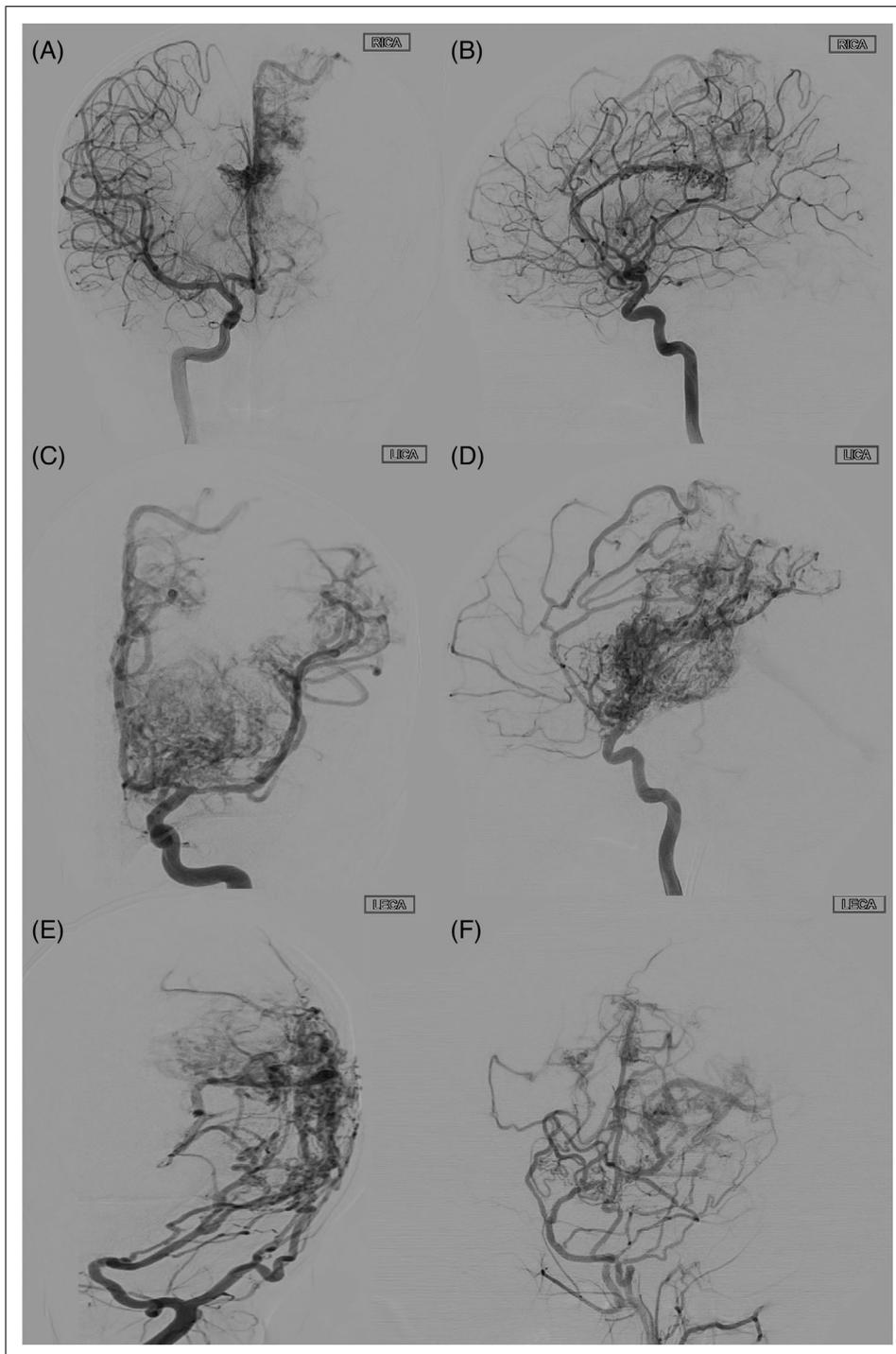


Figure 4. Postsurgical conventional angiography. Digital subtraction angiography images following selective catheterization of the right internal carotid artery (Subplots **A** and **B**), left internal carotid artery (Subplots **C** and **D**), and left external carotid artery (Subplots **E** and **F**) showing stability of the presurgical findings of CPA on both ICA territories, and a patent indirect bypass on the left with extensive extracranial to intracranial revascularization. CPA indicates cerebral proliferative angiopathy; and ICA, internal carotid artery.

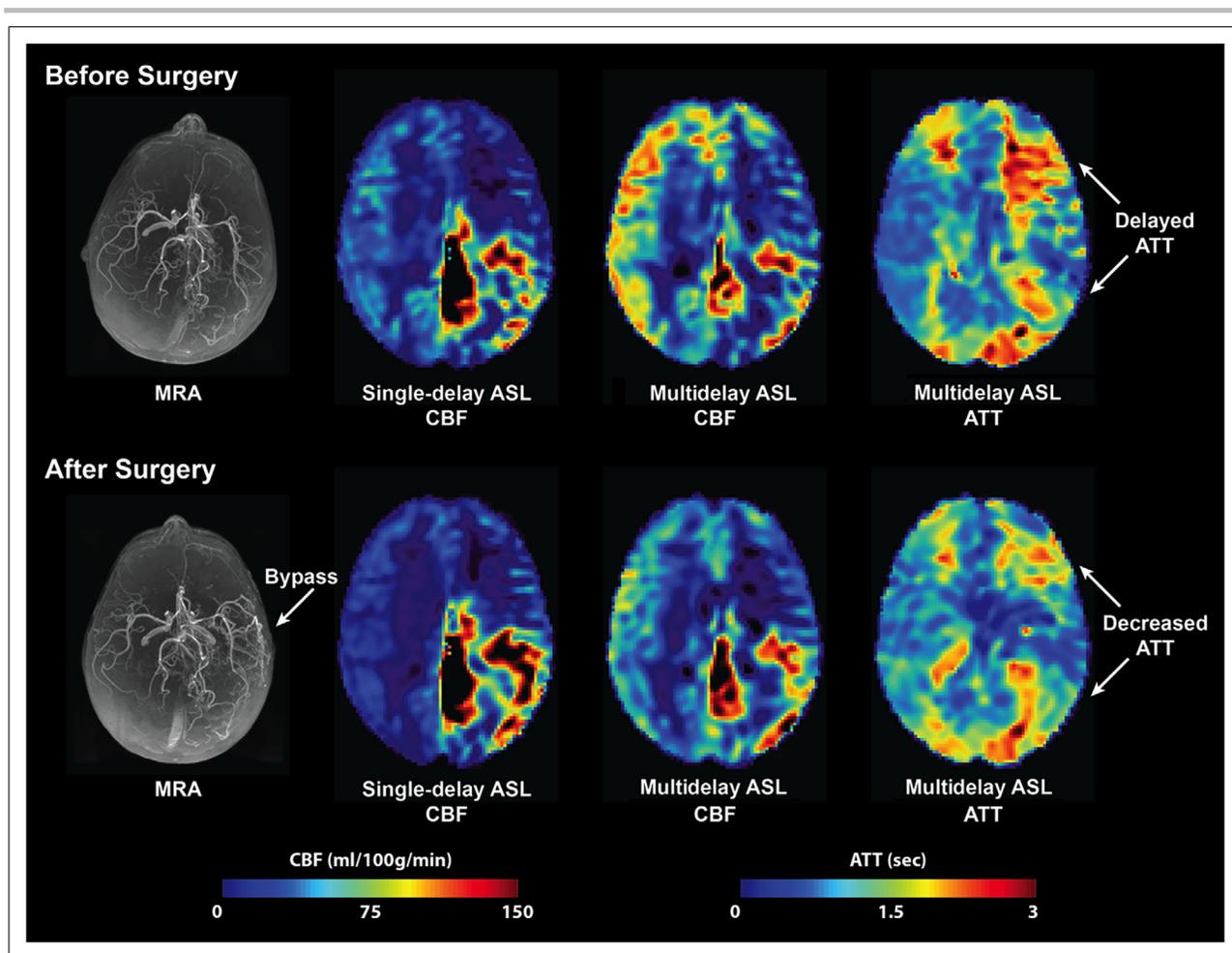


Figure 5. MRA and ASL perfusion comparison before and after bypass surgery. MRA, CBF, and ATT maps of the patient with CPA. For both single-delay and multidelay ASL, a high CBF can be observed near regions affected by CPA. Before surgery, delayed ATT can be seen in these regions. After the bypass surgery, ATT in regions affected by CPA decreased. ASL indicates arterial spin labeling; ATT, arterial transit time; CBF, cerebral blood flow; CPA, cerebral proliferative angiopathy; and MRA, magnetic resonance angiography.

ARTICLE INFORMATION

Received July 29, 2024; Accepted November 4, 2024

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Acknowledgments

This work was supported by the American Heart Association (Grant: 23SCE-FIA1141920).

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