JVIN Journal of Vascular and Interventional Neurology
OFFICIAL JOURNAL OF THE ZEENAT QURESHI STROKE INSTITUTE

Use of Arterial Spin-Labeling in Patients with Aneurysmal Subarachnoid hemorrhage

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Abstract

Delayed cerebral ischemia (DCI) due to cerebral vasospasm following aneurysmal subarachnoid hemorrhage (aSAH) has long been recognized as a major source of morbidity and mortality. Early detection of cerebral vasospasm and identification of patients who are likely to become symptomatic is crucial to guide aggressive medical and/or endovascular interventions. Magnetic resonance imaging using arterial spin-label (ASL) is a noninvasive mean for assessing cerebral blood flow and is based on direct magnetic labeling of arterial blood water protons. The diagnostic role of ASL in acute ischemic stroke, epilepsy, and neurodegenerative disorders has been explained in multiple studies but its ability to predict vasospasm in aSAH has not been published before. The purpose of this study is to highlight the diagnostic implications of different perfusion patterns of ASL in patients with aSAH which can be utilized to prevent DCI in such patients when other commonly used modalities are not available, contraindicated, or fail to detect vasospasm.

Keywords

Aneurysmal subarachnoid hemorrhage; magnetic resonance imaging; arterial spin-label; delayed cerebral ischemia

INTRODUCTION

An estimated 6 million (or 1 in 50) people in the United States have an unruptured brain aneurysm and the annual rate of brain aneurysmal rupture is approximately 8–10 per 100,000 population. The annual incidence of in-hospital deaths from aneurysmal subarachnoid hemorrhage (aSAH) in the United States is estimated to be around 6700, however, the mortality rates have declined during the last few decades (a recently estimated mortality rate of ~33%) because of advances in treatment and ability to better prevent and cope with serious complications related to SAH, including delayed cerebral ischemia (DCI) [1,2].

DCI is usually defined as the onset of focal neurological deficits (such as hemiparesis, aphasia, apraxia, hemianopia, or neglect) or at least a two points decrease on the Glasgow coma scale (either on the total score or on one of its individual components), lasting for at least one hour which is not apparent immediately after aneurysm occlusion, and cannot be attributed to other causes by means of clinical assessment, CT or MRI scanning of the brain, and appropriate laboratory studies [3]. The main preceding factor of DCI is cerebral vasospasm, the delayed narrowing of large-capacitance arteries at the base of the brain following SAH, and is seen by angiography in 30%–70% of patients and nearly 50% of them develop DCI. The peak time of vasospasm following SAH is between 5 and 14 days with gradual resolution over 2–4 weeks [1,2].

The most important factor which determines outcome after SAH, including Level 1 trauma centers, is DCI due to cerebral vasospasm following aneurysmal SAH. Hence, early detection of cerebral vasospasm and identification of patients who are likely to become symptomatic is crucial to guide aggressive medical and/or endovascular interventions aimed at preventing DCI [3]. Unfortunately, at this time, there is no accurate and reliable noninvasive method to predict early and delayed vasospasm. If patients at risk could be identified prior to

Vol. 10, No. 3, pp. 10–14. Published May, 2019.

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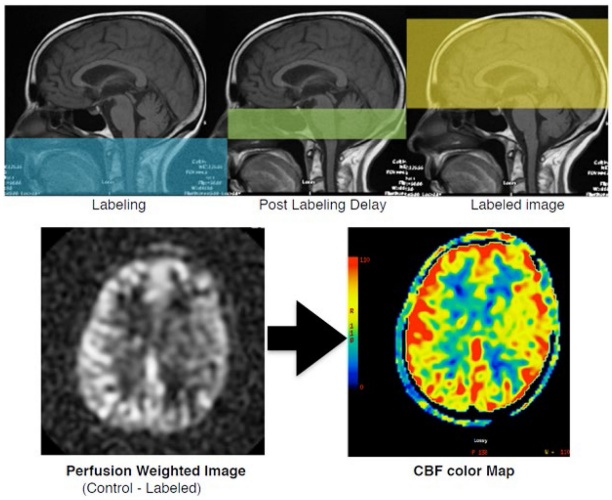


Figure A. ASL labeling technique: the arterial blood water is magnetically labeled caudal to the area of interest with the application of an inversion pulse. Following a delay to allow the labeled blood water to diffuse into the brain tissue and alter the total tissue magnetization, a second image is obtained (tagged image). This process is repeated without the application of an inversion pulse to obtain a control image. The tagged image and the control image are subtracted to produce a perfusion image which reflects the amount of arterial blood delivered, expressed in units of mL/100 g/min.

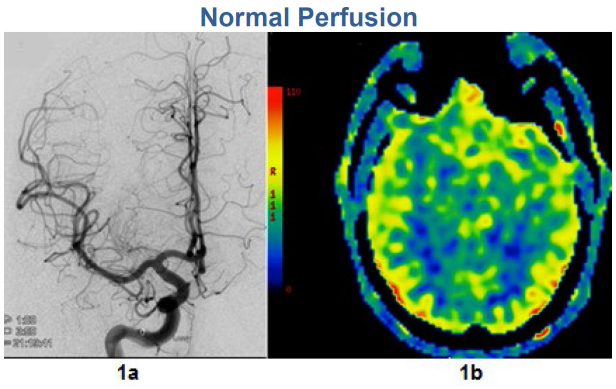


Figure 1a. showing normal digital subtraction angiogram (DSA) without any evidence of vasospasm. Figure 1b showing normal ASL imaging: there is a symmetric flow between the two hemispheres, cortical gray matter exhibits slightly higher signal intensity than white matter from using the same coefficient called baseline magnetization artifact. High signal intensity in the occipital region is due to an activation of the visual areas in the MRI environment. (The tagged image and the control image are subtracted to produce a perfusion image which is expressed in units of mL/100 g/min.)

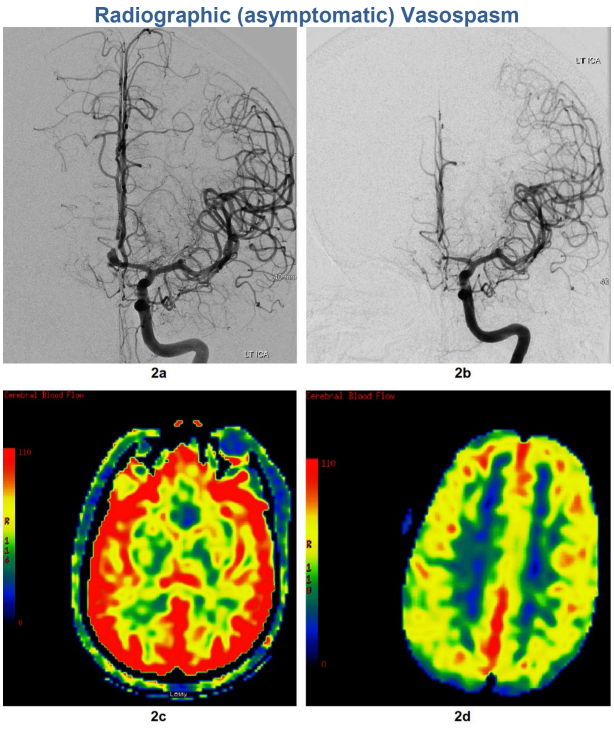
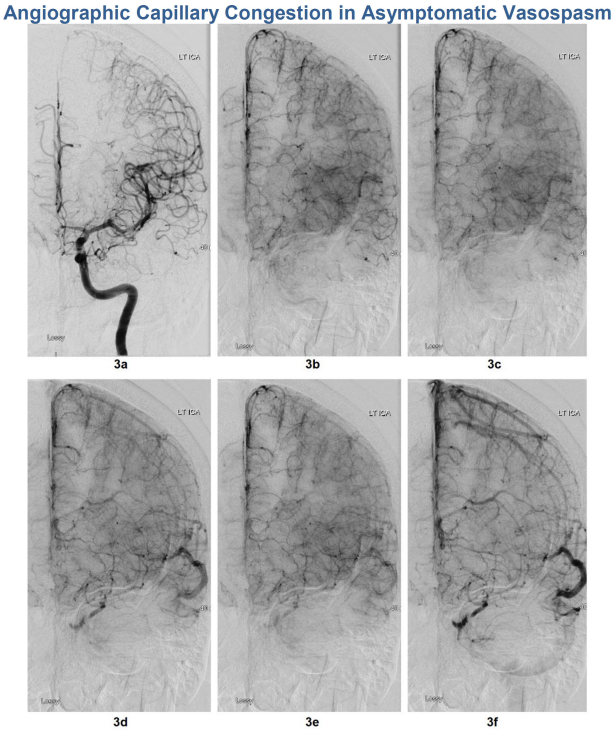


Figure 2a:DSA at day 0, no evidence of vasospasm, MCA and ACA territories opacify in the midarterial phase symmetrically and contributing to the watershed area equally.
Figure 2b: DSA at day 8 showing vasospasm, there is a delay in the ACA territory opacification with the MCA contributing to the watershed area, as well the ACA territories via pial collateral.
Figure 2c: ASL at day 8 showing vasospasm with intact collaterals.
Figure 2d: ASL at day 16 showing resolution of vasospasm.

the development of DCI, this may improve the morbidity and mortality associated with aneurysmal SAH, as well as reduces the length of stay in the intensive care unit. The purpose of this study is to determine the role of magnetic resonance (MR) imaging using arterial spin-label (ASL) in identifying patients at risk of delayed vasospasm to significantly reduce the number of days spent in the NICU.

PRINCIPLES OF USING ASL

Various imaging modalities are being used at neuro-critical care units across the US for early detection and guiding the management of vasospasm, including CT angiography, CT perfusion, perfusion-weighted imaging, and positron emission tomography but they all require use of contrast or radioactive substance, making their use challenging in certain patient populations [2,4].



Figures 3 a–f. Angiographic images from the patient presented in Figure 3 (AP view in 2 fps from the midarterial phase 3a to the early venous phase 3f).

ASL is a noninvasive mean for assessing cerebral blood flow (CBF)/cerebral perfusion and was first introduced in 1991 by Williams *et al.*[5], since then, this technique has been further optimized to create numerous labeling approaches which are being utilized in increasing number of clinical applications, including assessment of perfusion territories of the individual cerebral arteries in ischemic stroke, arteriovenous malformation, epilepsy, tumors, and neurodegenerative disorder [6–9]. The most prominent advantage that ASL has over other means of assessing cerebral perfusion is its noninvasiveness. Unlike other means of assessing cerebral perfusion, it does not require an exogenous contrast making it an excellent choice for initial or follow-up studies even in the special patient population, including children and patients with contrast allergy or renal failure.

ASL imaging technique is based on direct magnetic labeling of arterial blood water protons before it flows into the tissue of interest by using inversion radiofrequency (RF) pulses (Figure A). This labeling can be achieved by two methods, which differ in the spatial extent and duration of the labeling, called pulsed ASL (PASL) and continuous ASL (CASL) [9,10].

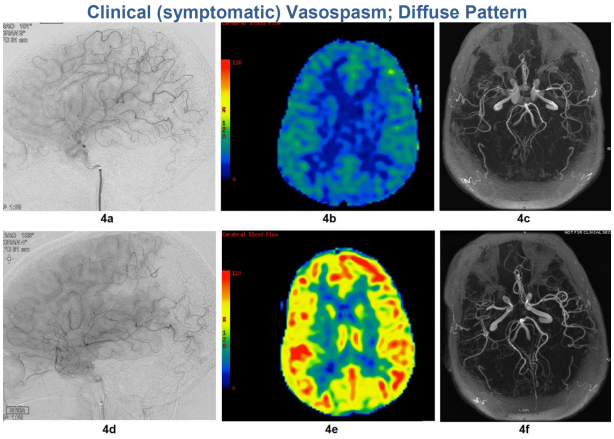


Figure 4a:Angiogram at day 0 demonstrates no evidence of vasospasm or capillary venous defects.
Figure 4b: MRA on day 8 shows angiographic vasospasm (patient is asymptomatic at this point).
Figure 4c: ASL on day 8 shows global hypoperfusion (ominous sign) consistent with compromised cerebral perfusion. This is likely due to the inability of failing pial collaterals and precapillary vessels to maintain CBF as a result of vasospasm.
Patient develops focal neurologic symptoms on day 10 and is taken emergently for intraarterial vasodilator therapy.
Figure 4d: DSA at day 10 shows a large area of oligemia in the posterior parietal and temporal vascular territory consistent with DCI resulting from cerebral vasospasm.
Figure 4e: MRA on day 21 shows resolving angiographic vasospasm.
Figure 4f: ASL on day 21 shows recovery of CBF.

In PASL, a single RF pulse is used to invert (label) a large volume of blood using a thick labeling plane for a total duration of typically 10–20 ms. A control image without any labeling of blood is also performed and the perfusion-weighted image is obtained by the subtraction of labeled image from the control image. In CASL, flowing blood spins are inverted continuously over a long period of time (typically 1–3 s) using a thin labeling plane which applies a constant gradient in conjunction with constant RF application for the duration of the labeling. This process is also known as flow-driven adiabatic inversion. A combination of both methods is pseudo-CASL (pCASL) where the constant RF application is split into a train (as many as 1000) of short RF pulses applied in succession (i.e., every ms) [11]. The labeling efficiency of pCASL has been determined to be superior to CASL and PASL; hence, it is the recommended labeling scheme for cerebral perfusion imaging [7–9,12].

ASL has the ability to label single vessels independently (unlike most perfusion imaging techniques where perfu-

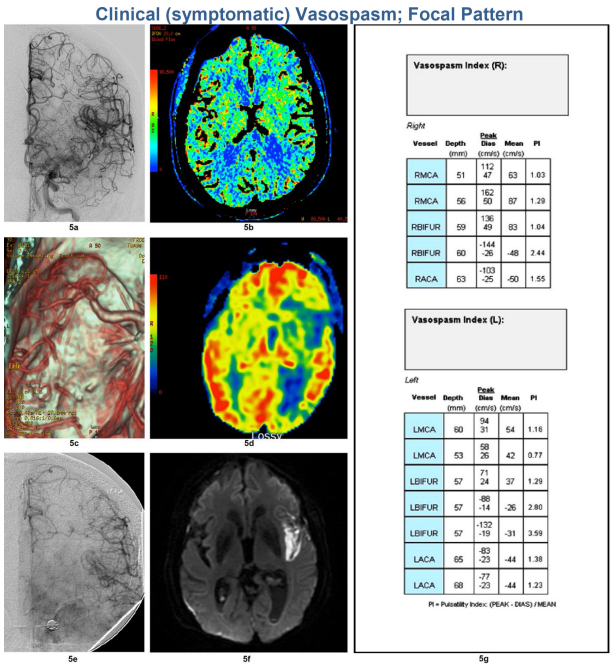


Figure 5a:DSA at day 0 shows no evidence of vasospasm or capillary venous defects.
On day 8, the patient develops fluctuating symptoms of altered level of consciousness, aphasia, and right upper extremity weakness.
Figure 5b: Stat CTP shows no perfusion deficits; Figure 5c: CTA shows proximal left MCA stenosis. Figure 5d: ASL on day 8 identifies focal decreased CBF in the left insular cortex and temporal/occipital areas. Figure 5e: DSA confirms vasospasm with a large area of oligemia consistent with DCI. Figure 5f: Follow-up MRI confirms an acute ischemic stroke in the involved territory. Figure 5g: TCD on day 7 (prior to symptom onset) was also unable to detect vasospasm.

sion maps include contributions from all the cerebral vessels), allowing it to not only identify different perfusion territories but also quantify the actual contribution of individual collateral arteries to the perfusion of the brain. Additionally, vascular reactivity (using acetazolamide challenge) and autoregulation status/cerebrovascular reserve capacity (percentage CBF change between baseline and vasodilatory challenge) can be assessed within the same scan session which makes it an ideal tool for assessment of vascular disorders. Because of the noninvasive nature of ASL, the measurements can be easily repeated without any need for optimization in between and may show hemodynamically-compromised brain regions that appear normal on the standard MR imaging protocol [13].

CLINICAL APPLICATIONS OF DIFFERENT PERFUSION PATTERNS OF ASL IN PATIENTS WITH VASOSPASM FOLLOWING ANEURYSMAL SAH

The diagnostic role of ASL in acute ischemic stroke, epilepsy, and neurodegenerative disorders has been explained in multiple studies but its ability to predict vasospasm in SAH has not been published before. We aim to highlight the diagnostic implications of high- and low-perfusion patterns of ASL in patients with aneurysmal SAH which can be utilized to prevent DCI in such patients when other commonly used noninvasive modalities are not available, contraindicated, or fail to detect vasospasm.

Normal perfusion

There is symmetric perfusion between the two hemispheres; cortical gray matter exhibits slightly higher signal intensity compared with white matter reflecting the physiologic hemodynamic differences between these tissues. There may be comparatively higher signal intensity in the occipital region as a result of the activation of the visual areas in the MRI environment [Figure 1a and 1b]. By convention, the redder the perfusion map is, the higher the perfusion is; and likewise; the darker the perfusion is, the lower the perfusion (CBF) is.

Radiographic (asymptomatic) vasospasm

In the setting of vasospasm, there is increased recruitment of pial collaterals and also vasodilatation of precapillary vessels in an attempt to maintain CBF. The capillary phase of CBF is also prolonged in order to increase the extraction of oxygen which results in an increase in the cerebral blood volume (CBV) in the affected territory. Increased arterial–capillary–venous phase results in increased arterial spins in the cortex interpreted on ASL as increased flow [Figures 2a–d and 3a–f].

Angiographic Capillary Congestion in Asymptomatic Vasospasm

CBV is preserved as a result of increased recruitment of pial collaterals and also vasodilatation of precapillary vessels distal to the vasospasm. The capillary phase appears congested and prolonged which corresponds to an increase in CBV. Increased arterial–capillary–venous phase (nearly double the baseline angiogram) results in increased arterial spins in the cortex interpreted on ASL as hyperperfusion. 3a–f]

Clinical (symptomatic) vasospasm

Once the maximal autoregulatory vasodilation crosses the threshold of collaterals failure and venous collapse, bioenergetic cell death ensues with focal neurologic symptoms. ASL perfusion map shows hypoperfusion consistent with compromised cerebral perfusion. The pattern of hypoperfusion can be diffuse [Figure 4a—f] or focal [Figure 5a—g], depending on the extent of vasospasm and collateral failure.

CONCLUSION

ASL is a noninvasive mean for assessing CBF/cerebral perfusion and does not require an exogenous contrast making it an excellent choice for initial or follow-up studies even in critically ill patients or those with renal failure.

Its diagnostic role in acute ischemic stroke, epilepsy, and neurodegenerative disorders has already been explained in multiple studies but its ability to predict vasospasm in SAH has not been published before. Unlike other noninvasive perfusion methods, ASL also has the ability to label single vessels independently, allowing it to quantify the actual contribution of individual collateral arteries to the perfusion of the brain.

We highlight the clinical application of different perfusion patterns of ASL in patients with subarachnoid hemorrhage.

Acknowledgements

None.

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