Arterial Spin Labeling MRI in Carotid Stenosis: Arterial Transit Artifacts predict symptoms

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Summary Statement: Arterial Transit Artifacts on Arterial Spin Labeling MRI were the only factor associated with recent ischemic symptoms in participants with carotid stenosis.

Key Results:

- Arterial Transit Artifact (ATA) was present in 16/16 participants with severe stenosis (>70%), p <.001), and were associated with absence of anterior communicating artery (11/16, p=.003).
- ATA was the best predictor of recent symptoms in internal carotid artery stenosis (13/16 participants with ATA had symptoms, p=004).
- All participants with severe ATAs were symptomatic (6 /13 symptomatic participants with ATA, p=.002)

Abbreviations: ICA = internal carotid artery, ASL = arterial spin labeling, PWI = perfusion weighted imaging, ATA = arterial transit artifact, IPH = intraplaque hemorrhage, TIA = transient ischemic attack, CBF = cerebral blood flow, TOF = time of flight, DSC = dynamic susceptibility contrast, PLD = post-labeling delay

Abstract

Background: Internal carotid artery (ICA) stenosis carries a higher risk of stroke. While many investigations have focused on morphology and plaque composition as signs of plaque vulnerability, very few studies analyzed the brain hemodynamic changes as a risk factor.

Objective: To use 3T MRI methods including contrast-enhanced MR angiography, carotid plaque imaging and Arterial Spin Labelling (ASL) to identify imaging parameters that best distinguish between asymptomatic and symptomatic participants with carotid stenosis.

Material and Methods: Participants with carotid stenosis from two ongoing prospective studies (ISRCTN registry number 97744893)**,** who underwent ASL and carotid plaque imaging using 3T MRI in the same setting, from 2014 to 2018. Participants were assessed clinically for recent symptoms (transient ischemic attack or stroke) and divided equally into symptomatic and non-symptomatic groups. Blinded to the symptomatic status, MRI were analyzed for the degree of stenosis, plaque surface morphology, presence of intraplaque hemorrhage (IPH), circle of Willis collaterals, and the presence and severity of arterial transit artifacts (ATAs) on ASL. MRI findings were correlated with symptomatic status using t-tests and Fisher's exact test.

Results: 44 participants (71 +/- 10 years, 31 men) were evaluated. ATAs were only seen in participants with a >70% stenosis (16/28, p<.001) and were associated with absence of anterior communicating artery (13/16, p=.003). There was no association between history of symptoms and degree of stenosis (>70%=27, <70%=17, p=.54), IPH (present=12, absent=32, p=.31), and plaque surface morphology (irregular/ulcerated=17, smooth=27, p=.54). However, participants with ATAs (n=16) were more likely to be symptomatic than those without ATAs (n=28) (p=.004). Symptomatic status also was associated with the severity of ATAs (p=.002).

Conclusion: Arterial transit artifacts were the only factor associated with recent ischemic symptoms in participants with carotid stenosis whereas the degree of stenosis, plaque ulceration or IPH were not associated with symptomatic status.

Introduction

Symptomatic cervical internal carotid artery stenosis can be asymptomatic or present with transient ischemic attack (TIA), stroke, or ocular ischemia. The TOAST (Trial of Org 10172 in Acute Stroke Treatment) and updated ASCOD (atherosclerosis, small-vessel disease, cardiac pathology, other causes, dissection) classifications of ischemic stroke etiology define carotid stenosis of 50-99% to indicate large vessel atherosclerotic disease as the likely cause of stroke in the absence of other competing causes.(1,2) Both asymptomatic and symptomatic carotid stenosis carry a higher risk of recurrent ischemic stroke, which can be reduced by medical and/or surgical treatments.(3,4)

Artery-to-artery embolism is the most common postulated mechanism by which carotid stenosis causes stroke or TIA. Hemodynamic etiology is thought to be responsible for only a minority of strokes caused by hypoperfusion in borderzone territories.(5) Recent investigations have therefore focused on the composition and morphology of atherosclerotic plaques with the aim of identifying vulnerable plaques with a higher risk of future thrombo-embolic ischemic events,(6–11) in particular intraplaque hemorrhage (IPH).(6)

Individuals with carotid stenosis are rarely investigated with MRI techniques that assess hemodynamic impairment, such as dynamic susceptibility contrast perfusion weighted imaging (DSC-PWI) or arterial spin-labeling (ASL).(12,13) DSC-PWI, widely investigated in acute stroke, is used for selecting patients presenting between 6 and 16 hours after stroke onset for thrombectomy.(14) But comparatively few MRI studies have investigated hemodynamic changes in carotid stenosis using either DSC-PWI or ASL.(15,16)

Unlike DSC-PWI, ASL does not require the injection of an exogenous contrast medium and uses labeling of endogenous water molecules. This method is being increasingly used in clinical practice.(12,13) ASL allows quantification of cerebral blood flow (CBF) but also visual assessment of arterial transit artifacts (ATAs). ATAs indicates the delayed arrival of blood in the corresponding vascular territory (17,18) and appear as bright signals in the vessels overlying the brain surface. ATAs represent labeled blood that has not yet reached the brain parenchyma at the time point of image acquisition, which occurs if the arterial transit time is greater than the post-labeling delay (ATAs are a pathophysiological phenomenon rather than an artifact, but for consistency we used the original name).(19) The arterial transit time is not only influenced by a carotid stenosis but also by cardiac output and presence of intracranial stenoses.

Our hypothesis is that hemodynamic impairment in patients with ICA stenosis may be a source of symptoms, along other previously considered risk factors. We used a combination of 3T MRI methods including contrast-enhanced MR angiography, carotid plaque imaging, and assessment of cerebral perfusion with ASL in participants with carotid stenosis with the aim to identify imaging parameters that distinguish best between asymptomatic and symptomatic participants.

Materials and Methods

Participants

Suitable participants were recruited from two prospective studies of participants with carotid artery stenosis at our institution: the second European Carotid Surgery Trial (ECST-2) (ISRCTN registry number 97744893; full protocol can be accessed at www.isrctn.com/ISRCTN97744893) and the Structural and Hemodynamic Imaging in carotid Plaque study (SHIP), funded by National Institute for Health Research (UK). Both studies had been approved by the local ethics committee and all participants gave written consent. The main inclusion criteria for ECST-2 were adult participants (≥ 18 years) who had either symptomatic or asymptomatic carotid stenosis of ≥50% calculated with NASCET (North American Symptomatic Carotid Endarterectomy Trial) criteria, with a carotid artery risk score indicating a 5-year ipsilateral stroke risk of <20%.(20,21) Full inclusion and exclusion criteria for ECST-2 are available on www.ecst2.com.(22) For SHIP, adult participants were included who had carotid stenosis ≥50% on either duplex ultrasound, CT angiography, or MR angiography. Recruitment took place in United Kingdom between 2014 and 2018 and all participants where imaged on the same 3T MRI system. For ECST-2 consecutive series of eligible participants were recruited or were randomly assigned to SHIP if inclusion criteria weren't met.

Inclusion criteria for the present study were participation in one of the two studies above and availability of cerebral perfusion imaging with pseudo-continuous arterial spin-labeling (pCASL) as well as high resolution carotid plaque imaging performed in the same sitting. Exclusion criteria were ICA occlusion or blood flow delays that weren't caused by ICA stenosis alone (such as low cardiac output or tandem stenosis) (Figure 1). All participants were clinically assessed by a stroke neurologist with experience ranging from 10 to 25 years. TIA was defined by distinct focal neurological dysfunction or monocular blindness with clearing of sign and symptoms within 24 hours, even if imaging showed a relevant infarct. Amaurosis fugax was defined as sudden, reversible loss of vision, lasting up to 30 minutes with complete and rapid recovery. Stroke was defined by one or more minor (non-disabling) completed strokes with persistence of symptoms or signs for more than 24h.

MRI Protocol

All imaging was performed on 3T Philips Achieva MRI system (Philips Healthcare, Best, The Netherlands), using a 16 channel neuro-vascular coil.

Carotid plaque imaging used T1W (pre- and post-gadolinium injection, fat suppression; TR=604, TE=27) (16 slices, slice thickness=3mm), time of flight (TOF, 3D fast gradient-echo; TR=25, TE=3.5), contrast-enhanced MR angiography (3D spoiled fast gradient-echo; TR=4.7, TE=1.7).

Brain imaging used T2W (axial fast gradient-echo; TR=3000, TE=80); T1W (3D magnetization-prepared fast gradient-echo; TR=6.5, TE=3.1), FLAIR (3D turbo spin-echo inversion recovery; TR=4800, TE=270), DWI (b-value=1000s/mm^2; TR=2913, TE=94), pCASL (axial echo-planar imaging (EPI): 20 slices, slice thickness=5mm, TR/TE=4400/15ms, SENSE=2.3, labeling duration=1650ms, post-labeling delay=1800ms, 30 control/label pairs, fat and background suppression). Full protocol is available on Supplement Table 1.
ASL perfusion-weighted imaging (ASL-PWI) was automatically generated by the scanner software (Achieva R3.2.1, 5.1.7, and 5.4.1; 2012, 2015, and 2018; Philips Healthcare, Best, The Netherlands) by averaging individual control-label subtractions.

Image Analysis

Two neuroradiologists with 5 (ADN) and 26 (HRJ) years of experience in neuroradiology, independently assessed the MRI, both in the same month, blinded to the symptomatic status. They evaluated: degree of stenosis; plaque surface characteristics; presence of intraplaque hemorrhage (IPH); collateral circulation of the circle of Willis; presence and severity of ATAs on ASL-PWI. Kappa statistic was calculated. For disagreements a consensus was reached.
The degree of stenosis was measured on MR angiography according to NASCET criteria,(21) and the surface morphology of the plaques was described on MR angiography (using on the following three categories: smooth, irregular and ulcerated) (Figure 2).
IPH was considered to be present when the atherosclerotic plaque appeared hyperintense on both the T1 fat saturated images and the TOF source data (Figure 3), based on previous studies.(7,9,10,23,24)
The primary collateral pathways of the circle of Willis were assessed on contrast-enhanced MR angiography using a 5-point grading system proposed by Maas and colleagues.(25)
ASL-PWI were assessed without any additional post-processing steps for CBF quantification. We adopted a previously established 4-point grading system to assess the ASL signal on the subtraction images: 0, no or minimal ASL signal; 1, moderate ASL signal with ATA; 2, high ASL signal with ATA; and 3, normal perfusion without ATA. Representative images are shown in Figure 4.(19,26,27)

We also dichotomized the data into groups with impaired perfusion (grade 0, 1 and 2), and normal perfusion without ATA (grade 3).

Statistical Analysis

We used t-tests to compare continuous traits and Fisher's exact test for categorical traits. To explore associations of ATA with symptomatic status adjusted for other risk factors we used logistic regression. We only adjusted for one risk factor at a time; adjustment for all covariates simultaneously was not possible due to the sample size. We considered a two-sided p-value <.05 as statistically significant. We did not

adjust for multiple comparisons; primary interest was in the relationship between ATA and symptomatic status. We used Stata Statistical Software 15.1 (StataCorp LLC, College Station, TX, USA) for all analyses.

Results

Participant Characteristics

Initially 50 participants were included in this study, but six were excluded for the following reasons: three participants had ICA occlusions, two participants had insufficient ASL signal due to low cardiac output and one participant had additional marked bilateral middle cerebral artery stenoses (full flow chart in Figure 1). Of 44 eligible participants, the mean age was 71 (SD=10) and 31 were men (Table 1). Asymptomatic (n=22) and symptomatic participants (n=22) had similar age at baseline (70 vs 72 years, p=.51). Of the 22 symptomatic participants, nine had ischemic stroke, four had amaurosis fugax, and nine had TIA. Stenosis >70% of the ICA of the side of interest was present in 27/44 participants (61%), IPH was present in 12/44 participants (27.3%), and 17/44 participants (39%) had ulcerated or irregular ICA plaques.

Inter-reader Agreement

There was no difference between the two readers in identifying ATAs. Differences were encountered in ATA grading (κ=.913), plaque morphology (κ=.953), IPH (κ=.861), for which an agreement was reached after joint review. For two IPH participants there was no hyperintensity in TOF source data, so they were classified as “no IPH”; one participant had a small portion of hyperintensity in both sequences that was not seen by one reader, hence it was converted into “IPH present”. Regarding plaque morphology the disagreement consisted on a small image defect that in the end was classified as ulceration rather than irregularity.

Presence of ATAs

ATAs were present in 16/44 participants (36%). Compared to participants without ATAs participants with ATAs were older (mean age=76 vs 68 years, p=.004), ATAs were only found in participants with >70% carotid stenosis. Of 44 participants, 16 (36.3%) had both ATA and >70%, 11 participants (25%) had >70% stenosis without ATA, and 17 (38.6%) had <70% stenosis without ATA. No participants with <70% stenosis had ATA.

The presence of ATA was associated with the number and type of primary circle of Willis collaterals in the individual participants (Figure 5). Presence of at least one ipsilateral circle of Willis collateral was evaluated in 43 of 44 participants (one patient did not undergo to intracranial MRI angiogram). Presence of circle of Willis collaterals was more frequent in participants without ATAs (25/27, 92.6%) compared to participants with ATAs (7/16, 56%) (p=.001; Table 1). In particular, anterior communicating artery was present in the majority of participants without ATA (22/27, 81%) but in a minority of participants with ATA (5/16, 31%) (p=.003).

Features associated with symptomatic versus asymptomatic participants

We investigated which features were most strongly associated with symptomatic status (Figure 6). The proportion of symptomatic participants was not significantly different in participants with (56%, 15/27) and without (41%, 7/17) >70% stenosis (p=.54), with (67%, 8/12) vs without (44%, 14/32) IPH (p=.31), and when comparing participants with smooth (56%, 15/27) vs ulcerated plaques (41%, 7/17) (p=.54). However, participants with ATAs were more likely to be symptomatic (13/16, 81%) than those without ATAs (9/28, 32%) (p=.004) (Table 2). Additionally, all six participants (100%) with more severe ATAs (grade 1) and seven of ten participants (70%) with less severe ATAs (grade 2) were symptomatic, compared to 9 of 28 (32%) participants without ATAs.

Discussion

Recent studies and stroke risk criteria in carotid stenosis focused on morphology and composition of plaque, while very few tried to examine a possible association between symptoms and hemodynamic modifications. In this study we assessed the association of ATA on ASL-PWI with recent symptoms and compared it to conventional structural parameters. The presence of ATA was strongly associated with a history of recent cerebrovascular symptoms and was the best discriminator between symptomatic and asymptomatic stenosis (13/16, p=.004), whereas the degree of stenosis (15/27, p=.54), plaque ulceration (15/27, p=.54) or IPH (8/12, p=.31) were not associated with symptomatic status (Figure 6). This is, to our knowledge, the first study to compare carotid plaque imaging and ASL-PWI in carotid stenosis, thereby obtaining information about carotid plaque vulnerability and cerebral hemodynamics.

We found an association between presence of ATA and age (mean age=76 vs 68 years in participants with and without ATA, respectively). However, the association between symptomatic status and ATA was not driven by the association of ATA with advancing age; asymptomatic and symptomatic participants had a similar age at baseline (70 vs 72 years).

ATAs were only found in participants with >70% carotid stenosis, implying that a lesser degree of stenosis does not cause a sufficient enough prolongation of the arterial transit time to produce ATAs. The presence of ATA was associated with the number and type of primary circle of Willis collaterals, particularly the absence of the anterior communicating artery was strongly associated with ATAs and be regarded as an imaging marker that reflects both flow limitation by carotid stenosis and effectiveness of the primary collateral pathway.

There is evidence from previous non-ASL based studies that hemodynamic parameters differ between participants with symptomatic and asymptomatic carotid stenosis. Hu and colleagues found that a longer cerebral circulation time on DSA was more strongly associated with symptomatic status than the degree of stenosis.(28) A study using gadolinium-based DSC-PWI found that participants with symptomatic carotid stenosis had an increase in mean transit time and a lower CBF in the ipsilateral hemisphere.(15) ASL has the advantage over DSC-PWI that it does not require gadolinium injection.

Recently, Hartkamp and colleagues used ASL to perform measurements of CBF and cerebrovascular reactivity (CVR) in participants with symptomatic and asymptomatic carotid stenosis or occlusion.(29) The calculation of CVR and CBF from ASL requires several of post-processing steps, dedicated software, and

injection of acetazolamide, whereas ATAs can be detected by simple visual inspection of ASL-PWI, making this a much more widely useable imaging marker in clinical practice.

IPH is associated with a higher risk of future TIA or stroke, both in symptomatic and in asymptomatic participants with carotid stenosis.(30–32) In these meta-analyses the hazard ratios for subsequent ipsilateral TIA or stroke ranged from 5.86 to 11.71 for symptomatic participants and from 3.50 to 3.66 for asymptomatic participants. Two studies investigated IPH as possible discriminator between symptomatic and asymptomatic carotid stenoses.(10,11) One defined symptomatic by the presence of DWI positive lesions (rather than by clinical symptoms) and found higher prevalence of IPH in the symptomatic stroke participants.(11) The other study found only a marginal association between symptomatic status and IPH (86% vs 33%, p=.055).(10)

The highest correlation for IPH area with histology was with magnetization-prepared RAGE (MPRAGE) imaging (r=0.813), followed by TOF (r=0.745), and fast spin-echo (r=0.497) imaging, as studied by Ota and colleagues.(33) 3D MPRAGE has been recently recommend as sequence of choice for IPH detection.(34) One could argue that 3D MPRAGE might have improved the detection of small IPHs.(10,11,30–32). In our study we required the presence of hyperintense signal of both the T1 spin-echo and TOF source data for the diagnosis of IPH, based on findings by Cappendijck and colleagues,(35) who demonstrated that high signal on T1 spin-echo may be caused by fibrous tissue and give false positive results, whereas some of the previous investigators used a less stringent definition.

A subgroup analyses of the ECST,(36) indicated that an irregular or ulcerated plaque surface shown on intra-arterial angiography was associated with a higher risk of recurrent stroke compared with a smooth plaque surface (HR=2.03). We found that irregular or ulcerated plaques were present both in symptomatic and asymptomatic participants and that plaque surface characteristics were not a discriminating feature between the two. A previous MRI study comparing 13 symptomatic and 84 asymptomatic participants found that ulcerations seen on MR angiography correlated with symptomatic status only in severe stenosis (70%-99%) but not in mild to moderate stenosis (30-69%).(10)

The strength of our study lies in highly standardized imaging protocol, which combined the use of two advanced MRI techniques assessing the carotid plaque and cerebral perfusion at the same time.
Our findings suggest that impaired cerebral hemodynamics play a greater role in the mechanism of TIA and stroke than currently appreciated. Should future studies show that ATAs not only predict recent stroke, but are also associated with a higher risk of future TIA and stroke, ASL may be useful in selecting participants for carotid revascularization. Such studies are currently in progress in our unit.

Our study had some limitations. The relatively small sample size had statistical power to detect only strong associations with symptomatic status, which could in part explain lack of association between symptomatic stenosis, plaque ulceration and IPH. Also, some of the participants were recruited for the ECST-2 that investigates participants with a low or medium calculated 5-year risk of stroke, which could introduce some selection bias. But this was counterbalanced by the inclusion of participants from the SHIP study, which comprises higher risk participants scheduled for endarterectomy, who were usually not suitable for recruitment to ESCT-2. However, there are no concerns about ATA's influencing patient selection, since they were unknown at the time of recruitment.

A technical limitation is our choice of a post-labeling delay (PLD) of 1.8sec. Our study started before the publications of the International Society for Magnetic Resonance in Medicine (ISMRM) white paper,(37) which recommends a PLD of 2.0 sec for healthy subjects over the age of 70 years and for clinical adult patients. As ATAs occur if the arterial transit time is longer than the PLD, it is possible that our PLD of 1.8 sec has led to an increased presence of ATAs.

Furthermore, there are variations in technical implementation of pCASL between different vendors: we used a 2D EPI readout, whereas other vendors use a 3D gradient and spin-echo (GRASE) or a 3D FSE stack of spirals. 3D readouts are characterized by through plane blurring that could potentially reduce the conspicuity of ATAs. Similarly, a different conspicuity of ATAs might be observed at lower field strengths due to shorter blood water protons relaxation times or pulsed ASL due to inferior labeling bolus compared to pCASL. Although ATAs have previously been reported in a range of vascular pathologies, scanned at different scanners and with different PLDs,(17,19,27,38) further studies, using other platforms with a recommended PLD of 2 sec, will be necessary to confirm that the results of our study are more widely applicable.

In conclusion, ATA is a simple parameter derived from ASL-PWI, which can be analyzed by visual inspection without requiring complex post-processing. We found that ATA is strongly associated with recent ischemic symptoms and is a much better predictor of recent symptoms in participants with carotid stenosis than the degree of stenosis, plaque surface characteristics, or IPH. ATAs are a physiological parameter at brain tissue level, which reflect the interplay between multiple "downstream factors" such as cardiac output, severity of stenosis, and state of intracranial collateral circulation. Our findings open an avenue for future larger

scale prospective studies using ASL-PWI as a marker for risks of recurrent TIAs or stroke and assessment of therapeutic interventions such as carotid endarterectomy.

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Characteristics		All participants	ATA absent	ATA present	p-value
Age (mean years (+/-SD))		71 (+/- 10)	68 (+/- 9)	76 (+/- 8)	.004
Men		31/44 (70.5%)	19/28 (67.9%)	12/16 (75.0%)	.74
Smoking Status	Never	22/44 (50.0%)	14/28 (50.0%)	8/16 (50.0%)	.33
	Former	12/44 (27.3%)	6/28 (21.4%)	6/16 (37.5%)	
	Current	10/44 (22.7%)	8/28 (28.6%)	2/16 (12.5%)	
Diabetes		14/44 (31.8%)	11/28 (39.3%)	3/16 (18.8%)	.19
Hypertension		36/44 (81.8%)	21/28 (75.0%)	15/16 (93.8%)	.22
Hypercholesteremia		30/44 (68.2%)	18/28 (64.3%)	12/16 (75.0%)	.52
Ulcerated/irregular plaque		17/44 (39%)	9/28 (32%)	8/16 (50%)	.34
Carotid Stenosis >70%		27/44 (61%)	11/28 (39%)	16/16 (100%)	<.001
Intraplaque hemorrhage		12/44 (27.3%)	8/28 (28.6%)	4/16 (25.0%)	>.99
Number of Circle of Willis collaterals					
0		11/43 (25.6%)	2/27 (7.4%)	9/16 (56.3%)	.001
≥1		32/43 (74.4%)	25/27 (92.6%)	7/16 (43.8%)	
Number of Circle of Willis collaterals					
0		11/43 (25,6%)	2/27 (7.4%)	9/16 (56.3%)	.001
1		26/43 (60.5%)	19/27 (70.4%)	7/16 (43.8%)	
2		6/43 (14.0%)	6/27 (22.2%)	0/27 (0.0%)	
PCOM present		11/43 (25.6%)	9/27 (33.3%)	2/16 (12.5%)	.12
ACOM present		27/43 (62.8%)	22/27 (81.5%)	5/16 (31.3%)	.003

Table 1: Participant characteristics by presence or absence of arterial transit artifact (ATA). ACOM = anterior communicating artery; PCOM = posterior communicating artery; SD = standard deviation.

		ATA		
		Present	Absent	Total
Symptoms	Present	13	9	22
	Absent	3	19	22
	Total	16	28	44

Table 2: Number of participants for presence of arterial transit artifact (ATA) in relation to symptoms. p = .004

Supplemental Table 1 – All abbreviations need to be spelled out .

Figure Legends

Figure 1. Study flow chart. pCASL = pseudo-continous arterial spin labeling.

Figure 2. Morphology of plaque
Plaque morphology evaluated on MR angiogram and intraplaque hemorrhage. A smooth plaque (arrow head); B irregular (curved arrow); C ulcerated (white arrow).

Figure 3. Intraplaque hemorrhage
Non-contrast MRI of a female participant (55 years old). A Axial T1 fat saturated sequence; B Axial Time of flight (TOF) source data. Hyperintensity of the plaque (white arrow) in both sequences was considered intraplaque hemorrhage.

Figure 4. Arterial transit artifact (ATA) evaluation
Non-contrast MRI of three participants. From left to right: axial pseudo-continuous arterial spin labeling (pCASL), axial diffusion weighted imaging (DWI), axial T2 fast spin-echo (T2FSE). A male participant (77 years old) with severe (grade G1) ATA on the left side, there is marked swirling hyperintensity representing blood vessels and no signal in the cortex (white arrows); B female participant (86 years old) with moderate (grade G2) ATA in the left side, both hyperintensity of the blood vessels and cortex are present (arrow heads); C male participant (56 years old) with normal cortex signal and no ATA (grade G3). DWI and T2FSE sequences are in comparison to show that no acute nor chronic lesion are present in the site where ATA appears.

Figure 5. Circle of Willis composition
Status of anterior communicating artery (ACOM) and posterior communicating artery (PCOM) collaterals ipsilateral to the Carotid Artery Stenosis, comparison between participants with and without arterial transit artifacts (ATAs) ($p = .001$).

Figure 6. Data correlation with symptoms
Percentage of participants symptomatic by arterial transit artifact (ATA) and markers of high-risk. G1 = grade 1 ATA (severe); G2 = grade 2 ATA (moderate); G3 = grade 3 (normal brain perfusion without ATA); irreg./ulc. = irregular or ulcerated.