HHS Public Access

Author manuscript

J Stroke Cerebrovasc Dis. Author manuscript; available in PMC 2015 October 13.

Published in final edited form as:

J Stroke Cerebrovasc Dis. 2015 January ; 24(1): 171–175. doi:10.1016/j.jstrokecerebrovasdis.2014.08.001.

The Impact of Absent A1 Segment on Ischemic Stroke Characteristics and Outcomes

Amir Shaban, MD[*], **Karen Albright, DO, MPH**[†,‡,§], **Brittany Gouse, BS**[*], **Alexander George, BS**[*], **Dominique Monlezun, BA**[*], **Amelia Boehme, MSPH**[†], **T. Mark Beasley, PhD**[‖], and **Sheryl Martin-Schild, MD, PhD**[*]

[*]Sroke Program, Department of Neurology, Tulane University School of Medicine, New Orleans, LA

[†]Department of Epidemiology, School of Public Health, University of Alabama at Birmingham, Birmingham, AL

[‡]Health Services and Outcomes Research Center for Outcome and Effectiveness Research and Education (COERE), Birmingham, AL

[§]Center of Excellence in Comparative Effectiveness Research for Eliminating Disparities (CERED) Minority Health & Health Disparities Research Center (MHRC), Birmingham, AL

[‖]Department of Biostatistics, School of Public Health, University of Alabama at Birmingham, Birmingham, AL

Abstract

Background—A1 segment is the proximal portion of anterior cerebral artery. Absence of the A1 segment can compromise anterior cerebral collateral blood flow. Few studies have examined the association of an absent A1 segment and ischemic stroke outcome. We sought to determine the association between A1 absence and affected vessel territory, stroke volume, and outcomes among patients with acute ischemic stroke (AIS).

Methods—A retrospective review of prospectively identified patients with AIS from July 2008 to March 2013 was performed. Patients without intracranial vascular imaging were excluded. We compared patients with absent A1 to patients with bilateral A1 segments in terms of demographics, stroke severity (as measured by National Institute of Health Stroke Scale [NIHSS]), vascular distribution, and in-hospital mortality using the chi-square test and logistic regression.

Results—Of the 1146 patients with AIS and intracranial vascular imaging, 5.9% patients (n = 68) had absent A1. Compared with other AIS patients, those with absent A1were older (65 vs. 63 years old, respectively, $P = .016$). There was no difference between groups in terms of the vascular distribution or the side of the stroke. The median volume of the infracted tissue was similar across the groups even when it was stratified according to the Treatment of Acute Stroke Trial classification. Patients with an absent A1 had twice higher odds of in-hospital mortality

Address correspondence to Sheryl Martin-Schild, MD, PhD, Department of Neurology, Stroke Program, Tulane University School of Medicine, 131 S. Robertson Street, Suite 1340, New Orleans, LA 70112. Smartin2@tulane.edu.

(odds ratio, 2.4; 95% confidence interval, 1.1-5.2; P = .028); however, significance was lost after adjusting to age, NIHSS at baseline, and glucose on admission. Other outcome measures were similar across the groups.

Conclusions—In our sample, patients with an absent A1 segment did not have a specific vascular distribution, larger infarct volume, or worse outcomes.

Keywords

Stroke; ischemic; cerebral circulation; mortality; magnetic resonance angiography; computed tomography angiography

Introduction

Anatomically intact circle of Willis is associated with better outcome in patients with acute ischemic stroke (AIS).[1] Because only 42%-50% of healthy individuals are believed to possess a complete circle of Willis configuration, it is made apparent that variations in circle of Willis anatomy and ultimately collateral capacity are relatively common in the population.[2-4]

Previous anatomic and radiographic studies have indicated that congenital abnormalities of the A1 segment are commonly observed. The reported prevalence of hypoplasia of the A1 segment in healthy individuals varies between 1% and 13%.[4-7] The complete absence of the A1 segment is much less common than A1 segment hypoplasia, ranging from 1% to 6%.[5,8-10] A prior study has demonstrated that the incidence of A1 segment hypoplasia is significantly higher in patients with AIS than in healthy controls, suggesting that impaired collateral blood flow due to A1 segment hypoplasia may be a contributing factor for AIS.[5] Collateral support in the anterior portion of the circle of Willis is provided through interhemispheric blood flow across the anterior communicating artery providing the opportunity for reversal of flow in the proximal anterior cerebral artery (ACA) in the setting of internal carotid artery (ICA) occlusion, adding to cerebral blood flow provided by the existing extracranial collaterals.[11,12] Previous studies have shown that in the case of absent A1, both ACAs are perfused by 1 ICA with associated lower flow rate through the other ICA on the side of absent A1.[13] Several computational models of cerebral flow dynamics have shown that A1 absence had the most considerable negative impact on blood flow of any common circle of Willis anomaly.[13-15]

In the light of the previous research, we hypothesized that absent A1 segment is associated with higher rates of ACA territory infarcts, larger stroke volumes, and worse outcomes.

Methods

Patients

We conducted a retrospective analysis on prospectively identified patients who presented consecutively to our medical center with AIS between July 2008 and March 2013. Patients who did not receive cerebrovascular imaging during their clinical course (magnetic resonance angiography [MRA], time-of-method [TOF], or computed tomographic

angiography [CTA]) were excluded from analysis. Clinical variables were abstracted from our prospective institutional review board–approved stroke registry.[16]

Definitions

Using MRA and CTA, we classified patients into 2 groups: patients with an absent A1 and patients who had intact bilateral A1 segments. An intact A1 segment was defined as an A1 segment that extended from the ICA to the ipsilateral ACA (A2 segment). Complete absence of the A1 segment was indicated in patients with lack of communication between the ICA and the ipsilateral ACA. Patients with hypoplastic A1 segment with atretic communication between ICA and ACA were classified as intact A1. The categorization of stroke etiology was determined using Treatment of Acute Stroke Trial [TOAST] classification.[17] Patients who were discharged home and to inpatient rehabilitation were considered to have a favorable discharge disposition. Neuroworsening was defined as an increase in National Institute of Health Stroke Scale [NIHSS] by 2 points within 24 hours.[18]

Imaging

CTA and MRA were interpreted by a trained research fellow (A.S.). A1 classification was confirmed by a board certified vascular neurologist (S.M.S.). We used the image processing program Centricity PACS (GE Healthcare Milwaukee, WI) to calculate the stroke volume for patients with absent A1 segment and a random sample of patients with intact A1 segment. The infarct area was manually tracked using the region of interest tool on each diffusion-weighted imaging slice, then multiplied by the slice thickness.

Statistical Analysis

We compared admission demographics, initial stroke severity as measured by the baseline NIHSS, vascular distribution of infarction, TOAST classification, and outcomes in patients with absent A1 and patients with intact A1. Categorical data were compared using the Pearson chi-square or Fisher exact test, where appropriate. Continuous data (presented as medians with ranges) were compared using Wilcoxon rank sum test. All tests were performed at the $\alpha = .05$ level and were 2-sided. As this was an exploratory analysis, no adjustments were made for multiple comparisons.[19] The retrospective chart review was approved by the Institutional Review Board at the Tulane University (IRB protocol number 297713-1).

Results

Of 1243 AIS patients who presented to our hospital during the study period, 1146 patients met the inclusion criteria. Of these, 44.2% (507 of 1146) were women and 66.3% (760 of 1146) were black. The median age was 63 years. In our sample, we detected absent A1 in 5.9% (68 of 1146). Of these, 44 were on the right side and 24 on the left side.

MRA was performed in 1064 patients; of these, 427 patients also had CTA conducted during their hospital stay. MRA was able to correctly identify 25 of 25 absent A1 segments that were detected using CTA and correctly ruled out absent A1 in 399 of the 402 ruled out by CTA. Using CTA as the gold standard, the sensitivity of MRA for detecting absent A1 in

our sample was 100% (95% confidence interval [CI], 83.4%-100%) while specificity was 99% (95% CI, 97.6%-99.8%). We found no association between absent A1 and side of stroke; 22patients had stroke on the side of absent A1, whereas 28 had stroke on the contralateral side; 11patients had bilateral strokes, stroke was unable to be documented in 5 patients, and 2 patients did not have magnetic resonances imaging.

Patients with absent A1were older (65 vs. 63 years old, respectively, P =.016). We found no difference in the rest of baseline demographics, NIHSS on admission, or TOAST etiology (Table 1). Rate of thrombolytic treatment was similar for patients with absent A1 and patients with intact bilateral A1 (21.7% vs. 25.3%, respectively, P =.695).

There was no significant difference in the vessel involvement among patients with absent A1 and those with intact A1. The median stroke volume was calculated for the 2 groups (2603 mm^3 for absent A1 vs. 3725 mm^3 for patients with intact A1, P = .430). The median stroke volume for patients with cardioembolic strokes was (9849 mm^3 for absent A1 vs. 11569 mm^3 for patients with intact A1, P = .911). The median stroke volume for patients with large vessel disease strokes was (4677 mm^3 for absent A1 vs. 13776 mm^3 for patients with intact A1, P = .320). The median stroke volume for patients with small vessel disease strokes was (657 mm^3 for absent A1 vs. 695 mm^3 for patients with intact A1, P = 1.000). The median stroke volume for patients with a TOAST classification other than cardioembolic large or small vessel disease was (62772 mm^3 for absent A1 vs. 3566 mm^3 for patients with intact A1, P = .018). There was no difference in the volume of strokes on the side of absent A1 to stroke contralateral to the absent A1 (median 3214 mm^3 vs. 2299 mm^3, P =.796).

Patients with an absent A1 had twice higher odds of in-hospital mortality (odds ratio, 2.4; 95% CI, 1.1-5.2; P = .028); however, significance was lost after adjusting to age, NIHSS at baseline, and glucose on admission (P = .182). The 2 groups had similar rates of favorable discharge disposition (P =.175). There was no difference in NIHSS or mRS on discharge (Table 2). The groups also had similar rates of neuroworsening events (P = .567).

Conclusions

Absent A1 is a rare variant of anterior circulation. Very little is known about the prevalence and relevance of absent A1 among patients with ischemic stroke. The scarce data available in the literature suggests that the frequency of A1 complete absence is 1%-5% in the general population.[5,8-11] Hypoplastic A1 was more frequently reported in 1%-13%.[5] Our sample had a marginally higher frequency of absent A1 segment than the general population 5.9%; this is in line with a previous study suggesting higher rates of absent A1 among patients with AIS compared with the general population.[5]

There are 2 perspectives derived from the literature to understand the relevance of absent A1 segment in AIS patients. The first is the possibility that absent A1 may cause an intrahemispheric collateral circulation failure; furthermore, the A1 segment of the ACA is the source of numerous penetrating striatal arteries that supply the anterior hypothalamus, septum pellucidum, and the anterior and inferior portions of the corpus striatum.[5] It would

be expected that absent A1 may increase the risk of stroke in the ACA territory on the side of the absent A1 segment; however, our data showed that the odds of a stroke being on the side of absent A1 versus the other side was no greater than the flip of a coin. We also were unable to detect significant difference in the distribution of vascular involvement comparing patients with absent A1 and intact A1. One would also expect that patients with absent A1 may suffer from larger strokes; however, our study showed that there was no difference in the stroke volume across the groups. When the stroke volume was compared for cardioembolic, large vessel, and small vessel subtypes, stroke volume was similar for absent and intact A1 segment. These findings suggest that our initial assumption was not correct, and based on our results absent A1 segment does not affect stroke location or volume. The second perspective of the relevance of absent A1 is that the A1 absence may affect the hemodynamics of blood flow throughout the circle of Willis overall.[13-15] It would also be expected that absent A1 may be associated with worse outcomes. In our study, we were not able to detect a significant difference in the mRS score on discharge, in-hospital length of stay, discharge disposition, or in-hospital mortality, after adjusting for known covariates.

Our study was limited by its retrospective nature and the small number of patients with this rare variant of circle of Willis. Higher prevalence of absent A1 among ischemic stroke patients may be explained by higher false positive values occurring when MRA TOF was used to detect vascular anomalies; 60% of our patients had only MRA TOF done without validating the results with CTA. Previous studies have shown that CTA has a higher sensitivity and positive predictive value than MRA and is recommended over TOF MRA for detection of intracranial stenosis and occlusion.[20] Considering that most of the subjects were screened using MRA TOF, it could be that many of the absent A1 patients had a hypoplastic rather than a completely absent A1. For the previous reason, in one of our subanalyses, we limited the comparison with the patients who had absent A1 on CTA; we found no significant difference in the stroke territory compared with patients with present A1. It is also possible that in the setting of hemispheric infarctions, our ability to distinguish a congenital absence of an A1 segment from a complete occlusion is impaired. In this case, some cases of “absent A1” may actually represent acutely occluded A1 segments and our prevalence and findings of increased mortality may be inaccurate.

In summary, to the contrary to our hypotheses, our study did not show any association of absent A1 segment with ACA strokes. Moreover, stroke volume for each of the 3 major TOAST categories was similar for absent A1 and intact A1 groups. Absent A1 was not associated with worse stroke outcome compared with intact A1. Absent A1 may affect the collateral circulation and the hemodynamics throughout circle of Willis; however, this variant did not show any clinical relevance in our study population.

References

1. Schellinger PD, Köhrmann M, Liu S, et al. SENTIS Trial Investigators. Favorable vascular profile is an independent predictor of outcome: a post hoc analysis of the safety and efficacy of NeuroFlo Technology in Ischemic Stroke trial. Stroke. 2013; 44:1606–1608. [PubMed: 23549132]
2. Kapoor K, Singh B, Dewan LI. Variations in the configuration of the circle of Willis. AnatSciInt. 2008; 83:96–106.

3. Lippert, H.; Pabst, R. Arterial variations in man: classification and frequency. Munich: J.F. Bergmann. Verlag; 1985.
4. Krabbe-Hartkamp MJ, van der Grond J, de Leeuq FE, et al. Circle of Willis: morphologic variation on three-dimensional time-of-flight MR angiograms. Radiology. 1998; 207:103–111. [PubMed: 9530305]
5. Chuang YM, Liu CY, Pan PJ, et al. Anterior cerebral artery A1 segment hypoplasia may contribute to A1 hypoplasia syndrome. EurNeurol. 2007; 57:208–211.
6. Alpers BJ, Berry RB, Paddison RM. Anatomical studies of the circle of Willis in normal brain. AMA Arch Neurol Psychiatry. 1959; 81:409–418. [PubMed: 13636509]
7. Puchades-Orts A, Nombela-Gomez M, Ortuno-Pacheco G. Variation in form of circle of Willis: some anatomical and embryological considerations. Anat Rec. 1976; 185:119–123. [PubMed: 1267194]
8. Niederberger E, Gauvrit JY, Morandi X, et al. Anatomic variants of the anterior part of the cerebral arterial circle at multidetector computed tomography angiography. J Neuroradiol. 2010; 37:139–147. [PubMed: 20346510]
9. Perlmutter D, Rhoton AL Jr. Microsurgical anatomy of the anterior cerebral-anterior communicating-recurrent artery complex. J Neurosurg. 1976; 45:259–272. [PubMed: 948013]
10. Uchino A, Nomiyama K, Takase Y, et al. Anterior cerebral artery variations detected by MR angiography. Neuroradiology. 2006; 48:647–652. [PubMed: 16786350]
11. Kane AG, Dillon WP, Barkovich AJ, et al. Reduced caliber of the internal carotid artery: a normal finding with ipsilateral absence or hypoplasia of the A1 segment. AJNR Am J Neuroradiol. 1996; 17:1295–1301. [PubMed: 8871715]
12. Liebeskind DS. Collateral circulation. Stroke. 2003; 34:2279–2284. [PubMed: 12881609]
13. Moore S, David T, Chase JG, et al. 3D models of blood flow in the cerebral vasculature. J Biomech. 2006; 39:1454–1463. Epub 2005 Jun 13. [PubMed: 15953607]
14. Alastruey J, Parker KH, Peiro J, et al. Modelling the circle of Willis to assess the effects of anatomical variations and occlusions on cerebral flows. J Biomech. 2007; 40:1794–1805. [PubMed: 17045276]
15. Ferrandez A, David T, Brown MD. Numerical models of autoregulation and blood flow in the cerebral circulation. Comput Methods Biomech Biomed Engin. 2002; 5:7–19. [PubMed: 12186730]
16. Siegler JE, Boehme AK, Dorsey AM, et al. A comprehensive stroke center patient registry: advantages, limitations, and lessons learned. MSRJ. 2013; 2:021.
17. Adams HP Jr, Bendixen BH, Kappelle LJ, et al. Classification of subtypes of acute ischemic stroke. Definitions for use in multicenter clinical trial Stroke. 1993; 24:35–41.
18. Siegler JE, Boehme AK, Kumar AD, et al. What change in the National Institutes of Health Stroke Scale should define neurologic deterioration in acute ischemic stroke? J Stroke Cerebrovasc Dis. 2013; 22:675–682. [PubMed: 22727922]
19. Bender R, Lange S. Adjusting for multiple testing–when and how? J Clin Epidemiol. 2001; 54:343–349. [PubMed: 11297884]
20. Bash S1, Villablanca JP, Jahan R, et al. Intracranial vascular stenosis and occlusive disease: evaluation with CT angiography, MR angiography, and digital subtraction angiography. AJNR Am J Neuroradiol. 2005; 26:1012–1021. [PubMed: 15891154]

Table 1

Demographics

Demographics	A1 absent	A1 present	*P* value
Age, median (min-max) [IQR], y	65 (29-97) [57-79]	63 (19-103) [54-73]	.016*
Gender, female, n (%)	31/68 (45.6)	476/1078 (44.2)	.818
Race, n (%)			.673
White	15/68 (21.1)	321/1073 (29.9)	
Black	51/68 (75.0)	709/1073 (66.1)	
HLD, n (%)	35/67 (52.2)	439/1065 (41.2)	.199
HTN, n (%)	58/67 (86.6)	815/1067 (76.4)	.155
DM, n (%)	22/66 (36.3)	352/1063 (33.1)	.971
Smoking, n (%)	20/67 (29.9)	377/1055 (35.7)	.329
Admission NIHSS, median (min-max) [IQR]	5 (0-29) [2.5-10.5]	5 (0-39) [3-12]	.676
Prior stroke, n (%)	32/67 (47.8)	422/1077 (39.2)	.299
tPA was given, n (%)	19/68 (27.9)	309/1078 (28.7)	.898
TOAST, n (%)			.292
Cardioembolic	16/68 (23.5)	247/1074 (23.0)	
Large vessel	15/68 (22.1)	237/1074 (22.1)	
Small vessel disease	21/68 (30.9)	217/1074 (20.2)	
Cryptogenic, >1 cause	1/68 (1.5)	36/1074 (3.4)	
Cryptogenic, no cause	9/68 (13.2)	221/1074 (20.6)	
Other	6/68 (8.8)	116/1074 (10.8)	
ACA involved in the stroke, n (%)	9/68 (13.2)	97/1078 (9.0)	.242
MCA involved in the stroke, n (%)	25/68 (36.8)	509/1078 (47.2)	.094
PCA involved in the stroke, n (%)	5/68 (7.4)	138/1078 (12.8)	.187

Abbreviations: ACA, anterior cerebral artery; DM, diabetes mellitus; HLD, hyperlipidemia; HTN, hypertension; IQR, interquartile range; MCA, middle cerebral artery; NIHSS, National Institute of Health Stroke Scale; PCA, posterior cerebral artery; TOAST, Treatment of Acute Stroke Trial; tPA, tissue plasminogen activator.

*Statistical significance was defined as $p < 0.05$.

Table 2

Outcomes

Outcomes	Absent A1	A1 present	*P* value
NIHSS at discharge, median (min-max) [IQR]	3 (0-42) [1-13]	2 (0-42) [1-7]	.147
mRS on discharge, median (min-max) [IQR]	3 (0-6) [1-4]	3 (0-6) [1-4]	.149
Length of stay, median (min-max) [IQR]	4 (1-44) [3-8]	5 (0-57) [2-9]	.679
Death, n (%)	8/67 (11.9)	57/1072 (5.3)	.023*
Favorable disposition, n (%)	43/62 (69.4)	802/1038 (77.3)	.152
NIHSS discharge–NIHSS admission, median (min to max) [IQR]	−1 (−23 to 34) [−4 to 1]	−1 (−23 to 42) [−4 to 0]	.224
mRS 0-1, n (%)	17/67 (25.4)	341/1045 (32.6)	.218
mRS 0-2, n (%)	25/67 (37.3)	491/1045 (47.0)	.124
mRS 5-6, n (%)	14/67 (20.9)	145/1045 (13.9)	.112
Neuroworsening, n (%)	23/68 (33.8)	322/1055 (30.5)	.567

Abbreviations: IQR, interquartile range; mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale.

*Statistical significance was defined as $p < 0.05$.