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# Transcranial Doppler and magnetic resonance angiography assessment of intracranial stenosis: An analysis of screening modalities

**Ashkan Mowla, Banafsheh Shakibajahromi[1], Rasadul Kabir[2], Zsolt Garami[3,4], John J. Volpi[2]**

*Department of Neurological Surgery, Division of Endovascular Neurosurgery, Keck School of Medicine, University of Southern California, Los Angeles, CA, [2]Department of Neurology, Houston Methodist Neurological Institute, [3]Institute for Academic Medicine, Research Institute, [4]Vascular Ultrasound Laboratory, Houston Methodist Hospital, Weill Cornell Medical College, Houston, TX, USA, [1]Clinical Neurology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran*

**Address for correspondence:**
Dr. Ashkan Mowla, Department of Neurological Surgery, Division of Endovascular Neurosurgery, Keck School of Medicine, University of Southern California, 1200 North State St., Suite 3300, Los Angeles, CA 90033, USA.
E-mail: mowla@usc.edu

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**Abstract:**

**BACKGROUND:** Time-of-flight (TOF) magnetic resonance angiography (MRA) of the head and transcranial Doppler (TCD) are used to diagnose intracranial stenosis, an important cause of ischemic stroke. We aimed to compare TCD findings with TOF-MRA results in a population of patients with symptoms of cerebrovascular disease in whom both tests were done within a short intervening period of each other.

**METHODS:** This is a retrospective, single-center study. Among adult patients referred for symptoms of cerebrovascular disease in both outpatient and inpatient settings, those who received a TCD with adequate insonation of all intracranial arteries and underwent MRA within 3 months intervals of TCD were included in this study. We evaluated the agreement between the results of these two modalities, and also assessed sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of TCD through receiver-operating characteristic (ROC) curve analysis, while MRA considered as a comparator.

**RESULTS:** Among eighty included patients, 720 arteries were examined. An overall significant agreement of 96.5% was observed between TCD and MRA (Kappa = 0.377, $P < 0.001$). Compared to MRA, TCD had sensitivity of 42.1%, specificity of 99.6%, PPV of 72.7%, and NPV of 98.4% (ROC area: 0.708 [0.594–0.822]). TCD is specifically accurate in evaluating middle cerebral artery (MCA) (ROC area = 0.83).

**CONCLUSIONS:** The high NPV of TCD in our study indicates the utility of TCD as a diagnostic test to exclude the presence of intracranial stenosis. This study supports TCD as a convenient, safe, and reproducible imaging modality applicable in the screening of intracranial stenosis, especially to evaluate MCA.

**Keywords:**

Intracranial stenosis, magnetic resonance angiography, screening, stroke, transcranial Doppler sonography

## Introduction

Intracranial stenosis is an important cause of ischemic stroke and an independent risk factor for stroke recurrence.[1] The presence of intracranial atherosclerosis is associated with an increased risk of recurrent stroke ranging from 10% to 50% per year.[2]

Diagnostic evaluation of a stroke patient typically includes screening for intracranial stenosis with one of several common imaging modalities. Conventional digital subtraction angiography (DSA) is



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considered the gold standard diagnostic modality,[3] but it is not the preferred test because it is invasive and incurs significant costs and specialized practitioners. Less costly non-invasive options for screening include CT angiography (CTA), Time-of-flight (TOF*)* magnetic resonance angiography (MRA) of the head, and transcranial Doppler (TCD).[4] CTA is most commonly performed in acute evaluations and requires radiation and administration of iodinated dye. MRA has the advantage of requiring neither radiation nor dye and has shown to be a highly sensitive and specific technique to evaluate the patency of intracranial vasculature.[5] While MRA is often preferred in nonacute settings, patient characteristics (such as body size, claustrophobia, the presence of metallic implants, or foreign bodies) as well as the cost of imaging, and availability in some areas limits its use. In addition, MRA and CTA machines are often off-site from outpatient clinic settings and require additional patient time and scheduling. TCD, on the other hand, is a portable, convenient, and repeatable bedside test that can be performed without radiation in any setting at a relatively low cost. While TCD is more operator dependent, high-quality studies are possible with proper training.[6]

In this analysis, we compared TCD findings with TOF-MRA results in a population of patients who referred for symptoms of cerebrovascular disease in whom both tests were done within a short intervening period of each other.

## Materials and Methods

This is a retrospective, prospectively collected data set from a single center. A population of 388 adults (≥18 years old) patients who were referred for symptoms of cerebrovascular disease in both outpatient and inpatient settings, were screened for inclusion into this study because they had received a TCD with adequate insonation of all intracranial arteries. The examined arteries included nine arterial segments: Bilateral middle cerebral artery (MCA), bilateral anterior cerebral artery (ACA), bilateral posterior cerebral artery (PCA), bilateral vertebral artery (VA), and basilar artery (BA). TCD was done within 10 days of the symptoms of the ischemic event. Patients who did not have complete TCD or had poor temporal acoustic windows were excluded from the study. In this population, both TOF-MRA of the head and TCD were obtained within 3 months of each other in 83 patients. Three patients were excluded due to poor quality of MRA from motion degradation. TCDs were interpreted by a stroke neurologist board certified in neurosonology. MRAs were read by a board-certified neuroradiologist who was blinded to the TCD results.

Among patients in whom there was at least one artery with a discordant result between both tests, seven had cerebral angiogram within 3 months of TCD and MRA. Cerebral angiograms were all read by a separate board-certified interventional neuroradiologist who was blinded to the TCD results but had access to the MRA images and results.

The MRA examinations were performed on a 1.5 T scanner using a 3D flow compensated gradient echo sequence. TCD examination was done on Power M-Mode TCD Doppler (ST3, Spencer Technologies, Seattle, WA) using previously published diagnostic criteria and IAC accredited protocol and interpretations. TCD values normal range for mean flow velocities 20–80 cm/s and pulsatility index values 0.6–1.2.

The institutional IRB approved the study and waived the need for obtaining informed consent, as the study was retrospective and no personal information of patients was used.

### Statistical analysis

Mean ± SD and range were reported for quantitative variables and frequencies were reported for qualitative variables. Inter-rater agreement was performed to detect the agreement between the results of TCD and MRA in total, and for each artery as an independent variable. We categorized the findings of each modality into three groups based on clinical relevance: (1) No stenosis (2) stenosis present but <50% (3) stenosis of 50%–100%. The agreement was defined according to the kappa values.[7] Due to the small number of patients with available DSA, agreement analysis between TCD and DSA, and MRA and DSA was not feasible. Therefore, we only reported the frequencies and relative frequencies of discordant arteries between TCD and MRA, which were in concordance with the cerebral angiogram in cases with available DSA. In addition, we considered MRA as the comparator and assessed sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) with binomial 95% confidence interval for TCD through receiver-operating characteristic (ROC) curve analysis in the total number of the arteries and also every single artery, separately. The area under the ROC curve was reported. For this analysis, we considered the stenosis ≥50% as the positive test result and the stenosis <50% as the negative result for both MRA and TCD. $P < 0.05$ was considered significant. We applied STATA version 12 for the statistical analysis.

## Results

Of 388 consecutive patients, eighty met the inclusion criteria for our study. The mean age was 58.4 (±17.9) ranging from 20 to 95 years old. The mean time interval between the two modalities was 23.0 ± 27.5 days. Sixteen patients (20.0%) had intracranial stenosis in at least one artery on at least one imaging modality. In seven patients, (8.7%), both TCD and MRA showed at least one stenotic artery.

A total of 720 arteries were evaluated. In 25 arteries (3.47%) of 12 patients, discordant results were observed [Table 1].

The agreement between TCD and MRA for evaluating each of the intracranial arteries is shown in Table 2 separately. According to our analysis, the agreement between these two modalities is significant in evaluating all intracranial arteries ($P < 0.05$) except for RACA, RPCA, and LPCA. Overall, a significant agreement of 96.5% was observed between TCD and MRA with Kappa = 0.377. In 15 arteries (of seven patients with available cerebral angiogram) with discordant results, angiogram results favored MRA in 10 cases (67%) and TCD in 5 cases (33%). Table 3 shows the sensitivity, specificity, PPV, NPV, and area under the ROC curve for TCD with MRA as the comparator. The overall sensitivity and specificity of TCD compared to MRA were 42.1% and 99.6%, respectively. TCD had a total PPV of 72.7%, and an NPV of 98.4%. The area under the ROC curve was 0.708 (0.594–0.822), in total, and was the most for MCA (0.83 [0.623–1])).

**Table 1: Number of arteries with different degrees of stenosis examined by transcranial Doppler and magnetic resonance angiography**

| TCD | MRA | | | Total |
|---|---|---|---|---|
| | NS | L50 | M50 | |
| NS | 687 | 8 | 11 | 706 |
| L50 | 3 | 0 | 0 | 3 |
| M50 | 3 | 0 | 8 | 11 |
| Total | 693 | 8 | 19 | 720 |

NS: No stenosis, L50: Stenosis <50%, M50: Stenosis more than 50%, TCD: Transcranial Doppler, MRA: Magnetic resonance angiography

**Table 2: Agreement between transcranial Doppler and magnetic resonance angiography (3 categories: No stenosis, stenosis <50% and stenosis more than 50%)**

| Artery | Agreement (%) | κ | *P* |
|---|---|---|---|
| RMCA | 95.0 | 0.480 | <0.001 |
| RACA | 96.25 | −0.008 | 0.564 |
| RPCA | 95.0 | −0.019 | 0.586 |
| RVA | 98.75 | 0.661 | <0.001 |
| BA | 97.50 | 0.490 | <0.001 |
| LMCA | 96.25 | 0.554 | <0.001 |
| LACA | 96.25 | 0.391 | <0.001 |
| LPCA | 97.5 | 0.00 | 0.500 |
| LVA | 96.25 | 0.389 | <0.001 |
| Total | 96.53 | 0.377 | <0.001 |

RMCA: Right middle cerebral artery, RACA: Right anterior cerebral artery, RPCA: Right posterior cerebral artery, RVA: Right vertebral artery, BA: Basilar artery, LMCA: Left middle cerebral artery, LACA: Left anterior cerebral artery, LPCA: Left posterior cerebral artery, LVA: Left vertebral artery

## Discussion

Our study included 720 arteries examined by both TCD and TOF-MRA in eighty symptomatic patients, and we observed a significant agreement in 96.5% of arteries between the modalities. However, this agreement is considered poor according to the kappa value classification.[7] Prior series suggested a poor agreement between TCD and CTA of the head.[8] Our results indicated that TCD and MRA had the strongest agreement in evaluating both MCAs, BA, and RVA. According to ROC analysis, TCD is specifically accurate in evaluating MCA (ROC area = 0.83). In a previous comparison between TCD and CTA findings, TCD was mostly accurate in diagnosing MCA stenosis and had the least accuracy in evaluating VA.[9] Our results showed a nonsignificant agreement in the ACA and PCA, a finding that was influenced by the relatively lower frequency of stenosis in these arteries. Another possible explanation for this finding is that TCD measures velocity only and there may be vessels in which luminal narrowing is detected on MRA, but the residual flow is sufficient to result in no significant increase in mean flow velocity in the ACA and PCA arteries. Our findings support the use of TCD for the screening of MCA and vertebrobasilar stenosis, but leaves open the question of accuracy in the ACA and PCA. Further studies with a larger sample size may better elucidate whether the discordance is a limitation of TCD or a sampling error unique to this data set.

We reported the total sensitivity of 42%, the specificity of 99.6%, PPV of 73%, and NPV of 98.4% for TCD in comparison to MRA. The sensitivity of TCD in the current study is lower than the previous reports.[10,11] In a recent meta-analysis of TCD diagnostic accuracy, the summary estimates for sensitivity and specificity of TCD compared to MRA/intra-arterial angiography were 82% and 92%, respectively.[12] The different established diagnostic criteria of TCD among different centers may account for the differences in the reported sensitivities for TCD. Furthermore, relatively few patients underwent DSA, so our comparator was MRA and while TOF-MRA has high sensitivity and specificity for the detection of intracranial stenosis, it remains possible that limitations of MRA may account for some of the error attributed to TCD.[5] A strength of this analysis is that it included both inpatient and outpatient cases, and most of our patients were not evaluated in the setting of an acute ischemic stroke. Likely as a consequence of outpatient testing, we observed higher variability in the time interval between TCD and MRA compared to other data sets[8,10,13] and this is a possible contributor to the discrepancy in results.

The high NPV of TCD in our study indicates the utility of TCD as a diagnostic test to exclude the presence

**Table 3: Sensitivity, specificity, positive predictive value, negative predictive value and area under receiver-operating characteristic curve for transcranial Doppler (2 categories: No stenosis /stenosis <50% and stenosis more than 50%)**

| Artery | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) | ROC area (%) |
|---|---|---|---|---|---|
| MCA | 66.7 (22.3-95.7) | 99.4 (96.4-100) | 80.0 (28.4-99.5) | 98.7 (95.4-99.8) | 0.83 (0.623-1) |
| ACA | 25.0 (0.63-80.6) | 100.0 (97.7-100.0) | 100.0 (2.5-100.0) | 98.1 (94.6-99.6) | 0.625 (0.38-0.87) |
| PCA | 0.0 (0.0-97.5) | 98.7 (95.5-99.8) | 0.0 (0.0-84.2) | 99.4 (96.5-100.0) | 0.494 |
| BA | 33.3 (0.84-90.6) | 100.0 (95.3-100.0) | 100.0 (2.5-100.0) | 97.5 (91.2-99.7) | 0.667 (0.34-0.993) |
| VA | 20.0 (0.50-71.6) | 100.0 (97.6-100.0) | 100.0 (2.5-100.0) | 97.5 (93.7-99.3) | 0.60 (0.404-0.796) |
| Total | 42.1 (20.3-66.5) | 99.6 (98.8-99.9) | 72.7 (39.0-94.0) | 98.4 (97.2-99.2) | 0.708 (0.594-0.822) |

MCA: Middle cerebral artery, ACA: Anterior cerebral artery, PCA: Posterior cerebral artery, VA: Vertebral artery, BA: Basilar artery, PPV: Positive predictive value, NPV: Negative predictive value, ROC: Receiver-operating characteristic

of intracranial stenosis. This could be of particular clinical importance in centers with limited access to more advanced neurovascular imaging modalities to decide if a patient needs to be transferred to an advanced tertiary center. In addition, TCD application can reduce the cost of unnecessary further radiological work-ups. Conversely, the relatively low PPV suggests that positive results on TCD require follow-up imaging for confirmation. This result is in concordance with the "the stroke outcomes and neuroimaging of intracranial atherosclerosis (SONIA) trial" study.[14]

One strength of the present study is that all major intracranial arteries were examined separately by the two modalities. This allows the comparison of the utility of TCD for each artery and in total.

In this study, our methods defined specific cut-off values for mean flow velocity to categorize TCD findings. The data set is limited in this regard and does not allow reconsideration of different cut-off values. Our data set are also limited in that DSA was not performed in all patients. We are also unsure if sampling bias occurred since patients with abnormal TCD were more probable to undergo further investigations such as MRA.

## Conclusion

This study supports TCD as a convenient, safe, and reproducible imaging modality with wide applications in the screening of cerebrovascular diseases, including intracranial stenosis. TCD is highly recommended to rule out the presence of intracranial stenosis and has the most accuracy in evaluating MCA.

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### Conflicts of interest
There are no conflicts of interest.

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