

Accuracy of Transcranial Doppler Compared With CT Angiography in Diagnosing Arterial Obstructions in Acute Ischemic Strokes

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Background and Purpose—Patients with acute ischemic stroke and intracranial arterial obstructions have a poor prognosis and a high probability of deteriorating at 24 hours. We aimed to evaluate the diagnostic accuracy of power motion mode Doppler (PMD-TCD) compared with CT angiography as standard in diagnosing intracranial arterial obstructions in patients presenting with ischemic stroke of <24 hours.

Methods—Consecutive patients presenting with acute ischemic stroke to the emergency department underwent high-resolution brain CT angiography and PMD-TCD within a 6-hour difference.

Results—A total of 100 patients were included. PMD-TCD demonstrated 34 intracranial occlusions and CTA 33. There were 6 false-positives and 4 false-negative diagnoses with PMD-TCD. PMD-TCD had a positive likelihood ratio of 13.7, a negative likelihood ratio of 0.19, sensitivity of 81.8%, and specificity of 94% for detecting an arterial occlusion in any specific artery. Results for the middle cerebral artery were: positive likelihood ratio 24.6, negative likelihood ratio 0.045, sensitivity 95.6%, and specificity 96.2%. For the anterior circulation, the results were: positive likelihood ratio 18.5, negative likelihood ratio 0, sensitivity 100%, and specificity 94.5%. For the posterior circulation, the results were: positive likelihood ratio >1000, negative likelihood ratio 0.42, sensitivity 57.1%, and specificity 100%. The post-test probability for any occluded artery when PMD-TCD was positive increased for any admission National Institutes of Health Stroke Scale score but was especially remarkable for National Institutes of Health Stroke Scale scores between 7 and 15 points.

Conclusions—PMD-TCD is valid compared with CT angiography for the diagnosis of arterial occlusions in patients with acute ischemic stroke, especially in middle cerebral artery obstructions. (*Stroke*. 2009;40:2037-2041.)

Key Words: Doppler ultrasound ■ intracranial arterial diseases ■ sensitivity ■ specificity ■ stroke ■ ultrasonography

Patients with acute ischemic stroke that have intracranial arterial obstructions have poorer prognosis and a higher probability of deteriorating at 24 hours with a lower response to intravenous recombinant tissue plasminogen activator.¹⁻³ These patients could benefit from intra-arterial, mixed intra-venous-intra-arterial thrombolysis,^{4,5} or therapies to increase cerebral perfusion^{6,7} or neuroprotection.⁸

There have been efforts to develop clinical scales that predict arterial occlusions, but their accuracy is not higher than 85% and restricted to the middle cerebral artery.⁹

Various diagnostic examinations are being used increasingly in the emergency room (ER) as the standard to identify intracranial vascular lesions as accurately and as fast as possible. CT angiography (CTA)^{10,11} and MR angiography

(MRA)^{12,13} are popular noninvasive techniques used to determine the status of the intracranial arteries. CTA is available in many hospitals and is generally more readily accessible than MRA in the ER. Nevertheless, its use is limited by renal failure and allergies to intravenous contrast.¹⁴ Transcranial Doppler (TCD) sonography is also used for this purpose.¹⁵ TCD is valid compared with digital subtraction angiography^{16,17} and has recently been shown to be valid compared with CTA.¹⁸ TCD has the advantage of being a bedside examination, repeatable, and less expensive than CTA.¹⁹

A new TCD technology, power motion mode Doppler (PMD-TCD), is thought to increase the speed by which acoustic windows are found and arteries.^{20,21} However, the rate of

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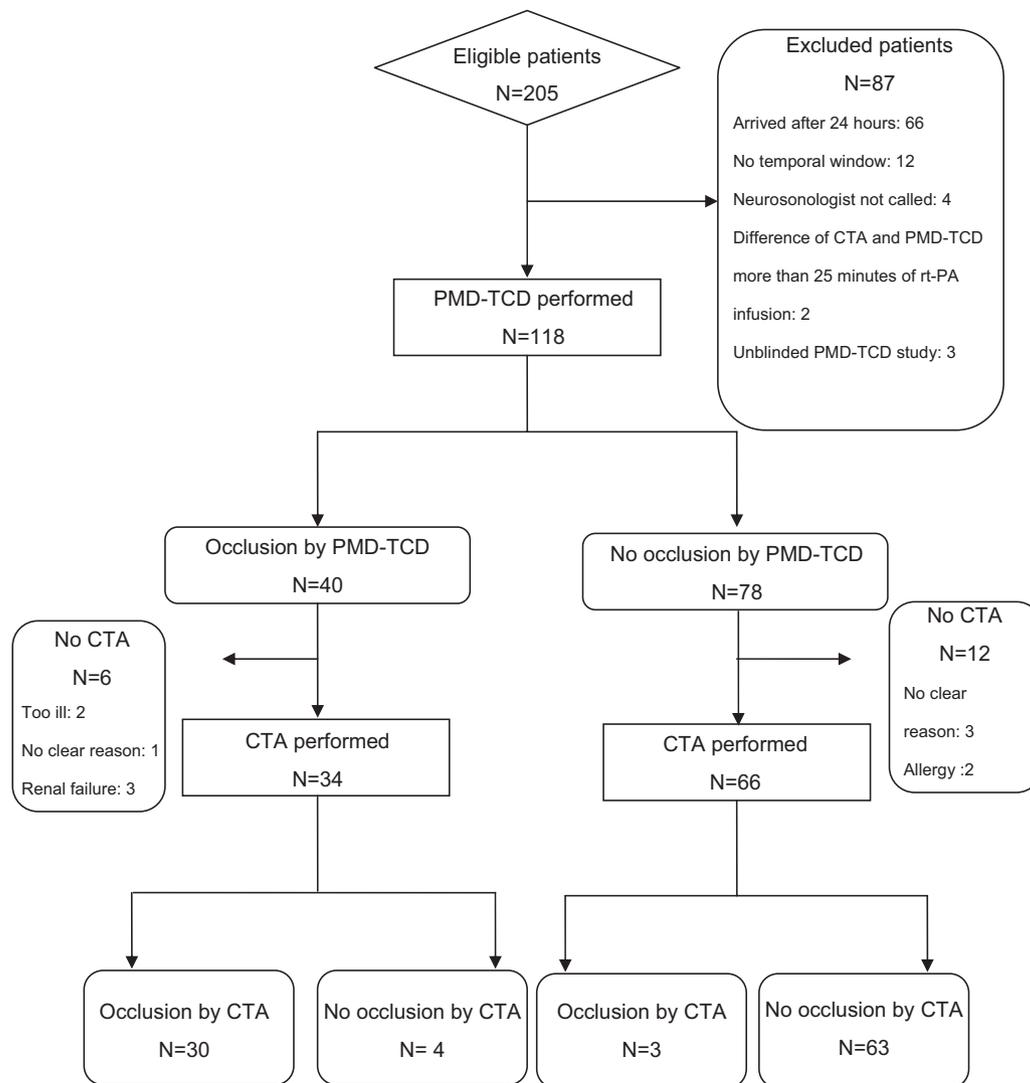


Figure. Flow diagram of the study of the accuracy of TCD versus CTA in diagnosing acute arterial obstructions in ischemic stroke.

successful identification of obstructed intracranial vessels with PMD-TCD only, when compared with CTA, is not known.

We aimed to evaluate the validity and diagnostic accuracy of PMD-TCD compared with CTA as the standard in diagnosing acute intracranial arterial obstructions or occlusions in patients presenting to the ER with ischemic stroke of <24 hours.

Patients and Methods

Clínica Alemana is a private teaching not-for-profit hospital of 350 beds serving a population of approximately 120 000 inhabitants in the northeast of Santiago, Chile. Patients with ischemic stroke are seen by the neurologist on call and a stroke fellow in the first 15 to 30 minutes of arrival to the ER. After initial clinical evaluation, all patients with suspected stroke are studied with an institutional imaging protocol consisting of noncontrast brain CT scan and, in those without contraindications, spiral CTA of intracranial arteries and diffusion-weighted MRI. Additionally, since 2005, all patients arriving <24 hours of symptom onset are evaluated with TCD using power motion PMD-TCD (PMD-100; Spencer Technologies) as part of the neurovascular diagnosis. All TCD studies were performed by an experienced sonographer certified by the American Society of Neuroimaging who was informed about the patients' main symptoms. In this investigation, we present data collected prospectively between April 2005 and January 2007 in which the sonographer,

who was not the treating physician, was blind to the results of the CTA performed usually earlier during the study period.

A standardized, rapid (lasting <15 minutes) insonation protocol was used and arterial stenosis or occlusions were diagnosed according to the criteria described by Demchuck et al adding PMD-TCD criteria for arterial occlusions.^{16,21} All results were interpreted immediately after insonation.

We choose CTA as our standard because of its elevated potential for application in acute cerebral ischemia and increasing use.^{10,11} Brain CTA scans were obtained with a Siemens Sensation 16 multidetector helical scanner. CT scans were performed with 0.75-mm slice thickness and 0.5-mm intervals during a bolus injection of 80 mL of contrast material at a rate of 5 mL per second. Explorations from C2 cervical level to the vertex were performed. Multiplanar reformats were created in the axial, coronal, and sagittal planes. When no reconstitution of distal flow was detected on an artery, arterial obstruction was diagnosed; in these cases, an additional 3-dimensional reconstruction with volume rendering was done. The neuroradiologist on call informed the CTA immediately on site. They were also blind to the results of PMD-TCD.

During the study period, patients who were eligible for intravenous thrombolytic therapy were treated according to the National Institute of Neurological Diseases and Stroke trial protocol²² and monitored with PMD-TCD according to the Combined Lysis of Thrombus in Brain Ischemia Using Transcranial Ultrasound and

Table 1. Baseline Characteristics of the Study Sample and Times to Examinations

Variables	N=100
Mean age, years (range)	69.9 (42–93)
Male sex, %	56
Mean admission NIHSS (SD)	7.9 (6.7)
Median admission NIHSS, range	1–32
Hypertension, %	71
Diabetes mellitus, %	37
Hypercholesterolemia, %	25
Smoking, %	24
Heart disease, %	37
Mean time from symptom onset to examination, minutes (SD)	361 (321)
CTA	391 (324.5)
PMD-TCD	468 (343.2)

Systemic tPA (CLOTBUST) study.²³ To allow comparisons between CTA and PMD-TCD, patients who received intravenous thrombolysis were only included if they had both examinations performed before the first 25 minutes of recombinant tissue plasminogen activator infusion.

Patients without temporal windows were excluded from the analysis as well as those who had contraindications for CTA. No adverse events were reported with CTA or PMD-TCD.

The study was reviewed by the local ethics and scientific committee and the methodology accepted as justified and respectful of patients' rights.

Statistical Analysis

Likelihood ratios, sensitivity, specificity, and their respective 95% CIs²⁴ as well as diagnostic accuracy were calculated to estimate PMD-TCD validity in detecting arterial occlusions in all arteries, middle cerebral artery (MCA), anterior circulation (MCA, anterior cerebral artery, and terminal internal carotid), posterior circulation (vertebral, basilar, and posterior cerebral arteries), any intracranial occluded artery, and the combination of the major arteries of the anterior and posterior circulation, which we defined as central arteries (terminal internal carotid artery, MCA–M1, basilar artery) were compared with CTA. We calculated the post-test probabilities of arterial occlusion diagnosed by PMD-TCD using Fagan's nomogram²⁵ and the probability of arterial occlusion according to admission National Institutes of Health Stroke Scale (NIHSS) score as pretest probability. Pretest probabilities were calculated using previous publications comparing admission NIHSS scores and MRA¹² and also admission NIHSS scores and digital subtraction angiography.^{26,27} The study is reported according to the STAndards for the Reporting of Diagnostic accuracy studies (STARD) criteria.²⁸

Results

During the study period, of 205 consecutive patients with acute ischemic stroke seen at the ER of Clínica Alemana, 100

were included. The flow diagram of the study and causes of exclusion from analysis are shown in the Figure. The characteristics of the study sample are shown in Table 1. The mean (SD) time from "symptom onset" to CTA was 391 (324.5) minutes and to PMD-TCD was 468 (343.2) minutes; the mean difference of time between both examinations was 77.8 (88.5) minutes. Seven PMD-TCD examinations were performed before CTA. In 60% of patients, both tests were performed with less than a 1-hour difference between them. In 29%, the difference was between 61 minutes and 180 minutes and in 11%, the difference was more than 181 minutes but less than 360 minutes.

PMD-TCD demonstrated 34 intracranial occlusions and CTA 33. Compared with CTA, PMD-TCD showed 6 false-positives and 4 false-negative diagnoses.

PMD-TCD had a positive likelihood ratio (PLR) of 13.7, a negative likelihood ratio (NLR) of 0.19, sensitivity (Se) of 81.8%, and specificity (Sp) of 94% for detecting an arterial occlusion in any specific artery compared with CTA.

The results for the middle cerebral artery were: PLR 24.55, NLR 0.045, Se 95.6%, and Sp 96.15%. For the anterior circulation, the results were: PLR 18.5, NLR 0, Se 100%, and Sp 94.5%. For the posterior circulation, the results were: PLR >1000, NLR 0.42, Se 57.1%, and Sp 100%. For detecting any overall occluded artery, PMD-TCD demonstrated a PLR of 15.2, a NLR of 0.09, a Se of 90.9%, and a Sp of 94%. For detecting an occlusion of central arteries, the results were: PLR of 70.3, a NLR of 0.08, a Se of 91.3%, and a Sp of 98.2%. The diagnostic accuracy of PMD-TCD was high as shown in Table 2.

The posttest probability for any occluded artery when PMD-TCD was positive increased for any admission NIHSS score but was especially remarkable for NIHSS scores between 7 and 15 points when compared with unselected patients whose occlusions were diagnosed by MRA (Table 3). The posttest probability for an anterior circulation artery occlusion increased from to 63%–97% to 94%–99% in selected patients with NIHSS >10 points diagnosed by digital subtraction angiography. In the posterior circulation, the posttest probability of an occlusion was less notable compared with the probability of occlusion diagnosed by digital subtraction angiography in a selected sample.

During the study period, a total of 18% patients were thrombolized.

Discussion

Our study shows that PMD-TCD is accurate in detecting arterial occlusions in unselected patients with acute ischemic

Table 2. PLRs, NLRs, Sensitivities, Specificities, and Diagnostic Accuracy for Each Artery With Corresponding 95% CIs

Artery	PLR (95% CI)	NLR (95% CI)	Se (95% CI)	Sp (95% CI)	Diagnostic Accuracy
Any specific artery	13.7 (5.2–35.9)	0.19 (0.09–0.4)	81.8 (68.7–95.0)	94 (88.3–99.7)	90
MCA	24.6 (8.1–74.7)	0.045 (0.006–0.30)	95.6 (87.3–100)	96.2 (91.7–100)	96
Anterior circulation	18.5 (7.1–48)	0 (0–NA)	100 (100–100)	94.5 (89.4–99.7)	96
Posterior circulation	>1000 (NA–infinity)	0.42 (0.18–1)	57.1 (20.4–93.8)	100 (100–100)	97
Central occlusion	70.3 (10–494.8)	0.08 (0.02–0.3)	91.3 (79.7–100)	98.2 (96.1–100)	97
Any overall artery	15.2 (5.8–38.6)	0.09 (0.03–0.28)	90.9 (81.1–100)	94 (88.3–99.7)	93

NA indicates not applicable.

Table 3. Pretest Probabilities and Likelihood Ratios of TCD Results and Post-test Probabilities of Any Arterial Occlusion in Patients With Acute Ischemic Strokes

NIHSS Score on Admission	Pretest Probability (%) of an Arterial Occlusion*	Artery	Likelihood Ratio for PMD-TCD Result of an Arterial Occlusion	Posttest Probability (%) of Any Arterial Occlusion
0–6	0	Any artery	15	20
7–15	43	Any artery	15	90
>16	78	Any artery	15	97

*Unselected sample of patients with stroke. Occlusion diagnosed by MRA from study by Derex et al.

stroke compared with CTA, particularly in anterior circulation arteries, MCA, and central arteries (combination of the major arteries of the anterior and posterior circulation), where PLRs were >10 indicating a large and often conclusive increase in the likelihood of an arterial occlusion and a negative NLR of <0.1 , indicating a very low likelihood of arterial occlusion when normal.

In acute occlusions of posterior circulation arteries, PMD-TCD demonstrated a very high positive posttest probability of occlusion but a lower posttest probability of nonocclusion when compared with CTA.

We found that PMD-TCD increases remarkably the probability of ruling in or ruling out an arterial occlusion in patients with admission NIHSS scores of 7 to 15. These are patients in whom the pretest probability of an arterial occlusion is intermediate with great uncertainty as whether the arteries are open. This is very important because occlusions are associated with an increased probability of clinical deterioration within the next 24 hours. If PMD-TCD shows an arterial occlusion, patients in this category could benefit greatly not only from thrombolysis, but also from monitoring of permeabilization and more aggressive therapy, if necessary.

In selected patients (nonlacunar, <80 years old, or with NIHSS ≥ 5 points), the pretest probability of an occlusion diagnosed by digital subtraction angiography in patients with NIHSS ≥ 10 was high according to 2 studies, so a positive PMD-TCD increases the likelihood less dramatically.

Our findings are similar to those obtained by Demchuk et al,¹⁶ who studied the reliability of single-gated TCD in intracranial occlusions, and Tsvigoulis et al,¹⁸ who demonstrated the accuracy of intracranial ultrasound (using single-gated and PMD-TCD) compared with CTA showing a high sensitivity and specificity of TCD in detecting alterations on any artery, especially MCA. Similar results had been obtained previously by Ley-Pozo²⁹ and Camerlingo³⁰ in anterior circulation artery occlusions. In posterior circulation arteries, our results are in agreement with the reports by Brandt³¹ and Tsvigoulis³² who found that TCD had lower sensitivity but high specificity in the diagnosis of occlusive disease. This is probably related to the high frequency of morphological variants in the posterior circulation. Different from the study of Tsvigoulis et al,¹⁸ we excluded patients with transient ischemic attacks, because these patients have a very low pretest probability of an occlusion and thus could bias the results toward a greater diagnostic accuracy for ruling out occlusions with PMD-TCD. Likewise, we excluded cases with poor sonographic windows from the analysis to evaluate the validity of examinations performed in optimal conditions. Our findings differ from those obtained by Suwanwela et al³³

who studied the validity of TCD in MCA M1/M2 occlusions compared with CTA with poor results. This could be explained by the long time delay between CTA and ultrasonography in their study, which may give time to spontaneous dissolution or reocclusion of the affected arteries. In our study, the maximum delay between the standard and PMD-TCD was 359 minutes with a mean of 85.2 minutes, guaranteeing minimum biological changes in this time period.

We have shown that PMD-TCD is valid compared with CTA in the diagnosis of arterial occlusions in patients with acute ischemic stroke, similar to the results obtained with single-gated TCD and a small time delay to the examination used as the gold standard.^{16,29,30}

The main strengths of our study are that it was conducted in a normal clinical setting in all consecutive patients with acute ischemic strokes who had an acoustic window that allowed TCD examination. There was a very little time difference between CTA and PMD-TCD. It was unbiased as to time from symptom onset and time or day of the week. Most CTAs were performed before PMD-TCD; therefore, there was no influence on whether to perform the study.

Our study has limitations. Some patients were excluded because they did not have acoustic windows and others because they had contraindications for CTA; also because of chance we did not examine any patient with anterior cerebral artery occlusion, which is one of the arteries with lowest sensitivity for TCD diagnosis. This could bias our results toward a greater accuracy of PMD-TCD. Furthermore, the number of cases with posterior circulation occlusion was limited, so the conclusions regarding validity of the test in this territory are less robust. Another limitation of this study is that we did not test interrater or intrarater reliability of PMD-TCD.

Conclusions

PMD-TCD is valid compared with CTA for the diagnosis of arterial occlusions in patients with acute ischemic stroke, especially in the MCA, and can be implemented in many ERs that have less access to CTA or MRA. Patients with intermediate clinical probabilities of an arterial occlusion can greatly benefit from a rapid, low-cost examination performed at the ER, which can discriminate those patients who should be closely monitored and treated more aggressively.

Disclosures

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