

## Validation of Transcranial Doppler with CT Angiography in Cerebral Ischaemia: A Preliminary Pilot Study in Singapore

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### Abstract

**Introduction:** Transcranial Doppler (TCD) is an established tool for the non-invasive assessment of cerebral blood flow. Since TCD results vary with the skills and experience of the sonographer, it requires validation against contrast angiography. We evaluated the diagnostic accuracy of TCD against computed tomography angiography (CTA) and the feasibility of the latter as an additional screening tool in our acute ischaemic stroke patients. **Materials and Methods:** Our stroke unit manages about 700 patients annually. Acute stroke patients undergo TCD for vascular assessment of major arteries of the circle of Willis. Randomly selected acute stroke patients with significant stenosis on TCD underwent high-resolution cranial CTA with multidetector helical scanner. CTA was performed within 24 hours of TCD and images were interpreted by a neuroradiologist blinded to TCD findings. An independent neurosonologist re-evaluated TCD if CTA findings were contradictory. Additional information by either modality was also noted. **Results:** Fifteen patients (12 men, mean age 61 ± 15 years) with cerebral ischaemia and moderate (>50%) stenosis in ≥1 large intracranial arterial segment on routine TCD were evaluated by CTA. Compared with 21 segments of significant stenosis on CTA, TCD showed 16 true-positive, 3 false-positive and 5 false-negative results (sensitivity: 76.2%, positive predictive value: 84.2%). In 3 cases, TCD showed findings complementary to CTA (real-time embolisation, collateral flow patterns, evidence of distal M2 branch occlusion). **Conclusion:** TCD in our neurovascular laboratory shows a satisfactory agreement with cranial CTA in evaluating patients with cerebral ischaemia. TCD can provide additional real-time dynamic findings complementary to information provided by CTA.

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**Key words:** Cerebral ischaemia, CT angiography, Transcranial Doppler

### Introduction

Transcranial Doppler (TCD) is routinely performed to assess the blood flow in patients with cerebral ischaemia and provides important real-time information about cerebral haemodynamics. TCD can aid in the diagnostic work-up by detecting, localising and grading the severity of intracranial arterial obstruction.<sup>1,2</sup> However, owing to variations in experience and technical skills, cerebrovascular ultrasound is often criticised for its “operator-dependence”.<sup>3</sup> Validation of TCD findings against contrast angiography may enhance the reliability of the results of the former in a neurovascular laboratory.<sup>4</sup> Cranial computer tomography angiography (CTA) is a useful non-invasive tool for imaging the major arteries of the circle of Willis.<sup>5,6</sup> Limited data are available

regarding the correlation of TCD and CTA findings in cerebral ischaemia.<sup>7-9</sup>

CTA is not routinely used as a screening tool in acute cerebral ischaemia in our institution. We undertook this pilot study with the aim of evaluating the diagnostic accuracy of TCD against CTA in our neurovascular laboratory. Additionally, we assessed the feasibility of performing the latter as an initial screening tool in patients with suspected acute cerebral ischaemia, especially if an experienced sonographer is not readily available.

### Materials and Methods

Our neurovascular laboratory routinely uses 2-MHz power-motion or single-channel TCD (Companion III,

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Nicolet-Viasys) as a non-invasive screening test in the evaluation of patients with cerebral ischaemia. A standard TCD employs ultrasound insonation through “trans-orbital”, “trans-temporal”, “sub-occipital” and “trans-foraminal” acoustic windows as per standard insonation protocols to identify arterial vaso-occlusive diseases and various intracranial flow patterns.<sup>10</sup> Stroke neurologists credentialed in cerebrovascular ultrasound (VKS, BPLC) used the previously published diagnostic criteria to interpret the TCD findings.<sup>1,2,10</sup> Specifically, we used a mean flow velocity of 80 cm/s as the cut-off for a moderate stenosis in middle cerebral artery (MCA), since it has been used in most of the previously validated studies with fairly good accuracy parameters.<sup>11</sup> We included patients with acute ischaemic stroke as well transient ischaemic attacks (TIA). We adopted the World Health Organization (WHO) definition of acute stroke as “rapidly developing signs of focal (or global) disturbance of cerebral function lasting >24 hours (unless interrupted by surgery or death), with no apparent nonvascular cause”. Patients whose focal neurological deficits resolved within 24 hours, without any therapeutic intervention, were labelled as TIA.

High-resolution brain CTA was performed on a 4-slice multidetector helical scanner (Siemens VolumeZoom, Erlangen, Germany) in patients without any evidence of intracranial bleeding and no contraindication for CTA (contrast medium allergy or serum creatinine levels >110 mmol/L). CTA images were obtained during a bolus injection of 70 mL to 100 mL of contrast with bolus-tracking done using a threshold level of 800 HU. Scan parameters were as follows: slice thickness 1 mm; no slice gap; field of view 200 mm; matrix 512 x 512; 230-250 mAs. Coverage was from the base of skull to the vertex. The source images were reformatted into 3 mm-thick axial, coronal and sagittal images.

The degree of stenosis was defined as the narrowest vessel diameter divided by a normal diameter of the vessel. The choice of a normal diameter was made according to a standard algorithm of selection of an unaffected denominator (choice 1 = prestenotic segment, choice 2 = poststenotic segment, choice 3 = feeding vessel). The reduction of narrowest diameter of the residual lumen to <50% was considered to represent a significant intracranial artery stenosis. Intracranial artery occlusion was diagnosed when no reconstitution of distal flow was detected.

Neuroradiologist interpreting the CTA films was blinded to the TCD findings. These CTA reports were used to compare the TCD findings and determine true-positive, true-negative, false-positive, and false-negative ultrasound results for TCD. We assessed the sensitivity and positive predictive value of TCD performed in the neurovascular laboratory of our tertiary care centre.

## Results

A total of 15 patients (12 men, mean age  $61 \pm 15$  years) with cerebral ischaemia (13 with acute ischaemic stroke and 2 with TIA) and a moderate (>50%) stenosis in  $\geq 1$  large intracranial arterial segments on routine TCD were randomly selected for this preliminary validation study. The demographic characteristics and vascular risk factors in our study population are shown in Table 1. The average time spent performing and processing CTA images in our study was 12 minutes (range, 10 to 25).

The findings obtained by TCD were evaluated with CTA, performed within 24 hours of the former (Table 2). Patients with an insufficient temporal acoustic “window” on TCD were not included due to technically incomplete assessment of the circle of Willis. Various intracranial artery stenosis or occlusion in the 15 cases as determined by TCD were: proximal middle cerebral artery (MCA, n = 7), distal (MCA, n = 3), supraclinoid C1 internal carotid artery (n = 3), ICA siphon (n = 2), posterior cerebral (PCA, n = 1), basilar artery (n = 1) and vertebral artery (n = 2). Six of the 15 patients evaluated with TCD revealed significant

Table 1. Baseline Characteristics, TCD and CTA Findings of the Study Population (n = 15)

Variable	No.
<i>Baseline characteristics</i>	
Mean age (years, SD)	61
Male gender	12
Hypertension	13
Diabetes mellitus	6
Ischaemic heart disease	2
Hypercholesterolaemia	12
Atrial fibrillation	2

Table 2. Abnormal Findings in Individual Arterial Segments Noted on CTA with the Accuracy Parameters of Transcranial Doppler

Arterial segment	CT angiography		Transcranial Doppler	
	Abnormal	True positive	False negative	False positive
M1 MCA	7	7	0	0
M2 MCA	4	3	1	0
TICA	2	2	0	1
ICA SIPHON	0	0	0	2
PCA	3	1	2	0
BA	2	1	1	0
VA	3	2	1	0

BA: basilar artery; ICA: internal carotid artery; M1 MCA: M1 segment of middle cerebral artery; M2 MCA: M2 segment of middle cerebral artery; TICA: terminal or C1 segment of intracranial internal carotid artery; PCA: posterior cerebral artery; VA: vertebral artery

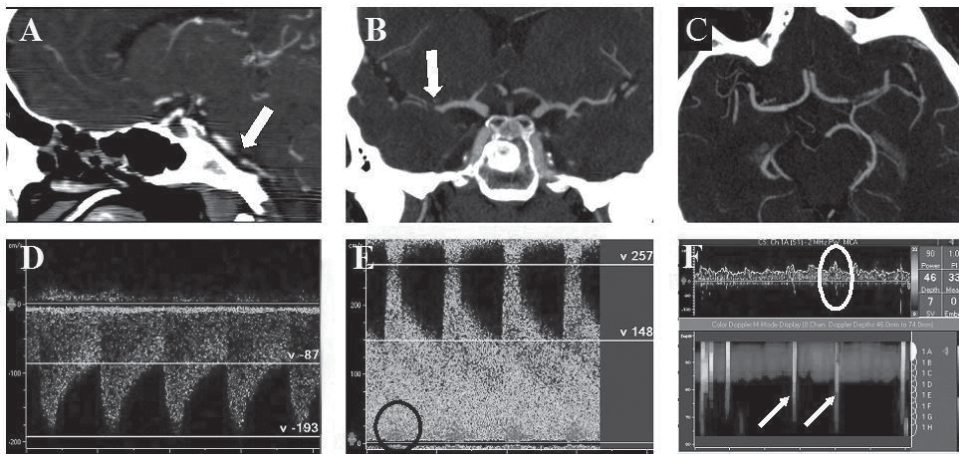


Fig.1. Correlation and complementary information by TCD and CTA. A high-grade stenosis in the mid-basilar artery is demonstrated in CTA (arrow in A) with a markedly elevated flow velocity (193/87 cm/s) noted on spectral TCD (D). Similarly, a severe stenosis in right MCA (arrow in B) is accompanied by a very high velocity (257/148 cm/s) on TCD (E). A systolic bruit is clearly demonstrated in the spectrum (circles in E). CTA shows normal filling (C) of both MCA and ACA in a patient with recurrent transient episodes of right-sided weakness. TCD shows real-time spontaneous embolic signals (F), noted both in the spectral (inside the circle in the upper frame) as well as in the M-mode display (arrows in the lower frame).

vaso-occlusive lesions in more than 1 intracranial segment, providing a total of 19 segments.

A total of 21 segments with intracranial stenosis were identified on CTA. Compared with these 21 segments of significant stenosis on CTA, TCD showed 16 true-positive, 5 false-negative and 3 false-positive results (sensitivity: 76.2%, positive predictive value: 84.2%) (Table 2). False-negative results were made in the assessment of both posterior as well as anterior circulation. Two false-positive TCD cases [minimal flow velocities in distal basilar artery and anterior cerebral artery (ACA)] occurred because of suboptimal angle of insonation, while in 1 case compensatory flow increased through the posterior communicating artery in the presence of ipsilateral carotid artery occlusion misidentified as proximal MCA occlusion. In one tPA-treated patient's baseline (before the tPA bolus dose), TCD disclosed stenotic waveforms (moderately elevated mean flow velocity 118 cm/sec) in proximal MCA. CTA performed next day revealed a normal MCA filling, thus representing a recanalised artery. However, the focal stenosis in the left distal vertebral artery was still observed on CTA.

Three cases showed TCD findings complementary to the information provided by CTA (real time embolisation in 2 patients and collateralisation of flow with extracranial internal carotid artery disease in 1 patient). Three correlative and complementary studies are presented in Figure 1. One patient, without any vascular risk factors, revealed Moya Moya disease pattern on CTA, but was diagnosed as having multiple intracranial arterial stenoses by TCD.

## Discussion

Our preliminary validation study shows a satisfactory agreement between the various TCD findings and CTA. TCD performed in our neurovascular laboratory not only matched CTA results in a significant proportion of cases, but also provided some additional real-time haemodynamic

information, important for the management of patients with cerebral ischaemia.

CTA has recently been introduced as a new sensitive and specific tool for the assessment of cerebral vasculature.<sup>5,6,8</sup> CTA is preferable to magnetic resonance angiography (MRA) since the depiction of the anatomy of the circle of Willis by the former is more reliable.<sup>12</sup> In a previous study, we reported unsatisfactory correlations between MRA and TCD performed in our institution.<sup>13</sup> CTA has an excellent yield in the diagnosis of intracranial steno-occlusive disease (sensitivity 100%, positive predictive value 93.4%) when compared to digital subtraction angiography (DSA).<sup>7</sup>

Individual accuracy parameters for TCD against CTA in the present report are comparable to the previous studies investigating a smaller number of cases.<sup>9,14</sup> In a relatively larger recent study, we reported approximately similar findings in acute stroke patients undergoing TCD examination performed in the emergency room employing a "fast-track" insonation protocol as well as an emergent CTA.<sup>8</sup> However, our findings differed considerably with the poor correlation of TCD with CTA (in patients with distal M1 or M2 disease) reported by Suwanwela et al.<sup>7</sup> Their study provides a good comparison since, like our report, TCD and CTA were performed within 2 and 7 days after the onset of cerebral ischaemia. A longer time interval between CTA and TCD may occur due to thrombus propagation, dissolution or reocclusion.

While CTA demonstrates the filling and patency of cerebral vasculature, TCD can provide real-time flow findings, collateral flow patterns and spontaneous embolic signals.<sup>15</sup> Performed within a reasonable time period of each other, CTA and TCD may provide complementary and clinically relevant information.<sup>8</sup> Various applications of CTA (perfusion studies with or without acetazolamide)<sup>16</sup> and TCD (vasomotor reactivity and assessment of "dynamic" and "static" cerebral autoregulation)<sup>17</sup> may add to the quantitative assessment of cerebral haemodynamics.

This study was aimed to assess the reliability of TCD performed in our neurovascular laboratory as well as the feasibility of performing a rapid CTA in acute cerebral ischaemia. The limitations of our study include the need for considerable skills and expertise to perform and interpret TCD accurately. This validation pilot study has a small number of subjects and this limits our interpretation of the results and their generalisation. Our 15 patients provided us with a significant number of individual arterial segments for comparison between CTA and TCD. (Theoretically, each patient would provide data from one ICA siphon, one terminal ICA, one M1 MCA, one M2 MCA, one ACA, one P1 PCA, one P2 PCA, one vertebral artery on each side in addition to the basilar artery. These add up to 17 arterial segments per patient, and in total 255 segments. The analysis of all these arterial segment could provide us with a specificity of 98.7% and a negative predictive value of 97.9%). However, due to a limited number of subjects, we hesitate to make claims for such accuracy parameters for TCD performed in our laboratory.

Our study also identified clinical situations when TCD and CTA may not be reliably interpreted. While TCD faces a limited visualisation of the distal basilar artery or distal M2 due to awkward insonation angles, the presence of adjacent skull bone mars the information in CTA images. Our results should not lead to the inference that TCD is superior to CTA, and is a possible substitute for the assessment of cerebral vasculature and cerebral haemodynamics. We evaluated CTA in a pre-selected group (by TCD) of patients and additionally, only a small number of patients were included in this pilot validation study.

In conclusion, TCD can reliably identify a substantial proportion of steno-occlusive arterial lesions in cerebral ischaemia, confirmed by contrast angiography. The determination of the vascular cause and localisation of the underlying vascular occlusion are important in the assessment of patients with cerebral ischaemia. As TCD requires an experienced operator, CTA, due to its speed and accuracy, may be introduced as an initial screening tool for patients so that there will not be any delay in initiation of thrombolytic therapy. Since TCD and CTA, especially when performed within a short time interval, may compensate for each other's shortcomings, both of these modalities can provide valuable information for better understanding of cerebral haemodynamics and the management of patients with cerebral ischaemia.

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