Transcranial Color-Coded Duplex Sonography and Digital Subtraction Angiography in Acute Stroke Patients

Farhad Assarzadegan
Shahid Beheshti University of Medical Sciences
Foroogh Mohammadi
Shahid Beheshti University of Medical Sciences
Behnam Safarpour Lima
Shahid Beheshti University of Medical Sciences
Behnam Mansouri
Shahid Beheshti University of Medical Sciences
Seyed Hossein Aghamiri
Shahid Beheshti University of Medical Sciences
Navideh Sahebi Vaighan (navideh.sahebi@sbmu.ac.ir)
Shahid Beheshti University of Medical Sciences

Research Article

Keywords: stroke, transcranial color-coded duplex sonography, digital subtraction angiography

Posted Date: February 15th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-189444/v1

Abstract

Background: Stroke is the most common neurological disorder with a high incidence in Middle-eastern regions. We aimed to assess the diagnostic accuracy of transcranial color-coded duplex sonography (TCCS) for detection of cerebral artery stenosis compared to digital subtraction angiography (DSA) as a gold standard method.

Methods: Eighty patients presenting with symptoms of cerebral ischemia were enrolled in the study. They were examined by color-coded Doppler and TCCS to determine stenosis of extracranial and intracranial arteries, respectively. DSA was performed 24-48 hours after the initial examination. The sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and accuracy of TCCS in comparison to DSA was calculated. The agreement between the two methods was determined by kappa statistics.

Results: Eighty patients (60% male, 40% female) with a mean age of 61.32±12.6 years were included. In 65% of cases, pathology in carotid artery was responsible for ischemia. We did not observe any abnormalities in the anterior cerebral artery (ACA), posterior cerebral artery (PCA) as well as basilar artery (BA). The agreement between TCCS and DSA in various arterial vessels were 0.9 for common carotid artery (CCA), 0.86 for internal carotid artery (ICA), 0.78 for middle cerebral artery (MCA), and 0.86 for vertebral artery (VA). The sensitivity, specificity, PPV, NPV, accuracy, and kappa value of TCCS for detection of stenosis regarding the arterial segments were 84.8%, 81%, 92.6%, 65.4%, 83.8, and 0.71, respectively.

Conclusion: TCCS is a valuable, non-invasive, and repeatable method to investigate cerebral artery stenosis with high diagnostic accuracy.

Background

Stroke is considered as the second most common cause of death and disability-adjusted life year (DALY), globally [1]. Although age–standardized stroke death rate and incidence have been decreased in developed countries, it is still prevalent with increasing incidence especially in east Asia, southern sub-Saharan Africa, and Middle-Eastern regions [2, 3]. According to a systematic review done by Hosseini et.al, the incidence rate of stroke in different age groups of Iranian population accounted 23 to 103 per 100000 person [4].

Acute occlusion of cervical or intracranial arteries is the leading cause of ischemic stroke which accounts for approximately 87 % of all stroke events [5, 6]. Significant stenosis of carotid artery with subsequent embolism or hypoperfusion is seen in twenty percent of ischemic stroke patients [7, 8]. Atherosclerosis is a primary mechanism of stenosis and occlusion of intracranial great arteries responsible for ischemic stroke in 8–29 % of general population [9, 10]. In the middle aged population asymptomatic atherosclerosis of carotid artery is common. On the other hand, 8–15 % of patients with ischemic stroke had internal carotid artery stenosis as a result of atherosclerosis [11, 12]. Patients with total carotid artery occlusion are at increased risk of recurrence about 6 percent per year which could be up to 10 percent with diminished cerebral blood flow reserve capacity although the best therapy [13]. In about 70% of patients presenting with ischemic stroke during the first 6 hours of onset of symptoms, arterial occlusion is detectable [5, 14]. Therefore, diagnosing intracranial arteries stenosis is crucial to manage the stroke and identify high risk patients for vascular events [15]. In addition, early evaluation of intracranial arteries is considered as criterion of effective treatment in many countries [16].

Digital subtraction angiography (DSA) is the "gold standard" for the assessment of cerebral artery stenosis despite some limitations. It is expensive, invasive, and hemodynamic changes are not presented [17]. Nevertheless, other modalities such as magnetic resonance angiography (MRA) as well as computed tomography angiography (CTA) used in stroke patients especially with growing use of mechanical thrombectomy, are not available on a 24/7 basis worldwide. Lesion’s morphology and real time hemodynamic information are not determined in these two modalities [16]. Moreover, patients who undergo CTA are exposed to ionizing radiation and are at risk of contrast induced nephropathy and allergic reactions [17].

Ultrasound is the safest imaging modality applicable at bedside by which frequent evaluation and real time monitoring are attainable [18]. Vessel wall and plaques in the extracranial arteries has been assessed for more than four decades by brightness-mode (B-mode) of ultrasound imaging [16]. In 1982, Aaslid et al. introduced transcranial Doppler (TCD) as a successful insonation of intracranial arteries via skull by placement of a probe of a ultrasound Doppler instrument in the temporal area [19]. Despite the advancement in the technology of TCD, which made it applicable of use in a broad range in clinical practice, it has some limitations. These limitations including poor spatial resolution, identification of blood vessels based on indirect parameters, nonvisualization of anatomical landmarks, incorrect blood velocity benchmark (metric), and misordered distinct blood vessels in presence of normal anatomic variants were the reasons for invention of transcranial color duplex sonography (TCCS) [20]. It provides two-dimensional imaging of intracranial structures and color Doppler description of vasculature additionally to hemodynamic information [21]. By B-mode parenchymal structures and by color-coded flow blood flow is visible simultaneously [22]. TCCS has some advantages in diagnosing intra-axial intracranial hematomas (intraparenchymal hematomas), extra-axial intracranial hematomas (epidural and subdural hematomas), brain midline shift, hydrocephaly, brain tumors, cerebral aneurysms, and arteriovenous malformations [21]. Although real-time dynamic morphological information is achieved via color or power Doppler flow imaging of TCCS [23], it has been reported that only 55–80% of basal cerebral arteries can be determined via unenhanced TCCS [24].

In the present study we aimed to appraise the accuracy of color-coded Doppler sonography for detection of extra- and intracranial stenosis in comparison to DSA as a gold standard.

Materials And Methods

Study population

Men and women aged over 18 years old with clinical signs and symptoms of cerebral ischemia who were admitted within six hours of onset of symptoms between January 2018 and February 2020 were eligible. Hemorrhagic stroke, receiving anticoagulant drugs, suffering from blood dyscrasia, hepatic and renal failure, bronchial asthma, history of endarterectomy, pregnancy, allergy to iodine contrast material, and poor acoustic window for TCCS were exclusion criteria.

On admission all patients underwent carefully neurologic examination and patient age and gender, history of underlying disease such as hypertension, diabetes, hyperlipidemia, and hypercoagulopathy were collected.

Transcranial color-coded sonography (TCCS)

An expert neurologist with at least 5 years of experience of the Doppler sonography of cerebral supplying arteries (F.A) examined extracranial and intracranial arteries with TCCS prior to DSA. No contrast enhancement was used. A high resolution color-coded duplex sonography system with a linear probe 5–10 MHz (high frequency) for the cervical arteries and phased-array probe 2–5 MHz (low frequency) for intracranial arteries was used.

Cervical Doppler was performed to evaluate left and right common carotid arteries, extracranial internal carotid arteries, and vertebral arteries. In addition, intracranial internal carotid artery, anterior cerebral artery (ACA), middle cerebral artery (MCA), and posterior cerebral artery (PCA) were examined through transtemporal window. Through transoccipital (also called transforaminal) window terminal vertebral arteries and proximal basilar arteries were evaluated. The results reported as normal and stenotic. The stenosis was sub-classified as < 50%, 50–69%, 70–99% and 100% (occluded). Velocity criteria for grading the stenosis was based on the consensus panel gray scale and Doppler US criteria for diagnosis of ICA stenosis [26]. The crucial peak systolic velocity (PSV), end diastolic velocity (EDV), and the peak systolic internal carotid artery/common carotid artery (ICA/CCA) velocity ratio were assessed. PSV and EDV were measured in three segments: pre-stenotic, stenotic, and post-stenotic. Occlusion was considered when the color signals or pulse-waved Doppler was absent. Details of ultrasound grading criteria for carotid and intracranial stenosis are shown in Tables 1 and 2.

Table 1
Ultrasound grading criteria for intracranial stenosis (1–3)

Vessel	Mild stenosis < 50%	Moderate stenosis 50–69%	Severe stenosis ≥ 70%
M1-MCA	PSV ≥ 155 cm/sec	PSV ≥ 220 cm/s	PSV _220 cm/s or variable PSV Distal M1/M2 post-stenotic FP Raised V mean ipsilateral A1 and/or P2-PCA
M2-MCA	PSV ≥ 100 cm/s	PSV ≥ 140 cm/s	PSV _140 cm/s or variable PSV Distal M2 post-stenotic FP
A1-ACA	PSV ≥ 120 cm/s	PSV ≥ 155cm/s	PSV _155 cm/s or variable PSV A2 post-stenotic FP Raised V mean ipsilateral M1 or P2-PCA and/or contralateral A1
P1-P2-PCA	PSV ≥ 100 cm/s	PSV ≥ 145 cm/s	PSV _145 cm/s or variable PSV Distal PCA post-stenotic FP Raised V mean ipsilateral M1 and/or A1
BA	PSV ≥ 100 cm/s	PSV ≥ 140 cm/s	PSV _140 cm/s or variable PSV Distal BA/PCA post-stenotic FP
V4-VA	PSV ≥ 90 cm/s	PSV ≥ 120 cm/s	PSV _120 cm/s or variable PSV Distal VA/BA post-stenotic FP

ACA: anterior cerebral artery, BA: basilar artery, EDV: end-diastolic velocity, FP: fellow pattern, MCA: middle cerebral artery, PCA: posterior cerebral artery, PSV: peak systolic velocity

Table 2
SRU Consensus Conference Criteria for the Diagnosis of ICA Stenosis (4)

Primary Parameters Additional Parameters				
Degree of Stenosis (%)	ICA PSV (cm/second)	Plaque Estimate (%)	ICA/CCA PSV Ratio	ICA EDV (cm/second))
Normal	<125	None	<2.0	<40
< 50%	<125	< 50	<2.0	<40
50–69	125–230	≥ 50	2.0–4.0	40–100
≥ 70 but less than near occlusion	>230	≥ 50	>4.0	>100
Near occlusion	High, low, or undetectable	Visible	Variable	Variable
Total occlusion	Undetectable	Visible, no detectable lumen	Not applicable	Not applicable
CCA: common carotid artery, EDV: end diastolic velocity, ICA: internal carotid artery, PSV: peak systolic velocity				

Digital subtraction angiography

Under local anesthesia DSA was carried out in radiology department after selective injection of 8–10 ml contrast material in vertebral and internal carotid arteries via femoral artery by experienced neurologist (B.M), who were unaware of ultrasonography results. It was performed within 24–48 hours after onset of symptoms. Finding of DSA were used as the gold standard for statistical analysis. Stenosis was determined by the ratio of the vessel's lumen diameter at the site of stenosis to the diameter of the vessel distal to the stenosis [27]. In the absence of complete filling, arterial occlusion was reported.

Statistical analysis

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) software (version 20). The sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), quadratic weighted and unweighted kappa was calculated.

Results

Cervical and intracranial arteries of 80 patients who fulfilled the eligibility criteria of the study were examined by TCCS and DSA. The study group contained 48 (60%) males and 32 (40%) females. The mean age of patients was 61.32 ± 12.6 years. Eighty-five percent of patients were suffering from an underlying disease. The clinical and characteristic variables were shown in Table 3. The time between the two examinations did not exceed 48 hours in any case. The mean interval of time between two methods was 27.1 ± 2.5 hours.

Among the 1040 vessel segments examined by TCCS, in 129 segments stenosis was detected. The number and grade of stenosis (< 50%, 50–69%, and 70–99%) were as follows: CCA (5, 1, 2), ICA (36, 19, 15), MCA (5, 4, 1), VA (2, 2, 9). In addition, in one MCA, 15 vertebral, and 9 ICA segments occlusion was reported. None of our patients showed stenosis in ACA, PCA, and basilar arteries. After conducting DSA, 98 of 129 cases of stenosis were confirmed (CCA:5, ICA:60, MCA:9, and VA:24). The detailed results of both examinations are shown in Table 4 and Table 5.

To appraise the agreement between two methods, the kappa statistics was measured with seven degrees : <0, less than chance agreement; 0.01–0.2, slight agreement; 0.21–0.4, fair agreement; 0.41–0.6, moderate agreement; 0.61–0.8, substantial agreement; 0.81–0.99, almost perfect agreement; 1, perfect agreement [31].

As is shown in Table 6, weighted kappa values were 0.9 for CCA (almost perfect agreement), 0.86 for ICA (almost perfect agreement), 0.78 for MCA (substantial agreement), and 0.82 for VA (almost perfect agreement) ($p < 0.001$). The Sensitivity, specificity, predictive values, accuracy as well as kappa values are reported in Table 6.

In subgroup analysis, we found fair agreement between TCCS and DSA for detecting mild ($k = 0.41$), moderate ($k = 0.41$), and severe ($k = 0.53$) grade of stenosis by calculating unweighted kappa, whereas almost perfect agreement was observed for occluded vessels ($k = 0.90$) ($p < 0.001$). On the other hand, overall quadratic weighted kappa revealed substantial agreement between two modalities (quadratic weighted $k = 0.71$, CI: 0.52–0.91, $p < 0.001$). The sensitivity, specificity, PPV, NPV, and accuracy of TCCS were 84.8%, 81% 92.6% 65.4%, and 83%. The validity and reliability indexes are shown in Table 7.

Table 3
Patient Characteristic

	Number of patients (n = 80)
Sex	48 (60%)
Male	32 (40%)
Female	
Mean ages in year (range)	61.32 (25–86)
Past Medical History	66/80 (85.5%)
DM	27/80 (33.8%)
HTN	56/80 (70%)
HLP	23/80 (28.7%)
Cardiac disease	42/80 (52.5%)
Hypercoagulopathy	1/80 (1.3%)
Smoking	11/80 (13.8%)
Diagnosis	72 (90%)
Cerebral ischemic infarct	
Transient ischemic attack	8 (10%)
Territory	52 (65%)
Carotid artery	11 (13.8%)
MCA	0
ACA	0
PCA	27 (33.8 %)
VA	0
BA	

ACA = anterior cerebral artery, BA = basilar artery, DM = diabetes mellitus, HTN = hypertension, HLP = hyperlipidemia, MCA = middle cerebral artery, PCA = posterior cerebral artery, VA = vertebral artery

Table 4
Number of diseased vascular segments detected by Digital Subtraction Angiography

Degree of stenosis					
Vascular segment	**Normal**	**< 50%**	**50–69%**	**70–99%**	**Occlusion**
CCA	151	4	2	3	0
ICA	93	28	11	19	9
MCA	147	2	3	7	1
ACA	160	0	0	0	0
PCA	160	0	0	0	0
VA	127	7	5	9	12
BA	80	0	0	0	0

CCA: common carotid artery, ICA: internal carotid artery, MCA: middle cerebral artery, ACA: anterior cerebral artery, PCA: posterior cerebral artery, VA: vertebral artery, BA: basilar artery

Table 5
Number of diseased vascular segments detected by Transcranial Color-coded duplex Sonography

Degree of stenosis					
Vascular segment	**Normal**	**< 50%**	**50–69%**	**70–99%**	**Occlusion**
CCA	150	5	2	3	0
ICA	81	36	19	15	9
MCA	149	5	4	1	1
ACA	160	0	0	0	0
PCA	160	0	0	0	0
VA	132	2	2	9	15
BA	80	0	0	0	0

CCA: common carotid artery, ICA: internal carotid artery, MCA: middle cerebral artery, ACA: anterior cerebral artery, PCA: posterior cerebral artery, VA: vertebral artery, BA: basilar artery

Table 6

Validity and reliability indexes of TCCS in comparison to DSA for detection of hemodynamically significant (≥ 50%) and normal/hemodynamically non-significant (< 50%) stenosis in various vascular segments

Vascular segment	Sensitivity	Specificity	PPV	NPV	Accuracy	kappa
CCA	100%	100%	100%	100%	100 %	0.9
ICA	87.1%	89.8%	84.4%	91.7%	88.8%	0.86
MCA	60%	100%	100%	94.6%	93.8%	0.78
VA	83.3%	94.6%	87%	93%	91.3%	0.86

CA: common carotid artery, ICA: internal carotid artery, MCA: middle cerebral artery, VA: vertebral artery, TCCS: Transcranial Color-coded Doppler Sonography, DSA: Digital Subtraction Angiography

Table 7

Validity and reliability indexes of TCCS for detection of cervical and intracranial arteries abnormalities in comparison to DSA

Parameter	Value (95% confidence intervals)
Sensitivity	84.8% (72.5–92.4)
Specificity	81% (57.4–93.7)
PPV	92.6% (80.2–97.5)
NPV	65.4% (44.4–82.1)
Positive LR	12.5 (4.9–32.2)
Negative LR	0.5 (0.3–0.9)
Kappa	0.71 (0.52–0.91)
Accuracy	83.8%

TCCS: Transcranial Color-coded Doppler Sonography, DSA: Digital Subtraction Angiography, PPV: Positive Predictive Value, NPV: Negative Predictive Value, LR: likelihood ratio.

Discussion

Transcranial ultrasound, as noninvasive neurovascular imaging, can be used in acute ischemic stroke patients to detect normal, stenosed as well as occluded vessels [32]. In the current study, we compared the pathology of cervical and intracranial arteries by TCCS to the gold standard method, DSA. Significant stenosis (> 50%) in carotid artery was reported in 65% of patients. Vertebral artery was responsible for the patients' symptoms in about 30% of cases.

Ultrasound of carotid artery provides precious information about echogenicity of plaque, ulceration, risk of thrombosis, and rupture [9]. Comparing color-coded Doppler sonography to DSA to detect common carotid abnormalities showed almost perfect agreement (k = 0.9) with 100% sensitivity, 100% specificity, and 100% accuracy. In three cases, sonography reported mild stenosis (< 50%) while the report of DSA was normal. Contrarily, one patient with normal sonography was diagnosed with mild stenosis by DSA. As is apparent, these discrepancies were observed in stenosis less than 50%, which was reported by Baumgartner et al., who stated that the prevalence of false-positive findings in mild stenosis increases up to three times [33]. Our results indicated fair agreement between these two methods for the detection of a mild grade of stenosis (k = 0.41).

TCCS detected stenosis of ICA with high sensitivity (87.1%), specificity (89.8%), accuracy (88.8%) as well as almost perfect agreement level which was comparable to the study of Simon et al. who reported 90.9% sensitivity with high specificity (98.1%) and almost perfect agreement level [18]. Navarro et al. found 90% sensitivity and 83% specificity of TCD in the diagnosis of abnormalities in terminal ICA [34]. Other research reported high accuracy of TCCS in the diagnosis of hemodynamically significant stenosis of intracranial arteries [15].

In the present study, TCCS could only detect 60% of the patients with significant symptomatic MCA stenosis (> 50%) diagnosed by DSA. The investigation of Chen et al. showed a sensitivity of 54% with low PPV (10.5%) compared to angiography in detection of MCA stem occlusion [35]. Although TCCS detected 6 out of 10 cases with significant (> 50%) stenosis, in two cases with severe stenosis the grade of stenosis was misdiagnosed. Half of four patients with missed diagnosis of severe MCA stenosis by TCCS were female with a mean age of 70 years old. It has been announced that some undesired conditions of acoustic window, like the skull eburnation, especially in women in the menopausal or climacteric period, led to vague or non-visualization and consequently misdiagnosis. It emphasizes the importance of clinical symptoms in the diagnosis of vascular occlusion [35]. Furthermore, one male patient had simultaneous occlusion in the ipsilateral ICA. Some possible reasons for such discrepancies between TCCS and DSA diagnosis could be described by the collateral circulation of occlusive vessels [36]. Recanalization of the MCA occlusion which may happen within several days to more than one week may contribute to differences in TCCS and DSA [35]. In a study by Gerriets et al., the symptomatic MCA examination was possible only in 55% of patients by unenhanced TCCS. The diagnosis was confirmed in 97% after performing angiography [37]. This is also reported by another survey in which only 52 % of patients with symptomatic MCA pathology were determined by unenhanced TCCS [38]. Poster with his colleges found 97% sensitivity of TCCS in detecting MCA stenosis in comparison to CTA [39]. The study by Simon et.al, compared TCCS to MRA which showed 70% and 33.3% sensitivity for detection of stenosis in M1 and M2 segments, respectively. They found a moderate level of agreement in M1 segment whereas just fair agreement was observed for M2 segment [18]. Bar et al. performed CTA and TCCS in patients with ischemic stroke within the three hours of symptoms onset and three months later. They revealed 92.3% sensitivity, 94.4% specificity, and 87.1% accuracy of TCCS in the diagnosis of MCA main stem occlusion [5].

The diagnosis and classification of VA stenosis by sonography are challenging because asymmetry in VA is prevalent and hypoplastic, and also, it could terminate in the posterior inferior cerebellar artery.

Moreover, contralateral VA pathology or severe stenosis of the carotid arteries may influence the blood flow in VA because of collaterals' recruitment [16]. Examination of VA arteries by TCCS showed high sensitivity (83.8%), specificity (94.6%), accuracy (91.3%), and kappa value (0.86). In the study by Simon et al., sensitivity, specificity, and agreement level were reported 72.7%, 99.4%, and 0.81, respectively [18].

Stroke as a result of ACA occlusion is less common compared to MCA. Furthermore, the accuracy of TCCS in the detection of ACA occlusion is not well studied [40]. In our study, TCCS and DSA examinations did not report any abnormality in ACA. The sensitivity and specificity of 100% with the almost perfect agreement have been reported previously [18].

P2 segment of PCA is one of the most common sites of intracranial arterial stenosis [40]. The diagnosis of PCA occlusion by TCCS may be demanding because of frequent variation like fetal type PCA which arises directly from ICA as well as misinterpreting the nearby superior cerebellar artery as the PCA [40]. In our study, none of our patients presented with symptomatic PCA stenosis, and investigation by two methods did not discover any pathology. Evaluation of PCA in a study revealed 33.3% sensitivity, 98.1% specificity, 50% PPV, and NPV 98.2% because of the distal part of P1 or P1-P2 junction stenosis with poor angle correction [18].

Because basilar artery occlusion is life-threatening, early accurate diagnosis is crucial. However, visualization of the distal part of the basilar artery by TCCS is somehow tricky, especially in obese patients with short necks or in patients with variation in the morphology of vessels. These difficulties could be overcome by the transtemporal approach instead of transformainal [40]. In this study, the primary evaluation of basilar arteries by TCCS was normal with a confirmatory DSA test.

In all evaluated cerebral arteries, we found high PPV and NPV indicative of a lower portion of false-positive and false-negative results, respectively. Overall sensitivity, specificity, PPV, NPV, accuracy as well as kappa value of TCCS for detection of cervical and intracranial arteries pathologies were 84.8%, 81%, 92.6%, 65.4%, 83.8%, and 0.71, respectively. The study of Hou et al. revealed 72.9% sensitivity, 82.9% specificity, 78.2% accuracy, 74.9%PPV, 77.3% NPV, and kappa 0.56 [36]. In addition, the investigation of the accuracy of TCCS by Roubec et al. in 67 patients, showed higher sensitivity, specificity, and NPV with lower PPV and agreement in comparison to our results [41].

In nine patients of our study, TCCS detected severe stenosis which was consistent with the patients' symptoms while DSA did not confirm any pathology. This discrepancy could be explained by the hypothesis that with the increasing the interval of time between the onset of stroke and angiographic examination vessel recanalization rapidly occurs [42]. In the current study, a fair agreement between these two methods was observed for diagnosis of mild to severe stenosis while for occlusion detection almost perfect agreement was found.

The present study has both strengths and limitations. Despite most previous studies, all cerebral arteries of the anterior and posterior cerebral circulation were examined with a more detailed classification of stenosis into mild (< 50%), moderate (50–69%), severe (70–99%) as well as occlusion. In this study, we combined TCCS with color-coded Doppler sonography of the extracranial carotid artery to provide additional information. Digital subtraction angiography has been used as a gold standard method. On the other hand, we did not use an ultrasound contrast agent, and DSA was performed at least 24 h after TCCS.

TCCS is a noninvasive, safe, and inexpensive method which can be performed at the bedside, and provides a more precise measurement of cerebral blood flow velocities than transcranial Doppler through color imaging of course of the intracranial vessels. Blood flow velocities of extracranial vessels in the neck help interpretation of cerebral blood flow velocities [17]. Furthermore, TCCS could be used to follow up of patients who require further monitoring of the disease progression. However, it has some limitations. Proper interpretation requires an experienced sonographer as well as adequate temporal bone window [41]. An Ultrasound contrast agent helps to overcome this limitation.

Conclusion

In conclusion, our study indicated high sensitivity, specificity and accuracy of TCCS for the detection of vascular abnormalities in patients presenting with ischemic symptoms.

Abbreviations

ACA: anterior cerebral artery

BA: basilar artery

CCA: common carotid artery

DSA: digital subtraction angiography

ICA: internal carotid artery

MCA: middle cerebral artery

PCA: posterior cerebral artery

TCCS: transcranial color-coded duplex sonography

VA: vertebral artery

Declarations

Ethics approval and consent to participate: This single-center, prospective study was consistent with the principles of the Declaration of Helsinki [25] and approved by local Ethics Committee of Shahid Beheshti medical University. Written informed consent was obtained from each patient

Consent for publication: Not applicable

Availability of data and materials: The data of the present study are available from corresponding author for reasonable request.

Competing interests: The authors declare that they have no competing interests

Funding: The present study was not funded.

Authors' contributions: F.A designed, supervised and performed TCCS. F.M, collected and analyzed the data. B.S.L designed and collected the data. B.M performed DSA. S.H.A collected the data. N.S.V analyzed the data and wrote the manuscript. All authors have read and approved the paper, and contributed to this work.

Acknowledgements: We thank all patients participating in the current study.

References

1. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: A systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012;380:2095–128.
2. Krishnamurthi R V., Feigin VL, Forouzanfar MH, Mensah GA, Connor M, Bennett DA, et al. Global and regional burden of first-ever ischaemic and haemorrhagic stroke during 1990-2010: Findings from the Global Burden of Disease Study 2010. Lancet Glob Heal. 2013;1:e259–81.
3. Gorelick PB. The global burden of stroke: persistent and disabling. Lancet Neurol. 2019;18:417–8.
4. Hosseini AA, Sobhani-Rad D, Ghandehari K, Benamer HTS. Frequency and clinical patterns of stroke in Iran - Systematic and critical review. BMC Neurol. 2010;10:1–10.
5. Bar M, Školoudík D, Roubec M, Hradílek P, Chmelová J, Czerný D, et al. Transcranial duplex sonography and CT angiography in acute stroke patients. J Neuroimaging. 2010;20:240–5.
6. Roger VL, Go AS, Lloyd-Jones DM, Adams RJ, Berry JD, Brown TM, et al. Heart disease and stroke statistics-2011 update: A report from the American Heart Association. Circulation. 2011;123:e18–209.
7. Sacco RL. Extracranial carotid stenosis. N Engl J Med. 2001;345:1113–8.
8. Kernan WN, Ovbiagele B, Black HR, Bravata DM, Chimowitz MI, Ezekowitz MD, et al. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2014;45:2160–236.
9. Kargiotis O, Safouris A, Magoufis G, Georgala M, Roussopoulou A, Stamboulis E, et al. The Role of Neurosonology in the Diagnosis and Management of Patients with Carotid Artery Disease: A Review. J Neuroimaging. 2018;28:239–51.

10. Craig DR, Meguro K, Watridge C, Robertson JT, Barnett HJ, Fox AJ. Intracranial internal carotid artery stenosis. Stroke. 1982;13:825–8.
11. Members WG, Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, et al. Executive Summary: Heart Disease and Stroke Statistics–2016 Update: A Report From the American Heart Association. Circulation. 2016;133:447–54.
12. Flaherty ML, Kissela B, Khoury JC, Alwell K, Moomaw CJ, Woo D, et al. Carotid artery stenosis as a cause of stroke. Neuroepidemiology. 2013;40:36–41.
13. Flaherty ML, Flemming KD, McClelland R, Jorgensen NW, Brown RD. Population-based study of symptomatic internal carotid artery occlusion: incidence and long-term follow-up. Stroke. 2004;35:e349–52.
14. Fieschi C, Argentino C, Lenzi GL, Sacchetti ML, Toni D, Bozzao L. Clinical and instrumental evaluation of patients with ischemic stroke within the first six hours. J Neurol Sci. 1989;91:311–21.
15. Valaikiene J, Schuierer G, Ziemus B, Dietrich J, Bogdahn U, Schlachetzki F. Transcranial color-coded duplex sonography for detection of distal internal carotid artery stenosis. Am J Neuroradiol. 2008;29:347–53.
16. Vosko MR, Newell DW, Alexandrov A V. Transcranial and Cervical Ultrasound in Stroke. In: Primer on Cerebrovascular Diseases. Elsevier; 2017. p. 702–7.
17. Nasr N, Ssi-Yan-Kai G, Guidolin B, Bonneville F, Larrue V. Transcranial color-coded sonography to predict recurrent transient ischaemic attack/stroke. Eur J Neurol. 2013;20:1212–7.
18. Simon B, Mani SE, Keshava SN, Alexander M, Aaron S. Role of noninvasive imaging of cerebral arterial system in ischemic stroke: Comparison of transcranial color-coded doppler sonography with magnetic resonance angiography. J Clin Imaging Sci. 2018;8.
19. Aaslid R, Markwalder TM, Nornes H. Noninvasive transcranial Doppler ultrasound recording of flow velocity in basal cerebral arteries. J Neurosurg. 1982;57:769–74.
20. Olatunji RB, Ogbole GI, Atalabi OM, Adeyinka AO, Lagunju I, Oyinlade A, et al. Role of transcranial colour-coded duplex sonography in stroke management-Review article. West African J ultrasound. 2015;16:33.
21. Blanco P, Abdo-Cuza A. Transcranial Doppler ultrasound in neurocritical care. J Ultrasound. 2018;21:1–16.
22. Schulte-Altedorneburg G, Droste DW, Popa V, Wohlgemuth WA, Kellermann M, Nabavi DG, et al. Visualization of the basilar artery by transcranial color-coded duplex sonography: Comparison with postmortem results. Stroke. 2000;31:1123–7.
23. Wang Y, Chen JM, Liu X, Wang J, Li LH, Deng JP, et al. Evaluation of the combined application of ultrasound imaging techniques for middle cerebral artery stent surveillance and follow-up study. PLoS One. 2013;8:e79410.
24. Baracchini C, Viaro F, Favaretto S, Palmieri A, Kulyk C, Causin F, et al. Safety and Tolerability of SonoVue® in Patients with Large Artery Anterior Circulation Acute Stroke. J Neuroimaging. 2017;27:409–13.

25. PP R. Human experimentation. Code of ethics of the world medical association. Declaration of Helsinki. Br Med J. 1964;2:177.
26. Grant EG, Benson CB, Moneta GL, Alexandrov A V, Baker JD, Bluth EI, et al. Carotid artery stenosis: gray-scale and Doppler US diagnosis—Society of Radiologists in Ultrasound Consensus Conference. Radiology. 2003;229:340–6.
27. Committee NASCETS. North America Symptomatic Carotid Endarterectomy Trial: methods, patient characteristics and progress. Stroke. 1991;22:711–20.
28. Rogge A, Doepp F, Schreiber S, Valdueza JM. Transcranial Color-Coded Duplex Sonography of the Middle Cerebral Artery: More Than Just the M1 Segment. J Ultrasound Med. 2015;34:267–73.
29. Baumgartner RW, Baumgartner I, Mattle HP, Schroth G. Transcranial color-coded duplex sonography in unilateral flow-restrictive extracranial carotid artery disease. Am J Neuroradiol. 1996;17:777–83.
30. Danyel LA, Hadzibegovic S, Valdueza JM, Tietze A, Fuchs S, Schreiber SJ, et al. Classification of Intracranial Stenoses: Discrepancies between Transcranial Duplex Sonography and Computed Tomography Angiography. Ultrasound Med Biol. 2020;46:1889–95.
31. Viera AJ, Garrett JM. Understanding interobserver agreement: The kappa statistic. Fam Med. 2005;37:360–3.
32. Tsivgoulis G, Alexandrov A V., Sloan MA. Advances in transcranial Doppler ultrasonography. Curr Neurol Neurosci Rep. 2009;9:46–54.
33. Baumgartner RW, Mattle HP, Schroth G. Assessment of≥ 50% and< 50% intracranial stenoses by transcranial color-coded duplex sonography. Stroke. 1999;30:87–92.
34. Navarro JC, Mikulik R, Garami Z, Alexandrov A V. The accuracy of transcranial Doppler in the diagnosis of stenosis or occlusion of the terminal internal carotid artery. J Neuroimaging. 2004;14:314–8.
35. Chen Y-C, Chen S-T, Chen C-J, Lee T-H. Absent middle cerebral artery signal in transcranial color-coded sonography: a reliable indicator of occlusion? Cerebrovasc Dis. 2005;20:251–7.
36. Hou WH, Liu X, Duan YY, Wang J, Sun SG, Deng JP, et al. Evaluation of transcranial color-coded duplex sonography for cerebral artery stenosis or occlusion. Cerebrovasc Dis. 2009;27:479–84.
37. Gerriets T, Goertler M, Stolz E, Postert T, Sliwka U, Schlachetzki F, et al. Feasibility and validity of transcranial duplex sonography in patients with acute stroke. J Neurol Neurosurg Psychiatry. 2002;73:17–20.
38. Goertler M, Kross R, Baeumer M, Jost S, Grote R, Weber S, et al. Diagnostic impact and prognostic relevance of early contrast-enhanced transcranial color-coded duplex sonography in acute stroke. Stroke. 1998;29:955–62.
39. Postert T, Braun B, Meves S, Koster O, Przuntek H, Weber S, et al. Contrast-enhanced transcranial color-coded sonography in acute hemispheric brain infarction. Stroke. 1999;30:1819–26.
40. Sauerbruch S, Schlachetzki F, Bogdahn U, Valaikiene J, Holscher T, Harrer J. Application of transcranial color-coded duplex sonography in stroke diagnosis. Curr Med Imaging. 2009;5:39–54.

41. Roubec M, Kuliha M, Jonszta T, Procházka V, Fadrná T, Filip M, et al. Detection of intracranial arterial stenosis using transcranial color-coded duplex sonography, computed tomographic angiography, and digital subtraction angiography. J Ultrasound Med. 2011;30:1069–75.
42. Allendoerfer J, Goertler M, von Reutern G-M. Prognostic relevance of ultra-early doppler sonography in acute ischaemic stroke: a prospective multicentre study. Lancet Neurol. 2006;5:835–40.