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RESEARCH ARTICLE

Role of Transcranial Doppler Ultrasonography in Detecting and Excluding Ischemic Stroke in the Emergency Department: A Prospective Observational Study

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ABSTRACT

Introduction: To determine whether color doppler ultrasonography (CDUS) and transcranial Doppler ultrasonography (TCD) can be used as an alternative test to cranial computed tomography angiography (CTA) by detecting vascular occlusions at the bedside in the emergency department (ED).

Methods: This is a prospective, observational, and single-center study. It was performed on patients aged 18 years and older who were examined with a preliminary diagnosis of ischemic stroke and presented to an ED within the first 48 hours after the onset of symptoms. TCD, CDUS and vertebral artery doppler ultrasound were performed on one hundred and three patients. Computed tomography angiography was conducted as well and TCD and CDUS findings were compared.

Results: Over one month, thirty-three patients were included in the study. The median age of the patients was 67 (52.5–78), and 57.6% (n=19) were male. When the TCD findings were compared with the gold standard (CTA), the negative predictive value of TCD for middle cerebral artery (MCA) was 96.5%. Both right and left carotids could be visualized optimally in all patients with CDUS. In the vertebral artery ultrasound examination, the right and left vertebral arteries were optimally visualized in all patients. Left vertebral artery ultrasound and CTA findings were completely compatible.

Conclusion: Transcranial Doppler ultrasonography, a fast, inexpensive, non-invasive, and reproducible method, may have a role in the early detection or exclusion of ischemic strokes where time is critical. This suggests that TCD may be a helpful method in the ED for the early exclusion of acute MCA occlusions.

Keywords: Cranial CT angiography, color Doppler, emergency department, transcranial Doppler

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INTRODUCTION

Ischemic stroke is a clinical manifestation that results in loss of neurologic function and cell death in the affected area due to sudden interruption in cerebral blood flow. Stroke is a leading cause of adult death and disability and burdens healthcare costs yearly (1). The primary objective in treating an ischemic stroke is to promptly restore blood flow following the onset of symptoms (2). Large vessel occlusion is the occlusion of major, proximal cerebral arteries, comprising 24–46% of acute ischemic strokes (AIS) when involving both A2 and P2 segments of the anterior and posterior cerebral arteries (3). Due to involvement of the proximal vascular system, critical brain regions are often affected, leading to significant neurological deficits (4). Large vessel occlusion constitutes 29.3% of AIS cases and has an incidence rate of 24 per 100,000 people per year, with the majority occurring in the anterior circulation (5,6).

Highlights

- **TCD could be an alternative to CT angiography in ischemic stroke.**
- **TCD can be used in the early period when CTA imaging cannot be performed.**
- **Ultrasound can be used in the ER to determine etiology in stroke patients.**

Cranial computed tomography (CT) and diffusion-weighted magnetic resonance imaging (DWI MRI) are the basic radiological methods used in the emergency department (ED) to diagnose ischemic stroke. Computed tomography is a valuable imaging modality for easy access and rapid evaluation and is successful in excluding hemorrhagic stroke (7,8). Contrast-enhanced CT angiography (CTA) provides visualization of the great vessels and ring of Willis; It helps to see stenosis and occlusions

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quite reliably (9). Diffusion-weighted magnetic resonance imaging is superior to CT for diagnosing acute ischemic stroke in patients presenting within 12 hours of symptoms (10). For this reason, DWI is frequently preferred in the ED (11).

Color Doppler ultrasonography (CDUS) and Transcranial Doppler ultrasonography (TCD) of the carotid and vertebral arteries are non-invasive methods for neurovascular evaluation of extracranial and intracranial great vessels. Color Doppler ultrasonography is 81-98% sensitive and 82–89% specific for detecting the internal carotid artery's significant stenosis (>50%) (12). The use of TCD has been increasing recently to detect occlusion in intracranial vessels (13,14). On the other hand, factors such as device quality, technician's experience, and patient's vascular anatomy are among the factors affecting the success of TCD (15).

With TCD, large vessel occlusion can be detected early and if thrombolytic therapy is given, its effectiveness can be monitored (16,17). This study aims to determine whether CDUS and TCD can be used as an alternative test to CTA by detecting vascular occlusions at the bedside in the ED.

METHODS

Study Setting and Study Design

This research was planned as prospective, observational, and single-center. Hacettepe University Ethical Committee approval was obtained (Date: January 2, 2018, Decision no: GO 18/18). The study was performed between July 1, 2018, and August 1, 2018, at Hacettepe University Adult ED in Türkiye. It is a tertiary academic emergency service in the city center and is easily accessible. There are 35,000 patient visits annually.

Participant Selection and Measurements

The number of patients with a preliminary diagnosis of ischemic stroke who admitted to the ED was 103. The inclusion criteria were as follows: to admit on the study date, to be 18 years of age or older, to agree to participate in the study (with the consent of the patient or their relatives), to have been examined with a preliminary diagnosis of ischemic stroke, to present in the first 48 hours from the onset of symptoms. We could not perform TCD imaging on some patients because they were not cooperative, and we could not perform CTA imaging on some patients because they were unstable. In this case, these patients were excluded from the study because the presence of occlusion could not be evaluated. The flow chart of the study is shown in Figure 1.

Gender, age, history, medications, time from the onset of the complaint to the ED admission, and preliminary diagnosis were recorded in the patient study form. All patients underwent non-contrast cranial CT to exclude hemorrhagic stroke and preliminary diagnoses were confirmed by DWI MRI.

Transcranial Doppler ultrasonography, CDUS and Vertebral artery Doppler ultrasound were performed in all patients. Emergency physician who perform vertebral artery Doppler ultrasound, TCD, and CDUS have previously received advanced ultrasound training (4 hours theory and 20 hours practical course at Hacettepe University Neurology Department). Ultrasound was applied at the bedside; measurements were made with Philips EPIQ 5G ultrasound device using linear and sector probes. The physician, who completed the imaging with ultrasound, performed the procedure without knowing the other imaging results of the patients. This procedure was performed by a single emergency physician. It was decided that the emergency physician would be observed by a neurologist with more than ten years of experience in TCD before starting to perform the procedure in the study. This procedure was performed on patients before performing CT and MRI imaging, avoiding loss of time in imaging.

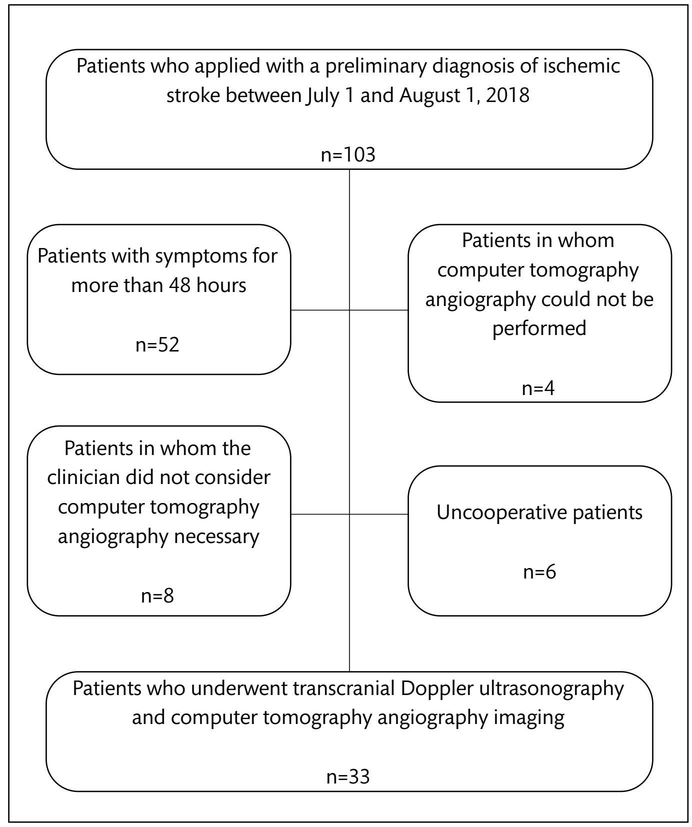

Figure 1. A flowcharts illustrating of the study.

Cases with >70% stenosis and complete occlusion in vertebral artery Doppler ultrasound and CDUS evaluations were considered pathological (12). Common carotid artery and internal carotid artery were examined in CDUS, but only stenosis in the internal carotid artery was considered pathological. Flow in MCAs in TCD was performed according to thrombolysis in brain ischemia (TIBI) flow grading classification. Those with TIBI 0 were deemed pathological (18).

Computed tomography angiography was performed on the patients, and TCD and CDUS findings were compared. Computed tomography angiography included imaging of the head and neck arteries and cases with >70% stenosis and complete occlusion in internal carotid artery, MCA and vertebral artery were considered pathological. CTAs were evaluated by a radiologist with 18 years of experience and a neurologist with 29 years of experience; these evaluations were considered the gold standard. There was no disagreement between the neurologists and radiologists.

Statistical Analysis

IBM Statistical Package for Social Sciences (SPSS) program version 23 (IBM Corp, Armonk, NY) program was used to analyze the data. For the descriptive statistics of numerical data, mean and standard deviation values were used for normally distributed data, and numbers and percentages were used for qualitative data. Median (Interquartile range, Q1-Q3) was used for data that did not show normal distribution. The McNemar test was used in the dependent groups to compare the mean of the two groups. For statistical significance, $p<0.05$ was considered significant.

RESULTS

A total of thirty-three eligible patients were included in the study and all of them were diagnosed with stroke. The median age of the patients was 67 (52.5–78), and 57.6% (n=19) were male. The patients' two most common comorbid diseases were hypertension 45.5% (n=15) and coronary artery disease 27.3% (n=9). 36.4% (n=12) of the patients were using antihypertensive drugs. The median time from the onset of symptoms to admission to the ED was 3 (2–7.5) hours. Cardiac thrombus was detected on echocardiography in only one (3.0%) patient. Symptoms were observed on the left side in 60.6% (n=20) of the patients. Descriptive data of the patients are shown in Table 1.

In the ultrasonographic examination of the right MCA with TCD, an optimal image could not be obtained in 3 (9.1%) patients due to the anatomical structure of the temporal window. We have added the TCD image of a patient with MCA occlusion findings in our study as Figure 2. No pathology was observed in the right MCA in 2 (6.1%) patients in the CTA. When the TCD findings were compared with the gold standard (CTA), the sensitivity for the right MCA was 100%, and the specificity was 92.8%; the positive predictive value was 50%, and the negative predictive value could not be calculated. In the ultrasonographic examination of the left MCA, an optimal image could not be obtained in 3 (9.1%) patients due to the anatomical structure of the temporal window. Pathology was observed in the left MCA in 4 (12.1%) patients in the CTA. When the TCD findings were compared with the gold standard (CTA), the sensitivity was 0%, and the specificity was 100% for the left MCA; while the positive predictive value could not be calculated, the negative predictive value was 93.3%. When both MCAs are evaluated together with TCD, their sensitivity is 50%, specificity is 96.50%. The positive predictive value is 50%, and the negative predictive value is 96.50% (Table 2).

Table 1. Descriptive data of the patients

Features (n=33 patients)	Values
Age, year, median (IQR)	67 (52.5–78)
Gender (n, %)	
Male	19 (57.6%)
Female	14 (42.6%)
Comorbidity (n, %)*	
Diabetes	8 (24.2%)
Hypertension	15 (45.5)
Stroke	6 (18.2%)
Coronary Artery Disease	9 (27.3%)
Malignancy	3 (9.1%)
Other	12 (36.4%)
Medications (n, %)*	
Antihypertensive	12 (36.4%)
Antiplatelet	5 (15.2%)
Anticoagulant	6 (18.2%)
Other	13 (39.4%)
Symptom duration, hours [median (IQR)]	3(2–7.5)
Thrombus in echocardiography	
Yes	1 (3.0%)
No	32 (97.0%)
Symptom side	
Right	13 (39.4%)
Left	20 (60.6%)

*There were patients with multiple comorbidities and multiple medicine use.

Both right and left carotids could be visualized optimally in all patients with CDUS. On CTA, pathology was observed in the right carotid in 1 (3.0%) patient. When CDUS findings of the right carotid were compared with CTA, the sensitivity was calculated as 100%, and the specificity as 100.0%; the positive predictive value was 100%, and the negative predictive value could not be calculated. In CTA, pathology was observed in the left carotid in 3 (9.1%) patients. When CDUS findings of the left carotid were compared with CTA, the sensitivity was 66.67%, and the specificity was 100%; the positive predictive value was 100.0%, and the negative predictive value was 96.77% (Table 3).

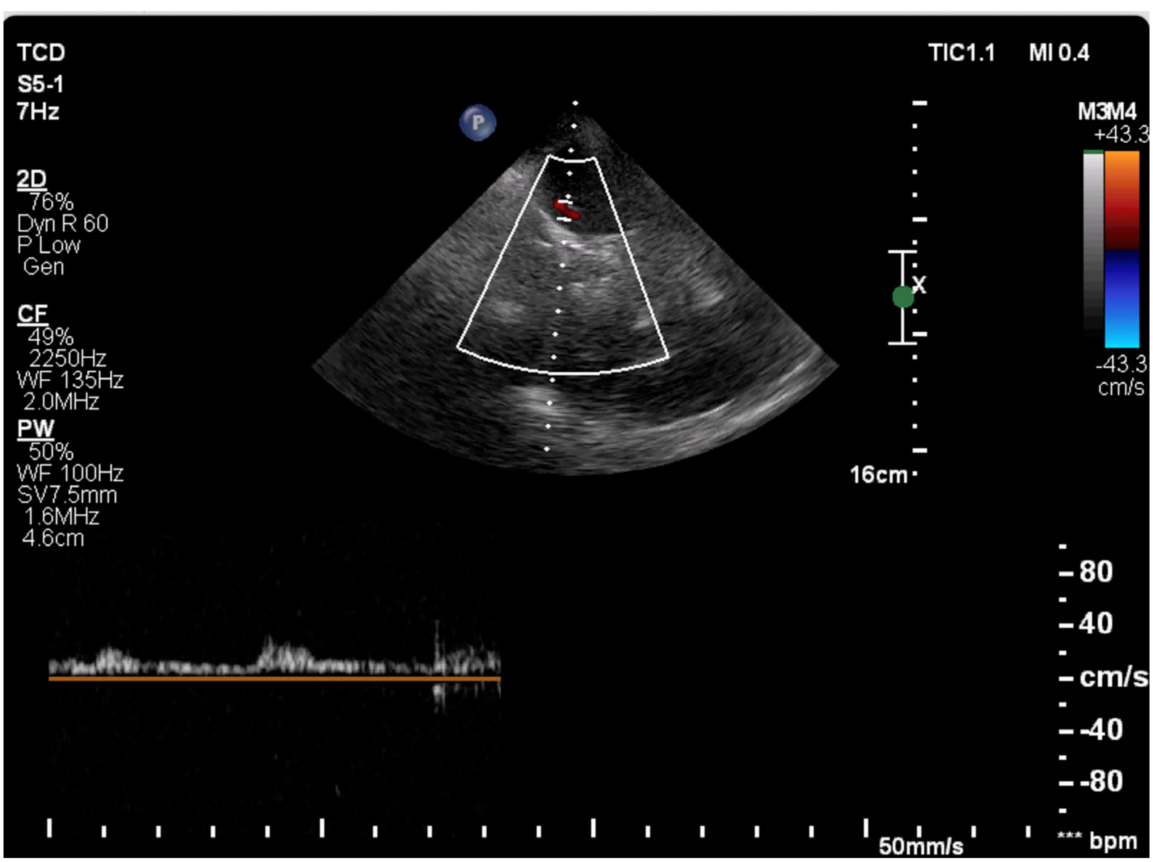

Figure 2. Middle cerebral artery stenosis transcranial Doppler ultrasonography imaging.

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Table 2. Comparison of transcranial doppler ultrasonography findings with cranial CT angiography

		CTA		
		Pathology (+)	Pathology (-)	Total
TCD Right MCA	Pathology (+)	2 (6.1%)	2(6.1%)	4 (12.1%)
	Pathology (-)	0 (0.0%)	26 (78.8%)	26 (78.8%)
	Could not image	0 (0.0%)	3 (9.1%)	3 (9.1%)
Total		2 (6.1%)	31 (93.9%)	33 (100.0%) (p>0.05)
TCD Left MCA	Pathology (+)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Pathology (-)	2 (6.1%)	28 (84.8%)	30 (90.9%)
	Could not image	2 (6.1%)	1 (3.0%)	3 (9.1%)
Total		4 (12.1%)	29 (87.9%)	33 (100.0%) (p>0.05)

CTA: cranial computer tomography angiography; MCA: middle cerebral artery; p value was obtained by McNemar test; TCD: transcranial Doppler ultrasound.

Table 3. Comparison of color Doppler ultrasonography findings with cranial CT angiography

		CTA		
		Pathology (+)	Pathology (-)	Total
CDUS Right Carotid	Pathology (+)	1 (3.0%)	0 (0.0%)	1 (3.0%)
	Pathology (-)	0 (0.0%)	32 (97.0%)	32 (97.0%)
Total		1 (3.0%)	32 (97.0%)	33 (100.0%) (p>0.05)
CDUS Left Carotid	Pathology (+)	2 (6.1%)	0 (0.0%)	2 (6.1%)
	Pathology (-)	1 (3.0%)	30 (90.9%)	31 (93.9%)
Total		3 (9.1%)	30 (90.9%)	33 (100.0%) (p>0.05)

CDUS: carotid color Doppler ultrasonography, CTA: cranial computer tomography angiography; p value was obtained by McNemar test.

Table 4. Comparison of vertebral artery ultrasound findings with cranial CT angiography

		CTA		
		Pathology (+)	Pathology (-)	Total
Right vertebral artery	Pathology (+)	4 (12.1%)	2 (6.1%)	6 (18.2%)
	Pathology (-)	2 (6.1%)	25 (75.7%)	27 (81.8%)
Total		6 (18.2%)	27 (81.8%)	33 (100.0%) (p>0.05)
Left vertebral artery	Pathology (+)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Pathology (-)	0 (0.0%)	33 (100.0%)	33 (100.0%)
Total		0 (0.0%)	33 (100.0%)	33 (100.0%) (p>0.05)

CTA: cranial computer tomography angiography; p value was obtained by McNemar test.

In the vertebral artery ultrasound examination, the right and left vertebral arteries were optimally visualized in all patients. In the CTA, pathology was observed in the right vertebral artery in 6 (18.2%) patients. When the right vertebral artery ultrasound findings were compared with CTA, the sensitivity was 66.6%; specificity was calculated as 92.6%; positive predictive value was 66.6%; negative predictive was calculated as 92.6%. No pathology was observed in the left vertebral artery in any patient in CTA. Left Vertebral artery ultrasound and CTA findings were completely compatible (Table 4).

DISCUSSION

This study aimed to compare ultrasonography, an inexpensive and easily accessible method, with CTA for the early diagnosis of ischemic stroke in the ED and to demonstrate whether it can be an alternative diagnostic test.

Middle cerebral artery is the most affected cerebral vessel in acute ischemic stroke (13,14). Acute occlusion of large vessel can cause severe functional morbidity and even mortality (19). Toni et al. stated the sensitivity of TCD to be 40% and its negative predictive value to be 96.5% (14). Alexandrov et al. found a negative predictive value of 89% in their study (13). The main reasons that complicate the detection of MCA with TCD are patient incompatibility and closed sonic temporal window (20–22). Our study revealed the sensitivity of TCD to be 50% and the specificity to be 96.5%. In 9.1% (n=3) of the patients, imaging could not be achieved because the trans-temporal acoustic window was closed. It explains the low sensitivity.

Ischemic stroke is associated with many comorbid diseases. In our study, hypertension was found the most in patients. Grau et al. found that 66.6% of acute stroke patients included in their study had hypertension, 44% had diabetes, and 24% had coronary artery disease (23). In the study of Ingal et al., 44% of the patients had hypertension (24). Our study detected coronary artery disease and diabetes following hypertension in patients. Data support that these diseases are the leading risk factors for acute ischemic stroke.

In ischemic stroke, cell damage begins from the first minutes of occlusion, when symptoms begin, and the extent of the damage increases as time passes (25). Therefore, the time from the onset of symptoms to admission to the ED affects the diagnosis and treatment process. It has been shown in many studies that only up to half of the patients (21–51%) can present to the ED in the first 4 hours (26–29). Our study's median admission time was 3 (2–7.5) hours, and 63.6% (n=21) of the cases presented to the ED within the first 4 hours. This situation can be explained by the fact that our hospital is in the city center and the ease of access to health in our country.

Cardioembolism is one of the most common causes of ischemic stroke. The findings we can detect in echocardiography in cardioembolic strokes are low ejection fraction, intracardiac thrombus, heart valve pathologies and aneurysms, dilatation, and wall motion disorders (23,30,31). In their study, Nakibuuka et al. found intracardiac thrombus on echocardiography in 2.3% of acute stroke cases (30). Wrigley et al. detected intracardiac thrombus in 0.9% of the cases (32). Our study caught intracardiac thrombus in 3% of the cases. Despite the definition of intracardiac thrombus as an etiological cause, its low frequency may be related to the low prevalence of detection methods.

The presence of steno-occlusive lesions in the carotid arteries is another crucial risk factor for stroke (33). Color Doppler ultrasonography is one of the most commonly used methods to demonstrate stenosis in the carotid artery and is considered an alternative to CTA (34). In the review of Nederkoorn et al., the sensitivity of stenosis detection with CDUS was reported as 96% and the specificity as 100% (35). Blakeley et al. found the sensitivity of stenosis detection with CDUS to be 86% and the specificity to be 98% (36). We found the sensitivity of CDUS to indicate critical stenosis or occlusion as 66.7% and 100% for the right and left carotid, respectively, and the specificity as 100%. Lower sensitivity was detected in the right carotid due to the low number of cases and anatomical defects that cause difficulties in providing optimal imaging.

Sonographic diagnosis of vertebral arteries flow pathologies is more difficult due to anatomical variability and orientation problems. Khan et al. compared the vertebral artery color Doppler ultrasound with CTA and found the sensitivity of ultrasound to be 70.2% and the specificity to be 97.7% (37). While our study found the left vertebral artery Doppler ultrasound results to be entirely similar for CTA, it revealed a sensitivity of 66.6% and a specificity of 92.6% in right vertebral artery imaging.

Limitations

Our primary limitation is that our study was conducted in a single center, by a single user, and that it was not applied to a wider population. Although all patients who consented to the study were included in the specified study period, the small sample size should not be ignored when interpreting the results. Its accuracy can be increased with multicenter and international studies.

The use of ultrasound is becoming increasingly common in EDs. Our data indicate that TCD, a fast, inexpensive, non-invasive, and reproducible method, may have a role in the early detection or exclusion of ischemic strokes where time is critical. The negative predictive value of TCD for both MCA was 96.50%. This suggests that TCD may be a helpful method in the ED for the early exclusion of acute MCA occlusions. However, the necessity of observation and research in groups with more patients should be addressed.

Ethics Committee Approval: Hacettepe University Ethical Committee approval was obtained (Date: January 2, 2018, Decision no: GO 18/18).

Informed Consent: Informed consent was obtained from all subjects.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept- İA, EMA, BE, MAT; Design- İA, BE; Supervision- MAT, BE, İA; Resource- İA, BE; Materials- İA, BE; Data Collection and/or Processing- İA, EA, MAK; Analysis and/or Interpretation- İA, MCD; Literature Search- İA, YÖ; Writing- İA, MA, MCD, BE; Critical Reviews- BE, MCD, MAT.

Conflict of Interest: The authors declared that there is no conflict of interest.

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