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Original article

# Transcranial Duplex in Prediction of Cerebrovascular Events after Transient Ischemic Attacks

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**Abstract:**

**Background:** Transient ischemic attack (TIA) is an independent risk factor of recurrent stroke. TIA Patients with intracranial or extracranial arterial stenosis are at high risk of recurrent stroke**.** Early assessment of intracranial and extracranial vessels is important to assess risk. **Aim of the work:** This study was conducted to assess the value of transcranial Doppler (TCD) ultrasonography to predict the occurrence of cerebrovascular events after TIA**. Patient and Methods:** This study was carried out in neuropsychiatry department in Benha University Hospital , it was conducted on 75 patients presented with TIA, transcranial and extracranial Doppler were done for each patient **.Results :** During follow up of the patients, 17(22%) out of studied sample experienced an ischemic stroke or TIA, TCD showed intracranial stenosis in 15(20%) patients, ECD (Extracranial Doppler )showed plaques of extracranial arteries in 18(24%) patients and stenosis of theses arteries in 9(12%) patients. Multivariate logistic regression analysis revealed stenosis detected by TCD and ECD was a predictor for cerebrovascular event (TCD: Odds ratio= 8.977 & 95% Confidence interval ranged from 1.889 – 42.652, P value was 0.006; ECD: Odds ratio = 26.169 & 95% Confidence interval ranged from 3.875 – 176.722, P value was 0.001).

**Conclusion:** TIA patients with abnormal TCD finding are high risk to develop further cerebral ischemic events. In addition, TCD is important diagnostic and prognostic procedure in patients with TIA.

**Key Words**: Transient Ischemic Attack; Ultrasonographic and Cerebrovascular Events.

**Abbreviation: BA** (basilar artery), **ACA** (anterior cerebral artery), **PCA**(posterior cerebral artery), **IMT**(intima media thickness)

## Introduction

TIA is a major risk factor for future ischemic stroke, with the greatest risk occurring in the period immediately after TIA. The odds ratio for ischemic stroke following TIA is 30.4 during the first 30 days, 18.9 at one to three months, 3.16 at four to six months, and 1.87 after five years ***(1).***

A high proportion of strokes are due to embolic (arteroembolic or cardioembolic) occlusion of intracranial arteries. Early assessment of intracranial and extracranial vessels is critical in assessing risk. Patients with persistent intracranial occlusions have a four-fold increase in risk of developing recurrent stroke ***(2).*** So, early identification and definitive management has been shown to improve outcomes and reduce the proportion of patients experiencing a disabling stroke after TIA ***(3).***

Assessment of the cerebral vasculature can be performed by employing transcranial Doppler (TCD) ultrasound, the only non-invasive examination that provides a reliable evaluation of intracranial blood flow patterns in real-time, adding physiological information to the anatomical information obtained from other neuroimaging modalities. TCD is relatively cheap, can be performed bedside, and allows monitoring both in acute emergency settings as well as for prolonged periods with a high temporal resolution making it ideal for studying dynamic cerebrovascular responses ***(4)***.

Transcranial Doppler ultrasonography is also a useful adjunct to traditional imaging techniques in the diagnosis and management of acute intracranial large vessel occlusion. This imaging technique correctly identified middle cerebral arteryocclusions with a sensitivity and specificity ≥ 90% ***(5).***

The current data suggests that the prognosis becomes worse with increasing degree of stenosis and with increasing number of affected vessels. It has been claimed by some to be the most common cause of stroke world-wide (***6).***

The presence of intracranial atherosclerosis is associated with an increased risk of recurrent stroke ranging from 10 to 50% per year ***(7)***. Vulnerable plaques that are prone to rupture and cause

distal embolism can be detected with ultrasonography ***(8).***

Evaluation of TIA should be done urgently with imaging and laboratory studies to decrease the burden of future strokes. Modifiable risk factors should be identified and treated. Immediate therapeutic interventions should be initiated. This may substantially reduce the risk of recurrent strokes or future TIA ***(9).***

## Patients and Methods

This is a prospective study which was carried out in neuropsychiatry department of Benha University Hospital, between Decembers 2018 to June 2019. It included 75 patients of TIA fulfilling its criteria.

**Inclusion criteria:** All patients of TIA fulfilling criteria of it.

**Exclusion criteria:**

- Patients with amaurosis fugax were not included in the study, as data suggest pathogenic and prognostic differences between transient eye and brain ischemic syndromes.
- Patients were excluded for the following reasons: competing differential diagnosis as assessed by the attending neurologist:
    - Migraine.
    - Epilepsy.
    - Functional disorder.
    - Peripheral dizziness.
    - Syncope.
    - Hypertensive crisis.

Approval of ethical committee was done and all of patients were subjected to the following procedures after taking their verbal consent:

 Medical history.

 Physical and neurological examinations .

 Electrocardiogram .

 Laboratory: Routine investigation to exclude metabolic disorders

- Liver function test.
- Kidney function test.
- Lipid profile.
- Complete blood count.

Radiological:

- CT brain to exclude acute infarction or any structural brain lesions.
- MRI brain with diffusion weighted imaging to exclude to exclude acute infarction.
- Transthoracic ECHO to detect possible cardiac causes of embolism.
- Extracranial carotid artery duplex and transcranial color duplex sonography.

**Extracranial carotid artery duplex and transcranial color duplex sonography:**

They were performed at Benha Neurology department, at neurovascular ultrasonographic laboratories, by Phillips clear vue 650 ultrasound.

**(a)Transcranial color duplex sonography**:

It was performed for each patient and findings were classified according to Badawy *et al.,**(10)*** classification.

1) MCA (middle cerebral artery) occlusion, when no flow signal was detected in the symptomatic MCA while it was present in the ipsilateral anterior cerebral artery and posterior cerebral artery.

2) *MCA asymmetry*, when the side-to-side flow velocity difference is more than 30%.

3) *Normal MCA*, when side-to-side flow velocity difference is less than 30%.

4) *No temporal bone window*, when normal extracranial internal carotid artery findings are associated with no flow signal in the symptomatic MCA, ipsilateral anterior cerebral artery and posterior cerebral artery (these cases were excluded).

**(b) Extracranial Carotid duplex:**

Carotid arteries were being considered normal if the intima- media thickness is < 1.0 mm, no plaque detected and peak systolic velocity (PSV) at the proximal internal carotid artery (PSVICA was less than 125 cm/s. Carotid atherosclerotic disease was considered present if the intima-media complex showed diffuse thickening (≤ 1.0 mm) or if carotid plaques were detected. Pulsed Doppler signals were routinely recorded from the CCA (common carotid artery) just proximal to the bifurcation, the origin of the external carotid artery, proximal, mid and if accessible distal ICA. They were recorded in the longitudinal view with less than 60° insonation angle. PSV and end diastolic velocities were being recorded at the proximal ICA, the distal CCA and the PSV ICA/CCA ratio were being calculated. In case of a stenosis on B-mode and color Doppler imaging, the Doppler signal was being recorded from the site of maximum stenosis i.e. from the area of maximum flow turbulence on color Doppler imaging.

**Statistical methods:**

Data management and statistical analysis were done using SPSS vs.25.

(IBM, Armonk, New York, United states ).

Numerical data was summarized as means and standard deviations. Categorical data

was summarized as numbers and percentages.

Comparisons between two groups were done using Mann Whitney U test for numerical data. Categorical data was compared using Chi-square test or Fisher's exact test if appropriate.

Logistic regression analysis was done for prediction of cerebrovascular events. Odds ratios with 95% confidence intervals were calculated for predictors.

All P values were two sided. P values less than 0.05 were considered significant.

## Results:

- The mean age of our patients was 61 years with standard deviation of 7 years. The majority were males (7.3%) while females represented (26.7%), 77.3% had hypertension, 66.7% had diabetes and 49.3% were smokers **(table 1).**
- Eighteen (24%) patients had plaques of extracranial arteries and 9 (12.0%) of them showed stenosis **(table 2).**
- Twenty percent of patients showed stenosis by trans-cranial Doppler and Rt MCA (33.3%) was the most affected (**table 3).**
- Ischemic heart disease was significantly higher in those with cerebrovascular events (47.1%) compared to those without (15.5%). P value was 0.006. And, mean ejection fraction was lower in those with cerebrovascular events (49.47%) compared to those without (56.8%). P value was 0.03 **(table 4).**
- Transcranial Doppler stenosis was significantly higher in those with cerebrovascular events (58.8%) compared to those without (8.6%). P value was <0.001 and Rt MCA flow velocity was significantly higher in those with cerebrovascular event (101 cm/s) compared to those without cerebrovascular event (77 cm/s). P value was 0.009 **(table 5).**
- Extracranial Doppler plaques were significantly higher in those with cerebrovascular events (64.7%) compared to those without (12.1%). P value was <0.001 and stenosis was significantly higher in those with cerebrovascular events (41.2%) compared to those without (3.4%). P value was <0.001 **(table 6).**
- Multivariate logistic regression revealed that stenosis detected by trans-cranial Doppler was a predictor for cerebrovascular event (OR = 8.977 & 95% CI ranged from 1.889 – 42.652). P value was 0.006 **(table 7).**

- Multivariate logistic regression revealed that stenosis detected by extra cranial Doppler was a predictor for cerebrovascular event (OR = 26.169 & 95% CI ranged from 3.875 – 176.722). P value was 0.001 **(table 8).**

**Table (1):** General characteristics of the whole study sample:

| | **The studied group(75)** |
|---|---|
| **Age Mean± SD** | 61 ±7 |
| **Gender** | 55(73.3) |
| **Male** | 20(26.7) |
| **Female** | |

**Table (2):** Stenosis and site of affection according to extra-cranial Doppler:

| | | |
|---|---|---|
| **Plaques** | Present | 18 (24.0) |
| **Stenosis** | Yes | 9 (12.0) |
| **Affection** | Lt ICA | 4 (44.4) |
| | Rt ICA | 5 (55.6) |

**Table (3):** Stenosis and site of affection according to Trans-cranial Doppler:

| | | **n (%)** |
|---|---|---|
| **stenosis** | **Yes** | 15 (20.0) |
| **Affection** | **Rt BA** | 2 (13.3) |
| | **Lt ACA** | 1 (6.7) |
| | **Lt MCA** | 1 (6.7) |
| | **Lt MCA & ACA** | 1 (6.7) |
| | **Lt MCA & PCA** | 1 (6.7) |
| | **Rt ACA** | 1 (6.7) |
| | **Rt MCA** | 5 (33.3) |
| | **Rt MCA & ACA** | 2 (13.3) |
| | **Rt PCA** | 1 (6.7) |

**Table (4):** Cardiac risk factors in those with and without cerebrovascular events:

| | | **Cerebrovascular event** | | |
|---|---|---|---|---|
| | | **Yes (n = 17)** | **No (n = 57)** | **P value** |
| **IHD** | n (%) | 8 (47.1) | 9 (15.5) | 0.006 |
| **Atrial fibrilation** | n (%) | 4 (23.5) | 14 (24.1) | 0.959 |
| **Rheumatic heart disease** | n (%) | 0 (0.0) | 1 (1.7) | 1.0 |

| | | | | |
|---|---|---|---|---|
| **Prothetic valve** | n (%) | 2 (11.8) | 5 (8.6) | 0.695 |
| **Ejection fraction** | Mean ±SD | 49.47 ±12.99 | 56.8 ±10.9 | 0.03 |

**Table (5)**: Flow velocity and stenosis by trans-cranial Doppler in those with and without cerebrovascular events:

| | | Cerebrovascular event | | |
|---|---|---|---|---|
| | | **Yes (n = 17)** | **No (n = 57)** | **P value** |
| **Rt MCA (cm/s)** | Mean ±SD | 101 ±34 | 77 ±20 | 0.009 |
| **Rt PCA (cm/s)** | Mean ±SD | 51 ±10 | 50 ±14 | 0.558 |
| **Rt ACA (cm/s)** | Mean ±SD | 56 ±34 | 45 ±19 | 0.151 |
| **Rt ICA (cm/s)** | Mean ±SD | 45 ±5 | 42 ±6 | 0.089 |
| **Rt BA (cm/s)** | Mean ±SD | 34 ±20 | 36 ±14 | 0.03 |
| **Rt vertebral (cm/s)** | Mean ±SD | 45 ±12 | 41 ±12 | 0.244 |
| **Lt MCA (cm/s)** | Mean ±SD | 81 ±35 | 70 ±23 | 0.581 |
| **Lt PCA (cm/s)** | Mean ±SD | 48 ±19 | 47 ±10 | 0.401 |
| **Lt ACA (cm/s)** | Mean ±SD | 61 ±35 | 51 ±8 | 0.784 |
| **Lt ICA (cm/s)** | Mean ±SD | 40 ±10 | 50 ±9 | 0.002 |
| **Lt BA (cm/s)** | Mean ±SD | 31 ±5 | 33 ±6 | 0.37 |
| **Lt vertebral(cm/s)** | Mean ±SD | 46 ±14 | 43 ±13 | 0.365 |
| **Stenosis** | n (%) | 10 (58.8) | 5 (8.6) | <0.001 |

Mann Whiney U test was used. Chi-square test was used for stenosis

**Table (6):** Flow velocity and stenosis by extra-cranial Doppler in those with and without cerebrovascular events:

| | | Cerebrovascular event | | |
|---|---|---|---|---|
| | | **Yes (n = 17)** | **No (n = 57)** | **P value** |
| **Rt CCA (cm/s)** | Mean ±SD | 57 ±11 | 56 ±16 | 0.143 |
| **Rt ICA (cm/s)** | Mean ±SD | 77 ±31 | 60 ±18 | 0.063 |
| **Rt ECA (cm/s)** | Mean ±SD | 71 ±15 | 68 ±13 | 0.179 |
| **Rt Vert (cm/s)** | Mean ±SD | 34 ±7 | 38 ±13 | 0.761 |
| **Rt IMT (mm)** | Mean ±SD | 0.27 ±0.42 | 0.08 ±0.12 | 0.778 |
| **Lt CCA (cm/s)** | Mean ±SD | 66 ±19 | 64 ±18 | 0.79 |
| **Lt ICA (cm/s)** | Mean ±SD | 80 ±57 | 63 ±34 | 0.276 |
| **Rt ECA (cm/s)** | Mean ±SD | 67 ±18 | 66 ±12 | 0.746 |
| **Lt Vert (cm/s)** | Mean ±SD | 41 ±11 | 38 ±9 | 0.538 |

| | | | | |
|---|---|---|---|---|
| **Lt IMT (mm)** | Mean ±SD | 0.13 ±0.23 | 0.07 ±0.02 | 0.279 |
| **Plaques** | Yes n (%) | 11 (64.7) | 7 (12.1) | <0.001 |
| **Stenosis** | Yes n (%) | 7 (41.2) | 2 (3.4) | <0.001 |

Mann Whiney U test was used. Chi-square test was used for stenosis

**Table (7):** Logistic regression analysis for prediction of cerebrovascular event using trans-cranial Doppler:

| | B | Wald | OR | 95% C.I. for OR | P value |
|---|---|---|---|---|---|
| **Smoking** | 0.921 | 1.724 | 2.511 | 0.635 - 9.925 | 0.189 |
| **IHD** | 0.36 | 0.101 | 1.433 | 0.155 - 13.259 | 0.751 |
| **Ejection fraction** | -.011 | 0.064 | 0.989 | 0.909 - 1.077 | 0.8 |
| **Total Cholesterol ( mg/dl)** | 0.009 | 0.299 | 1.009 | 0.977 - 1.041 | 0.585 |
| **Stenosis by trans-cranial Doppler** | 2.195 | 7.618 | 8.977 | 1.889 - 42.652 | 0.006 |

B = regression coefficient OR = Odds ratio 95% CI = 95% Confidence interval

**Table (8):** Logistic regression analysis for prediction of cerebrovascular event using extra-cranial Doppler:

| | B | Wald | OR | 95% C.I. for OR | P value |
|---|---|---|---|---|---|
| **Smoking** | 1.017 | 1.823 | 2.764 | 0.632 - 12.087 | 0.177 |
| **IHD** | 1.13 | 0.706 | 3.096 | 0.222 - 43.18 | 0.401 |
| **Ejection fraction** | -.023 | 0.218 | 0.978 | 0.889 - 1.075 | 0.64 |
| **Total Cholesterol (mg/dl)** | 0.022 | 1.353 | 1.022 | 0.985 - 1.061 | 0.245 |
| **Stenosis by extra cranial Doppler** | 3.265 | 11.223 | 26.169 | 3.875 - 176.722 | 0.001 |

B = regression coefficient OR = Odds ratio 95% CI = 95% Confidence interval

## Discussion

Tansient ischemic attack is a medical emergency and an independent risk factor for ischemic stroke ***(11).*** So, management of TIA is important because potentially fatal ischemic strokes can be prevented ***(12).***

Prompt assessment and early treatment by stroke specialists in dedicated TIA clinics can decrease this risk by 80% ***(13).***

Doppler ultrasound (Duplex) is the most widely used modality and is recommended by the guidelines from joint American

scientific societies ***(14).*** Therefore, it is important for urgent ultrasound carotid Doppler and TCD to be performed in these high-risk patients ***(15***).

This study is a prospective cohort study made in neuropsychiatry department at Benha university hospital, aimed to assess the value of transcranial (TCD) and extracranial Doppler (ECD) ultrasonography to predict the occurrence of cerebrovascular events after transient ischemic attacks.

The studied sample was 75 patients of transient ischemic attacks fulfilling criteria of it. In this study the mean age of the studied sample was 61 ±7 years. The number of male patients with transient ischemic attack in this study was 55 patients (73.3%) compared to 20 female patients (26.7 %).

The present study demonstrates that TIA patients with ultrasonographic evidence of extracranial or intracranial steno occlusive disease are at high risk of further cerebral ischemic events during follow up of the patients for 6 months. During follow-up of the patients, 17(22%) out of the studied sample with either stenoocclusive disease in ECD or pathological findings in TCD, had suffered a new cerebrovascular events which was statistically significant.

This was consistent with another study ***(16***) who revealed that in TIA patients, ischemic strokes often occur early after the first presenting clinical features especially in the first 7 days.

Also, this is consistent with **Coutts study *(17)*** who revealed that TIAs or minor strokes will have a stroke within the next 90 days and the highest risk period being the first 24 hours.

In this study 15 (20 %) out of total studied sample showed stenosis by trans-cranial Doppler. Stenosis was significantly higher in those patients with further cerebrovascular events during follow up. And, 10 of 17 patients who had suffered a new cerebrovascular events, had stenosis compared to those without cerebrovascular events.

This is consistent with **Figueiredo et al., study *(18)*** they revealed that intracranial atherosclerotic disease is increasingly recognized as a major cause of ischemic stroke and is an independent risk factor for recurrence of stroke, depending on sex and race. It accounts for approximately 8% of ischemic strokes. Patients with a previous transient ischemic attack or ischemic stroke secondary to intracranial stenosis have a 12%–14% risk of subsequent stroke in the 2

years after the event, despite treatment with antithrombotic medication.

As an additional result of the present study that MCA was the most common affected artery. The most frequent affection was Rt MCA (33.3%).

This is consistent with another study ***(19),*** they reported that TCD is almost 100% specific and 93% sensitive for identifying the MCA ischemia, whereas MRA had 74% specificity and only 46% sensitivity in the assessment of intracerebral arteries. Moreover, TCD can be used in emergency department as bed side tool and provide real time information about cerebral blood flow (CBF).

Also, the present study showed importance of atherosclerotic carotid diseases on development of TIA or ischemic stroke. Stenosis and plaques were found in 18 (24.0%) of patients.

As regarding carotid atherosclerosis as a risk factor of further cerebrovascular events, the number of patients having plaques in extracranial arteries was significantly higher in those with cerebrovascular events. As, 11 (64.7%) of patients who had suffered new cerebrovascular events during follow up, had plaques in extracranial arteries compared to those without (12.1%). Also, stenosis was significantly higher in those with cerebrovascular events as 7(41.2%) of the patients who had suffered new cerebrovascular events compared to those without (3.4%).

This is consistent with **Fernandes *et al.,(20)* study as they** revealed that the highest risk of large artery stroke appears to be among patients with the highest degree of carotid stenosis, a history of diabetes, presence of asymptomatic carotid plaques, or a combination of these factors.

And, Carotid artery stenosis is a consequence of systemic atherosclerotic disease. Thus, any risk factor predisposing a patient to progressive atherosclerosis can potentially manifest itself as stenosis of the carotid artery with resultant ischemic stroke and or TIA like symptoms. Risks include smoking, hyperlipidemia, male gender, and age ***(21,22).***

As, regarding IHD as a risk factor, 17(23%) out of total studied sample had IHD and 8 (47%) out of 17 of patients who had suffered anew cerebrovascular event had IHD which is statistically significant.

This is consistent with another study **(23)** that revealed that patients with TIA/stroke with coexisting stable atherosclerotic cardiovascular disease (coronary or peripheral artery disease) have been shown

previously to be at high absolute risk of recurrent stroke and coronary events.

Multivariate analysis revealed that stenosis detected by trans-cranial Doppler and extracranial Doppler was a predictor for cerebrovascular event which is statistically significant.

So, the combination of TCD and carotid ultrasound in patients with acute ischemic stroke is a noninvasive portable method that allows the detection of poor prognosis findings and assists therapeutic decision-making with high accuracy when compared with digital subtraction angiography ***(18)***.

## Conclusion

TCD was found to have diagnostic and prognostic role in TIA patients. The presence of intracranial arterial stenosis was found to predict recurrence cerebrovascular events.

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