Research Article

Electrocardiographic and Echocardiographic Findings of Patients With Non-hemorrhagic Stroke

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Abstract
Background: Stroke is a significant cause of morbidity and mortality worldwide. The association between non-hemorrhagic stroke and some electrocardiographic and echocardiographic findings shows its potential cardiac source. This study aimed to evaluate electrocardiographic and echocardiographic findings of patients with non-hemorrhagic stroke.
Methods: This cross-sectional study included 134 patients with non-hemorrhagic stroke admitted to the neurology ward of Shahid Mohammadi hospital, Bandar Abbas, Iran, from 2018 to 2019. Patients' characteristics including age, gender, family history of stroke, diabetes, hypertension, dyslipidemia, inadequate physical activity, and smoking were recorded. All patients underwent electrocardiography (ECG) and echocardiography.
Results: The patients' mean age was 68.57±12.08 years. Additionally, 84 patients (62.7%) were male. The most common risk factor was dyslipidemia (72.4%) followed by hypertension (64.9%), diabetes (45.5%), smoking (44.8%), and family history of stroke (17.2%). Inadequate physical activity was found in 69.4% of the patients. The most common ECG finding was old myocardial infarction (MI) accounting for 24.6% of the patients, followed by atrial fibrillation (AF) (14.9%) and new MI (3.7%). The most common echocardiographic finding was significant mitral regurgitation (MR) (23.1%), followed by left ventricular systolic dysfunction (21.6%), significant tricuspid regurgitation (TR) (11.2%), mitral stenosis (MS) (4.5%), aortic stenosis (AS) (4.5%), and mitral annulus calcification (MAC) (2.2%).
Conclusion: The most common echocardiographic and ECG findings of patients with non-hemorrhagic stroke in this study were MR and old MI and the most common risk factor was dyslipidemia.
Keywords: Stroke, Electrocardiography, Echocardiography, Cardioembolism, Iran

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Background

An acute neurologic deficit attributable to brain ischemia or hemorrhage is regarded as a stroke. Ischemic stroke is among the most common causes of morbidity and mortality worldwide (1). The causes of ischemic stroke can be brain tissue hypoperfusion, thrombi, or emboli; however, the cause is undetermined in approximately one-third of ischemic strokes, which are termed as "cryptogenic strokes" (2).

Since the 5-year-recurrence rate of ischemic stroke after the first episode is estimated to be 30% (3), diagnostic workup can determine the underlying mechanism and contribute to the prevention of a second stroke (4). While the cardiac source of emboli accounts for 15%-40% of all strokes (5), cardiac emboli appear to cause more severe strokes compared to other types of ischemic strokes (6). Nevertheless, cardioembolism and recurrent stroke can be prevented in high-risk patients by a wide range of medications, including anticoagulants, antiarrhythmics, antihypertensives, and lipid-lowering agents (7).

Noteworthy, electrocardiography (ECG) and echocardiography can identify almost all major causes of cardioembolic stroke (8). On the other hand, some ECG and echocardiography findings have been reported to be associated with ischemic stroke (9, 10). Studies have demonstrated that more than 90% of stroke patients show some changes in ECG (11). Furthermore, echocardiography findings such as patent foramen ovale (PFO), atrial septal aneurysm, cardiac tumors, and valvular diseases have been found to be associated with stroke (12).

In this study, we aimed to investigate electrocardiographic and echocardiographic findings of patients with non-hemorrhagic stroke.

Materials and Methods
Participants

In this cross-sectional study, we evaluated 134 patients with an acute focal neurologic deficit admitted to the neurology ward of Shahid Mohammadi hospital, Bandar

Abbas, Iran, from March 2018 to December 2019. All patients who presented to Shahid Mohammadi Hospital with symptoms of acute and new focal neurologic deficit and were admitted to the neurology ward were included in the study.

Patients with hemorrhagic lesions in the computed tomography (CT) scan diagnosed by an expert neurologist were excluded from the study.

Sample size was calculated to be 134 patients, with 95% confidence level and d = 0.05, taking into account the maximum and minimum ratio of cardiac embolism.

Study Design

After explaining the purpose and providing detailed information about the method of the study, written informed consent was obtained from all the participants. Demographic features including age and gender were recorded for each patient. Patients with a family history of stroke were also noted. Potential risk factors for stroke, including diabetes, hypertension, dyslipidemia, inadequate physical activity, and smoking were evaluated. Diabetes was defined as fasting plasma glucose ≥126 mg/dL or receiving oral or injectable medications for diabetes. Hypertension was defined as systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg, or the use of antihypertensive agents. Dyslipidemia was defined as any of the following abnormalities: total cholesterol ≥240 mg/dL, triglyceride > 200 mg/dL, low-density lipoprotein ≥160 mg/dL (in both men and women), and/or high-density lipoprotein < 40 mg/dL in men or < 50 mg/dL in women (13).

Patients who smoked cigarettes, waterpipe, or tobacco were regarded as smokers. In addition, adequate physical activity was defined as walking 30 minutes a day for at least 5 days a week and individuals lacking this amount of activity were regarded as having inadequate physical activity.

All patients underwent ECG by a cardiology resident and ECG findings including arrhythmias such as atrial fibrillation (AF) were evaluated. Moreover, ST segment changes and old or new myocardial infarction (MI) were investigated. All participants also underwent echocardiography by a general cardiologist and some were reevaluated by an expert echocardiologist. Left ventricular (LV) function, presence of thrombi in the LV, valvular diseases, especially mitral stenosis (MS) and mitral annulus calcification (MAC), and PFO were evaluated. Interatrial septum was assessed for the presence of aneurysms. An ejection fraction (EF) lower than 45% was regarded as LV dysfunction. If atrial septal aneurysm or redundant atrial septum was present , echocardiography with intravenous contrast (agitated saline) was performed to rule in/out PFO and interatrial shunt. Although the severity of valvular disease was evaluated, only moderate to severe valvular dysfunction was included in the final analysis.

Data Analysis

The Statistical Package for the Social Sciences (SPSS) software version 25.0 (Armonk, NY: IBM Corp.) was used for data analysis. Mean ± standard deviation, frequency, and percentage were used to describe the results. Chi-square and Fisher's exact tests were used to compare qualitative data. P values ≤0.05 were regarded as statistically significant.

Results

Of the 134 patients with non-hemorrhagic stroke included in this study, with a mean age of 68.57 ± 12.08 years, 84 (62.7%) were male and 50 (37.3%) were female. The family history of stroke was found in 23 (17.2%) patients. The most common risk factor was dyslipidemia (72.4%), followed by hypertension (64.9%), diabetes (45.5%), and smoking (44.8%). Additionally, 69.4% of patients had inadequate physical activity (Table 1).

ECG and echocardiography findings are presented in Table 2. The most common ECG finding was old MI accounting for 24.6% of the patients, followed by AF (14.9%) and new MI (3.7%). None of the participants had prolonged QT. The most common echocardiographic finding was significant (moderate to severe) mitral regurgitation (MR) (23.1%), followed by LV systolic dysfunction (21.6%), significant (moderate to severe) tricuspid regurgitation (TR) (11.2%), MS (4.5%), aortic stenosis (AS) (4.5%), and MAC (2.2%). PFO, cardiac tumors, and intracardiac emboli were not observed in echocardiography. Moreover, due to the unavailability of the appropriate probe for transesophageal echocardiography (TEE), the left atrial appendage could not clearly be evaluated for the presence of a clot.

The associations of the findings of history, ECG, and echocardiography with gender, age, and family history of stroke are demonstrated in Table 3. There was a male predominance in hypertension (71.4% vs. 54%, $P = 0.041$); however, inadequate physical activity ($P = 0.001$), AF ($P = 0.006$), and significant MR ($P = 0.021$) were significantly more frequent in women compared to men. Family history of stroke and MS were significantly more common in patients aged < 60 years ($P < 0.001$ and $P = 0.003$, respectively) while inadequate physical activity, old MI, LV systolic dysfunction, and significant MR and TR were significantly more prevalent in those aged ≥75 years ($P < 0.05$). Furthermore, a significantly higher

Table 1. General Characteristics of the Study Population

Variables	Number (%)
Family history of stroke	23 (17.2)
Diabetes	61 (45.5)
Hypertension	87 (64.9)
Dyslipidemia	97 (72.4)
Smoking	60 (44.8)
Inadequate physical activity	93 (69.4)

Table 2. ECG and Echocardiography Findings in the Study Population

Variables	Number (%)
New MI	5 (3.7)
Old MI	33 (24.6)
AF	20 (14.9)
LV systolic dysfunction	29 (21.6)
AS	
Mild	4 (3.0)
Moderate	2 (1.5)
MS	
Mild	5 (3.7)
Moderate	1 (0.7)
MR	
Mild	21 (15.7)
Moderate	27 (20.1)
Severe	4 (3.0)
TR	
Mild	1 (0.7)
Moderate	11 (8.2)
Severe	4 (3.0)
AR (mild)	2 (1.5)
Atrial septal aneurysm	1 (0.7)
Elongated eustachian valve	2 (1.5)
Mitral annulus calcification	3 (2.2)

Abbreviations: MI, myocardial infarction; AF, atrial fibrillation; LV, left ventricle; AS, aortic stenosis; MS, mitral stenosis; MR, mitral regurgitation; TR, tricuspid regurgitation; AR, aortic regurgitation

number of patients without a family history of stroke had inadequate physical activity, old MI, LV systolic dysfunction, and significant MR ($P < 0.05$).

Discussion

In the current study, the most common ECG finding in patients with non-hemorrhagic stroke was old MI (24.6%), followed by AF (14.9%), and new MI (3.7%). Meanwhile, prolonged QT was not observed in any of the patients. Furthermore, by evaluating the ECG findings, we found that AF was significantly more frequent in women compared to men. In addition, old MI was significantly associated with patients' age. In a study conducted by Indurkar et al, the most common ECG abnormalities in ischemic stroke patients were U-wave (51.47%), prolonged QT (346.76%), inverted T-wave (30.88%), and ST segment depression (30.88%), respectively (14). Our findings were only consistent with the results of the study conducted by Indurkar et al in terms of ST-T changes, considering that 28.3% of our patients had ST-T changes. Given the fact that most ECG findings are representative of patients' basic heart condition in both studies, it appears that the difference in the results of this study and ours can be due to the severity of the underlying cardiac diseases in either study population. The results obtained by Khechinashvili et al (15) were also similar to the findings of the study by

Indurkar et al (14).

Niveditha et al demonstrated that the most common ECG abnormalities in ischemic stroke patients were U-wave (50%), prolonged QT (0.45 ± 0.08 ms), and inverted T wave (29.4%) (16). Additionally, Waldenhjort et al found new AF in 8.6% of patients with ischemic stroke or transient ischemic attack who did not have a history of AF prior to the occurrence of stroke (17). AF found in 14.9% of our patients might be new AF or previous silent AF that has become more prominent after stroke and therefore recognizable. Stone et al had only investigated the presence of inverted T-wave (cerebral T-wave) in stroke patients and found it in 2.1% of their patients (18), while this was not seen in any of our participants. It is noteworthy that the reported ECG findings in some studies were based on the results of Holter monitoring, while ECG at rest was performed in our study, which can be the reason for the discrepancies between studies. Furthermore, Wasser et al demonstrated that most changes in management decisions are based on findings of Holter monitoring and this method should be paid more attention in future guidelines (1).

LV systolic dysfunction was observed in 21.6% of our patients. Contrarily, by evaluating 143 young patients with cryptogenic ischemic stroke using TEE, Jecmenova et al found LV systolic dysfunction in 3 (2%) patients (19). One reason for this discrepancy can be the patients' basic heart conditions before stroke which might have been different from ours. Another reason is that we regarded EF < 45% as LV systolic dysfunction while Jecmenova et al defined it as EF < 40%. Quite comparable with our findings, LV systolic dysfunction was found in 29.4% of patients in the study by Niveditha et al (16) and in 23.5% in the study by Indurkar et al (14).

We did not find PFO in any of our patients. Meanwhile, Jecmenova et al observed PFO accompanied by prominent right-to-left shunt in 24% of their patients (19). Moreover, Wasser et al showed that 10% of the patients had either atrial septal aneurysm or PFO (1). Furthermore, PFO was observed in 2.7% of patients with cryptogenic stroke by Marino et al (10). The primary difference between these three studies with ours is their method of assessment. In other words, they used TEE which is more sensitive and specific while TEE was not available for us, leading to the underdiagnosis of some features in our study, including PFO for which TEE is the gold standard of diagnosis. In addition, the study population in the study by Marino et al was patients with cryptogenic stroke (10), which is different from ours (non-hemorrhagic stroke).

In the current study, medical history findings (i.e., risk factors) of ischemic stroke were dyslipidemia (72.4%), hypertension (64.9%), diabetes (45.5%), smoking (44.8%), and family history of stroke (17.2%), respectively. In addition, 69.4% of patients had inadequate physical activity. Besides, the prevalence of hypertension was significantly higher in men, while the prevalence of

Table 3. Findings of History, ECG, and Echocardiography by Gender, Age, and Family History of Stroke

Variable	Gender, No. (%)			Age, No. (%)				Family history of stroke, No. (%)		
	Male (n = 84)	Female (n = 50)	*P* value[a]	< 60 y (n = 33)	60-74 y (n = 56)	≥75 y (n = 45)	*P* value[a]	No (n = 111)	Yes (n = 23)	*P* value[a]
Family history of stroke	14 (16.7)	9 (18.0)	0.843	13 (39.4)	10 (17.9)	0 (0.0)	<0.001	-	-	-
Diabetes	35 (41.7)	26 (52.0)	0.245	15 (45.5)	22 (39.3)	24 (53.3)	0.371	49 (44.1)	12 (52.2)	0.482
Hypertension	60 (71.4)	27 (54.0)	0.041	22 (66.7)	34 (60.7)	31 (68.9)	0.674	75 (67.6)	12 (52.2)	0.159
Dyslipidemia	57 (67.9)	80 (40.0)	0.128	21 (63.6)	38 (67.9)	38 (84.4)	0.078	82 (73.9)	15 (65.2)	0.389
Smoking	41 (48.8)	38 (19.0)	0.224	19 (57.6)	24 (42.9)	17 (37.8)	0.206	46 (41.4)	14 (60.9)	0.088
Inadequate PA	50 (59.5)	43 (86.0)	0.001	9 (27.3)	40 (71.4)	44 (97.8)	<0.001	84 (75.7)	9 (39.1)	0.001
New MI	3 (3.6)	2 (4.0)	1.000[b]	0 (0.0)	4 (7.1)	1 (2.2)	0.303[b]	5 (4.5)	0 (0.0)	0.587[b]
Old MI	20 (23.8)	13 (26.0)	0.776	0 (0.0)	6 (10.7)	27 (60.0)	<0.001	32 (28.8)	1 (4.3)	0.013
LV systolic dysfunction	16 (19.0)	13 (26.0)	0.345	1 (3.0)	5 (8.9)	23 (51.1)	<0.001	29 (26.1)	0 (0.0)	0.004
AF	7 (8.3)	13 (26.0)	0.006	5 (15.2)	5 (8.9)	10 (22.2)	0.176	19 (17.1)	1 (4.3)	0.196[b]
AS	3 (3.6)	3 (6.0)	0.671[b]	2 (6.1)	0 (0.0)	4 (8.9)	0.060[b]	5 (4.5)	1 (4.3)	1.000[b]
MS	2 (2.4)	4 (8.0)	0.195[b]	5 (15.2)	0 (0.0)	1 (2.2)	0.003[b]	6 (4.5)	0 (0.0)	0.589[b]
Significant MR	14 (16.7)	17 (34.0)	0.021	1 (3.0)	7 (12.5)	23 (51.1)	<0.001	30 (27.0)	1 (4.3)	0.019
Significant TR	8 (9.5)	7 (14.0)	0.427[b]	0 (0.0)	3 (5.4)	12 (26.7)	<0.001[b]	15 (13.5)	0 (0.0)	0.073[b]
AR (mild)	2 (2.4)	0 (0.0)	0.529[b]	0 (0.0)	2 (3.6)	0 (0.0)	0.510[b]	1 (0.9)	1 (4.3)	0.315[b]
Atrial septal aneurysm	1 (1.2)	0 (0.0)	1.000[b]	0 (0.0)	1 (1.8)	0 (0.0)	1.000[b]	1 (0.9)	0 (0.0)	1.000[b]
Elongated Eustachian valve	1 (1.2)	1 (2.0)	1.000[b]	0 (0.0)	1 (1.8)	1 (2.2)	1.000[b]	2 (1.8)	0 (0.0)	1.000[b]
MAC	1 (1.2)	2 (4.0)	0.555[b]	0 (0.0)	2 (3.6)	1 (2.2)	0.788[b]	3 (2.7)	0 (0.0)	1.000[b]

Abbreviations: N, number; PA, physical activity; MI, myocardial infarction; LV, left ventricle; AF, atrial fibrillation; AS, aortic stenosis; MS, mitral stenosis; MR, mitral regurgitation; TR, tricuspid regurgitation; AR, aortic regurgitation; MAC, mitral annulus calcification.
[a] Analyzed by Chi-square test.
[b] Analyzed by Fisher's exact test.

inadequate physical activity was significantly higher in women. Additionally, a significant correlation was found between inadequate physical activity and age. In the study conducted by Niveditha et al, hypertension was observed in 48.5%, diabetes in 17.6%, and smoking in 27.9% (16) of the ischemic stroke patients. The comparison of their results with ours shows that the prevalence of the risk factors of ischemic stroke was higher in the patients of the current study. These risk factors in the study by Waldenhjort et al included smoking (4%), diabetes (17%), and hypertension (64%) (17). Their findings are only in line with our results regarding hypertension. Dyslipidemia was found in 26.9% of the patients in the study by Menon et al (20), which is very different from the frequency of dyslipidemia in our study (72.4%), most probably due to different definitions of dyslipidemia. Hypertension was found in 56.1% and smoking in 31% of the patients in the same study (20).

The most common echocardiography finding of the current study was significant MR (23.1%), followed by significant TR (11.2%), AS (4.5%), MS (4.4%), MAS (2.2%), AR (1.5%), elongated Eustachian valve (1.5%), and atrial septal aneurysm (0.7%). No cardiac tumors or intracardiac thrombi were observed. Moreover, we were not able to visualize thrombi in the left atrial appendage due to the unavailability of a TEE probe. On the other hand, MR was significantly more frequent in women

compared to men and there was a significant association between age and the presence of MR, MS, and TR. In the study by Jecmenova et al, significant valvular disease was found in 3 patients (2%), one of whom had AS with severe calcification, one had a bicuspid aortic valve, and the other had chronic MR. Additionally, another patient had left atrial myxoma (19). In the study by Indurkar et al, no thrombi were found in the left atrial appendage by either 2D or 3D echocardiography. However, mitral and aortic valve abnormalities were found in 28% and 6% by 2D echocardiography and 24% and 6% by 3D echocardiography, respectively (14). The difference between their findings and ours can stem from different general features of the study populations, the evaluation method of these findings (TEE or TTE), the experience of the echocardiologist in this regard, and different quality and accuracy of the echocardiography devices used in each of the studies.

One limitation of the current study was that because of the occurrence of the coronavirus disease 2019 (COVID-19) pandemic, many patients could not be reevaluated by an experienced echocardiologist. Another limitation was the unavailability of a TEE probe which led to the assessment of all features by TTE.

Conclusion
Based on the results of the current study, the most

frequent echocardiographic and ECG findings of patients with non-hemorrhagic stroke were MR and old MI while the most common risk factor was dyslipidemia. In our patients, ECG and echocardiography contributed to the diagnosis of the cardiac source of non-hemorrhagic stroke and the associated cardiac conditions.

Authors' Contribution
Concept: FM; design: FM and MN; supervision: OE; data: FM; analysis: HY; writing: MN; critical revision: RER.

Conflict of Interests
The authors declare that they have no conflict of interest.

Ethical Approval
The present study received ethics approval from the Ethics Committee of Hormozgan University of Medical Sciences (IR. HUMS.REC.1398.417). Additionally, it complies with the statements of the Declaration of Helsinki. Written informed consent was obtained from all the participants or their guardians.

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