# The evaluation of left ventricular diastolic dysfunction in patients with non-hemorrhagic stroke and atrial fibrillation

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**Short Communication**

## Abstract

**BACKGROUND:** Atrial fibrillation (AF) is the most common tachyarrhythmia and an important risk factor for thromboembolic stroke. $CHA_2DS_2$-VASc score was introduced for assessment of embolic events and as criteria for starting anticoagulants. This study was performed to evaluate the left ventricular diastolic dysfunction (LVDD) in patients with non-hemorrhagic stroke and AF.

**METHODS:** This cross-sectional study consisted of 76 consecutive patients with suspected non-hemorrhagic stroke referred to the Cardiology Department of Alzahra and Ayatollah Kashani hospitals in Isfahan, Iran, during 2015-2016. Demographic, anthropometric and clinical characteristics were evaluated for all patients at baseline. $CHA_2DS_2$-VASc score was calculated for all. All eligible patients underwent transthoracic echocardiogram (TTE) and LVDD was measured in the patients.

**RESULTS:** The mean age of the patients was 64.64 ± 5.95 years and 28 subjects (36.8%) were women. The most common underlying disease in the patients was hypertension (HTN) (65.8%). Median (range) $CHA_2DS_2$-VASc score was 4 (1-7). Four patients (5.3%) had paroxysmal AF and 16 cases (21.1%) had LVDD. Analysis showed that LVDD in patients with non-hemorrhagic stroke and coexisting AF was not associated with $CHA_2DS_2$-VASc score (r = 0.151, P = 0.192).

**CONCLUSION:** LVDD is not associated with $CHA_2DS_2$-VASc score in patients with non-hemorrhagic stroke and coexisting AF.

**Keywords:** Left Ventricular Dysfunction, Stroke, Atrial Fibrillation

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## Introduction

Atrial fibrillation (AF), as the most common tachyarrhythmia, affects more than 5% of adults aged 65 years. This arrhythmia is progressive and its prevalence rises with increasing age.[1] AF is associated with some conditions and cardiovascular diseases in 80% of patients.[2] AF, as compared with sinus rhythm, is associated with a higher incidence of death, stroke, and coronary events.[3] Non-valvular AF is the most common cause of stroke due to cardiac embolism so that the risk of stroke in patients with AF is 3 to 7 times more than patients without AF.[4] In patients with known risk factors for stroke, anticoagulant therapy has a particular importance.[5,6]

So far, various scoring systems have been developed to determine the risk of stroke in patients with AF, but none of them are considered the echocardiographic variables. Recently, $CHA_2DS_2$-VASc score was introduced for assessment of embolic events and as criteria for starting anticoagulants. The main components of this scoring system include congestive heart failure or left ventricular systolic dysfunction, hypertension (HTN), older age, diabetes mellitus (DM), prior stroke or transient ischemic attack (TIA) or thromboembolism, vascular disease and being woman, but left ventricular diastolic dysfunction (LVDD) are not placed in the criteria.[7,8] AF in patients with LVDD is caused stasis and stroke by increasing left ventricular and left atrial end-diastolic pressure.[9,10]

Regarding the predictive role of above factors for hemorrhagic stroke and LVDD, these two variables may be related.[11] Due to lack of sufficient studies in the world, this study was performed to assess the relationship between LVDD and non-hemorrhagic stroke in patients with atrial

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fibrillation. According to the absence of LVDD in $CHA_2DS_2$-VASc score (despite encompassing systolic dysfunction) and the recent establishment of new LVDD assessment criteria in patients with AF and due to lack of sufficient studies in the world, this article had been designed to evaluate the importance of LVDD in the occurrence of thromboembolic events.

## Materials and Methods

The cross-sectional study consisted of 76 consecutive patients with suspected non-hemorrhagic stroke referred to the cardiology department of Alzahra and Ayatollah Kashani hospitals in Isfahan, Iran, between April 2015 and March 2016. Demographic characteristics of the patients such as age and sex were recorded in the checklist. Anthropometric and clinical evaluations were performed for all patients at baseline. The patients' height and body weight were measured, and their body mass index (BMI) was calculated as follows: weight in kilograms divided by the square of the height in meters ($kg/m^2$). A complete medical history and physical examination were performed for all patients. A history of smoking, diabetes mellitus, hypertension and vascular disease was taken. In a 2-year period, patients with suspected stroke were under initial assessment including history, physical examination and imaging by the resident or specialist of neurology. After confirming the diagnosis of non-hemorrhagic stroke, the eligible patients with coexisting AF in the electrocardiogram (ECG) were selected for the study.

The study was approved by the Human Subjects Committee at Isfahan University and conformed to the ethical guidelines of the 2013 Declaration of Helsinki.[12] Written informed consent was obtained from all participants before enrollment.

Inclusion criteria were all patients with non-hemorrhagic stroke and coexisting AF and having consent to participate in the study. Exclusion criteria were all patients with heart valve stenosis, moderate or severe valve regurgitation, left ventricular ejection fraction (LVEF) < 45%, heart valve surgery, pacemaker insertion, New York Heart Association (NYHA) class IV for congestive heart failure (CHF), other arrhythmias such as ventricular tachycardia (VT) or supraventricular tachycardia (SVT) and lack of consent to participate in the study.

Regarding obtained data from the patients with non-hemorrhagic stroke, $CHA_2DS_2$-VASc score was calculated for all of them and they received necessary neurologic treatment and care in the course of hospitalization (if $CHA_2DS_2$-VASc score ≥ 2, anticoagulant was required). Simultaneously, the patients underwent transthoracic echocardiogram (TTE) by Samsung Medison and GE Vivid 3 echocardiography machines to assess LVDD. To evaluate LVEF of the patients, three echocardiographic methods were used including M-mode fractional shortening, Simpson's method and Eyeball estimation in several consecutive turns. If LVEF ≥ 45% was confirmed and the patients did not have the exclusion criteria, they were enrolled and LVDD evaluation was performed as following steps: 1- Measurement of left ventricle inflow velocities including E velocity, deceleration slope (DT), a velocity and duration, 2- Measurement of left atrial inflow including peak systolic velocity, peak diastolic velocity, atrial velocity peak and duration, 3- Measurement of mitral annulus velocity by Doppler tissue imaging including early myocardial velocity (E') and atrial myocardial velocity (A'). Due to the lack of A velocity and atrial myocardial velocity (A') in patients with AF, American Society of Echocardiography (ASE) guidelines 2016 [13] were used to assess LVDD as follows: 1- Peak acceleration rate of mitral E velocity (≥ 1,900 $cm/s^2$), 2- Isovolumetric relaxation time (IVRT) (≤ 65 ms), 3- Deceleration time (DT) of pulmonary venous diastolic velocity (≤ 220 ms), 4- E/Vp ratio (≥ 1.4), 5- Septal E/e' ratio (≥ 11). Two above items including DT and E/Vp ratio were not measured in this study due to technical problems and needing to transesophageal echocardiography (TEE).

All statistical analysis was performed using SPSS software (version 24, IBM Corporation, Armonk, NY, USA). The qualitative variables were described with number and percentage. Quantitative variables were described using mean ± standard deviation (SD), median (range) and interquartile range (IQR). To analyze the correlation between LVDD and $CHA_2DS_2$-VASc score, Spearman correlation was used. Chi-square test was used to evaluate the difference between categorical variables in two groups. $P < 0.050$ was considered statistically significant at 95% confidence interval (95% CI).

## Results

A total of 76 patients with non-hemorrhagic stroke and coexisting AF completed the study. The mean age of the patients was 64.64 ± 5.95 years (range = 54-78). Baseline characteristics are shown in table 1. The results of echocardiographic

evaluations of the patients are shown in table 2. These results are only a status report and the control group does not exist.

**Table 1.** Baseline characteristics of patients (n = 76) with non-hemorrhagic stroke and coexisting atrial fibrillation (AF)

| Characteristic | Statistics |
|---|---|
| Age > 75 (year) | 4 (5.7) |
| Sex (woman) | 28 (36.8) |
| Smoker | 12 (15.8) |
| DM | 14 (18.4) |
| HTN | 50 (65.8) |
| Vascular disease | 13 (17.1) |
| $CHA_2DS_2$-VASc | 4.0 (1-7) |
| BMI ($kg/m^2$) | 25.83 ± 1.77 |

Data are shown as number (%) or mean ± standard deviation (SD) or median (range)
BMI: Body mass index; DM: Diabetes mellitus; HTN: Hypertension

Analysis showed that LVDD in patients with non-hemorrhagic stroke and coexisting AF was not correlated with $CHA_2DS_2$-VASc score (r = 0.151, P = 0.192).

**Table 2.** Echocardiographic parameters in the patients (n = 76) with non-hemorrhagic stroke and coexisting atrial fibrillation (AF)

| Parameter | Statistics |
|---|---|
| Heart rate (bpm) | 74.51 ± 6.16 |
| LVEF (%) | 55.00 ± 4.40 |
| E (cm/s) | 1.32 ± 0.43 |
| Septal E/e' (ratio) | 9.78 ± 1.16 |
| IVRT (ms) | 77.17 ± 10.76 |
| LVDD | 16 (21.1) |
| Paroxysmal AF | 4 (5.3) |

Data are shown as n (%) or mean ± standard deviation (SD)
AF: Atrial fibrillation; LVEF: Left ventricular ejection fraction; E: Peak acceleration of mitral E wave; IVRT: Isovolumetric relaxation time; LVDD: Left ventricular diastolic dysfunction

The assessment of variables in patients with $CHA_2DS_2$-VASc score ≥ 2 showed that there was a significant difference between the patients with and without LVDD it in terms of sex (P = 0.037), smoking (P = 0.032), DM (P = 0.001) and vascular disease (P = 0.020), but It was not significantly different regarding age (P = 0.655), BMI (P = 0.274) and HTN (P = 0.255) (Table 3). In addition, in terms of echocardiographic parameters, there was a significant difference between two subgroups of LVDD (with or without) in terms of E index (P < 0.001), septal E/e' ratio (P < 0.001) and IVRT (P < 0.001). However, it was not significantly different regarding paroxysmal AF (P = 0.345), heart rate (P = 0.860) and LVEF (P = 0.145).

## Discussion

In this study, patients with non-hemorrhagic stroke with coexisting AF were evaluated in relation to LVDD and its association with $CHA_2DS_2$-VASc score. About one-fifth of the patients had LVDD. A limited number of patients were over 75-year old (about 5%), and about one-third were women. Most patients (over 70%) were overweight or obese. The most common underlying disease in the patients was HTN (about two-thirds) and less than one-fifth had DM or vascular disease, or were smokers. All of the patients had a $CHA_2DS_2$-VASc score ≥ 2, and so they needed anticoagulant therapy. None of the patients had bradycardia or tachycardia, and none of them had LVEF less than 50%. Few patients had paroxysmal AF (about 5%). Echocardiographic parameters such as peak acceleration of mitral E wave, septal E/e' ratio and IVRT were abnormal. Being woman, smoking, DM and vascular diseases had significant effects on LVDD, but over 75-year age, overweight or obesity and HTN did not significantly affect LVDD.

**Table 3.** Distribution of left ventricular diastolic dysfunction (LVDD) in baseline clinical characteristics of the subjects with $CHA_2DS_2$-VASc score ≥ 2

| Characteristic | Diastolic Dysfunction | | P |
|---|---|---|---|
| | Yes | No | |
| | n = 16 | n = 60 | |
| Sex (man) | 6 (37.5) | 42 (70.0) | 0.037 |
| Smoke | 0 (0.0) | 18 (30.0) | 0.032 |
| HTN | 13 (81.2) | 41 (68.3) | 0.255 |
| DM | 8 (50.0) | 6 (10.0) | 0.001 |
| Vascular | 7 (43.7) | 8 (13.3) | 0.020 |
| Paroxysmal AF | 0 (0.0) | 4 (6.7) | 0.345 |

Data are shown as number (%)
HTN: Hypertension; DM: Diabetes mellitus; AF: Atrial fibrillation

In addition, echocardiographic parameters such as E index, E/e' ratio and IVRT had significant relationships with LVDD, while heart rate, LVEF and paroxysmal AF (no persistent) had no significant relations with LVDD.

AF is the most commonly associated illness in hospitalized patients, which is the cause of nearly 25% of stroke cases in the 80-89 age groups.[14] In patients with persistent AF or prolonged paroxysmal AF that have risk factors for stroke, anticoagulant therapy with warfarin is recommended, with the goal of maintaining the international normalized ratio (INR) between 2 and 3.[4,5,15] Aspirin is used in a small number of patients who are not at risk or when warfarin is contraindicated. However, aspirin is less effective in preventing thromboembolism than is warfarin. Despite the easier treatment, the strength of aspirin in preventing thromboembolism is much less than warfarin and should only be considered in low-risk patients. The risk of stroke in these patients is high (1% per year), but due to the high prevalence of this arrhythmia, prevention of these events in patients is important. Warfarin reduces this chance by about 75%, but aspirin has about one-third of warfarin effects on stroke prevention.[4,5] Various studies have been done on the classification of AF patients to determine the high or low risk of thromboembolic events, such as stroke. The $CHA_2DS_2$-VASc score is one of the scoring and risk assessment systems, that has been much considered in recent years. The American College of Chest Physicians recommends treatment with warfarin in patients with $CHA_2DS_2$-VASc score $\geq 2$.[4,5,14]

Few studies have been conducted to evaluate the presence of LVDD and estimate $CHA_2DS_2$-VASc score to predict the non-hemorrhagic stroke.[16,17] The only available study in this field is a study by Kosiuk et al. to investigate the association between LVDD and stroke in patients with AF.[18] Their results showed that 37% of stroke patients had LVDD. Also, the $CHA_2DS_2$-VASc score was higher in patients with LVDD. There was a statistically significant relationship between $CHA_2DS_2$-VASc score and LVDD ($r = 0.392$, $P = 0.001$). In addition, LVDD compared to $CHA_2DS_2$-VASc score was a stronger predictor of stroke in AF patients. However, in the present study, the frequency of LVDD in patients with non-hemorrhagic stroke and coexisting AF was approximately 20% that was about half of the rate reported in the study of Kosiuk et al.[18]

Two studies can be different. In Kosiuk et al.[18] they worked on patients with strokes of different origin, including strokes with and without AF, as well as cryptogenic stroke. The authors analyzed the complex relationships among LVDD, cerebral ischemic events, and AF. But in the present study, only patients with non-hemorrhagic stroke were investigated.

## Conclusion

The results of this study showed that LVDD in patients with non-hemorrhagic stroke and coexisting AF is not associated with $CHA_2DS_2$-VASc score.

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## Conflict of Interests

Authors have no conflict of interests.

## References

1. Go AS, Hylek EM, Phillips KA, Chang Y, Henault LE, Selby JV, et al. Prevalence of diagnosed atrial fibrillation in adults: National implications for rhythm management and stroke prevention: the AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study. JAMA 2001; 285(18): 2370-5.
2. Chambers PW. Lone atrial fibrillation: Pathologic or not? Med Hypotheses 2007; 68(2): 281-7.
3. Aronow WS. Management of the older person with atrial fibrillation. J Gerontol A Biol Sci Med Sci 2002; 57(6): M352-M363.
4. Elezi S, Qerkini G, Bujupi L, Shabani D, Bajraktari G. Management and comorbidities of atrial fibrillation in patients admitted in cardiology service in Kosovo-a single-center study. Anadolu Kardiyol Derg 2010; 10(1): 36-40.
5. Agarwal S, Bennett D, Smith DJ. Predictors of warfarin use in atrial fibrillation patients in the inpatient setting. Am J Cardiovasc Drugs 2010; 10(1): 37-48.
6. Altmann DR, Kuhne M, Sticherling C, Osswald S, Schaer BA. Use of the CHADS2 risk score to guide antithrombotic treatment in patients with atrial fibrillation-room for improvement. Swiss Med Wkly 2010; 140(5-6): 73-7.
7. O'Brien PJ, Thiemann DR, McNamara RL, Roberts JW, Raska K, Oppenheimer SM, et al. Usefulness of transesophageal echocardiography in predicting

mortality and morbidity in stroke patients without clinically known cardiac sources of embolus. Am J Cardiol 1998; 81(9): 1144-51.
8. Zabalgoitia M, Halperin JL, Pearce LA, Blackshear JL, Asinger RW, Hart RG. Transesophageal echocardiographic correlates of clinical risk of thromboembolism in nonvalvular atrial fibrillation. Stroke Prevention in Atrial Fibrillation III Investigators. J Am Coll Cardiol 1998; 31(7): 1622-6.
9. Demircelik MB, Cetin M, Cicekcioglu H, Ucar O, Duran M. Effect of left ventricular diastolic dysfunction on left atrial appendage function and thrombotic potential in nonvalvular atrial fibrillation. Anadolu Kardiyol Derg 2014; 14(3): 256-60.
10. Sarrafzadegan N, Sadeghi M, Gharipour M, Talaiei M, Shafie D, Aghababaie E. Left ventricular diastolic function in subjects with metabolic syndrome: Isfahan Cohort Study. Iran Heart J 2013; 13(4): 63-71.
11. Aalami Harandi S, Sarrafzadegan N, Sadeghi M, Talaei M, Dianatkhah M, Oveisgharan S, et al. Do cardiometabolic risk factors relative risks differ for the occurrence of ischemic heart disease and stroke? Res Cardiovasc Med 2016; 5(1): e30619.
12. World Medical Association Declaration of Helsinki: Ethical principles for medical research involving human subjects. JAMA 2013; 310(20): 2191-4.
13. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF 3rd, Dokainish H, Edvardsen T, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: An update from the American society of echocardiography and the European association of cardiovascular imaging. J Am Soc Echocardiogr 2016; 29(4): 277-314.
14. Hopps S, Marcy TR. Warfarin versus aspirin: Using CHADS2 to guide therapy for stroke prevention in nonvalvular atrial fibrillation. Consult Pharm 2009; 24(11): 841-4.
15. Medi C, Hankey GJ, Freedman SB. Atrial fibrillation. Med J Aust 2007; 186(4): 197-202.
16. Schaer BA, Zellweger MJ, Cron TA, Kaiser CA, Osswald S. Value of routine holter monitoring for the detection of paroxysmal atrial fibrillation in patients with cerebral ischemic events. Stroke 2004; 35(3): e68-e70.
17. Todo K, Moriwaki H, Saito K, Naritomi H. Frequent premature atrial contractions in stroke of undetermined etiology. Eur Neurol 2009; 61(5): 285-8.
18. Kosiuk J, Breithardt O, Bode K, Kornej J, Arya A, Gaspar T, et al. Left ventricular diastolic dysfunction and thromboembolic risk in atrial fibrillation: Diastolic dysfunction and thromboembolic risk in AF. Int J Cardiol 2013; 168(1): 547-8.

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