Original Paper

Factors Associated with Stroke in Atrial Fibrillation. A Retrospective Study

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ABSTRACT: Aim. The aim of our study was to retrospectively evaluate known factors such as CHA2DS2-VASc, but, also, new factors (such as left atrial remodeling), associated with the development of stroke in patients with atrial fibrillation (AFi). Material and Methods. We performed a retrospective study in which 251 patients with AFi were included. 47 patients had an ischemic stroke before the diagnosis of AFi, at the time of diagnosis or after AFi was diagnosed. The CHA2DS2-VASc score was analyzed for all patients together with other left atrial remodeling parameters. Results. We observed that among the patients with ischemic stroke approximately 61.70% were over 72.5 years old compared to those without stroke who presented this age in a proportion of only 44.61% (OR=2.001, P=0.0367). The CHA2DS2-VASc score had the greatest statistical impact for stroke, as expected. Patients with a CHA2DS2-VASc score >4.5 presented stroke in a proportion of 87.23% compared to CHA2DS2-VASc <4.5 who had stroke only in a proportion of 12.77% (OR=11.51, P=<0.0001). Regarding left atrial remodeling parameters, low LA ejection fraction was associated with a high percentage of stroke among patients (61.70%) compared to those with LA EF>34.5% who had stroke only in a percentage of 38.30% (OR= 2.124, P=0.0238). Conclusions. Although the CHA2DS2-VASc score remains a good factor for predicting the association of AFi with ischemic stroke, echocardiographic parameters for the evaluation of the left atrium can be used as new risk factors for predicting the occurrence of ischemic stroke in patients with AFi.

KEYWORDS: *Stroke, atrial fibrillation, risk factors.*

Introduction

Nonvalvular atrial fibrillation (AFi) is a significant and separate risk factor for stroke [1].

However, the actual stroke rate may differ greatly among patients with AFi, which is crucial in determining the potential advantages of identifying additional risk factors for stroke in this disease.

AFi is becoming more common worldwide, both in terms of new cases and the total number of cases [2].

According to Framingham Heart Study (FHS) data, the occurrence of atrial fibrillation has tripled in the last 50 years [3].

In 2016, the Global Burden of Disease project estimated that there were approximately 46.3 million people worldwide affected by AFi [4].

In 2004, the lifetime chance of developing AFi was estimated to be approximately 1 in 4 for white men and women over the age of 40 [5].

Ten years later, lifetime risk increased to approximately 1 in 3 for white people and 1 in 5 for color people [6].

In the United States, approximately 3 to 6 million people are affected by AFi, with estimates indicating that this number will increase to approximately 6 to 16 million by the year 2050 [7].

The prevalence of atrial fibrillation (AFi) in Europe was approximately 9 million in 2010 among people aged 55 years and it is estimated to increase to 14 million by 2060 [8].

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By 2050, it is estimated that approximately 72 million people in Asia will be diagnosed with atrial fibrillation, and approximately 3 million of them will experience AFi-related strokes [9].

Previous cohort studies have shown that approximately 20% to 30% of ischemic stroke patients have AFi either before, during, or after the initial event [10].

While the CHA_2DS_2-VASc score is commonly used in Europe and the United States to assess the risk of thromboembolism in patients with nonvalvular AFi, there are many other risk factors not yet considered in the new guidelines for AFi and stroke [11].

The aim of our study was to retrospectively evaluate known factors such as CHA_2DS_2-VASc, but, also, new factors (such as left atrial remodeling), that are associated with the development of stroke in patients with atrial fibrillation.

Material and Methods

We performed a retrospective study in which 251 patients with atrial fibrillation were finally analyzed.

Among them, 47 patients had an ischemic stroke before the diagnosis of atrial fibrillation, at the time of diagnosis or after atrial fibrillation was diagnosed.

The study design is presented in Figure 1.

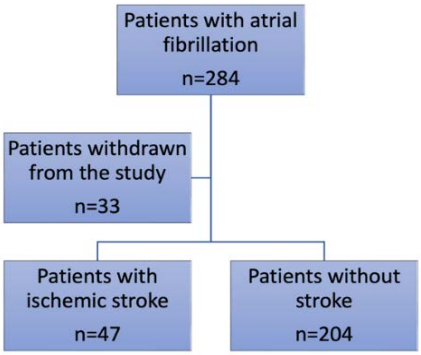

Figure 1. Design of the study.

The patient's data were taken from the medical records of the Timisoara Municipal Emergency Clinical Hospital and of the Timisoara Cardiovascular Disease Institute, between January 2021 and December 2022.

The study was approved by the Ethics Committee of the University of Medicine and Pharmacy "Vitor Babes", Timisoara, Romania (No 82/2020).

Inclusion criteria

The patients included in the study suffered from atrial fibrillation (paroxysmal, persistent, or permanent) at the time of evaluation or had a documented history of atrial fibrillation.

Atrial fibrillation was documented by 12-lead electrocardiogram, rhythm strip, or Holter electrocardiogram.

The duration of atrial fibrillation was at least 30 seconds.

Age over18 years was an inclusion criteria, as well as the patient's acceptance for using data from their medical records for scientific research.

Exclusion criteria:

-patients with significant mitral, aortic, and tricuspid valvulopathy

-patients with prosthetic heart valves

-congenital heart disease

-patients with significant severe hematological, oncological and liver diseases

-acute myocardial infarction and coronary syndromes defined as cardiac arrest, electrical or hemodynamic instability with cardiogenic shock or mechanical complications

-acute pulmonary edema defined as acutely decompensated state due to either cardiac or noncardiac etiologies

-severe pulmonary thromboembolism defined as hemodynamic instability: cardiac arrest, obstructive shock, persistent hypotension

-end stage heart failure

-severe renal disease defined as KDIGO stage G5 GFR<15ml/min/1.73m2 or patients in hemodialysis program.

The CHA_2DS_2-VASc score (congestive heart failure/LV dysfunction (1 point), hypertension (1 point), age ≥75 years (2 points), diabetes mellitus (1 point), stroke (2 points), vascular disease (1 point), (female) sex category (1 point) and age 65-74 years (1 point), was analyzed for all patients included in our study.

Biological samples were collected when patients were admitted to the emergency department as well as during hospitalization.

Echocardiographic left atrium assessment

Ultrasound images were explored with patients in left lateral decubitus position, using a GE VIVID E90 machine (Vivid E90, GE Health Medical, Milwaukee, WI, USA) with simultaneous ECG recording.

The echocardiographic assessment was carried out using conventional perspectives and procedures.

The following parameters were studied:

- LA volume and shape
- LA function

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The LA assessment guideline states that when tracing the borders of the LA, the confluence of the pulmonary veins and the LA appendage should be excluded (Figure 2).

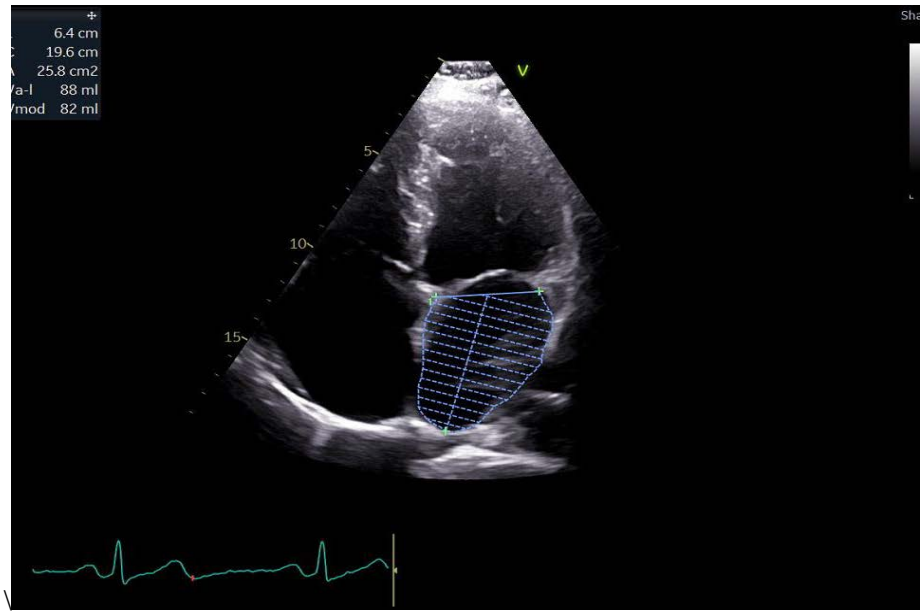

Figure 2. Example of ellipsoid left atrium (LA) shape.

The most common echocardiographic methods for assessing LA function include volumetric analysis.

The LA ejection fraction was defined as [(LA Volume max-LA Volume min)/LA Volume max]X100.

Also, LA shape evaluation was performed.

Trapezoidal shape (remodeling) was defined if the basal dimension (LAb) was larger than the transverse dimension (LAt).

The basal dimension of the LA (LAb) was defined as the maximal transverse distance at the base of LA apical four chamber view (Figure 3).

The transverse dimension was defined as LA mid-transversal diameter.

Each LA was approximated in shape with an ellipsoid and a trapezoid.

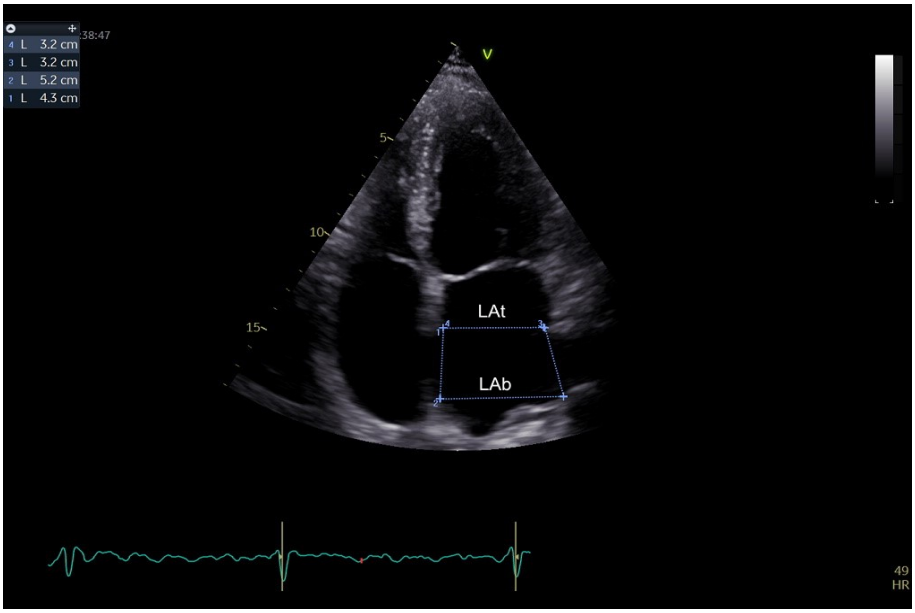

Figure 3. Example of trapezoidal LA shape: LAb>LAt.

Statistical analysis

All data from our study were imported into Microsoft Office Excel 2019 (Microsoft Corporation, Redmond, Washington, DC, USA) and later statistically analyzed in GraphPad software (Version 10.0, San Diego, CA, USA).

Fisher exact test was used for the comparative analysis of proportions.

Thus, the odds ratio value was calculated for the selected risk factors.

To compare the mean of two groups, we used the student t-test.

For the analysis of cut-off values, we used ROC (Receiver operating characteristic) curves. In all cases, the value P <0.05 was selected as having statistical significance.

Results

In this study, from the 251 patients diagnosed with atrial fibrillation (AFi) included in the final analysis, 47 had an ischemic stroke (before, during or after the AFi diagnosis) and 204 were without stroke.

To determine the cut-off values, we used ROC curves and Area under the ROC curve (AUC).

Thus, for age the value of 72.5 years was established (AUC=0.5909), for the CHA_2DS_2-VASc value the value of 4.5 (AUC=0.8475), for the left atrium (LA) the value of 33, 5cm2 (AUC=0.5500), LA volume of 132ml (AUC=0.5448) and LA ejection fraction of 34.5% (AUC=0.5415).

All this is shown in Figure 4.

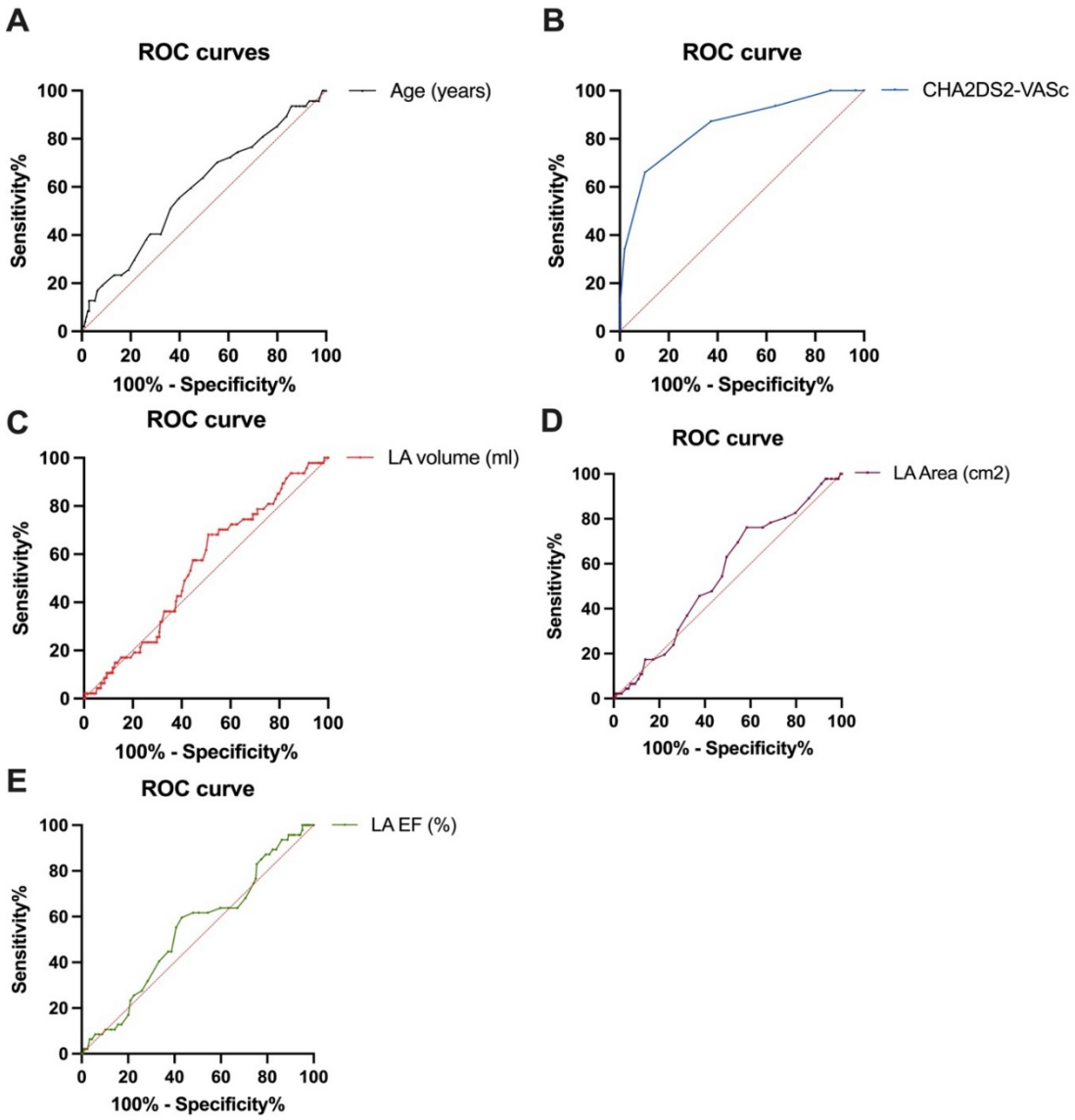

Figure 4. ROC curves for determining cut-off values. A. Determining the cut-off value for the age of the patients B. Determining the cut-off value for the CHA_2DS_2-VASc score. C. Determining the cut-off value for the left atrium volume (LA)-ml. D. Determining the cut-off value for LA area (cm2). E. Determining the cut-off value for LA ejection fraction (%).

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We observed that among the patients with ischemic stroke approximately 61.70% were over 72.5 years old compared to those without stroke who presented this age in a proportion of only 44.61% (OR=2.001, 95% CI=1.057 to 3.829, P=0.0367).

Regarding the gender of the patients, men were diagnosed with stroke in a lower percentage (48.94%) than women (51.06%), but without registering a statistically significant difference (OR=1.263, 95% CI=0.6619 to 2.395, P=0.5164).

The CHA_2DS_2-VASc score had the greatest statistical impact for stroke, as expected.

Patients with a CHA_2DS_2-VASc score >4.5 presented stroke in proportion of 87.23% compared to CHA_2DS_2-VASc <4.5 who had stroke only in proportion of 12.77% (OR=11.51, 95 % CI= 4.654 to 26.58, P= <0.0001).

Regarding left atrial remodeling parameters, low LA ejection fraction was associated with a high percentage of stroke among patients in our study (approximately 61.70%) compared to those with LA EF>34.5% who had stroke only in a percentage of 38.30% (OR= 2.124, 95% CI=1.121 to 4.068, P= 0.0238).

Although there was no statistically significant difference among them, patients who presented an LA volume greater than 132ml presented stroke in an increased percentage (57.45%) compared to a low LA volume (OR=1.676, 95% CI=0.8905 to 3.102, P=0.1443).

Likewise, patients who had a LA area >33.5cm2 had a larger stroke compared to patients with a smaller LA, but still without a statistically significant difference (OR=1.519, 95% CI=0.8076 to 2.808, P=0.2572).

Although the patients who presented the trapezoid shape of the LA presented stroke in percentage of 85.11%, no statistically significant difference was noticed among them either (OR=2.057, 95% CI=0.8673 to 5.128, P=0, 1302).

All clinical-pathological characteristics are shown in Table 1, while in Figure 5 the Odds ratio values accompanied by the values of the corresponding confidence interval are highlighted.

		Without Stroke (n=204, 81,2%)	Stroke (n=47, 18,8%)	P value	OR (and reciprocal)	Min int	Max int
Age (years)		71,43±8,837	74,4±9,219	0,0399*			
	<72,5	113 (55,39%)	18 (38,30%)	0,0367#	0,4998	0,2611	0,9463
	>72,5	91 (44,61%)	29 (61,70%)		2,001	1,057	3,829
Gender	Female	116 (56,86%)	24 (51,06%)	0,5164#	0,7916	0,4175	1,511
	Male	88 (43,14%)	23 (48,94%)		1,263	0,6619	2,395
AFi	Fd/Parox/Pers	115 (56,37%)	19 (40,43%)	0,0433#	0,5252	0,2794	0,991
	Perm.	89 (43,63%)	28 (59,57%)		1,904	1,009	3,579
CHA_2DS_2-VASc		3,961±1,316	5,915±1,316	<0,000*			
	<4,5	128 (62,75%)	6 (12,77%)	<0,000#	0,08689	0,03762	0,2149
	>4,5	76 (37,25%)	41 (87,23%)		11,51	4,654	26,58
Trapezoid shape of LA	Yes	150 (73,53%)	40 (85,11%)	0,1302#	2,057	0,8673	5,128
	No	54 (26,47%)	7 (14,89%)		0,4861	0,195	1,153
LA area (cm2)		33,95±9,252	34,80±7,833	0,5601*			
	< 33.5	106 (52,94%)	20 (42,55%)	0,2572#	0,6584	0,3561	1,238
	> 33.5	98 (47,06%)	27 (57,45%)		1,519	0,8076	2,808
LA V (ml)		135,9±60,72	139,8±50,48	0,6822*			
	<132	113 (55,39%)	20 (42,55%)	0,1443#	0,5965	0,3224	1,123
	>132	91 (44,61%)	27 (57,45%)		1,676	0,8905	3,102
LA EF (%)		36,56±12,68	34,51±11,18	0,3090*			
	<34,5	88 (43,14%)	28 (61,7%)	0,0238#	2,124	1,121	4,068
	>34,5	116 (56,86%)	19 (38,3%)		0,4709	0,2458	0,8922

Table 1. The clinical-pathological features of the patients included in our study. AFi-atrial fibrillation. Fd/Parox/Pers-First diagnosed/Paroxysmal/Persistent. LA-left atrium. V-volume (ml). EF-ejection fraction. * t student test. # Fisher exact test. OR-odds ratio. Min int and Max int-the minimum and maximum values of the 95% confidence interval.

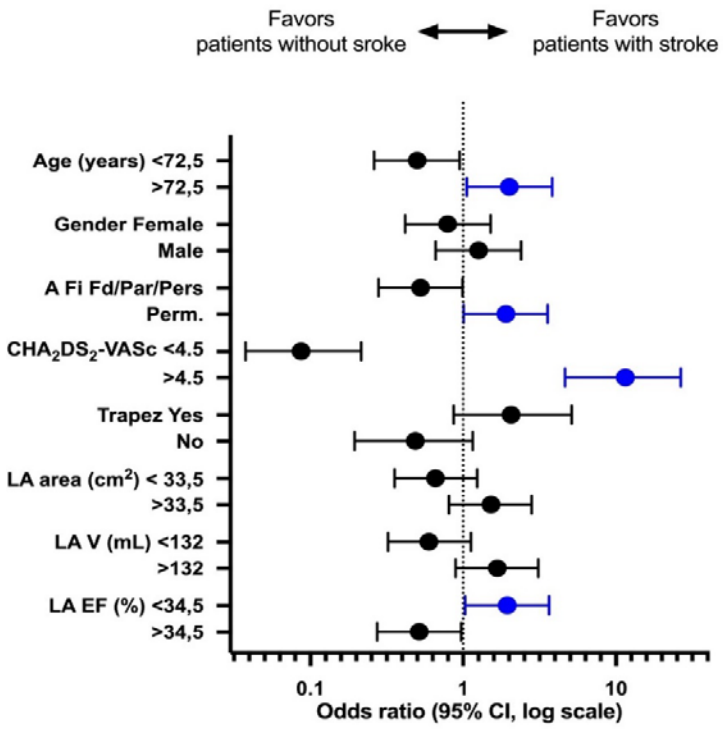

Figure 5. Odds ratio and its reciprocal. CI= confidence interval. AFi-atrial fibrillation. Fd/Parox/Pers-Firstdiagnosed/Paroxysmal/Persistent. LA-left atrium. V-volume (ml). EF-ejection fraction. Blue color-P <0.05.

Discussions

One of the most common arrythmias found in clinical practice is represented by atrial fibrillation, with a prevalence of approximately 2%-4% in general population [12].

Because in many cases patients are asymptomatic, atrial fibrillation remains undiagnosed until the appearance of complications.

Therefore, the total prevalence is probably much higher [13].

Atrial remodeling, that consists in electrical and structural remodeling, is considered to be the substrate of atrial fibrillation [14].

Previous studies have shown that left atrium dimensions are related to electrical remodeling and that in many cases it has an asymmetrical shape, also known as trapezoidal shape, defined by a transverse dimension smaller than a basal dimension, that is caused by the atrialization of pulmonary veins [15,16]

Structural remodeling of the left atrium consists in architectural changes, at macro-but also microscopic levels, changes that are caused by non-modifiable factors as genetics or age, as well as those modifiable factors such as congestive heart failure, hypertension, obesity, ischemia, obstructive sleep apnea, valvular heart disease and inflammation [17].

The majority of these factors can be found in CHA_2DS_2-VASc score, that is widely used to stratify thromboembolic risk in patients with atrial fibrillation, and several studies suggested that this score is associated with left atrial remodeling [18-24]

Therefore, not only we can use this score when we are facing a patient with diagnosed atrial fibrillation, but we could also use this as a predictor for future development of this arrythmia.

For example, Aksoy et al. [25] in a prospective study that included 696 patients with ST-segment elevation myocardial infarction, knowing that atrial fibrillation is the most common type of supraventricular arrythmia following this event, have shown that CHA_2DS_2-VASc score predicted new-onset atrial fibrillation and it was significantly higher in this group of patients [25].

Congestive heart failure, one of the components of this score, is commonly associated with elevated left ventricular filling pressure.

The burden caused by diastolic dysfunction on the left atrium walls, eventually leads to a larger volume of the atrium [26].

And as we already know, left atrium enlargement is strongly associated with atrial fibrillation onset.

Furthermore, hypertension is the most prevalent factor for atrial fibrillation, and it is associated with cardiac hypertrophy and atrial

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dilation, which are directly proportional to its severity.

If it remains untreated, as time passes, hypertension leads to cell apoptosis, scarring and fibrosis of the atrium.

In addition, electrical remodeling occurs, expressed through a slower atrial conduction, a higher refractory period [17] and a prolongation in P-wave duration on electrocardiogram.

Also, patients with hypertension have increased levels of angiotensin II, that generates interstitial fibrosis in cardiac muscle [14].

Another CHA_2DS_2-VASc component is age, that is a non-modifiable factor for atrial remodeling.

As the Framingham study shows, the incidence of atrial fibrillation increases with aging.

It is known that this process leads to uncoupling connections between atrial fibers, that eventually result in a higher susceptibility for atrial fibrillation [17].

Prolonged hyperglycemia, caused by insulin resistance or insulin deficiency, depending on which type of diabetes mellitus we are referring to, leads to multiple side effects, including structural remodeling of the cardiac muscle.

It has been shown that this pathological condition is associated with an increased amount of collagen that is stored between the fibers of cardiac muscle, leading to interstitial fibrosis.

In addition, hyperglycemia is also related to a glycation process of proteins and lipids, resulting in advanced glycation end-products.

According to previous studies, these products can contribute to muscle stiffness, through profibrotic signaling and fibroblast proliferation.

If in type 1 diabetes mellitus, insulin therapy can prevent some of these problems, in type 2, which is the most common type, therapy may not be as effective because of insulin resistance.

In many cases, diabetes mellitus is associated with hypertension and obesity, also known as metabolic syndrome.

An important aspect of obesity is that adipose tissue can adhere and infiltrate the myocardium, and as we know, this type of tissue can be a substrate for arrythmias [14].

As previous studies have shown, a greater percentage of strokes occur in patients that are in sinus rhythm, not in atrial fibrillation, as we would expect.

There has been determined that left atrial volume could be a predictor of stroke, not only in patients without a history of atrial fibrillation, but also in those without neurological events [26].

Limitations of the study:

The main limitations of our study are represented by the relatively small group of patients due to the inclusion criteria, patients with ischemic stroke in whom AFi was later diagnosed.

Moreover, the size of the study group showed a trend of thromboembolic risk and not an exhaustive statistic.

For this reason, there is reasonable suspicion regarding the superior significance of the AS remodeling.

Conclusions

Although the CHA_2DS_2-VASc score remains a good factor for predicting the association of atrial fibrillation with ischemic stroke, echocardiographic parameters for the evaluation of the left atrium (for example, decreased EF LA) can be used as new risk factors for predicting the occurrence of ischemic stroke in patients with atrial fibrillation.

Conflict of interests

None to declare.

References

1. Hart RG, Pearce LA, McBride R, Rothbart RM, Asinger RW. Factors associated with ischemic stroke during aspirin therapy in atrial fibrillation: analysis of 2012 participants in the SPAF I-III clinical trials. The Stroke Prevention in Atrial Fibrillation (SPAF) Investigators. Stroke, 1999, 30(6):1223-1229.
2. Kornej J, Börschel CS, Benjamin EJ, Schnabel RB. Epidemiology of Atrial Fibrillation in the 21st Century: Novel Methods and New Insights. Circ Res, 2020, 127(1):4-20.
3. Schnabel RB, Yin X, Gona P, Larson MG, Beiser AS, McManus DD, Newton-Cheh C, Lubitz SA, Magnani JW, Ellinor PT, Seshadri S, Wolf PA, Vasan RS, Benjamin EJ, Levy D. 50 year trends in atrial fibrillation prevalence, incidence, risk factors, and mortality in the Framingham Heart Study: a cohort study. Lancet, 2015, 386(9989):154-162.
4. Benjamin EJ, Muntner P, Alonso A, Bittencourt MS, Callaway CW, Carson AP, Chamberlain AM, Chang AR, Cheng S, Das SR, Delling FN, Djousse L, Elkind MSV, Ferguson JF, Fornage M, Jordan LC, Khan SS, Kissela BM, Knutson KL, Kwan TW, Lackland DT, Lewis TT, Lichtman JH, Longenecker CT, Loop MS, Lutsey PL, Martin SS, Matsushita K, Moran AE, Mussolino ME, O'Flaherty M, Pandey A, Perak AM, Rosamond WD, Roth GA, Sampson UKA, Satou GM, Schroeder EB, Shah SH, Spartano NL, Stokes A, Tirschwell DL, Tsao CW, Turakhia MP, VanWagner LB, Wilkins JT, Wong SS, Virani SS; American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart Disease and Stroke Statistics-2019 Update: A Report from the American Heart Association. Circulation, 2019, 139(10):e56-e528.

5. Lloyd-Jones DM, Wang TJ, Leip EP, Larson MG, Levy D, Vasan RS, D'Agostino RB, Massaro JM, Beiser A, Wolf PA, Benjamin EJ. Lifetime risk for development of atrial fibrillation: the Framingham Heart Study. Circulation, 2004, 110(9):1042-1046.
6. Mou L, Norby FL, Chen LY, O'Neal WT, Lewis TT, Loehr LR, Soliman EZ, Alonso A. Lifetime Risk of Atrial Fibrillation by Race and Socioeconomic Status: ARIC Study (Atherosclerosis Risk in Communities). Circ Arrhythm Electrophysiol, 2018, 11(7):e006350.
7. Miyasaka Y, Barnes ME, Gersh BJ, Cha SS, Bailey KR, Abhayaratna WP, Seward JB, Tsang TS. Secular trends in incidence of atrial fibrillation in Olmsted County, Minnesota, 1980 to 2000, and implications on the projections for future prevalence. Circulation, 2006, 114(2):119-125.
8. Krijthe BP, Kunst A, Benjamin EJ, Lip GY, Franco OH, Hofman A, Witteman JC, Stricker BH, Heeringa J. Projections on the number of individuals with atrial fibrillation in the European Union, from 2000 to 2060. Eur Heart J, 2013, 34(35):2746-2751.
9. Chiang CE, Wang KL, Lip GY. Stroke prevention in atrial fibrillation: an Asian perspective. *Thromb Haemost*, 2014, 111(5):789-797.
10. Essa H, Hill AM, Lip GYH. Atrial Fibrillation and Stroke. *Card Electrophysiol Clin*, 2021, 13(1):243-255.
11. Okumura K, Tomita H, Nakai M, Kodani E, Akao M, Suzuki S, Hayashi K, Sawano M, Goya M, Yamashita T, Fukuda K, Ogawa H, Tsuda T, Isobe M, Toyoda K, Miyamoto Y, Miyata H, Okamura T, Sasahara Y; J-RISK AF Research Group. Risk Factors Associated with Ischemic Stroke in Japanese Patients With Nonvalvular Atrial Fibrillation. *JAMA Netw Open*, 2020, 3(4):e202881.
12. Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomström-Lundqvist C, Boriani G, Castella M, Dan GA, Dilaveris PE, Fauchier L, Filippatos G, Kalman JM, La Meir M, Lane DA, Lebeau JP, Lettino M, Lip GYH, Pinto FJ, Thomas GN, Valgimigli M, Van Gelder IC, Van Putte BP, Watkins CL; ESC Scientific Document Group. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. Eur Heart J, 2021, 42(5):373-498.
13. Turakhia MP, Shafrin J, Bognar K, Trocio J, Abdulsattar Y, Wiederkehr D, Goldman DP. Estimated prevalence of undiagnosed atrial fibrillation in the United States. PLoS One, 2018, 13(4):e0195088.
14. Jansen HJ, Bohne LJ, Gillis AM, Rose RA. Atrial remodeling and atrial fibrillation in acquired forms of cardiovascular disease. Heart Rhythm O2, 2020, 1(2):147-159.
15. Cozma D, Popescu BA, Lighezan D, Lucian P, Mornos C, Ginghina C, Dragulescu SI. Left atrial remodeling: assessment of size and shape to detect vulnerability to atrial fibrillation. Pacing Clin Electrophysiol, 2007, 30 Suppl 1:S147-50.
16. Floria M, Blommaert D, Lacrosse M, Ambarus V, Dormal F, Dabiri Abkenari L, Jamart J, Rezus C, Cozma D, De Roy L. Assessment of left atrial shape and volume in structural remodeling secondary to atrial fibrillation. J Interv Card Electrophysiol, 2009, 25(3):167-170.
17. Pathak R, Lau DH, Mahajan R, Sanders P. Structural and Functional Remodeling of the Left Atrium: Clinical and Therapeutic Implications for Atrial Fibrillation. J Atr Fibrillation, 2013, 6(4):986.
18. Thomas L, Abhayaratna WP. Left Atrial Reverse Remodeling: Mechanisms, Evaluation, and Clinical Significance. JACC Cardiovasc Imaging, 2017, 10(1):65-77.
19. Li Y, Ding W, Wang H, Song N, Lin L, Wang Z, Zhong M, Zhang Y, Zhang W. Relationship of CHA2DS2-VASc and CHADS2 score to left atrial remodeling detected by velocity vector imaging in patients with atrial fibrillation. PLoS One, 2013, 8(10):e77653.
20. Vitali F, Serenelli M, Airaksinen J, Pavasini R, Tomaszuk-Kazberuk A, Mlodawska E, Jaakkola S, Balla C, Falsetti L, Tarquinio N, Ferrari R, Squeri A, Campo G, Bertini M. CHA2DS2-VASc score predicts atrial fibrillation recurrence after cardioversion: Systematic review and individual patient pooled meta-analysis. Clin Cardiol, 2019, 42(3):358-364.
21. Vatan MB, Yılmaz S, Ağaç MT, Çakar MA, Erkan H, Aksoy M, Demirtas S, Varım C, Akdemir R, Gündüz H. Relationship between CHA2DS2-VASc score and atrial electromechanical function in patients with paroxysmal atrial fibrillation: A pilot study. J Cardiol, 2015, 66(5):382-387.
22. Park JH, Joung B, Son NH, Shim JM, Lee MH, Hwang C, Pak HN. The electroanatomical remodelling of the left atrium is related to CHADS2/CHA2DS2VASc score and events of stroke in patients with atrial fibrillation. Europace, 2011, 13(11):1541-1549.
23. Tsai CF, Huang PS, Chen JJ, Chang SN, Chiu FC, Lin TT, Lai LP, Hwang JJ, Tsai CT. Correlation Between CHA_2DS_2-VASc Score and Left Atrial Size in Patients With Atrial Fibrillation: A More Than 15-Year Prospective Follow-Up Study. Front Cardiovasc Med, 2021, 8:653405.
24. Allessie M, Ausma J, Schotten U. Electrical, contractile and structural remodeling during atrial fibrillation. Cardiovasc Res, 2002, 54(2):230-246.
25. Aksoy F, Baş HA, Bağcı A, Oskay T. The CHA2DS2-VASc score for predicting atrial fibrillation in patients presenting with ST elevation myocardial infarction: prospective observational study. Sao Paulo Med J, 2019, 137(3):248-254.
26. Abhayaratna WP, Seward JB, Appleton CP, Douglas PS, Oh JK, Tajik AJ, Tsang TS. Left atrial size: physiologic determinants and clinical applications. J Am Coll Cardiol, 2006, 47(12):2357-2363.

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