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# **PhD THESIS**

**- A B S T R A C T -**

**CHA2DS2VASc VS REMODELLING THE SHAPE AND  
VOLUME OF THE LEFT ATRIUM IN PATIENTS WITH  
ATRIAL FIBRILLATION**

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## INTRODUCTION

Atrial fibrillation, the most common adult arrhythmia, is a huge burden on patients, clinicians, and worldwide health systems. The big problem of this arrhythmia is the risk of systemic thromboembolism, especially cerebral thromboembolism, with catastrophic consequences: mortality in one year - 50%, very high rate of permanent motor and cognitive disabilities.

Significant research efforts and resources are being directed toward gathering extensive knowledge on the mechanisms behind atrial fibrillation, its natural course, and efficient medical treatments, and new data is being developed and published on frequently. The intricate nature of atrial fibrillation requires a multifactorial, holistic, and multidisciplinary approach to managing patients with this particular arrhythmia, as well as a proactive role in collaboration with doctors.

In 10% of ischemic strokes, non-valvular atrial fibrillation (NVAf) is detected retroactively. Milder, or even asymptomatic forms of NVAf have shown high mortality, thrombotic risk and deterioration of cognitive function. The current guidelines for the diagnosis and treatment of AF contain “grey areas”, such as the one related to anticoagulant treatment in men with CHA<sub>2</sub>DS<sub>2</sub>-VASc score 1 and women with score 2. Moreover, parameters such as renal function, patient weight or left atrium remodelling are missing from the recommended guidelines scores. Vulnerable categories of patients including the elderly population, high hemorrhagic risk patients or patients with newly diagnosed paroxysmal episodes of atrial high rate at device interrogation are at risk of underestimating the thrombotic risk.

From all of the risk stratification models the CHA<sub>2</sub>DS<sub>2</sub>-VASc score is the most widely utilised stroke risk score. In patients with CHA<sub>2</sub>DS<sub>2</sub>-VASc score = 0 or (1 in females) no anticoagulation is recommended according to the European Society of Cardiology (ESC) guidelines. The risk stratification stroke scores are designed to be simple and practical, but these risks score such CHA<sub>2</sub>DS<sub>2</sub>-VASc score do not incorporate parameters that are known to predict high thrombo-embolic risk, such as echocardiographic parameters including LA volume and the trapezoidal form of the LA, biochemical (inflammation status, Troponin and NT-proBNP), or coagulation parameters. The integration of the echocardiography parameters to the CHA<sub>2</sub>DS<sub>2</sub>-VASc score may improve risk stratification of AF patients.

Atrial fibrillation is not a benign clinical entity and poses a significant risk of ischemic-thromboembolic stroke, heart failure, cardiovascular and overall mortality.

An increase in the LA volume defines the anatomical remodeling of the LA. The echocardiographic measurement/parameters including LA volume, ejection fraction, etc. and speckle tracking echocardiography has the ability to detect LA remodeling associated with AF. The studies have shown that anatomical and functional LA remodeling is independently and

strongly associated with AF. The most accurate parameter reflecting the anatomical remodelling of the LA has been demonstrated to be the LA volume.

The European Society of Cardiology has developed guidelines for the management of atrial fibrillation that require the use of the CHA2DS2-VASc score as a prognostic model for stroke in patients with atrial fibrillation.

Unfortunately, until now, the relationship between the systemic thromboembolic accident and remodeling / inflammation of the left atrium is not considered a parameter of the risk computer. According to the latest ESC guideline, including EHRA, only the CHA2DS2-VASc score is evaluated for the prophylaxis of systemic thromboembolism by high-performance oral anticoagulation, respectively from score 2 in men and score 3 in women.

Given that atrial fibrillation is at least as significantly related to systemic inflammatory status, platelet activation, and direct evidence of left atrial dilation / remodelling, this could be proposed as an improvement in risk assessment, in addition to assessing the CHA2DS2-VASc score. Moreover, in the current ESC guideline, the methodology of echocardiographic measurement of the left atrium, only in volume, not in geometry, is incomplete and often leads to inaccurate conclusions.

The purpose of this research project is to provide an improvement in the management /treatment of patients with atrial fibrillation by studying not only the remodeling of the shape and volume of the left atrium but also the endothelial-systemic inflammation, parameters that are not currently used to calculate the risk of systemic embolism (excluding the CHA2DS2-VASc score).

After an introduction to the concept of atrial remodeling, ways to evaluate left atrium remodeling systems will be approached: shape, linear dimensions, area and volume. Starting from the evaluation indications in the guides and the insufficient characterization of the left atrium, the concept of deformed trapezoidal shape and the relationship with the possibility of calculating the volume of the left atrium using the cone trunk formula, and not the rotating ellipsoid will be described.

Another objective of the doctoral study project is to establish the additional information provided by the remodeling of the left atrium in the decision of long-term oral anticoagulation in patients with a low CHA2DS2-VASc score, knowing the need to stratify the risk of stroke in individuals with atrial fibrillation and even those with sinus rhythm.

Paroxysmal atrial fibrillation, from unsustainable to sustained, is analyzed as an electrophysiological concept, not only from an electrical point of view, but also in relation to geometric changes that can be observed through associated imaging data.

We will not limit ourselves to the new measurements proposed in the evaluation of LA dimensions and geometry, but we will associate these data with the feasible and affordable

evaluation of the markers of systemic inflammation - ESR (erythrocyte sedimentation rate), CRP-hs, and fibrinogen.

Of course, the prognostic data will be confirmed by following at least 2 years of enrolled patients and by careful monitoring of anticoagulation, regardless of the type of anticoagulant prescribed - VKA or NOAC.

### **Aim and objectives**

The aim of the thesis is to analyze the relationship between the CHA2DS2-VASc score, LAV and geometry, and inflammation in patients with atrial fibrillation for the purpose of predicting their additive value to improve prognosis and understanding of therapy strategy.

#### **Main objectives:**

- to analyze the LA geometry in patients with atrial fibrillation
- the assessment of LAV
- to examine the bidirectional correlation between CHA2DS2-VASc score and LA volume and shape in studied patients.
- to analyze the relation between CHA2DS2-VASc score and inflammation in selected patients.

#### **Secondary objectives:**

- to evaluate the correlation between LA function and dilatation in patients with concomitant AF and HF
- to analyze the potential relationship between LA remodeling and inflammation
- to examine the correlation between CHA2DS2-VASc score and LA function, size and shape.
- STROKE relation to studied parameters.

The research was carried out within the Timisoara Institute of Cardiovascular and Heart Diseases and the Municipal Emergency Clinical Hospital, Internal Medicine Department for the period January 2021- december 2022. This is a prospective and observational study, and consecutive hospitalized patients were included for different reasons. Usual clinical, biochemical, and echocardiographic examinations were performed on the patients.

#### **Inclusion criteria:**

The included patients were in atrial fibrillation (paroxymal, persistent, or permanent) at the time of evaluation or had a documented history of atrial fibrillation. The biological evaluation focused on the evaluation of inflammatory markers: ESR, CRP-hs, and fibrinogen.

Atrial fibrillation was documented by 12-lead electrocardiogram, rhythm strip, or Holter electrocardiogram. The duration of atrial fibrillation lasted at least 30 seconds.

**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 oedema 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/1.73m<sup>2</sup> or patients in hemodialysis program.

**Methods**

**Basic data**

Baseline data included:

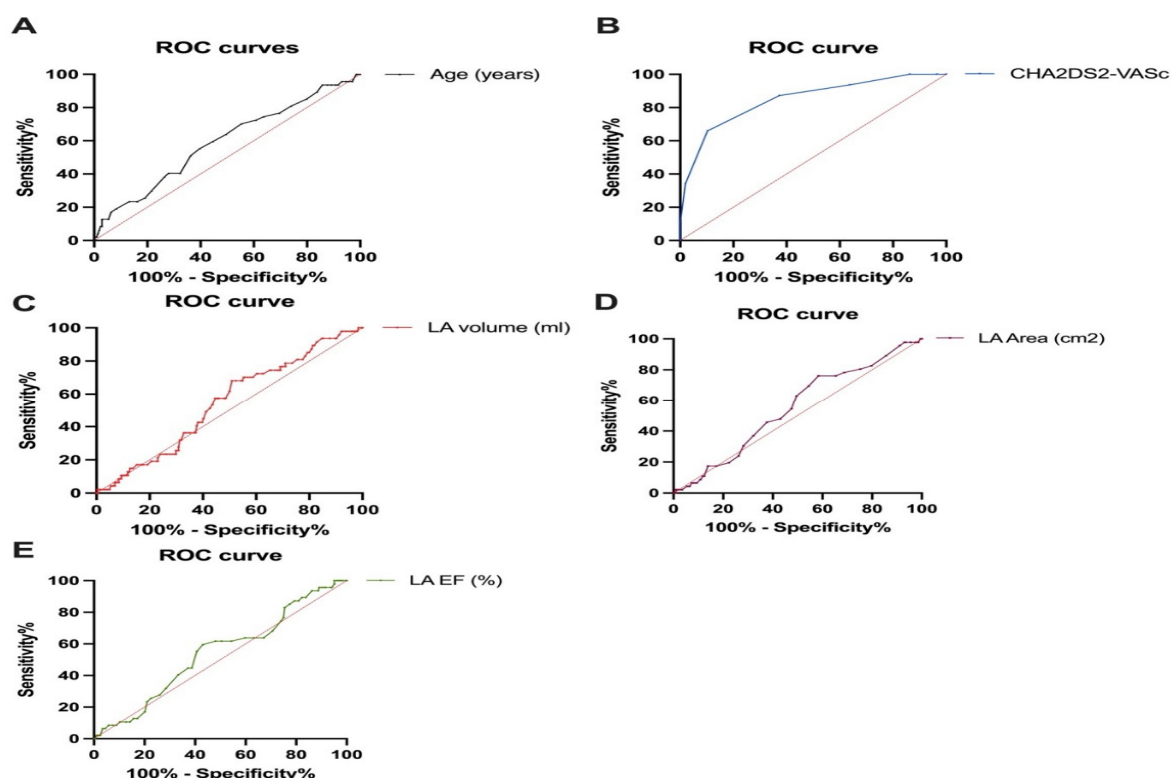
- age/gender/sex
- standard 12-lead ECG with scrolling speed of 25mm/s at admission
- dynamic 12-lead ECG were analyzed.
- category/classification of AF
- presence of following comorbidities:
  - arterial hypertension  
Stages: stage1: uncomplicated,  
stage2: asymptomatic disease, stage3: established disease,  
Grading high normal:130-139/85-89mmHg, Grade1:140-159/90-99mmHg, Grade2:160-179/100-109mmHg, Grade3: >180/110mmHg),
  - coronary heart disease
  - chronic kidney disease CKD stages/GFR (ml/min/1.73m<sup>2</sup>: G1: GFR>90, G2:60-89, G3a:45-59, G3b:30-44, G4:15-29, G5:<15),

- diabetes mellitus,
- heart failure: HFrEF (EF<40%), HFmrEF (EF:40-49%), HFpEF (EF>50%),
- dyslipidemia (hypercholesterolemia, hypertriglyceridemia),
- pulmonary disease (bronchial asthma, pulmonary emphysema, chronic obstructive pulmonary disease),
- peripheral artery disease,
- stroke, TIA, ESUS (embolic stroke of undetermined source) at interrogation
- CHA2DS2-VASc score
- HAS-BLED score
- Complete basic echocardiographic data: LVEF, LVEDV, Simpson EF, LAV, LA surface, TR velocity
- general biological data: lipid status, blood count (CBC), Creatinine, Urea, GFR, Uric acid, blood glucose, liver enzyme (alanine transaminase (ALT) and aspartate transaminase (AST))

## Results

A retrospective analysis was conducted, analyzing a total of 251 individuals diagnosed with atrial fibrillation. Out of the total, 47 individuals experienced an ischemic stroke either before, at the time of, or after being diagnosed with atrial fibrillation.

In order to establish the cut-off values, we employed ROC curves and calculated the Area under the ROC curve (AUC).



**Figure 19. 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 CHA2DS2-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 (%).**

The following values were established: 72.5 years for age (AUC=0.5909), 4.5 for CHA2DS2-VASc value (AUC=0.8475), 33.5cm<sup>2</sup> for left atrium (LA) value (AUC=0.5500), 132ml for LA volume (AUC=0.5448), and 34.5% for LA ejection fraction (AUC=0.5415).

Our observation revealed that 61.70% of patients with ischemic stroke were over the age of 72.5, but only 44.61% of those without stroke were in this age group. The odds ratio (OR) was calculated to be 2.001, with a 95% confidence interval (CI) ranging from 1.057 to 3.829. The p-value associated with this finding was 0.0367.

When it comes to the gender of the patients, a slightly higher percentage of women (51.06%) were diagnosed with stroke compared to males (48.94%). However, this difference is not statistically significant (OR=1.263, 95% CI=0.6619 to 2.395, P=0.5164).

The CHA2DS2-VASc score had the most significant statistical influence on stroke, as anticipated. Patients with a CHA2DS2-VASc score of more than 4.5 had a stroke rate of 87.23%, whereas those with a CHA2DS2-VASc score of 34.5% had a stroke rate of just 38.30% (odds ratio = 2.124, 95% confidence interval = 1.121 to 4.068, p-value = 0.0238).

Although there was no statistically significant difference, individuals with a left atrial (LA) volume more than 132ml had a higher proportion (57.45%) of stroke compared to those with a low LA volume (OR=1.676, 95% CI=0.8905 to 3.102, P=0.1443).

Similarly, patients with a left atrial (LA) area more than 33.5cm<sup>2</sup> experienced a higher incidence of stroke compared to individuals with a smaller LA size, but this difference was not statistically significant (odds ratio [OR]=1.519, 95% confidence interval [CI]=0.8076 to 2.808, p=0.2572).

Although the patients with a trapezoid-shaped left atrium had a stroke rate of 85.11%, there was no statistically significant difference seen among them (OR=2.057, 95% CI=0.8673 to 5.128, P=0.1302).

Individuals diagnosed with hypertension had a greater occurrence of inflammation (98.20% vs to 91.67% in those without inflammation), with an odds ratio of 4.970 (95% confidence range 1.326 to 17.94, p = 0.0181).

Heart failure patients had a significantly greater proportion of individuals with an inflammatory condition (85.63% versus 73.81% without inflammation, odds ratio = 2.114, 95% confidence range 1.115 to 4.126, p = 0.0256).

Additionally, it was noted that individuals who had both atrial fibrillation and inflammation had a higher occurrence of ischemic heart disease (83.33% compared to 16.67% in patients without inflammation). The odds ratio was calculated to be 2.992, with a 95% confidence interval ranging from 1.364 to 6.378. The p-value was determined to be 0.0062.

Patients with atrial fibrillation and elevated inflammatory status had a greater incidence of stroke compared to patients without inflammation. The stroke rate was 22.75% in patients with inflammation, whereas it was 10.71% in patients without inflammation. The odds ratio was 2.455, with a 95% confidence range of 1.161 to 5.425. The p-value was 0.0253.

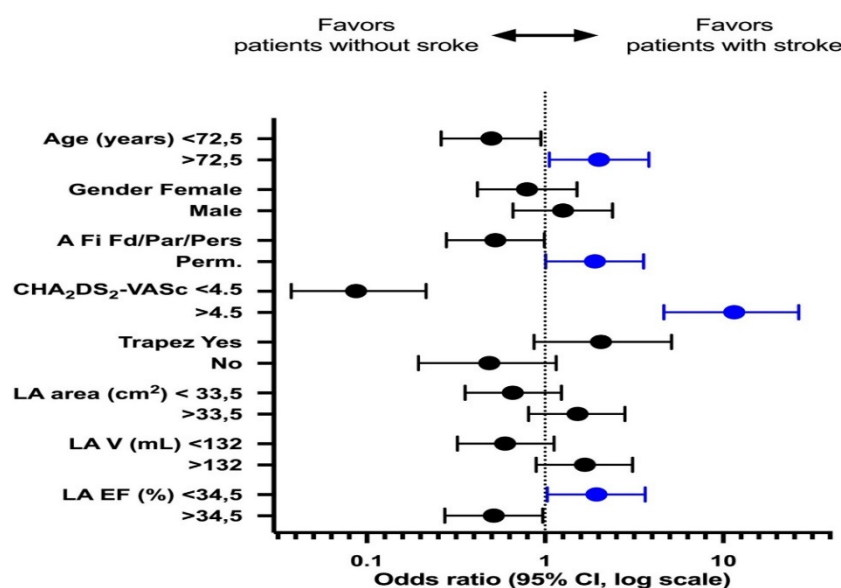


Figure 20. Odds ratio and its reciprocal. CI= confidence interval. AFi-atrial fibrillation. Fd/Parox/PersFirstdiagnosed/Paroxysmal/Persistent. LA-left atrium. V-volume (ml). EF-ejection fraction. Blue color- P <0.05



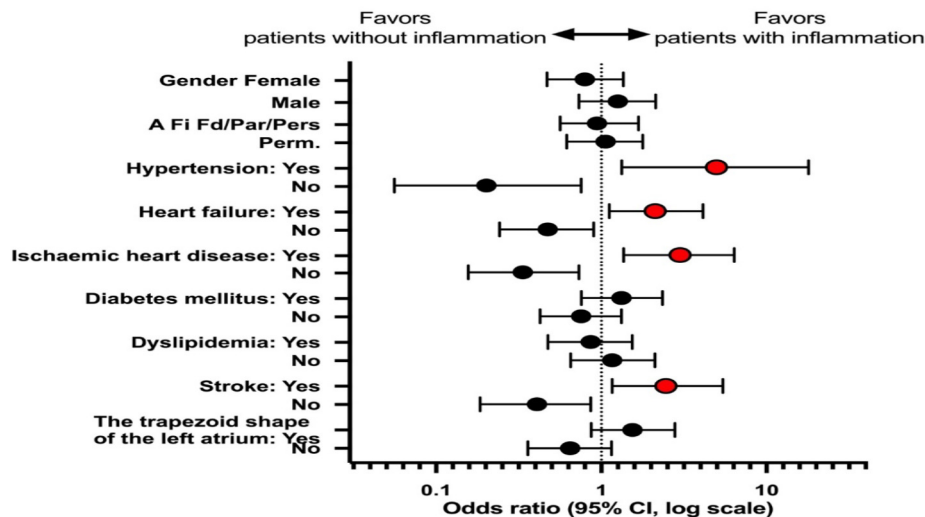


Figure 28. Odds ratio (OR) and its inverse. CI stands for confidence interval. A Fi - atrial fibrillation. Fd - First diagnosed, Parox - Paroxysmal, Pers - Persistent. Red color - P < 0.05.

## Discussion

Atrial fibrillation is the most frequent arrhythmia in clinical practice, affecting 2%-4% of the general population. Retroactively, non-valvular atrial fibrillation (NVAf) is identified in 10% of ischemic strokes. Upon reflection, the European register (EORP-AF) highlights several unexpected elements, despite just 1 year of monitoring. Initially, the seemingly less severe kinds - those without symptoms or just discovered - have the greatest mortality and score for thrombotic complications.

Furthermore, the lack of thrombotic risk evaluation based on renal function (in the CHA2DS2-VASc score) is associated by a consistent decline in renal function, even within the indicated short time period. It is important to consider the decline in cognitive function, which can be caused by both endothelial and implicit hemodynamic mechanisms, as well as repeated micro-embolic events. Additionally, there is a progressive deterioration of the heart's ability to contract, leading to significant impairment in blood flow.

The latest ESC guideline on the diagnosis and treatment of AF provides a more comprehensive approach to managing this arrhythmia. It emphasizes the importance of considering the underlying causes and associated health conditions. The primary focus is not only on extending lifespan but also on improving the overall quality of life. This involves addressing issues such as correcting abnormal heart rhythm and heart rate, optimizing hemodynamic function, motor abilities, and psychological well-being. Additionally, the guideline emphasizes the significance of effectively managing any coexisting health conditions.

Left atrium remodeling should be given particular importance when evaluating the risk of thrombosis. This is because fibrotic atrial cardiomyopathy is associated with embolic strokes of unknown origin, even in individuals without atrial fibrillation. However, it is important to distinguish between left atrium enlargement and LA cardiomyopathy, as AF electroconversion appears to be safe even in individuals with LA dilatation.

LA remodeling refers to the process of making changes to the structure, function, and/or electrical properties of the left atrium in response to factors such as increased pressure or volume, metabolic changes, or electrical stress. The primary disorders that negatively affect the function of the left atrium include heart failure, arterial hypertension, and valvular heart disease.

However, even individuals with frequent premature ventricular contractions still showed evidence of subclinical left atrial remodeling.

According to the LA evaluation guideline, when outlining the boundaries of the left atrium, the point where the pulmonary veins and the LA appendage come together should be left out. The 2019 recommendations mandate the use of LA volume assessment as the optimal method for evaluating LA size. Nevertheless, the precise demarcation of the boundary between the left atrium (LA) and pulmonary veins (PV) remains undefined, and the significance of the PV antrum in influencing the expansion of the LA has not been acknowledged or thoroughly examined. Thus, there is a significant area that has not been thoroughly investigated, which involves redefining a more exact echocardiographic assessment of the left atrium (LA). Although echocardiography is a cost-effective and readily available method, it falls short in terms of accuracy compared to the gold standard of computed tomography (CT) or magnetic resonance imaging (MRI). Patients having AF ablation can be readily assessed using direct comparative assessment, which involves the use of 3D CT evaluation of the left atrium (LA) and a comprehensive echocardiographic evaluation of the LA.

The structural remodeling of the left atrium (LA) is an intricate manifestation of an underlying condition known as atrial cardiomyopathy. This condition is linked to a higher likelihood of developing atrial fibrillation (AF), even in persons who are otherwise in good health. Precise visualization of LA structural remodeling offers valuable prognostic insights and has an impact on treatment decisions. It may also be relevant to consider in the decision-making process for anticoagulation, particularly for specific patient populations.

The inflammatory state is a crucial factor in the development of several cardiovascular conditions, such as atrial fibrillation. Recent findings indicate that inflammation plays a role in the process of left atrial remodeling, emphasizing the complex relationship between inflammation and cardiovascular well-being.

Inflammation facilitates the stimulation and penetration of immune cells, such as macrophages and lymphocytes, into the tissue of the left atrium. These immune cells secrete pro-inflammatory cytokines, chemokines, and growth factors, which initiate a series of molecular and cellular processes that result in fibrosis, hypertrophy, and electrical remodeling of the atrial tissue. These modifications contribute to irregularities in the structure of the atria and instability in electrical activity, which increases the likelihood of developing and sustaining atrial fibrillation (AF).

Inflammatory mediators, including C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF- $\alpha$ ), have been linked to left atrial enlargement and fibrosis, which are both indicators of left atrial remodeling.

Additionally, the presence of inflammation-induced oxidative stress and the generation of reactive oxygen species (ROS) might stimulate the activation of fibroblasts and the accumulation of collagen in the atrial tissue, hence exacerbating left atrial remodeling.

To summarize, inflammation is a vital factor in the development and progression of atrial fibrillation since it significantly contributes to the pathophysiology of left atrial remodeling. The stimulation of immune cells and the secretion of pro-inflammatory substances launch a series of events that result in alterations in the structure and function of the left atrium. Gaining a comprehensive understanding of how inflammation and left atrial remodeling interact might offer valuable knowledge on new treatment targets and techniques for preventing and managing atrial fibrillation (AF). Additional investigation is necessary to clarify the fundamental processes and assess the effectiveness of therapies that target inflammation in reducing left atrial remodeling and enhancing cardiovascular outcomes.

The uncertainty about the involvement of developing and less fully studied stroke risk factors, as previously mentioned, persists. Nevertheless, by conducting thorough clinical investigations, we can get a more profound comprehension and improve our capacity to develop more personalized treatments for preventing primary and subsequent strokes. A crucial area for future investigation should focus on evaluating the effects of left atrium remodeling, inflammation, and genetics on anticoagulation therapy for atrial fibrillation in a specific subgroup of elderly patients aged 80 or above. This is important because the demographics and risk factors in this age group of stroke patients differ significantly.

Due to the absence of symptoms in many situations, atrial fibrillation often goes untreated until issues arise. Hence, it is quite likely that the overall prevalence is far greater. Atrial remodeling, encompassing both electrical and structural changes, is regarded as the underlying cause of atrial fibrillation.

Prior research has indicated a correlation between the size of the left atrium and electrical changes in the heart. It has been observed that the left atrium often has an asymmetrical shape, referred to as a trapezoidal shape, where the transverse dimension is

smaller than the basal dimension. This shape is a result of the pulmonary veins becoming part of the atrium.

Structural remodeling of the left atrium involves alterations in its architecture at both macroscopic and microscopic levels. These changes are influenced by factors that cannot be modified, such as genetics and age, as well as modifiable factors including congestive heart failure, hypertension, obesity, ischemia, obstructive sleep apnea, valvular heart disease, and inflammation.

The bulk of these characteristics are included in the CHA<sub>2</sub>DS<sub>2</sub>-VASc score, which is often used to assess the risk of thromboembolism in patients with atrial fibrillation. Multiple studies have indicated that this score is linked to left atrial remodeling. Hence, this score can be utilized not only in the management of patients already diagnosed with atrial fibrillation, but also as a prognostic indicator for the likelihood of developing this arrhythmia in the future.

Aksoy et al. conducted a prospective study involving 696 patients with ST-segment elevation myocardial infarction. They found that atrial fibrillation, the most common type of supraventricular arrhythmia after this event, was predicted by the CHA<sub>2</sub>DS<sub>2</sub>-VASc score. Furthermore, the score was significantly higher in patients who developed new-onset atrial fibrillation. Congestive heart failure, a component of this score, is frequently linked with increased left ventricular filling pressure. Diastolic dysfunction exerts pressure on the walls of the left atrium, resulting in an increase in atrial volume.

Left atrium enlargement is closely linked to the beginning of atrial fibrillation, as we are previously aware. In addition, hypertension is the most common cause contributing to atrial fibrillation. It is also linked to cardiac hypertrophy and atrial dilatation, with the severity of both conditions being directly related to the severity of hypertension. Untreated hypertension can result in cell death, as well as scarring and fibrosis of the atrium over time.

Regarding C-reactive protein (CRP) levels, it is important to note that this inflammatory biomarker is non-specific in nature and has a high level of repeatability. The liver is the primary site of synthesis. It is largely generated there as a reaction to inflammatory cytokines. Studies discussed in the literature suggest that persons with a diagnosis of atrial fibrillation had higher levels of C-reactive protein (CRP) in their blood compared to those without a history of atrial fibrillation. Furthermore, those with ongoing atrial fibrillation exhibit elevated levels of CRP in contrast to those with intermittent AF.

Higher levels of circulating C-reactive protein (CRP) appeared to be associated with the recurrence of atrial fibrillation after electrical cardioversion and catheter ablation. Our study demonstrates a direct relationship between levels of C-reactive protein (CRP) and risk factors for stroke, such as diabetes and hypertension, in individuals with atrial fibrillation.

And yet, newer medical reports have shown that diabetes mellitus is not a major predictor of atrial fibrillation risk (see HARMS<sub>2</sub>-AF score). The most current approach remains

the association of individually determined genetic risk with clinical risk (e.g. CHARGE-AF) and biological markers (especially NT proBNP). This multimodal approach is much more effective for AF prediction, and thrombogenic in particular, but is still less accessible in many communities.

Nevertheless, AF remains a complex condition that is not fully understood, both in terms of how patients perceive it and how medical professionals approach preventive anticoagulation. Additionally, there are still high rates of illness and death associated with AF, particularly among individuals over the age of 70. Failure to comply, adhere to, and endure with these drastic therapies might result in a bitter failure. Therefore, providing education to health-care networks, particularly patients, and implementing intra-family supervision of medicine administration and avoidance of life-threatening behaviors, result in significant improvements in both the number of lives saved and overall quality of life.

Additional study is required to authenticate and assess the effectiveness of the new thrombotic risk ratings in various patient groups. Furthermore, continuous progress in precision medicine and the incorporation of genetic and biomarker data may enhance and individualize the evaluation of thrombotic risk in AF. This is a dilemma for any contemporary healthcare system.

And even if it were no longer a dilemma, it remains a financial and technical problem, especially in communities less helped by efficient health systems. We continue to rely on screening and prevention methods as cheap and simple as possible to apply, even in the detection of paucisymptomatic AF, but AF remains a segment of severe pathology, with often adverse consequences, which requires a strictly individualized, technological and competent approach, not cheap, expeditious and impersonal.

Our study has demonstrated that people with atrial fibrillation and an elevated inflammatory state also have additional coexisting conditions, including hypertension, heart failure, ischemic heart disease, chronic kidney disease, and stroke. These data indicate a new direction for research focused on understanding the molecular mechanisms behind the findings in our study. Additionally, they suggest the need to assess the effectiveness of new anti-inflammatory drugs in improving the pathological conditions associated with our study and reducing the burden of atrial fibrillation.

While the CHA2DS2-VASc score is still a reliable predictor of the link between atrial fibrillation and ischemic stroke, new risk factors such as echocardiographic parameters, specifically decreased EF LA, can also be used to predict the occurrence of ischemic stroke in patients with atrial fibrillation even if it means a laborious activity and an extra effort for treating doctors and health systems.

The main limitation of our studies is related to the size of the studied groups, in order to be able to develop an exhaustive statistic. However, despite this claim, many studies that required strong risk scores, such as ATRIA, ABC, GARFIELD-AF, used smaller batches.

## **CONCLUSIONS**

1. Nonvalvular AF is a severe condition, despite an often-inconclusive symptomatology. Unfortunately, with age, its presence is more and more frequent. The increase in life expectancy has caused in recent decades a marked increase in the incidence and prevalence of this arrhythmia.
2. The consequence of this pathology is most often neglected. Unfortunately, apart from consequences such as impairment of general condition due to globally altered hemodynamics, decreased cardiac systolic function, cognitive decline, progressive regression of renal function, etc., the most severe consequence of unsupervised and uncontrolled AF is the increased incidence of systemic thrombo-embolic accidents, namely cerebral ones, with catastrophic consequences, both in terms of fatality and severe impairment of motor and cognitive function, with very high social and family price.
3. All cerebral and systemic ischemic thrombo-embolic risk assessments have been followed, in recent decades, the most recognized and recommended by guides, the applied risk score being CHA2DS2-VASc, score based on history and comorbidities installed in patients with any form of nonvalvular atrial fibrillation, according to the current definition of EHRA.
4. It has been affirmed, in recent years, the need for a more complex assessment of the anticoagulation need and for a better forecast of the evolution of patients with nonvalvular AF, beyond the ischemic (CHA2DS2-VASc) and hemorrhagic (HAS-BLED) scores, considering both the direct and iatrogenic pathological risk, respectively the safety of the anticoagulant treatments undertaken.
5. The models of anticoagulation – indirect – Antivitamin K, direct – activated antifactors II and X, lately – in the study – antifactor XI – have shown, in most of them, certain advantages, but also undesirable effects, major, sometimes fatal bleeding.
6. For this reason, finding new decision makers on oral anticoagulation requirements is really essential.
7. We proposed, in our studies, the implementation of morphology and function criteria of the left atrium, the one involved in the phenomenon of parietal thrombosis and embolic source for systemic circulation.

8. Both the remodeling of the left atrium, with its physiological structure of rotating ovoid that undergoes under certain circumstances a transformation into a cone trunk (trapezoid at 2D echocardiographic observation), and the increase in LA volume, along with affecting its ejection fraction, most often neglected in the evaluation of the patient in any form of AF, appeared to have a major impact on the incidence of thrombotic accidents.
9. Moreover, endothelial dysfunction – systemic inflammation, and implicitly endothelial inflammation causes increased thrombogenicity of the atrial endothelium, respectively increased susceptibility to atrial thrombosis in altered hemodynamics of LA.
10. Our paper presents certain evidence regarding the left atrial morphological and functional component in increasing the risk of systemic thrombus-embolism, and, in particular, cerebral, which constitutes the importance and value of this research.
11. Thus, we propose a routine evaluation of these pathological components for the superior assessment of thrombo-embolic risk, beyond the CHA2DS2-VASc risk score mechanically applied and exclusively for the anticoagulation decision, a therapeutic intervention as necessary as it is accompanied by iatrogenic risk, in case of unjustified use.
12. We believe that this contribution is not without importance in a life-saving therapeutic decision and unequivocal quality of life. Of course, complementing the current decision coordinated by a single risk score requires an amplified and specialized activity, correctly said individualized, all the more necessary in a radical therapeutic decision, such as indefinite anticoagulation.