

Development of predictive models for the recurrence of atrial fibrillation after interventional treatment, based on the quantification of calcium score and other imaging parameters

Atrial fibrillation (AF) is the most common supraventricular arrhythmia, which, due to heart failure and associated thromboembolic complications, presents high rates of mortality and morbidity worldwide. Catheter ablation aims to achieve electrical isolation of tissue with arrhythmic potential within the pulmonary veins (PV).

In recent years, radiofrequency ablation and cryoablation treatments had known a significant evolution in the field of interventional cardiology. These techniques have become increasingly used for the management of AF. The recurrence of AF after ablation remains a significant problem, and is affecting between 20 and 40% of patients. The evaluation of treatment success is mainly based on the absence of AF-specific symptoms during the post-interventional follow-up period.

Therefore, this doctoral thesis was aimed to achieve the following main objectives within the two sub-studies:

- Evaluation the role of imaging parameters determined by echocardiography and cardiac computed tomography angiography (CCTA) in predicting the risk of arrhythmia recurrence after ablation in paroxysmal and persistent AF, over a one-year follow-up period.
- Investigating the relationship between the volume of the left atrial (LA) determined by CCTA and different cardiovascular risk factors and imaging parameters, as well as examining the correlation between the degree of LA dilatation and the frequency of emergency hospitalizations. In addition, we assessed the rate of AF recurrence after ablation treatment, as well as the impact of invasive treatment on emergency hospitalizations for heart failure and arrhythmia.

Accurate determination of LA size and function can provide essential information to clinicians regarding the prognosis and appropriate treatment of AF. Multimodal imaging allows for a comprehensive assessment of LA anatomy and function in AF patients. The most accurate and reliable method for determining LA volume is CCTA. The results have demonstrated that both LA volume (LA vol) and indexed LA volume (iLA vol) have a significant correlation with AF recurrence in both univariate and multivariate analyses. These findings are supported by similar studies, in which LA vol was identified as an independent predictor of AF recurrence. ROC curve analysis revealed a significant cut-off value of iLA vol $\geq 51.1 \text{ mm}^3/\text{m}^2$ (AUC=0.82, $p < 0.001$) for identifying patients at high risk of recurrence after PVI.

Following the assessment of LA dilation, it has been demonstrated that LA volume has a significant impact on the number of emergency hospitalizations, primarily manifested by left ventricular failure, which increases proportionally with the degree of atrial dilation. The hospitalization rate was 30% for reduced LA volumes but can increase up to 76% in cases of large atrial volumes. Another important observation was that in cases of moderate dilated LA, pharmacological cardioversion was mainly used for rhythm control, but in patients with highly dilated LA, electrical cardioversion was required to a greater extent. This procedure can significantly prolong the hospitalization time for patients, thereby increasing treatment costs.

Patients with AF recurrence after ablation exhibited significantly larger iRA vol and iBA vol. Subjects with an increased iRA vol, with a cut-off value of $\geq 35.4 \text{ mm}^3/\text{m}^2$, were more susceptible to AF recurrence (AUC=0.83, $p < 0.001$). The described results indicated that, in addition to the pathophysiological mechanisms within the LA and PV that lead to the onset or recurrence of AF, there are other triggering factors and substrates for the arrhythmia, and indexed RA volume plays a significant role in AF recurrence. There is a bidirectional pathophysiological mechanism between LA dilation and AF, as follows: fibrosis at the level of LA

leads to the appearance of areas with slow conduction and altered repolarization, which can serve as sources of atrial rotors, shifting the focus of initiation and persistence of AF from the VP to the atrium.

Several pathophysiological mechanisms linking coronary atherosclerosis and the risk of developing AF have been described, but the exact pathogenic processes through which coronary atherosclerosis leads to AF development are not fully understood. Elevated coronary calcium score (CS) correlates well with subclinical inflammatory processes that may lead to myocardial damage and atrial inflammation. Our data have highlighted that elevated CS levels and moderate stenosis, predominantly located at the level of the right coronary artery (which is responsible for the vascularization of the atria in most patients), are associated with LA enlargement and the onset of atrial recurrence after ablation. Multivariable analysis has shown that stenosis at the RCA level can be an independent factor in arrhythmia recurrence.

Epicardial adipose tissue (EAT) can affect cardiac structure and function through mechanisms that includes: fibro-fatty infiltration of atrial myocardium, increased intramyocardial lipid content, and secretion of pro-inflammatory and pro-fibrotic cytokines, ultimately leading to LA dilation. Our findings have highlighted that localized EAT at the LA level significantly correlates with LA enlargement ($p=0.006$), supporting the hypothesis that EAT may play a role in structural changes and the pathophysiology of atrial remodeling. Following the analysis between EAT and AF recurrence, it was demonstrated that total EAT was significantly associated with AF recurrence (AUC=0.706, 95% CI: 0.56–0.82, $p=0.006$). However, in multivariable analysis, the above finding was not identified as an independent predictive factor, unlike regional LA- and RA-EAT, which appear to be independent factors for arrhythmia recurrence. ROC analysis demonstrated that regional EAT at both the LA and BA levels has significant prognostic value in AF recurrence, with an AUC of 0.855 (95% CI: 0.72–0.93) for LA-EAT ($p<0.0001$) and an AUC of 0.827 (95% CI: 0.69–0.91) for RA-EAT ($p<0.0001$).

Based on the data from this study, we can observe that ablation treatment has significantly improved the quality of life for patients and reduced the number of emergency hospitalizations, regardless of LA volume. This indicates that, despite the higher recurrence rate observed in cases with larger LA volumes, ablation treatment plays a crucial role in the management and improvement of the condition for this category of patients.

Conclusions

Patients with increased indexed atrial volumes, a larger diameter of the LA, and elevated CS before ablation are at significantly higher risk of AF recurrence at the 12-months follow-up after ablation. Thus, iLA vol, iRA vol, and iBA vol can be used as predictive factors for AF recurrence following the ablation procedure. These measurements are relevant regardless of age, cardiovascular risk factors, the type of AF, and comorbidities.

The assessment of EAT and coronary atherosclerosis through non-invasive cardiac imaging, particularly based on CCTA, can play a significant role in determining prognosis and selecting patients for ablation treatment. LA dilation can be influenced by factors such as right atrial volume, LA-EAT, and stenoses located at the level of the RCA. Therefore, when evaluating the size and function of the LA, these non-invasive multimodal parameters should be taken into account in the pre-procedural assessment of patients undergoing ablation.

Ablation treatment can contribute to improving the quality of life for patients and reduce the frequency of emergency hospitalizations, thereby having a favorable impact on the long-term management of patients with AF. The use of pre-procedural imaging assessment and non-invasive parameters can lead to a more precise selection of patients and improve the prognosis regarding AF recurrence after ablation. Therefore, these findings can bring both medical and economic benefits by enhancing treatment outcomes and reducing the need for emergency hospitalizations.