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ȘCOALA DOCTORALĂ DE
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DOCTORAL THESIS

DETECTION OF CORONARY LESIONS WITH A HIGH RISK OF ATRIAL FIBRILLATION USING ADVANCED ARTIFICIAL INTELLIGENCE TECHNIQUES

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- ABSTRACT -

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1. INTRODUCTION

Cardiovascular diseases (CVD) represent the leading cause of morbidity and mortality worldwide, posing a major public health challenge. According to recent epidemiological data, they account for a substantial number of premature deaths and place a considerable burden on healthcare systems, both through the direct costs of medical care and the indirect socio-economic impact resulting from reduced productivity in the working population. The increasing prevalence of associated risk factors, such as obesity, arterial hypertension, diabetes mellitus, dyslipidemia, and physical inactivity, amplifies the magnitude of this problem and reinforces the status of CVD as one of the most pressing global public health priorities.

Atrial fibrillation (AF) is often described as the “silent epidemic” of the 21st century due to its rising prevalence and significant impact on public health. Its insidious progression, frequently characterized by asymptomatic or minimally symptomatic forms, leads to diagnostic delays, thereby increasing the risk of severe complications, such as stroke and heart failure.

Over the past decade, accumulating evidence has implicated inflammation in the pathogenesis of AF. Inflammation appears to play a key role both in the initiation and perpetuation of the arrhythmia, as well as in the development of the associated prothrombotic state. Epicardial adipose tissue (EAT) is now recognized not merely as an energy reservoir, but as a metabolically and endocrinologically active organ with a direct role in cardiovascular pathophysiology. Periatrial and pericoronary adipose tissue exhibit distinct inflammatory profiles, with direct implications for cardiac structure and function. For the pericoronary compartment, advances in computed tomography (CCTA) imaging have enabled the quantification of inflammation through the Fat Attenuation Index (FAI). This radiomic marker reflects tissue composition and the degree of inflammatory activation, offering superior predictive value compared to traditional anatomical markers.

CCTA provides the opportunity to integrate imaging biomarkers of inflammation and metabolism through quantification of epicardial adipose tissue volume and FAI analysis. Characterizing the quality of EAT through CT density analysis (FAI) allows for the assessment of local inflammation and the risk of major cardiovascular events.

2. STUDY OBJECTIVES

My doctoral research was designed to investigate the interaction between coronary inflammation, epicardial adipose tissue (EAT), and atrial remodeling in relation to atrial fibrillation (AF). Accordingly, the primary objectives of this doctoral work were:

- **To explore the relationship between pericoronary adipose tissue (PCAT) inflammation**, quantified by the Fat Attenuation Index (FAI) and FAI Score, and the presence of AF in patients undergoing CCTA for suspected coronary artery disease (CAD).
- **To evaluate regional variations in coronary inflammation** in patients with AF, with particular emphasis on differences between the left and right coronary circulation.
- **To quantify EAT volumes**—total, peri-atrial, and bi-atrial—as well as atrial volumetric parameters (LAV and LAVI), and to analyze their association with AF.
- **To investigate the combined predictive performance of CCTA-derived imaging biomarkers** (EAT volume, LAVI, FAI Score, and CAD-RADS classification) for AF risk stratification.
- **To integrate modern AI-assisted risk assessment tools**, such as the CaRi-Heart® score and syngo.via Frontier® modules, in order to validate their applicability in non-invasive prediction of arrhythmic risk.

This study was based on the hypothesis that inflammatory changes in adipose tissue adjacent to the coronary arteries, together with structural atrial remodeling, synergistically contribute to AF susceptibility, and that these processes can be detected using advanced CCTA-derived imaging biomarkers.

3. MATERIALS AND METHODS

The research was designed as a **retrospective, observational, single-center study**, conducted at the Advanced Multimodal Cardiac Imaging Research Center, Romania. A total of **203 patients** who underwent **128-slice CCTA** were included, encompassing **over 600 coronary segments** (LAD, LCX, RCA) available for **pericoronary FAI analysis**.

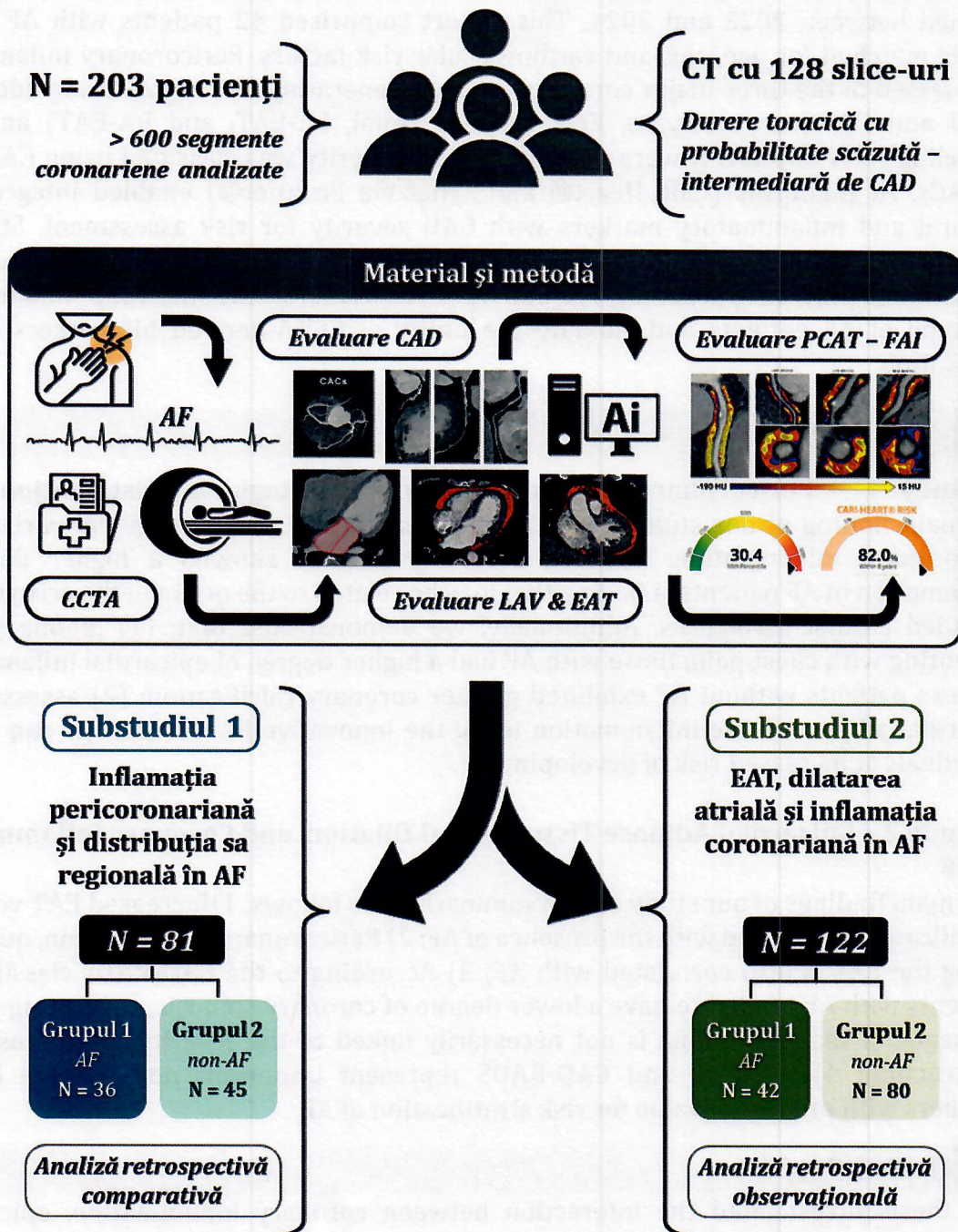


Figure 10. Patient selection process and organization of the two sub-studies included in the analysis. **Substudy1:** Pericoronary inflammation and its regional distribution in AF, including 81 patients (Group 1: AF, n = 36; Group 2: non-AF, n = 45), retrospective comparative analysis. **Substudy2:** Relationship between EAT, atrial dilation, and coronary inflammation in AF, including 122 patients (Group 1: AF, n = 42; Group 2: non-AF, n = 80), retrospective observational analysis.

Substudy 1 was a retrospective comparative analysis including 81 patients (mean age 64.7 ± 7.8 years) examined between 2021 and 2023. Of these, 36 had documented AF, while 45 served as controls. For each patient, PCAT was assessed in the three major coronary arteries (LAD, LCX, RCA), resulting in the analysis of 243 coronary segments. The main biomarkers were FAI-HU and the FAI Score, adjusted for age and sex. Regional variations in coronary inflammation were investigated, with a particular focus on the left coronary circulation. Additional parameters analyzed included CACs, coronary stenosis severity, echocardiographic left atrial size, and the CaRi-Heart® Risk score. The objective was to identify a distinct pattern of pericoronary inflammation in AF patients and potential regional differences associated with the arrhythmogenic substrate.

Substudy 2 was a retrospective observational analysis including 122 patients examined between 2022 and 2024. This cohort comprised 42 patients with AF and 80 controls matched for age, sex, and cardiovascular risk factors. Pericoronary inflammation was assessed in the three major coronary arteries, generating 366 segments. In addition to FAI-HU and FAI Score analyses, EAT volumes (total, LA-EAT, and BA-EAT) and atrial remodeling (LAV and LAVI) were quantified. CAD severity was classified using CAD-RADS and CACs. AI platforms (CaRi-Heart® and syngo.via Frontier®) enabled integration of structural and inflammatory markers with CAD severity for risk assessment. Statistical analyses included group comparisons, regression models, and ROC analyses to evaluate diagnostic and predictive accuracy. The aim was to characterize the structural-inflammatory phenotype of AF patients and validate the utility of CCTA-derived biomarkers for risk stratification.

4. RESULTS

Substudy 1 - Pericoronary Inflammation and Its Regional Distribution in AF

The main finding of our study was that patients with AF exhibit regional variations in pericoronary inflammation. The left coronary arteries showed a higher degree of inflammation in AF patients, a finding that may be related to the origin of the arrhythmia in left-sided cardiac structures. Additionally, we demonstrated that: (1) among patients presenting with chest pain, those with AF had a higher degree of epicardial inflammation, whereas patients without AF exhibited greater coronary calcification; (2) assessment of epicardial adipose tissue inflammation using the innovative FAI technology can identify individuals at increased risk of developing AF.

Substudy 2 - Epicardial Adipose Tissue, Atrial Dilatation, and Coronary Inflammation in AF

The main findings of our study can be summarized as follows: 1) Increased EAT volume is significantly associated with the presence of AF; 2) Pericoronary inflammation, quantified using the FAI, is also correlated with AF; 3) According to the CAD-RADS classification, patients with AF tended to have a lower degree of coronary stenosis, suggesting that the presence of the arrhythmia is not necessarily linked to the severity of atherosclerotic obstruction; 4) EAT, FAI, and CAD-RADS represent important non-invasive imaging markers with predictive value for risk stratification of AF.

5. DISCUSSION

This thesis investigated the interaction between coronary inflammation, epicardial adipose tissue (EAT), and atrial remodeling in relation to atrial fibrillation (AF). Across the two substudies, it was demonstrated that patients with AF exhibit a distinct coronary and epicardial inflammatory profile, characterized by increased PCAT-FAI values and larger EAT volumes, along with marked left atrial dilation, compared to individuals without AF.

By integrating multimodal imaging data, CCTA becomes a tool capable not only of diagnosing obstructive coronary artery disease but also of identifying patients at high risk for AF, stroke, or major coronary events. The simultaneous assessment of atrial structural parameters (LAV, LAVI), atherosclerotic scores (CAC, CAD-RADS), imaging-derived inflammatory markers (FAI), and AI-generated data enables the development of personalized therapeutic strategies aimed at both prevention and treatment. In an era where cardiovascular medicine is increasingly moving toward personalized and predictive approaches, the results of this thesis support the integration of advanced imaging biomarkers into routine clinical practice.

The findings of this thesis highlight the crucial importance of integrating CCTA-derived imaging parameters for a comprehensive cardiovascular risk assessment, with particular emphasis on the relationship between CAD and AF. Over the past two decades, CCTA has evolved from a method primarily used for diagnosing coronary obstructions to a multimodal tool that allows analysis of atherosclerotic plaques, assessment of EAT, quantification of LAV and LAVI, and characterization of perivascular inflammation via FAI. This transition represents a major advance in cardiovascular imaging, extending its applicability from simple morphology to a functional and biological characterization of cardiovascular disease.

6. CONCLUSIONS

The results presented in this thesis demonstrate that the integrated use of CCTA imaging, combined with structural, functional, and inflammatory markers and supported by AI platforms, represents a promising strategy for the comprehensive assessment of patients with coronary artery disease and atrial fibrillation. This multimodal approach has the potential to redefine the understanding and management of cardiovascular risk, contributing to more precise, efficient, and personalized patient care.

7. ORIGINALITY OF THE THESIS

A major novelty of this research lies in the use of AI-based analysis platforms, such as CaRi-Heart® and syngo.via Frontier®. These tools facilitated the automated and standardized processing of imaging data, reducing inter- and intra-observer variability and enhancing the reproducibility of results. Furthermore, AI enabled the simultaneous integration of structural, inflammatory, and clinical markers into a unified predictive model capable of providing personalized estimates of cardiovascular risk. This approach aligns with current trends in medicine, where AI algorithms play an increasingly important role in early diagnosis, risk stratification, and guidance of individualized therapeutic decisions.