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Programvezető: Dr. Merkely Béla, egyetemi tanár

Témavezető: Dr. Szegedi Nándor, egyetemi docens

Integrated Optimization of Atrial Fibrillation Catheter Ablation: Advances in Pre-Procedural Imaging, Determinants of Lesion Formation, Anatomical Predictors of Recurrence, and Procedural Efficiency

PhD thesis

Gábor Orbán, MD

Semmelweis University Doctoral College
Cardiovascular Medicine and Research Division

Supervisor: Nándor Szegedi, MD, PhD

Official reviewers: Károly Altdorfer, MD, PhD
Dorottya Debreceni, MD, PhD

Head of the Complex Examination Committee: Alán Alpár, MD, PhD, DSc

Members of the Complex Examination Committee:
László Cervenák, MD, PhD
Mihály Kovács, MD, PhD

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LIST OF ABBREVIATIONS

AF: atrial fibrillation

AAD: antiarrhythmic drug

ACS: acute coronary syndrome

ACT: activated clotting time

AHRE: atrial high-rate episode

AI: artificial intelligence

AV: atrioventricular

BB: beta-blocker

BMI: body mass index

BNP: B-type natriuretic peptide

BOOST: Bright-blood and black-BlOOd phase SensiTive

bpm: beat per minute

CA: catheter ablation

CAD: coronary artery disease

CCB: calcium channel blocker

CCS: chronic coronary syndrome

CF: contact force

CI: confidence interval

CMR: cardiac magnetic resonance

CPAP: continuous positive airway pressure

CT: computed tomography

CV: cardioversion

CTA: computed tomography angiography

ECG: electrocardiogram

ECV: electrical cardioversion

eGFR: estimated glomerular filtration rate

ESC: European Society of Cardiology

HF: heart failure

HFrEF: heart failure with reduced ejection fraction

HR: hazard ratio

ID: impedance drop

INR: international normalized ratio

iLAV: indexed left atrial volume

IQR: interquartile range

LA: left atrium *or* left atrial

LAA: left atrial appendage

LAEF: left atrial ejection fraction

LAV: left atrial volume

LAVi: body surface area-indexed left atrial volume

LA SV: left atrial stroke volume

LA SVi: body surface area-indexed left atrial stroke volume

LGE: late gadolinium enhancement

LIPV: left inferior pulmonary vein

LSPV: left superior pulmonary vein

LVEF: left ventricular ejection fraction

NOAC: novel oral anticoagulant

NT-proBNP: N-terminal pro-B-type natriuretic peptide

OAC: oral anticoagulation

OR: operating room

OSA: obstructive sleep apnea

PFA: pulsed-field ablation

PV: pulmonary vein

PVI: pulmonary vein isolation

RCT: randomized controlled trial

RF: radiofrequency

RFCA: radiofrequency catheter ablation

RIPV: right inferior pulmonary vein

RSPV: right superior pulmonary vein

SCAF: subclinical atrial fibrillation

SD: standard deviation

SEC: spontaneous echo contrast

NSR: normal sinus rhythm

TEE: transesophageal echocardiography

TIA: transient ischemic attack

vHPSD: very high-power, short-duration *or* very high-power short duration

VKA: vitamin K antagonist

1. INTRODUCTION

1.1. Atrial fibrillation in general

1.1.1. Definition

Atrial fibrillation (AF) is a supraventricular tachyarrhythmia characterized by high-frequency (400-600 beats per minute), uncoordinated, and chaotic electrical activation of the atria, leading to the cessation or severe reduction of organized atrial systole (1). On electrocardiogram (ECG), AF is identified by the absence of P-waves and, in the absence of complete atrioventricular (AV) block, irregular R-R intervals. Clinical AF refers to symptomatic or asymptomatic AF that is unequivocally confirmed on ECG, either by a 12-lead recording or other ECG-recording modalities (1). Device-detected atrial high-rate episodes and subclinical AF are increasingly recognized through implanted and wearable monitoring devices but require careful interpretation and confirmation of the recorded rhythm (1-3).

1.1.2. Epidemiology and clinical significance

AF is the most common sustained cardiac arrhythmia worldwide among adults (2, 4). Globally, AF has reached epidemic proportions: the latest Global Burden of Disease analyses estimate that roughly 4.5 million new cases occur each year and about 340 000 deaths are attributable to it, with hypertension identified as the leading contributory risk factor (5). The 2024 European Society of Cardiology (ESC) guideline underscores the accelerating global burden of AF: in 2019 some 59.7 million people were already living with the arrhythmia, and incident cases are doubling every few decades (1). Demographic modelling for the European Union projects the number of adults older than 55 years with AF to rise from 8.8 million in 2010 to approximately 17.9 million by 2060, while annual new diagnoses are expected to increase from ~1.2 million in 2010 to ~2.6 million by 2030 (6, 7). Contemporary ESC Atlas data place Hungary's age-standardized AF prevalence at about 1.3% in men (1 340 per 100 000) and 0.8% in women (831 per 100 000), translating into more than 120 000 affected individuals, with national registry analyses indicating that roughly 0.4-0.5% of adults receive a new AF diagnosis each year (1).

AF is associated with substantial clinical burden, primarily through its strong links to stroke and heart failure (HF). Among all cardiovascular conditions, AF is one of the most powerful risk factors for ischemic stroke, increasing the risk 3- to 5-fold, and accounting for approximately 20% of all strokes (8). The annual stroke risk rises steeply with age, from 1.5% in patients aged 50–59 years to >23% in those over 80 years, even in the absence of additional risk factors (9). In parallel, AF and HF frequently coexist and share bidirectional pathophysiological mechanisms. Although their causal relationship is complex and not fully elucidated, AF can directly compromise cardiac output via shortened diastolic filling time, loss of atrial systole, elevated ventricular filling pressures, and sustained tachycardia leading to myocardial dysfunction – a phenomenon referred to as tachycardia-induced cardiomyopathy (10). The presence of AF in HF patients worsens prognosis, increases hospitalization risk, and complicates management strategies (11).

1.1.3. Pathomechanism

In simplified terms, and according to our current understanding, three factors contribute to AF initiation and maintenance.

1.1.3.1. Triggers of AF

The initiation of AF typically requires focal ectopic activity, most often originating from myocardial sleeves extending into the pulmonary veins (PVs) (12). These triggers may involve abnormal automaticity or triggered activity, particularly under conditions of calcium-handling disturbances such as delayed after-depolarizations, which are common in electrically remodelled atrial tissue (13). In the presence of a vulnerable substrate (as described in the next subsection), these ectopic impulses can initiate and sustain AF episodes.

1.1.3.2. Atrial substrate: electrical and structural remodelling

Once initiated, AF is perpetuated by an underlying atrial substrate characterized by electrophysiological and structural changes, recently defined as “atrial cardiomyopathy” (14). Electrical remodelling emerges in response to rapid and irregular atrial activation, leading to shortening of the action potential duration and the effective refractory period, which promotes reentry circuits and enhances susceptibility to abnormal impulse formation. Additionally, impaired calcium cycling increases the likelihood of delayed after-depolarizations, further sustaining arrhythmia (13, 15).

Structural remodelling is dominated by fibroblast-to-myofibroblast transdifferentiation and excessive deposition of collagen-rich extracellular matrix (16). Although the newly formed scar initially provides mechanical stability to the atrial wall and prevents dilation, progressive fibrosis eventually leads to atrial stiffening, disruption of gap junction continuity, and conduction slowing or block, all of which contribute to the development of a spatially heterogeneous, arrhythmogenic substrate (16, 17).

1.1.3.3. Systemic conditions promoting AF

In addition to local atrial changes, several cardiovascular and extracardiac conditions contribute to atrial remodelling and thus promote the onset and maintenance of AF. These include chronic hypertension, valvular heart disease (e.g., mitral stenosis), endocrine imbalance (hyper- or hypothyroidism), obesity, diabetes, and respiratory conditions such as obstructive sleep apnea (OSA) (18, 19). These systemic contributors to AF will be discussed in greater detail in later sections.

1.1.3.4. Pathophysiology of stroke in AF

Given the well-established association between AF and thromboembolic events and considering that ischemic stroke represents the most serious and feared complication of AF, it is essential to briefly outline the underlying pathophysiological mechanisms. Stroke in the context of AF primarily results from a prothrombotic state driven by atrial dysfunction. Hypokinesia leads to reduced endothelial shear stress, which promotes the expression of plasminogen activator inhibitors (17). In addition, ischemia induced inflammation enhances endothelial adhesion molecule expression and promotes endothelial detachment, resulting in tissue factor release into the bloodstream (20). AF itself further exacerbates these mechanisms, supporting its progressive nature and the need for timely intervention (13).

1.1.4. Etiology

Table 1 lists the principal factors that trigger AF, organized into two categories: cardiovascular determinants and non-cardiovascular contributors (1, 14). Aging and male gender are the most significant non-modifiable risk factors for AF. Ethnicity also plays a role in the likelihood of developing AF, with Caucasians being more susceptible than African Americans (21).

Table 1. Etiology of atrial fibrillation. Cardiovascular and non-cardiovascular factors and conditions associated with atrial fibrillation are listed. Compiled from published literature and guideline sources (1, 14).

Cardiovascular	**Non-cardiovascular**
Hypertension	Hyperthyroidism
Coronary artery disease	Obstructive sleep apnea
Myocardial infarction	Obesity
Valvular heart disease	Diabetes
Heart failure	Metabolic syndrome
Cardiomyopathies	Pulmonary diseases
Myocarditis and pericarditis	Pheochromocytoma
Pulmonary artery hypertension	Systemic infections/inflammation
Congenital heart disease	Excess alcohol intake
History of cardiac surgery	Drugs
Brady-tachy syndrome	Electrolyte imbalance
Systemic disease affecting the heart (amyloidosis, metastatic heart tumors)	Chronic kidney disease
Peripheral arterial disease	Physical inactivity
Primary arrhythmia syndromes and accessory pathways	Genetic predisposition / Genetic factors

1.1.5. Classification

Over time, several different AF classifications have emerged and been used; however, traditionally, the five types of AF are distinguished based on occurrence, duration of AF

episodes, and cessation of episodes (22). The types include first diagnosed, paroxysmal, persistent, long-standing persistent, and permanent AF.

When both paroxysmal and persistent AF occur, classification is based on the more frequent type. Although AF type classification is clinically useful, data from continuous long-term ECG monitoring with implantable devices demonstrate that these clinical labels often poorly reflect the actual temporal persistence of the arrhythmia (23-25). In addition, another classification criterion is based on valvular involvement and comorbidities. Valvular AF refers to AF in patients with moderate or severe mitral stenosis or those with mechanical heart valves in any position. Non-valvular AF encompasses all other AF cases. It is also important to note that this classification significantly impacts a key aspect of AF management - anticoagulation. However, recently, this valve-based categorization has been criticized due to potential inaccuracies (2, 26). Other classification systems focus on the presence or absence of patient symptoms, while some attempt categorization based on potential underlying causes of AF, such as postoperative AF; however, clinical evidence regarding the use of these classification systems is currently lacking (22, 27, 28).

1.2. Symptoms and clinical presentation

The symptoms of AF can vary widely, often influenced by the ventricular rate, with AF typically presenting as tachycardia but occasionally manifesting as bradycardia. Common AF-related symptoms include palpitations, shortness of breath, and fatigue, but patients may also complain of chest tightness or pain, dizziness, fainting, sweating, and nausea (29-33). Individuals with paroxysmal AF report more symptoms (80%) compared to those with persistent and permanent AF (76% and 51%), with the latter groups more commonly experiencing shortness of breath, fatigue, and exercise intolerance (34). It is important to note that the symptoms of AF patients are often related to undiagnosed or inadequately treated comorbidities (e.g., HF) (35). Nevertheless, it is crucial to emphasize that a significant proportion of AF cases can be asymptomatic, termed "silent atrial fibrillation", the prevalence of which has greatly increased in recent decades thanks to implantable cardiac electronic devices and wearable smart devices for monitoring heart rhythm (36, 37).

1.3. Diagnosis

Clinical suspicion of AF may arise during physical examination from the irregular and inconsistent nature of the pulse, which is subsequently confirmed by characteristic ECG findings. A standard 12-lead ECG typically records 10 seconds of rhythm, whereas on single- or multiple-lead monitoring devices, episodes lasting ≥30 seconds have generally been regarded as sufficient for diagnosis (1). However, this threshold is largely consensus-based and supported by limited evidence (1). Diagnostic documentation should demonstrate the absence of identifiable P-waves and, in the absence of complete AV block, an irregular beat-to-beat R–R interval (3, 38, 39).

1.4. Treatment

The effective and successful treatment of patients with AF ideally requires an interdisciplinary care team that conducts integrated patient care in a coordinated and personalized manner (40). The treatment plan initially put together may require significant changes over time due to the emergence of new risk factors or symptoms, the progression of the disease, and the introduction of new treatment options (2). The AF-CARE pathway, introduced in the 2024 ESC Guidelines, builds on the five-step management scheme introduced in the 2016 guidelines and the ABC pathway proposed in 2020. It gives more emphasis to early risk factor and comorbidity management, but stroke prevention with anticoagulation remains the key priority in AF care. Robust data indicate that systematic management of comorbidities improves symptoms, reduces thromboembolic risk, enhances survival, and increases the effectiveness of rhythm and rate control. These principles are embedded within the broader AF CARE model of the most recent guideline, which provides structured algorithms for first diagnosed, paroxysmal, persistent, and permanent AF, covering all key aspects of care, including anticoagulation, symptom control, comorbidity management, and ongoing reassessment (1, 41).

1.4.1. Comorbidities

When managing AF, it is crucial to recognize that cardiovascular risk factors, comorbidities, and lifestyle habits not only increase the risk of AF onset but also contribute to its progression (35).

Obesity, associated with a higher body mass index (BMI), increases the risk of AF, along with AF-bound complications like stroke and worsening comorbidities (42, 43). Intensive weight loss and comprehensive cardiovascular risk management lowers AF recurrence risk and reduces symptoms (44, 45). Obesity also hampers the long-term success of rhythm control methods like catheter ablation (CA), as several studies have shown a significantly higher risk of AF recurrence in obese patients post-ablation (44, 46, 47). Alcohol consumption and smoking can also affect the onset and recurrence of AF (48-50). Moderate physical activity reduces AF risk, but there is an increased incidence among elite athletes (51-53).

Hypertension, a key risk factor for AF, is associated with a 1.7-fold increased risk of developing AF compared to normotensive individuals (54, 55). Additionally, hypertension exacerbates AF complications and increases the risk of stroke (56). Treating high blood pressure is essential for patients with AF, and studies suggest aiming for systolic/diastolic values below 130/80 mm Hg in the AF patient population (57, 58).

AF and HF exhibit a bidirectional relationship and frequently co-occur. HF is not only significant due to its coexistence but also represents a clear thromboembolic risk factor (59). Moreover, the presence of HF substantially influences therapeutic decision-making, particularly the choice of rate control agents if this strategy is pursued. Detailed considerations regarding AF rate control, including drug selection in patients with concomitant HF, are discussed in Section 1.4.3.

In patients with AF and concomitant HF, amiodarone is considered the safest antiarrhythmic drug (AAD) (1, 60). Moreover, CA of AF has been shown to improve not only symptoms, exercise capacity, quality of life, and left ventricular ejection fraction (LVEF), but also overall mortality in patients with AF and HF (61). The CASTLE-AF randomized controlled trial (RCT) enrolled patients with symptomatic paroxysmal or persistent AF and HF (New York Heart Association class II-IV, LVEF ≤35%) who had an implanted defibrillator. They were randomly assigned to receive either CA or medical therapy (rate or rhythm control), both on top of guideline-directed HF treatment. The trial showed that CA significantly reduced the composite endpoint of death from any cause or hospitalization for worsening HF compared to medical therapy alone (62). Detailed discussion of AF rhythm control strategies is provided in Section 1.4.4.

During acute coronary syndrome (ACS), the occurrence of AF varies widely, ranging from 2-23%, and the risk of AF may increase by 60-77% in patients who have experienced myocardial infarction (63, 64). AF alone can also increase the risk of ST-elevation myocardial infarction and non-ST-elevation ACS (65, 66), with 10-15% of AF patients undergoing percutaneous coronary intervention for coronary artery disease (CAD) (67).

Moreover, chronic coronary syndrome (CCS) is also associated with significant risk of AF. In the CLARIFY registry of stable outpatients with CCS, atrial fibrillation or flutter was present in 7.1% of patients at baseline. During five years of follow-up, new-onset AF occurred in 5% and was strongly associated with increased risk of cardiovascular death, non-fatal myocardial infarction, stroke, HF hospitalization, and major bleeding (68). Therefore, optimal management of CCS is also crucial for the prevention of AF and the care of patients with existing AF.

Diabetes, especially in younger patients, is an independent risk factor for AF, with at least twice the prevalence of AF among diabetic patients (69, 70). The severity of microvascular complications in diabetes may correlate with AF incidence (71, 72), and both type 1 and type 2 diabetes can increase the risk of stroke (73, 74).

Furthermore, OSA is also a well-established risk factor for AF (75, 76). A prospective analysis found that approximately 50% of AF patients had OSA (76), and OSA may reduce the effectiveness of AADs, electrical cardioversion (ECV), and CA in AF patients (77). Continuous positive airway pressure (CPAP) therapy is the most appropriate treatment for OSA, which can have a favorable impact on the recurrence of AF (78, 79). Other studies and recent meta-analyses have shown that optimal CPAP treatment improves rhythm control in AF patients and reduces the frequency of recurrence after ablation (80, 81).

1.4.2. Anticoagulation

AF increases the risk of ischemic stroke roughly five-fold, yet this excess hazard is heterogeneous and modulated by individual comorbidities and biological markers (82). Contemporary risk stratification therefore moves beyond solely assessing traditional clinical factors. Although the CHA_2DS_2-VASc score remains a convenient guide (83), the 2024 ESC guidelines now recommend using the simplified CHA_2DS_2-VA score, which excludes the sex category (1). Oral anticoagulation (OAC) is indicated at ≥2 points, a

threshold generally corresponding to an annual thromboembolic risk of ≥2%, and should be considered at 1 point, where the estimated annual risk is approximately 1-2%, after shared decision-making (14). Clinicians are urged to incorporate additional risk modifiers – e.g., chronic kidney disease (84), malignancy, atrial enlargement, obesity, smoking, ethnicity – and to acknowledge emerging biomarkers [troponin, N-terminal pro-B-type natriuretic peptide (NT-proBNP), growth differentiation factor 15, cystatin C, interleukin-6] that refine residual stroke risk (85, 86). However, while biomarker-guided anticoagulation strategies are still under evaluation, current guidelines recommend using validated clinical risk scores (e.g., CHA_2DS_2-VA) alongside individualized assessment of comorbidities, bleeding risks, and patient preferences. Since absolute stroke risk varies case by case, there is no fixed threshold for initiating anticoagulation; however, most risk models consider an annual stroke risk of approximately 0.6–1.0% sufficient to justify lifelong OAC (1).

Vitamin K antagonists (VKAs) remain an effective option for stroke prevention in AF, with a general INR target of 2.0–3.0 (Class I, Level B). VKAs are to be preferred in the presence of mechanical heart valves and moderate to severe mitral stenosis (87). In patients with mechanical prosthetic valves, higher targets are recommended according to valve type and location: for bileaflet or newer-generation mechanical aortic valves without risk factors, an INR of 2.5 is advised, whereas in the presence of risk factors or in the mitral or tricuspid position the target is 3.0; for older-generation valves, an INR of 3.5 is recommended (1, 88, 89). Under optimal control, VKAs have been shown to reduce the risk of stroke by approximately 64% and all-cause mortality by 26% (90). However, since the recommended INR range is narrow, regular INR monitoring, dose adjustment, and adherence to dietary recommendations affecting vitamin K intake are crucial, and both efficacy and safety correlate strongly with the proportion of time in therapeutic range (78). Studies show that if TTR exceeds ≈70%, warfarin can reach the efficacy profile of novel oral anticoagulants (NOACs) while maintaining a low bleeding risk (91, 92). The SAMe-TT_2R_2 score helps predict which patients are unlikely to achieve high TTR; in such cases transition to a NOAC is advisable (93).

The 2024 ESC guideline now prefers NOACs (apixaban, dabigatran, edoxaban, rivaroxaban) as first-line therapy in most non-valvular AF, reserving VKAs chiefly for AF patients with mechanical heart valves or moderate-to-severe MS. RCTs demonstrate

that NOACs are noninferior to VKAs in preventing stroke and systemic embolism, and they confer a lower all-cause mortality (94). Compared to VKAs, NOACs significantly reduce the risk of intracranial hemorrhage, as shown in major randomized trials (95-98). However, gastrointestinal bleeding risk varies by agent: rivaroxaban and high-dose dabigatran are associated with increased gastrointestinal bleeding (99, 100), while apixaban has a more favorable profile (94). Large observational cohorts have corroborated these efficacy and safety advantages in everyday practice (101-106).

Antiplatelet agents alone do not provide adequate stroke prevention in AF, and dual antiplatelet therapy carries substantial bleeding risk – particularly in older patients – without sufficient thromboembolic protection in AF patients (107, 108). Consequently, current guidelines do not recommend antiplatelet therapy for stroke prevention in AF.

1.4.3. Rate control

Rate control therapy aims to maintain ventricular rate within a range that alleviates symptoms. The 2024 ESC guideline acknowledges that evidence comparing different rate targets or pharmacological strategies remains limited; a lenient resting heart rate target (<110 bpm) is generally acceptable, while stricter control is typically used in patients with persistent symptoms or concern for tachycardia-induced cardiomyopathy (1, 109-112).

The choice of rate-control therapy should be individualized according to symptoms, left ventricular systolic function, comorbidities, and potential side effects (1).

- **BBs** (e.g., bisoprolol, metoprolol, nebivolol, betaxolol) remain first-line agents for acute and chronic ventricular rate control in AF. Selective BBs are preferred for their efficacy and safety. In patients with heart failure with reduced ejection fraction (HFrEF), BBs are appropriate when clinically stable; during acute decompensation, continuation, dose reduction, or temporary withholding should be individualized according to blood pressure, perfusion, congestion, bradycardia, and the need for inotropic support (1, 113).
- **Non-dihydropyridine CCBs** , such as verapamil and diltiazem, can provide rapid rate control but are considered safe only in patients with preserved LVEF (i.e., LVEF >40%). They are contraindicated in HFrEF because of their negative

inotropic effects and should not be co-administered with BBs due to the risk of clinically significant bradycardia or advanced AV block (1, 114).

- **Digoxin and digitoxin** provide additional rate control, particularly at rest, and are therefore more appropriate as adjunctive agents than as first-line therapy for acute rate control (1). Associations between digoxin use and increased mortality in non-randomized studies are likely attributable to confounding by indication, as these drugs are often prescribed in older, frail patients with advanced HF, chronic kidney disease, or hypotension (115-120). The 2024 ESC guideline recommends initiating digoxin at low maintenance doses and regular monitoring to maintain serum concentrations within the 0.5-0.9 ng/mL range (1).
- In hemodynamically stable patients with HFrEF and rapid AF, rate control can be achieved with **combination therapy** using a BB and digoxin when clinically appropriate (1).
- Permanent pacemaker implantation followed by AV node ablation represents a **non-pharmacological rate control strategy**, generally reserved for patients in whom all pharmacological and catheter-based approaches have failed or are contraindicated. This approach is associated with a low procedural complication rate and favorable long-term outcomes in this selected population (121-123).

1.4.4. Rhythm control

Rhythm control in AF aims to restore and maintain sinus rhythm. These include direct interventions such as ECV, pharmacological cardioversion (CV) using AADs, and CA (discussed in detail in the 1.5. section and subsections). In addition, comprehensive cardiovascular risk modification plays a supportive role by improving long-term rhythm control outcomes (124-126). In hemodynamically unstable AF patients, emergency ECV is the preferred approach. In stable patients, pharmacological CV using AADs or elective hybrid (ECV with AAD) or sole ECV can be attempted (127, 128). For CV of hemodynamically stable AF lasting ≥24 h or of unknown onset, the 2024 ESC guideline mandates either a minimum of 3 weeks of therapeutic OAC or a transesophageal echocardiography (TEE) demonstrating a thrombus-free LAA before the procedure (1). In contrast, hemodynamically unstable patients require immediate ECV without delaying the procedure for pre-procedural anticoagulation or TEE. In all cases, anticoagulation should be started or continued as soon as possible and maintained for at least 4 weeks

after CV, regardless of CHA_2DS_2-VA score (1). In newly diagnosed, hemodynamically stable AF without significant structural or ischemic heart disease, intravenous vernakalant, flecainide, or propafenone are considered first-line agents for pharmacological CV. If structural heart disease is present (e.g., cardiomyopathy, coronary artery disease, or HFrEF), or if these rapid-acting agents are contraindicated, intravenous amiodarone is recommended, although the onset of action may be delayed by several hours (129, 130).

1.5. Catheter Ablation

According to the 2024 ESC guideline on AF, CA has moved to the forefront of rhythm control: it is recommended as a first-line therapy (Class I, Level A) for symptomatic paroxysmal AF, even before any trial of class I or III antiarrhythmic medication, following shared decision-making. For persistent AF, ablation remains strongly recommended (Class I, Level A) once a class I or III drug has proved ineffective or intolerable; however, it may also be considered as an initial option (Class IIb, Level C) in carefully selected patients. This upgrade reflects accumulating evidence that early ablation can secure durable sinus rhythm and better quality of life in appropriately chosen individuals (1).

The gold standard strategy for AF CA is the antral circumferential isolation of the PVs [i.e., pulmonary vein isolation (PVI)], which can be achieved either by point-by-point ablation or with so-called single-shot ablation devices (2, 131, 132).

1.5.1. Cryoablation

Cryoablation and radiofrequency (RF) ablation, the latter of which is discussed in the following subsection, create lesions through thermal energy transfer. Unlike RF ablation, cryoablation induces lesion formation through convective cooling, where a cryocatheter absorbs heat from the surrounding tissue, leading to tissue cooling. This cooling process causes cold-induced cellular damage through two mechanisms. Firstly, it results in direct cellular damage due to freezing, caused by intra- and extracellular ice crystal formation and the accompanying osmotic stress. Secondly, it leads to cold-induced microcirculatory insufficiency, resulting in localized ischemic cell death (133, 134).

The isolation of PVs using cryothermal energy is most commonly performed with the cryoballoon catheter. The procedure is carried out as follows: each PV is selectively cannulated under fluoroscopic guidance, aided by the use of contrast injection. Once proper positioning is achieved, a balloon is inflated at the ostium to establish stable contact between the vein wall and the catheter's cryothermal application surface. This ensures consistent energy delivery throughout the ablation. Cryoenergy is then applied, inducing tissue necrosis around the antral regions of the PVs (135, 136). However, because fluoroscopic imaging and verification are required for each PV, cryoballoon ablation may be associated with increased fluoroscopy time and radiation exposure (137). Designed to deliver a single-shot circumferential lesion around each PV, the cryoballoon streamlines PVI, making the procedure easier to master and markedly shortening the operator learning curve compared with point-by-point RF ablation (138).

The FIRE and ICE trial demonstrated comparable efficacy between second-generation cryoballoon and radiofrequency catheter ablation (RFCA) in the treatment of paroxysmal AF. Safety profiles were also similar; the most frequent complication was transient phrenic nerve injury associated with cryoablation. (135, 139, 140). However, evidence from subsequent studies showed that cryoballoon ablation may be less effective in certain anatomical variants, such as the presence of a left long common trunk (141) – defined as a single ostium draining both the left superior and inferior PVs, with a shared segment of at least 10 mm before bifurcation. Other potentially limiting anatomical features include extra PVs or markedly oval PV ostia (141, 142). Complication rates may also vary depending on such anatomical variations (143).

1.5.2. Radiofrequency ablation

PVI was first performed using point-by-point RFCA guided by fluoroscopy, following the discovery that ectopic foci within the PVs often initiate AF. This foundational approach was described by Haïssaguerre et al. in 1998, marking the beginning of catheter-based AF ablation (12); early trials showed that RFCA of the PV ostia is safe and effective for AF (144). Over the subsequent two decades most centers have adopted contact force-sensing, irrigated point-by-point RF catheters guided by 3D electroanatomical mapping, a shift that removes the geometric constraints of a circular device and lets operators tailor lesion sets to each patient's highly variable PV anatomy (39). The price of this flexibility is procedural: creating a continuous, transmural ring from dozens of individual lesions

prolongs procedure and fluoroscopy times, and requires a steeper learning curve, particularly during an operator's first 50-100 cases (145). Point-by-point RFCA has been proven effective in reducing symptoms related to rhythm disturbances in both paroxysmal and persistent AF cases (146, 147). In RFCA, the lesion formation occurs through two distinct phases: resistive and conductive tissue heating (148). During the resistive phase, the electrical current applied to the tissue immediately causes heating in the superficial layer, as the tissue surrounding the electrode acts as an electrical resistor, generating heat due to RF alternating current. In the conductive phase, the heat produced during the resistive phase penetrates deeper tissue layers. Conductive heating is a passive process; its depth is influenced by time and linked to the heat produced during the resistive phase and the quantity of energy applied (149). Figure 1 shows how lesions are created during RF ablation.

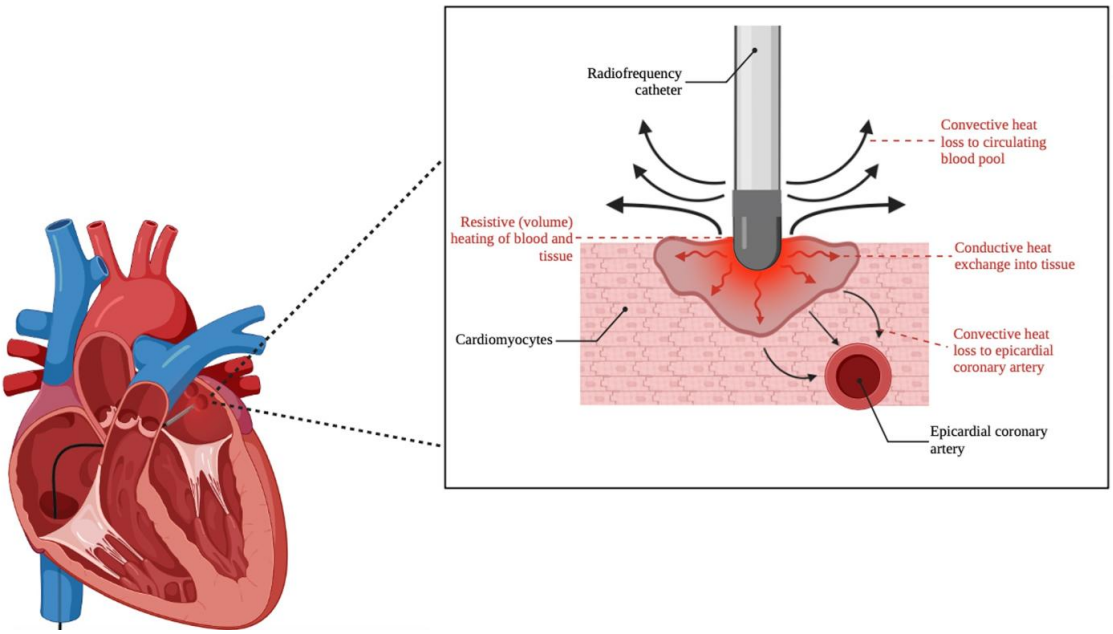


Figure 1. Lesion formation during radiofrequency ablation. Redrawn based on the schematic illustration by Nath, S et al., 1994 (148), with permission from Wiley.

In conventional point-by-point RFCA, energy is typically delivered at low-to-moderate power settings of 20-40 W for 20-60 seconds per lesion, often with a target contact force (CF) of 10-20 g (150). High-power short-duration strategies aim to reduce the relative contribution of conductive heating by delivering higher power over a shorter time period. This increases the proportion of resistive heating, shortens each application, and may

improve lesion delivery by reducing the time during which stable catheter-tissue contact must be maintained (151).

During very high-power, short-duration (vHPSD) ablation, energy is delivered at power levels above conventional high-power short-duration settings (typically up to 50 W), with power settings of 70-90 W applied for only a few seconds per application (152); no consensus definition exists, and settings and energy-control modes vary between technologies (151). The most extensively studied protocol, used in the present thesis, delivers 90 W for 4 seconds in a temperature-controlled mode (152, 153), whereas power-controlled 70 W protocols have also been reported as vHPSD (154, 155). Clinical studies of the 90 W/4 s temperature-controlled protocol (hereafter, the term vHPSD refers exclusively to this specific ablation setting) suggest that it is effective and safe, with shorter procedure and RF application times than conventional RF ablation and non-inferior arrhythmia outcomes in randomized controlled trials (152, 153, 156-159). The technical details of the vHPSD workflow used in the present dissertation are described in section 3.2.

Reducing the proportion of conductive tissue heating may also be advantageous from a safety perspective, because prolonged conductive heating can damage extracardiac structures adjacent to the left atrial (LA) wall. For instance, in the case of the posterior wall, a prolonged phase of conductive heating could result in harming the esophageal wall, potentially leading to ulceration and the development of an atrioesophageal fistula (160-164). Moreover, vagal nerve damage can result in gastroparesis (165, 166).

1.5.3. Pulsed-field ablation

In recent years, one of the innovations in the CA of AF is pulsed-field ablation (PFA). The potential of PFA lies in its ability to target cardiomyocytes precisely and selectively in areas of concern while minimizing damage to other types of tissue (e.g., neurons, endothelial cells, esophageal smooth muscle), thus reducing the risk of potentially serious complications (e.g., PV stenosis, phrenic nerve palsy, atrioesophageal fistula) (167-169). PFA's mechanism of action is irreversible electroporation. Momentary electric fields are generated in rapid succession by the ablation catheter, causing the formation of pores in the membranes of cardiac muscle cells (170). Since different types of cells are sensitive to electromagnetic fields with different characteristics, cardioselective ablation is

assumed to occur during PFA. Pore formation is initially reversible with early pulses but becomes irreversible once the cumulative energy of subsequent pulses exceeds the membrane's ability to reseal. The cell contents exit through these pores, resulting in non-thermal cell death (170). Figure 2 illustrates the mechanism of lesion formation during PFA.

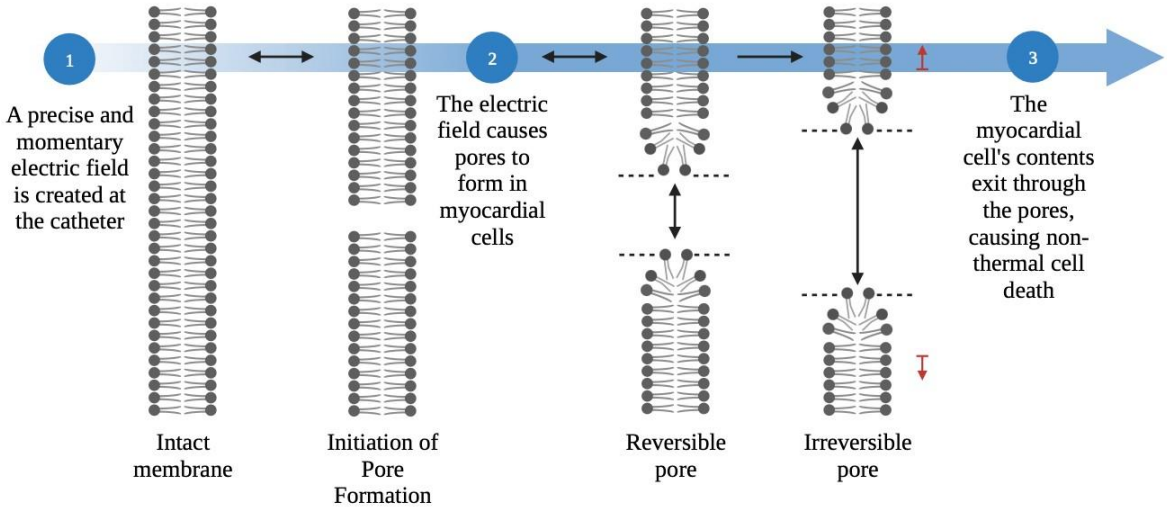


Figure 2. Lesion formation during pulsed-field ablation. Based on Kotnik, T et al., 2012 (171). © 2012 IEEE. Used with permission from IEEE.

It is important to mention that various PFA techniques differ, with the Farapulse system (Boston Scientific, Corp, Marlborough, MA, USA) being the one with a substantial wealth of data (172-174). Accordingly, the safety and efficacy data discussed below primarily refer to this system, unless otherwise specified. Contemporary evidence confirms the favorable safety of PFA. The MANIFEST-17K registry reported a major-complication rate of ≈1% with no esophageal injury, PV stenosis or persistent phrenic palsy (175). The ADVENT trial likewise showed PFA to be non-inferior to conventional thermal ablation for both safety and one-year efficacy (176). Beyond its favorable safety profile, PFA is considered a breakthrough innovation because it may simplify and standardize AF ablation. Contemporary PFA platforms are predominantly large-footprint, single-shot systems that allow rapid PVI with less dependence on point-by-point lesion formation, catheter stability, and operator-specific lesion delivery. Therefore, PFA may improve procedural reproducibility, shorten procedure times, and reduce the impact of operator experience on workflow efficiency (172, 177-180). These

advantages may facilitate wider adoption of AF ablation, although current single-shot PFA systems may offer less flexibility for individualized lesion sets than conventional point-by-point RF ablation (181-183).

Among PFA-related adverse events, coronary vasospasm has received increasing attention. According to the literature, such events most commonly occur during ablation along the mitral isthmus. In a single-center study of 17 PFA cases that included a mitral isthmus line ablation, vasospasm occurred in 7 patients (41%), and the rate was particularly high (7 of 9 patients, 78%) when the mitral isthmus line was situated superiorly (184). These findings should, however, be interpreted with caution as they derive from a small cohort. Larger registries such as the MANIFEST-17K (> 17,000 PFA cases) reported coronary spasm in only 0.14% of patients, the majority of whom were asymptomatic, and the episodes resolved quickly, usually within 5 minutes, with or without nitroglycerin administration (175). Overall, coronary vasospasm appears to be a rare and transient complication, but vigilance and readiness to treat with vasodilators remain advisable during procedures (185). Transient phrenic nerve palsy (stunning) has been reported during PFA, especially when ablating near the right superior PV or superior vena cava, although persistent phrenic nerve palsy is exceedingly rare (186, 187). Furthermore, initial concerns suggested that lesions delivered without adequate catheter-tissue contact could result in intravascular hemolysis and subsequent hemolysis-associated acute kidney injury (188). However, contemporary data from large registries such as EU-PORIA and the randomized ADVENT trial have not demonstrated any clinically significant evidence of hemolysis or acute kidney injury associated with PFA, suggesting that such complications are rare (172, 176).

Finally, adopting PFA generally calls for a deeper level of anaesthesia – typically deep sedation or even general anaesthesia – in contrast with the conscious sedation protocols commonly used for most RF procedures. This change in sedation strategy introduces additional anaesthetic steps, particularly the induction and emergence phases, which can lengthen the total time spent in the operating room (i.e., room time) (172, 189).

1.6. Pre-procedural imaging prior rhythm control of AF

Pre-procedural cardiac imaging in AF serves mainly two purposes: (i) exclusion of left atrial appendage (LAA) thrombus before ECV or CA; and (ii) in the ablation setting,

delineation of LA size, PV morphology, and relevant anatomical variants for procedural planning. LAA thrombus can be excluded with TEE, intracardiac echocardiography (ICE), or contrast-enhanced cardiac computed tomography (CT) or cardiac magnetic resonance (CMR) (1).

For ECV, imaging may be omitted only when AF duration is confidently ≤24 hours or when ≥3 weeks of uninterrupted therapeutic anticoagulation has been documented; otherwise, a TEE-guided strategy is recommended. In patients undergoing CA under therapeutic OAC, LAA thrombus exclusion is not universally required, but imaging should be considered in those at high thromboembolic risk (Class IIa, Level B) (1). According to our institutional protocol, to maximize safety – and given the availability of experienced TEE operators – all patients scheduled for elective ECV undergo TEE irrespective of prior anticoagulation.

For CA specifically, a secondary imaging objective is accurate anatomic assessment. Contrast-enhanced cardiac CT has become the first-line modality for this purpose in our practice because it simultaneously excludes LAA thrombus and provides high-resolution LA/PV geometry; it also enables screening of the coronary arteries for CAD (190, 191).

CMR offers a radiation-free alternative; late gadolinium enhancement (LGE) sequences can visualize atrial fibrosis, a substrate associated with post-ablation arrhythmia recurrence (192, 193). However, contrast-enhanced CMR is time-consuming and less accessible, requires gadolinium administration, and may be contraindicated in claustrophobia or in patients with non-MRI-conditional devices (167). Transthoracic echocardiography is routinely used to document left ventricular systolic function before either ECV or ablation, with CMR reserved when additional characterization is required (62, 194, 195).

Accordingly, imaging should be tailored to the planned intervention – TEE for rapid thrombus exclusion before ECV; contrast-enhanced CT or CMR for comprehensive anatomic assessment before ablation – while balancing each modality's constraints (radiation exposure, contrast use, access, and patient preference).

Table 2 highlights the strengths of the mentioned modalities in different aspects of cardiac assessment, indicating their capabilities in terms of anatomy, function, and LAA thrombus detection.

Table 2. Pre-procedural left atrial imaging modalities for LAA thrombus exclusion and anatomical assessment in AF. Compiled from published literature and guideline sources (1, 2). Abbreviations: AF = atrial fibrillation; CMR = cardiac magnetic resonance; CT = computed tomography; LAA = left atrial appendage; TEE = transesophageal echocardiography.

	TEE	Cardiac CT	CMR
Anatomy	+	+	+
Function	+		+
Detection of LAA thrombus	+	+	+

1.7. Factors predicting atrial fibrillation recurrence

In AF management and ablation procedures, predicting AF recurrence is of paramount concern. More accurate recurrence prediction allows clinicians to focus on patients with higher risk of recurrence after AF ablation. Recent studies have aimed to identify parameters that can predict disease recurrence following AF ablation (196-198).

Consistent with the “C” (Comorbidity management) pillar of the AF-CARE framework, tight control of co-existing conditions reduces post-ablation recurrence.

Beyond comorbidities, LA anatomy can also play a significant role in recurrence determination. A larger LA diameter was identified as an independent predictor of AF recurrence (198, 199). Furthermore, higher LA volumes and larger PV diameters are considered potential predictors of AF recurrence risk following RFCA (200). Epicardial adipose tissue volumes around the left atrium (LA) may also play a role in determining the success of CA (198). In particular, adipose tissue surrounding the LAA is associated with recurrence (201). Another parameter measurable via cardiac CT angiography, right coronary artery stenosis, has also been associated with recurrence (198). Furthermore,

LAA volume and mitral regurgitation were identified as independent predictors for AF recurrence (202).

In a post hoc analysis of the DECAAF II trial involving patients with persistent AF undergoing CA, marked regional and patient-specific variations in LA fibrosis were observed, highlighting the heterogeneity of the arrhythmogenic substrate. The left PV antral region exhibited the highest fibrosis percentage, and regional fibrosis of the LAA was identified as a significant predictor of AF recurrence in patients who received CMR-guided fibrosis ablation. These findings suggest the heterogeneity of atrial cardiomyopathy and remodeling in relation to AF recurrence (203).

Regarding laboratory parameters, inflammation is recognized as a pivotal factor in AF initiation and progression. The C-reactive protein to albumin ratio has emerged as an independent predictor of AF recurrence (204). Furthermore, higher post-ablation high-sensitivity CRP levels have been associated with AF recurrence (205). Additionally, an elevated preoperative uric acid/creatinine ratio was found to be independently associated with a higher risk of AF recurrence following CA (206). Moreover, in patients with persistent AF without HF, higher baseline brain natriuretic peptide levels were linked to an increased risk of arrhythmia recurrence following PVI (207). Lower baseline levels of NT-proBNP, angiopoietin-2, and bone morphogenetic protein 10 have been linked to a higher probability of remaining in sinus rhythm after CV or ablation; however, these biomarkers are currently investigational and have no routine role in identifying patients with higher risk of AF recurrence (208).

In summary, several factors, including inflammation, cardiac anatomy, comorbidities and specific biomarkers, have been found to predict AF recurrence after ablation procedures, underscoring the multifaceted nature of this condition's prognosis.

2. OBJECTIVES

Our research objective was to carry out four sequential studies that span the entire CA pathway for AF: enhancing the efficiency of pre-procedural imaging, refining the intraprocedural ablation technique, identifying post-procedural predictors of recurrence, and assessing time- and resource-efficiency across the full workflow.

Consequently, our research objectives were as follows:

2.1. Comparing a novel non-contrast-enhanced cardiac MR sequence with TEE and left atrial contrast-enhanced CT in pre-procedural imaging in AF patients

In this study, our primary aim was to evaluate the feasibility of the novel non-contrast-enhanced Bright-blood and black-BlOOd phase SensiTive inversion recovery (BOOST) CMR sequence (209-211) for pre-procedural LAA thrombus assessment, using TEE as the clinical reference modality. We also compared patients' subjective experiences during TEE and CMR examinations using a custom-developed distress questionnaire. As a secondary exploratory objective, we assessed whether BOOST CMR could provide clinically useful anatomical information for CA planning, including comparison with contrast-enhanced LA CT in the subset of patients in whom both modalities were available.

2.2. Assessing the influence of the distance between the left superior pulmonary vein and the left atrial appendage on recurrence of atrial fibrillation after ablation

In this retrospective study, we aimed to evaluate whether the proximity of the left atrial appendage (LAA) to the left superior pulmonary vein (LSPV) plays a role in the recurrence of AF following CA for paroxysmal AF.

2.3. Examining the characteristics of very high-power, short-duration radiofrequency applications

We focused on investigating the relationships between various ablation parameters, including CF, power, ID, and temperature, and evaluated their impact on lesion formation when utilizing the new vHPSD ablation settings for RFCA.

2.4. Comparing room times between pulsed-field ablation and very high-power short-duration ablation

Lastly, our goal was to prospectively compare the room time [defined as the interval from patient entry into the operating room (OR) to exit] and procedural subsections' times of PFA and vHPSD procedures. Based on these comparisons, we aimed to draw broader conclusions about workflow efficiency, recurrence rate, and resource utilization in AF care when using these two cutting-edge ablation technologies.

3. METHODS

All four studies were carried out in accordance with the Declaration of Helsinki and Hungarian regulations. The prospective imaging pilot study "Use of a new non-contrast-enhanced BOOST cardiac MR sequence before electrical cardioversion or ablation of atrial fibrillation" received approval from the Hungarian Medical Research Council (IV/4962-3/2021/EKU), and every participant signed written informed consent. The procedural investigation "Characteristics of Very High-Power, Short-Duration Radiofrequency Applications" was authorized by the Semmelweis University Regional and Institutional Committee of Science and Research Ethics (SE RKEB No.: 278/2020), which waived additional study-specific consent because all patients had already consented to the ablation procedure. In the retrospective study 'Abutting Left Atrial Appendage and Left Superior Pulmonary Vein Predicts Recurrence of Atrial Fibrillation After Point-by-Point Pulmonary Vein Isolation', the requirement for ethics approval was waived by the SE-RKEB due to its non-interventional design. Finally, the prospective workflow study "Comparison of room times between pulsed-field ablation and very high-power short-duration ablation" was approved by the Hungarian Medical Research Council (BM/5584-1/2024), and all enrolled patients provided written consent for data collection and analysis.

3.1. Imaging-based studies: study design and statistical analysis

Two of our studies focused on the role of cardiac imaging in AF, addressing both pre-procedural assessment and anatomical predictors of post-ablation recurrence. The first study investigated the diagnostic performance and patient experience of TEE and a novel non-contrast-enhanced CMR sequence (BOOST), while the second study evaluated a specific anatomical relationship derived from contrast-enhanced cardiac CT as predictors of AF recurrence. Both studies were conducted at the Heart and Vascular Center of Semmelweis University in Budapest, Hungary.

3.1.1. General imaging methodology

TEE was used for thrombus exclusion, while contrast-enhanced cardiac CT provided detailed anatomical characterization of the LA and PVs while also providing information

regarding the existence of LAA thrombi. In the CMR study, the novel BOOST sequence was used to assess both anatomy and LAA thrombus status.

Cardiac CT was acquired on a 256-slice Brilliance iCT 256 scanner in prospective ECG-triggered axial mode (tube current 100–120 kV, 200–300 mAs, 128 × 0.625 mm collimation, 270 ms rotation). To optimize image quality, whenever the resting heart rate exceeded 60 beats per minute we administered metoprolol – up to 100 mg orally or 20 mg intravenously – to slow down the heart rate, and we gated the acquisition to mid-diastole using a 3–5% padding window (73–83% of the RR interval) to minimize motion artefact. A four-phase protocol injected 85–95 mL Iomeprol 400 at 4.5–5.5 mL/s under LA bolus tracking, followed by 0.8 mg sublingual nitroglycerin.

During the TEE procedure, patients received conscious sedation. We used an Epiq CV-X system with either an X7-2T or an X8-2T xMATRIX transducer with a frequency range of 8.0–2.0 MHz, positioned at the appropriate level within the esophagus. The recorded images were stored in a Picture Archiving and Communication System (PACS) for later evaluation.

Imaging datasets were evaluated by experienced operators, and measurements were performed using dedicated post-processing software.

3.1.2. Comparing a novel non-contrast enhanced CMR sequence with TEE in pre-procedural imaging in AF patients

This prospective study was conducted at the Heart and Vascular Center of Semmelweis University in Budapest, Hungary, between May 2021 and June 2022. The study aimed to enroll patients with symptomatic AF who were scheduled for either ECV or RFCA following an outpatient evaluation and subsequent scheduling for a TEE examination.

As part of the pre-procedural imaging, each patient in the study underwent a BOOST CMR scan, followed by a TEE examination 2-3 hours later. The status of LAA, as described by both modalities, was compared for each patient. It is important to note that LA contrast-enhanced CT scans were also conducted in a subset of patients scheduled for ablation, in addition to the TEE and BOOST examinations. CT imaging was not mandatory in the study protocol, because the primary aim was to compare BOOST CMR with TEE for LAA thrombus assessment. Among patients scheduled for ablation, the

decision to perform CT was made according to routine institutional practice and the preference of the operating electrophysiologist. In these cases, CT scans were typically performed before the CMR examination as part of routine pre-ablation planning. Electrophysiologists assessed the utility and applicability of the BOOST and CT images for ablation planning, considering the LA anatomy and the positioning of the PVs provided by the two imaging modalities. A subjective scale ranging from 1 to 10 was used to assign values to the usability of the BOOST and CT images, which were subsequently compared. In addition, pulmonary vein ostial areas were compared between BOOST and contrast-enhanced CT as a secondary exploratory anatomical analysis in the subset of patients with both imaging modalities available. TEE was performed as described in the previous section. For CMR scans, we employed a 1.5T MR scanner, specifically the MAGNETOM Aera by Siemens Healthcare, Germany. Our comprehensive imaging protocol included capturing balanced steady-state free precession (bSSFP) cine images from various angles, such as the 2-chamber view, 4-chamber view, left ventricle outflow tract, and a modified 2-chamber long-axis slice optimized for the visualization of the LAA. Additionally, we utilized a specialized 3D whole-heart BOOST prototype sequence that performed with T2-preparation pre-pulse (T2prep) and MT preparation (MTC). The BOOST acquisitions covered the entire LA, including the PV ostia and the LAA, with an isotropic spatial resolution of 1.4 × 1.4 × 1.4 mm. The scans were performed without the use of contrast agents. Data acquired from the CMR scans were analyzed using Medis Suite 4.0 software, developed by Medis Medical Imaging Software in Leiden, The Netherlands. CMR-derived LA volumetric and functional parameters were assessed descriptively to characterize the imaging dataset and were not considered primary outcome measures. LA contrast-enhanced CT scans were performed as described in section 3.1.1.

Within one week, we assessed patients' subjective experiences of TEE and BOOST using a customized 20-item questionnaire developed by our research team. The first two sections addressed the clarity of pre-procedural information, perceived mental and physical discomfort, and the subjective length of the examination. The final section asked participants to indicate their preferred modality for a potential future examination and to explain their choice in a free-text response. Clinical staff conducted the interviews, addressed any patient questions, and recorded all responses.

Normality of continuous variables was assessed with the Shapiro-Wilk test. To evaluate the associations between specific groups, Fisher's exact test was utilized to examine contingency. The Mann-Whitney U test was employed to compare continuous variables. A two-tailed p-value of less than 0.05 was considered statistically significant. The statistical analyses were conducted using IBM SPSS 25 and GraphPad Prism 9.1.2.

3.1.3. Assessing the influence of the distance between the left superior PV and the LAA on the recurrence of AF after ablation

We conducted a retrospective study at the Heart and Vascular Center of Semmelweis University in Budapest, Hungary, based on data from January 2014 to December 2017. The study focused on consecutive patients who had undergone point-by-point RFCA for paroxysmal AF and who had undergone pre-procedural LA contrast-enhanced cardiac CT in order to comprehensively assess the LA anatomy. We excluded patients from the study if they had non-paroxysmal AF, had previously undergone LA ablation procedures, had LA CT scans with inadequate image quality for LA anatomy assessment, or had not received point-by-point ablation.

Cardiac CT was performed as described above. Images were reconstructed at 0.8 mm thickness with 0.4 mm overlap. LA and LAA borders – including PV ostia and the mitral annulus – were segmented on three-dimensional volume-rendered reconstructions using EP Planning software (Philips IntelliSpace Portal). Three experienced readers, blinded to outcomes, reached consensus on LAA morphology, classifying each appendage as cauliflower, windsock, chicken wing or swan; they also measured LAA volume, orifice area and the minimal endocardial distance between LAA and the LSPV. A distance <2 mm defined an abutting LAA–LSPV relationship, whereas ≥2 mm was non-abutting. Figure 3 contrasts CT images of non-abutting versus abutting LAA-LSPV anatomies.

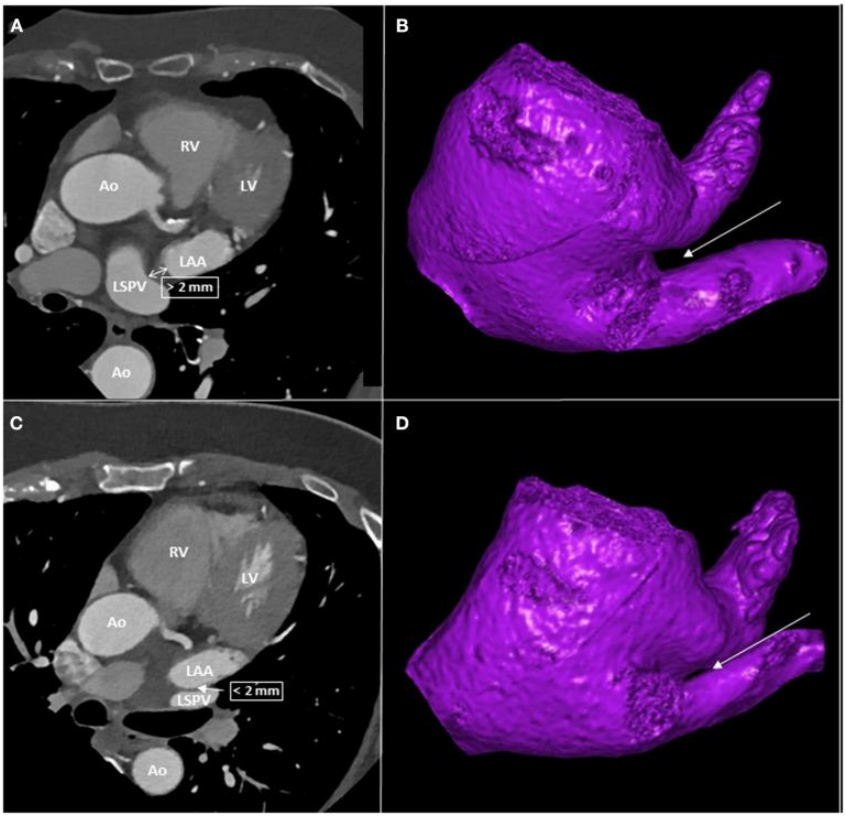


Figure 3. CT examples of non-abutting (A-B) and abutting (C-D) LAA-LSPV relationships. Axial scans (A, C) and corresponding caudal 3D reconstructions (B, D; LIPV removed for clarity) show the measured LAA-LSPV gap (arrows). Abbreviations: Ao = aorta; CT = computed tomography; LAA = left atrial appendage; LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein; LV = left ventricle; RV = right ventricle. Reproduced from Szegedi, N et al., Frontiers in Cardiovascular Medicine, 2022, under the terms of the Creative Commons Attribution License (CC BY) (212).

Within 24 hours prior to RFCA, all patients underwent TEE to exclude thrombus, assess for spontaneous echo contrast (SEC) or sludge, and measure peak LAA emptying velocity as described previously.

All ablations were performed under conscious sedation by operators performing >100 AF ablations annually. Patients attended follow-up visits at 3, 6, and 12 months and at least annually thereafter. Each visit included clinical evaluation and a 24-hour Holter ECG, with additional appointments arranged for any symptomatic episodes. Recurrence was defined as any atrial tachyarrhythmia lasting ≥30 seconds documented beyond a 90-day blanking period.

The distribution of continuous variables was assessed using the Shapiro-Wilk test. Normally distributed variables are reported as mean ± standard deviation (SD), whereas non-normally distributed variables are presented as median (interquartile range, IQR). Categorical variables are summarized as counts and percentages. Group comparisons were performed using appropriate parametric or non-parametric tests. Predictors of AF recurrence were assessed using univariable and multivariable Cox proportional hazards regression. Kaplan-Meier analysis was used to estimate event-free survival, with between-group differences evaluated by the log-rank test. Statistical significance was defined as a two-sided p-value <0.05. Statistical analysis was performed using R 3.6.1.

3.2. Novel ablation technology-based studies: study design and statistical analysis

Another two of our studies focused on CA technologies in AF, examining both lesion formation characteristics and procedural efficiency. While the first study investigated the biophysical parameters of vHPSD RF ablation, the second study compared procedural workflow and room times between PFA and vHPSD ablation. Again, both studies were conducted at the Heart and Vascular Center of Semmelweis University in Budapest, Hungary, and involved experienced operators performing a high volume of AF ablations annually.

3.2.1. Very high-power, short-duration ablation methodology

All procedures involved femoral venous access. Transseptal puncture was performed under fluoroscopy guidance and pressure monitoring to access the LA, followed by systemic anticoagulation with intravenous heparin to maintain an activated clotting time (ACT) of approximately 350 seconds.

After successful LA entry, a fast anatomical map of the LA was generated using a 3D electroanatomical mapping system (CARTO3, Biosense Webster, Inc., Irvine, CA, USA) with a mapping catheter.

Very high power, short duration ablation was performed using the QDOT Micro ablation catheter (Biosense Webster, Inc., Irvine, CA, USA) with temperature-controlled settings. During vHPSD ablation, 90 watts of power was applied for 4 seconds with an irrigation rate of 8 ml/min. Six thermocouples are integrated into the catheter tip to monitor temperature (Figure 4). When RF application commences, a short cooling phase precedes

energy delivery, followed by rapid power escalation. Power delivery is continuously modulated according to the maximum temperature measured at the catheter tip. The target temperature was set at 55°C, with a cut-off temperature of 65°C.

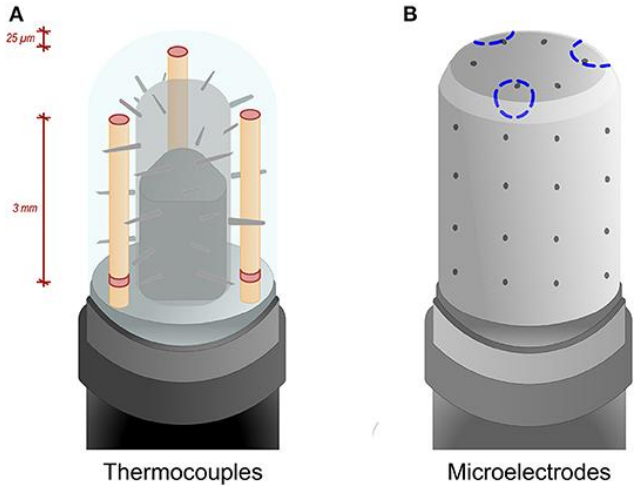


Figure 4. (A, B) QDOT Micro Ablation Catheter (Biosense Webster, Irvine, CA, USA) Illustration. (A) The ablation catheter has six thermocouples (red disks) at the tip for accurate temperature measurement, with distal thermocouples located 25 µm from the tip and proximal ones 3 mm back. (B) Additionally, the tip contains three microelectrodes (blue dotted circles), each with a surface area of 0.17 mm² and spaced 1.5 mm apart. Reproduced from Orbán, G et al., Frontiers in Cardiovascular Medicine, 2022, under the terms of the Creative Commons Attribution License (CC BY) (213).

Point-by-point RF applications were delivered around the antra of the ipsilateral PVs to achieve complete electrical isolation. Interlesion distances between neighboring points were maintained below 5 mm (Figure 5). PVI was verified by the presence of both entrance and exit block. First-pass isolation was defined as confirmation of both blocks following the first-pass circumferential ablation. If disconnection was not achieved after the initial circumferential ablation, additional vHPSD applications were delivered to achieve complete isolation.

Patients without complications were typically discharged the day after the procedure.

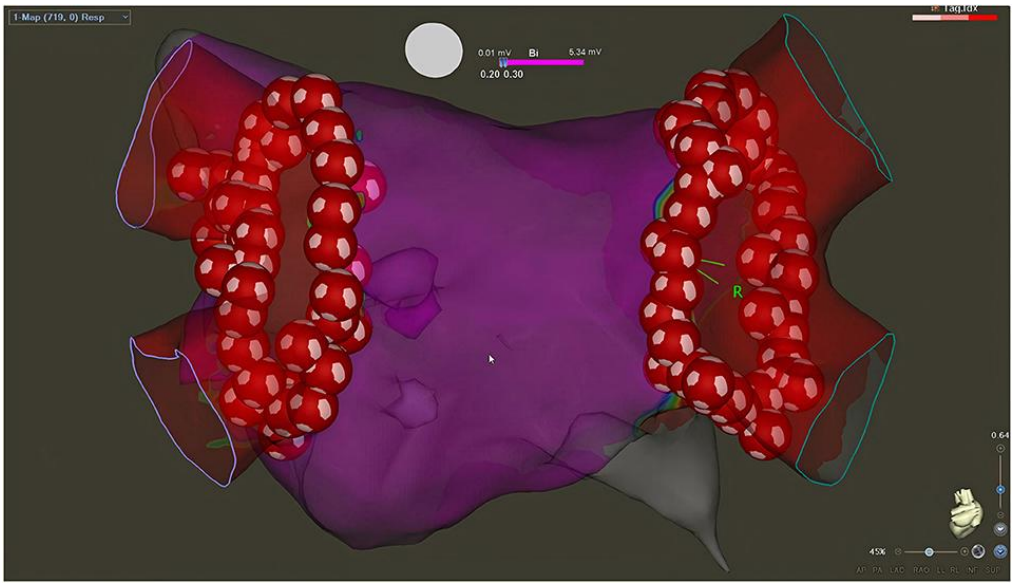


Figure 5. Postero-anterior left atrial voltage map after successful vHPSD PVI. The CARTO 3 (Biosense Webster, Inc., Irvine, CA, USA) map demonstrates a continuous lesion set with interlesion spacing <5 mm throughout. Abbreviations: PVI = pulmonary vein isolation; vHPSD = very high-power short-duration. Reproduced from Orbán, G et al., Frontiers in Cardiovascular Medicine, 2022, under the terms of the Creative Commons Attribution License (CC BY) (213).

3.2.2. Examining the characteristics of very high-power, short-duration radiofrequency applications

In our prospective single-center study conducted at the Heart and Vascular Center of Semmelweis University in Budapest, Hungary, we enrolled consecutive patients undergoing their first RFCA for AF. The procedures were performed under conscious sedation by highly experienced operators who each perform over 100 AF ablations per year. RFCA was performed as described in the previous section.

We systematically recorded data for each vHPSD application, including mean delivered power, temperature change, maximum temperature, generator ID, mean CF, minimum CF, and maximum CF.

We scheduled outpatient clinical follow-up visits 3 and 6 months after the procedure. During these follow-up visits, patients underwent clinical assessments, and 24-hour Holter ECG monitoring was conducted. Recurrence of AF was defined as the presence of any atrial tachyarrhythmia lasting for more than 30 seconds.

Normality was assessed with the Shapiro-Wilk test. Variables that proved non-Gaussian were summarized as median values with IQRs. Differences between groups were assessed using the Mann-Whitney U test, while associations between procedural metrics were quantified with Spearman's rank correlation coefficient. All analyses were executed in IBM SPSS Statistics 25 and GraphPad Prism 9.1.2.

3.2.3. Comparison of room times between pulsed-field ablation and very high-power short-duration ablation

Between November 2023 and July 2024, we prospectively enrolled adult patients scheduled for CA of AF at our clinic. Each participant underwent either vHPSD ablation or PFA using the Farapulse system (Boston Scientific, Corp, Marlborough, MA, USA).

All procedures were performed by the same five physicians, each of whom was experienced in both PFA and RF-based AF ablation and had extensive prior experience with both techniques. Physicians were categorized into two groups according to their lifetime number of AF ablation procedures: experienced operators (300–1000 procedures; n = 3) and expert operators (>1000 procedures; n = 2).

Very high-power short-duration ablation was performed as described above.

Due to local insurance policies, some PFA cases were redo cases. PFA was performed using single transseptal access with the same ACT goal of 350 s through iv. sodium-heparine. The ablation catheter (Farawave catheter) was introduced through the Faradrive sheath into the LA and connected to the Farastar ablation generator. Subsequently, PVI was performed with PFA as follows: 4-4 applications in basket and flower configurations, with a 30-degree catheter rotation after 2 applications in each configuration. Since no CF feedback was available with the Farawave catheter, ICE and fluoroscopy was utilized to assess catheter tissue contact, position and PV anatomy. Every PFA case included full PVI, with complete rePVI for reinforcement in all redo cases, and operators were allowed to extend PFA beyond PVI (e.g., posterior wall isolation, mitral isthmus ablation, roof isolation) as per their clinical judgement. Given that local electrograms disappear immediately after pulsed-field energy delivery, we believe that the post-ablation waiting period and repeated assessments of PV disconnection appear to have limited value in the context of PFA. Therefore, we considered it reasonable to evaluate the success of PVI only after ablating the given PV, without reassessing at the end of the procedure.

Sedation adhered to contemporary anaesthesiology standards (214). Very high-power short-duration ablation was typically performed under conscious sedation, while PFA procedures were usually carried out under deep sedation, with general anesthesia reserved for selected cases.

To compare procedural time efficiency, we recorded the duration of the entire electrophysiology laboratory process and of each discrete procedural segment listed below:

- Door-in to puncture time: Time from entering the OR to the first femoral vein puncture.
- Puncture to transseptal time: Time from first femoral puncture to successful transseptal puncture.
- Transseptal to first ablation time: Time from the transseptal puncture to the first ablation lesion.
- Ablation time: Time from the first to the last ablation lesion.
- Last ablation to sheath-out time: Time from the last ablation lesion to sheath removal.
- Sheath-out to door-out time: Time from sheath removal to leaving the OR.
- LA dwell time: Time from the transseptal puncture to sheath removal.

Continuous variables were expressed as mean ± SD or median (IQR), as appropriate, while categorical variables were reported as frequencies and percentages. Between-group comparisons were performed using parametric or non-parametric tests according to the distribution of the data. Statistical significance was defined as a two-tailed p-value <0.05.

4. RESULTS

4.1. Comparing a novel non-contrast-enhanced cardiac MR sequence with TEE and left atrial contrast-enhanced CT in pre-procedural imaging in AF patients

4.1.1. Study cohort

Of the 80 patients initially screened, nine were excluded because of contraindications for CMR (five due to claustrophobia and four due to magnetic foreign bodies). Data from the remaining 71 patients (age 65 years [57–72], 38% female) were analyzed. Baseline comorbidities, renal function, LVEF, and anticoagulation regimens are summarized in Table 3.

Table 3. Baseline characteristics of the study population. Continuous variables are expressed as medians and interquartile ranges. Reproduced from Orbán, G et al., Frontiers in Cardiovascular Medicine, 2023, under the terms of the Creative Commons Attribution License (CC BY) (215). Abbreviations: AF = atrial fibrillation; BMI = body mass index; CAD = coronary artery disease; CTI = cavotricuspid isthmus; ECV = electrical cardioversion; eGFR = estimated glomerular filtration rate; LMWH = low-molecular-weight heparin; LVEF = left ventricular ejection fraction; PVI = pulmonary vein isolation; RFCA = radiofrequency catheter ablation; TIA = transient ischemic attack.

Patient characteristics (n=71)	
Age (years)	65 (57-72)
Female, n (%)	27 (38)
AF type	
Paroxysmal, n (%)	37 (52)
Persistent, n (%)	34 (48)
BMI (kg/m^2)	28 (26-32)
Hypertension, n (%)	55 (77)
Hyperlipidemia, n (%)	36 (51)
Diabetes, n (%)	16 (23)
CAD, n (%)	15 (21)
Prior stroke/TIA, n (%)	2 (2.8)

Other thromboembolic events, n (%)	3 (4.2)
CHA_2DS_2-VASc score	2 (2-4)
Thyroid gland disease, n (%)	13 (18)
Prior RFCA, n (%)	23 (32)
PVI, n (%)	16 (23)
CTI ablation, n (%)	3 (4.2)
PVI+CTI ablation, n (%)	4 (5.6)
eGFR (ml/min/1.73 m^2)	71 (60-89)
LVEF (%)	55 (52-59)
Reason for admission	
RFCA, n (%)	47 (66)
ECV, n (%)	24 (34)
Anticoagulants used prior to imaging (n=71)	
Rivaroxaban, n (%)	21 (29.6)
Apixaban, n (%)	20 (28.2)
Dabigatran, n (%)	12 (16.9)
Edoxaban, n (%)	9 (12.7)
Vitamin-K antagonists, n (%)	5 (7)
LMWH, n (%)	1 (1.4)
None, n (%)	3 (4.2)

4.1.2. Imaging results and detection of LAA thrombus

BOOST CMR and TEE were in agreement regarding the absence of thrombus in 67 patients (94%) and identified thrombus concordantly in one case (Table 4 and Figure 6). Three discordant or indeterminate findings merit explicit mention. First, in one ablation candidate who underwent all three imaging modalities, TEE could not exclude thrombus because of dense sludge. Contrast-enhanced CT yielded similarly inconclusive findings. In contrast, BOOST CMR clearly excluded the presence of a thrombus. Anticoagulation was continued without modification, and repeat TEE and CT performed three months later were both negative. The patient subsequently underwent successful ablation without thromboembolic complications. Second and third, BOOST

CMR was inconclusive in two patients due to AF-related motion artefact. In one of these cases, TEE was likewise inconclusive because of dense sludge, while in the other, TEE definitively excluded thrombus. Across the entire cohort, no peri-procedural or three-month thromboembolic events occurred. BOOST acquisition was longer than TEE [40 (30-45) vs 7 (5-9) min, respectively, $p < 0.0001$].

Table 4. Imaging results. Continuous variables are expressed as medians and interquartile ranges. Reproduced from Orbán, G et al., Frontiers in Cardiovascular Medicine, 2023, under the terms of the Creative Commons Attribution License (CC BY) (215). Abbreviations: CMR = cardiac magnetic resonance; LAA = left atrial appendage; SEC = spontaneous echo contrast; TEE = transesophageal echocardiography.

Imaging results (n=71)	
CMR duration (min)	40 (30-45)
TEE duration (min)	7 (5-9)
LAA emptying velocity (cm/s)	53 (37-71)
SEC detected by TEE, n	4
Both TEE and CMR excluded thrombus, n	67
Both TEE and CMR showed thrombus, n	1
Inconclusive TEE result, but CMR excluded thrombus, n*	1
Both TEE and CMR uncertain about thrombus, n*	1
Inconclusive CMR result, but TEE showed thrombus, n	1

**In these cases, dense LAA sludge prevented definite exclusion of organized thrombus.*

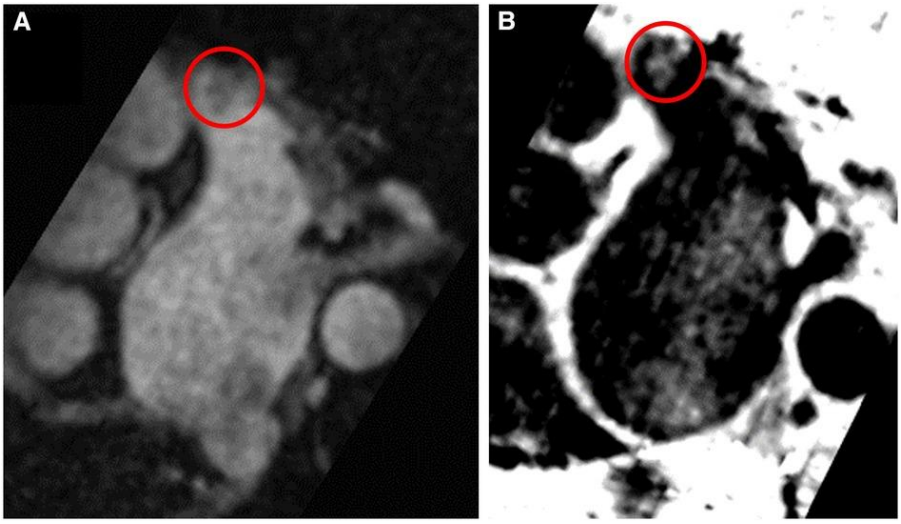


Figure 6. Left atrial appendage thrombus (circled in red) on T2prep BOOST CMR images. Panel (A): magnitude image of T2prep BOOST. Panel (B): dark-blood image of T2prep BOOST. Abbreviations: BOOST = Bright-Blood and Black-Blood Phase Sensitive; CMR = cardiac magnetic resonance; T2prep = T2-preparation. Reproduced from Orbán, G et al., Frontiers in Cardiovascular Medicine, 2023, under the terms of the Creative Commons Attribution License (CC BY) (215).

4.1.3. Pulmonary vein anatomy and ostial measurements

Among the 25 patients who underwent both BOOST CMR and contrast-enhanced CT, PV ostial areas did not differ between the two modalities (all $p > 0.05$; Table 5).

Table 5. Pulmonary vein ostial areas measured by BOOST CMR and contrast-enhanced CT in patients who underwent both imaging modalities. Continuous variables are expressed as medians and interquartile ranges. Reproduced from Orbán, G et al., Frontiers in Cardiovascular Medicine, 2023, under the terms of the Creative Commons Attribution License (CC BY) (215). Abbreviations: BOOST = Bright-Blood and Black-Blood Phase Sensitive; CMR = cardiac magnetic resonance; CT = computed tomography; LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein.

	BOOST CMR	Contrast-enhanced CT	p-value
RSPV (mm^2)	299 (267-393)	312 (269-377)	0.51
RIPV (mm^2)	284 (244-394)	309 (244-439)	0.64
LSPV (mm^2)	267 (208-321)	276 (208-350)	0.71
LIPV (mm^2)	268 (213-392)	274 (247-393)	0.69

4.1.4. LA function measured with CMR

CMR cine images yielded functional data: when recorded in sinus rhythm (52% of scans) median left atrial ejection fraction (LAEF) was 53 (44-60) %; while in patients with ongoing arrhythmia the LAEF was 19 (12-29) %. Volumetric measurements are detailed in Table 6.

Table 6. Left atrial parameters recorded by CMR. Continuous variables are expressed as medians and interquartile ranges. Reproduced from Orbán, G et al., Frontiers in Cardiovascular Medicine, 2023, under the terms of the Creative Commons Attribution License (CC BY) (215). Abbreviations: CMR = cardiac magnetic resonance; LA = left atrial; LAEF = left atrial ejection fraction; LAV = left atrial volume; LAVi = body surface area-indexed left atrial volume; LA SV = left atrial stroke volume; LA SVi = body surface area-indexed left atrial stroke volume; NSR = normal sinus rhythm.

Left atrial parameters	
Patients in NSR during CMR, n (%)	37 (52)
Patients in non-NSR during CMR, n (%)	34 (48)
LAEF of patients in NSR (%)	53 (44-60)
LAEF of patients in non-NSR (%)	19 (12-29)
Minimum LAV (mL)	53 (43-107)
Maximum LAV (mL)	106 (87-137)
Minimum LAVi (mL/m^2)	26 (21-51)
Maximum LAVi (mL/m^2)	50 (43-67)
LA SV (mL)	35 (26-52)

LA SVi (mL/m^2)	17 (11-25)

4.1.5. CMR image utility in ablation planning, patient experience

Among the 25 patients who had both LA contrast-enhanced CT and BOOST CMR, electrophysiologists rated the CT image quality higher [CT: 8 (7–9) vs. BOOST CMR: 6 (5–7); $p < 0.0001$] yet considered BOOST CMR suitable for procedural planning in 43 of 47 RFCA cases (91 %). Figure 7 below illustrates why: even though the LA reconstruction based on contrast-enhanced CT (panel A) appears marginally crisper than the BOOST-based model (panel B), both renderings provide equivalent anatomical detail for safe, wide antral PVI planning (Figure 7).

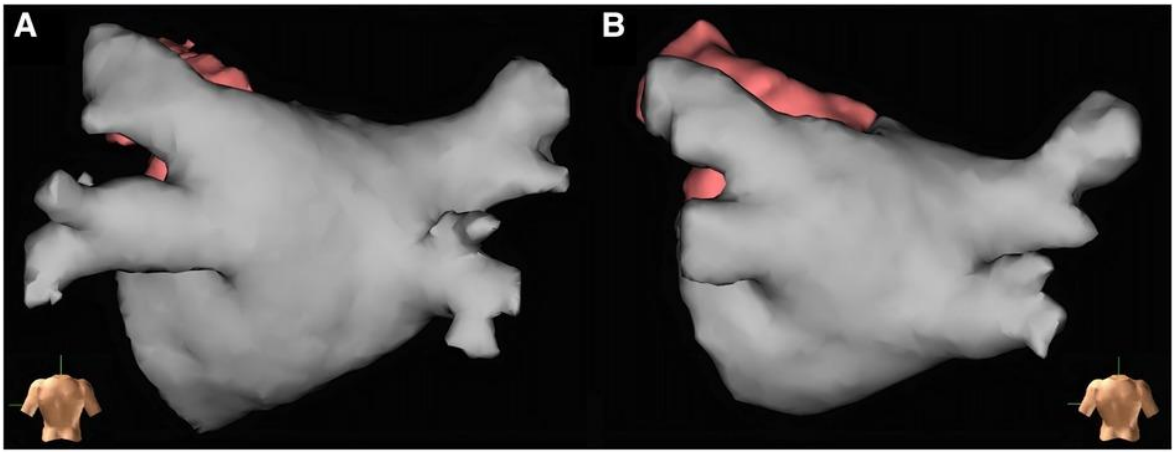


Figure 7. 3D reconstruction of the left atrium for ablation planning. Both images originate from the same patient and were created in the ENSITE (Abbott Laboratories, Abbott Park, IL, USA) mapping system. Panel A: model derived from contrast-enhanced CT. Panel B: model derived from non-contrast-enhanced BOOST bright-blood CMR, demonstrating similar 3D image quality. Abbreviations: BOOST = Bright-Blood and Black-Blood Phase Sensitive; CMR = cardiac magnetic resonance; CT = computed tomography. Reproduced from Orbán, G et al., Frontiers in Cardiovascular Medicine, 2023, under the terms of the Creative Commons Attribution License (CC BY) (215).

Of the 54 questionnaire respondents, 67% reported at least mild pain during TEE, whereas only one patient (1.9%) felt mild discomfort during CMR ($p < 0.0001$). When asked about a hypothetical future examination for the same indication, half of the patients were reluctant to undergo TEE again, compared with only 7.4% for CMR ($p < 0.0001$). Overall,

89% would choose CMR over TEE, citing greater comfort and the absence of gagging or nausea, whereas the remaining 11% preferred TEE because they found the CMR frightening or too long.

4.2. Assessing the influence of the distance between the left superior pulmonary vein and the left atrial appendage on recurrence of atrial fibrillation after ablation

4.2.1. Study cohort

We included 428 patients (61 ± 11 years, 36% female) in the analysis. Table 7 details participants' anthropometric characteristics, cardiovascular comorbidities, and the key imaging and procedural parameters.

Table 7. Baseline patient and procedural characteristics stratified by AF recurrence. Continuous variables are expressed as mean ± standard deviation. For LAA morphology, the p-value refers to the overall comparison across morphology categories. Reproduced from Szegedi, N et al., Frontiers in Cardiovascular Medicine, 2022, under the terms of the Creative Commons Attribution License (CC BY) (212). Abbreviations: AF = atrial fibrillation; BMI = body mass index; CAD = coronary artery disease; E/A = early-to-late transmitral flow velocity ratio; eGFR = estimated glomerular filtration rate; iLAV = body surface area-indexed left atrial volume; LA = left atrium; LAA = left atrial appendage; LAAV = left atrial appendage volume; LSPV = left superior pulmonary vein; LVEF = left ventricular ejection fraction; TIA = transient ischemic attack.

Patient characteristics (n=428)				
	All patients (n=428)	**No AF recurrence (n=285)**	**AF recurrence (n=143)**	**p-value**
Age (years)	61 ±11	60±11	62±10	0.108
Female, n (%)	152 (36)	89 (31)	63 (44)	**0.010**
BMI (kg/m^2)	29±5	29±4	29±5	0.492
Hypertension, n (%)	287 (67)	187 (66)	100 (70)	0.385
Hyperlipidemia, n (%)	96 (22)	64 (23)	32 (22)	1.00
Diabetes, n (%)	56 (13)	40 (14)	16 (11)	0.451
Stroke/TIA, n (%)	34 (8)	21 (7)	13 (9)	0.572

CAD, n (%)	37 (9)	22 (8)	15 (11)	0.364
Thyroid gland disease, n (%)	48 (11)	30 (11)	18 (13)	0.520
eGFR (mL/min/1.73m²)	76±14	76±15	76±14	0.590
LVEF <50%, n (%)	26 (6)	12 (4)	14 (10)	**0.031**
iLAV (mL/m²)	51±15	50±15	52±16	0.220
E/A ratio	1.2±0.4	1.2±0.4	1.1±0.4	0.368
LAAV (mL)	7±3	7±3	7±3	0.282
LAA flow velocity (cm/s)	37±16	37±15	39±16	0.156
LAA orifice area (mm²)	381±130	371±132	400±124	**0.023**
Procedure characteristics (n=428)				
Procedure time (min)	93±28	96±30	89±24	0.074
LA time (min)	61±24	62±22	59±28	0.424
Fluoroscopy time (min)	9±7	9±8	9±4	0.855
cauliflower, n (%)	227 (53)	155 (54)	72 (50)	0.776
windsock, n (%)	130 (30)	86 (30)	44 (31)	
chicken wing, n (%)	48 (11)	30 (11)	18 (13)	
swan, n (%)	23 (5)	14 (5)	9 (6)	
LAA abutting LSPV, n (%)	232 (54)	145 (51)	87 (61)	0.064

4.2.2. Recurrence of AF

AF recurrence occurred in 33% of patients. The median recurrence-free survival of 21 months (IQR 9-43). Female sex was more frequent in the recurrence group (44% vs. 31%; p = 0.010), as was reduced LVEF (10% vs. 4%; p = 0.031). Indexed LA volume did not differ significantly (52 ± 16 ml vs. 50 ± 15 ml; p = 0.220), whereas LAA orifice area was larger in the recurrence group (400 ± 124 mm² vs. 371 ± 132 mm²; p = 0.023). One- and two-year success rates were similar between procedures performed with and without CF-sensing catheters (86% vs. 83% at 1 year, respectively, p = 0.419; 75% vs. 75% at 2 years, respectively, p = 0.697) and between CARTO (Biosense Webster, Inc., Irvine, CA, USA) and ENSITE (Abbott Laboratories, Abbott Park, IL, USA) systems

(86% vs. 83% at 1 year, respectively, p = 0.419; 75% vs. 75% at 2 years, respectively, p = 0.894).

4.2.3. Predictors of AF recurrence

In the univariable analysis, female sex (HR 1.45; 95% CI 1.04-2.01; p = 0.028), LAA flow velocity (HR 1.01; 95% CI 1.00-1.02; p = 0.022), LAA orifice area (HR 1.00; 95% CI 1.00-1.00; p = 0.028), and abutting LAA-LSPV (HR 1.53; 95% CI 1.09-2.14; p = 0.013) were associated with AF recurrence. In the multivariable model, abutting LAA-LSPV remained the only independent predictor (adjusted HR 1.55; 95% CI 1.04-2.31; p = 0.030). Kaplan-Meier curves illustrating AF recurrence-free survival according to abutting LAA-LSPV status are shown in Figure 8, and full Cox regression results are presented in Table 8.

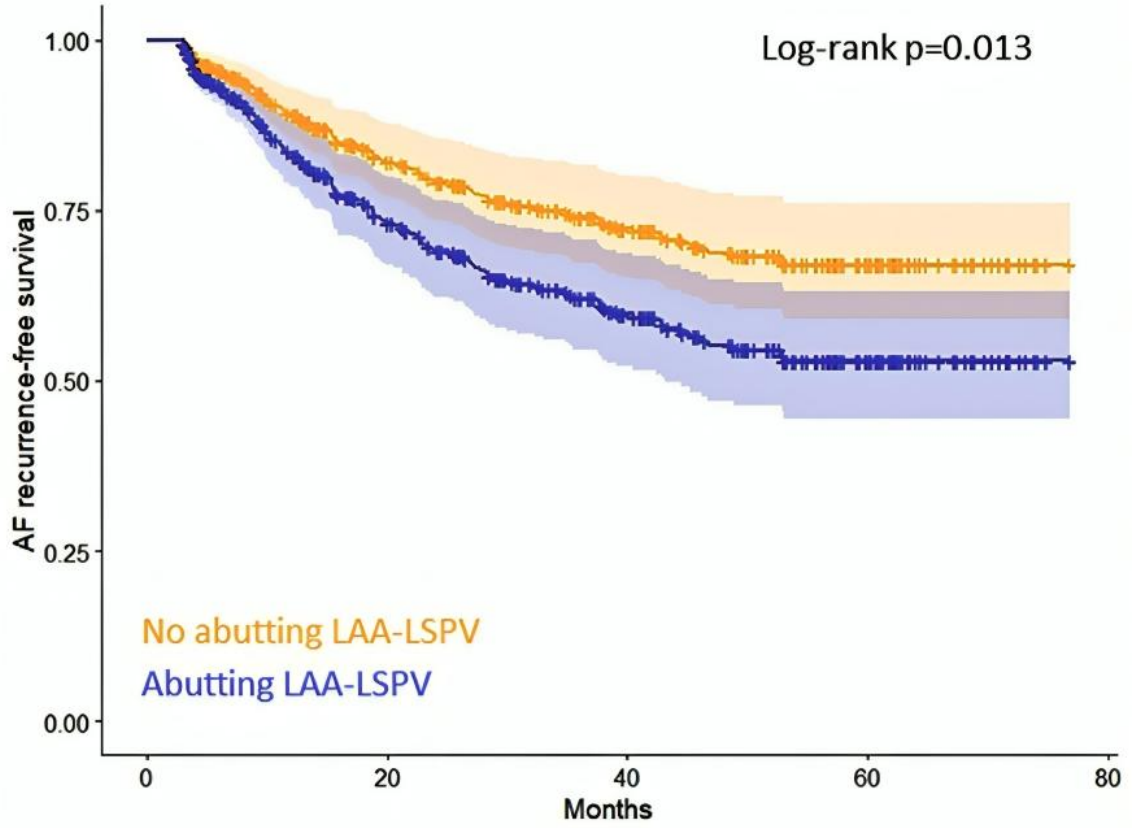


Figure 8. Kaplan-Meier curves of AF recurrence-free survival according to the presence or absence of abutting LAA-LSPV anatomy. Abbreviations: AF = atrial fibrillation; LAA = left atrial appendage; LSPV = left superior pulmonary vein. Reproduced from Szegedi, N et al., Frontiers in Cardiovascular Medicine, 2022, under the terms of the Creative Commons Attribution License (CC BY) (212).

Table 8. Cox regression analysis of AF recurrence predictors. Cauliflower LAA morphology served as the reference category. Reproduced from Szegedi, N et al., Frontiers in Cardiovascular Medicine, 2022, under CC BY license (212). Abbreviations: AF = atrial fibrillation; CI = confidence interval; E/A = early-to-late transmitral flow velocity ratio; eGFR = estimated glomerular filtration rate; HR = hazard ratio; iLAV = body surface area-indexed left atrial volume; LAA = left atrial appendage; LSPV = left superior pulmonary vein; LVEF = left ventricular ejection fraction; Ref. = reference.

	Univariable analysis			Multivariable analysis		
	HR	**95% CI**	**p-value**	**HR**	**95% CI**	**p-value**
Age	1.01	0.99-1.02	0.444	1.01	0.97-1.02	0.800
Female	1.45	1.04-2.01	**0.028**	1.42	0.94-2.15	0.097
Body mass index	1.02	0.98-1.06	0.310	1.01	0.97-1.06	0.522
Hypertension	0.98	0.68-1.40	0.910	0.97	0.61-1.35	0.900
Hyperlipidemia	0.86	0.58-1.28	0.465	0.83	0.53-1.31	0.429
Diabetes	0.73	0.43-1.23	0.234	0.90	0.51-1.60	0.722
Stroke/transient ischemic attack	1.07	0.63-1.83	0.792	0.69	0.32-1.49	0.347
Obstructive coronary artery disease	1.11	0.65-1.90	0.698	1.86	0.98-3.52	0.057
Thyroid gland disease	1.09	0.66-1.78	0.741	1.01	0.55-1.84	0.987
eGFR <60 mL/min/1.73m^2	1.38	0.94-1.51	0.097	1.37	0.88-2.13	0.163
LVEF <50%	1.67	0.96-2.90	0.069	1.40	0.68-2.89	0.357
iLAV	1.01	1.00-1.02	0.149	1.00	0.99-1.02	0.871
E/A ratio	0.80	0.50-1.28	0.352	0.80	0.48-1.34	0.394
LAA volume	1.04	0.99-1.10	0.103	1.02	0.95-1.09	0.622
LAA flow velocity	1.01	1.00-1.02	**0.022**	1.01	1.00-1.02	0.087
LAA orifice area	1.00	1.00-1.00	**0.028**	1.00	1.00-1.00	0.327
LAA morphology						
cauliflower	Ref.	-	-	Ref.	-	-
windsock	1.13	0.78-1.65	0.511	1.35	0.88-2.08	0.166
chicken wing	1.22	0.73-2.05	0.447	1.51	0.81-2.82	0.197
swan	1.46	0.73-2.92	0.286	1.73	0.79-3.76	0.168
LAA abutting LSPV	**1.53**	**1.09-2.14**	**0.013**	**1.55**	**1.04-2.31**	**0.030**

4.2.4. Subgroup analysis of cases with contact force-sensing catheters

In the contact force-sensing catheter subgroup (n = 220), abutting LAA-LSPV predicted recurrence in univariable analysis (HR 1.68, 95 % CI 1.05–2.66; p = 0.029) but did not remain significant after adjustment (adjusted HR 1.73, 95 % CI 0.95–3.17; p = 0.075).

4.3. Examining the characteristics of very high-power, short-duration radiofrequency applications

4.3.1. Study cohort

Data of 85 consecutive patients [median age 65 (59–71) years, 34% female] were analyzed. Detailed demographics can be found in Table 9.

Table 9. Baseline patient and procedural characteristics of the vHPSD RF ablation cohort. Continuous variables are expressed as medians and interquartile ranges. Reproduced from Orbán, G et al., Frontiers in Cardiovascular Medicine, 2022, under the terms of the Creative Commons Attribution License (CC BY) (213). Abbreviations: AF = atrial fibrillation; BMI = body mass index; CAD = coronary artery disease; LA = left atrial; RF = radiofrequency; TIA = transient ischemic attack, vHPSD = very high-power short-duration.

Patient characteristics (n=85)	
Age (years)	65 (59-71)
Female, n (%)	29 (34)
AF type	
Paroxysmal, n (%)	51 (60)
Persistent, n (%)	34 (40)
BMI (kg/m^2)	29 (26-31)
Hypertension, n (%)	64 (75)
Hyperlipidemia, n (%)	18 (21)
Diabetes, n (%)	15 (18)
Prior stroke/TIA, n (%)	4 (5)
CAD, n (%)	16 (19)
Thyroid gland disease, n (%)	6 (7)

CHA_2DS_2-VASc score	3 (1-4)
Procedure characteristics (n=85)	
Procedure time (min)	70 (60-90)
LA dwell time (min)	49 (42-58)
Fluoroscopy time (min)	7 (5-11)
RF time (s)	312 (237-365)

4.3.2. Analysis of vHPSD ablation points, procedural outcomes

A total of 6,551 vHPSD RF points were collected and analyzed. Detailed lesion information can be found in Table 10. The bilateral first-pass isolation rate was 84%. The rate of AF recurrence six months after ablation was 7%. There were no instances of steam pop or major complications. Only one case of groin hematoma occurred, which did not necessitate further intervention.

Table 10. Baseline characteristics of vHPSD lesions. Variables are expressed as medians and interquartile ranges. Reproduced from Orbán, G et al., Frontiers in Cardiovascular Medicine, 2022, under the terms of the Creative Commons Attribution License (CC BY) (213). Abbreviations: vHPSD = very high-power short-duration.

Mean delivered power (W)	84 (84-86)
Maximum temperature (°C)	48 (45-50)
Temperature change (°C)	13 (11-16)
Generator impedance drop (Ω)	8 (6-10)
Contact force (g)	14 (10-21)
Minimum contact force (g)	6 (3-11)
Maximum contact force (g)	24 (17-35)

4.3.3. Correlations between RF application parameters

CF demonstrated a significant positive correlation with both the maximum temperature (Spearman's $\rho = 0.4208$, $p < 0.0001$) and temperature change (Spearman's $\rho = 0.4562$, $p < 0.0001$), as illustrated in Figure 9A-B. Conversely, there was a negative correlation

between CF and the mean delivered power (Spearman's ρ = -0.09272, $p < 0.0001$), as depicted in Figure 9C.

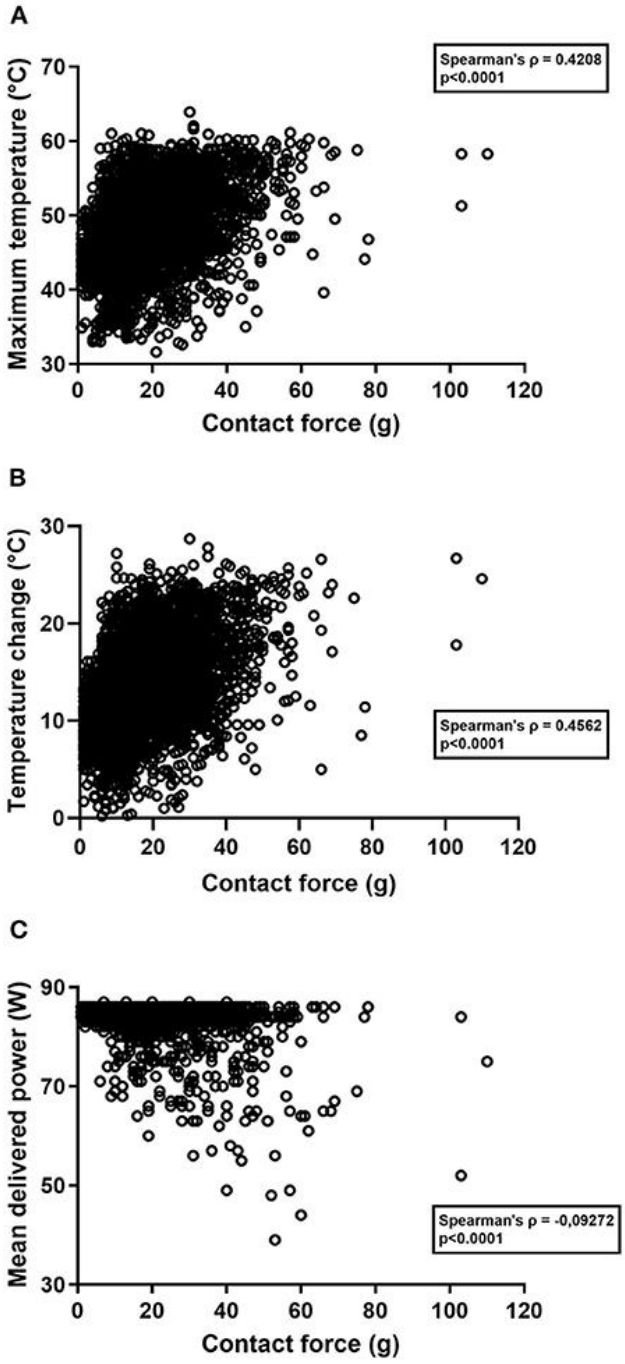


Figure 9. (A–C) Scatter plots showing correlations between different parameters registered during vHPSD ablation. Panel A: correlation between CF and the maximum temperature. Panel B: correlation between CF and temperature change. Panel C: correlation between CF and the mean delivered power. Abbreviations: CF = contact force; vHPSD = very high-power short-duration; ρ = correlation coefficient. Reproduced from Orbán, G et al., Frontiers in Cardiovascular Medicine, 2022, under the terms of the Creative Commons Attribution License (CC BY) (213).

ID showed statistically significant positive correlations with maximum temperature (Spearman's ρ = 0.3730), temperature change (ρ = 0.3822), and CF (ρ = 0.1907), while a weak but statistically significant negative correlation was observed with mean delivered power (ρ = −0.0718) (all p < 0.0001).

The catheter's thermocouples registered significantly higher maximum temperatures during lesions that were created with a CF of 5 grams or more, in contrast to those with a CF below 5 grams [48 (45-51) vs. 44 (42-46) °C, respectively, p < 0.0001], as illustrated in Figure 10.

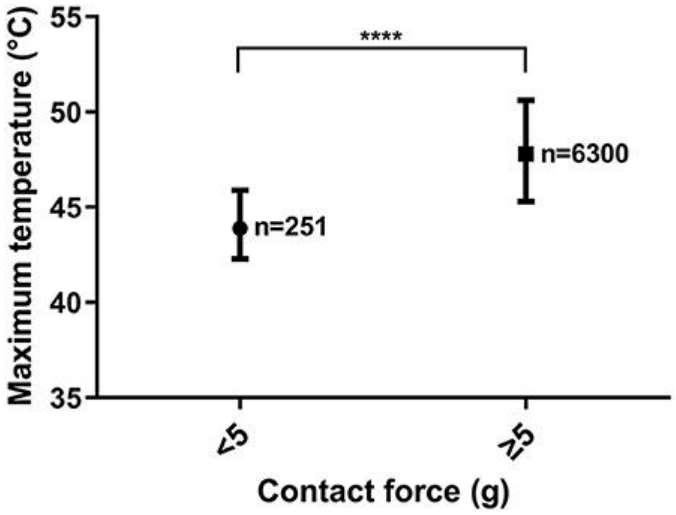


*Figure 10. Maximum temperature according to contact force during vHPSD ablation. Lesions created with CF <5 g are compared with those created with CF ≥5 g; median values with interquartile ranges are shown. Abbreviations: CF = contact force; vHPSD = very high-power short-duration; **** = p < 0.0001. Reproduced from Orbán, G et al., Frontiers in Cardiovascular Medicine, 2022, under the terms of the Creative Commons Attribution License (CC BY) (213).*

4.4. Comparing room times between pulsed-field ablation and very high-power short-duration ablation

4.4.1. Study population

We included 131 patients [66 (55-71) years, 86 (66%) had paroxysmal AF]. Eighty-seven (66%) patients underwent PFA, and 44 (34%) underwent vHPSD ablation. Baseline characteristics of the study population are shown in Table 11.

Table 11. Baseline characteristics of the study population and subpopulations. Continuous variables are expressed as mean ± SD or median (IQR), according to

normality. For AF type, the p-value refers to the overall comparison across AF type categories. Reproduced from Orbán, G et al., Heart Rhythm O2, 2025, licensed under Creative Commons Attribution 4.0 (CC BY 4.0) (216). Abbreviations: AF = atrial fibrillation; BMI = body mass index; CAD = coronary artery disease; iLAV = body surface area-indexed left atrial volume; IQR = interquartile range; LA = left atrial; LVEF = left ventricular ejection fraction; PAD = peripheral artery disease; PFA = pulsed-field ablation; PVI = pulmonary vein isolation; SD = standard deviation; TIA = transient ischemic attack; vHPSD = very high-power short-duration.

	All patients (n = 131)	**PFA (n = 87)**	**vHPSD (n = 44)**	**p-value**
Age (years)	66 (55-71)	65 (55-71)	69 (55-73)	0.127
Female, n (%)	44 (34)	30 (35)	14 (32)	0.093
BMI (kg/m^2)	28 (26-32)	29 (26-32)	28 (25-31)	0.479
AF type				
Paroxysmal, n (%)	86 (66)	52 (60)	34 (77)	0.096
Persistent, n (%)	42 (32)	32 (37)	10 (23)	
Long-standing persistent, n (%)	3 (2)	3 (3)	0 (0)	
Hypertension, n (%)	94 (72)	64 (74)	30 (68)	0.518
Diabetes, n (%)	22 (17)	18 (21)	4 (9)	0.088
Hyperlipidemia, n (%)	61 (47)	44 (51)	17 (39)	0.176
Thyroid gland disease, n (%)	15 (12)	9 (10)	6 (14)	0.545
CAD, n (%)	25 (19)	16 (18)	9 (21)	0.776
Prior stroke/TIA, n (%)	8 (6)	7 (8)	1 (2)	0.192
PAD, n (%)	3 (2)	3 (3)	0 (0)	0.213
Prior PVI, n (%)	19 (15)	19 (22)	0 (0)	**0.001**
LVEF (%)	57 (52-63)	55 (51-61)	59 (54-65)	0.142
iLAV (mL/m^2)	53 (41-63)	55 (42-65)	49 (39-58)	0.139
LA transverse diameter (mm)	45 ± 8	46 ± 7	43 ± 8	0.052
LA longitudinal diameter (mm)	55 (50-60)	56 (51-60)	54 (48-58)	0.133

4.4.2. Procedural phases and their durations

Median room time was markedly shorter with PFA than with vHPSD [71 (64-80) min vs 88 (75-100) min, respectively, ($p < 0.001$)]. Almost all other procedural phases were likewise shorter during PFA (all $p < 0.001$), except the door-in to puncture and puncture to transseptal intervals, which showed no difference (both $p > 0.05$). By contrast, the sheath-out to door-out interval was longer in PFA cases ($p < 0.001$). Fluoroscopy exposure was significantly higher in the PFA group [PFA: 8 (6-12) vHPSD: 5 (3-7) min, $p<0.001$]. Figure 11 and Table 12 summarize the time measurements of each procedural subsection and their differences.

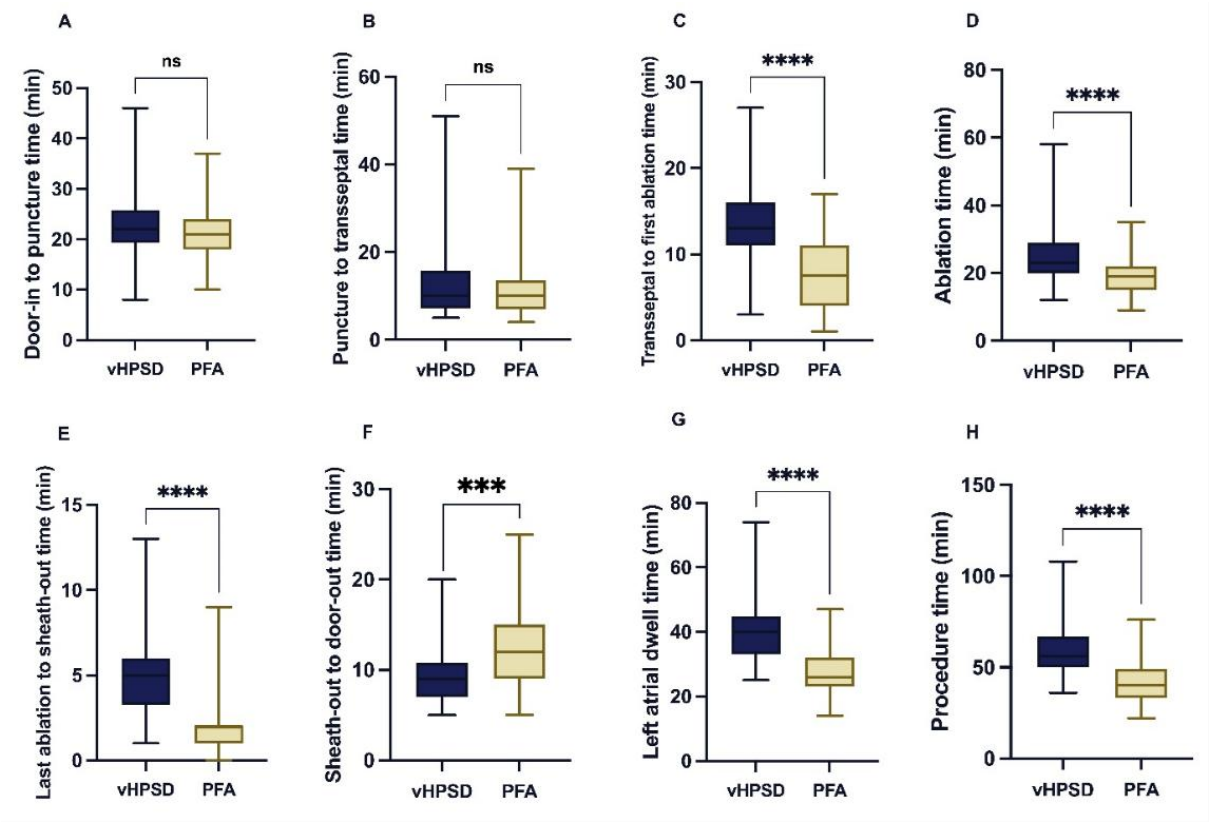


*Figure 11. Duration of procedural subsections in the PFA and vHPSD groups. Abbreviations: LA = left atrium; min = minutes; ns = not significant; PFA = pulsed-field ablation; vHPSD = very high-power short-duration; *** = p < 0.001; **** = p < 0.0001. Reproduced from Orbán, G et al., Heart Rhythm O2, 2025, licensed under Creative Commons Attribution 4.0 (CC BY 4.0) (216).*

Table 12. Procedural characteristics. Continuous variables are expressed as mean ± SD or median (IQR), according to normality. For anaesthesia type, the p-value refers to the overall comparison across anaesthesia categories. Reproduced from Orbán, G et al., Heart Rhythm O2, 2025, licensed under Creative Commons Attribution 4.0 (CC BY 4.0) (216). Abbreviations: IQR = interquartile range; NA = not applicable; PFA = pulsed-field ablation; SD = standard deviation; vHPSD = very high-power short-duration.

	All patients (n = 131)	**PFA (n = 87)**	**vHPSD (n = 44)**	**p-value**
Door-in to puncture time (min)	21 (18-25)	21 (18-24)	22 (19-26)	0.222
Puncture to transseptal time (min)	10 (7-14)	10 (7-14)	10 (7-16)	0.657
Mapping time (min)	NA	NA	9 ± 4	NA
Transseptal to first ablation time (min)	10 ± 5	8 ± 4	14 ± 4	**<0.001**
Ablation time (min)	20 (16-25)	19 (15-22)	23 (20-29)	**<0.001**
Last ablation to sheath-out time (min)	2 (1-5)	2 (1-2)	5 (3-6)	**<0.001**
Sheath-out to door-out time (min)	10 (8-14)	12 (9-15)	9 (7-11)	**<0.001**
Left atrial dwell time (min)	29 (24-38)	26 (23-32)	40 (33-45)	**<0.001**
Procedure time (min)	44 (37-56)	40 (33-49)	56 (50-67)	**<0.001**
Room time (min)	75 (68-88)	71 (64-80)	88 (75-100)	**<0.001**
Anaesthesia types				
Conscious sedation, n (%)	39 (30)	0 (0)	39 (89)	**<0.001**
Deep sedation, n (%)	88 (67)	83 (95)	5 (11)	
General anaesthesia, n (%)	4 (3)	4 (5)	0 (0)	

4.4.3. Efficacy and safety

All PVs were electrically isolated in every patient, and first-pass isolation was achieved in 89% of vHPSD cases. Four complications (3%) occurred, with no significant between-

group difference ($p > 0.05$): one groin hematoma in each group, neither requiring intervention; transient ST-segment elevation in one PFA case, with coronary angiography excluding CAD and spontaneous resolution within minutes; and one major complication, an arteriovenous fistula at the femoral access site in a PFA patient, requiring vascular surgery the following day. Median hospital stay was 1 day [IQR 1-1] in both groups ($p > 0.05$). At 6-month, AF recurrence occurred in 16% of patients, with no significant between-group difference ($p > 0.05$). Post-procedural AAD use was prospectively recorded and did not differ between groups ($p > 0.05$). Exploratory analysis showed no significant association between AAD use at 6 months and arrhythmia recurrence ($p > 0.05$).

4.4.4. Influence of operator experience on room time

In both operator groups, PFA was associated with significantly shorter room times than vHPSD. Among expert operators, median room time was 69 minutes (IQR 60-74) with PFA compared with 80 minutes (72-87) with vHPSD ($p < 0.001$). This difference was more pronounced among experienced operators: median room time was 76 minutes (66-87) with PFA compared with 98 minutes (89-115) with vHPSD ($p < 0.001$) (Figure 12).

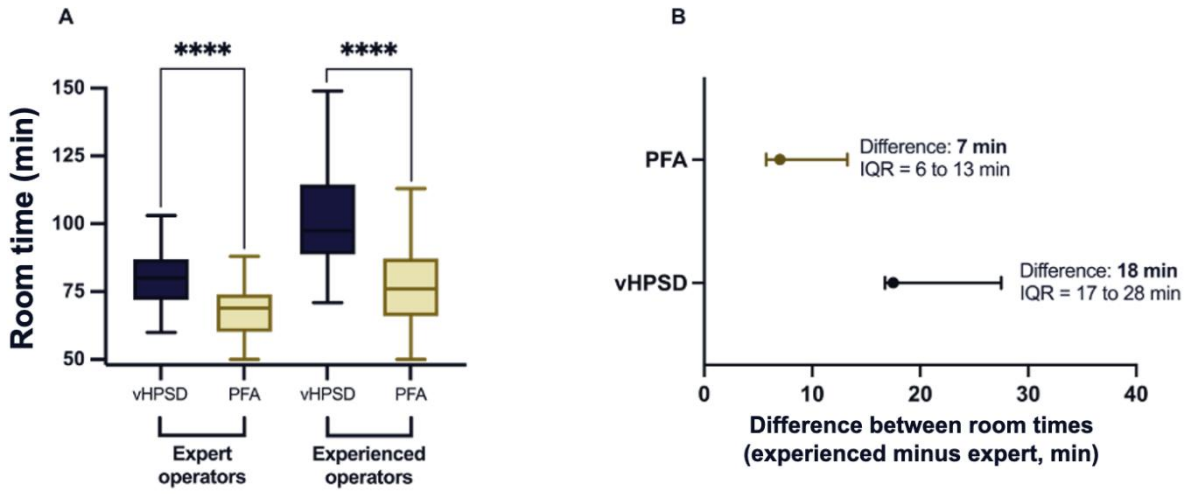


*Figure 12. Subgroup analysis of room times according to operator experience. Abbreviations: AF = atrial fibrillation; IQR = interquartile range; OR = operating room; PFA = pulsed-field ablation; vHPSD = very high-power short-duration; **** = $p < 0.0001$. Reproduced from Orbán, G et al., Heart Rhythm O2, 2025, licensed under Creative Commons Attribution 4.0 (CC BY 4.0) (216).*

5. DISCUSSION

5.1. Imaging in atrial fibrillation: from pre-procedural assessment to prediction of recurrence

Cardiac imaging plays a central role in the management of AF, both in the pre-procedural setting and in the identification of factors associated with post-ablation recurrence (1). In our work, we investigated two complementary aspects of imaging: the optimization of pre-procedural imaging for thrombus exclusion and anatomical assessment, and the use of imaging-derived anatomical relationships to predict AF recurrence.

In our first study, we evaluated a novel non-contrast-enhanced CMR sequence (BOOST) in comparison with TEE and contrast-enhanced cardiac CT. The main focus of this component was LAA thrombus assessment and patient experience, whereas the comparison with contrast-enhanced CT and the assessment of LA functional parameters were secondary exploratory analyses based on the available imaging data. Our results demonstrated that BOOST imaging is feasible and provides clinically relevant information both for thrombus exclusion and for anatomical assessment prior to CA. Importantly, BOOST allows imaging without the use of contrast agents or ionizing radiation.

When imaging is needed for exclusion of LAA thrombi, the 2024 ESC AF guideline designates TEE as the gold standard for this purpose (1). When TEE is not feasible or is declined, cardiac CT with a dedicated delayed-contrast protocol, CMR or, in experienced centers, intracardiac echocardiography may be used as validated alternatives (1, 217-220). While TEE delivers very high diagnostic accuracy (>95% sensitivity, ≈100% specificity), it remains operator-dependent and may be ambiguous in cases with complex LAA anatomy, dense SEC, or sludge; moreover, it is semi-invasive, often uncomfortable, and carries a small but relevant risk of oropharyngeal or esophageal injury (221). On the other hand, cardiac CT, although a validated alternative, exposes patients to ≈2–3 mSv of ionizing radiation (217), requires iodinated contrast with attendant risks of allergy and nephrotoxicity (222). Furthermore, CT is susceptible to false-positive filling defects unless a ≥3–6 min delayed phase is acquired (219), and its diagnostic performance varies with scanner protocol, center expertise and AF related rhythm irregularity (190). Similarly, contrast-enhanced CMR – particularly delayed-enhancement imaging – has proven effective for detecting LAA thrombus. Nevertheless, its applicability is limited in

patients with impaired renal function and, in rare cases, by contrast agent hypersensitivity (220, 223).

The BOOST CMR sequence addresses key limitations of other imaging alternatives by avoiding ionizing radiation, contrast administration, and renal dependency, while simultaneously providing bright- and black-blood 3D datasets (209, 210). In our study, BOOST excluded LAA thrombus in 67 of 71 patients (94%) in concordance with TEE findings (Table 4), demonstrating good agreement in a clinical setting. One patient had inconclusive results on both TEE and contrast-enhanced CT, while BOOST showed no thrombus. However, due to the absence of exclusion by a validated imaging reference, this case cannot be interpreted as confirmation of a thrombus-free status, even though no clinically manifest thromboembolic event occurred during the three-month follow-up period without any change in the anticoagulation regimen. Delayed-enhancement CMR could have been considered as a supplementary modality in such uncertain cases, given its previously reported high sensitivity and specificity for thrombus detection (220, 224), although its superiority over TEE or CT is not established. Finally, while BOOST reliably identified large thrombi, the isotropic resolution used here (1.4 × 1.4 × 1.4 mm) may limit its ability to detect smaller thrombi; higher-resolution protocols (e.g. 1.2 × 1.2 × 1.2 mm) warrant future investigation.

Beyond thrombus exclusion, pre-procedural imaging can also help characterize LA and PV anatomy, because specific variants can affect both ablation outcome and device choice (23, 24, 33–35). In our institution contrast-enhanced CT is our current standard, yet electrophysiologists who reviewed both CT and BOOST images from patients who underwent both modalities agreed that, despite slightly lower image quality, BOOST still supplied adequate information required for procedural planning. Moreover, to support this point, PV ostial area measurements did not differ between modalities (all $p > 0.05$). Consequently, BOOST could eventually replace contrast-enhanced LA CT, particularly in younger patients or those with renal impairment, while simultaneously obviating TEE for LAA thrombus screening.

TEE's esophageal intubation causes notable distress: two-thirds of patients reported at least mild pain, whereas only one patient felt mild discomfort during CMR, and 89% would choose CMR for future imaging in case of LAA thrombus exclusion ($p < 0.0001$).

Taken together, these results support a more individualized approach to pre-procedural imaging in AF, where the choice of imaging modality should be tailored based on patient characteristics, clinical indication, and local expertise. In this context, non-contrast-enhanced CMR techniques such as BOOST may have an increasing role in the future.

Beyond its role in modality selection, the same pre-procedural imaging dataset can be further leveraged to extract anatomical features with prognostic relevance.

Once an LAA thrombus has been ruled out, the same pre-procedural imaging set is analyzed to define LA and PV anatomy, information essential for planning PVI. In the cohort from our retrospective study focusing on anatomical predictors, an abutting LAA-LSPV configuration (defined as an endocardial distance of <2 mm between the LAA and the LSPV measured on pre-procedural contrast-enhanced CT) was present in 54% of the patients and emerged as the strongest independent predictor of post-ablation recurrence.

Although the specific link between an abutting LAA-LSPV and recurrence is novel, other anatomical studies support that myocardial bulk in this region affects ablation lesion durability and recurrence. A three-dimensional CT wall thickness study showed that segments which later reconnect are significantly thicker, with the greatest differences at the LSPV ridge and carina (225). A separate cohort linked a broad (rectangular) LA ridge to higher one-year AF recurrence, again implicating local myocardial bulk (226). Finally, thorough electroanatomical mapping studies identified epicardial conduction through the ligament of Marshall that can bypass an apparently complete ostial line; focal ablation at the anterior LSPV carina eliminated these connections (227). Taken together, these studies suggest that when the LAA is in direct apposition to the LSPV (endocardial gap <2 mm), the thicker atrial ridge and residual epicardial fibers make durable isolation harder to achieve – providing a plausible mechanistic basis for the higher recurrence risk we observed. The 54% prevalence observed in our cohort is difficult to compare directly with previous literature, because earlier studies mainly assessed left lateral ridge width or morphology rather than the minimal endocardial distance between the LAA and LSPV (228, 229). Nevertheless, these studies consistently indicate substantial anatomical variability in this region, and some have linked ridge morphology or dimensions to AF recurrence after ablation (230, 231). Thus, our study extends previous work by introducing a quantitative, reproducible CT-based definition of abutting LAA-LSPV anatomy and demonstrating its association with post-ablation recurrence.

This result is clinically significant for several reasons. First, the abutting LAA-LSPV arrangement was common in our cohort, affecting more than half of the studied patients. Second, it can be quickly recognized on routine contrast-enhanced CT images because the gap between the LAA and the LSPV can be measured in seconds with good reproducibility. Unlike age or overall atrial size, which are general predictors of recurrence but cannot be addressed during ablation planning or the procedure itself, the presence of an abutting LAA-LSPV is a local anatomical feature that can directly guide precise lesion delivery: a gap under 2 mm implies a thicker LA ridge and possible epicardial connections, so additional lesions along the ridge or the ligament of Marshall may improve long-term isolation. Including this simple measurement in the standard contrast-enhanced cardiac CT report could refine the patient's risk-and-benefit assessment and help operators plan a more tailored ablation strategy.

Overall, these results emphasize that pre-procedural imaging serves a dual role AF, informing both procedural planning and risk stratification through detailed assessment of LA and PV anatomy.

5.2. Lesion formation and procedural efficiency in contemporary ablation technologies

In the present work, also we investigated two closely related aspects of CA in AF: lesion formation characteristics during vHPSD RF ablation, and procedural efficiency as reflected by room time and procedure duration in vHPSD and PFA.

Importantly, both analyses are centered around vHPSD ablation, which provides a common procedural and technological framework linking lesion formation characteristics with overall procedural performance.

In conventional RFCA of AF, lesion quality is assessed using composite metrics – Ablation Index, Lesion Size Index, and real-time local ID – but these surrogates cannot be applied to vHPSD lesions, where power and time are fixed at baseline (although can be modified automatically or manually during the ablation) and the QDOT Micro catheter (Biosense Webster, Irvine, CA, USA) lacks integrated local impedance sensing (232-234). Although generator ID has been proposed as an alternative (235, 236), it correlates only weakly with lesion quality (237).

Gutbrod et al. showed that local impedance – a marker of tissue contact – increases steeply as CF rises, but plateaus once CF reaches about 5 g, indicating no meaningful

additional tissue contact beyond this threshold (238). Our data mirror this observation: CF ≥5 g produced significantly higher maximum electrode temperatures, indicating larger resistive heating zones (18). Because the QDOT Micro (Biosense Webster, Irvine, CA, USA) houses six thermocouples within 3 mm of the tip, the generator can run in temperature-control mode: when rising CF drives maximum temperature toward the target temperature of 55 °C, delivered power is automatically reduced. As a result, higher CF values were associated with higher peak temperatures but lower mean power showing effective feedback regulation without compromising lesion efficacy (239-241).

Prior studies with conventional power settings recommended a CF window of 10–30 g for durable lesions (242, 243). In our vHPSD series, CF as low as 5 g sufficed for optimal tissue heating, and values well above the manufacturer's 5-25 g guideline occasionally occurred – up to 50 g – without steam pops or perforation, presumably because the algorithm promptly curtailed power once the temperature target was met (244). Such transient CF spikes may arise under conscious sedation when patient movement alters catheter stability (245).

In summary, during vHPSD ablation, maximum temperature significantly correlates with CF. Moreover, a CF ≥5 g achieves higher tissue heating and, therefore, is likely to yield better LA lesions, although lesion size was not measured in this study.

Beyond lesion formation, the same vHPSD-based procedural framework also allows evaluation of overall procedural efficiency in comparison with emerging ablation technologies.

PFA proved faster than vHPSD ablation, even though vHPSD represents the fastest RF option nowadays. Median room time was 17 minutes shorter with PFA, and the procedure time averaged 40 minutes versus 56 minutes for vHPSD. Two mechanistic differences explain this gap. First, PFA does not require electroanatomical mapping, which is reflected in a markedly shorter transseptal to first ablation time (8 minutes for PFA vs 14 minutes for vHPSD). Second, catheter navigation and manipulation appear less complex with a large footprint PFA system, as cumulative ablation time is lower than with the point-by-point vHPSD approach (19 minutes vs 23 minutes).

Reductions in skin-to-skin procedure time and LA dwell time with PFA mirror those reported in earlier comparisons with thermal ablation technologies. In the ADVENT trial,

LA dwell time was 29% shorter and overall procedure time 14% shorter with PFA compared to thermal ablation; both statistically significant (176). A single-center study comparing PFA with cryoballoon PVI in 400 patients (200 per group) found a significant reduction in procedure time in favor of PFA (246).

Although vHPSD requires placement of skin patches for the mapping system and the preparation of two transseptal sheaths, door-in to puncture time remained similar (21 min vs 22 min), reflecting the experience of our EP laboratory staff. Fluoroscopy time and dose were higher with PFA, consistent with the findings of ADVENT trial (176), because the absence of LA mapping necessitates greater reliance on fluoroscopic guidance. Despite this, radiation exposure still remains well below that of other percutaneous cardiology procedures (e.g., coronary angiography) (247, 248).

PFA demands deeper anaesthesia (249, 250), lengthening sheath-out to door-out time (12 min vs 9 min), yet overall room time still favored PFA (71 min vs 88 min) thanks to shorter intraprocedural phases. Saving approximately 17 min per case could permit one extra procedure after every four, without worsening 6-month recurrence rates.

Our cohort experienced three minor and one major complication, with no difference in hospital stay between PFA and vHPSD. These findings are consistent with previous literature: the MANIFEST-PF survey reported a major complication rate of 1.6% and a minor rate of 3.9% for PFA (249), while the Q-FFICIENCY trial documented a 3.6% primary adverse-event rate after vHPSD ablation (251).

Operators were classified by volume: experts (> 1,000 prior AF ablations) versus experienced (< 1,000). In expert-performed PFA cases, median room time was 69 minutes versus 76 minutes for experienced operators – a modest 7-minute difference most probably without relevant clinical impact. By contrast, vHPSD showed an 18-minute expert-experienced gap (80 min vs 98 min). The EU-PORIA registry likewise found no significant variation in PFA procedural times or complication rates across operator-experience levels (172). Given that AF ablation is the most commonly performed electrophysiology procedure, PFA's relative operator-independence represents a meaningful advance in standardizing efficiency and outcomes.

5.3. Limitations

Several limitations of the present dissertation should be acknowledged. The investigations were conducted within a single high-volume tertiary cardiovascular center,

using institution-specific imaging protocols, ablation strategies, operator experience, and procedural workflows. Although this ensured methodological consistency, it may limit generalizability to centers with different patient populations, imaging availability, ablation technologies, or peri-procedural routines. In addition, several analyses were observational, retrospective, or non-randomized, which limits causal interpretation. Recurrence assessment was based on clinically indicated follow-up and ECG-documented arrhythmia episodes, without systematic invasive or continuous rhythm monitoring. Therefore, asymptomatic or short-lasting AF recurrences may have remained undetected, and the true recurrence burden may have been underestimated.

Regarding the BOOST CMR component, the number of patients was relatively limited, and the prevalence of LAA thrombus was low; therefore, the positive predictive value of the sequence could not be reliably assessed. TEE served as the reference modality, but inconclusive cases with dense sludge highlight the uncertainty of thrombus assessment. Only a subset of patients underwent contrast-enhanced CT, and the ability of BOOST CMR to detect smaller thrombi may be influenced by spatial resolution. The follow-up period was short and mainly suitable for detecting procedure-related neurological events.

Regarding the abutting LAA-LSPV analysis, the retrospective design limits conclusions. Post-procedural AAD use was not systematically collected and therefore could not be included in the recurrence analysis. Although entrance and exit block were confirmed during the index procedures, potential capture from non-ostial LSPV segments was not systematically investigated. In addition, ablations were guided by the lesion quality parameters available at that time, and this anatomical predictor should be validated using contemporary ablation technologies and lesion assessment tools.

The vHPSD RF ablation analysis was based on a single-arm clinical cohort with a limited number of patients, although the number of analyzed RF applications was high. Actual lesion dimensions could not be directly assessed, and only mid-term clinical follow-up was available. Therefore, the relationship between the observed biophysical parameters and long-term outcome requires further investigation. The safety profile also cannot be fully characterized from this sample size.

Finally, the comparison of PFA and vHPSD ablation was observational and non-randomized. Although baseline characteristics were largely comparable, the higher rate of prior PVI in the PFA group may have influenced procedural metrics. Procedures were

performed by operators with different experience levels, and procedure times may also have been affected by modality-specific workflow differences, including transseptal access strategy. Moreover, the findings primarily apply to the Farapulse PFA system (Boston Scientific, Corp, Marlborough, MA, USA) and should not be automatically generalized to other PFA platforms.

6. CONCLUSIONS

This dissertation set out to test four practical questions, each touching a key stage of contemporary AF ablation. First, the non-contrast-enhanced BOOST CMR sequence matched TEE in excluding clinically relevant LAA thrombus in 94% of the patients and provided sufficient PV anatomical detail for ablation planning in 91% of cases, although contrast-enhanced CT still delivered superior image quality. Moreover, patients overwhelmingly preferred CMR over TEE. This novel sequence may therefore pave the way for a new pre-procedural imaging paradigm prior to both ECV and AF ablation. Second, a simple anatomical metric – abutting LAA and LSPV – proved to be an important independent predictor of post-ablation recurrence, highlighting a subgroup that may benefit from additional lesion sets. Third, temperature-controlled vHPSD ablation demonstrated that a CF of approximately 5 g is sufficient for effective lesion creation. Once this threshold is reached, the generator's rapid feedback maintains optimal tissue heating without delivering excess power, thereby limiting the risk of complications while ensuring adequate lesion formation. Finally, PFA shortened room time (overall time spent in the OR by a patient) by 17 minutes compared with the fastest RF technology (i.e., vHPSD ablation), achieved this consistently across different operator experience levels, and maintained comparable safety and six-month efficacy. Taken together, these findings confirm that non-contrast-enhanced CMR imaging, targeted anatomy-based risk stratification, contact force-guided and temperature-controlled very high-power short-duration RF energy delivery, and non-thermal workflows can collectively make AF ablation safer, quicker, more effective, and more patient-centered.

7. SUMMARY

Atrial fibrillation continues to face limitations in long-term treatment success due to PV reconnection, anatomical variability, and procedural inefficiencies, which restrict the ability to deliver treatment to more patients. This thesis explored key elements along the AF ablation workflow, including pre procedural imaging, lesion delivery parameters, anatomical predictors of recurrence, and procedural efficiency, aiming to streamline strategies that improve safety, efficacy and procedural capacity.

We first evaluated a novel non-contrast enhanced CMR sequence as an alternative to TEE and contrast-enhanced CT for pre-procedural LAA thrombus exclusion and anatomical planning. BOOST CMR reliably ruled out LAA thrombus, provided accurate LA and PV anatomical assessment, and was substantially better tolerated by patients. Beyond pre-procedural imaging, we also investigated the prognostic value of patient-specific anatomical factors. In a cohort examined with pre-procedural contrast-enhanced CT, an abutting LAA-LSPV – defined as an endocardial distance <2 mm between the two structures – was present in more than half of the patients and emerged as the strongest independent predictor of post-ablation AF recurrence. This observation identifies a high-risk anatomical subgroup that may benefit from localized intensified lesion delivery. We then focused on determinants of effective lesion delivery during RF ablation. We analyzed procedural characteristics of vHPSD RFCA and found that peak temperature significantly correlated with CF. A CF ≥5 g was associated with higher tissue heating, whereas occasional higher CF values (i.e., >25 g) were not linked to complications. These findings highlight the central role of adequate CF in ensuring lesion quality and procedural safety during vHPSD ablation. Finally, we compared PFA and vHPSD ablation. PFA shortened room time by 17 minutes and reduced the duration of most procedural subsections, regardless of operator experience, with no difference in safety or 6-month efficacy. Such reduction translates into the capacity to perform an extra procedure after every 4 cases.

Together, these studies demonstrate how advanced imaging, anatomical risk stratification, optimized lesion delivery parameters, and improved procedural efficiency can improve AF ablation workflows. Integrating these elements into clinical practice may help increase procedural capacity, reduce recurrences, and improve outcomes.

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9. BIBLIOGRAPHY OF THE CANDIDATE'S PUBLICATIONS

Publications related to the thesis:

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