Diploma thesis

Patients with atrial fibrillation undergoing catheter ablation with innovative therapies – a single center experience

submitted by

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Graz, 25.07.2023

Affidavit

I hereby declare that I did write the following diploma thesis by myself and without any assistance from third parties. Furthermore, I confirm that no sources have been used in the preparation of this thesis other than those indicated in the thesis itself.

Graz, 25.07.2023 Anja Reischl eh.

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List of abbreviations

AAD	Antiarrhythmic drug
AP	Action potential
BMI	Body Mass Index
BPM	Beats per minute
Ca^{2+}	Calcium
CIED	cardiac implantable electronic device
CTI	Cavotricuspidal isthmus
DADs	Delayed afterdepolarizations
DOACs	Direct oral anticoagulants
EADs	Early afterdepolarizations
ECG	Electrocardiogram
EHRA	European Heart Rhythm Association
ESC	European Society of Cardiology
K^{+}	Potassium
LIPV	Left inferior pulmonary vein
LSPV	Left superior pulmonary vein
LVEF	Left ventricular ejection fraction
Na^{+}	Sodium
NT-proBNP	N-terminal prohormone of brain natriuretic peptide
OAC	Oral anticoagulation
PFA	Pulsed field ablation
PVI	Pulmonary vein isolation
RIPV	Right inferior pulmonary vein

RSPV	Right superior pulmonary vein
RF	Radiofrequency (energy)
RFA	Radiofrequency ablation
RR	Riva-Rocci
RV	Right ventricle

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// Zusammenfassung

Hintergrund: Vorhofflimmern (AF) ist nach wie vor die häufigste Tachyarrhythmie bei Erwachsenen. Die Morbidität und Mortalität bei Patient*innen mit Vorhofflimmern ist im Vergleich zu Patient*innen im Sinusrhythmus wesentlich höher. Es gibt bereits verschiedene Behandlungsmöglichkeiten zur Wiederherstellung des Sinusrhythmus, aber die Katheterablation bietet die besten Chancen auf dauerhaften Erfolg. Die meisten etablierten Energiequellen für die Pulmonalvenenisolation (PVI) wie Radiofrequenz- und Kryoablation haben ihre Grenzen hinsichtlich Wirksamkeit und Sicherheit. Neue Ablationstechniken werden ständig entwickelt, mit dem Ziel die Sicherheit und Wirksamkeit zu verbessern. Die Elektroporation (PFA) ist eine nicht-thermische Technik, bei der kurze, hochenergetische elektrische Impulse unter Verwendung irreversibler Elektroporation erzeugt werden. Dadurch hat sie das Potenzial, den Ablationserfolg zu verbessern und die Komplikationen der PVI zu verringern.

Methode: Alle Patient*innen, bei denen an der Universitätsklinik für Kardiologie der Medizinischen Universität Graz eine Elektroporation-PVI durchgeführt wurde, wurden retrospektiv analysiert. Die statistische Analyse wurde mit Excel und SPSS durchgeführt.

Ergebnisse: 155 Patient*innen wurden in die Analyse einbezogen (39% weiblich, 62±9 Jahre). Zwei Drittel der Patient*innen hatten paroxysmales Vorhofflimmern und bei 6% aller Patient*innen wurde zusätzlich Vorhofflattern diagnostiziert. Eine First-Pass-Isolation wurde bei 83% aller Patient*innen erreicht. Bei 17% der Patient*innen wurde die Ablation aufgrund von Lücken, hauptsächlich im Bereich der linken superioren Pulmonalvene, nachgeholt. Die Dauer des Ablationsverfahrens betrug 76±30 Minuten und 118±27 Minuten, wenn zusätzlich eine Ablation für Vorhofflattern durchgeführt wurde. Bei 79% der Patient*innen konnte bei der Nachuntersuchung nach einem Jahr kein Wiederauftreten einer Vorhofarrhythmie festgestellt werden. Ein Rezidiv trat bei 21% der Patient*innen nach 77±91 Tagen auf, wobei sich 10 Patient*innen innerhalb des ersten Jahres einem erneuten Eingriff unterziehen mussten. Am häufigsten wurden Lücken in der rechten inferioren Pulmonalvene und im Bereich der Ridge der linken

Pulmonalvenen sowie im Bereich der Carinae beobachtet. Größere Komplikationen traten nicht auf.

Schlussfolgerung: Die Elektroporation stellt eine neue nicht-thermische Ablationstechnik mit vielversprechenden Erfolgsraten und niedrigen Komplikationsraten dar. Es besteht jedoch Bedarf an prospektiven multizentrischen Studien mit hohen Fallzahlen, um bessere Schlussfolgerungen hinsichtlich der Sicherheit und Wirksamkeit der gepulsten Feldablation zu ziehen

Abstract

Background: Atrial fibrillation (AF) remains the most common tachyarrhythmia in adults. The morbidity and mortality in patients with AF are much higher compared to patients in sinus rhythm. There are already various treatment options for restoring sinus rhythm, but catheter ablation offers the best chance of lasting success. Most established energy sources for pulmonary vein isolation (PVI) such as radiofrequency and cryoablation have their limitations concerning efficacy and safety. New ablation techniques are constantly being developed with the goal of improving safety and efficacy. Pulsed field ablation (PFA) is a non-thermal technique generating short, high-energy electrical pulses using irreversible electroporation and thus has the potential to improve ablation success and reduce complications of PVI.

Method : All patients that underwent a PFA-PVI at the Department of Cardiology of the Medical University of Graz were retrospectively analyzed. The statistical analysis was performed using Excel and SPSS.

Results: 155 patients were included in the analysis (39% female, 62±9 years). Two-thirds of the patients had paroxysmal atrial fibrillation and 6% of all patients were additionally diagnosed with atrial flutter. First-pass isolation was achieved in 83% of all patients. 17% of the patients received a touch-up ablation because of gaps, mainly in the region of the left superior pulmonary vein. Ablation procedure time was 76±30min and 118±27min when additionally, ablation for atrial flutter was performed. 79% of patients were free of recurrence of any atrial arrhythmia at the one year follow up. Recurrence occurred in 21% of patients after 77±91 days with 10 patients undergoing a redo procedure within the first year. Most commonly gaps of the right inferior pulmonary vein and in the ridge area of the left pulmonary veins as well as in the area of the carinae was observed. No major complication occurred.

Conclusion: Pulsed field ablation represents a new non-thermal ablation technique with promising success rates and low complication rates. However, there is a need for prospective multicenter studies with high case numbers to draw better conclusions regarding the safety and efficacy of pulsed field ablation.

Introduction

1. Atrial Fibrillation

Atrial fibrillation (AF) is defined as a tachycardic, irregular arrhythmia which has its origin in the left atrium of the heart. It leads to uncoordinated depolarizations of the atrial myocardium that can reach frequencies above 300 beats per minute (bpm), resulting in ineffective atrial contractions. (1, 2)

In the electrocardiogram (ECG, *Figure 1*) no clear P waves can be distinguished. The atrioventricular node, when functioning adequately, can filter the high frequencies of the atrium in patients with AF, which can result in lower ventricular frequencies, typically below 150 bpm. Nevertheless, the ventricular activity may also remain irregular. (1, 2)

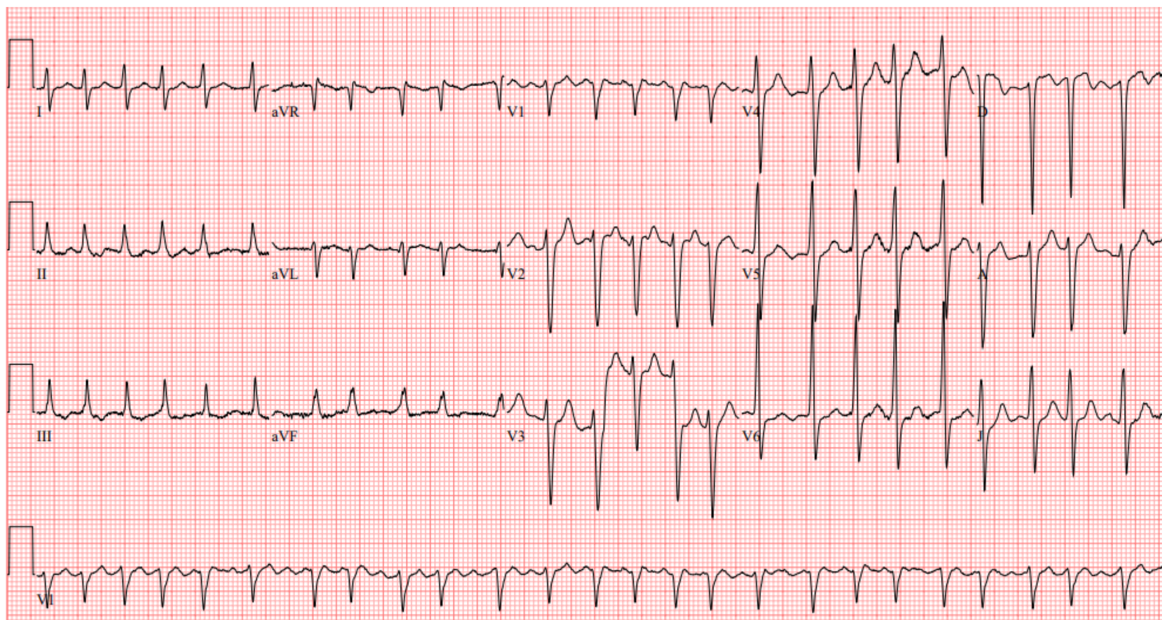

Figure 1 Example ECG tachycardic conducted AF

1.1. Diagnostic

For the clinical diagnosis of AF, rhythm documentation using either a single-lead ECG recording with a minimum duration of 30 seconds, or a standard 12-lead ECG is required. (1)

Therefore, the European Society of Cardiology (ESC) has defined the following criteria for the diagnosis of AF using an ECG:

- “Absolutely irregular RR intervals
- no discernible, distinct P waves
- an episode lasting at least 30 seconds” (1)

However, ECGs of this type are only a momentary recording of electrical signals and arrhythmias that occur outside of this period are missed. For this reason, continuous ECG monitoring systems have been developed to address these limitations. For ambulatory detection of arrhythmias, so-called Holter monitors are commonly used. The different types of cardiac monitoring are listed in *Table 1* below. (3)

Device	Maximum Duration of Monitoring
12-lead ECG	Single timepoint
Holter monitoring	Several days
Patch monitor	1–3 weeks
External loop recorder	1 month
Implantable loop recorder	3 years
Cardiac implantable electronic devices (CIED)	Indefinite
Wearable cardioverter defibrillator	Indefinite
Smartphone monitor	Indefinite
Mobile cardiac telemetry	1 month

Table 1 Cardiac monitoring devices (3)

For atrial arrhythmias detected by a CIED (Pacemaker, implantable cardioverter defibrillator), episodes lasting more than 5 to 6 minutes are considered “high atrial frequency episodes”. The clinical relevance and therapeutic strategy of incidental detection of asymptomatic AF episodes in CIED patients is still under investigation. (1)

Also, the increasing digitalization offers new techniques for digital ECG analysis through wearable, injectable devices, or also smart textile-based garments. This opens new possibilities for the detection and diagnosis of AF, as it could be used to personalize therapy and risk stratification. Several studies are currently underway to evaluate such possibilities and to define appropriate treatment pathways based on such tools. (1, 3)

1.2. Epidemiology

AF is the most common sustained form of cardiac arrhythmia in adults. Worldwide, the number of AF patients was approximately 43.6 million people in 2016. One in three middle-aged adults will be affected during their lifetime. Austria is among the countries with the highest prevalence (>900/100,000), along with the United States, Canada, Norway, Sweden, and Finland. (1) According to the study by Lipi, Sanchies-Gomar, and Cervellin, the estimated global incidence in 2017 was 31% higher than it was in 1997, and the worldwide prevalence also increased by 33% over the past 20 years. As seen in the figure 2 **Error! Reference source not found.**, t he prevalence of AF is expected to continue to rise sharply in the upcoming years. (4)

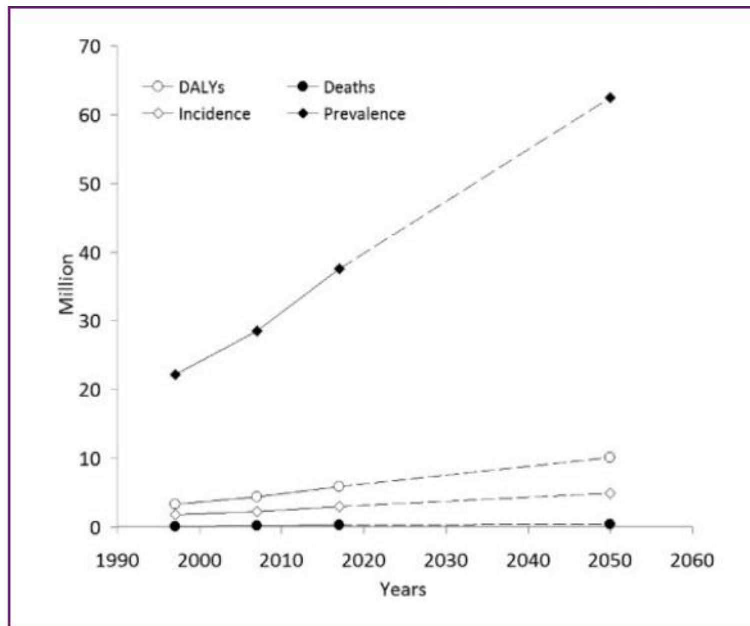

Figure 2 Worldwide burden of AF (4)

This is partly due to the fact that life expectancy and thus the number of people affected is increasing, and partly due to the rise in risk factors, technical improvements, better methods of prognosis and growing awareness among the public and doctors. (5)

1.3. Classification

There are different types of AF. For the respective classification, the most important factors are the consideration of the duration of the AF episodes and the clinical manifestation of the arrhythmia. Basically, a classification is made among the following types: paroxysmal, persistent, long-standing persistent and permanent. (2, 6)

Paroxysmal AF refers to episodes that occur spontaneously, usually lasting several minutes to hours but no longer than seven days, and spontaneously convert back to sinus rhythm. (6)

Persistent AF lasts between seven days and twelve months and often requires pharmacological or electrical therapy to return to normal rhythm. Duration beyond seven days lowers the chance of spontaneous cardioversion. (2)

Long-standing persistent AF is defined as a continuous episode of AF for more than 12 months but the therapeutic strategy is still rhythm control. (6)

Permanent AF means that cardiac arrhythmia is continuously present. This may be either the first occurrence or preceded by recurrent self-terminating episodes. Attempts to restore sinus rhythm have either not been attempted or have failed. This form is also referred to as accepted permanent AF. (2, 6)

However, this classification only refers to the duration of AF episodes and the temporal pattern of AF, which may not provide holistic care, as AF is a complex disease. For this reason, the European Society of Cardiology proposed a paradigm shift toward a structured characterization of AF (*Figure 3*) in its latest guideline, called the 4S-AF Scheme. (Stroke, Symptoms, Severity of AF burden and Substrate) (7)

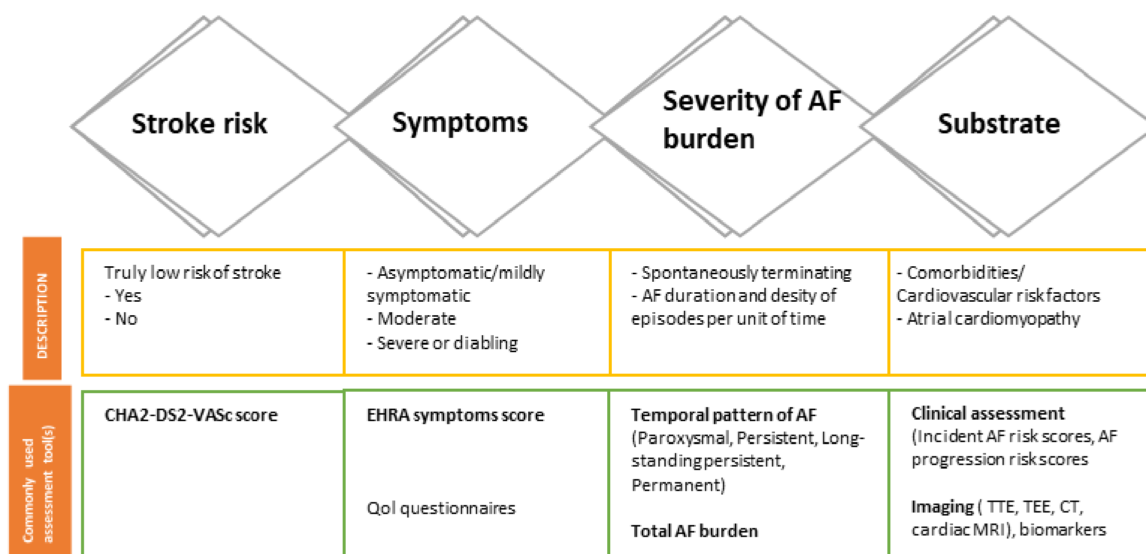

Figure 3 4S-AF Scheme (7)

Stroke Risk: Stroke is the second leading cause of death worldwide after ischemic heart disease and AF is an important risk factor, as the disease leads to a five-fold higher risk of stroke and a two-fold increase in mortality. The currently routinely used CHA_2DS_2 VASc score is used to assess the risk of a stroke. (*Table 2*) The CHA_2DS_2 VASc score is an acronym for Congestive heart failure, Hypertension, Age ≥ 75a, Diabetes, Stroke, Vascular disease, Age > 65a, Sex category female. The score can reach a maximum value of 9 and as the score increases, the annual risk for a

thromboembolic event increase. The incidence of stroke at 1 year follow-up is estimated to be 0.2% in patients with a score of 0 and to patients with a score of 9 to 14.4%. (8)

Risk factor	Points
Congestive heart failure	+1
Hypertension	+1
Age ≥ 75 y	+2
Diabetes mellitus	+1
Previous stroke, transient ischemic attack, or thromboembolism	+2
Vascular disease	+1
Age 65 – 74y	+1
Female gender	+1

Table 2 CHA_2DS_2 VASc score (8)

Symptoms: In AF, the clinical symptoms are extremely broad and frequently depend on the heart rate that is being transmitted. Some patients experience symptoms such as palpitations, chest pain, dyspnea, fatigue, and dizziness, which can usually lead to a decrease in quality of life. Younger patients are more likely to experience palpitations as well as chest pain, while shortness of breath as well as fatigue predominate in older people. Symptoms are usually most severe at the onset of the disease, when episodes are usually paroxysmal, and the heart rate is fast. As the disease progresses, the symptoms usually decrease. The resulting subjective distress for the patient is classified and evaluated using the European Heart Rhythm Association (EHRA) score (*Table 3*). (6)

EHRA I	**No symptoms**
EHRA IIa	Mild symptoms. No impairment of daily life.
EHRA IIb	Mild symptoms. No impairment of daily life, but patient troubled by symptoms
EHRA III	Severe symptoms. Impairment of everyday life.
EHRA IV	Severe disabling symptoms. Unable to cope with everyday life

Table 3 EHRA classification (1)

There are also some people who experience no symptoms. This can be found as incidental finding in routine health check-ups or might be discovered during routine follow-up of CIED such as pacemaker checks. (6)

It is important to note that AF is associated with increased morbidity and mortality in patients. In addition to the common symptoms, complications such as ischemic stroke, vascular dementia, depression, and heart failure may occur. (1)

Severity of AF burden: This domain deals with the duration and density of AF episodes and the termination of these episodes. Here, the guidelines continue to recommend using the classification according to the temporal pattern (paroxysmal, persistent, or permanent). However, with the ever-advancing portable and deployable technologies for long-term monitoring, the description and classification of AF burden will change soon. (7)

Substrate: This deals with the pathophysiology of AF, which is very complex. The focus is on the enlargement, dysfunction and fibrosis of the left atrium as well as existing comorbidities. Cardiovascular risk factors as well as comorbidities are a routine part of a clinical examination of every patient. For the evaluation of the left atrium, transthoracic echocardiography should be used primarily, as it is widely used in routine clinical practice and provides basic information. (7)

1.4. Risk factors

The range of conditions that cause AF or that promote the progression of AF is broad. Some modifiable as well as non-modifiable risk factors have now been identified. Non-modifiable risk factors include age as well as sex, with age being the most important risk factor. The risk for developing AF doubles with each decade of life. While the incidence in patients aged 55 to 59 years is 1.1 per 1000 person-years, it is 20.7 per 1000 person-years in patients over 80 years. (9)

Gender also influences the occurrence of AF. It has been observed that women suffer more frequently from the symptoms of AF and have a higher heart rate than male patients. However, women have a 46% lower risk of AF compared to men. The Medicare database shows that between 1993 and 2007, the incidence in men was of 35 per 1000 person-years and the incidence in women was 25 per 1000 person-years. (9)

Furthermore, there are numerous modifiable risk factors and some of the best described modifiable factors that increase the risk of AF are shown in *Figure 4*.

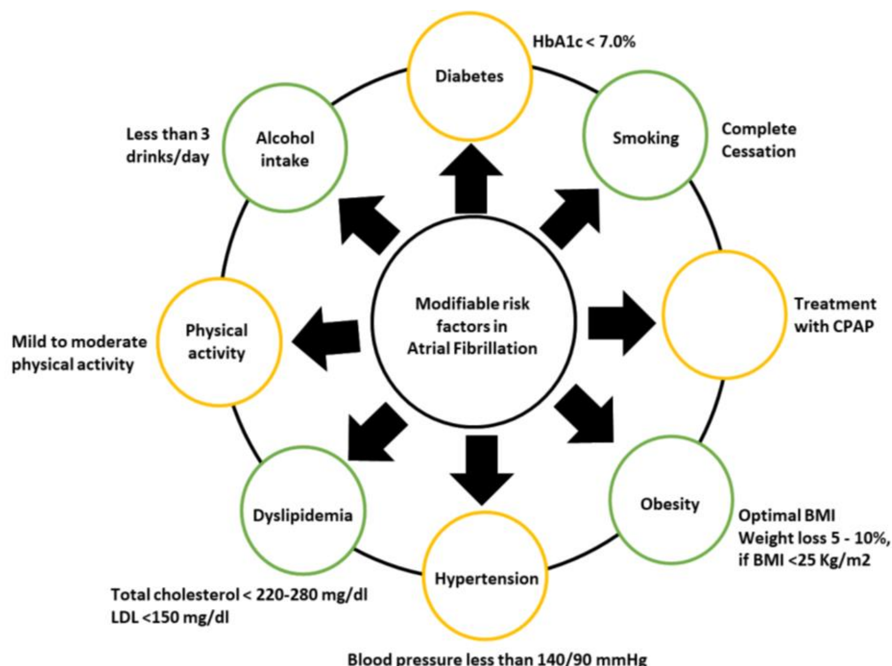

Figure 4 Modifiable risk factors (10)

The knowledge of these risk factors can be used to reduce the risk potential by appropriate lifestyle changes and to determine the indication for screening and intervention. (1)

1.5. Cardiac electrophysiology

To understand the pathophysiological mechanisms of AF, it is important to understand the electrophysiological basis of the heart. *Figure 5* illustrates the action potential (AP) and the different ion channels. The cells of the myocardium have a resting membrane potential of about -85 mV, and this corresponds largely to the potassium (K^+) equilibrium potential. An AP requires sodium (Na^+), calcium (Ca^{2+}), and K^+ channels. Depolarization of the cells occurs through the activation of fast Na^+ channels, resulting in a repolarization of the membrane to about +40mV. Subsequently, the Na^+ channels are inactivated. At this point, in the refractory phase, it is impossible or very difficult to trigger re-excitation. Thus, an increase in the inward ionic current (Ca^{2+} and Na^+) would prolong the refractory period, and an increase in the outward current (K^+) would shorten it. The plateau phase follows, during which there is a slow depolarizing Ca^{2+}- influx. When the Ca^{2+} channels are inactivated and the outward K^+ current reaches its peak, we are already in the repolarization phase. (11)

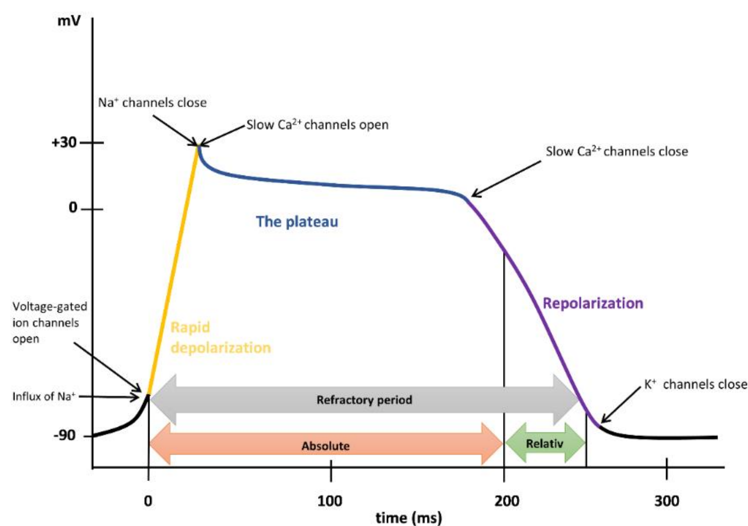

Figure 5 Action potential of the heart (11)

Another important component of the natural electrophysiology of the heart are the connexins. These are proteins found in the junctions between cardiomyocytes and are responsible for the ion permeability between the cells. This allows normal propagation of the electrical impulse. (11)

1.5.1. Pathophysiology

The pathophysiology of AF is very complex. In recent decades, more and more has become known about the mechanisms, even though they have not yet been fully explored. (12) Currently, a multifactorial genesis is assumed, since AF can occur both in a healthy heart as well as in structural heart disease, but is very commonly associated with typical risk factors. (13)

As early as 1998, Haissaguerre et al identified focal sources in the pulmonary veins that can trigger episodes of AF by intracardiac mapping. (14) Other localizations (superior vena cava, posterior wall of the left atrium, coronary sinus, intraatrial septum) are also possible. (13) Ectopic activity is caused by abnormal local spontaneous discharges that may be due to delayed or early afterdepolarizations (*Figure 6*). Delayed afterdepolarizations (DADs) are membrane potential oscillations that occur after complete repolarization of the triggering AP. DADs are favored by conditions leading to Ca2+ overload, such as ischemia, tachycardia, adrenergic stimulation, and low extracellular K^+ concentration. Early afterdepolarizations (EADs) occur under bradycardic conditions with normal Ca^{2+} levels. These are membrane oscillations that are usually triggered during phase 2 or phase 3 of the action pause, when the membrane potential of the AP is less negative. This can lead to atrial premature contractions and tachycardia. (12)

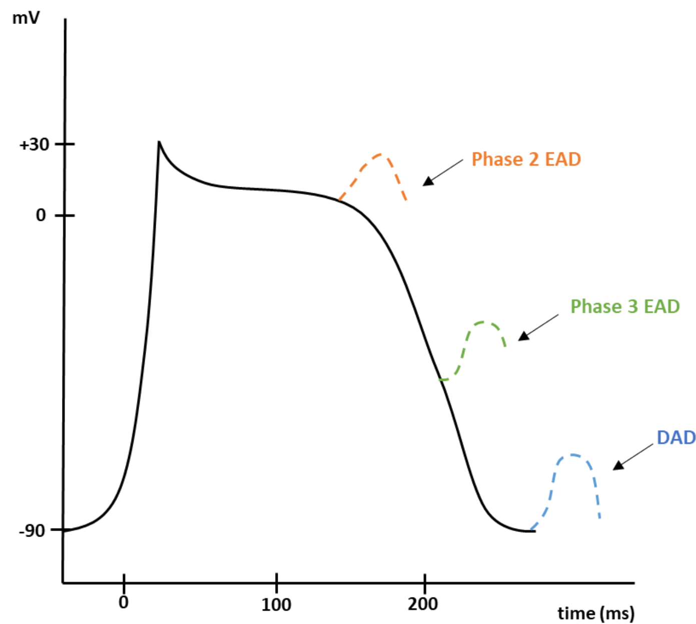

Figure 6 EADs and DADs (15)

In AF, remodelling is detected on a structural as well as on an electrophysiological level. Certain clinical conditions cause changes in the atrium and, consequently, the electrophysiological characteristics of AF change with different pathophysiological consequences. For example, 60% to 80% of patients with AF have been diagnosed with hypertension. Approximately one-third of all AF patients have coronary artery disease and 30 to 40% have heart failure (New York Heart Association II - IV). All these factors lead to dilatation and remodeling of the atrium. There are changes in ion channel function and Ca^{2+} homeostasis, as well as structural changes, such as hypertrophy of myocardial cells, activation of fibroblasts and tissue fibrosis. The changes in the structure of the myocardium also disrupt the conduction of the electrical impulse. As a result, there is a decrease in conduction velocity, which favors reentry mechanisms. This may favor the occurrence of triggers for AF and increase the formation of substrates which then maintain the AF. (12)

Neurogenic stimuli also play an important role in the development and maintenance of AF. Vagal activation can modulate acetylcholine-dependent potassium currents, leading to a reduction in AP duration and thus stabilizing reentry circuits. (12)

Changes in structure and function are also caused by AF itself, explaining the progression of the disease. (16)

1.6. Therapeutic options in AF

According to ESC guidelines, the "ABC" pathway (see Figure 6) can be used for the treatment of AF. This provides a simple strategy to remind clinicians of the holistic approach when treating patients. After all, because AF has tremendous complexity, it is even more important to provide an integrated care to improve patient outcomes. The ABC pathway includes the items: A - anticoagulation, B - better symptom control, and treatment of C - cardiovascular risk factors and comorbidities. (1, 17)

1.6.1. A – Anticoagulation to avoid stroke

The main priority in the treatment of AF is stroke prevention, because 20-25% of all strokes are caused by AF and studies have shown that AF-related strokes are more severe than strokes of other origin. (12)

Estimation of thromboembolic risk and probability of bleeding complications are important for proper stroke prevention. In clinical routine, the CHA_2DS_2 VASc score for thromboembolic risk (see chapter 1.3)**Classification** and the HAS-BLED score for bleeding probability are routinely used. (1)

Anticoagulation is clearly recommended in male patients with a score of ≥2 and in female patients with a score of ≥3. The decision about anticoagulation in male patients with a score of 1 and female patients with a score of 2 should be made on an individual basis. The bleeding risk is not incorporated in the CHA_2DS_2 VASc score but should also be considered. Different types of oral anticoagulants (OACs) are used, namely vitamin K antagonists (VKA) for valvular AF and direct oral anticoagulants (DOACs) for nonvalvular AF. The most used DOACs are the factor Xa inhibitors (Apixaban, Rivaroxaban, and Edoxaban) and the direct thrombin inhibitor dabigatran. While there are numerous studies confirming the benefit of warfarin in reducing the risk of stroke in patients with AF, DOACs have been shown to be safer than Warfarin in several clinical trials. (8)

The HAS-BLED score (*Table 4*) is used to estimate the risk of bleeding in patients with AF with an indication for anticoagulation. (1)

HAS-BLED	Criteria	Points
H	**Uncontrolled hypertension** ➔ Systolic blood pressure > 160 mmHg	1
A	**Abnormal renal/liver function** ➔ Dialysis, transplantation, serum creatinine > 200 µmol/l, liver cirrhosis, bilirubin > x2 upper limit normal, Aspartate aminotransferase / Alanine transaminase /Alkaline phosphatase > x3 upper limit normal	1 or 2
S	**Stroke** ➔ Previous ischemic or hemorrhagic strokes	1
B	**Bleeding history or predisposition** ➔ Previous severe bleeding or anemia or severe thrombocytopenia	1
L	**Labile international normalized ratio** ➔ Time in therapeutic range < 60% in patients on VKA	1
E	**Elderly (age over 65)** ➔ Age > 65 years or extreme frailty	1
D	**Drugs/alcohol concomitantly** ➔ Concomitant use of antiplatelet agents or nonsteroidal anti-inflammatory drugs and/or excessive alcohol consumption	1 or 2
	Maximum Score	**9**

Table 4 HAS-BLED-Score (1)

As shown in the table above, a maximum of nine points can be achieved. A score ≤ 2 is associated with a low to moderate risk of bleeding, while a score > 2 is expected to indicate a high risk of bleeding. However, a high bleeding score is not a contraindication for anticoagulation and should be compared to the thromboembolic risk. The decision should be made after a profound risk-benefit analysis. Rather, it is important to identify bleeding risk factors and to treat treatable factors as best as possible. (1)

Absolute contraindications to anticoagulation are active and clinically relevant bleeding, diseases with a relevant bleeding risk and clinical conditions with a high bleeding potential, such as intracranial hemorrhages and neoplasms with a high bleeding risk. (1)

1.6.2. B – better symptom control

Symptom control is the second pillar of the ABC pathway and is critical to patient management. Symptom-based therapy for patients with AF includes rate or rhythm control using antiarrhythmic drugs (AAD), cardioversion, or interventional therapy. (1) Often, after initiation of acute treatment, AF spontaneously converts to sinus rhythm. If it persists, however, a decision must be made whether to attempt to reduce the ventricular rate while leaving the rhythm unchanged (rate control) or to restore sinus rhythm (rhythm control). (18)

1.6.3. Rate control

Rate control is an important element of AF treatment in permanent AF. The goal is to achieve an appropriate resting heart rate of less than 110 beats per minute, but without restricting the patient too much during exercise. Basically, there are two procedures to choose from. One option is drug-based rate control with beta-blockers, the Ca^{2+} antagonists like diltiazem, or verapamil, and/or digitalis. In the pharmacological field, beta-blockers represent the first-line therapy. (1)

Patients with a left ventricular ejection fraction (LVEF) of 40% or more are recommended beta-blockers or diltiazem or verapamil. If the LVEF is below this mark, a combination of the beta-blocker with digoxin can be considered. If this does

not achieve the target rate, cardiac glycosides, non-dihydropyridine calcium channel blocker, and amiodarone can be considered in addition. (1)

If again no therapeutic success is achieved, a “pace and ablate” approach can be a bailout strategy. That means that a cardiac resynchronization device is implanted followed by a consecutive atrioventricular node ablation to control the heart rate. (1)

1.6.4. Rhythm control

Rhythm control is an attempt to restore and maintain sinus rhythm. Therapeutic intervention options include electrical and pharmacological cardioversion, AAD, and catheter ablation. (1) Especially in patients with severe symptomatic limitations, such as dyspnea or a performance kink, and with a high chance of success of sinus rhythm, this treatment method should be sought. (18)

Cardioversion is the method of choice to achieve acute rhythm regulation in hemodynamically unstable AF patients. In stable patients, either pharmacological or electrical cardioversion can be attempted. (1) It is important to start a three-week anticoagulant therapy before the first attempt of arrhythmia therapy, which must be continued for another four weeks after successful therapy to minimize the risk of thromboembolic complications. If there is no sufficient anticoagulation before the intervention, a transoesophageal echocardiography must be performed to exclude left atrial thrombi. (18)

Pharmacological cardioversion with vernakalant, flecainide, or propafenone are recommended for recent-onset AF. However, vernakalant should not be used in patients with recent acute coronary syndrome or severe heart failure, and propafenone should not be used in severe structural heart disease. Intravenous injection of amiodarone is recommended in patients with heart failure and/or structural heart disease. (1)

Catheter ablation is a long-lasting alternative therapeutic option for symptomatic patients, see chapter 1.7. (1)

1.6.5. C - Cardiovascular risk factors and comorbidities

Another important aspect in the treatment strategy is the identification and management of concomitant diseases, cardiometabolic risk factors, and lifestyle modification to reduce the risk of developing AF and to improve the success of therapy in case of existing arrhythmia. Major cardiovascular risk factors include obesity, arterial hypertension, alcohol abuse, nicotine abuse, diabetes, sleep apnea, and physical inactivity. These lead to increased cardiac remodeling and thus favor the formation of the substrate for the arrhythmia. A lifestyle intervention may lead to a reduction in AF burden and alleviate the severity of symptoms. Numerous studies, such as the FIT project, the HUNT study, or the CARDIO-FIT Study, showed that a higher cardiorespiratory fitness was associated with a lower long-term risk of cardiovascular disease and all-cause mortality in individuals with AF. (19-21) Patients with hypertension or sleep apnea are recommended to be screened for AF, and if arrhythmia is already present, attention should be paid to good blood pressure control and optimal treatment of sleep apnea to reduce the occurrence, progression, recurrence, and symptoms of AF. (1)

1.7. Catheter ablation

Catheter ablation represents an important and durable strategy to control rhythm in patient with AF. (22) Several prospective randomized trials have shown that catheter ablation is more effective as initial treatment for paroxysmal disease compared with AAD. But because of the invasive character of the procedure, there is a risk of major complications such as atrio-oesophageal fistula, stroke, or cardiac tamponade. (23) Current guidelines recommend catheter ablation in patients with paroxysmal or persistent AF who are symptomatic and intolerant or refractory to AAD. (22, 23)

However, there are certain patients with symptomatic PAF in whom catheter ablation should be considered as first-line therapy. This applies, for example, to patients with atrial fibrillation and heart failure with reduced ejection fraction. In these cases, catheter ablation appears to have significant advantages over pharmacological therapy, such as improvement in left ventricular ejection fraction,

exercise capacity, and quality of life. In addition, catheter ablation has been shown to eliminate reversion pauses and reduce the need for permanent pacemaker implantation in patients with concomitant tachycardia-bradycardia syndrome. Catheter ablation may also be an important option for the initial treatment of athletes in whom medical therapy may impair performance. (22)

The foundation for the development of catheter ablation of AF was laid in 1998, when Haissaguerre et al observed that ablation of focal sources in the pulmonary veins, could lead to suppression of recurrent AF episodes. (14)

So, the main goal of interventional therapy for AF is circumferential electrical isolation of all pulmonary veins. (24) Additional ablations such as roof lines, posterior box isolation, mitral isthmus isolation, targeting non pulmonary vein triggers or vein of Marshall alcohol ablation may be performed for persistent AF, but its benefits remain largely unproven are currently studied in clinical trials. (22)

The most established energy forms used for PVI are either radiofrequency (RF) energy or freezing (“cryoablation”). These ablation strategy result in electrical isolation of the tissue around the pulmonary veins and consecutively stop the propagation of the arrhythmia. The thermal energy causes tissue necrosis and subsequently non-conductive myocardial scar tissue develops. (25)

Radiofrequency ablation represents the most used technology, followed by cryoballoon ablation. Through the "Fire and Ice" study, which compared the two ablation methods, it was demonstrated for the first time that cryoballoon ablation was not inferior to radiofrequency ablation. (26) Both methods of PVI are considered equivalent by the ESC guidelines based on the results of several randomized trials and arerecommended for symptomatic treatment of AF. (1) However, controlling ablation using heat or cold can be challenging, resulting in incomplete pulmonary vein isolation or excessive ablation with collateral injury to surrounding structures, which is why it requires new technologies. (27) There are already several new technology in various stages of development, mainly focused on achieving permanent isolation of veins, shorter procedure duration and improved safety. (22)

1.7.1. Radiofrequency ablation

Radiofrequency ablation has been used in the treatment of cardiac arrhythmias since 1987. In this procedure, a high-frequency current of 500 kHz is generated, which is applied via the tip of an ablation catheter in a point-by-point mode. Temperatures between 40 and 90 degrees Celsius are reached, which leads to desiccation of the cells and subsequently to coagulation necrosis, resulting in small homogeneous lesions. The size of the lesion depends on the temperature at the boundary between the electrode and the endocardium, the diameter and length of the distal electrode, and on the heat loss through the blood flow. (26)

In the last few years, radiofrequency ablation has been accompanied using 3D electro anatomical mapping systems (*Figure 7*). This displays electro anatomical information in real time and creates a precise three-dimensional catheter visualization, resulting in a reduction in procedure time, perfusion time and dose, and complication rate. (27) The two most used mapping systems are Carto3® (Biosense Webster) and EnSiteNavX Velocity® (St Jude Medical). While the CARTO system uses a magnetic field for catheter navigation, the NavX system uses only impedance measurement. (28)

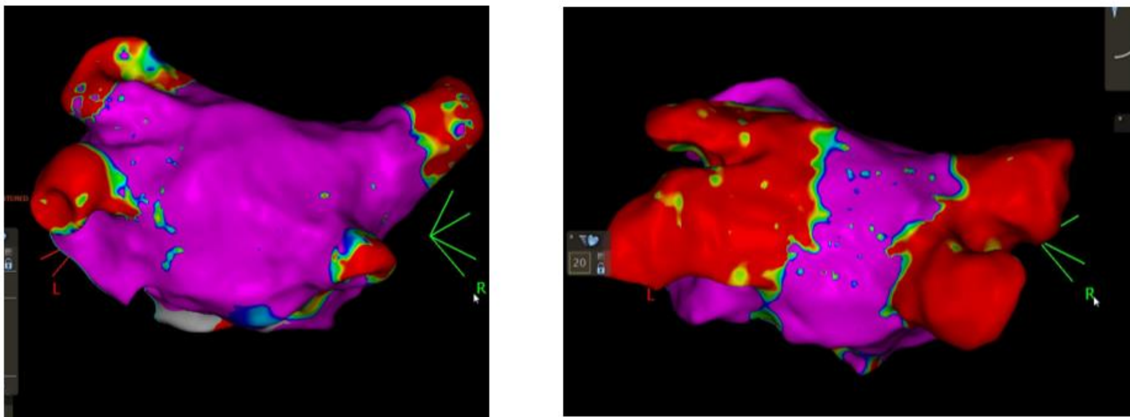

Figure 7 Example of CARTO mapping of a real-world patient within this registry before ablation (left) and after ablation (right).

Although radiofrequency has been the most used energy source for ablations for the past three decades, significant complications can occur, including pulmonary

vein stenosis, incomplete pulmonary vein isolation, and damage to surrounding structures, such as the right phrenic nerve or the oesophagus. In addition, radiofrequency ablation results in heat loss due to the high blood flow through the area to be treated, which can be overcome by higher power. However, this also increases the risk of mechanical complications, such as steam bubbles or cardiac perforation with might result in consecutive cardiac tamponade or lethal complications. (29)

1.7.2. Cryoablation

Cryoballoon ablation (*Figure 8*) is a procedure to isolate the pulmonary veins in AF by using cold to create a lesion around the pulmonary vein confluence. However, the formation of these lesions is very complex and involves both, the freezing cycle and the unfreezing process. (30)

The cryoballoon consists of an inner and an outer balloon. At the proximal end of the balloon is a temperature probe that allows the temperature to be always monitored during ablation. The standard refrigerant for cryocatheter ablation is nitrous oxide because it is readily available and can be stored in its liquid phase without additional refrigeration when pressurized in a gas tank. The cryogen is introduced in liquid form through a very fine injection tube into the inner balloon, where the pressure is released, causing the cryogen to expand and vaporize. (30)

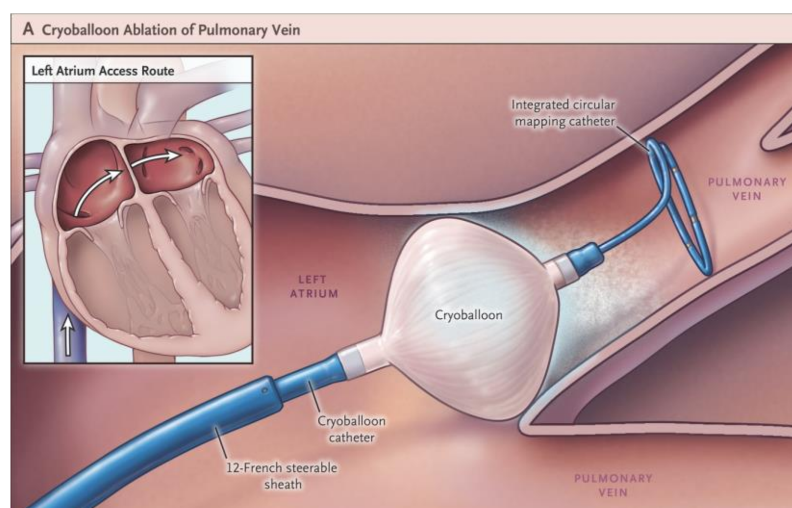

Figure 8 Cryoballoon (31)

The cryotechnique makes use of the Joule-Thompson effect, which allows temperatures of -30 to -90 degrees Celsius to be reached.(30, 32) The cold leads to extracellular ice crystal formation as well as osmotic stress, resulting in cell damage. Furthermore, there is a failure of microcirculation, which additionally leads to ischemic cell death. (33)

While cryoablation is a faster ablation method compared to radiofrequency, there is also an increased risk of injury to the phrenic nerves and oesophagus. (29)

1.7.3. Pulsed field ablation (PFA)

Pulsed field ablation (PFA) is a new ablation technique that does not require thermal energy. It involves the use of novel energy sources that cause lesions in the tissue by means of short, pulsed electric fields with high amplitude, a process known as electroporation. (27, 29, 34)

This technology has already been used for several years in oncology, where reversible electroporation is used. In the field of cardiac ablation, irreversible electroporation is used. In reversible electroporation, the pores in the cell membrane reverse after application of the electric field and the cell survives. In contrast, in irreversible electroporation, the pores do not reverse, and homeostatic changes occur, leading to cell death. (29, 31)

Vessels or nerve tissue are significantly more resistant to electroporation than the target tissue, such as tumor cells or myocytes. (34) In fact, myocytes have one of the lowest thresholds for these fields among cell types. (31) Due to this tissue-specific property, PFA has an increased safety profile compared to radiofrequency or cryoablation, which have been used up to now. (34)

1.7.3.1. Technique

As explained above the PFA uses electroporation. Electroporation is the increase in permeability of a plasma cell membrane because of an applied electric field. This causes a change in potential at the plasma cell membrane and pore formation, which increases the permeability. The high-voltage electric filed are applied near the target tissue, resulting in increased membrane permeability and subsequent cell

death. (27, 29, 31, 34) Due to the short pulse duration, these high-voltage electric fields can produce irreversible electroporation with very little heating. Whether reversible or irreversible pore formation occurs in the cell membrane depends on the strength of the electric field. The heat is dissipated by the cooling effect of conduction and convection. This results in a non-thermal ablation method. (27)

Thus, there are three mechanisms underlying the operation of irreversible electroporation:

1. the electrical formation of aqueous pores in the lipid bilayer.
2. the structural damage of the non-polar tails
3. the damage of voltage-dependent ion channels (35)

With the help of a generator, it is possible to generate these high-energy fields and precisely transfer them to an ablation catheter. For pulmonary vein isolation, specially designed catheters are used to achieve optimal irreversible electroporation. These are 12-F catheters, with 5 arms, each with 4 electrodes. (34) This catheter is placed in two different configurations, called "basket" and "flower" of the pulmonary veins, as you can see in *Figure 9*. Four pulses of 2000 volts are delivered per position, with the catheter rotating 36 degrees after two pulses to cover the entire antral circumference of the vein. The system is available with two different catheter diameters, 31 mm and 35 mm. (35) In addition to the current voltage, the duration (nanoseconds to milliseconds), the frequency, and the number of phase changes of the electric field are important. This allows tissue-specific pulses to be generated. (34)

Various catheter designs are now being developed, and catheters previously used in thermal procedures are also being modified for use with PFA. (35)

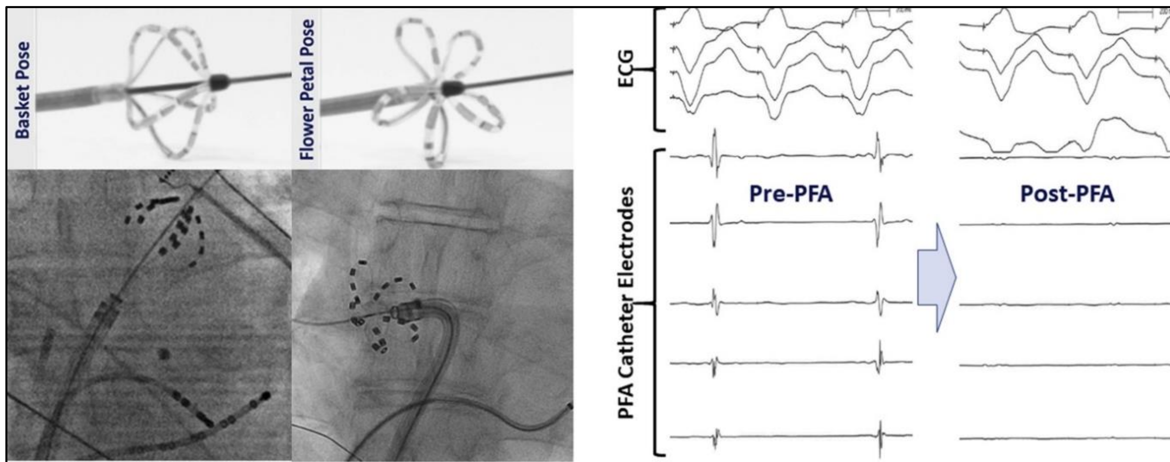

Figure 9 PFA ablation (31)

While thermal ablation methods require adequate contact pressure and several minutes of energy delivery to achieve an effective transmural lesion, PFA does not require any contact pressure. Complete isolation of all pulmonary veins is possible even with an electric field that only exists for nano- to milliseconds. To avoid possible ventricular arrhythmias, ECG-triggered delivery of the electric field to the R-wave during ventricular depolarization is attempted. (27, 34)

1.7.3.2. Safety and efficacy

A crucial difference to the previously used energy forms is the tissue specificity. As mentioned above, the sensitivity of the cardiac muscle is very high compared to the surrounding structures. The threshold of cardiomyocytes is 400 V/cm. In comparison, the threshold for surrounding structures, such as the endothelium of the esophagus, is 1750 V/cm and for nerve tissue, such as the phrenic nerve, it is as high as 3800 V/cm. (37) Even within the heart, different regions have different sensitivities to electroporation. For example, the ventricular endocardium is more sensitive than the epicardium. It is not fully clear why each tissue responds differently to electric fields ,but a correlation between cell size, orientation, membrane properties, and sensitivity to nonspecific entry of cations is suspected. (27)

In thermal procedures, injury to the esophagus with formation of an atrio-oesophageal fistula and the phrenic nerve represent significant complications (*Figure 10*). (27, 34, 35)

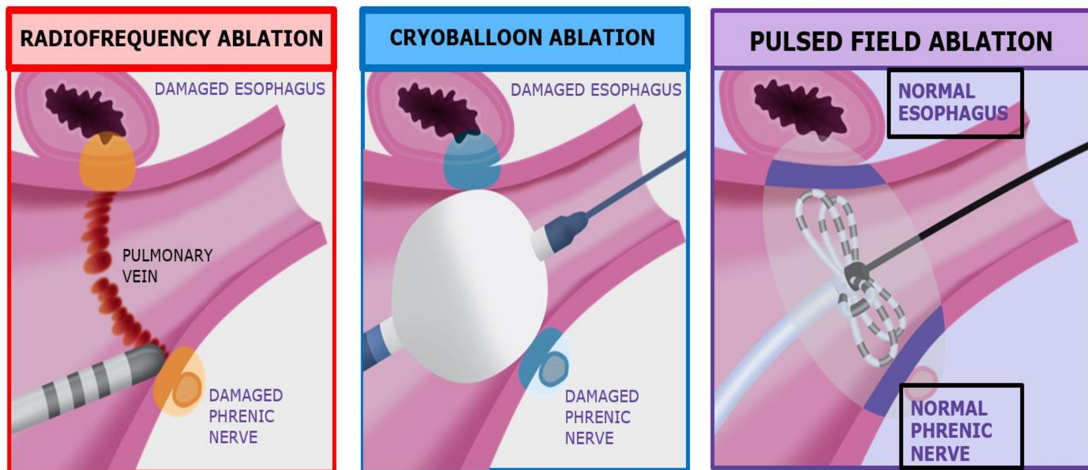

Figure 10 Differences between thermal methods and PFA methods regarding esophageal and phrenic injuries.(31)

Koruth et al tested 2020 the effects of PFA and RFA on pig models. Four discrete sites of the esophagus were targeted in 10 pigs. The PFA method was used in 6 pigs and the RFA method in 4 animals. After 25 days, the esophagus was pathologically examined. All RFA animals showed esophageal lesions while no lesions appeared in the PFA models. (36) The PFA benefits shown in this novel porcine model have been not only shown in preclinical evaluations, but also in clinical trials for the treatment of patients with paroxysmal and persistent AF, like in the IMPULSE, PEFCAT, and PECAT2 trials, as well as the PERsAFOne trial. (37) In terms of efficiency, these studies showed that PVI by PFA results in excellent PVI durability as well as a low 1-year rate of recurrence of atrial arrhythmias. In all 121 patients, 100% pulmonary vein isolation was achieved during ablation with PFA. 110 patients underwent pulmonary vein remapping after ~93.0 ± 30.1 days to assess pulmonary vein isolation. Durable PVI was found in 64.5% of patients. (38) The retrospective Manifest-AF study, which examined all patients at the 24 clinical centers that used the PFA catheter after regulatory approval, showed that no esophageal or phrenic injuries occurred in 1758 patients. However, pericardial tamponade occurred in 0.97% and stroke in 0.4%, indicating a need for improvement. (37)

2022 Reddy et al published the results of his study "Coronary Arterial Spasm During Pulsed Field Ablation to Treat AF," where they investigated the vasospastic potential of PFA lesion sets near coronary arteries as well as further away. Coronary

vasospasm was not induced during PFA at points that were distant from coronary arteries. However, when energy was delivered in proximity to a coronary artery, as during cavotricuspidal isthmus (CTI) ablation, PFA provoked vasospasm. Nitroglycerin was used to counteract this phenomenon. (39)

2. Methods

AF ablation registry

Every patient that underwent an ablation procedure for AF at the Department of Cardiology of the Medical University of Graz was included in a web-based registry retrospectively. By the end of January 2023, a total of 1184 patients had been entered into the ablation registry. A total of 1430 ablations (1184 first time and 246 re-ablations) had been performed. The distribution of the different ablation techniques is shown in

Table 5.

Technique	Number of ablations
RF	1195
Cryoballoon	80
PFA	155

Table 5 Distribution of the different techniques in the webbased registry of Graz

The ethics application no 31-036 ex 18/19 has been approved by the local ethics committee.

A retrospective analysis of all patients undergoing a PFA procedure was performed. Procedures were performed with either the Biosense Webster or Boston/Farapulse PFA system.

Patient specific data were obtained from the hospital information system called “openMEDOCS” (open Medical and nursing Documentation and Communication network of Styria). Parameters were taken from the patients' admission and discharge documents, the ablation procedure protocol, nursing documentation and echocardiography reports.

The AF registry captures baseline characteristics, echocardiographic and laboratory data as well as relevant risk scores such as the CHA_2DS_2 VASc and the HAS-BLED score. Furthermore, data concerning the ablation procedure is collected there. These include the following: indication for ablation as well as AF type (paroxysmal, persistent, long-standing persistent), procedure details such as the applied technique, radiation dose, duration of the procedure and ablation-related complications. Acute and chronic success in terms of arrhythmia freedom is recorded in the ablation result. After the procedure, a bedside echocardiography is performed to rule out pericardial effusion and a 12-lead ECG is performed to monitor the rhythm. A check-up and a 24h ECG are also recommended after 3 and 12 months.

Statistical analysis

Continuous variables are presented as mean ± standard deviation, or median and range (min;max). Categorical variables are presented as percentages (%) and counts. Statistical analyses were performed using SPSS 27 (IBM, Armonk, New York, USA).

3. Results

Baseline characteristics

Within the AF ablation registry, 155/1184 (13%) patients were identified who were treated with PFA between June 2021 and January 2023. These 155 consecutive patients were 62±9 years old (39% female). At baseline, the mean Body Mass Index (BMI) was 28±5 kg/m² with 120 patients (77%) being overweight/pre-obese or obese per definition (BMI>24.9kg/m2), see *Table 6*.

The most present comorbidity was arterial hypertension in 55% of the patients, followed by diabetes in 7% of the patients. The median CHA_2DS_2 VASc score was 2 [0;5]. The mean left atrial diameter was 46±8 mm and the mean LVEF was 61±7%. The ratio of patients with paroxysmal AF to those with persistent AF was approximately 2:1, and 4/155 patients (2,6%) had long standing persistent AF, see details in *Figure 11*

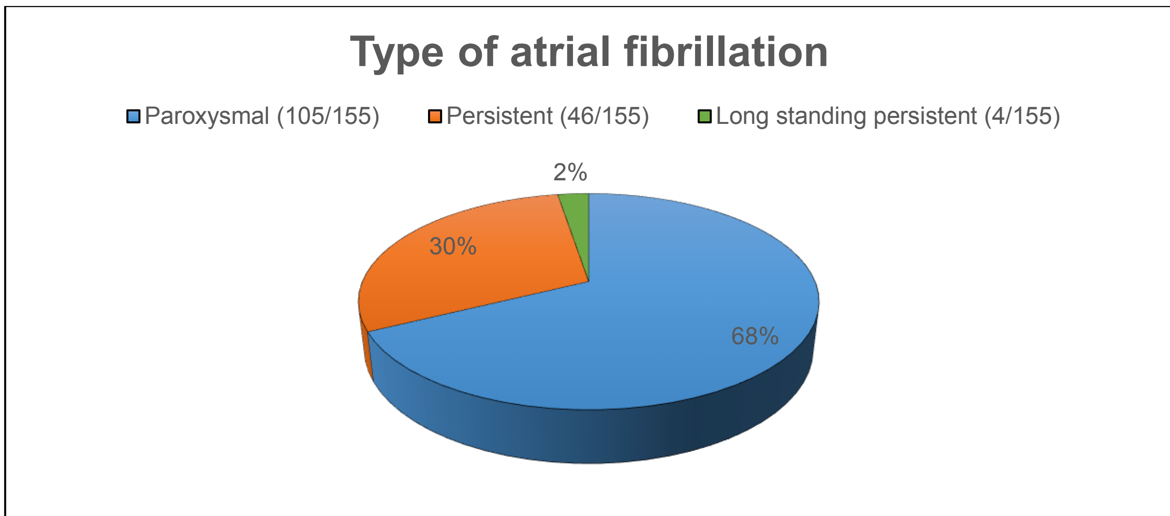

Figure 11 Type of AF

124/155 (80%) have been pre-treated with an anticoagulant agent before procedure, 3/124 (2,4%) have been treated with a VKA, 121/124 (97,6%) with DOACs, and 31/155 (20%) without OACs.

139/155 (90%) were pre-treated with an AAD before ablation: 36/155 patients (23%) received a class I AAD, 112/155 (72%) a class II AAD, and 42/155 (27%) amiodarone. 16/155 patients (10%) were not taking an antiarrhythmic drug, 87/155 (56%) were taking one antiarrhythmic drug, and 52/155 (34%) were taking either a class 2 AAD + a class 1 AAD or a class 2 AAD + amiodarone.

Characteristics	Parameter
Height (cm)	176±10
Weight (kg)	86±18
BMI normal (18,5 – 24,9)	35 (22,5%)
BMI overweight (25-29,9)	71 (46%)
BMI obese (30-34,9)	35 (22,5%)
BMI extremely obese (>35)	14 (9%)

HAS BLED	0 [0;3]
NT-proBNP (pg/ml)	194 [6;2258]
Creatinine (mg/dl)	0,98±0,23

Table 6: Baseline characteristics

Ablation procedure

All ablation procedures take place under deep sedation with propofol and fentanyl and as a standard procedure a coronary sinus catheter for exit/entrance block testing and a right ventricle (RV) catheter were placed at the beginning of the procedure. The RV threshold was tested before ablation starts to have a back-up stimulation electrode in place in case severe bradycardia happened.

At procedure start, 65% of all patients were in sinus rhythm, 31% of patients were in AF and 3% showed atrial flutter on ECG. During the procedure another 9/155 (6%) patients were diagnosed with atrial flutter.

Following the local protocols, all patients received 1 mg i.v. of atropine before the ablation starts to prevent bradycardia.

The mean procedure duration for the PFA ablation method was 76±30 min. The shortest procedure had a duration of 26 min and the longest procedure lasted for 175 min. X-ray dose required an average of 15±15 cm^{2}Gy (1.14; 110 cm^{2}Gy). The PFA Farapulse system was used in 147 patients and the PFA Biosense system in 8 patients. In every patient where typical right atrial flutter was also diagnosed during the procedure, CTI ablation was performed using the Thermocool 3.5 catheter and radiofrequency. A system switch to radiofrequency was performed due to reported potential complications in right atrial ablation with PFA resulting in longer procedure times.

Successful isolation was tested via exit and entrance pacing, with a first pass isolation achieved in 83% of patients. The remaining 17% of patients required additional PFA applications. A total of 40 insufficient isolated veins in 27 patients were detected: 42.5% involved the left superior pulmonary vein (LSPV), 22.5% the

left inferior pulmonary vein (LIPV), and 17.5% each the right inferior (RIPV) and superior pulmonary veins (RSPV), see *Figure 12*.

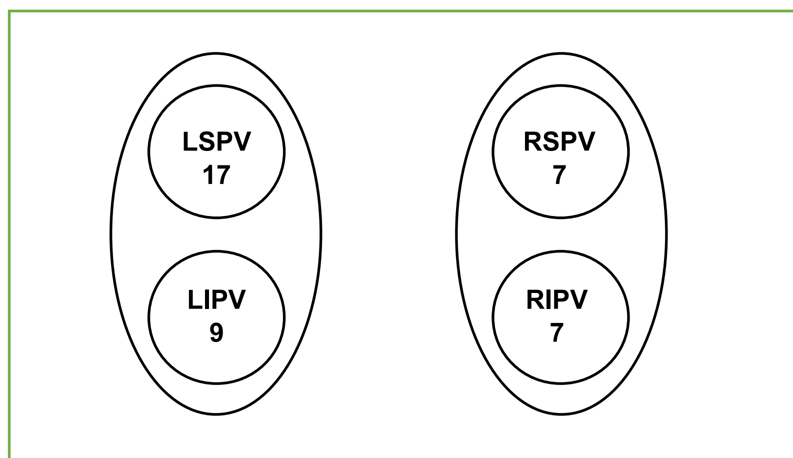

Figure 12 Insufficient veins at the first ablation

At the end of the procedure, the primary PVI success rate was 100%, there were no catheter-related complications. One patient moved at a wake episode during sedation and suffered from a slight skin lesion on his left knee (2,5cm) which did not lead to a prolonged stay in hospital and could be treated with band-aid. One patient experienced a marked vagal reaction with sinus arrest during ablation in the LSPV region. There was rapid improvement after atropine was given and the intrinsic conduction system did not suffer any persistent damage. No pacemaker was needed, and the patient was able to leave the hospital as planned on the day after the procedure.

After ablation, an AAD was recommended: Class I antiarrhythmics in 47/155 patients (30%), 111/155 (72%) Class II and 45/155 (29%) amiodarone. 12/155 patients (8%) were not taking an antiarrhythmic drug, 83/155 (53%) were taking one antiarrhythmic drug, and 60/155 (39%) were taking either a class 2 AAD + a class 1 AAD or a class 2 AAD + amiodarone. All patients were additionally prescribed a proton pump inhibitor for 4 weeks after ablation.

After a mean follow-up time of 275±152 days, a secondary success rate of 123/155 (79%) was observed. Recurrence occurred in 32/155 (19%) during the median days of 33 [1;348]. To date, a re-do procedure has been performed in 10/155 (6,5%).

20/32 (62,5%) patients had another episode of atrial arrhythmia within the blanking period (<90 days, median days 9 [1;71]), 12/32 (37,5%) patients had a recurrence after blanking period (>90 days, median days 142 [96;348]) resulting in 10/32 (31,25%) re-do procedures. This time the procedure was performed with a 3D mapping system and radiofrequency ablation to localize gaps and focused target the gaps only. A total of 29 gaps occurred. All patients had a reablation of the right inferior pulmonary vein and in 50% of the patients the ridge of the left pulmonary veins was incomplete. Furthermore, additional ablations were necessary in the carina regions, see *Figure 13.*

Gaps localization at second ablation after recurrence

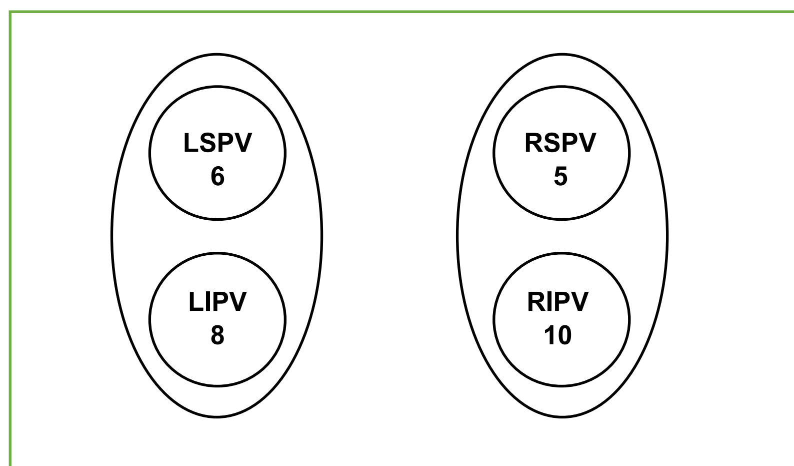

Figure 13 Gaps localization at second ablation after recurrence

To identify factors influencing the procedure success, certain subgroups were analyzed with a Kaplan-Meier curve to see whether there is a difference in arrhythmia freedom. After 365 days, 79% of patients, including patients undergoing a re-do-procedure, were free from recurrences (*Figure 14*).

Arrhythmia-free survival for AF

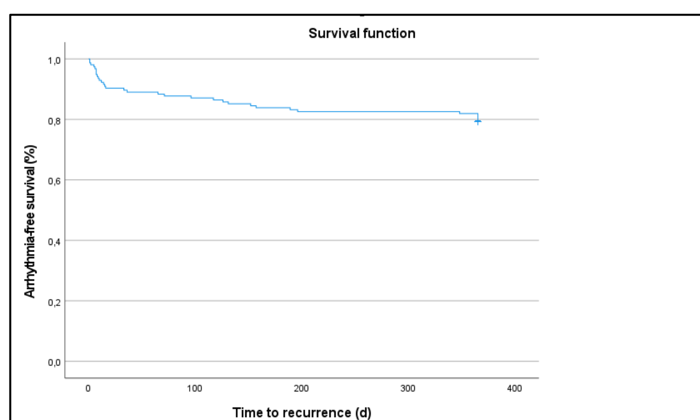

Figure 14 Kaplan-Meier curve for arrhythmia-free survival for AF

In addition, there are no significant differences between women and men in the recurrence of AF. (*Figure 15)*

Arrhythmia-free survival for AF separated by gender

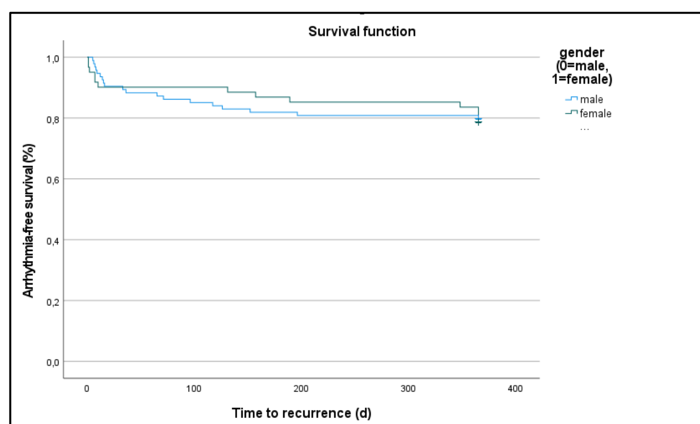

Figure 15 Kaplan-Meier curve for arrhythmia-free survival for AF separated by gender.

There is also no statistically significant difference between paroxysmal and persistent AF as you can see in *Figure 16*, what might be caused by low numbers in this study. In both types, approximately 80% were free of recurrence after 365 days. Patients with longstanding AF were approximately 25% recurrence-free after 365 days, although no significant conclusion can be drawn regarding the total number of 4 patients.

Arrhythmia-free survival for AF separated by type of AF

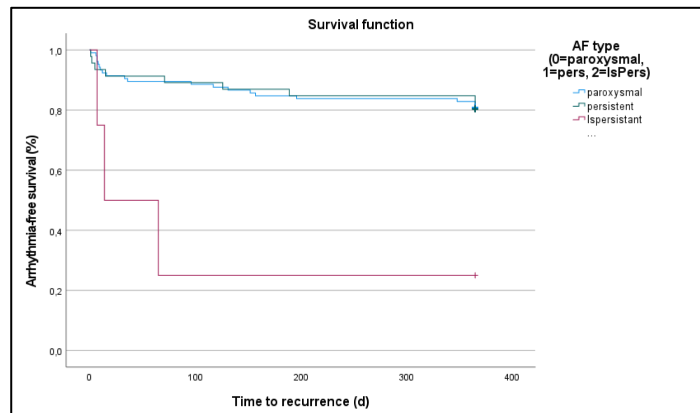

Figure 16 Kaplan-Meier curve for arrhythmia-free survival for AF separated by the type of AF.

4. Discussion

We analyzed the first 155 consecutive patients in a single-center registry who underwent PFA ablation at the Department of Cardiology of the Medical University of Graz. With a first-pass isolation rate of 83% and a primary PVI pass rate of 100%, PFA demonstrates a high success rate.

Comparison to previous ablation methods

Murray et al (2018) performed a meta-analysis to compare radiofrequency ablation and cryoballoon ablation techniques. The analysis was conducted on the four large trials FIRE and ICE (2016), Cryo vs RF (2015), FREEZE AF (2015), and the Cor trial (2014). (26, 40-43)

After 365 days, approximately 79% of the 155 patients treated with PFA were free of recurrence. This compares to 69% for radiofrequency ablation and 72% for cryoablation in one year. (40) Thus, this comparison shows that the PFA method is promising in terms of arrythmia free time. *Table 7* shows the values of the individual studies.(40)

Study	**Radiofrequency**	**Cryoballoon**
Kuck (2016)	77%	79%

Hunter (2015)	47%	67%
Luik (2015)	61%	61%
Perez (2014)	68%	48%

Table 7 Arrythmia free time of the individual studies (40)

Procedure time

There are also significant differences between the previous methods and the new PFA method in terms of procedure duration. With the PFA method, the average procedure duration was 75±31 minutes. Compared to the previous ablation method, the average procedure time was 171±46 minutes.(40) This establishes the PFA method as a significantly faster ablation method. In the following *Table 8* you can see the average procedure times of the different studies.

Study	Radiofrequency	Cryoballoon
Kuck (2016)	141±54,4	124±39
Hunter (2015)	211±60,7	167±48,9
Luik (2015)	174±11.9	161±44,7
Perez (2014)	173±63	215±53

Table 8 Average procedure time in minutes plus SD of the different studies(40)

X-ray dose

Another difference can also be clearly seen in the X-ray dose used. The average X-ray dose for radiofrequency ablation and cryoballoon ablation was about 56.0 Gy-cm^2 in the Freeze AF Study. (41) In contrast, the X-ray dose for the PFA method was about 15.11 Gy-cm^2. Thus, with the new ablation method, X-ray radiation can be significantly reduced.

Complications

Although patients did not experience catheter-related complications, one patient experienced sinus arrest, but this quickly resolved, and the patient was able to leave the hospital the next day as planned and without a pacemaker.

Sinus arrest has occasionally been observed during catheterization of AF. Mostly seen as pre-automatic pause when AF converts to sinus rhythm. However, the exact mechanism of this phenomenon is still uncertain. It is suspected to be a dysfunction of the sinus node, which could be caused by the electrical remodeling of the atrium due to AF. (44) Sinus arrest may be a vagal response that is common during PVI ablation. Feng Hu et al (2019) found that prior ablation of the right anterior ganglion plexus veins could inhibit a vagal response. (45)

As described in literature, no other tissues were harmed (oesophagus, nervus phrenicus), while no specific follow-up was performed due to the real-world retrospective character of this study.

Baseline characteristics

As can be seen in the following *Table 9*, the baseline characteristics of the studied patient population show typical features for patients undergoing AF ablation in terms of age, BMI, concomitant diseases, CHA_2DS_2 VASc score, HAS-BLED score, type of AF, and echocardiographic data.

Characteristics	European registry (46)	Graz Registry (PFA)
Age (years)	58 ± 10	62 ± 9
Male	68%	61%
BMI	28±5	28±5
Hypertension	55%	55%
Diabetes mellitus	10%	7%
CHA_2DS_2 VASc score	1,48±1,2	1,75±1,4

HAS-BLED SCORE	0,48±0,69	0,48±0,62
Paroxysmal AF	68%	68%
Persistent AF	27%	30%
Longstanding AF	5%	2%
Left atrial diameter (mm)	43±7	46±8
LVEF	60%	62%

Table 9 Baseline characteristics of the European registry and the registry of Graz

4.1. Limitation

This is a retrospective analysis from one treatment center representing real-world data from a non-selected cohort. Therefore, the follow-up was not structured, no specific follow-ups were performed, only symptomatic recurrences were captured.

4.2. Conclusion

Pulsed field ablation is a new non-thermal ablation technique that provides safe and effective ablation. This real-world study confirms what several studies (IMPULSE, PEFCAT, PECAT2 trials, Manifest-Af study) have already shown: this method has a high success rate as well as a high safety rate.

There is a need for prospective multicenter studies with high case numbers to draw better conclusions regarding the patient population and the safety and efficacy of pulsed field ablation. However, the results obtained so far show that pulsed field ablation is a fast and safe alternative to existing thermal ablation methods.

In summary, the PFA method is a fast, effective, and safe method for ablation of AF and could further improve the risk-benefit profile in the long term. Compared to radiofrequency ablation and cryoballoon ablation, the procedure time is significantly shorter, and the X-ray exposure is lower compared to cryoablation. Also, in terms of arrhythmia free time, the PFA method is shown to be very effective with 79% at one year and there are no long-term complications in this cohort.

However, there is currently no possibility to treat other arrhythmias such as atrial flutter with PFA, which means that if one notices atrial flutter during ablation, one must switch to an RF catheter, which significantly prolongs the procedure.

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