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# Long-term outcomes after catheter ablation of atrial fibrillation: single centre experience

## Dolgoročni izidi po katetrski ablaciji preddvorne fibrilacije in izkušnje Kliničnega oddelka za kardiologijo UKC Ljubljana

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**Ključne besede:**
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## Abstract

**Background:** Catheter ablation has been widely adopted for the treatment of atrial fibrillation (AF). We have already reported on early and mid-term ablation outcomes. Our aim is to report on long-term clinical outcomes.

**Methods:** We performed a follow-up on all patients in whom the first catheter ablation was performed between 2003 and 2009 due to antiarrhythmic drug-refractory paroxysmal or persistent AF. We also considered ablation procedures for typical atrial flutter (AU) performed after 1999. Complete electrical isolation of the pulmonary veins (PV) was the primary ablation target. The fluoroscopy and lasso-catheter guided segmental radiofrequency ablation procedure was performed. For typical AU, cavotricuspidal isthmus linear ablation was performed. Patients were followed up for at least 5 years after the complete PV isolation, up to a telephone call in April 2020, or death. They were classified as: a) *successful*, in stabile sinus rhythm with up to 5-minute mild palpitations, without regular antiarrhythmic drug (AAD) treatment, b) *partially successful*, mainly in sinus rhythm with rare AF/AU episodes up to once a year and periodic AAD treatment, and c) *unsuccessful*, with frequent AF/AU episodes despite AAD or with long-term persistent AF/AU. Ablation due to recurrent AF/AU was repeated only after a blanking of period of three months. Recurrent AF/AU was documented with serial ECGs or Holter monitoring. The results were evaluated by Kaplan-Meier analysis, t-test and Fisher's test. $P < 0.05$ was considered significant.

**Results:** We included 128 patients (95 male, 33 female, median age at the first ablation procedure was 54.5 years, range 19–75 years). On average, 1.7 ablation procedures per patient for AF or 2 procedures per patient considering also AU ablations were done. The follow-up was successful in 117 patients (85 male, 32 female) on average for 11.7 years (median 140 months, range 21–230). Ten patients died (6 male, 4 female); death was not related to ablation procedure. The most frequent comorbidities were malignant disease and thyroid dysfunction. The probability of stabile sinus rhythm after 10 years of follow-up was 50%, with first-year drop of 15% and a linear drop of 4% per year afterwards. Ablation procedure was *successful* in 54 patients (46%), *partially successful* in 25 (21%) and *unsuccessful* in 38 patients (33%, worse in females, $p < 0.05$). Only 46 (16%) ablation procedures were performed over the last 10 years. Thirty-eight patients (32%) were treated with AADs, mainly with amiodarone and propafenone. Tamponade was the only serious complication in 5 patients (4%); none of them needed surgical intervention.

**Conclusion:** Catheter ablation of AF is a reasonably long-term successful, safe and, according to reported data, cost-efficient procedure, and therefore recommended for the majority of patients with AF. In addition, elimination of reversible risk factors, appropriate AAD treatment and anticoagulation are of great importance for thorough management of patients with AF.

## Izvleček

**Izhodišče:** Katetrska ablacija je danes uveljavljena metoda zdravljenja preddvorne fibrilacije (AF). O zgodnjih in srednjeročnih izidih smo že poročali. Tokrat želimo predstaviti še dolgoročne klinične izide.

**Metode:** Spremljali smo vse bolnike, pri katerih smo v obdobju 2003–2009 prvič opravili katetrsko ablacijo paroksizmalne ali vztrajajoče AF zaradi neučinkovitosti antiaritmičnega zdravljenja. Upoštevali smo tudi ablacijske posege zaradi tipične atrijske undulacije (AU) po letu 1999. Glavni cilj ablacijskega posega je bil popolna električna osamitev pljučnih ven (PV). Uporabili smo metodo segmentne radiofrekvenčne ablacije s fluoroskopskim nadzorom in beleženjem elektrogramov na krožnem katetru »laso«. Pri bolnikih s tipično AU smo opravili linijsko ablacijo kavotrikuspidalne ožine. Bolnike smo spremljali vsaj 5 let po doseženi popolni osamitvi PV oz. do telefonskega razgovora v aprilu 2020 oz. do morebitne smrti. Razvrstili smo jih v tri skupine: a) *uspešne*, tj. v stabilnem sinusnem ritmu z nemotečimi palpitacijami do 5 min, brez rednega antiaritmičnega zdravljenja, b) *delno uspešne*, ko so bili pretežno v sinusnem ritmu, z epizodami dokumentirane AF/AU do enkrat letno in tudi občasno uporabo antiaritmičnih zdravil v ustreznih odmerkih in c) *neuspešne*, tj. s pogostimi epizodami AF/AU, neučinkovitim antiaritmičnim zdravljenjem v ustreznih odmerkih ali z dolgotrajno vztrajajočo AF/AU. Ablacijski poseg smo ponovili zaradi recidiva AF/AU, vendar ne prej kot po 3 mesecih. Ob sumu na ponovitev aritmije smo naročili serijske posnetke EKG in Holterjevega monitoriranja. Podatke smo vrednotili s Kaplan-Meierjevo analizo, testom-t in Fisherjevim testom. Vrednost $p < 0,05$ je bila značilna.

**Rezultati:** V raziskavo smo uvrstili 128 bolnikov (95 moških, 33 žensk; mediana starost pri prvem posegu zaradi AF je bila 54,5 let, rang 19–75), pri katerih smo opravili povprečno 1,7 ablacijskega posega zaradi AF oziroma 2 posega, če smo upoštevali še ablacije AU. Spremljanje je zaključilo 117 bolnikov (85 moških in 32 ženskah) po povprečno 11,7 letih (mediana 140 mesecev, rang 21–230 mesecev). Umrlo je 10 bolnikov (6 moških, 4 ženske), nihče pa zaradi ablacijskega posega. Od soobolevnosti sta bili v ospredju maligna bolezen in ščitnična disfunkcija. Verjetnost za ohranitev stabilnega sinusnega ritma je bila po 10 letih približno 50-odstotna. Po 15-odstotnem padcu verjetnosti za sinusni ritem v prvem letu je bil padec nato linearen, in sicer 4 % letno. Ablacijsko zdravljenje je bilo *uspešno* pri 54 bolnikih (46 %), *delno uspešno* pri 25 (21 %) in *neuspešno* pri 38 bolnikih (33 %, manj uspešno pri ženskah, $p < 0,05$). V zadnjih 10 letih spremljanja smo opravili manjši del ablacijskih posegov – 46 (16 %). Antiaritmična zdravila je prejemalo 38 bolnikov (32 %), pretežno amiodaron in propafenon. Med ablacijskim posegom smo povzročili tamponado pri 5 bolnikih (4 %). Nihče od njih ni potreboval kirurškega posega. Drugih večjih zapletov ni bilo.

**Zaključek:** Ablacijsko zdravljenje AF je dolgoročno dovolj uspešno, varno in po podatkih drugih avtorjev tudi cenovno učinkovito. Zato ga lahko priporočimo večini bolnikov z AF. Za celostno obravnavo bolnikov z AF pa so pomembni tudi: ureditev odpravljivih dejavnikov tveganja, antiaritmično zdravljenje in kakovostno antikoagulacijsko zdravljenje.


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## 1 Introduction

Atrial fibrillation (AF) is the most common heart rhythm disorder. The incidence of AF increases after the age of fifty and reaches a 10% prevalence in the elderly (1). In recent years, the number of patients with AF has been increasing due to an ageing population, an epidemic of hypertension, diabetes and obesity, and long-term survival of heart patients, as well as effective diagnosis. Therefore, AF poses an increasing health challenge. A patient with AF attacks has a poor quality of life due to the symptoms and frequent doctor visits. In addition, a patient with AF who suffers from an associated disease and is in old age (high value of CHA2DS2-VASc scores) has a 4- to 5-times higher risk of stroke and twice as much mortality as those without AF (2). Finally, AF and heart failure interact negatively in the form of a positive feedback loop, which is seen in one third of heart failure or AF patients.

Catheter ablation is a well-established non-pharmacological method of treatment of AF with the indication class IA for the paroxysmal form, IIa for the persistent form and IIb for the long-term persistent form of AF (3-5). We introduced this method into clinical practice in 2003. Early and medium-term outcomes have already been reported (6,7). This time, we want to present long-term clinical outcomes in the same group of patients.

## 2 Methods

### 2.1 Patients

The study included a cohort of consecutive patients who underwent catheter ablation of symptomatic paroxysmal or persistent AF in the period from September 2003 to November 2009 due to unsuccessful antiarrhythmic drug treatment. All were initially less than 76 years old, with a left ventricle ejection fraction above 40% and a left atrium diameter below 50 mm. Some patients had previously (for the first time in 1999) undergone catheter ablation of typical atrial flutter (AU), which was considered in this study. The date of termination of health insurance in the hospital information system meant the date of death. The research was approved by the Republic of Slovenia National Medical Ethics Commission (KME 72/07/07).

### 2.2 Catheter ablation

The ablation method has already been presented in detail (6-8). Briefly: a) all of the patients underwent transesophageal echocardiogram the day before the procedure to rule out the presence of blood clots; b) the procedure was performed under local anaesthesia, with mild sedation, thorough analgesia and anticoagulation with unfractionated heparin – the activated coagulation time was 300–350 s; c) the transseptal puncture and the guidance of the electrode catheters were performed under fluoroscopic supervision, and after 2010, also with the help of intracardiac echocardiography (ICE); d) around the ostium of all pulmonary veins (PV), we performed a circular segmental radiofrequency (RF) ablation procedure until the removal of venous electrograms on a circular 20-electrode lasso catheter in the ostium of the PV; e) we used irrigated-tip ablation catheters arch-D or -F, RF energy 25–35 W and 40 W on the cavotricuspidal isthmus (CTI), up to a maximum of 43°C (Biosense-Webster, Diamond-Bar, California). The goals of ablation were: a) complete electrical ostial and antral isolation of all PV, b) removal of all spontaneous focal atrial activity, and c) bidirectional CTI conduction block in patients with documented typical AU. In

the initial learning period, we performed ablation procedures in several sessions; for example, first the CTI block, in the second session the isolation of two veins, etc. The procedure was repeated in case of recurrence of AF/AU after more than 3 months, if antiarrhythmic drug treatment was not effective. We ablated the conduction gaps at sites of previous ablation lines and spontaneous focal activity. In patients with atypical AU (all non-CTI-dependent AUs; the slow conduction velocity site is usually in the left atrium), we used 3-dimensional electroanatomic mapping (CARTO and CartoSound, Biosense-Webster, Diamond-Bar, California) and the stimulation technique with concealed entrainment. The position of the oesophagus was shown fluoroscopically with a sip of barium contrast or demonstrated with the CartoSound system. In some patients with persistent AF, where we failed to interrupt AF by PV isolation, fragmented atrial electrograms were also ablated along lines (linear) connecting the upper PV, the oval foramen (foramen ovale) with the right upper PV or mitral annulus, and the left lower PV with mitral annulus. Fractionated electrograms had a tachycardia cycle below 140 ms, at least a 3-phase complex shape, and an amplitude of 0.05–0.5 mV. If sinus rhythm was not achieved by ablation, electrical or pharmacological cardioversion was performed. PV isolation was then completed in the sinus rhythm. After 2010, linear defragmentation was abandoned.

## 2.3 Follow-up

Treatment with antiarrhythmic drugs (amiodarone, propafenone, sotalol) was continued for at least 1 month after ablation and anticoagulant therapy (warfarin, dabigatran, rivaroxaban) for at least 2 months or continuously if the CHA2DS2-VASc score was two points or more. Patients were asked to return for a follow-up in 3–6 months, then in one year, and later in case of palpitations. In case of symptoms, patients were instructed to record the ECG with their doctor or at the emergency department and to provide us with these records. If the problems were relatively frequent, we also referred them for Holter monitoring. Patients were classified into three groups, according to the clinical evaluation of the ablation treatment success: a) *successful*, a stable sinus rhythm with up to 5-minute undisturbed palpitations and without regular antiarrhythmic drug treatment, b) *partially successful*, mainly in sinus rhythm with rare AF/AU episodes up to once a year and periodic AAD treatment, and c) *unsuccessful*, with frequent AF/AU episodes despite AAD or with long-term persistent AF/AU.

The analysis included all patients who were monitored on an outpatient basis for at least 5 years after complete isolation of PV, until the telephone interview in April 2020 that focused on symptoms and pharmacological and anticoagulant treatment, or until death.

## 2.4 Statistical methods

Descriptive statistical methods were used to show clinical features. The prevalence of sinus rhythm and AF in those over 30 years of age was shown graphically. We considered the periods of stable sinus rhythm until the first onset of palpitations and between individual ablation procedures. The probability of maintaining sinus rhythm after ablation procedures was assessed by Kaplan-Meier analysis. Endpoints were time of death, time of onset of long-term persistent AF, arrhythmia at last check-up after at least five years, and arrhythmia in April 2020. An unpaired two-tailed t-test was used

to compare quantitative variables, and Fisher's test was used to compare attribute variables. The p value <0.05 was statistically significant. We used the freely available statistical program MedCalc version 19.2.6 (MedCalc Software Ltd, Ostend, Belgium).

## 3 Results

The study included 128 patients (95 men, 33 women; median age at first ablation procedure due to AF was 54.5 years, range 19–75). This time, we also included a patient in whom the procedure was terminated prematurely due to tamponade and later did not have an ablation procedure, and a patient who had a surgical ablation procedure first and only later a catheter procedure. The clinical characteristics of our patients at the end of the follow-up and the results of ablation treatment are shown in Table 1. There were 23 (19%) patients with malignant disease, most often with breast cancer – 3 times and prostate cancer – 3 times; with lung cancer, melanoma, colon cancer, chronic lymphocytic leukaemia, skin cancer – 2 times; individual cases of carcinoma of the pancreas, kidney, bladder, testis, uterus, floor of the mouth, and polycythaemia rubra vera. There were no significant differences between the sexes in the prevalence of hypothyroidism (women 22%, men 10.5%, p = NS) and hyperthyroidism (women 7%, men 6%, p = NS). Patients with valve disease or congenital heart defect were few (after insertion of mitral valve and plastic repair of tricuspid valve – 1, after insertion of aortic valve – 1, after atrial septal defect surgery – 1, with mitral valve prolapse – 1), also diabetics – 6 and patients with chronic kidney disease – 2 (estimated glomerular filtration rate <60 ml/mi/1.75 m2). In one patient, we also performed ablation of the accessory pathway and in another, ablation of AV nodal reentrant tachycardia.

Patients were followed for an average of 11.7 years (median 140 months, range 21–230). Follow-up was successful in 117 patients (85 men and 32 women). Ten patients died (6 men, 4 women). The estimated annual mortality for men was 539.8/100,000 and for women 1036/100,000; the total mortality was 667.7/100,000. The cause of death was ischaemic stroke in a 20-year-old man with dilated cardiomyopathy in whom the ablation procedure was unsuccessful and who, in spite of the recommendation, did not receive anticoagulant treatment. A 56-year-old man and an 80-year-old woman died of malignant progression, a 69-year-old woman of heart failure and valvular heart disease, a 77- and 80-year-old woman of hypertension, and a 68-year-old man of ischaemic disease; the cause of death is unknown in the 57-, 60- and 66-year-old men. The mean age at death was over 20 years lower in men than in women (54.5 vs. 76 years, p <0.05). None of the deaths were directly related to the ablation procedure, meaning no one died in the first three months after the procedure.

The probability of maintaining a stable sinus rhythm was approximately 50% after 10 years (Figure 1). After a quick, i.e. 15% drop in the first year the drop was then linear – 4% per year. Ablation treatment was successful in 54 patients (46%, 12 women), partially successful in 25 (21%, 3 women) and unsuccessful in 38 patients (33%, 17 women, p <0.05) (Table 1). The number and types of ablation procedures performed are shown in Figure 2. Most often, we performed electrical isolation of all PV in one session (4PV). If we consider only ablations due to AF (n = 217), we performed an average of 1.7 procedures per patient. In the last 10-year follow-up, we performed ablation in a small proportion

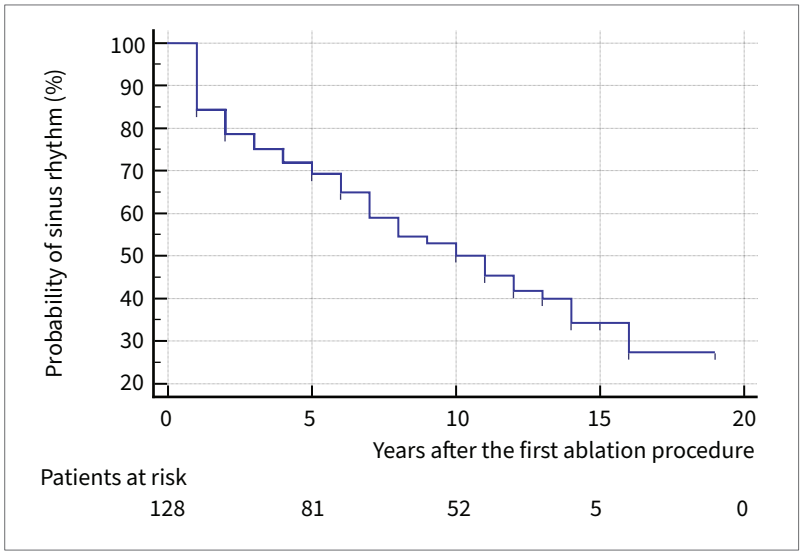


**Figure 1:** The likelihood of maintaining a stable sinus rhythm in our patients after an average of 1.7 ablation procedures due to AF and an average of 11.7 years of follow-up. Ten years after the first ablation procedure, the probability of maintaining sinus rhythm is 50%. After an initial rapid decline in the first year, this probability decreases linearly – 4% per year. The early fall can be the result of an inadequate indication as well as a poorly performed ablation procedure due to a deficient technique, difficult anatomy, myocardial thickness or shortcomings of the ablation method itself.

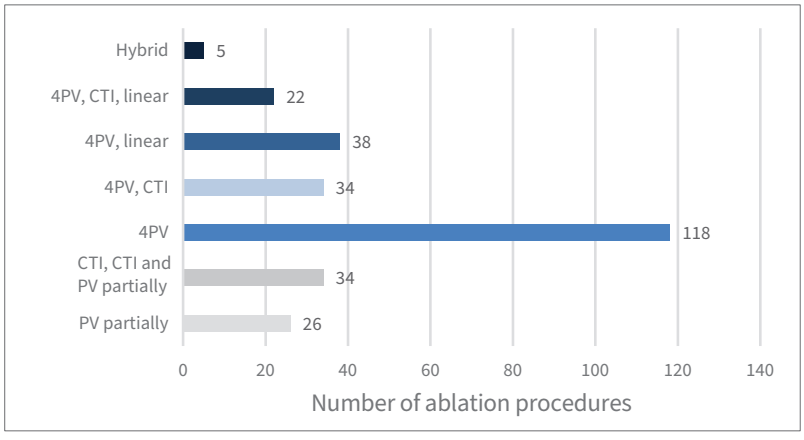


**Figure 2:** Number of ablation procedures by type. In 128 patients, 277 ablation procedures were performed in 20 years (average 2 procedures per patient); only 46 (16%) after 2010. If we consider only ablation procedures due to AF (n = 217), we performed an average of 1.7 procedures in each patient. The generally accepted ablation goal is complete electrical isolation of the pulmonary veins (4PV) and in those with typical AU also linear CTI block, which we do today in one session. Hybrid - simultaneous endoscopic surgical and percutaneous coronary cardiac ablation; PV – pulmonary veins; 4PV – electrical isolation of all pulmonary veins in one session; CTI – linear ablation of cavotricuspidal isthmus; linear ablations connecting the anatomical structures in the left atrium in a straight line.

**Table 1:** Clinical features of 128 patients and outcome of ablation treatment for the period 2003–2020.

| Clinical features | |
|---|---|
| Age at first ablation procedure (median, rank) | age 54,5 (19–75) |
| Number of patients | 128 |
| Women | 33 (26%) |
| -age | age 55 (34–75) |
| Men | 95 (74%) |
| -age | age 54 (19–69) |
| Arterial hypertension | 77 (60%) |
| Thyroid dysfunction* | 24 (20%) |
| Malignant disease | 23 (19%) |
| Asthma, chronic bronchitis, sleep apnoea** | 17 (13%) |
| Thromboembolic event, bleeding*** | 15 (12%) |
| Conduction Disorder **** | 13 (10%) |
| Coronary/peripheral artery disease | 9/2 (8%) |
| Rheumatoid arthritis, ulcerative colitis, pancreatitis, psoriasis, pericarditis | 9 (7%) |
| Dilated/hypertrophic cardiomyopathy | 6/3 (7%) |
| Ethilism | 9 (7%) |
| Obesity (BMI > 35) | 9 (7%) |
| Ulcer and reflux disease, hiatal hernia | 8 (6%) |
| Diabetes | 6 (5%) |
| Family history of AF | 5 (4%) |
| No associated diseases | 22 (19%) |
| PAF at first ablation | 104 (81%) |
| PeAF at first ablation | 24 (19%) |
| Ablation of a typical AU (after 1999) | 45 (35%) |
| Only typical AU at first ablation | 16 (12,5%) |
| Antiarrhythmic treatment | 38 (32%) |

| Clinical features | |
|---|---|
| Number of all ablation procedures# | 277 (2 per patient) |
| - number of complete ablation procedures due to AF | 217 (1,7 per patient) |
| - 1 procedure | 43 (34%) |
| - 2 procedures | 42 (33%) |
| - 3 procedures | 26 (20%) |
| - > 3 procedures | 17 (13%) |
| - tamponade | 5 (4%) |
| Tracking time, median (rank) | 140 months (21–30) |
| Number of patients with follow-up | 117 (91%) |
| - SR | 54 (46%) |
| - SR, rare PAF | 25 (21%) |
| - PAF, long-term PEAF/atypical AU | 38 (33%) |
| Deceased | 10 (6 men, 4 women) |
| Annual mortality | men 539,8/100.000; women 1030/100.000 |
| Long-term clinical benefit | ~50% |

* hyperthyroidism (n = 8, men = 6), hypothyroidism (n = 16, men = 9), goitre, strumectomy, adenoma, amiodarone toxicity;
** asthma (n = 10), chronic obstructive pulmonary disease (n = 6), sleep apnoea (n = 1);
*** ischaemic stroke (n = 6), transient ischaemic attack (TIA) (n = 4), peripheral embolic event (n = 2), subdural haematoma (n = 2), carotid-cavernous fistula;
**** sinoatrial disease, left- and right bundle branch block, PQ > 200ms;
# also, ablation procedures due to typical and atypical AU and procedures with partial isolation of the pulmonary veins.

BMI – body mass index (kg/m2), PAF/PeAF – paroxysmal and persistent atrial fibrillation, typical AU – cavotricuspidal isthmus-dependent atrial undulation, SR – sinus rhythm, long-term PeAF/atypical AU – long-term persistent AF or atypical AU, CTI – cavotricuspidal isthmus.

of patients – 46 (16%) procedures. Thirty-eight patients received antiarrhythmic drugs (32%; amiodarone – 17, of which at a dose of 50–100 mg daily – 9; propafenone 12, of which with AF attacks only – 9; sotalol – 5, ranolazine – 2, sotalol and propafenone – 1, dronedarone – 1).

During the ablation procedure, we induced tamponade in 5 patients (4%). Tamponade was managed in all patients by pericardial drainage without surgery. In the first months after the procedure, no one suffered from simptomatic PV stenosis, oesophageal damage, or stroke. Figure 3 shows the prevalence of sinus rhythm and AF/AU with respect to age after the age of 30. We also considered the sinus rhythm period until the appearance of first palpitations and the period of stable sinus rhythm after ablation procedures. The hypothetical prevalence of sinus rhythm and AF/AU, discounting the effects of ablation procedures, is shown in Figure 4. Without the ablation treatment, all of our patients would have AF after the age of 70 and more than 50% after the age of 50.

Of the 117 patients, 33 (28%, 14 women, 19 men) developed long-term persistent AF or atypical AU at a median age of 65. This occurred on average 5 years (range 1–12) after the first ablation due to persistent AF and typical AU (51%) or due to paroxysmal AF (49%). There was a statistically significant higher proportion of long-term persistent AF and atypical AU in women than in men (44% vs. 22%, $p < 0.05$). There were more men than women in the subgroup without associated diseases, but the difference was not statistically significant (men 22%, women 9%, P = NS).

## 4 Discussion

This study addresses a small cohort of patients with early-onset AF who

underwent their first ablation procedure due to AF more than 10 years ago. Three quarters are men in their fifties, hypertensive individuals – 1.5 times more in the group than in the population (60% vs. 41.2% in the 55–64 age group) (9), with high comorbidity of malignancies – 4 times more (196/1000 vs. 47.7/1000) (10) and thyroid diseases - 5 times more (17.5/1000/year vs. 2.9/1000/year) (11) and 1,5 times more asthma or chronic bronchitis than the estimated prevalence in the population (13% vs. 9%) (Table 1). Comorbidity therefore plays an important role in the aetiology of AF in most of our otherwise younger patients. An interesting fact is the high prevalence of malignant diseases, which is not mentioned in the literature (5). The causes can be found in the systemic nature of the malignancy, in the cardiotoxicity of cytostatic treatment and radiation, and in the long follow-up period. Thyroid disease has been very common, especially in men, in whom thyroid disease is on average five times less common than in women (12). A high percentage of thyroid disease can also be attributed to the side effects of amiodarone, an antiarrhythmic drug, which causes thyroid dysfunction in 15–20% of patients (13). The calculated annual mortality of men and women in our group is difficult

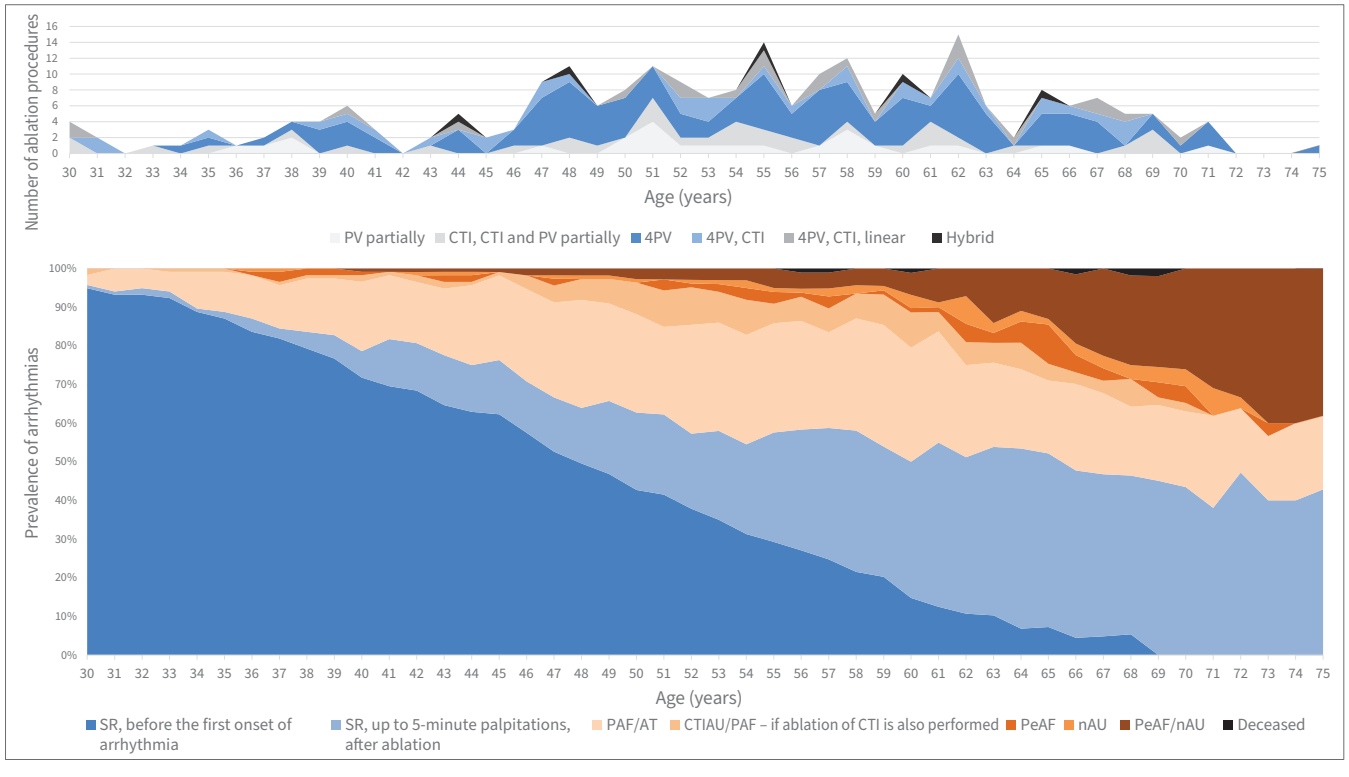


**Figure 3:** The prevalence of sinus rhythm and atrial tachyarrhythmias is shown above, and types and number of ablation procedures according to the age of the patients below. In dark blue, the prevalence of sinus rhythm until the appearance of the first palpitations before the ablation procedure is shown, and in light blue, a stable sinus rhythm after the ablation procedure. Ablation interventions reduced the prevalence of AF (compare with Figure 4).
SR – sinus rhythm; PAF/AT – paroxysmal atrial fibrillation and atrial tachycardia; long-term PeAF – long-term persistent atrial fibrillation; CTIAU – atrial undulation of cavotricuspidal isthmus;
PV – pulmonary veins; CTI – cavotricuspidal isthmus; 4PV – electrical isolation of all pulmonary veins; linear – ablations connecting the anatomical structures in the left atrium in a straight line; hybrid – simultaneous endoscopic surgical and percutaneous coronary cardiac ablation.

to compare with epidemiological data in the general population, but the average age at death in our men was 20 years lower than in the general population, which places them among premature deaths (54.5 years vs. 74.1 years) and only 5 years lower in women (76 years vs. 81.5 years) (9). Although comparatively more female than male patients died in our group, men died significantly younger. Importantly, deaths were not directly related to AF ablation treatment.

The most important finding of this study is that the probability of maintaining a stable sinus rhythm ten years after the first ablation procedure is about 50% (Figure 1). This was achieved with an average of 1.7 ablation procedures due to AF per patient, or with two, if we also considered ablations of typical AU and partial isolation of PV in several sessions. After the initial 15% drop in the first year, the probability of maintaining sinus rhythm decreased linearly in the following years, by 4% per year. Our five-year result is almost exactly the same as the five-year results of Weerasooriya et al. (14), in a similar group of patients, by the same segmental circumferential ablation approach. An almost 10% better result was achieved by Ouyang F et al. (15) in 161 individuals, predominantly male, with paroxysmal AF and a normal left ventricular function. Paroxysmal AF, low comorbidity, and a better ablation method — complete circular PV isolation guided by electroanatomical mapping and two lasso catheters — and a reference institution with a large number of ablation procedures are some of the reasons for their better outcome. It is worth noting that our results are also statistically significantly better in patients with paroxysmal AF than in those with persistent AF (84% vs. 48%) (7). The

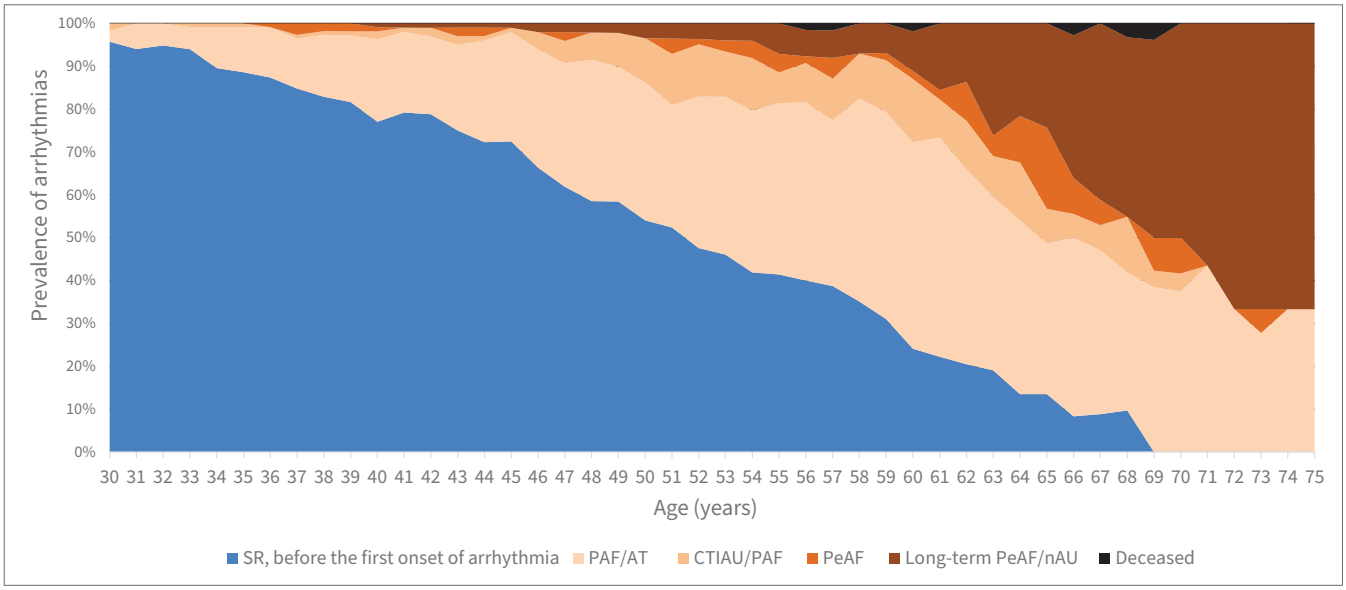


**Figure 4:** Hypothetical prevalence of sinus rhythm and atrial tachyarrhythmias in our group of patients according to age, if we remove the prevalence of re-established sinus rhythm after catheter ablation (see Figure 3). In dark blue, the prevalence of sinus rhythm until the appearance of the first palpitations is shown. More than 50% of patients would have AF in the sixth decade and all after the age of 70. We hypothesize that the probability of spontaneous establishment of a stable sinus rhythm is negligible.

SR – sinus rhythm; PAF/AT – paroxysmal atrial fibrillation and atrial tachycardia; CTIAU – atrial undulation of cavotricuspidal isthmus; PeAF – persistent AF; long-term PeAF/nAU – long-term persistent atrial fibrillation or atypical atrial undulation.

reports by others are similar (16). A common feature of all reports in the literature (16), as well as ours (Table 1), is the need for more ablation procedures to achieve a stable sinus rhythm in a higher percentage of patients. This is one of the shortcomings of AF ablation treatment despite significant technological and methodological improvements over the last 10 years.

Most AF/AU relapses in our group were early. Therefore, we performed more than 80% of ablation procedures in the early period. Early recurrences may be due to: a) inadequate indications in some patients (high comorbidity, prolonged persistent AF, older age, and large left atrium), b) poorly performed ablation procedure with incomplete PV isolation due to a deficient technique, difficult anatomy, or myocardial thickness, c ) technological shortcomings (only fluoroscopic control of ablation catheter guidance without the possibility of good control of tissue contact and position in the ostium of the pulmonary vein) and d) the ablation method itself used at that time (a segmental circumferential ablation guided by a lasso catheter is less effective than a contemporary complete circumferential ablation guided by 3-dimensional electroanatomical mapping). In addition, the larger number of interventions was also contributed by the initial strategy with partial isolation of PV and CTI ablation in several sessions.

Today, we know that complete and permanent electrical isolation of PV is key to the long-term success of AF ablation treatment (3-5). The cause of late relapses is most often the progression of structural atrial disease to so-called atrial cardiomyopathy (17). In these patients, atypical AU has been frequently encountered, which is otherwise an early complication of linear ablation approach (7). In most cases, atypical AU requires another ablation procedure because it is difficult to slow it down or stop it with medication, and after cardioversion, it is also likely to recur. During the procedure, thorough and well-chosen linear ablations are made, which interrupt the re-entrant depolarization around anatomical structures or areas of the scar, most often in the left atrium.

In addition to methodological factors, clinical factors are also important for the success of an ablation procedure. Clinical factors that predicted poorer ablation success in our group were: older age, female gender, persistent AF, abnormal PV anatomy with pronounced antrum, and comorbidity (7). The reports of other authors are similar. In addition to coronary disease, diabetes and uncontrolled hypertension, they also reported left ventricular ejection fraction below 50%, recurrence of AF in the first three months after ablation, large diameter or volume of the left atrium, obesity with a body mass index above 27–30 kg/m2, ineffective antiarrhythmic drug treatment, high CHA2DS2VASc scores, impaired renal function, and sleep-disordered breathing (18-20). Typical AU also predicted AF in 12.5% of our patients, similar to what others report (21). In modern treatment of a patient with AF, measures to control the reversible risk factors are very important. In addition to those mentioned above, are: sedentary lifestyle and smoking, as well as excessive aerobic exercise (22,23). This must be considered in predicting the success of an ablation procedure.

Catheter ablation of AF is today a safe and predictable treatment approach, which is more successful than antiarrhythmic drug treatment, with positive effects on the incidence of stroke and major bleeding, on quality of life and also on overall mortality (3-5,24-29). After ablation, there were significantly fewer

rehospitalizations and AF recurrences compared with antiarrhythmic drug treatment, and in patients with heart failure, there was lower overall mortality and less hospitalizations due to worsening of the heart failure (25,30). Without ablation, more than 50% of our patients would have AF after the age of 50, and all of them after the age of 70 (Figures 3 and 4). Among serious complications, there was only tamponade in 4%, which is within the reported range (31). Since we started using ICE to guide transseptal puncture, this complication is no longer documented. The results of the large, prospective, multicentre, randomized Cabana study definitively confirmed the safety of AF catheter ablation (26).

AAD treatment has its place in treating patients after AF catheter ablation, especially in the first three months after procedure, while the ablation injury is healing. In our group, a third of patients also received antiarrhythmic drugs chronically (especially those with partial success and without success). Amiodarone was most often prescribed long-term treatment, and propafenone for AF attacks. In 12% of patients, a stable sinus rhythm was achieved after ablation therapy with the addition of an antiarrhythmic drug that was not previously effective (7). Antiarrhythmic drug treatment effectively reduced the atrial extrasystole burden and the AF burden in patients after catheter ablation of paroxysmal AF (32). Therefore, some authors recommend antiarrhythmic drug treatment for all patients in the first year after ablation. They have reported good results (33).

The technology we use in ablation procedures has advanced greatly in the last 10 years. Today, we use a 3-dimensional electroanatomical mapping system with ICE and an ablation catheter that detects the contact force (CartoSound, SmartTouch ablation catheter, Biosense-Webster), while the burden of X-rays for the patient and the operator is negligible. When designing ablation with RF energy, in addition to power (W), ablation time, temperature and contact force, the distance between ablation points and impedance drop (CLOSE protocol, ablation index) are important (34,35) (Figure 5). A success rate of more than 90% has been reported after one year (35).

In younger patients with normal pulmonary vein anatomy, cryoballoon ablation (Medtronic, Minnesota) is sometimes chosen. A special balloon placed tightly on the opening of the pulmonary vein is used to cool the tissue in one or two 3-minute applications. The procedure is performed faster than with the RF energy of the catheter, so it can be offered to a wider circle of patients. However, patients tolerate cryoballoon ablation less well (nausea, headache, chest pain, vagal response, risk of phrenic nerve paresis), probably due to the larger area of concomitantly damaged tissue and transient interruption of blood flow to the PV. In our experience, there are more recurrences. In a prospective, multicentre, randomized study, there were no significant differences in performance or complications between RF catheter ablation and cryoballoon ablation (36).

The technology or tools available today are so advanced that there are no significant differences between them regarding the efficiency of PV isolation (RF energy, high power RF energy and short duration (37), cryoballoon ablation (36), electroporation (38), laser balloon (39), RF hot balloon (40), etc.). Therefore, it is important that we know how to choose the right candidates for ablation procedure. We still do not have clear recommendations on what to do if AF recurs or turns into long-term persistent AF despite PV isolation.

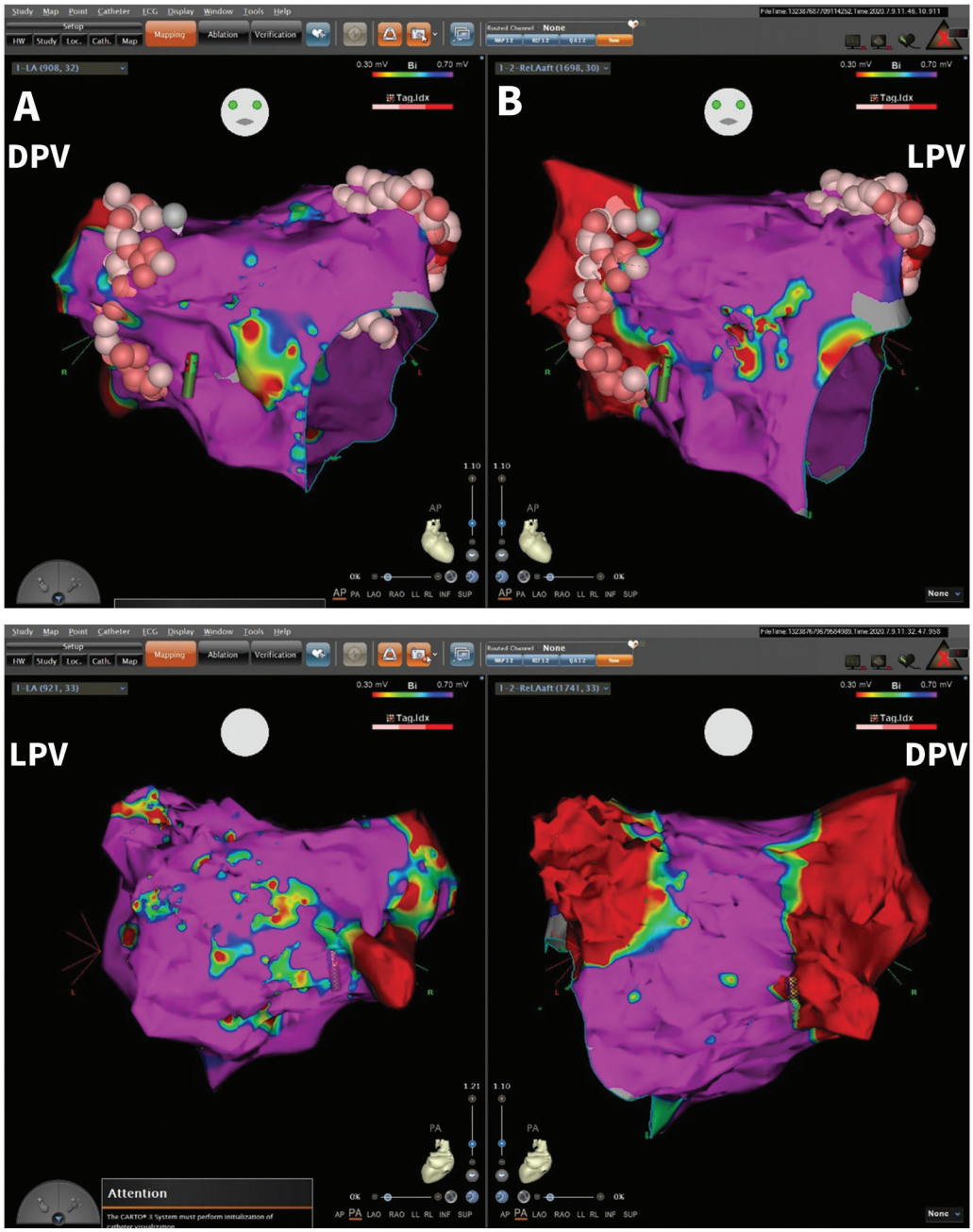


**Figure 5:** Mapping of the left atrium (CartoSound) from the front (above) and from the back (below) in a 40-year-old patient with persistent atrial fibrillation and no associated diseases. The area of atrial bipolar electrograms above 0.7 mV is shown in purple, and the smaller than 0.3 mV, mostly in the line of the pulmonary veins in red. The figures on the left (A) show the conditions before the electrical isolation of the pulmonary veins with radiofrequency catheter ablation, and on the right (B) at the end of the ablation procedure. Before ablation, there are many "purple" electrograms in the antral part of the left and right pulmonary veins, which indicates extensive ingrowth of the myocardium into the pulmonary veins. Above, the ablation points made around the openings of the pulmonary veins are shown in pink. The area of isolation in red is clearly separated from normal atrial electrograms in purple after ablation. We have reached the ablation goal, i.e. complete antral electrical isolation of the pulmonary veins. This is the main area of triggering and most likely also of maintenance of atrial fibrillation.
LPV – left pulmonary veins, DPV – right pulmonary veins

There were as many as a third of such patients in our group. For these patients, ablation of arrhythmogenic foci outside the PV area, additional linear ablations, ablation of fractionated electrograms during AF or sinus rhythm, isolation of the left auricle, isolation of the superior vena cava, ablation of rotor activity, isolation of the posterior wall of the left atrium or scar region (41) or epicardial and endocardial concomitant ablation surgery (hybrid surgery) have been recommended (42). However, these methods are not standardized, efficacy has not been proven, long-term outcomes are poor, or there are too many adverse events (41).

AF without associated diseases was present in one fifth of, as a rule, younger men, which indicates the primary arrhythmic cause, or that the disease or genetic background had not yet been clinically expressed. We often found a large common antral part of PV with a strong focal activity (Figure 5). Permanent isolation of this area was difficult to achieve in one session with the ablation technique of that time. Jahangir et al. (43) followed 76 AF patients who had no associated diseases for an average of 25 years. Five of them had long-term persistent AF at baseline and the others had an equal proportion of paroxysmal and persistent AF. 78% were men with an average age of 44 years. The cumulative probability that they would later have long-term persistent AF was 29 per cent after 30 years. There were no significant differences in mortality compared to the general population, but after 25 years, there was a significant difference in the prevalence of heart failure. However, more strokes and transient ischaemic attacks (TIAs) were also significant in those over 45 years of age and with the onset of comorbidity (e.g. hypertension). Ablation treatment of AF is, therefore, well justified even in patients without associated diseases, even if they are asymptomatic.

Individuals with extensive antral myocardium appear to be susceptible to AF (see Figure 5). There, AF is triggered and also maintained, which may be an individual pathoanatomical factor for the occurrence of AF. The initial electrical instability then leads to electrical, functional, and structural remodelation of the atrial myocardium due to AF itself. Comorbidity, genetic factors, and ageing further accelerate these processes. In individuals over the age of 60, the prevalence of long-term persistent AF in our group increased rapidly, especially in women (Figures 3 and 4). Characteristic of long-term persistent AF is that the atria are large, diastolic dysfunction of the left ventricular with elevated filling pressures is common, and systolic function is initially preserved. Diastolic dysfunction has several causes. Age-related changes in the myocardium with interstitial amyloid deposition are themselves of importance, followed by the structural changes due to long-term tachyarrhythmia (tachycardia-induced cardiomyopathy with impaired systolic function), changes due to hypertensive heart disease or hypertrophic cardiomyopathy (or other genetic cardiomyopathies and arrhythmias), changes due to heart valve disease, diabetes, ischaemic heart disease, obesity, etc. (17). In patients with long-term persistent AF, signs of right-side heart failure also appear at a later stage. In these patients, ablation is less successful. Among them, however, are also good candidates for ablation treatment, especially those in which the heart rate cannot be slowed down sufficiently with medication. Within a few months, tachycardia-induced cardiomyopathy develops. After successful ablation, electrical and structural recovery of the atria and a significant improvement of the left ventricular systolic function were noted (44).

The initial costs of ablation treatment are high, but this treatment is also cost-effective compared to antiarrhythmic drug treatment in the long run. We present the results of a cost analysis of a Canadian study with comparable ablation treatment prices. The initial average costs for ablation and antiarrhythmic drug treatment were EUR 6,864 and EUR 1,676 at today's Canadian dollar exchange rate, and after only two years the cumulative costs were the same – EUR 10,038 and EUR 9,440 (45). We can therefore conclude that ablation treatment was not only more successful for our patients, but significantly more cost-effective than antiarrhythmic drug treatment would have been 11.7 years after the first ablation procedure. A repeat ablation procedure makes this treatment more expensive, but in the last 10 years we have performed it in only a small proportion of patients (16%).

Our research has limited value due to the observational and partly retrospective nature of data acquisition as well as the small number of patients from single electrophysiological laboratory being included. Nevertheless, the results are interesting because they reflect the practical aspects of the treatment and are in line with the results in the literature. Since patients were not followed with an implantable loop recorder, we do not have data on silent episodes of AF/AU or on palpitations that did not occur due to AF/AU. However, our results are based on more than 10 years of morbidity and mortality data, which gives our results more weight. The reported results of catheter ablation of AF are more cost-effective today than they were in the first cohort of our patients more than 10 years ago, due to experience, technological advances and new methodology, but this will still have to be confirmed.

## 5 Conclusion

Ablation treatment of our patients with AF has been sufficiently successful, safe and cost-effective in the long run, so we recommend it to a wide range of well-selected patients. Today, in addition to ablation, all reversible risk factors must be eliminated, the added value of antiarrhythmic drug treatment must be considered, and quality anticoagulant treatment must be provided for comprehensive treatment. All this is in line with international recommendations. Nevertheless, one third of patients fall into chronic AF/AU, and in some, ablation is not effective despite complete PV isolation. Therefore, the ablation method needs to be further improved so that we can achieve a stable sinus rhythm in most patients with just one ablation procedure. Finally, AF ablation treatment needs to be brought closer to a wider range of patients, which is also the responsibility of health care policy.

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