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Clinical outcomes of radiofrequency catheter ablation of atrial fibrillation in octogenarians—10-year experience of a one high-volume center

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Abstract

Background Prevalence of atrial fibrillation (AF) increases with age. Radiofrequency catheter ablation (RFCA) is an established treatment option superior to antiarrhythmics (AAs). In this study, we investigated safety and efficacy of RFCA of AF in octogenarians. **Methods** From our database, we extracted procedural and follow-up data for patients ≥ 80 years with symptomatic AF undergoing RFCA and compared this population to RFCA patients ≤ 50 years. All patients underwent pulmonary vein isolation (PVI) supplemented by linear lesions in PVI-nonresponders. Arrhythmia-free survival was assessed using seven day Holter every three months post procedure. All patients completed their 12 months follow-up. **Results** Fifty patients aged ≥ 80 years (80.5 ± 1.6 years) were compared to 259 patients aged ≤ 50 years (43.5 ± 5.5 years). The RFCA complication rate did not vary between groups. No differences in procedural characteristics were seen after being analyzed by type of AF. Among patients with paroxysmal AF, 71.4% octogenarian *vs*. 84.7% young patients was free of any arrhythmia, without AAs, after single procedure. For non-paroxysmal AF, arrhythmia-free survival without AAs, was considerably lower (58.6% octogenarians *vs*. 81.2% younger patients, $P = 0.023$). If AAs were used, arrhythmia-free survival for paroxysmal AF increased to 90.5% and 92.1% in octogenarians and younger patients, respectively; and in non-paroxysmal AF it increased to 79.3% *vs*. 88.4%. **Conclusions** RFCA is a safe and effective strategy to achieve normal sinus rhythm in a highly selected group of octogenarians. Paroxysmal AF ablation in octogenarians has similar clinical effectiveness as that seen in much younger patients. Non-paroxysmal AF ablation has lower, but still reasonable clinical effectiveness.

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1 Introduction

Elderly patients are being referred more and more often for curative treatment of various arrhythmias and radiofrequency catheter ablation (RFCA) is increasingly considered safe and effective arrhythmia treatment for these older patients. Life expectancy continues to increase in developed countries and health care systems are going to have to cope with patients with multiple organ diseases. The incidence of some arrhythmias, especially atrial fibrillation (AF) and typical atrial flutter (AFL), are directly linked to advanced age,[1,2] while other arrhythmias, like atrioventricular reciprocating tachycardia (AVRT), are very rarely seen in the elderly since RFCA is usually offered to these patients during childhood or young adulthood, particularly if the accessory pathway is overt.

AF tends to be more debilitating in the elderly and the antiarrhythmic medications used to treat it are often poorly tolerated. For instance, the impact of AF on morbidity and mortality in octogenarians is huge: up to a quarter of strokes are attributable to AF and antithrombotic therapy is often challenging due to increased risk of bleeding.

RFCA of AF has been proven to be more effective than antiarrhythmic drugs.[3,4] However, significant concerns persist amongst general practitioners which have led them to preclude patients over 80 years from receiving adequate invasive arrhythmia therapy. These concerns usually include high complication rates due to advanced frailty, lower effectiveness, and lower patient compliance. These worries have led to a continued preference for pharmacological therapy over invasive treatment. These beliefs are underlined by the fact that octogenarians have been largely excluded from the

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majority of studies addressing the clinical benefit of RFCA. Therefore, in the present study, we report on the safety and effectiveness of RFCA for AF in octogenarians compared to patients aged ≤ 50 years, based on our experiences over a 10-year period.

2 Methods

We extracted data from the Ceske Budejovice Ablation Database, which includes 4608 patients that underwent RFCA of various cardiac arrhythmias from 2007–2016. We selected only patients aged ≥ 80 years (octogenarians) and ≤ 50 years (young patient group) at the time of ablation, who underwent selective ablation of AF. Standard definitions of paroxysmal, persistent, and long-standing persistent AF were used,[5] however, persistent and long-standing persistent AF were grouped together and henceforth will be referred to as non-paroxysmal AF. Transesophageal echocardiography (TEE) was performed one day before RFCA in all patients with non-paroxysmal AF regardless of the anticoagulation therapy regime. In patients with paroxysmal AF, TEE was only performed in patients with a subtherapeutic International Normalized Ratio (INR) that was detected within the 4-week period prior to the RFCA procedure or in patients not receiving anticoagulation therapy. Acute success rate, periprocedural and 30-day post-ablation complications, and other clinical and procedural characteristics, including the length of hospitalization were prospectively collected for all patients. A systematic follow-up of at least 1 year was routinely used for all patients and followed the common clinical practice in our center. One year arrhythmia-free survival was assessed using 7 days ECG Holter recordings at 3, 6, 9, and 12 months following the index procedure. AF or any other supraventricular tachycardia lasting > 30 s on any of the three 7 days Holter during the 12-month post-ablation period was considered a procedural failure, assessed separately on and off antiarrhythmic drugs.

2.1 Electrophysiological study and catheter ablation

All RFCA of AF were performed using a three-dimensional (3D) electro-anatomical (EAM) navigation system. For this purpose, the left femoral vein was used for introduction of one 11 F sheath for the intracardiac echocardiography (ICE) catheter and one 7 F sheath for the decapolar steerable coronary sinus (CS) catheter, and the right femoral vein was accessed twice for introduction of two transseptal (TS) sheaths. After a double TS puncture, two steerable TS sheaths (8F, Channel, Boston Scientific, USA) were introduced into the left atrium. In all AF ablation procedures, a circular mapping catheter (LASSO®, Biosense Webster) was positioned in both the right and left pulmonary veins (PVs) to confirm the endpoint of PV isolation by demonstrating the presence of both entry and exit blocks. After 3D reconstruction of the PVs and virtual left atrial anatomy using the CARTO XP and later the CARTO3 mapping systems (Biosense Webster), the image was merged with a previously acquired CT scan of the left atrium. RF energy was then applied using a 3.5 mm irrigated-tip ablation catheter (Navistar® or later ThermoCool® Smart Touch™, Biosense Webster). Ablation endpoints were PV isolation in all patients and in nonPVI-responders, additional posterior left atrial wall isolation (i.e., "box" lesion) and the mitral isthmus line were added (usually in non-paroxysmal AF patients). The endpoint for atrial tachycardia (AT) ablation, if detected, was identification of the narrow arrhythmia channel during perpetuating reentrant arrhythmia and termination by ablation, or termination by a focal ablation at the site of origin in case of focal ATs. Thereafter, non-inducibility of ATs was tested using incremental atrial pacing up to 300 beats/min. Anticoagulation with a loading dose of heparin 100 IU/kg (*i.v.*) followed by continuous infusion was begun immediately after the first TS puncture, with the target level of activated clotting time (ACT) reaching at least 300 s (optimum 300–350 s). No procedures were performed on uninterrupted Warfarin. Warfarin was restarted the day after the procedure and low-molecular weight heparin was administered subcutaneously as a bridge until a target INR level above 2.0 was reached.

2.2 Assessment of complications

All complications were recorded meticulously and were considered procedure-linked when they occurred within the 30-day post-procedure window. Major complications were defined as transient ischemic attack, stroke, pericardial tamponade, hemo- or pneumo-thorax, PV stenosis ≥ 50% (based on TEE measurement of PV flow velocity ≥ 100 cm/s), or severe bleeding from puncture sites or internal bleeding requiring catecholamine support or blood transfusions. Hematoma at access sites, arterio-venous (AV) fistula, pericardial effusion not requiring pericardiocentesis and PV stenosis < 50% (based on TEE measurement of PV flow velocity < 100 cm/s and absence of any symptoms), and groin hematoma prolonging hospitalization were considered minor complications.

2.3 Statistical analysis

Categorical parameters were described using absolute (relative) frequencies. Differences between groups were tested using the Fisher exact test. Continuous variables were described by the mean ± SD. Differences between groups,

for continuous variables, were tested using the Mann-Whitney *U* test. Time to arrhythmia recurrence was illustrated using the Kaplan-Meier estimate arrhythmia-free survival function and by the number of patients at risk. Differences between groups were tested using the Log-rank test. Statistical analyses were carried out using SPSS Statistics for Windows, version 24.0 (IBM Corp., Armonk, NY, USA).

3 Results

Out of 4608 patients in the ablation registry, 50 (1.1%) patients 80 years or older and 259 (5.6%) patients 50 years or younger, at the time of RFCA for AF, were identified. Table 1 summarizes the baseline clinical characteristics of the study population. Octogenarians were more often females (56% *vs*. 19%, $P < 0.001$), had a higher prevalence of hypertension (48% *vs*. 16%, $P < 0.001$) and diabetes (18% *vs*. 3.5%, $P = 0.001$), and had a more significant history of previous strokes (14% *vs*. 1.5%, $P < 0.001$). LA diameter was slightly larger in octogenarians, while the left ventricular ejection fraction was comparable. Significantly more younger patients were ablated for paroxysmal AF (73% *vs*. 42%, $P < 0.001$); a similar proportion of patients had taken at least one antiarrhythmic drug (64% *vs*. 63%), however, octogenarians had tried more different drugs compared to the younger patients (1.2 ± 0.8 *vs*. 0.7 ± 0.6, $P = 0.035$).

3.1 Procedural characteristics and complications

The main procedural characteristics of the two age groups are summarized in Table 2. There were no differences found in procedural characteristics (procedure time, fluoroscopy time) apart from the total RF time, which seemed to be higher in octogenarians (54.8 ± 39.8 min *vs*. 40.5 ± 20.2 min, $P = 0.019$). However, when analyzed according to the type of AF (paroxysmal *vs*. non-paroxysmal), the differences became statistically insignificant (Table 2), reflecting the higher proportion of patients with non-paroxysmal arrhythmia among the octogenarians. Additionally, the minor and major periprocedural complication rates were the same in octogenarians compared to the younger patients. Despite this fact, the mean in-hospital stay was approximately one-half day longer for octogenarians compared to the younger patients (4.3 ± 0.9 days *vs*. 3.9 ± 1 days, $P = 0.003$).

3.2 Clinical outcomes

All patients completed their 12 months follow-up using repeated seven days Holter ECG monitoring. After 12 months of follow-up, 32 (64%) of octogenarians *vs*. 217 (83.8%) of patients aged less than 50 years remained free from any AF recurrences and were off antiarrhythmic drugs after a single procedure ($P = 0.001$). When analyzed by type of arrhythmia, younger patients with paroxysmal AF showed slightly better, albeit statistically insignificant, arrhythmia-free survival compared to octogenarians (84.7% *vs*. 71.4%, $P = 0.1$). Thus, the majority of failures to sustain normal sinus rhythm were observed in the non-paroxysmal AF subgroup resulting in arrhythmia free survival in only 58.6% of octogenarians compared to 81.2% of younger patients ($P = 0.023$, Figure 1).

Table 1. Clinical characteristics of patients included in the study.

	Patients ≥ 80 yrs	Patients ≤ 50 yrs	*P* value
Number of patients	50	259	
Age, yrs	80.5 ± 1.6 (80–88)	43.5 ± 5.5 (19–50)	< 0.001
Female sex	28 (56%)	50 (19.3%)	< 0.001
Body mass index, kg/m^2	28.9 ± 4.1	29.2 ± 5.5	0.994
Type of atrial fibrillation			
Paroxysmal	21 (42%)	190 (73.4%)	< 0.001
Non-paroxysmal	29 (58%)	69 (26.6%)	
Hypertension	24 (48%)	42 (16.2%)	< 0.001
Diabetes mellitus	9 (18%)	9 (3.5%)	0.001
Prior stroke/Transitory ischemic attack	7 (14%)	4 (1.5%)	< 0.001
Coronary artery disease	7 (14%)	3 (1.2%)	< 0.001
Heart failure	2 (4%)	14 (5.4%)	0.999
Left atrial diameter, mm	45.5 ± 6.8	42.6 ± 7.3	0.011
Left ventricular ejection fraction	65.4% ± 6.8%	64.3% ± 9.2%	0.782
Number of patients receiving antiarrhythmic drugs, *n*(%)	32 (64%)	163 (62.9%)	0.999
Failed antiarrhythmic drugs	0.7 ± 0.6	1.2 ± 0.8	0.035

Data are presented as mean ± SD, mean ± SD (range) or *n* (%) unless other indicated.

Table 2. Main procedural characteristics of patients included in the study.

	Patients ≥ 80 yrs	Patients ≤ 50 yrs	*P* value
Total procedure time (all types of AF), min	149 ± 54	145 ± 51	0.729
Total procedure time (paroxysmal AF), min	122 ± 54	134 ± 47	0.136
Total procedure time (persistent AF), min	169 ± 46	177 ± 49	0.315
Fluoroscopy time (all types of AF), min	12.5 ± 10.5	11.2 ± 9.8	0.324
Fluoroscopy time (paroxysmal AF), min	9.7 ± 9.6	10.6 ± 9.5	0.557
Fluoroscopy time (persistent AF), min	14.6 ± 10.8	12.9 ± 10.3	0.379
RF application time (all types of AF), min	54.8 ± 39.8	40.5 ± 20.2	0.019
RF application time (paroxysmal AF), min	49.1 ± 42.3	34.3 ± 16.6	0.099
RF application time (persistent AF), min	58.9 ± 38.1	57.2 ± 19.8	0.594
Length of hospitalization, days	4.3 ± 0.9	3.9 ± 1	0.003
Periprocedural complications			
Stroke/TIA	0	0	
Tamponade	0	0	
Pericardial effusion	0	1 (0.4%)	
Major bleeding requiring blood transfusion	0	0	0.787
Pulmonary vein stenosis	0	0	
Minor bleeding	0	0	
AV fistula	0	1 (0.4%)	
Groin hematoma prolonging hospitalization	2 (4%)	9 (3.5%)	

Data are presented as mean ± SD. AF: atrial fibrillation; AV: arterio-venous; TIA: transitory ischemic attack.

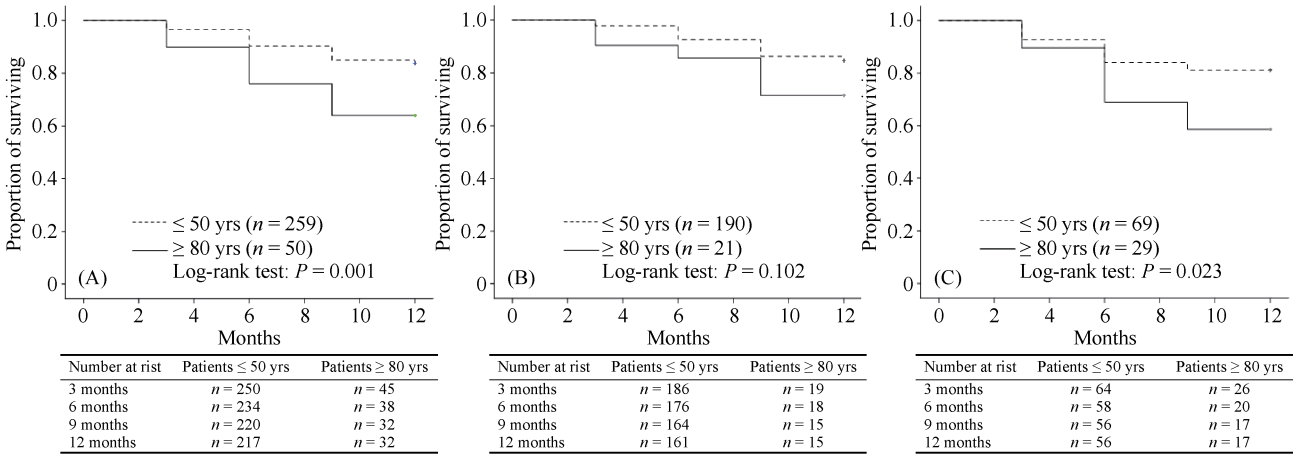
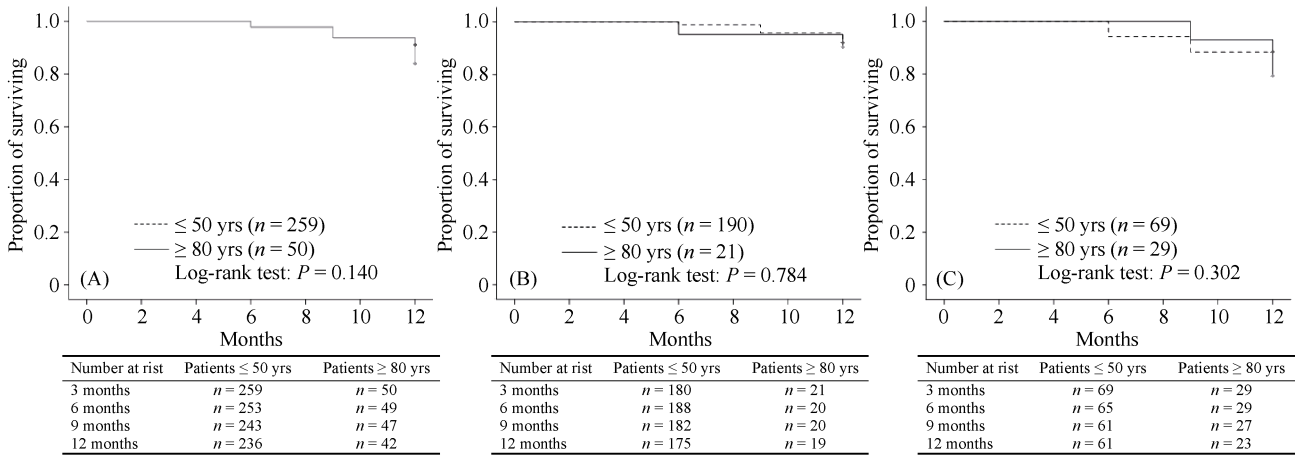


Figure 1. Kaplan-Meier estimates of arrhythmia-free survival off antiarrhythmic drugs. (A): significantly lower efficiency in octogenarians for the whole patient cohort; (B): differences in arrhythmia-free survival were not statistically significant for patients with paroxysmal atrial fibrillation; and (C): outcomes were apparently worse in octogenarians for patients with persistent atrial fibrillation.

For those taking antiarrhythmic medication, mainly amiodarone (90% in the octogenarians and 33.2% in the patients aged less than 50 years, $P < 0.001$), the overall one year AF-free survival increased to 84% of octogenarians and 91.1% of the younger patients ($P = 0.14$). Interestingly, even on previously ineffective antiarrhythmic drugs, the clinical results of both groups were comparable regardless of the type of AF, with an arrhythmia-free survival for paroxysmal AF of 90.5% and 92.1% ($P = 0.784$) and an arrhythmia-free survival for non-paroxysmal AF of 79.3% and 88.4% ($P = 0.302$) for octogenarians and younger patients, respectively (Figure 2).

No thromboembolic events occurred during the 12-month post RFCA period in either patient group. The majority of patients were on warfarin (or more recently, direct oral anticoagulant drugs) at the end of the 12-month follow-up period (88% of octogenarians and 61.8% of patients ≤ 50 years). No deaths were reported among the younger patients, while one octogenarian died of lung cancer 11 months after the index procedure. There were no cardiovascular-related hospitaliza-



Number at rist	Patients ≤ 50 yrs	Patients ≥ 80 yrs
3 months	*n* = 259	*n* = 50
6 months	*n* = 253	*n* = 49
9 months	*n* = 243	*n* = 47
12 months	*n* = 236	*n* = 42

Number at rist	Patients ≤ 50 yrs	Patients ≥ 80 yrs
3 months	*n* = 180	*n* = 21
6 months	*n* = 188	*n* = 20
9 months	*n* = 182	*n* = 20
12 months	*n* = 175	*n* = 19

Number at rist	Patients ≤ 50 yrs	Patients ≥ 80 yrs
3 months	*n* = 69	*n* = 29
6 months	*n* = 65	*n* = 29
9 months	*n* = 61	*n* = 27
12 months	*n* = 61	*n* = 23

Figure 2. Kaplan-Meier estimates of arrhythmia-free survival while taking previously ineffective antiarrhythmic medication: for the whole patient cohort (A), in patients with paroxysmal atrial fibrillation (B), and in patients with persistent atrial fibrillation (C).

tions among the octogenarians, while in the ≤ 50 years group, two patients were hospitalized due to acute myocardial infarction and one patient had an emergent hypertension crisis.

4 Discussion

To the best of our knowledge, this is the first study comparing procedural outcome of RFCA for AF in a significantly older patient group (i.e., octogenarians) directly with a patient group ≤ 50 years of age. The clinical implications of our study may be highly relevant. While younger populations with AF are usually referred, with no special concerns or restrictions, for RFCA soon after the first presentation of an arrhythmia, patient ≥ 80 years are frequently precluded from such invasive procedures for fear of higher complication rates and lower effectiveness of ablation treatment. As a result, antiarrhythmic therapy is used more extensively prior to an RFCA indication, which was also confirmed in this study. Our publication makes two very important points: (1) RFCA in octogenarians is safe; and (2) RFCA in octogenarians has similar, albeit for non-paroxysmal AF significantly lower, clinical effectiveness compared to the same procedures performed in a younger population.

AF is an arrhythmia with an increased prevalence in the elderly. Simultaneously, AF is associated with an increased risk of heart failure,[6,7] loss of cognitive functions,[8] and AF-related cerebrovascular accidents, all of which tend to be more devastating and debilitating in elderly patients.[7,9–11] Most publications on RFCA for AF were carried out in patients younger than 65 years and without significant comorbidities,[4,12,13] and the majority of studies that did address the issue of RFCA in older patients were not specifically focused on octogenarian patients.[14–18] So far, three studies have been published that specifically focused on octogenarians, all of which reported similar success and complication rates of RFCA compared to "younger" populations, which unlike our study, consisted of patients < 80 years of age.[19–21] No study to date has compared octogenarians with the presumably most suitable and relatively healthy patients of ≤ 50 years, an age at which the safety profile and clinical effectiveness of RFCA can be expected most favorable. In this respect, our study confirms and extends previous observations.

Our study shows that RFCA in octogenarians has a similar safety profile compared to younger patients, despite the higher incidence of comorbidities and female gender present in our study, with the latter being associated with higher complication rates.[22–24] No major adverse event occurred in either group of patients. Importantly, the procedural characteristics were also comparable, and we demonstrated that RFCA in older patients does not prolong either procedural time or X-ray exposure. Only the length of hospitalization was slightly prolonged, which in part might be explained by the presumption that octogenarians are more fragile and have diminished wound healing capability. Most likely this "general fear" influenced the physicians responsible for patients in the wards, since it was not justified by an observed increase in the number of complications among octogenarians. On the other hand, longer in-hospital stays of the elderly might very well reflect the greater care needed to adjust medications, especially anticoagulant therapy, and mange postprocedural fluid balance in this group.[19] Overall, the majority of published studies have not revealed increased numbers of complications among elderly patients undergoing RFCA for AF,[25] although some, typically single-center, studies have found an age-dependent increase in complication rates.[16,26] However, in 2010, the updated worldwide survey of AF ablation found comparable complication rates between patients of different age groups.[27]

Regarding clinical efficacy, octogenarians, if they presented with paroxysmal type of AF, both on and off antiarrhythmic drugs, had a similar 12-month arrhythmia-free survival compared to younger patients. Nevertheless, in the non-paroxysmal AF population ≥ 80 years, the clinical efficacy seemed to be significantly lower when off antiarrhythmic medication, reflecting typical outcomes thus far seen in published trials.[5] As such, it is also tempting to hypothesize that results of persistent AF ablation in younger patients (i.e., ≤ 50 years of age) are generally greater than reported in the "usual" patient groups aged between 60–70 years, most likely reflecting the underlying pathophysiology of AF in aging hearts. PV isolation, the cornerstone of ablation therapy, which was performed in all patients in our study, was probably sufficient to treat AF, even when presenting as a persistent arrhythmia, when performed in patients ≤ 50 years old. While in octogenarians, even though more extensive ablation lesions were performed in the left atrium, in addition to PV isolation, it was not enough to significantly impact the arrhythmogenic substrate and alleviate the AF.

Octogenarians have been reported to have increased amounts of extrapulmonary triggering foci,[20] paralleling significant changes in the atrial substrate leading to development of areas with regionally slowed conduction (especially in critical structures such as the coronary sinus and the crista terminalis), and the presence of diffuse areas with low voltages,[28] which may explain the generally lower efficacy of RFCA in procedures that stress only PV isolation and linear left atrial lines. More site-specific left and right atrial ablations are likely necessary to successfully cope with the arrhythmia. However, on antiarrhythmic drugs, the results seemed to be satisfactory. In our study, almost 80% of octogenarians with non-paroxysmal AF types did not experience further relapse over the 12-month follow-up period, when previously ineffective anti-arrhythmic therapy was reconstituted.

4.1 Study limitations

The major limitation was that this study was a retrospective analysis of the safety and clinical effectiveness of RFCA in octogenarians, although the data was collected prospectively. Since we serve as a tertiary high-volume center for RFCA, octogenarians referred for RFCA at our institution most likely represented a highly selected group of relatively vital, "biologically younger" individuals capable of understanding the principles of the procedure and capable of full cooperation before, during, and after the procedure. This referral bias may also explain the relatively low prevalence of structural heart disease, heart failure, and other age-associated comorbidities in our elderly population. Therefore, caution must be taken before generalizing our results to an unselected cohort of octogenarians with AF. Octogenarians constituted only 1.1% of the overall patient population referred for RFCA at our institution, thus our findings of similar effectiveness and safety of RFCA compared to younger patients might be underpowered to disclose differences in procedural outcomes between the two age groups. Last, this is a single center study with just two highly experienced physicians performing all ablation procedures under direct guidance of intracardiac echocardiography, which is being known to increase the safety of RFCA for AF.[22] Whether our experience can be generalized to less experienced physicians and institutions, which do not use complex periprocedural imaging, will require further assessment.

4.2 Conclusions

RFCA is a safe and effective strategy for achieving normal sinus rhythm in a highly selected group of octogenarians. Therefore, biologically vital individuals should not be discouraged from undergoing RFCA, especially in highly experienced centers. Age alone should not be considered a sufficient reason for nonintervention, especially given the possible benefits relative to the lower incidence of heart failure, cardioembolic events, and dementia. Paroxysmal AF ablation in octogenarians has similar clinical effectiveness as that seen in much younger patients, while persistent AF ablation has lower, although, still reasonable clinical value.

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