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Catheter ablation of atrial fibrillation in the elderly: Where do we stand?

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Abstract

Catheter ablation has emerged as an important therapy for the management of drug refractory symptomatic paroxysmal and persistent atrial fibrillation (AF). Although the elderly account for the majority of patients with AF, limited data exists regarding the use of catheter ablation for elderly patients with AF. As AF ablation has become more widespread, ablation techniques have improved and the complication rate has decreased. As a result, referrals of elderly patients for catheter ablation of AF are on the rise. Two retrospective analyses have recently demonstrated that catheter ablation of AF in the elderly can safely be performed and results are comparable to a younger population with up to 80% or more of patients maintaining sinus rhythm at 12 months follow-up. We compared the results of 15 consecutive patients ≥ 70 years old with symptomatic paroxysmal atrial fibrillation who underwent catheter ablation of AF at our institution to 45 randomly sampled younger patients. The primary endpoint of our study, presence of sinus rhythm in the absence of symptoms at 12 months follow-up, was present in 60% of elderly patients and 80% of younger patients (p = 0.17). There was no statistically significant difference in complication rate between the younger and elderly patients. In this article we present the results of our study and review the published literature to date regarding the clinical efficacy and safety of catheter ablation for AF in elderly patients with paroxysmal and persistent atrial fibrillation. (Cardiol J 2009; 16, 2: 113–120)

Key words: atrial fibrillation, catheter ablation, elderly patients

Introduction

The growing epidemic of atrial fibrillation (AF) presents new challenges for cardiovascular practitioners [1]. Already the most frequently encountered arrhythmia in clinical practice, the incidence and prevalence of AF appears to be on the rise. Census based projections estimate that by the year 2050, 12–15 million people in the United States will be affected by atrial fibrillation [2, 3]. That AF is a disease of the elderly is well established. Beginning at age 50, the prevalence of AF almost doubles with each decade of life; increasing from 0.5% at age 50––59 years to 5–7% or greater in those aged 70–79 years [4]. The median age of a patient with atrial fibrillation in the United States is 75 years and 70% of the AF burden in the United States is accounted for by patients aged 65 to 85 years of age [5, 6].

Beyond the shear numbers of elderly with AF, this population presents unique challenges to disease management. Elderly patients are more likely to have co-morbid illnesses including hypertension, congestive heart failure and left ventricular hypertrophy; placing them at increased risk for throm-

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boembolic complications with AF [7]. Age related senescence alters the pharmacokinetics of anti-arrhythmic agents making the metabolism less predictable and increasing the predilection for side-effects, including pro-arrhythmias [8–10]. Degenerative changes in the cardiac conduction system that occur with age predispose the elderly to sick sinus syndrome, otherwise known as tachycardia-bradycardia syndrome [7]. This predilection for tachycardia and sinus pauses (particularly during spontaneous cardioversion) makes pharmacologic rhythm control difficult to achieve in elderly patients with symptomatic paroxysmal and persistent atrial fibrillation. Additionally, patients with tachy-brady syndrome are often intolerant of atrioventricular (AV) nodal blocking agents required for adequate rate control, necessitating permanent pacemaker implantation [10].

Until recently, there has been a paucity of data regarding the use of catheter ablation for maintenance of sinus rhythm in the elderly population (particularly those ≥ 70 years of age). Elderly patients have largely been excluded from many AF ablation trials because of concerns regarding safety and efficacy of catheter ablation in these patients [11–13]. With increasing life expectancy, the elderly are the most rapidly expanding portion of our population, making AF an even more important public health concern [1, 14]. Given that elderly patients with symptomatic paroxysmal or persistent AF may be less tolerant of anti-arrhythmic agents than their younger counterparts, catheter ablation for the elderly could prove to be an important treatment strategy [7, 10].

Review of the literature

There are no randomized prospective trials comparing the safety and efficacy of catheter ablation for paroxysmal or persistent AF in the elderly to best medical therapy or alternative strategies such as AV node (AVJ) ablation plus pacemaker placement. Hsieh et al. [15] compared the long-term results (> 4 years) of 71 elderly patients (> 65 years old) with medically refractory paroxysmal AF that were assigned to either AVJ ablation plus single-chamber (VVI or VVIR) pacemaker placement versus AF ablation. The AF ablation strategy consisted of pulmonary vein isolation, ablation of non-pulmonary vein foci and cavotricuspid isthmus ablation. All pacemaker leads were positioned in the right ventricular apex. One patient in each arm had an unsuccessful ablation; thus 32 patients with AVJ ablation and 37 patients with AF ablation were followed for ≥ 52 months [15].

Atrial fibrillation was better controlled in the group with AVJ ablation and pacemaker placement than with AF ablation (100% *vs*. 81%, p = 0.013). Most other outcome variables favored the AF ablation strategy. In the AF ablation group, 30 (81%) patients remained free of symptomatic AF, with only 11% requiring anti-arrhythmic agents. 69% of patients in the AVJ ablation plus pacemaker group had persistent AF at the end of follow-up, compared to only 8% in the AF ablation group (p < 0.001). The incidence of congestive heart failure was significantly higher in the AVJ plus pacemaker strategy (53% *vs*. 24%, p = 0.001). Compared with pre-ablation values, there was a significantly greater increase in New York Heart Association (NYHA) class in the pacemaker group (1.4 ± 0.7 *vs*. 1.7 ± 0.9, p = 0.01) and no increase in NYHA class in the AF ablation group (1.2 ± 0.4 *vs*. 1.3 ± 0.6, p = 0.2). Additionally, the left verticular ejection fraction decreased in the AVJ ablation group from baseline to end of follow-up (51 ± 10% *vs*. 44 ± 8%, p = 0.01), but not with AF ablation (49 ± 10% *vs*. 46 ± 10%, p = 0.37) [15].

There were several limitations in the report by Hsieh et al. [15]. It was not a randomized controlled trial comparing the two treatment arms and the pacemaker strategy was non-physiologic. However, it was the first study to raise the question of whether an initial attempt at AF ablation would be reasonable for selected elderly patients with paroxysmal and persistent AF prior to performing the more permanent AV junctional ablation which leaves patients 100% pacemaker dependent. Additionally, 43 AF ablations were performed in the elderly population without any major complications including cardiac tamponade or cerebrovascular accident (CVA). A recently released, randomized controlled trial of AF ablation *vs*. AVJ ablation plus BiV pacemaker placement in patients with NYHA class II and III heart failure also favored an initial AF ablation strategy for improving heart failure symptoms. The mean age in this trial was 60 ± 8 years [16].

As AF ablation has become more widespread, the clinical population has broadened, providing us with greater insight into the potential efficacy in older patients as well as those with more advanced structural heart disease. Two larger analyses of efficacy, safety and outcomes of AF ablation in septugenarians have been published. Corrado et al. [17] reported a multi-center experience of 175 patients older than 75 years of age who underwent catheter ablation for symptomatic AF that was refractory to at least one antiarrhythmic drug (AAD) between 2001 and 2006. The ablation procedure consisted of pulmonary vein antrum isolation and isolation of

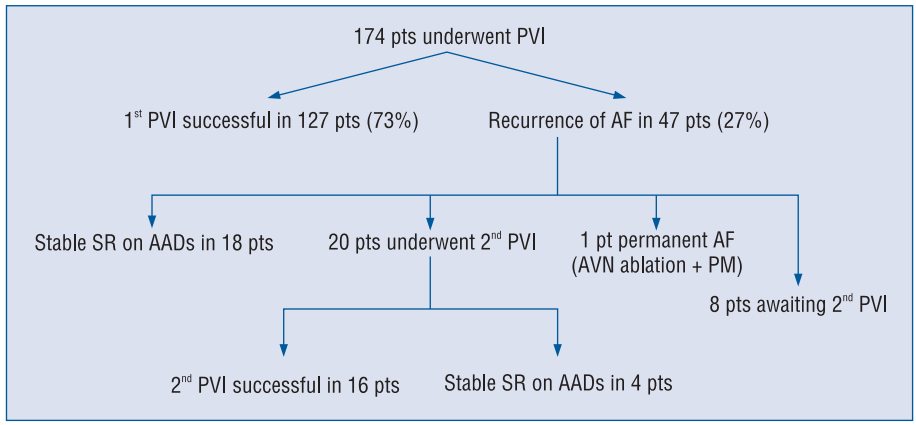

Figure 1. Results from the multicenter experience reported by Corrado et al. [17] for 174 patients over 75 years of age who underwent pulmonary vein isolation (PVI) for atrial fibrillation (AF); PM — pacemaker; AVN — atrioventricular node, SR — sinus rhythm, AADs — antyarrhythmic drugs (reproduced with permission from [17]).

the superior vena cava, guided by circular mapping catheter and intracardiac echo. Patients were followed-up at 3, 6, 9 and 12 months after the procedure and every 6 months, thereafter. During the first 5 months, patients were asked to transmit their rhythm three times daily and when they experienced symptoms of AF via an event recorder. Fourty-eight-hour Holter monitoring was performed at 3, 6, 9, and 12 months and then every 6 months [17].

The mean age in this study was 77 ± 6 years with 55% of patients having paroxysmal AF and 45% having non-paroxysmal AF. Mean ejection fraction and left atrial size were 53 ± 7% and 4.6 ± 0.6 cm, respectively. Mean follow-up was 20 ± 14 months. In keeping with the results of prior AF ablation trials in younger patients, 73% (127/174) maintained sinus rhythm (SR) after a single ablation procedure (Fig. 1) [11–13]. Among the 47 patients with recurrences, 18 maintained SR on anti-arrhythmic agents and 16/20 maintained SR after a 2nd procedure, with an additional 4/20 maintaining SR on AADs after the 2nd procedure. There were only two major complications out of 194 ablations; one intra-procedure CVA and one right hemothorax secondary to right internal jugular central line placement. Five to six months after successful ablation, warfarin was discontinued in 138/143 patients who were in SR in the absence of AADs. No thromboembolic events occurred in this group during a mean follow-up of 16 ± 12 months [17].

Although the multi-center experience reported by Corrado et al. [17] is a retrospective analysis that is subject to a referral bias of only "healthy" septugenarians, there was a remarkable rate of ablation success with 143/174 (82%) maintaining SR off AADs after two ablation procedures. An additional 22 patients were able to maintain SR with AADs. Thus 94% of patients were able to maintain SR at almost 2-years follow-up with an ablation strategy with a very low rate of major procedure related complications [17]. While the ablation success rate reported by Corrado et al. [17] seems almost prohibitively high for an elderly population, similar results were reported by Zado et al. [18] in their single-center experience.

Zado et al. [18] analyzed the procedural outcomes of 1165 patients with drug refractory AF who underwent 1506 ablation procedures between 2000 and 2007. The ablation procedure consisted of elimination of all provocable pulmonary vein triggers and non-pulmonary vein triggers of AF. For selected patients all four pulmonary veins were isolated. Follow-up patient monitoring consisted of both routine office follow-up and surveillance transtelephonic monitoring, as well as the ability to transmit symptomatic episodes. Patients were stratified by age group to < 65 years (n = 948), 65–74 years (n = 185) and ≥ 75 years (n = 32). The peri-procedural complication rate was low with no difference between the three age groups. In those older than 75 years of age, there was one CVA/transient ischemic attack (3%) and no pericardial effusions/tamponade requiring drainage compared to a 0.3% CVA/transient ischemic attack rate and a 0.8% pericardial effusion/tamponade rate in those < 65 years of age.

Among the 781 patients who completed the minimum 1-year of follow-up, there was no difference between the groups for ablation success. AF control rates (see Figure 2 for definition) were 89%,

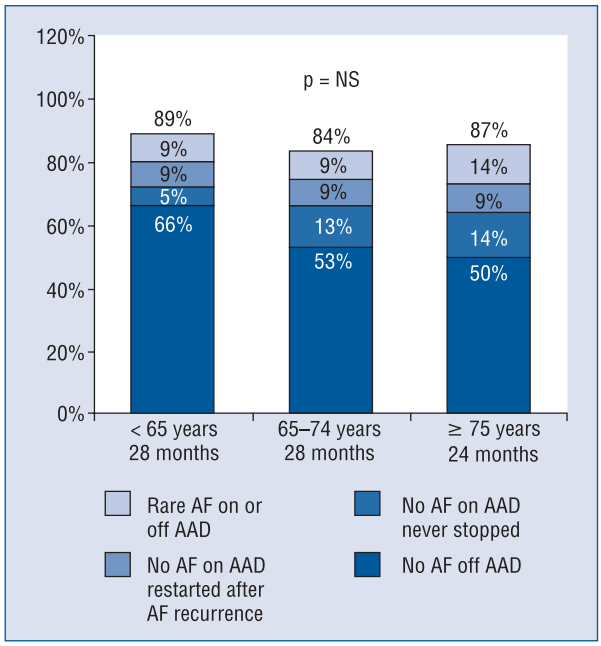

Figure 2. Results from the single center experience reported by Zado et al. [18] for the patients who completed at least 1-year follow-up from the last atrial fibrillation (AF) ablation procedure (n = 635 in group 1, n = 122 in group 2, n = 22 in group 3). Although there was a trend towards greater use of antiarrhythmic drugs (AADs) in older patients, there was no difference in AF control* between the three groups, p = NS (reproduced with permission from [18]); *defined as 1) no AF episodes on or off anti-arrhythmic therapy or 2) rare AF (≤ 6 AF episodes over the follow-up year and/or > 95% reduction in AF burden when monitoring was compared pre- and post-ablation

84% and 87%, among those aged < 65, 65–74, and > 75, respectively. There was also no difference between the percentages of patients with no reported AF during follow-up off anti-arrhythmic agents. There was a trend toward less repeat procedures among the oldest patients and more elderly patients were maintained on AAD therapy to achieve AF control (Fig. 2). Additionally, more elderly patients were maintained on AADs even in the absence of AF recurrence (5% group 1, *vs*. 13% group 2, *vs*. 14% group 3).

Our experience

We compared the procedural outcomes of 15 consecutive patients ≥ 70-year-old and 45 randomly selected patients < 70-year-old who underwent catheter ablation for paroxysmal AF between February 2003 and February 2007 at the Strong Memorial Hospital, University of Rochester Medical Center, Rochester, NY. Pulmonary vein isolation was performed in all patients using circumferential applications of radiofrequency energy and verified with a circular mapping catheter (Lasso Catheter, Biosense Webster, Inc, Diamond Bar, Calif). The ablation catheter used was an 8-mm nonirrigated tip (Navistar, Biosense Webster) in 8 of the elderly and 19 non-elderly patients. When the 3.5-mm irrigated tip catheter (Navistar Thermocool, Biosense Webster) became available, the remainder of the patient procedures were performed with this catheter (n = 7 in elderly group, n = 26 in non-elderly group). A power and temperature limit of 60 W and 60°C was used for the non-irrigated tip catheter. A power limit of ≤ 35 W with a tip temperature of ≤ 40°C was used for the irrigated tip catheter.

All patients were initially followed up at 3, 6 and 12 months. After the first year, they were followed at 3–6 month intervals. Electrocardiograms (ECGs) were performed at each follow-up visit. Twenty-four or 48-hour Holter monitoring was performed for any patient who reported recurrent symptoms of paroxysmal AF. The primary outcome was presence of normal sinus rhythm (NSR) in the absence of symptoms, on or off anti-arrhythmic agents, based on ECG or Holter monitoring at 12 months of follow-up. The secondary outcome was NSR and/or symptomatic improvement as reported by patients during routine follow-up. Symptoms or documentation of AF beyond 12 months were censored for the primary and secondary end-points.

Baseline characteristics of study patients were similar (Table 1). The mean age of our elderly population was 73 ± 2.2 years compared to a mean age of 51.9 ± 11.3 years in the younger group. A similar percentage of younger (24%) and elderly (20%) patients underwent a repeat ablation procedure. Median clinical follow-up was 586 days and 675 days in the young and elderly groups, respectively.

The primary outcome, presence of NSR in the absence of symptoms, was present in 9 (60%) of elderly patients and in 36 (80%) of younger patients at 12-months follow-up (p = 0.17, Table 2). The combined outcome of symptomatic improvement or NSR was present in 80% (n = 12) of elderly patients and 93% (n = 42) of younger patients (p = 0.16). There were three serious complications of pericardial tamponade: one in the older group and two in the younger one (7% *vs*. 4%; p = 1.00). At the end of follow-up, 30% of elderly patients (3/9) with successful ablations were still using anti-arrhythmic medications versus 8% among younger patients (p = 0.002). Additionally, 80% of the elderly patients remained on warfarin therapy, compared to 22% of the younger patients (p < 0.001).

Table 1. Baseline characteristics of patients undergoing atrial fibbrillation (AF) ablation by age category.

Clinical variables	Age < 70 (n = 45)	Age ≥ 70 (n = 15)	P
Age	52 ± 11	74 ± 2	< 0.001
Female	29%	20%	0.738
Ejection fraction (%)	54 ± 8	57±6	0.105
Ejection fraction ≤ 45%	13%	7%	0.668
Left atrial size [mm]	41 ± 6	43±5	0.151
Left atrial size ≥ 50 mm	4%	13%	0.258
AF duration > 60 months	24%	40%	0.324
Comorbidites			
Coronary artery disease	13%	20%	0.678
Hypertension	42%	40%	1.000
Diabetes	4%	7%	1.000
Medications at baseline			
ACE-inhibitors	27%	40%	0.347
Beta-blockers	40%	87%	0.002
Statins	27%	40%	0.347
Flecainide	24%	13%	0.485
Tikosyn	11%	47%	0.006
Propafenone	33%	20%	0.517
Sotalol	18%	7%	0.427
Amiodarone	9%	0	0.564
None	4%	13%	0.258

Table 2. Comparison of atrial fibrillation ablation outcomes at 1 year by age category.

	Age < 70 (n = 45)	Age ≥ 70 (n = 15)	P
NSR in the absence of symptoms at 12 months	36 (80.0%)	9 (60.0%)	0.169
NSR or symptomatic improvement	42 (93.3%)	12 (80.0%)	0.159
Remaining on anti-arrhythmic therapy (%)	7 (15.6%)	9 (60.0%)	0.002
With successful ablations who remained on anti-arrhythmic therapy (%)	3/36 (8%)	3/9 (33%)	< 0.05
Remaining on warfarin (%)	10 (22.2%)	12 (80.0%)	< 0.001
Complications	2 (4.4%)	1 (6.7%)	1.000

NSR — normal sinus rhythm

Discussion

As AF ablation has become a more mainstream therapy, the number of AF ablations performed has increased, the safety profile has improved and patient characteristics have evolved [19–21]. Gerstenfeld et al. [21] reported that between 1999 and 2005, patients undergoing AF ablation have become relatively older, with more persistent and permanent AF and larger left atrial size. A similar trend has been observed at our center with increasing referrals of elderly patients, as well as those with significant structural heart disease.

The AFFIRM trial demonstrated that rate control and anti-coagulation is an acceptable management strategy for elderly patients with AF [22]. However, AFFIRM did not address the needs of patients who are intolerant of AF due to loss of atrial contraction, irregularity of QRS intervals or tachy/brady syndrome refractory to standard rate and rhythm controlling agents. In the rate control arm of AFFIRM, radiofrequency ablation to modify or eliminate AV nodal conduction was used in 5.2% of patients after drug failure. 12.2% of the rate control arm crossed over to rhythm control during the study. Thus for 17.4% of the rate control arm in

AFFIRM, use AV nodal blocking agents alone was not a satisfactory clinical management strategy [22]. Furthermore, treatment analysis of both the AFFIRM and DIAMOND studies suggests that the presence of sinus rhythm is associated with improved survival [22–24]. Use of AAD in AFFIRM was associated with increased mortality, leaving open the question of whether a rhythm control strategy that relies less heavily on anti-arrhythmic agents might provide long-term survival benefit to patients [23].

In a recent editorial on management of AF in the elderly, Curtis et al. [9] remarked that given the potential adverse effects from long-term antithrombotic and anti-arrhythmic therapy in elderly patients, the role of AF ablation deserves further study. Also mentioned was that at this point there is too little data because elderly patients have largely been excluded from AF ablation trials [9]. The combined retrospective data from the three published series and the experience at our center indicates that AF ablation can be performed safely in a septuagenarian population [15, 17, 18]. While the data reviewed above also indicates that AF ablation appears to be efficacious in a septuagenarian population, randomized, prospective studies comparing AF ablation to rate control and rhythm control with AADs or both is certainly warranted.

One point of interest that emerged from review of the literature to date is the trend toward more elderly patients remaining on AADs after ablation, even in the absence of documented recurrent AF (Table 3). A potential explanation for this finding is that one of the goals of AF ablation in a younger population is to negate the need for long-term AAD therapy. For the elderly, symptom relief with control of AF may have been the objective of ablation in these retrospective series. Additionally, the substrate for initiation and perpetuation of AF in the younger and elderly population may differ. Aging is associated with electrical and structural atrial remodeling including changes in action potential shape and duration, enhanced dispersion of repolarization, and increased atrial fibrosis [25, 26]. Pulmonary vein isolation may not sufficiently eliminate the triggers for AF in an elderly compared to a younger population; although this remains to be proven.

Two final issues that merit discussion in regard to AF ablation in the elderly are how to define ablation success and whether or not discontinuation of anti-coagulation therapy should be an objective of AF ablation. Most randomized trials comparing AF ablation to AAD therapy define ablation success as freedom from recurrent AF at 1-year follow-up

Table 3. Summary of studies of atrial fibrillation (AF) ablation in the elderly.

Author	Patients (age range in years)	AF type (paroxysmal, persistent, chronic)	Mean-follow (months)	Outcome	Remaining on AAD's	Major complications
Hseih et al.	37 (72 ± 4)	Paroxysmal	52 ± 6	81% in SR	11%	0%
Corrado et al. (see Fig. 1)	174 (> 75)	Paroxysmal 55% Persistent 45%	20 ± 14	88% (127/143) SR off AAD's after 1st procedure 10.8% (16/143) SR off AAD's after 2nd procedure	13%	1%
Zado et al. (see Fig. 2)	635 (< 65) 124 (65–74) 22 (≥ 75)	65% paroxysmal** 62% paroxysmal 53% paroxysmal	27.6 ± 13.8 27.7 ± 13.6 23.8 ± 11.3	89% AF control* 84% AF control* 87% AF control*	20% 29% 37%	1.6% 1.7% 2.9%
Hall et al.	15 (73.6)	100% paroxysmal	56	60% in SR at 12 months 80% in SR or with symptomatic improvement	60%	6.6%
Santinelli et al. (abstract)	172 (> 80, mean age 83 ± 2)	35% paroxysmal 29% persistent 36% paroxysmal	18 ± 5	Overall success rate of 75% 90% paroxysmal 76% persistent 60% permanent	Not reported	5%

AAD — antiarrhythmic drug, SR — sinus rhythm; *defined as 1) no AF episodes on or off anti-arrhythmic therapy or 2) rare AF (≤ 6 AF episodes over the follow-up year and/or > 95% reduction in AF burden when monitoring was compared pre- and post-ablation; **percentage of paroxysmal per age group, other patients in each age group were non-paroxysmal AF

without AAD use based on Holter monitoring and patient reported symptoms [27–30]. From a clinical perspective, achieving a significant reduction in AF burden as reported by Zado et al. [18], regardless of AAD use may be an acceptable endpoint for a highly symptomatic elderly patient with paroxymal AF; even more so with persistent AF. However, to truly understand the efficacy of AF ablation in the elderly, initial randomized trials should objectively evaluate the same clinical endpoints as those performed to date in younger populations, specifically the ability to maintain SR off anti-arrhythmic agents. Perhaps pre-defined secondary endpoints for these trials could include: a reduction in AF episodes, ability to maintain sinus rhythm on AADs when AADs had previously failed, symptom reduction or other less stringent but still clinically relevant end-points.

In the series by Corrado et al. [17], warfarin was discontinued in 138/143 patients who maintained SR 5–6 months after AF ablation. No thromboembolic events occurred in this group during a mean follow-up of 16 ± 12 months. While Corrado et al. [17] are to be commended for their promising results, their findings must be interpreted in light of the yearly risk for CVA in an AF patient off anticoagulation, which ranges from 2.8% to 6.4% with $CHADS_2$ scores of 1–3 [31]. Discontinuation of warfarin following successful AF ablation in an elderly patient is extremely appealing in concept. Establishing the safety of this practice will require longer follow-up of ablation patients with inquiries specifically investigating rates and predictors of late recurrences of AF.

Conclusions

Elderly patients have historically been underrepresented in clinical trials. As physicians we are often left to extrapolate data and make our own conclusions as to whether or not we feel an elderly patient may benefit from a new technology that has proven effective in a younger cohort. Once the technology is used in enough elderly patients, retrospective analyses are carried out to assess the clinical efficacy. These analyses are often subject to bias and rightfully not accepted with the same degree of merit as randomized controlled trials. The elderly represent the fastest growing segment of our population and for this reason a conscious effort should be made to include these patients in our clinical trials and perhaps perform trials that specifically address the elderly population. Because atrial fibrillation is a disease in which the majority of patients are elderly, it behooves us to scientifically investigate the efficacy of catheter ablation in this ever expanding population. The retrospective analyses conducted to date indicate that catheter ablation of AF can be safely performed in an elderly population and appears to be beneficial. The next step is to perform large scale, randomized trials like AFFIRM to more definitively establish the role of catheter ablation in treating elderly patients with atrial fibrillation [22].

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