



# Percutaneous interventions in elderly patients with atrial fibrillation: left atrial ablation and left atrial appendage occlusion

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## 1 Introduction

Heart rhythm disturbances become of special importance when patients reach a senior age. Atrial fibrillation (AF) is the most prevalent arrhythmia among the old age groups, and its impact on morbidity and mortality becomes of paramount significance. In this population, AF is responsible for significant amount of thromboembolic cerebrovascular events, especially for disabling and fatal strokes.<sup>[1]</sup> Following announcement of the special issue of the *Journal of Geriatric Cardiology* devoted to heart rhythm disorders in the elderly, a number of submissions have been received with AF as the major topic of authors' researches.

Here we would like to introduce this special issue, which finally included clinical research papers on age-related differences in outcomes of AF catheter ablation, AF-related stroke hospitalizations, mortality predictors in patients with AF, stroke prevention using left atrial appendage (LAA) occluder implantation. Additionally, a clinical research paper describes predictors of heart rhythm disturbances in patients with obstructive sleep apnea and hypertension, and a paper describes ventricular tachycardia suppression by renal denervation in patients with left heart thrombosis and contraindications to conventional endocardial substrate modification.

Having included into the issue two controversial topics of special importance, AF catheter ablation and LAA occluder implantation in the elderly, we decided to discuss them in the light of other recently published studies.

## 2 Atrial fibrillation: risk-benefit considerations in elderly patients undergoing catheter ablation

AF ablation safety and efficacy have been evaluated in a

number of observational and randomized studies. It had been anticipated that age is associated with advanced myocardial fibrosis and an increased extent of arrhythmogenic substrate remodeling in both atria.<sup>[2,3]</sup> However, age-stratified histological evaluation revealed that myocardial fibrosis is robustly associated with the presence of AF, without correlation between patient age and changes in atrial tissue.<sup>[4]</sup> According to this latter finding, pulmonary vein isolation in elderly patients is thought to be as effective as in younger patients. On the other hands, older patients usually have more severe co-morbidities, and AF ablation can potentially be associated with more procedure-related complications.

Outcomes of ablation in septuagenarians and octogenarians have been evaluated by many groups around the world; however, the majority of those studies were single-center retrospective analyses, and only a few publications included data from prospective multicenter registries. We have identified 14 papers where age groups were studied separately, and efficacy and/or safety outcomes were clearly reported for patients >65/>75 years old (Table 1). Among these studies, 11 included a control group of younger patients. Twelve studies reported on 1<sup>st</sup> AF ablation procedure success (arrhythmia freedom with regular ECG screening), and 12 studies reported on detailed procedure-related major complications, that required additional interventions or prolonged hospital stay.

It was possible to extract data for comparison between older and younger age groups from 10 studies: six studies demonstrated no difference in efficacy and safety between groups;<sup>[6,8–11,14]</sup> one study showed that complications were more frequent in the older group;<sup>[15]</sup> one study showed that success rate was lower in the older group;<sup>[18]</sup> in one study the authors found that older patients had more major complications and poorer success rate of ablation;<sup>[16]</sup> and in

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**Table 1. Published analyses evaluating AF ablation efficacy and safety in old patients.**

	Old patient group definition	Number of old patients	Number of control patients	% of paroxysmal AF	Type of ablation	#Major complications, n (%) (older/younger patients)	Mean follow-up period, months	12-months arrhythmia freedom after 1 <sup>st</sup> ablation (older patients only)	Arrhythmia freedom after 1 <sup>st</sup> ablation at last follow-up (Older/younger patients)	Different outcome compared to a younger group
Corrado A, <i>et al.</i> <sup>[5]</sup>	> 75 yrs	174	No	55%	RF	5 (2.9%)	20	NA	73%	NA
Zado E, <i>et al.</i> <sup>[6]</sup>	> 75 yrs	32	1472	53%	RF	1 (3.1%)/24 (1.6%)	24	NA	50%/59.5%	No
Kusumoto F, <i>et al.</i> <sup>[7]</sup>	> 75 yrs	61	179	34%	RF	0/2 (1.1%)	12	60%	60%/88%	NA
Tan H, <i>et al.</i> <sup>[8]</sup>	≥ 80 yrs*	49	328	55%	RF	1(2%)/7(2.1%)	18	NA	70%/73%	No
Bunch TJ, <i>et al.</i> <sup>[9]</sup>	≥ 80 yrs	35	717	45.7%	RF	NA	12	78%	78%/75%	No
Santangeli P, <i>et al.</i> <sup>[10]</sup>	≥ 80 yrs	103	2651	25%	RF	1 (0.97%)/25 (0.9%)	18	NA	69%/71%	No
Lioni L, <i>et al.</i> <sup>[11]</sup>	> 65 yrs	95	225	100%	RF	3 (3.2%)/4 (1.7%)	34	57.9%	57.9%/67.4%	No
Metzner I, <i>et al.</i> <sup>[12]</sup>	≥ 75 yrs	94	No	59%	RF	7 (7%)	37	NA	38%	NA
Pott A, <i>et al.</i> <sup>[13]</sup>	> 75 yrs	40	No	77.5%	Cryo	1 (2.5%)	15	86.4%	77.5%	NA
Abugattas JP, <i>et al.</i> <sup>[14]</sup>	> 75 yrs	53	106	100%	Cryo	0/2 (1.9%)	13	81.1%	81.1%/84.9%	No
Moser J, <i>et al.</i> <sup>[15]</sup>	> 75 yrs	227	4222	59.9%	RF: 84.6%; Cryo: 15.4%	10 (4.4%)/12 (2.7%)	15.1	NA	NA	Yes, complications
Kautzner J, <i>et al.</i> <sup>[16]</sup>	> 70 yrs	394	2803	66.5%	RF	5.3%/3.2%	25	NA	44.2%/58.2%	Yes, complications and success
Kis Z, <i>et al.</i> <sup>[17]</sup>	> 65 yrs	80	310	90%	RF 39%; Cryo 61%	NA	72	NA	NA	No, complications
Bulava A, <i>et al.</i> <sup>[18]</sup>	> 80 yrs	50	259 (< 50 years old)	42%	RF	2 (4%)/11 (4.2%)	12	64%	64%/83.8%	Yes, success
Overall**	> 75 yrs	883 for safety analysis; 691 for efficacy analysis	9217 for safety analysis; 5712 for efficacy analysis	54.4%	RF: 80.6%; Cryo: 19.4%	28 (3.2%)/191 (1.9%)	Median 18 months, IQR (13.5; 24.75)	72.8%	65.7% <sup>†</sup> / 67.2% <sup>‡</sup>	Complications, <i>P</i> = 0.0433; Success, <i>P</i> = 0.42 <sup>††</sup>

#Severe procedure-related complications, requiring additional interventions; \*Although three groups of patients were studied (1<sup>st</sup> group ≥ 80 years old, 2<sup>nd</sup> group 70–79 years old, 3<sup>rd</sup> group 60–69 years old), only the 1<sup>st</sup> group was included into this pooled analysis; \*\*In total, data from 10 studies reporting on complications in patients > 75 years old was used, and data from 10 studies reporting on success rate in patients > 75 years old; †A value derived from six studies with available data; ††Between groups, as reported arrhythmia-free status at last follow-up visit, Chi-square test with two-tailed *P*; ‡A value derived from 12 studies with available data. AF: atrial fibrillation; Cryo: cryoballoon ablation; IQR: interquartile range (first and third quartiles); NA: non-available/not reported data; RF: radiofrequency ablation.

one study only complications were reported and there was no difference between groups.<sup>[17]</sup>

Since there was no common definition of the older age group in the studies, we combined data from reports dealing with patients > 75 years old. This pooled analysis in 10,100

subjects (883 patients > 75 years old and 9217 patients < 75 years) showed that procedure-related major complications were more frequently seen in older patients (3.2% vs. 1.9%, *P* = 0.0433). On the other hand, at a median of 18 months, the success rate of a single AF ablation procedure, defined

as no documented evidence of sustained atrial tachyarrhythmia, was not different between the older and younger groups (analyzed in 691 subjects >75 years old and in 5712 controls). Forest plot analyses of AF ablation success and procedure-related major complications from comparative studies (patients younger and older 75 years, each analysis included 7 studies) showed the same results, see Figures 1 and 2.

Considering these findings, we strongly believe that when symptomatic AF is refractory to antiarrhythmic medications, decision on referral of a patient for AF ablation should not be restricted to younger patients. However, patients of older age should be informed regarding the higher risk of complications.

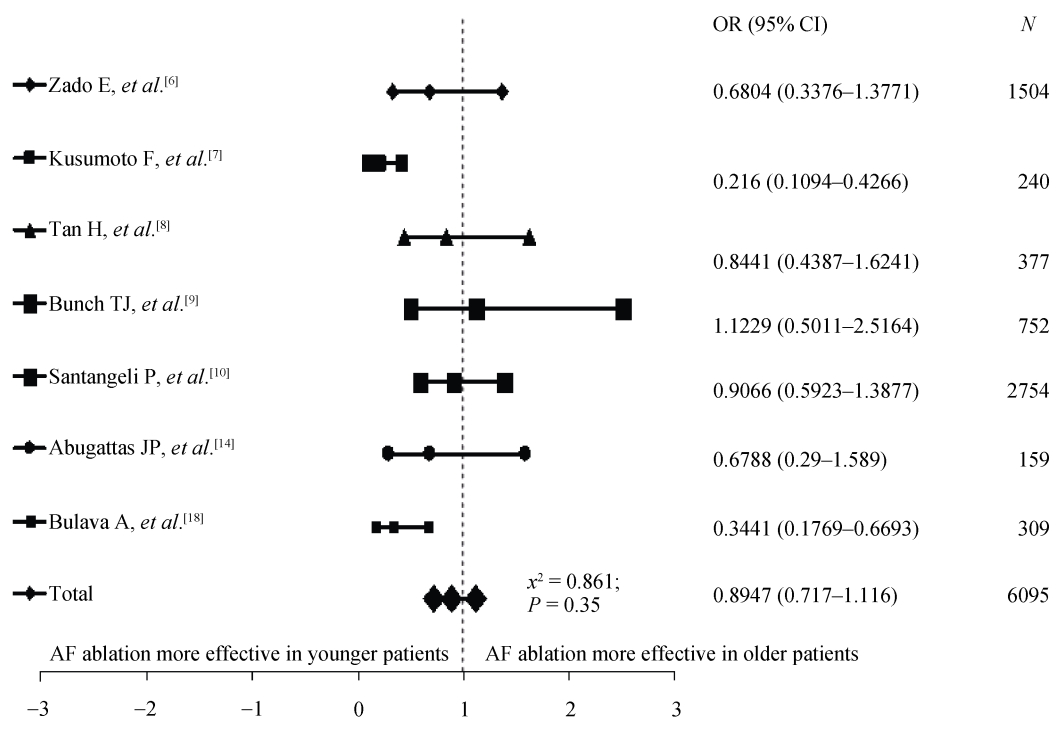
### 3 Left atrial appendage occlusion in elderly patients

Outcomes of interventional LAA occlusion have mainly been reported in observational studies and registries, and one occluder device has been investigated in comparison with oral anticoagulation in randomized trials.<sup>[19,20]</sup> It has been suggested that percutaneous LAA occlusion is

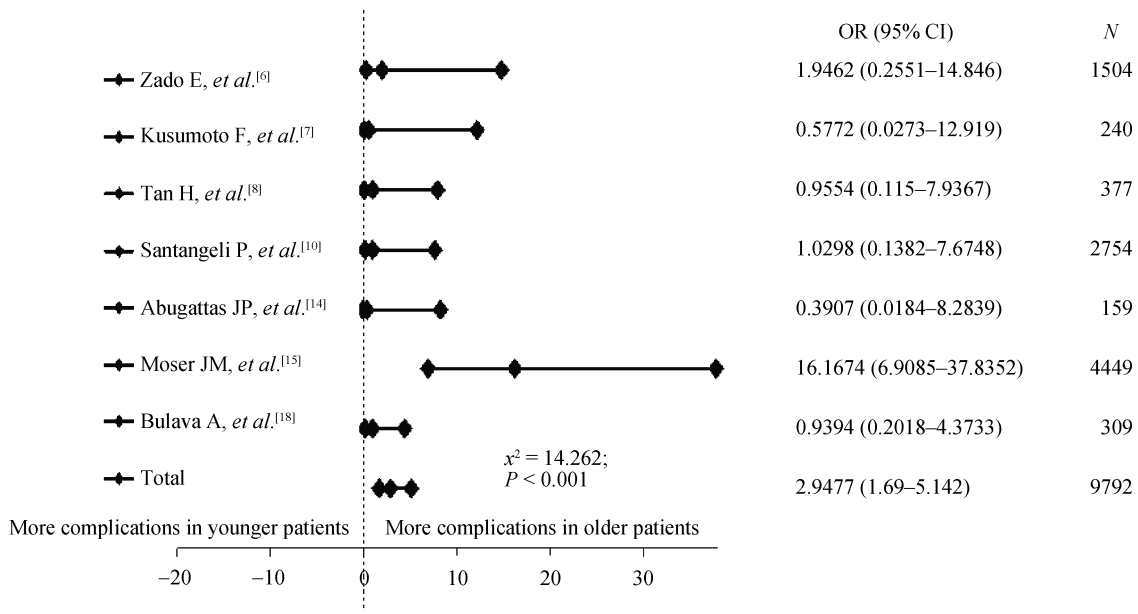
non-inferior to warfarin treatment regarding prevention of stroke and possibly associated with less bleeding events. Although the majority of published studies included elderly patients with a mean patient age ranging between 70 and 74 years, there is a lack of studies exclusively investigating safety and efficacy of LAA occlusion in patients over 75 years old. There is one sub-analysis showing higher bleeding events in patients >75 years after LAA occluder implantation compared to a younger group (4.4% vs. 1.4%).<sup>[21]</sup>

Oral anticoagulation therapy often remains underutilized in elderly AF patients, and adherence to therapy is sometimes a challenge in this subpopulation.<sup>[22]</sup> This is also exaggerated by the fact that frail patients are also at increased risk of stroke and bleeding.<sup>[23]</sup> Therefore, interventional percutaneous LAA occlusion is an attractive strategy in old patients, and implantation of this device could obviate the need for oral anticoagulation.

In this special issue of *Journal of Geriatric Cardiology* Davtyan K with co-authors describe their long-term experience with LAA occlusion in AF patients > 75 years old.<sup>[24]</sup> When these results are presented along with other reports on LAA occlusion, it seems that serious complications related to the implantation procedure vary from 0 to 5.1%, with a



**Figure 1. Forest plot analysis of AF ablation success in patients aged < 75 and > 75 years.** Only seven studies with evaluation of arrhythmia-free rate in patients >75 years old and a control group were included. No heterogeneity analysis was performed, since all studies were observational. Statistical analysis and graphical presentation were performed using Excel 2003 SP3 (Microsoft Corporation, USA). AF: atrial fibrillation.



**Figure 2. Forest plot analysis of major complications related to AF ablation in patients aged < 75 and > 75 years.** Only seven studies with evaluation of arrhythmia-free rate in patients > 75 years old and a control group were included. No heterogeneity analysis was performed, since all studies were observational. AF: atrial fibrillation.

mean rate 4.8% (Table 2). Regarding late events, smaller studies show a perfect protection from stroke, while a study with the largest cohort of old patients reveal 2.3% rate of

stroke/transient ischaemic attack (TIA) despite successful occluder implantation.

A warning finding among patients with an implanted

**Table 2. Results of percutaneous LAA occluder device implantation derived from studies reporting outcomes in elderly patients.**

	Gafoor S, <i>et al.</i> <sup>[25]</sup>	Freixa X, <i>et al.</i> <sup>[26]</sup>	Davtyan K, <i>et al.</i> <sup>[24]</sup>	Overall
Design	Retrospective	Retrospective analysis of prospectively collected data	Retrospective	All retrospective
Number of sites	Single-center	Multicenter	Single-center	
Definition of old patients	> 80 yrs	> 75 yrs	> 75 yrs	> 75 yrs
Control group	No	Yes (n = 376)	Yes (n = 54)	430
Number of old patients	75	452	18	545
Mean CHA <sub>2</sub> DS <sub>2</sub> -VASC	5.2	5.1	5.27	5.19
Devices	Watchman, ACP, PLAATO, Lariat, Coherex	ACP	ACP, Watchman	
Follow-up	1 yr	1.4 yrs	4 yrs	Median 1.4 yrs
Number of old patients with an implanted device and available follow-up data	75	430	18	523
Periprocedural complications in old patients				
Total major procedure-related complications	3 (3.9%)	23 (5.1%)	0	26 (4.8%)
Stroke/TIA	1 (1.3%)	3 (0.7%)	0	4 (0.7%)
Device embolization	0	4 (0.9%)	0	4 (0.7%)
Major bleeding	1 (1.3%)	6 (1.3%)	0	7 (1.3%)
Cardiac tamponade	0	10 (2.2%)	0	10 (1.8%)
Death	0	6 (1.3%)	0	6 (1.1%)
Late events in old patients				
Stroke/TIA	0	10 (2.3%)	0	10 (1.8%)
Device thrombus	1	NA	1	NA
Major bleeding	0	11 (2.6%)	0	11 (2%)
Death	2 (2.7%)	40 (9.3%)	3 (17%)	45 (8.3%)

Data are presented as n (%) unless other indicated. LAA: left atrial appendage; NA: non-available/not reported data; TIA: transient ischaemic attack.

LAA occluder is a thrombus on the device in the early and mid-term follow-up period. Thus, in a recent French multicenter observational study, which mainly comprised of 453 older patients (mean age 75 yrs), in whom either the Watchman or Amplatzer Amulet (Boston Scientific, USA) was implanted, the authors reported thrombus formation in 24/453 (5.3%) cases.<sup>[27]</sup> There was no statistical difference between two devices. Older age and a previous history of ischemic stroke independently predicted thrombus. The predictors of stroke/TIA during follow-up were vascular diseases ( $P = 0.002$ ) and thrombus on device ( $P = 0.008$ ).

According to the 2016 ESC atrial fibrillation management guidelines, LAA occluder implantation has IIb class indication for stroke prevention in patients with AF and contra-indications for long-term anticoagulant treatment.<sup>[1]</sup> We suggest that safety of LAA occlusion in elderly patients is under-investigated and a balance between potential benefit and risk of procedure-related and device-related adverse events should be considered in each individual patient.

In conclusion, we would like to emphasize that although there is a lack of systematic and prospective results on AF ablation in elderly patients, the existent data shows catheter ablation is favorable for the management of symptomatic arrhythmia. Efficacy of this procedure in old patients seems not significantly different compared to younger patients, but the higher risk of major complications should be considered.

At the same time, we call for more caution when LAA occluder implantation is considered in old patients. The procedure-related complication rate is considerable in this population, and this risk needs to be carefully weighed with potential benefit, especially understanding risk of ischemic stroke after successful LAA occluder implantation. There is no systematic comparison of percutaneous LAA occlusion efficacy with non-vitamin K direct oral anticoagulants.

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