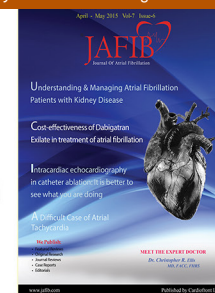




Original Research

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Influence of Age and Gender on Complications of Catheter Ablation for Atrial Fibrillation

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Abstract

Background: Despite catheter ablation (CA) has become an accepted treatment option for symptomatic, drug-resistant atrial fibrillation (AF), safety of this procedure continues to be cause for concern.

Objective: Aim of the present multicenter study was to assess the influence of age and gender on incidence and severity of early CA complications.

Methods: From January 1, 2011 to December 31, 2011, data from 2,323 consecutive patients who underwent CA (mean age 59.1±10.9; 72.3% male) for AF in 29 Italian centres were collected. All complications occurring to the patients from admission to 30th post-procedural day were recorded.

Results: Complications occurred in 94 patients (4.0%); of these 7 (0.30%) developed permanent sequelae. There was a significant trend toward a greater incidence of complications with increasing age-group. In particular, the incidence of complications was 35/1066 (3.3%) in patients < 60 year-old vs 59/1257 (4.7%) in those > 60 year-old (p=0.03). All 7 patients with permanent sequelae were older than 60. Females had a higher incidence of complications both among younger [13/231 (5.6%) vs 22/915 (2.5%), p=0.02] and older patients [32/405 (7.9%) vs 27/739 (3.5%) p=0.001]. In subjects older than 60, 5/405 (1.2%) females and 2/176 (0.3%) males (p=0.04) suffered from permanent sequelae.

Conclusions: Older patients and females are a subgroup at higher risk of complications during AF ablation. A particular care should be taken when performing CA in this clinical setting.

Introduction

Catheter ablation (CA) has become an accepted treatment option for recurrent, symptomatic, drug-resistant atrial fibrillation (AF). Isolating or encircling all accessible pulmonary veins (PVs) is identified as the cornerstone of any ablation approach. The number of operators and hospitals performing this procedure is increasing. Despite the satisfactory results justifying the introduction of CA in the international guidelines in selected patients also at an early AF management stage, safety of this procedure remains cause for concern.^{1,2} Complication rate range from 3.5% to 6.0%,³⁻¹⁰ but few data are present in Literature regarding the influence of age on incidence of complications.¹¹⁻¹⁴ Females are considered at higher risk of complications in all percutaneous procedures.^{15,16} Recently an higher risk of complications has been reported in female undergoing AF catheter ablation too.^{7-10,17} Aim of the present study was to

assess the influence of age and gender on incidence and severity of complications of CA for AF in an contemporary, unselected population of consecutive patients.

Methods

Study Population

Clinical and procedural data concerning consecutive patients who underwent CA for AF in 29 Italian electrophysiology laboratories between January 1 and December 31, 2011 were collected.

This observational study was approved by the local institutional review committees, and written informed consent was obtained from each patient.

Ablation

Details of anticoagulation strategy and ablation protocols have already been reported.⁸ Briefly, all ablation strategies aiming at isolating or encircling the PVs (radiofrequency ablation, circular multielectrode ablation, cryoablation) were included in the Registry. Additional linear lesions in the right or left atrium were also allowed.

Definitions

Major complications included all events that resulted in death or

Disclosures:
None.

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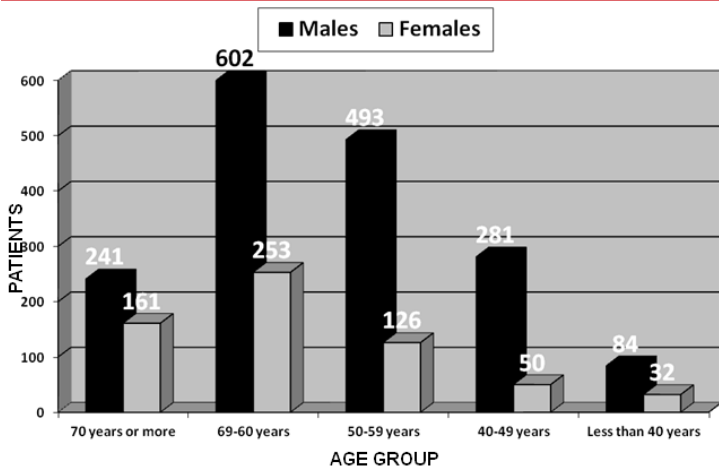


Figure 1: Distribution of age and gender among the study population. Males=black bar; females=grey bar. Absolute numbers are presented at the top of the bar

permanent injury, prolonged or required intervention for treatment, or required or prolonged hospital stay beyond the scheduled period. Early tachyarrhythmias (AF or atrial tachycardia/flutter) were not included even if they required cardioversion to be terminated.¹⁸

Permanent sequelae included all events that resulted in death or permanent injury.

Vascular complications included: femoral hematoma, arteriovenous fistula, femoral pseudoaneurysm, and subclavian hematoma.

Hemodynamic complications included: PV stenosis, cardiac tamponade, pericarditis, and hemothorax.

Ischaemic complications included: ischemic stroke, transient ischemic attack, and acute myocardial infarction.

Data Collection

The investigators were provided with the same data sheet for the collection of specific information on each ablation procedure. Data were gathered retrospectively by each investigator, and sent via a computerized database in Excel format (Windows 7, XP, or Mac) to the coordinating centre for analysis. Each author took responsibility for data integrity.

Statistical Analysis

Normally distributed continuous variables were expressed as mean

Table 1: Major complications occurred in the 2,323 enrolled patients

Complication	Patients
Vascular access complications	50 (2.2%)
Femoral hematoma	28
Arteriovenous fistula	13
Femoral pseudoaneurysm	7
Subclavian hematomas	2
Cardiac tamponade	12 (0.5%)
Pericarditis	14 (0.6%)
Transient ischemic attack	5 (0.2%)
Stroke	4 (0.15%)
Ischemic	3
Hemorrhagic	1
Phrenic nerve paralysis	3 (0.1%)
Hemothorax	3 (0.1%)
Others	3 (0.1%)

(SD) and compared with the Student's T-Test. Skewed variables were expressed as median (25-75 %iles) and compared with the run-sum test. Normality was assessed using the Shapiro-Wilk test. Categorical variables were presented as counts and percentages, and compared with chi-squared or Fisher's exact test, as appropriate. The Linear by Linear Association test was used to test for a linear trend in proportions of complications across age groups.

At multivariate analysis, a logistic regression model was designed and stepwise backward selection was performed in order to identify significant and independent predictors of complications. The starting model included: gender; age (< or > 59 years); left ventricular ejection fraction (< or > 57%); and mean procedural duration (< or > 147 minutes). The mean value was used as cut-off to categorize continuous variables (age, left ventricular ejection fraction, and mean procedural duration). A significant increase in risk was obtained if the 95% confidence interval exceeded 1 and the p value of the Wald test was <0.05.

Analysis was performed by means of SPSS (version 11.0, SPSS Inc., Chicago, Illinois, USA).

Results

Clinical And Procedural Data

The final patient cohort included 2,323 consecutive patients [median age 60 (52-67) years; 72.3% male]. Distribution of age and gender among the study population is shown in Figure 1.

An open irrigated-tip catheter was used in 2,169 cases (93.4%), while a cryo-balloon catheter and a circular multielectrode catheter were used in 97 (4.2%) and 57 patients (2.5%), respectively.

Major Complications

No procedure-related death was observed. Major complications occurred in 94 patients (4.0%) (Table 1). Seven (0.30%) of these patients developed permanent sequelae: 3 ischemic stroke (0.13%); 2 phrenic nerve paralysis (0.09%); 1 hemorrhagic stroke (0.04%); and 1 myocardial infarction (0.04%).

Influence of Age on Complications

There was a significant trend toward a greater incidence of complications with increasing age-group (Figure 2). In particular, the incidence of complications was 35/1066 (3.3%) in patients < 60 year-old vs 59/1257 (4.7%) in those > 60 year-old (p=0.03). All 7 patients with permanent sequelae were older than 60.

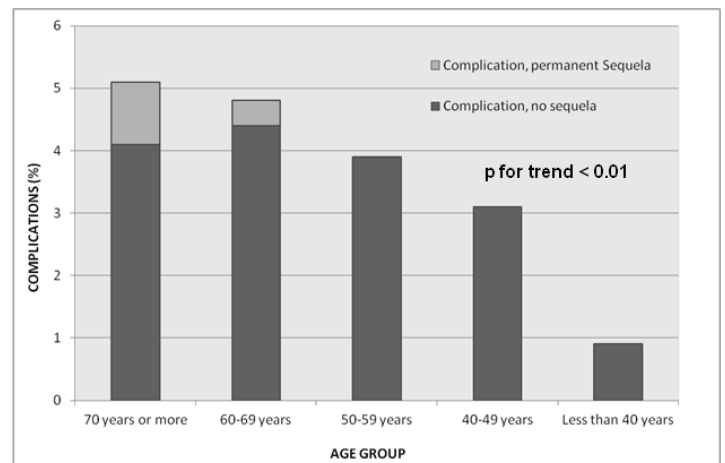


Figure 2: Distribution of complications among age groups. Major complications=grey bar; permanent sequela=black bar

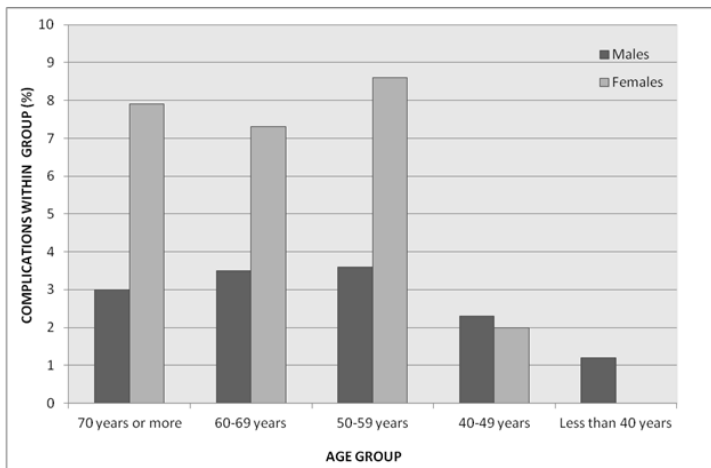


Figure 3: Incidence of major complications according to gender among age groups. Major complications=grey bar; permanent sequela=black bar

Influence of Gender on Complications

Complications occurred more frequently in females than in males [44/522 (8.4%) vs 50/1801 (2.8%), $p=0.001$]. Females had a higher incidence of complications both among younger (< 60 years) [13/208 (6.3%) vs 21/858 (2.4%), $p=0.01$] and older (> 60 years) patients [31/414 (7.5%) vs 29/843 (3.4%) $p=0.01$]. In subjects older than 60, 6/414 (1.45%) females and 1/843 (0.12%) males ($p=0.02$) suffered from permanent sequelae (Figure 3).

All types of complications (hemodynamic, vascular, and ischaemic) resulted significantly more frequent in females than in males (Figure 4).

At multivariate analysis, female gender (OR 2.643, 95% CI 1.686 to 4.143, $p<0.0001$) and longer procedural duration (OR 2.195, 95% CI 1.388-3.473, $p<0.001$) independently predicted a higher risk of procedural complications.

Discussion

Main Findings

In this large multicenter National study a greater incidence of complications after CA for AF was documented with increasing age. Permanent sequelae occurred only in older patients. Females presented a higher incidence of complications than males throughout all age-groups. All types of complications (hemodynamic, vascular, and ischaemic) resulted significantly more frequent in females than in males.

Influence of Age on Complications

Radiofrequency CA has emerged as an important treatment option for refractory AF. The incidence of AF is higher in the elderly,¹⁹ but this cohort of patients is usually underrepresented in clinical studies assessing the efficacy and safety of AF ablations. Moreover, elderly patients with AF undergoing CA are often female with a higher incidence of structural heart disease and/or hypertension. Randomized trials²⁰⁻²² have included few elderly patients, and the safety and efficacy of AF ablation was not adequately assessed in this subset. These limitations drove early guidelines for catheter ablation of AF to suggest a more conservative approach in the elderly. Recently, several Authors^{11-14,23} reported data on AF ablation in patients ≥ 66 years demonstrating that AF catheter ablation is safe and efficacious in older patients too. Thus, older age is not more considered a contraindication to AF CA in the recent guidelines.^{1,2}

Nevertheless, some concerns remain about the AF catheter ablation safety in the elderly. In several registries older age has been reported as a predictor of complication in AF catheter ablation. Shah et al⁷ among 4,156 patients who underwent an initial AF ablation, found a 5% of periprocedural complications. Older age, female sex, prior AF hospitalizations, and recent hospital procedure experience were associated with a higher risk of complications and/or 30-day readmission after AF ablation. Deshmukh et al⁹ reported data on 93801 patients with AF treated with catheter ablation from the Nationwide Inpatient Sample data set from 2000 to 2010. Catheter ablation of AF in older patients (age >80) was associated with a higher total complication rate (9.37 %) in comparison with younger patients (age <80, $p<0.001$). The results of our study confirms these findings showing a significant trend toward a greater incidence of complications with increasing age-group. Of note all 7 patients with permanent sequelae were older than 60. Although these data arise some concerns about the AF ablation in the elderly they seem to further support the safety of AF catheter ablation when used as first line therapy in younger patients. The lack of severe complications in these subgroup seems to confirm the data of Leong-Sit P et al²⁴ which demonstrated that in patients younger than 45 years, there is a lower major complication rate and a comparable efficacy rate, with a greater chance of being AF free without antiarrhythmic drugs.

Influence of Gender on Complications

Although women are undergoing fewer AF ablations procedures than men, female gender has been identified as a predictor of complications of AF ablation in several studies.^{7-10,17} Our results confirmed this finding.

The increased procedural risk for women undergoing AF ablation was consistent with a more than 2-fold higher risk of vascular complications than men^{15,16} during percutaneous coronary intervention. Smaller body size and vessels and higher levels of anticoagulation among women have been suggested⁷ as a possible explanation for the high percentage of vascular complication. The smaller body size of women carries also a smaller heart size. Smaller chamber size in women may theoretically restrict the manipulation of catheter, which leads to the lower success rate in women²⁵ and could increase the catheter manipulation related complications. Of note in our study.

female gender predict not only vascular complication but every kind of complications.

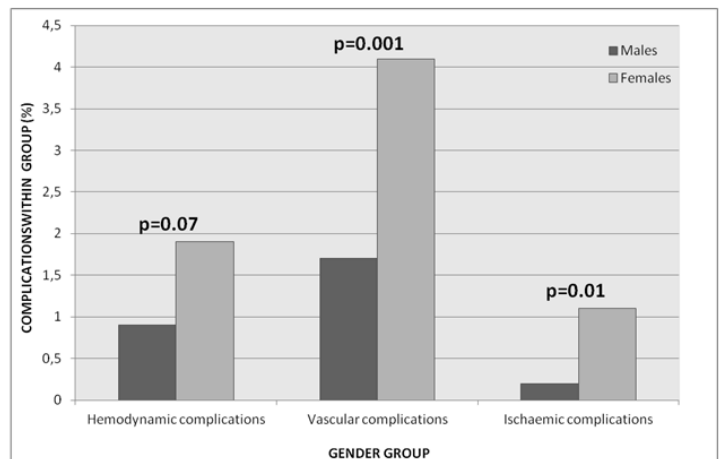


Figure 4: Incidence of different types of major complications according to gender. Males=black bar; females=grey bar

Conclusion

Older patients and females are a subgroup at higher risk of complications during AF ablation. Older patients were also affected by the most serious complications. Although women and patients ≥ 75 years are undergoing fewer AF ablations procedures than men and patients < 75 years a particular care should be taken when performing ablation in this clinical setting.

References

- January CT, Wann LS, Alpert JS, Calkins H, Cleveland JC, Cigarroa JE, Conti JB, Ellinor PT, Ezekowitz MD, Field ME, Murray KT, Sacco RL, Stevenson WG, Tchou PJ, Tracy CM, Yancy CW. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *Circulation*. 2014;130:2071-104.
- Camm AJ, Lip GYH, De Caterina R, Savelieva I, Atar D, Hohnloser SH, Hindricks G, Kirchhof P. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation. An update of the 2010 ESC Guidelines for the management of atrial fibrillation. Developed with the special contribution of the European Heart Rhythm Association. *Eur Heart J* 2012;33:2719-2747
- Cappato R, Calkins H, Chen SH, Davies W, Iesaka Y, Kalman J, Kim Y, Klein G, Packer D, Skanes A. Worldwide survey on methods, efficacy and safety of catheter ablation for human atrial fibrillation. *Circulation* 2005;111:1100-1105.
- Bertaglia E, Zoppo F, Tondo C, Colella A, Mantovan R, Senatore G, Bottoni N, Carreras G, Corò L, Turco P, Mantica M, Stabile G. Early complications of pulmonary vein catheter ablation for atrial fibrillation: A multicenter prospective registry on procedural safety. *Heart Rhythm* 2007;4:1265-1271.
- Cappato R, Calkins H, Chen SA, Davies W, Iesaka Y, Kalman J, Kim YH, Klein G, Natale A, Packer D, Skanes A, Ambrogi F, Biganzoli E. Updated Worldwide Survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. *Circ Arrhythm Electrophysiol* 2010;3:32-38.
- Baman TS, Jongnarangsin K, Chugh A, Suwanagool A, Guiot A, Madenci A, Walsh S, Ilg KJ, Gupta SK, Latchamsetty R, Bagwe S, Myles JD, Crawford T, Good E, Bogun F, Pelosi Jr F, Morady F, Oral H. Prevalence and predictors of complications of radiofrequency catheter ablation for atrial fibrillation. *J Cardiovasc Electrophysiol* 2011;22:626-631.
- Shah RU, Freeman JV, Shilane D, Wang PJ, Go AS, Hlatky MA. Procedural complications, rehospitalizations, and repeat procedures after catheter ablation for atrial fibrillation. *J Am Coll Cardiol*. 2012;59:143-149.
- Bertaglia E, Stabile G, Pappone A, Themistoclakis S, Tondo C, De Sanctis V, Soldati E, Tritto M, Solimene F, Grimaldi M, Zoppo F, Pandozi C, Augello G, Calò L, Pappone C. Updated national multicenter registry on procedural safety of catheter ablation for atrial fibrillation. *J Cardiovasc Electrophysiol*. 2013;24:1069-74.
- Deshmukh A, Patel NJ, Pant S, Shah N, Chothani A, Mehta K, Grover P, Singh V, Vallurupalli S, Savani GT, Badheka A, Tuliani T, Dabhadkar K, Dibu G, Reddy YM, Sewani A, Kowalski M, Mitrani R, Paydak H, Viles-Gonzalez JF. In-hospital complications associated with catheter ablation of atrial fibrillation in the United States between 2000 and 2010: analysis of 93 801 procedures. *Circulation*. 2013;128:2104-2112.
- Inoue K, Murakawa Y, Nogami A, Shoda M, Naito S, Kumagai K, Miyauchi Y, Yamane T, Morita N, Okumura K; Japanese Heart Rhythm Society Members. Clinical and procedural predictors of early complications of ablation for atrial fibrillation: Analysis of the national registry data. *Heart Rhythm*. 2014;11:2247-53.
- Zado E, Callans DJ, Riley M, Hutchinson M, Garcia F, Bala R, Lin D, Cooper J, Verdino R, Russo AM, Dixit S, Gerstenfeld E, Marchlinski FE. Long-term clinical efficacy and risk of catheter ablation for atrial fibrillation in the elderly. *J Cardiovasc Electrophysiol*. 2008;19:621-626.
- Kusumoto F, Prussak K, Wiesinger M, Pullen T, Lynady C. Radiofrequency catheter ablation of atrial fibrillation in older patients: outcomes and complications. *J Interv Card Electrophysiol*. 2009;25:31-35.
- Santangeli P, Di Biase L, Mohanty P, Burkhardt JD, Horton R, Bai R, Mohanty S, Pump A, Gibson D, Coutts L, Hongo R, Beheiry S, Natale A. Catheter ablation of atrial fibrillation in octogenarians: safety and outcomes. *J Cardiovasc Electrophysiol*. 2012 Jul;23(7):687-93.
- Zhang XD, Gu J, Jiang WF, Zhao L, Wang YL, Liu YG, Zhou L, Gu JN, Wu SH, Xu K, Liu X. The impact of age on the efficacy and safety of catheter ablation for long-standing persistent atrial fibrillation. *Int J Cardiol*. 2013;168:2693-2698.
- Argulian E, Patel AD, Abramson JL, Kulkarni A, Champney K, Palmer S, Weintraub W, Wenger NK, Vaccarino V. Gender differences in short-term cardiovascular outcomes after percutaneous coronary interventions. *Am J Cardiol*. 2006;98:48-53.
- Ahmed B, Piper WD, Malenka D, VerLee P, Robb J, Ryan T, Herne M, Phillips W, Dauerman HL. Significantly improved vascular complications among women undergoing percutaneous coronary intervention: a report from the Northern New England Percutaneous Coronary Intervention Registry. *Circ Cardiovasc Interv*. 2009;2:423-429.
- Zhang XD, Tan HW, Gu J, Jiang WF, Zhao L, Wang YL, Liu YG, Zhou L, Gu JN, Liu X. Efficacy and safety of catheter ablation for long-standing persistent atrial fibrillation in women. *Pacing Clin Electrophysiol*. 2013;36:1236-44.
- Calkins H, Kuck KH, Cappato R, Brugada J, Camm AJ, Chen SA, Crijns HJG, Damiano RJ, Davies W, DiMarco J, Edgerton J, Ellenbogen K, Ezekowitz MD, Haines DE, Haissaguerre M, Hindricks G, Iesaka Y, Jackman W, Jalife J, Jais P, Kalman J, Keane D, Kim Y-H, Kirchhof P, Klein G, Kottkamp H, Kumagai K, Lindsay BD, Mansour M, Marchlinski FE, McCharty PM, Mont L, Morady F, Nademanee K, Nakagawa H, Natale A, Nattel S, Packer DL, Pappone C, Prystowsky E, Raviele A, Reddy V, Ruskin JN, Shemin RJ, Tsao H-M, Wilber D. 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design. *Heart Rhythm* 2012;9:632-696.
- Go AS, Hylek EM, Phillips KA, Chang Y, Henault LE, Selby JV, Singer DE. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study. *JAMA*. 2001;285:2370-2375.
- Wazni OM, Marrouche NF, Martin DO, Verma A, Bhargava M, Saliba W, Bash D, Schweikert R, Brachmann J, Gunther J, Gutleben K, Pisano E, Potenza D, Fanelli R, Raviele A, Themistoclakis S, Rossillo A, Bonso A, Natale A. Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of symptomatic atrial fibrillation. A randomized trial. *JAMA* 2005;293:2634-2640.
- Oral H, Pappone C, Chugh A, Good E, Bogun F, Pelosi Jr F, Bates ER, Lehmann MH, Vicedomini G, Augello G, Agricola E, Sala S, Santinelli V, Morady F. Circumferential pulmonary vein ablation for chronic atrial fibrillation. *N Eng J Med* 2006;354:934-994.
- Stabile G, Bertaglia E, Senatore G, De Simone A, Zoppo F, Donnici G, Turco P, Pascotto P, Fazzari M, Vitale DF. Catheter ablation treatment in patients with drug-refractory atrial fibrillation: a prospective, multi-centre, randomized, controlled study (Catheter Ablation For The Cure Of Atrial Fibrillation Study). *Eur Heart J* 2006;27:216-221.
- Rojas F, Valderrábano M. Effect of Age on Outcomes of Catheter Ablation of Atrial Fibrillation. *JAFIB* 2013.
- Leong-Sit P, Zado E, Callans DJ, Garcia F, Lin D, Dixit S, Bala R, Riley MP, Hutchinson MD, Cooper J, Gerstenfeld EP, Marchlinski FE. Efficacy and risk of atrial fibrillation ablation before 45 years of age. *Circ Arrhythm Electrophysiol*. 2010;3:452-457.
- Dagres N, Clague JR, Breithardt G, Borggrefe M. Significant gender-related

differences in radiofrequency catheter ablation therapy. J Am Coll Cardiol. 2003;42:1103-1107.