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REVIEW

The effects of gender on electrical therapies for the heart: procedural considerations, results and complications

A report from the XII Congress of the Italian Association on Arrhythmology and Cardiostimulation (AIAC)

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Use of cardiac implantable devices and catheter ablation is steadily increasing in Western countries following the positive results of clinical trials. Despite the advances in scientific knowledge, tools development, and techniques improvement we still have some grey area in the field of electrical therapies for the heart. In particular, several reports highlighted differences both in medical behaviour and procedural outcomes between female and male candidates. Women are referred later for catheter ablation of supraventricular arrhythmias, especially atrial fibrillation, leading to suboptimal results. On the opposite females present greater response to cardiac resynchronization, while the benefit of implantable defibrillator in primary prevention seems to be less pronounced. Differences on aetiology, clinical profile, and development of myocardial scarring are the more plausible causes. This review will discuss all these aspects together with gender-related differences in terms of acute/late complications. We will also provide useful hints on plausible mechanisms and practical procedural aspects.

Keywords Gender • Sex • Arrhythmia • Review • Defibrillator • Ablation • CIED

Introduction

Despite the improvements in knowledge and technologies, in the 1990s the Society for the Advancement of Women's Health Research criticized the exclusion of women from most clinical research.[1] The differences between men and women go beyond sex hormones and anatomy, entailing all the aspects of human life. These factors reflect on the outcomes of the treatments we adopt in common clinical practice. This review will focus on the various effects of gender on electrical therapies for the heart: electrophysiology (EP) procedures with substrate ablation and treatments based on implantable devices for cardiac pacing/defibrillation (CIED).

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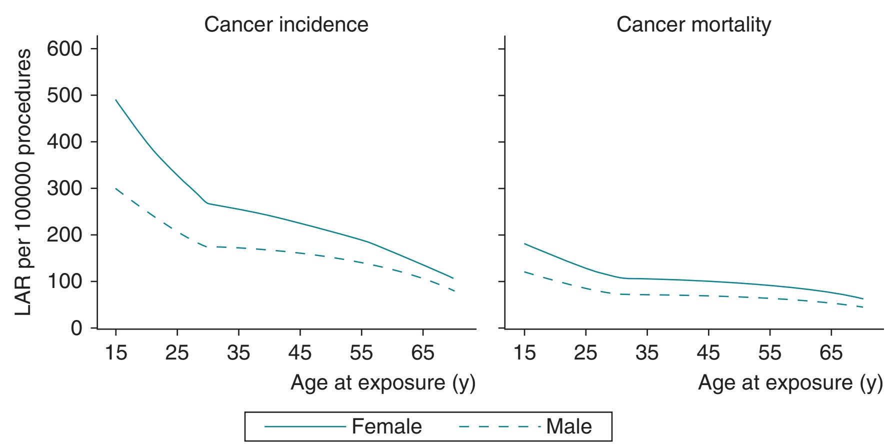

Figure 1 Lifetime attributable risk of cancer incidence and mortality induced by radiation exposure during RFA procedures by age at exposure for females and males, for a mean effective dose of 19.1 mSv per procedure. Modified from Casella *et al.*[4]

Procedural considerations

Radiation exposition

Radiation exposition is a known risk factor for cancer. About 1/1000 individuals will develop cancer from an exposure similar to what provided by CT scan or atrial fibrillation (AF) ablation.[2,3] Sensitivity to radiation is different between age and sex, being women of childbearing age the more sensitive (*Figure 1*).[4] After a 64-slice CT coronary angiography the lifetime risk of radiation-related cancer was reported to be 2.4–4.8 times greater in women.[5,6] Breast cancer accounted for up to 40% of the total cancer risk in younger women,[6] followed by lung cancer.[5] However, several technical limitations of these studies have been reported.[7] Lawler *et al.*[8] showed in population-based longitudinal cohort of 82 861 patients undergoing coronary angiography, that for each mSv women were more likely to develop a cancer than men also after adjusting for age, non-cardiac exposure, and covariates (HR 1.005 vs. 1.002). The increased risk of cancer was confirmed to be primarily due to lung cancer, while incidence of breast cancer did not reach statistical significance. This discordance with CT scan studies[5,6] is probably due to a more advanced age of patients (almost all >50 years)[8] explaining also why age was not a determinant of radiation-associated risk of cancer. Regarding CIED procedures, Pedersen *et al.* conducted a 'similar' population-based study on ICD recipients examining the risk of ICD-related cancer, by linking the Danish National Registry of Patients and the Danish Cancer Registry. They detected a 10% excess risk of cancers during a median follow-up of 2.8 years, confined to tobacco-related cancers in patients with ischaemic heart disease without difference between genders, showing that smoking habit was the plausible driver.[9] The authors concluded that the role of exposition for CIED therapy to promote cancer is marginal. However, three considerations should be raised: (i) The follow-up period was too short since previous studies showed a 5- to 10-year latency between radiation exposure and cancer development;[8] (ii) These findings may not be applied to CRT and complex procedures since patient can be exposed to a dose five-fold higher (on average 22 mSv vs. 4 mSv)[3,10]; (iii) All these data[5,6,8,9] derive from very large registries, enabling the evaluation of very rare events, but lacking of some important factors such as height, weight, and BMI that should be considered.[3]

Several mapping tools have been developed that can already permit 'near-zero' fluoroscopic exposure during ablation of supraventricular arrhythmias. The No-PARTY trial[11] evidenced that a 'near-zero' approach, for ablation of supraventricular arrhythmias, was associated with equivalent results, as compare to standard approaches, both in terms of success (97% vs. 96% at 6 months) and safety (complication rate of 0.01% vs. 0.01%) . The median reduction of exposure of about 8 mSv for patients and 24 microSv for the operators.[11] This lead to a 96% reduction of the risk of developing a procedure-related cancer (from 0.267% to 0.0089%). Moreover, in 72% of the patients radiation were not used at all. These results are really promising for women of childbearing age, since no definite data are currently available on the minimum 'safe' radiation exposure for women planning to become pregnant. Indeed, there are no studies aimed at clarifying how long it is advisable to wait before a pregnancy after an EP procedure, and how to manage a pregnant woman requiring an invasive approach for severe recurrent arrhythmias. However, there is a general agreement that, during pregnancy, an ablation procedure should be discouraged; then, in women with a history of major rhythm disturbances, an elective procedure should be programmed at least 6 months before planning a pregnancy.

Gender differences in peri-procedural sedation

Intravenous sedation represents a relevant issue in CIED and EP procedures since it can provide many benefits but also rise several concerns (see Supplementary material online, *Table S1*).[12] Notably, there is a continuum between sedation and general anaesthesia and scales have been developed to allow standardization.[12] Many patient-specific characteristics may affect pain/discomfort during procedures, but despite the broad number of studies, we still have conflicting evidence on the role of gender in pain perception.[13–15] Despite the relevance of the topic, only a limited number of investigations evaluated pain in EP/CIED procedures. Ezzat *et al.*[16] reported that excess of pain is the principal source of disappointment after AF ablation, with a high prevalence (about 56% of the patients). A Swedish study randomized 80 consecutive patients to pulmonary vein isolation under standard sedation (morphine plus diazepam) vs. an improved analgesic strategy (pre-medication with oral midazolam plus intravenous alfentanil and midazolam) with half of the patients treated with radiofrequency and the others with Cryo-ablation.[17] Women experienced more pain than men ($P = 0.01$), while both the active analgesic strategy and the use of Cryo-ablation was associated with a reduced discomfort. More recently, Bode *et al.*[18] provided a broader picture analysing the incidence of acute post-procedural pain in consecutive patients after EP (49) and CIED (53) procedures. Sixty per cent of the patients reported moderate-to-severe pain in the first 24 h despite the use of analgesics, especially back pain (44%) and at the site of the CIED pocket (39%). Female sex was the only variable significantly associated with early post-procedural pain at multivariate analysis ($P = 0.046$). Finally post-procedural pain is not limited to the acute phase, especially after CIED procedures, a phenomenon that can lead to prolonged disability of the ipsilateral arm in a significant portion of the patients.[19–21] Gender specific responses to sedation agents provide another source of variability both in terms of type/dose adjustment and occurrence of side effects,[22] which however still needs to be explored since women are often excluded also from basic/clinical studies of anesthesia.[23]

The effect of gender on CIED implanting technique

Previous studies on breast cancer showed that conserving surgery (vs. mastectomy) provided several benefits in terms of body image, psychological/social adjustment and compliance to overall treatment.[24,25] The ICD implanting technique evolved during time with the downsizing of the can moving from the abdomen to be subclavian area, initially submuscular and later subcutaneous.[26] In the same period Belott *et al*. reported two cases of a particular approach involving the deployment of the ICD lead through 1 cm incision to the surface of pectoralis muscle followed by a second 4 cm long inframammary incision to create the device pocket above the pectoralis muscle and behind the mammary glandule with tunnelization of the lead.[27] This approach was followed by a single-incision approach based on the puncture of the axillary vein based on a peripherally placed intravenous guidewire and creation of the subpectoral device pocket by an incision near the anterior axillary line.[28] The two larger experiences reported in literature come from Giudici *et al.*[29] and Persichetti *et al.*[30] Both groups created a retropectoral inframammary device pocket, while the difference was in the venous access that was axillary (Giudici *et al.*[29]) or subclavian (Persichetti *et al.*[30]) with a small separate incision followed by lead tunnelization. All these studies showed high level of CIED acceptance. However, it has to be underlined that despite being promising alternatives, we still lack of robust data with long-term follow-up of patients undergoing these implanting techniques: there are few studies and those that exist have enrolled a small number of patients, without direct comparison with standard approaches.[31,32] From a technical point of view higher impedances have been reported[33] without evident effects on defibrillation threshold. A more recent report on 20 patients with submammary (subglandular and above the pectoralis muscle) ICD showed a significative increase in ventricular pacing threshold an a reduction in lead impedance (from 0.6 ± 0.2 V and 621 ± 223 ohms vs. 1.6 ± 0.6 V and 471 ± 89 ohms) with 2 lead dislodgement and 3 late lead revision 15%).[32] The last technological advancements can potentially favour the development of more cosmetic approaches while providing several other benefits (*Figure 2*).[34,35]

Gender and outcomes of EP/CIED procedures

The effect of gender on outcomes after ICD implantation

The survival benefit provided by ICD in women is a subject of debate. Despite the absence of a clear gender effect showed by the original trials,[36–44] three metanalysis showed less benefit in female subjects.[45–47] However, under-representation of women in cardiac device trials (8–29%) limited these analyses. Focusing on real-life data there is general agreement with lower occurrence of appropriate ICD therapies in female subjects.[48–52] However, overall survival of implanted patients and benefit with respect to non-implanted subjects seems not to be affected by gender.[48,51–55] This can be explained by the higher prevalence in men of myocardial scarring (especially post-infarction) leading to a higher change of sudden death for shockable arrhythmias, while females die relatively more by asystole, pulseless electrical activity and pump failure.[56–59] The negative results of the recently published Danish Study to Assess the Efficacy of ICDs in Patients with Non-ischaemic Systolic Heart Failure on Mortality trial[60] may support this hypothesis since it evidenced that patients with non-ischaemic left ventricular dysfunction seem not to benefit from ICD despite indication to CRT without gender difference (at subgroup analysis).

There is a broad spectrum of mental symptoms/diagnoses in ICD carriers: anxiety is the most common with a prevalence between 7.6 and 46%, similarly depression is another typical disorder occurring in 14–41% of the subjects.[61] These factors and the broader concept of quality of life (QoL) are relevant since they have been associated with all-cause and cardiac-related mortality in patients with an ICD[62–65] and CRTD.[66,67] Several characteristics have been associated with poorer QoL and occurrence of anxiety/depression: ICD shock therapies, type D personality, non-CRT device, younger age and female gender. Females in particular, seem to express more anxiety (connected to procedure, shock, and death) and concerns for body image while depression seems to be equally expressed among the two sexes.[62–65,67–74] Notably, these studies present several limitations (patient selection, assessment measures, population size, time of administration since ICD implant, follow-up duration, and response rate) and adjusting for covariates has shown to decrease the gender-effect especially at long-term after CIED implant.[75] In any case according an adequate pre/post-procedural patient counselling, patient support and tailoring of CIED procedures may positively impact on these symptoms and QoL.[76–78]

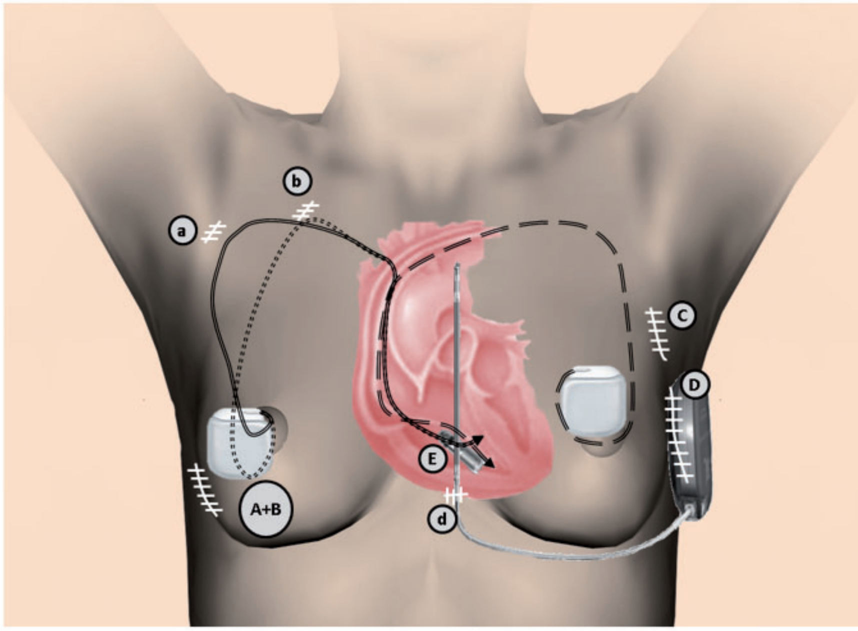

Figure 2 Schematic representation of the different aesthetical approaches reported in literature for implantation of CIED by (*A*) Giudici *et al.*[29] (*B*) Persichetti *et al.*[30] (*C*) Shefer *et al.*[28] For comparison new approaches based on recent leadless technologies for ICD (*D*)[34] and PM (*E*)[35] are reported. Incisions are reproduced with white lines, generator incision with capital letter and additional incisions with small letters. For graphical purposes, the devices implanted with A and B approaches are represented in the right side of the body, even if they are commonly performed on the left side.[29,30]

The effect of gender on response to CRT

Several randomized studies demonstrated a greater benefit of CRT in women than in men (*Table 1*).[79–86] This has been confirmed in real world settings,[87,88] also at long-terms.[89] Despite the increased prevalence of cardiovascular (hypertension, coronary artery disease, AF) and non-cardiovascular (diabetes, COPD, and chronic renal failure) comorbidities in the elderly, women present a higher response to CRT also in the advanced age.[90–93] The reason for these findings is unclear. Possible explanations are: (i) the higher risk of HF for women vs. men which may lead to boost the preventive effects of CRTD, (ii) a standard QRS duration of 10 ms lower in women vs. men[94] leading to a greater conduction disturbance and possibly to a greater chance of response. More recently, in the MADIT-CRT trial, women presented a higher performance with CRT-D (about 70% reduction in HF hospitalization or death) independently of QRS duration (< vs. > 150 ms).[83] This was confirmed by a FDA metanalysis[95] showing that women with a QRS 130–150 ms benefit more than men from CRT. Notably this is a IIA indication (ACCF/AHA/HRS guidelines).[96] However, while >50% HF patients are women only <25% of the enrolled patients in HF clinical trials are females.

Gender differences in acute complications of CIED procedures

Despite no difference in mortality found in real-life studies, several authors reported a greater incidence of CIED-related complications for female subjects, with an OR ranging between 1.32 to 1.55 for overall complications.[48,55,97–99] The National Cardiovascular Data Registry (NCDR) ICD Registry found a 32% greater incidence in overall in-hospital complications (4.4% vs. 3.3%, $P < 0.001$), mainly lead dislodgements, vessel injuries, pneumothorax, pericardial effusion.[99] This was confirmed also by the Ontario ICD Database which extended the perspective to post-discharge <45 days and <1 year (OR 1.50 and 1.55, respectively)[48] and a recently published metanalysis.[100] This also applies to pacemaker setting as shown by the analysis of two European registries: the Danish Pacemaker and ICD Register (DPIR)[101] and the database of the Institute of Quality Assurance Hessen (Germany).[98] Since the more frequently reported complications increased in women are lead dislodgements, vessel injuries, pneumothorax and pericardial effusion the principal explanations for these findings are: the sicker profile (in terms of aging, progression of cardiac disease, comorbidities), the smaller body size and the need for different device (more frequently CRT). Notably, these results were also confirmed after adjusting for the mentioned parameters in most of the reports, but it the high number of variables coupled with the low number of events and enrolled female subjects significantly limit any post-hoc ‘adjustment procedure’.

The effect of gender on CIED infection and lead extraction

According to current literature, males seem to be more vulnerable to many infectious pathogens[102] and in particular to community/hospital-associated bloodstream infections (BSI) and surgical site

Table 1 Main large randomized controlled trial (>200 patients) on CRT with the prevalence of women and outcomes

Study	Year	Procedure	Inclusion criteria	*N*	F (%)	Mean age (year)	Mean LVEF (%)	Primary endpoint	Average follow-up (months)	Global outcomes	Outcomes M vs. F
MIRACLE[79]	2002	CRT + MT vs. lone MT	CHF, NYHA III-IV + LVEF ≤ 35% LVEDD ≥55mm + QRS ≥130 ms 6MWT distance ≤450m	453	32	64.3	21.7	NYHA, 6MWD, QoL	6	CRT better 6MWD, NYHA, QoL.	F: reduced death or CHF hospitalization with CRT (P < 0.001 M: no difference[85]
COMPANION[80]	2004	CRT-D vs. CRT-P vs. MT	CHF, NYHA III-IV + LVEF ≤35% QRS ≥120ms + PR interval≥150 ms + SR	1520	33	68	22	Mortality/ hospitalization	15.7–16.2–11.9 per group	CRT-D (HR 0.80 P = 0.011) CRT-P (HR 0.81 P = 0.015)	Not significant difference
CARE-HF[81]	2005	CRT + MT vs. lone MT	CHF, NYHA III-IV + LVEF ≤ 35% and QRS ≥ 120 ms	812	26	66.5	25	Mortality/ hospitalization (CV)	29.4	CRT reduced mortality/ hospitalization (HR 0.63, P < 0.001)	M: 0.62 (0.49–0.79) F: 0.64 (0.42–0.97)
REVERSE[82]	2008	CRT on vs. CRT off	CHF, NYHA I-II + LVEF ≤40% + QRS ≥120 ms + LVEDD ≥55 mm	610	22	62	26	HF composite score	12	CRT less likely to worse (HR 0.70, P = 0.01)	M: 0.69 (0.43–1.11) F: 0.75 (0.26–2.19)
MADIT-CRT[83]	2009	CRT-D vs. lone ICD	CAD (NYHA I-II)/non-CAD (NYHA II) + SR + LVEF ≤35% + QRS ≥130 ms	1820	25	65	24	Mortality/non-fatal HF events	28	CRT-D <mortality/ non-fatal HF events (HR 0.66, P = 0.001)	M: 0.76 (0.59–0.97); F: 0.37 (0.22–0.61) F: greater benefit (P = 0.01)
RAFT[84]	2010	CRT-D vs. lone ICD	CHF, NYHA II-III + LVEF ≤30% + QRS ≥120ms + SR/AF with controlled heart rhythm (60-90 bpm)	1798	17	66	22.6	Mortality/CHF hospitalization	40	CRT-D <death rates/ CHF hospitalization (HR 0.75, P < 0.001)	No significant difference in hazard ratio

AF, atrial fibrillation; CAD, coronary artery disease; CHF, cronic heart failure; CRT, cardiac resynchronization therapy; CRT-D, cardiac resynchronization therapy with defibrillator; F, female; HR, hazard ratio; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end diastolic diameter; M, males; MT, medical therapy; N, number of patients; QoL, quality of life; SR, sinus rhythm; 6MWD, six minute walked distance; 6MWT, six minute walking test.

Table 2 Large cohort studies of CIED candidates/carriers reporting incidence of CIED infection by gender

Study	Years	Setting	*N*	Infection rate, %	Infection rates F/M, %	OR (95% CI)	P
Klug *et al.* (PEOPLE Study)[116]	January 1, 2000, December 31, 2000	Prospective	6319 pts	0.68	M: 0.79 F: 0.47	F: 0.74 (0.39-1.4)	NS
Uslan *et al.*[111]	1975, 2004	Retrospective, population-based cohort study	1524 pts	5.0	M: 6.1 F: 3.7		Not reported
Catanchin *et al.*[117]	1 January 1994, 31 December 2004	Retrospective	1481 PM/ICD procedures	1.6	M: 2.0 F: 1.1		0.01
Nery *et al.*[115]	1 July 2003, 20 March 2007	Prospective	2417 pts	1	M: 1.11 F: 0.9		NS
Johansen *et al.*[114]	1 January 1982, 31 December 2007	Prospective	56 657 PM/ICD procedures	1.0 (explantation for CDI)	M: 1.3 F: 0.8	F: 0.60 (0.51-0.71)	0.001
Sohail *et al.*[113]	1 January 2007, 31 December 2007	Retrospective cohort study	200 219 PM/ICD procedures	2.9	M: 3.1 F: 2.7		Not reported
Lin *et al.*[112]	1 January 1997, 31 December 2010	Retrospective, population-based cohort study	46 506 PM/ICD procedures	0.9	M: 1.11 F: 0.7	M: 1.66 (1.36-2.02)	0.001
Peterson et al.[99]	*January 2006, December 2007*	*Retrospective*	*161 470 ICD implantation*	*0.03*	*M: 0.03* *F: 0.03*		*NS*
Nowak et al.[98]	*2003, 2006*	*Retrospective*	*17 826 PM implantation*	*0.11*	*M: 0.12* *F: 0.10*		*NS*

CDI, cardiac device infection; CI, confidence interval; F, female; ICD, implantable cardioverter defibrillator; M, male; N, number of patients/procedures; NS, not significant; OR, odds ratio; PM, pacemaker.

infections (SSI)[103] due to various factors,[102,104–110] as confirmed by several observational cohort/population studies (*Table 2*).[98,99,111–117] Notably, the two studies showing no gender-effect on CIED infection (in italics in *Table 2*)[98,99] limited the analysis to pre-discharge complications, losing sensitivity to CIED infections which usually occur several months later (confirmed by the low prevalence reported).[118] When CIED infection occurs, the only effective approach is the complete extraction of all the PM/ICD system. Several authors reported that female sex and a BMI below 25 kg/m^2 are associated with an increased risk of peri-procedural complications. Smaller vessels and the higher chance of lesion by traction/pressure or the delivery of additional energies by powered sheaths can be an explanation to these findings.[119] Notably, a recent metanalysis did not confirm the presence of any association between female sex and outcomes both in terms of technical success and clinical outcomes.[120] However, male sex prevailed in all the studies included in the metanalysis, being ≥75% in one third of them (notably 6 studies did not reported gender prevalence at all).[120] Taken together these data show once again the limitations provided by existing literature in terms of statistical power for an adequate gender analysis of procedural outcomes incidence. The final results of the Electra registry will provide additional hints on this topic.[121]

The effect of gender on catheter ablation procedures

A large prospective cohort study[122] reported a success rate for AVNRT ablation of 98.1% and a recurrence rate of 1.5% at 63 ± 38 months. Young age (<20 years, OR 14.1) and female sex (OR 3.6) were the two independent predictors of late recurrence. The authors concluded that a more conservative approach could explain this finding[122] confirming the previous findings on a cohort study enrolling 894 patients.[123] Farkowski *et al.*[124] reported on a series of 82 patients undergoing ablation for AVNRT/AVRT showing an equivalent resource utilization in both genders in the year before the procedure but antiarrhythmic drugs were more often prescribed to women (30% vs. 8%). After ablation there was no difference in health-related quality of life (QoL) while females reported a significantly higher persistence of arrhythmia-related symptoms, especially 'heart skipping'. Regarding AF, women are referred to ablation less often than men (3% vs. 6%).[125,126] The results on ablation outcome from published cohorts are discordant: while some authors provided similar acute and late success rate,[127] other reported a lower success rate in female patients both in acute and at subsequent follow-up.[128–130] However, these findings can be attributable to a different level of disease progression/evolution before the procedure in the various cohorts, due to late referral (60 vs. 47 months)[127] with advanced left atrial remodelling (diameter 44.0 ± 6.5 vs. 40.6 ± 6.3 mm)[127] and high prevalence of long-standing persistent AF (27% vs. 20%)[128] showing non-pulmonary vein sites of firing (50.4 vs. 16.3%).[128]

The same authors also showed a higher incidence of procedure-related haematomas in women (2.1–6.8% vs. 0.7–0.9%). With regards to overall complications, the incidence of major complication has been reported to be about 4–5% for AF ablation,[129,131–133] with two major independent predictors of events, corresponding to advanced

Table 3 Large cohort studies (>1000 patients) comparing outcomes of catheter ablation for atrial fibrillation in women and men (percentage values and ORs have been reported only when $P < 0.05$ in the publication)

Study	Setting	*N*	F, %	Mean age	Follow-up (months)	CA outcome	Complications
Baman *et al.*[140]	Prospective	1642 procedures	26	60±10	N.R.	N.R.	F: higher ratio (OR = 2.32) of any complications.
Hoyt *et al.*[139]	Prospective	1190 procedures	23.6	58	3	N.R.	F: higher ratio (OR = 1.9) of major adverse events: lifethreatening, resulted in permanent harm, required intervention, or significantly prolonged hospitalization
Kaiser *et al.*[135]	Retrospective (medical claims)	21 091 patients	29	M: 58±11 F: 62±11	12	F: higher ratio of rehospitalization for AF (OR = 1.12), but less likely to have repeat AF ablation (OR = 0.92) or cardioversion (OR = 0.75)	F: higher risk of 30-day vascular complications(2.7% vs. 2.0%) and tamponade (3.8% vs. 2.9%)
Stabile *et al.*[138]	Prospective	2167 patients	25.2	60	1	N.R.	F: higher ratio (OR = 2.5) of complications requiring intervention or prolonged hospital stay.
Shah *et al.*[129]	Retrospective	4156 patients	29.3	61.7	1	N.R.	F: higher ratio (OR = 1.38) of inpatient complications or 30-days rehospitalization.
Takigawa *et al.*[137]	Prospective	1124 patients	23.1	M: 60±11 F: 63±9	31.7, after first CA	SR maintenance was similar between sexes after the first CA; for repeated procedures was significantly lower in females after the last CA	Incidence of procedure-related complications was similar between genders
Zylla *et al.*[136]	Retrospective	3652 patients	33	M: 59±11 F: 64±10	12	F: higher AF recurrence rates (50.2% vs. 45.4%; OR = 1.19)	F: higher ratio of major inhospital complications(1.9% vs. 0.8%) and femoral access site complications (6.2% vs. 3.3%)

N, number of patients/procedures; F, female; M, male; CA, catheter ablation; N.R., not reported; OR, odds ratio; AF, atrial fibrillation; SR, sinus rhythm.

age (OR 1.86 for age 65–74 vs. 18–44) and female sex (OR 1.38).[129] Since the major randomized controlled trial on AF ablation did not reported sex-specific analysis of the outcomes and complications,[134] data come from large cohort studies (*Table 3*).[129,135–140]

Notably, obesity is a further modifying factor, associated with an increased risk of procedural complications (Shoemaker *et al.*[141] reported an odds of complications increased 3.1-fold in patients with high BMI). Finally, no significant differences in the outcomes of ablation for atrial flutter and ventricular arrhythmias have been reported, although females were largely underrepresented in studies on ablation of ventricular arrhythmias.[142]

Conclusions

The available data summarized in this review support the presence of an influence of gender on several aspects of EP/CIED based therapies. In some cases the mechanism is better documented and characterized. Women receive greater benefit from CRT and CIED infection rate is inferior. However, women experience a higher rate of acute complications during CIED implantation and haematomas after EP ablation. Finally, EP/CIED procedure-related pain are more frequent in women. There are some topics discussed in this review for which clearly need further investigations. Females seem to receive lower benefit from ICD in primary prevention but the reason is still obscure. The more cosmetic CIED implanting techniques, while attractive to improve device acceptance, still need direct comparison to standard approaches to confirm an equivalent performance at long-term. The role of gender on the efficacy of EP ablation needs studies including a larger proportion of women. The higher complication risk reported by females undergoing lead extraction has not been confirmed in more recent investigations. These data highlight the need to design new clinical researches aimed at mitigating the existing gaps between men and women in this field.

Supplementary material

Supplementary material is available at *Europace* online.

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Treatment of intramural ventricular tachycardia in cardiac sarcoidosis with transcoronary ethanol ablation

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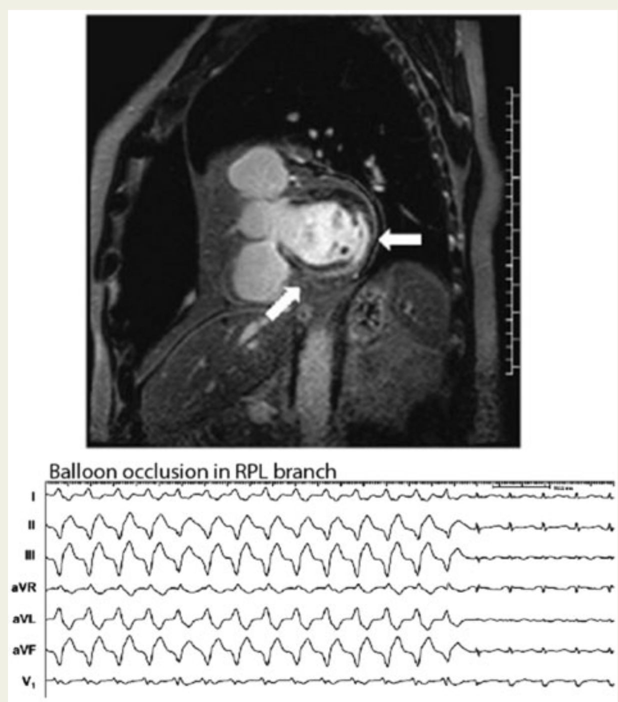
A 67-year-old man with sarcoidosis presented with recurrent ventricular tachycardia (VT) despite treatment with amiodarone. Cardiac magnetic resonance imaging demonstrated delayed enhancement of the mid-myocardium in the inferolateral wall and septum (Figure, upper panel) and cardiac positron emission tomography–computed tomography (PET-CT) showed a perfusion defect with increased uptake of 18F-fluorodeoxyglucose in the same region. Two inducible VTs were both mapped to the cardiac crux along the inferior interventricular septum (RBBB, superior axis and LBBB, superior axis, respectively). Prior attempts at radiofrequency (RF) catheter ablation, including epicardial and bipolar transmural RF ablation, as well as haemodynamic support with extracorporeal membrane oxygenation, were not successful. Because of VT storm, the patient underwent transcoronary ethanol ablation, which targeted a right posterolateral (RPL) branch which supplied this region. Balloon occlusion of the distal RPL during VT reproducibly terminated the tachycardia within 30–50 s (Figure, lower panel), and ethanol ablation prevented inducibility. During 2 years of follow-up, he required one other endocardial ablation to treat VT from a lateral LV location, and then had only one recurrence. We propose that alcohol ablation should be considered in patients with sarcoidosis who have intramural VTs that fail endocardial and epicardial ablation and are refractory to conventional therapy.



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