





Long-term observation in patients with implantable cardioverter-defibrillator with and without resynchronisation therapy

Obserwacja długoterminowa u pacjentów z wszczepialnym kardiowerterem-
-defibrylatorem i poddanych terapii resynchronizującej oraz bez niej

Agnieszka Kołodzińska¹ , Diana Paskudzka¹ , Anna Maria Gawatkiewicz^{1*}, Marcin Grabowski¹ ,
Andrzej Cacko¹ , Przemysław Stolarz¹ , Krzysztof Krasuski^{2,3} , Grzegorz Opolski¹ 

¹Department of Cardiology, Medical University of Warsaw, Warsaw, Poland

²Department of Medical Informatics and Telemedicine, Medical University of Warsaw, Warsaw, Poland

³Faculty of Mathematics and Information Science, Warsaw University of Technology, Warsaw, Poland

Abstract

Introduction. An implantable cardioverter-defibrillator (ICD) with or without resynchronisation therapy (CRT-D) is an effective treatment in heart failure patients (pts.).

Materials and methods. We retrospectively analysed 60 patients (50/60; 83.33% male) with implanted ICD or CRT-D followed-up in the Cardiology Department between May 1995 and February 2019 who had undergone at least one device exchange.

Results. Women rarely received ICD, and especially ICD with CRT-D, compared to men [9/26 females in ICD and 1/24 in CRT-D group ($p = 0.035$) OR 8.31 95% CI (0.98–70.56)] and presented higher left ventricular ejection fraction (LVEF) ($38.11 \pm 12.74\%$ vs. 29.65 ± 12.63 , $p = 0.027$). CRT-D in our patients was implanted mainly as primary prevention [22/25 vs. 18/35 ($p = 0.0726$) OR 6.93 95% CI (1.75–27.43)] and in patients with a lower LVEF compared to the ICD-only patients [24.75 ± 8.98 vs. $35.52 \pm 13.55\%$ ($p = 0.001$)]. Technical analysis of endocardial lead parameters at implantation and at the final follow-up revealed a decrease in impedance in cases of atrial, defibrillator and left-ventricular leads. In the ICD-only group, atrial impedance was 280.03 ± 335.3 vs. 218.29 ± 229.48 ohm ($p = 0.0018$), and defibrillator lead impedance was 768.66 ± 210.62 vs. 507.03 ± 131.67 ohm ($p < 0.001$) (at implantation vs. final follow-up respectively). In the ICD plus CRT-D group, mean atrial lead impedance was 511.05 ± 271.30 vs. 388.55 ± 231.75 ohm ($p = 0.007$), impedance of the defibrillator lead was 698.95 ± 165.45 vs. 547.13 ± 385.24 ohm ($p = 0.002$), and impedance of the left-ventricular lead was $1,036.28 \pm 337.34$ vs. 794.87 ± 274.99 ohm ($p < 0.001$).

Conclusion. Women receive CRT-D therapy less often than men. CRT-D is implanted in pts. with lower LVEF and mainly as primary prevention. All endocardial leads impedance decreased with the passing of time.

Key words: resynchronisation therapy, CRT, implantable cardiac defibrillator, ICD, heart failure, impedance lead

Folia Cardiologica 2019; 14, 2: 136–141

Introduction

Heart failure (HF) is a disease caused by cardiac dysfunction that is associated with high mortality. Among adults in developed countries, the prevalence of HF is about 1–2%. It is higher in older patients (pts.), reaching almost 10% among people aged above 70 years [1]. HF can be divided according to left ventricular ejection fraction (LVEF) into reduced ejection fraction (HFrEF) and preserved ejection fraction (HFpEF) [2]. It is important to note that different underlying aetiologies, demographics, and co-morbidities and varying responses to therapies are related to the degree of reduction of LVEF. Patients with HFpEF are older, more often female, and are less likely to have coronary artery disease compared to HFrEF pts [3, 4]. The treatment of HF has changed over the last 30 years, with nowadays implantable electronic devices and resynchronisation therapy more often being used [5–7]. Based on the current guideline criteria for a cardiovascular implantable electronic device (CIED), only 5–10% of pts with HF are indicated for CRT therapy and approximately 70% of them are responders. Wider QRS, left bundle branch block, non-ischaemic cardiomyopathy, and female gender are factors associated with a better response to CRT [8].

Despite the improvements in HF treatment, the disease is still associated with a poor prognosis. 20% of patients admitted to hospital due to HF die within the first year, and approximately 50% die within five years of diagnosis. Saxon et al. analysed the survival status in patients implanted with ICD and CRT devices from a single manufacturer across the United States. One- and five-year survival rates in 185,778 patients after ICD implantation were 92% and 68% respectively, and were 88% and 54% for CRT-D device recipients [9].

Endocardial lead problems may appear in the course of CIED therapy. Electrical integrity concerning electrical impedance is calculated by measuring the voltage (V) and the current (I) and by applying Ohm's law ($R = V/I$). The circuit comprises the connection between the generator's header and the lead, the conductors to the tip and ring electrodes, and the electrode-myocardial interface. The most common causes of lead failure are insulation break and conductor fractures. The aim of our study was to analyse the long-term follow-up in patients with ICD and CRT-D therapy.

Material and methods

60 patients (male 50/60; 83.33%) with implanted ICD or CRT-D who had been followed-up in the Cardiology Department between May 1995 and February 2019 who had undergone one or more device exchange due to the end of battery life were retrospectively analysed. ICD and CRT-D had been implanted according to the prevailing guidelines [5, 8]. ICD had been implanted in 35/60; 58.33% pts. (male 26/35; 74.29%) and ICD plus CRT-D in 25/60; 41.66% pts. (male 24/25; 96%). In the medical histories, coronary artery disease had been diagnosed in 41 (68.33%) pts., chronic heart failure in 56 (93.3%) pts., hypertension in 36 (60%) pts., atrial fibrillation in 36 (60%) pts., diabetes mellitus in 19 (31.67%) pts., chronic renal disease in 33 (55%) pts., and previous stroke in seven (11.67%) pts. The clinical characteristics of the patients are set out in Table 1.

Statistical analysis

All data were expressed as mean numbers with standard deviation (\pm SD). The variables were analysed with chi-square, Yates chi-square, Fisher exact tests, Shapiro-Wilk, Mann-Whitney and *t*-Student tests. *P*-value < 0.05 was

Table 1. Clinical characteristics of patients with implantable cardioverter-defibrillator (ICD) and patients with cardiac resynchronisation therapy with defibrillation (CRT-D)

Clinical characteristics	Patients with CRT-D therapy	Patients with ICD therapy	<i>p</i> value
Number of patients	25	35	<i>p</i> > 0.05
Male	24/25	26/35	<i>p</i> > 0.05
Age at first implantation	60.36 \pm 10.54	60.51 \pm 14.07	<i>p</i> > 0.05
Age at final intervention (replacement/up-grade)	66.08 \pm 10.31	68.43 \pm 13.87	<i>p</i> > 0.05
Chronic kidney failure	18 (72%)	15 (42.86%)	<i>p</i> > 0.05
Heart failure	25 (100%)	31 (88.57%)	<i>p</i> > 0.05
Hypertension	15 (60%)	21 (60%)	<i>p</i> > 0.05
Coronary artery disease	18 (72%)	23 (65.71%)	<i>p</i> > 0.05
Atrial fibrillation	17 (68%)	19 (54.29%)	<i>p</i> > 0.05
Diabetes mellitus	9 (36%)	10 (28.57%)	<i>p</i> > 0.05
History of stroke	4 (16%)	3 (8.57%)	<i>p</i> > 0.05

identified as statistically significant. Predictive values were calculated and 95% confidence intervals for odds ratios were presented.

Results

The 60 patients who had undergone ICD/CRT-D implantation were at a similar age at the time of implantation. Most of them had coronary artery disease, hypertension, and/or atrial fibrillation (Table 2). The mean dwell time of CIED therapy was 86.55 ± 36.11 months. Male patients were predominant. There were 9/26 females in the ICD group and 1/24 females in the CRT-D group ($p = 0.035$) OR 8.31 95% CI (0.98–70.56). Women presented with higher left ventricular ejection fraction compared to men $38.11 \pm 12.74\%$ vs. 29.65 ± 12.63 ($p = 0.027$). Patients with CRT-D when compared to those with ICD presented lower LVEF 24.75 ± 8.98 vs. $35.52 \pm 13.55\%$ ($p = 0.001$). CRT-D was mainly implanted as primary prevention 22/25 vs. 18/35 ($p = 0.0726$) OR 6.93 95% CI (1.75–27.43). Endocardial lead impedance in cases of atrial, defibrillator and left-ventricular leads were lower at the final follow-up compared to the values at implantation in both the ICD group and the CRT-D group (Table 3). In the ICD group, atrial impedance was 280.03 ± 335.3 vs. 218.29 ± 229.48 ohm ($p = 0.0018$), defibrillator lead impedance was 768.66 ± 210.62 vs. 507.03 ± 131.67 ohm ($p < 0.001$) (at implantation vs. final follow-up respectively). In the CRT-D group, the mean atrial lead impedance was $511.05 \pm$

271.30 vs. 388.55 ± 231.75 ohm ($p = 0.007$), impedance of the defibrillator lead was 698.95 ± 165.45 vs. 547.13 ± 385.24 ohm ($p = 0.002$), and impedance of the left-ventricular lead was $1,036.28 \pm 337.34$ vs. 794.87 ± 274.99 ohm ($p < 0.001$) at implantation vs. final follow-up respectively.

Discussion

8,467 ICD and 4,164 CRT devices were implanted in Poland in 2016 [10]. Implantable electronic devices for heart failure prolong a patient's life and, in cases of CRT-D, improve the quality of life. In our study, we took into consideration the clinical presentation of patients and endocardial lead technical parameters at implantation and at the final follow-up. Our main observation was gender-related. Women rarely receive ICD, and especially CRT-D, compared to men, and women present with higher LVEF. CRT-D in our patients was implanted mainly as primary prevention and in pts. with lower LVEF compared to ICD. Technical analysis of endocardial lead parameters at implantation and at final follow-up revealed a decrease in impedance in cases of atrial, defibrillator and left-ventricular leads.

Large ICD therapy-related trials such as MADIT, MADIT II, SCD-HeFT, MUSTT, and DEFINITE AVID have involved between 8% and 29% of women, while CRT trials such as MADIT-CRT and MIRACLE have contained a higher number of female patients (around 30%) [11–17]. In the MADIT trial, women were noted to have more advanced HF, as well as a higher incidence of hypertension, diabetes and

Table 2. Lead-associated electrical parameters at implantation in patients with implantable cardioverter-defibrillator (ICD) and patients with cardiac resynchronisation therapy with defibrillation (CRT-D)

Parameter	Patients with CRT-D therapy	Patients with ICD therapy	p value
Atrial lead pacing threshold	0.73 ± 0.59	0.34 ± 0.39	$p < 0.05$
Defibrillation lead pacing threshold	0.69 ± 0.2	0.66 ± 0.22	$p > 0.05$
Left ventricular lead pacing threshold	1.75 ± 1.71	None	None
Atrial lead impedance	511.05 ± 271.30	280.03 ± 335.30	$p < 0.05$
Defibrillation ventricular lead impedance	547.13 ± 385.24	768.66 ± 210.62	$p > 0.05$
Left ventricular lead impedance	$1,036.28 \pm 337.34$	None	None

Table 3. Lead-associated electrical parameters at final follow-up in patients with implantable cardioverter-defibrillator (ICD) and patients with cardiac resynchronisation therapy with defibrillation (CRT-D)

Parameter	Patients with CRT-D therapy	Patients with ICD therapy	p value
Atrial lead pacing threshold	0.67 ± 0.36	0.73 ± 0.27	$p > 0.05$
Defibrillation lead pacing threshold	0.97 ± 0.51	0.85 ± 0.26	$p > 0.05$
Left ventricular lead pacing threshold	1.71 ± 1.36	None	None
Atrial lead impedance	388.55 ± 231.75	218.29 ± 229.48	$p > 0.05$
Defibrillation ventricular lead impedance	698.95 ± 165.45	507.03 ± 131.67	$p > 0.05$
Left ventricular lead impedance	794.87 ± 274.99	None	None

left bundle branch block (LBBB) [18, 19]. MacFadden et al. analysed 5,213 HF patients who received primary and secondary prevention ICDs for up to one year [20]. Of the 921 women who received ICDs for primary prophylaxis, and the 367 who received ICDs for secondary prophylaxis, they found no difference in mortality between men and women. Myocardial scarring post-infarction is more often seen in men, and men with out-of-hospital sudden cardiac arrest are more likely to have VT/VF compared to women (41% vs. 30%). Women are more likely to have asystole (8.8% vs. 7%) or pulseless electrical activity (24% vs. 18%) than men [21]. Women were more likely to have HF, non-ischaemic cardiomyopathy, and advanced NYHA class, and were more likely to receive CRT-defibrillators (CRT-D) compared to men [22]. In the MADIT-CRT trial, women demonstrated a lower mortality rate than men. Enina et al. [23] observed that the best response to CRT therapy is associated with female gender. In our population, men were eight times more likely to receive CRT-D implantation than women. Moreover, female pts presented with a higher LVEF than male pts [23].

We observed long-term stable pacing thresholds of atrial, defibrillation and left ventricular leads, but lead impedance varied at implantation as opposed to at final follow-up. The

impedance increased with time in both ICD and CRT-D pts. Low impedance can be associated with insulation breaks, where a lead wire is exposed to a low resistance body fluid or another lead wire that induces a potential loss of capture or rapid battery depletion. Electrical dysfunction is usually related to a conducting wire fracture in cases of low-voltage circuits, where it can lead to oversensing, inappropriate shocks, and loss of capture. High-voltage circuit failure can lead to short circuiting with a failure to defibrillate [24]. In the literature, we found the devices most prone to failure to be Fidelis and Riata leads, 28% versus 15% respectively [25, 26]. Data has indicated that an impedance threshold above 100 ohm or an abrupt 75% increase in chronic impedance has identified a Fidelis fracture [27].

In CRT-D pts, primary prevention predominates, while in ICD pts primary and secondary prevention were balanced. The implantation of both ICD and CRT-D as primary and secondary prevention is associated with a decrease in the mortality rate [28–30].

Conflict(s) of interest

Marcin Grabowski – fees from: Cook, Medtronic, Abbott, Biotronik, Boston Scientific.

Streszczenie

Wprowadzenie. Wszczepialny kardiowerter-defibrylator (ICD) z terapią resynchronizującą (CRT-D) oraz bez niej stanowi efektywny element leczenia u pacjentów z niewydolnością serca.

Metody i wyniki. Sześćdziesięciu pacjentów (50/60; 83,33% mężczyzn) pozostających pod opieką kliniki kardiologii w latach od maja 1995 roku do lutego 2019 roku z wszczepionym ICD/CRT-D, u których wykonano przynajmniej jedną wymianę urządzenia, poddano retrospektywnej analizie. Kobiety rzadziej wszczepieniu zarówno ICD, jak i CRT-D niż mężczyznom (9/26 kobiet w grupie z ICD oraz 1/24 w grupie z CRT-D [$p = 0,035$], iloraz szans [OR] 8.31 95-proc. przedział ufności [CI] 0,98–70,56). Panie charakteryzowały się wyższą frakcją wyrzutową lewej komory (LVEF) ($38,11 \pm 12,74\%$ v. $29,65 \pm 12,63$ [$p = 0,027$]). U opisywanych chorych CRT-D wszczepiano głównie w ramach w prewencji pierwotnej (22/25 v. 18/35 [$p = 0,0726$], OR 6,93 95% CI 1,75–27,43) oraz u pacjentów z niższą LVEF niż u osób z ICD ($24,75 \pm 8,98$ v. $35,52 \pm 13,55\%$; $p = 0,001$). Analiza parametrów technicznych elektrod endokawitarnych wykazała obniżenie oporności, gdy porównano parametry z dnia wszczepienia i ostatniej wizyty kontrolnej. W grupie z wszczepionym ICD oporność elektrod przedsionkowych wynosiła $280,03 \pm 335,3$ w porównaniu z $218,29 \pm 229,48$ omów ($p = 0,0018$), a elektrod defibrylujących $768,66 \pm 210,62$ w porównaniu z $507,03 \pm 131,67$ omów ($p < 0,001$) (dzień implantacji v. ostatnia kontrola). W grupie poddanych CRT-D średnia oporność elektrod przedsionkowych wynosiła $511,05 \pm 271,30$ w porównaniu z $388,55 \pm 231,75$ omów ($p = 0,007$), elektrod defibrylujących $698,95 \pm 165,45$ w porównaniu z $547,13 \pm 385,24$ omów ($p = 0,002$), a elektrod lewokomorowych $1036,28 \pm 337,34$ w porównaniu z $794,87 \pm 274,99$ omów ($p < 0,001$), gdy porównano dzień implantacji z dniem ostatniej kontroli.

Wnioski. Kobiety podlegają terapii resynchronizującej znacznie rzadziej niż mężczyźni. Ponadto CRT-D poddano pacjentów z niższą LVEF, głównie w ramach prewencji pierwotnej. Oporność wszystkich elektrod ulegała obniżeniu z upływającym czasem.

Słowa kluczowe: terapia resynchronizująca, CRT, wszczepialny kardiowerter-defibrylator, ICD, niewydolność serca, oporność elektrod

References

- Ponikowski P, Voors AA, Anker SD, et al. Authors/Task Force Members, Document Reviewers, ESC Scientific Document Group. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J.* 2016; 37(27): 2129–2200, doi: [10.1093/eurheartj/ehw128](https://doi.org/10.1093/eurheartj/ehw128), indexed in Pubmed: [27206819](https://pubmed.ncbi.nlm.nih.gov/27206819/).
- Butler J, Fonarow GC, Zile MR, et al. Developing therapies for heart failure with preserved ejection fraction: current state and future directions. *JACC Heart Fail.* 2014; 2(2): 97–112, doi: [10.1016/j.jchf.2013.10.006](https://doi.org/10.1016/j.jchf.2013.10.006), indexed in Pubmed: [24720916](https://pubmed.ncbi.nlm.nih.gov/24720916/).
- Owan TE, Hodge DO, Herges RM, et al. Trends in prevalence and outcome of heart failure with preserved ejection fraction. *N Engl J Med.* 2006; 355(3): 251–259, doi: [10.1056/NEJMoa052256](https://doi.org/10.1056/NEJMoa052256), indexed in Pubmed: [16855265](https://pubmed.ncbi.nlm.nih.gov/16855265/).
- Rich JD, Burns J, Freed BH, et al. Beta-Blockers in Heart Failure Collaborative Group, Meta-Analysis Global Group in Chronic Heart Failure (MAGGIC), Meta-Analysis Global Group in Chronic Heart Failure (MAGGIC), Beta-Blockers in Heart Failure Collaborative Group, Meta-analysis Global Group in Chronic Heart Failure (MAGGIC), Meta-Analysis Global Group in Chronic Heart Failure (MAGGIC), Meta-Analysis Global Group in Chronic Heart Failure (MAGGIC) Investigators, Meta-analysis Global Group in Chronic Heart Failure (MAGGIC) Investigators, Meta-Analysis Global Group in Chronic Heart Failure (MAGGIC) Investigators, Meta-analysis Global Group in Chronic Heart Failure (MAGGIC). The survival of patients with heart failure with preserved or reduced left ventricular ejection fraction: an individual patient data meta-analysis. *Eur Heart J.* 2012; 33(14): 1750–1757, doi: [10.1093/eurheartj/ehr254](https://doi.org/10.1093/eurheartj/ehr254), indexed in Pubmed: [21821849](https://pubmed.ncbi.nlm.nih.gov/21821849/).
- Silvia GP, Blomström-Lundqvist C, Mazzanti A, et al. 2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC) Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC). *Eur Heart J.* 2015; 36(41): 2793–2867.
- Dickstein K, Vardas PE, Auricchio A, et al. ESC Committee for Practice Guidelines, Committee for Practice Guidelines of the European Society of Cardiology, ESC Committee for Practice Guidelines (CPG), ESC Committee for Practice Guidelines (CPG). 2010 Focused Update of ESC Guidelines on device therapy in heart failure: an update of the 2008 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure and the 2007 ESC guidelines for cardiac and resynchronization therapy. Developed with the special contribution of the Heart Failure Association and the European Heart Rhythm Association. *Eur Heart J.* 2010; 31(21): 2677–2687, doi: [10.1093/eurheartj/ehq337](https://doi.org/10.1093/eurheartj/ehq337), indexed in Pubmed: [20801924](https://pubmed.ncbi.nlm.nih.gov/20801924/).
- Swedberg K, Cleland J, Dargie H, et al. Task Force for the Diagnosis and Treatment of Chronic Heart Failure of the European Society of Cardiology. Guidelines for the diagnosis and treatment of chronic heart failure: executive summary (update 2005): the Task Force for the Diagnosis and Treatment of Chronic Heart Failure of the European Society of Cardiology. *Eur Heart J.* 2005; 26(11): 1115–1140, doi: [10.1093/eurheartj/ehi204](https://doi.org/10.1093/eurheartj/ehi204), indexed in Pubmed: [15901669](https://pubmed.ncbi.nlm.nih.gov/15901669/).
- Brignole M, Auricchio A, Baron-Esquivias G, et al. 2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy. Developed in collaboration with the European Heart Rhythm Association (EHRA). *Europace* 2013; 8: 1070–1118. doi: [10.1093/europace/eut206](https://doi.org/10.1093/europace/eut206).
- Saxon LA, Hayes DL, Gilliam FR, et al. Long-term outcome after ICD and CRT implantation and influence of remote device follow-up: the ALTITUDE survival study. *Circulation.* 2010; 122(23): 2359–2367, doi: [10.1161/CIRCULATIONAHA.110.960633](https://doi.org/10.1161/CIRCULATIONAHA.110.960633), indexed in Pubmed: [21098452](https://pubmed.ncbi.nlm.nih.gov/21098452/).
- Raatikainen MJ, Arnar DO, Merkely B, et al. A Decade of information on the use of cardiac implantable electronic devices and interventional electrophysiological procedures in the European Society of Cardiology countries: 2017 Report from the European Heart Rhythm Association. *Europace.* 2017; 19(suppl_2): ii1–ii90, doi: [10.1093/europace/eux258](https://doi.org/10.1093/europace/eux258), indexed in Pubmed: [28903470](https://pubmed.ncbi.nlm.nih.gov/28903470/).
- Moss AJ, Hall WJ, Cannom DS, et al. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. Multicenter Automatic Defibrillator Implantation Trial Investigators. *N Engl J Med.* 1996; 335(26): 1933–1940, doi: [10.1056/NEJM199612263352601](https://doi.org/10.1056/NEJM199612263352601), indexed in Pubmed: [8960472](https://pubmed.ncbi.nlm.nih.gov/8960472/).
- Buxton AE, Lee KL, Fisher JD, et al. A randomized study of the prevention of sudden death in patients with coronary artery disease. Multicenter Unsustained Tachycardia Trial Investigators. *N Engl J Med.* 1999; 341(25): 1882–1890, doi: [10.1056/NEJM199912163412503](https://doi.org/10.1056/NEJM199912163412503), indexed in Pubmed: [10601507](https://pubmed.ncbi.nlm.nih.gov/10601507/).
- Moss AJ, Zareba W, Hall WJ, et al. Multicenter Automatic Defibrillator Implantation Trial II Investigators. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. *N Engl J Med.* 2002; 346(12): 877–883, doi: [10.1056/NEJMoa013474](https://doi.org/10.1056/NEJMoa013474), indexed in Pubmed: [11907286](https://pubmed.ncbi.nlm.nih.gov/11907286/).
- Bardy GH, Lee KL, Mark DB, et al. For the Sudden cardiac death in heart failure trial (SCD-HeFT) investigators. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. *N Engl J Med.* 2005; 352: 225–37.
- Curtis LH, Al-Khatib SM, Shea AM, et al. Sex differences in the use of implantable cardioverter-defibrillators for primary and secondary prevention of sudden cardiac death. *JAMA.* 2007; 298(13): 1517–1524, doi: [10.1001/jama.298.13.1517](https://doi.org/10.1001/jama.298.13.1517), indexed in Pubmed: [17911496](https://pubmed.ncbi.nlm.nih.gov/17911496/).
- Kadish A, Dyer A, Daubert JP, et al. Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation (DEFINITE) Investigators. Prophylactic defibrillator implantation in patients with nonischemic dilated cardiomyopathy. *N Engl J Med.* 2004; 350(21): 2151–2158, doi: [10.1056/NEJMoa033088](https://doi.org/10.1056/NEJMoa033088), indexed in Pubmed: [15152060](https://pubmed.ncbi.nlm.nih.gov/15152060/).
- Woo GW, Petersen-Stejskal S, Johnson JW, et al. Ventricular reverse remodeling and 6-month outcomes in patients receiving cardiac resynchronization therapy: analysis of the MIRACLE study. *J Interv Card Electrophysiol.* 2005; 12(2): 107–113, doi: [10.1007/s10840-005-6545-3](https://doi.org/10.1007/s10840-005-6545-3), indexed in Pubmed: [15744462](https://pubmed.ncbi.nlm.nih.gov/15744462/).
- Arshad A, Moss AJ, Foster E, et al. MADIT-CRT Executive Committee. Cardiac resynchronization therapy is more effective in women than in men: the MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy) trial. *J Am Coll Cardiol.* 2011; 57(7): 813–820, doi: [10.1016/j.jacc.2010.06.061](https://doi.org/10.1016/j.jacc.2010.06.061), indexed in Pubmed: [21310317](https://pubmed.ncbi.nlm.nih.gov/21310317/).
- Tompkins CM, Kutiyifa V, Arshad A, et al. Sex Differences in Device Therapies for Ventricular Arrhythmias or Death in the Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy (MADIT-CRT) Trial. *J Cardiovasc Electrophysiol.* 2015; 26(8): 862–871, doi: [10.1111/jce.12701](https://doi.org/10.1111/jce.12701), indexed in Pubmed: [25929699](https://pubmed.ncbi.nlm.nih.gov/25929699/).

20. MacFadden DR, Crystal E, Krahn AD, et al. Sex differences in implantable cardioverter-defibrillator outcomes: findings from a prospective defibrillator database. *Ann Intern Med.* 2012; 156(3): 195–203, doi: [10.7326/0003-4819-156-3-201202070-00007](https://doi.org/10.7326/0003-4819-156-3-201202070-00007), indexed in Pubmed: 22312139.
21. Wigginton JG, Pepe PE, Bedolla JP, et al. Sex-related differences in the presentation and outcome of out-of-hospital cardiopulmonary arrest: a multiyear, prospective, population-based study. *Crit Care Med.* 2002; 30(4 Suppl): S131–S136, indexed in Pubmed: 11940787.
22. Peterson PN, Daugherty SL, Wang Y, et al. National Cardiovascular Data Registry. Gender differences in procedure-related adverse events in patients receiving implantable cardioverter-defibrillator therapy. *Circulation.* 2009; 119(8): 1078–1084, doi: [10.1161/CIRCULATIONAHA.108.793463](https://doi.org/10.1161/CIRCULATIONAHA.108.793463), indexed in Pubmed: 19221223.
23. Enina TN, Kuznetsov VA, Soldatova AM, et al. Gender in cardiac resynchronisation therapy. *J Cardiovasc Thorac Res.* 2018; 10(4): 197–202, doi: [10.15171/jcvtr.2018.34](https://doi.org/10.15171/jcvtr.2018.34), indexed in Pubmed: 30680077.
24. Kołodzińska A, Kutarski A. Lead insulation failure, a serious complication: risk factors and management. *Kardiol Pol.* 2015; 73(8): 585–591, indexed in Pubmed: 26528524.
25. Sung RK, Massie BM, Varosy PD, et al. Long-term electrical survival analysis of Riata and Riata ST silicone leads: National Veterans Affairs experience. *Heart Rhythm.* 2012; 9(12): 1954–1961, doi: [10.1016/j.hrthm.2012.08.006](https://doi.org/10.1016/j.hrthm.2012.08.006), indexed in Pubmed: 22871583.
26. Swerdlow CD, Gunderson BD, Ousdigian KT, et al. Downloadable software algorithm reduces inappropriate shocks caused by implantable cardioverter-defibrillator lead fractures: a prospective study. *Circulation.* 2010; 122(15): 1449–1455, doi: [10.1161/CIRCULATIONAHA.110.962407](https://doi.org/10.1161/CIRCULATIONAHA.110.962407), indexed in Pubmed: 20876433.
27. Koneru JN, Gunderson BD, Sachanandani H, et al. Diagnosis of high-voltage conductor fractures in Sprint Fidelis leads. *Heart Rhythm.* 2013; 10(6): 813–818, doi: [10.1016/j.hrthm.2013.02.027](https://doi.org/10.1016/j.hrthm.2013.02.027), indexed in Pubmed: 23454808.
28. Expósito V, Rodríguez-Mañero M, González-Enríquez S, et al. Primary prevention implantable cardioverter-defibrillator and cardiac resynchronization therapy-defibrillator in elderly patients: results of a Spanish multicentre study. *Europace.* 2016; 18(8): 1203–1210, doi: [10.1093/europace/euv337](https://doi.org/10.1093/europace/euv337), indexed in Pubmed: 26566939.
29. Almejadi F, Porta-Sánchez A, Ha ACT, et al. Mortality implications of appropriate implantable cardioverter defibrillator therapy in secondary prevention patients: contrasting mortality in primary prevention patients from a prospective population-based registry. *J Am Heart Assoc.* 2017; 6(8), doi: [10.1161/JAHA.117.006220](https://doi.org/10.1161/JAHA.117.006220), indexed in Pubmed: 28862957.
30. van Welsesens GH, van Rees JB, Borleffs CJ, et al. Long-term follow-up of primary and secondary prevention implantable cardioverter defibrillator patients. *Europace.* 2011; 13(3): 389–394, doi: [10.1093/europace/euq494](https://doi.org/10.1093/europace/euq494), indexed in Pubmed: 21208947.