International Journal of Cardiology 283 (2019) 122–127

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

# Incidence of appropriate anti-tachycardia therapies after elective generator replacement in patient with heart failure initially implanted with a defibrillator for primary prevention: Results of a meta-analysis

Roberto Rordorf [a,b,*,1], Stefano Cornara [a,b], Catherine Klersy [c], Simone Savastano [a,b], Alessandro Vicentini [a,b], Antonio Sanzo [a,b], Barbara Petracci [a,b], Stefano Ghio [d], Luigi Oltrona Visconti [d], Gaetano M. De Ferrari [a,b]

[a] Coronary Care Unit and Laboratory of Clinical and Experimental Cardiology–IRCCS Fondazione Policlinico San Matteo, Pavia, Italy
[b] Department of Molecular Medicine, University of Pavia, Pavia, Italy
[c] Service of Clinical Epidemiology & Biometry, IRCCS Fondazione Policlinico San Matteo, Pavia, Italy
[d] Division of Cardiology, – Fondazione IRCCS Policlinico San Matteo, Pavia, Italy

ARTICLE INFO

*Article history:*
Received 16 November 2018
Received in revised form 16 December 2018
Accepted 24 December 2018
Available online 2 January 2019

*Keywords:*
ICD
CRT-D
Heart failure
Generator replacement
Appropriate therapies
Meta-analysis

ABSTRACT

*Background:* Implantable cardioverter-defibrillator (ICD) is an effective therapy to reduce mortality in heart failure. When the ICD generator approaches the end of life, most of the patients undergo an elective generator replacement (GR) even if they no longer meet implantation criteria. Whether arrhythmic risk should be re-assessed at the time of GR is still an open question. The aim of our study was to assess, via a meta-analysis, the occurrence of appropriate ICD therapies after GR in patients stratified based on the presence/absence of ICD indication at the time of GR.

*Methods:* Via a systematic literature search for primary prevention studies (January 2000-September 2018), 2976 studies were analyzed. 6 studies were lastly included. Patients were categorized into two groups: "with ICD indication" in case of LVEF≤35% at the time of GR and/or appropriate therapies during the first ICD life; "without ICD indication" in case of a LVEF>35% and no previous ICD therapies. Incidences of appropriate ICD therapies were computed as number of events per 100 person-year.

*Result:* We included 478 pts. (65%) with and 255 patients (35%) without persistent ICD indication. The incidence of appropriate therapies was 12.3/100-person-year in patients with vs. 3.4 in patients without persistent ICD indication (2.98 fold higher risk of ICD therapies).

*Conclusion:* Patients who no longer meet ICD implantation criteria at the time of GR present a significantly lower risk of appropriate ICD therapies after GR. The results of this study underline the importance of an arrhythmic risk re-stratification at the time of GR.



## 1. Introduction

One of the leading causes of mortality in patients with heart failure and reduced left ventricular ejection fraction (LVEF) is sudden cardiac death. Implantable cardioverter defibrillator (ICD) therapy is an effective and established treatment for patients with heart failure for both primary and secondary prevention of sudden cardiac death. Current guidelines of the European Society of Cardiology (ESC) [1] and the American College of Cardiology Foundation/American Heart Association (ACCF/AHA) [2] recommend ICD therapy for primary prevention in symptomatic patients with LVEF ≤35% despite optimal medical therapy for ≥3 months, regardless of heart failure etiology.

Almost 80% of ICD implanted nowadays are for primary prevention [3]; in this subset the rate of appropriate device therapy ranges between 1.9% and 12%/year [4–7]. Accordingly, most of the patients reach the moment when the ICD generator approaches the end of its life without having received an appropriate device therapy during the ICD's first life. Nevertheless, they usually undergo an elective generator replacement (GR) even if they no longer meet implantation criteria. Moreover, at the time of GR patients are usually older and potentially with more comorbidities making the risk-benefit ratio of ICD therapy more debatable. Recent 2016 ESC HF guidelines outline the importance of a careful clinical evaluation of patients before GR in order to assess whether the clinical needs of the patients have changed as compared

* Corresponding author at: Coronary Care Unit and Laboratory of Clinical and Experimental Cardiology, IRCCS Fondazione Policlinico S. Matteo, P.le Golgi 19, 27100 Pavia, Italy.
*E-mail address:* r.rordorf@smatteo.pv.it (R. Rordorf).
[1] The first two authors equally contributed to the preparation of the manuscript.

https://doi.org/10.1016/j.ijcard.2018.12.068
0167-5273/

to the time of first implantation. This is of the utmost importance taking into consideration the fact that the average complications rate of GR is not trivial, ranging from 4% to 7.1% across different studies [8–10].

The aim of our study was to assess, via a meta-analysis of current literature, the occurrence of appropriate ICD therapies after generator replacement in patients subdivided into two groups based on the presence/absence of ICD indication at the time of GR.

## 2. Methods

The metanalysis was performed following the PRISMA statement indications [11].

### 2.1. Data search criteria

We performed an advanced search in the PubMed, Embase, Embase abstracts, WoS, WoS abstracts and Cochrane databases for studies evaluating the rate or appropriate ICD therapies in patient with and without ICD indication at the time of generator replacement, published from January 2000 to December 2017. Bibliographic search strategy is reported in Table e1 (supplemental material).

### 2.2. Study selection

First, all non-pertinent, duplicate, review, commentary or meta-analysis were excluded. 117 studies were evaluated for eligibility. Then 2 investigators (SC and RR) independently reviewed all full text to identify potentially relevant studies, who met the inclusion criteria. Great attention was paid to retrieve the information on the modality of follow up collection. Our inclusion criteria were: studies on ICD GR that included patients formerly implanted with a primary prevention indication, that required LVEF assessment at the time of GR and that reported the rate of appropriate ICD therapies after GR. When those data were not available, or not exactly specified, the study was excluded. We included all studies, both observational or clinical trials, comparing patients with or without indication for generator replacement, assessing the rate of appropriate ICD intervention over time and reporting left ventricular ejection fraction. Controversies were solved by discussion. Study flow chart is shown in Fig. e1 (supplemental material).

### 2.3. Data extraction

One independent investigator (SC), who was not personally involved in any of the included studies, performed the primary data abstraction from each report into prespecified forms. SC and RR, separately, reviewed data extrapolated from eligible articles and in case of discrepancies, they were solved by consensus. The extracted data included: the rate of appropriate ICD therapies after GR, the number of patients with and without ICD indication, age, sex, percentage of patients with CRT, months of follow-up, New York Heart Association functional class and the cause of chronic heart failure (simplified in ischemic/non-ischemic). Those information were collected at the time of GR and first implant, when available.

### 2.4. Data analysis

Our total population was stratified into two groups: 1) patients without persistent ICD indication at the time of GR, based on the absence of appropriate ICD therapies during the first ICD's life and with LVEF>35% at the time of GR; 2) patients with persistent ICD indication at the time of GR, based on the history of appropriate ICD therapies during the first ICD's life and/or with LVEF≤35% at the time of GR. The primary goal of our meta-analysis was to investigate the rate of appropriate antitachycardia ICD therapies after GR in patients with or without an ICD indication at the time of GR. A secondary analysis of the primary endpoint was performed including first those studies enrolling 100% CRT patients, and, secondly, the remaining studies. Incidences were computed from each article as the number of events per hundred person-year; Poisson 95% confidence intervals (95%CI) were also computed. A random effect meta-analysis was performed. Meta-analytic estimates were shown in Forrest plots. The presence of influential studies was excluded graphically by omitting each study in turn from the metanalysis. Patients and study characteristics were summarized over studies as median and 25th–75th percentiles. Stata 15.1 (SataCorp, College Station, TX, USA) was used for computation.

## 3. Results

### 3.1. Study identification

The process of studies screening and selection is showed in Fig. e1. Among the 2976 initially collected abstracts, 121 publications were further evaluated for eligibility. However, 115 of them were excluded for at least one of the following reasons: they did not present a follow-up, they did not report separated data for each group, enrolled secondary prevention patients, the study protocol was unclear or showed a lack of information, it was not clearly declared the appropriateness of ICD therapy. Finally, six relevant studies met the inclusion criteria and were included in the current meta-analysis.

### 3.2. Study population

The 6 studies [12–17] finally included were retrieved in just the last 4 years of literature review, 3 were published in 2016, 2 in 2014, 1 in 2017. Study design was observational retrospective in all cases. One study only reported adjustment for confounding [16]. A total of 733 patients were enrolled in our analysis, 255 in patients without persistent ICD indication and 478 in patients with persistent ICD indication. Baseline characteristics of the population and associations between persistent ICD indication and demographic and clinical variables are shown in Table 1. Among patients with persistent ICD indication 64% had an ischemic etiology, 87% were male and a CRT-D device was implanted in 58% of the patients. Among patients without persistent ICD indication 55% of patients were implanted with an ischemic etiology, 61% were male and a CRT-D device was implanted in 67% of the cases. The median follow-up after GR in the included studies was 26 months (25th–75th percentile: 25–39 months, see Table 1).

### 3.3. Incidence of events and outcomes

Table 2 shows the incidence of appropriate ICD therapies in patients with vs. without persistent ICD indication, expressed as incidence rates

**Table 1**
Differences in variables between patient with (1) and without (0) an ICD indication in each study and in the whole population.

| Variables | Dell'era | | Kini | | Madhavan | | Rordorf | | Sebag | | Madeira | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ICD indication | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1 |
| Number of patients | 52 | 114 | 59 | 93 | 25 | 66 | 41 | 66 | 39 | 68 | 39 | 82 | 255 | 478 |
| Number of appropriate therapy | 12 | 30 | 5 | 40 | 7 | 17 | 2 | 15 | 2 | 19 | 2 | 35 | 30 | 156 |
| Publication year | 2016 | | 2014 | | 2016 | | 2016 | | 2014 | | 2017 | | | |
| Follow-up (month) | 25 | | 42 | | 26 | | 25 | | 26 | | 39 | | 30.5 | |
| Age at replacement (mean ± SD) | 66 ± 11 | 67 ± 9 | 69 ± 9 | 67 ± 9 | 68 ± 10 | 71 ± 11 | 64 ± 11 | 64 ± 10 | 65 ± 10 | 65 ± 11 | 66 ± 10 | 65 ± 11 | 66 [64–68] | 66 [64–67] |
| Coronary artery disease (%) | 37% | 62% | 35% | 54% | 68% | 79% | 54% | 45% | 85% | 78% | 33% | 53% | 55% | 64% |
| Male sex (%) | 37% | 98% | * | * | 96% | 100% | 68% | 86% | 62% | 85% | 62% | 83% | 62%[61–68] | 86%[85–98] |
| LVEF at implant (mean ± SD) | 27 ± 5 | 25 ± 6 | * | * | 31 ± 8 | 37 ± 13 | 27 ± 6 | 22 ± 5 | 27 ± 7 | 26 ± 6 | 25 ± 6 | 24 ± 6 | 27 [27–27] | 25 [24–26] |
| LVEF at replacement (mean ± SD) | 45 ± 7 | 28 ± 7 | 49 ± 9 | 28 ± 7 | 49 ± 8 | 25 ± 11 | 47 ± 7 | 29 ± 9 | * | * | 48 ± 7 | 26 ± 7 | 48 [47–49] | 28 [26–29] |
| CRT (%) | 73% | 50% | 43% | 34% | 0% | 0% | 100% | 100% | 100% | 100% | 92% | 67% | 67% | 58% |

LVEF = left ventricular ejection fraction; CRT = Cardiac Resynchronization Therapy. *data not available.

**Table 2**
Incident of events in the 2 groups.

| First author | Publication year | Without persistent ICD indication | | | With persistent ICD indication | | |
|---|---|---|---|---|---|---|---|
| | | Event/year | LCI | UCI | Event/year | LCI | UCI |
| Sebag | 2014 | 2.33 | 0.28 | 8.42 | 12.70 | 7.65 | 19.83 |
| Dell'era | 2016 | 11.08 | 5.72 | 19.35 | 12.63 | 8.52 | 18.03 |
| Kini | 2014 | 2.42 | 0.79 | 5.65 | 12.29 | 8.78 | 16.73 |
| Madhavan | 2016 | 12.92 | 5.20 | 26.63 | 11.89 | 6.93 | 19.03 |
| Rordorf | 2016 | 2.34 | 0.28 | 8.46 | 10.91 | 6.11 | 17.99 |
| Madeira | 2017 | 1.58 | 0.19 | 5.70 | 13.13 | 9.15 | 18.27 |
| Total | | 3.43 | 1.06 | 5.80 | 12.36 | 10.31 | 14.41 |

LCI = 5% lower confident interval; UCI = 95% upper confident interval.

per 100 person-years, together with their 95% confident interval. The rate of events was 3.43/100 person/year (95% CI were respectively 1.06–5.80) in patients without vs. 12.36/100 person/year (95% CI were respectively 10.31–14.41), in patients with persistent ICD indication. Appropriate ICD therapies occurred with an almost 3-fold increased risk among patients with persistent ICD indication than in patients without a clear indication at the time of GR (Fig. 1). Fig. 2 shows the relative risk of appropriate ICD therapies when the analysis was limited to studies including only CRT patients; in this subgroup, patients with persistent ICD indication shown a 5-fold increased risk of an appropriate ICD therapies as compared to patients without persistent ICD indication at the time of GR. When the analysis was repeated excluding studies with 100% CRT patients there was still is a trend toward a statistically significance, with a 2-fold higher risk of appropriate ICD therapies in patients with persistent ICD indication.

## 4. Discussion

This systematic review and meta-analysis shows that patient with a persistent ICD indication at time of generator replacement present a significantly higher likelihood of appropriate ICD therapies compared with the subset of patient without a persistent ICD indication. The difference in arrhythmic risk is even more pronounced in patients implanted with a device for cardiac resynchronization therapy.

Indication for first-time ICD implantation is clearly established in current international guidelines, based on the evidence resulting from randomized clinical trials. On the contrary, neither clinical trials nor randomized studies have yet been performed to drive clinical decision when the ICD battery is exhausting and the benefit of ICD therapy after GR replacement is still unsettled. In the absence of clinical evidences, ICD is usually replaced in the majority of the patients in clinical practice without further investigations. More data are required to better understand the potential benefit of replacing an ICD especially in two categories of patients, those with a really poor prognosis and those who no longer meet ICD indication criteria at the time of generator replacement. Two previous studies concluded that ICD pulse generators should be replaced even in the presence of a significant improvement in ventricular function after initial ICD implantation [18,19]. However, both are limited by retrospective designs, [20] and drive their conclusion without any comparison with a control group.

The present meta-analysis was addressed to try and fill the gap in the current evidence-based knowledge. Firstly, we confirmed the absence of data from randomized clinical studies on this topic and therefore only retrospective studies, usually based on single center experience, were included. It is well recognized that retrospective observational studies, usually, better represent real life clinical scenarios, nevertheless they are limited by the absence of control for potential confounders. A randomized clinical trial on ICD generator replacement is definitely needed; in the absence of a randomized clinical trial, to the best of our knowledge, the present meta-analysis includes the largest number of patients in this field.

As was shown in previous studies [21], in this meta-analysis about one third of the patient who received an ICD for primary prevention at the time of the end of generator life, present a LVEF >35% and received no appropriate ICD therapies within first ICD's life. Patients in this subgroup were more likely to be women, with ischemic heart failure and were implanted with a CRT-D device, as reported previously [22,23].

It is well known that ICD therapy is an effective treatment for patients with a history of ventricular arrhythmias (secondary prevention); when a generator of a patients with previous appropriate ICD therapies during the first life of the device start to exhaust, the replacement is highly suggested. Less straightforward is the decision-making in patients without previous arrhythmias. It is acknowledged that the main variable affecting arrhythmic risk is left ventricular function [5], although using LVEF alone as a predictor of arrhythmic death may be limiting. The present study confirms the key role of LVEF also in the

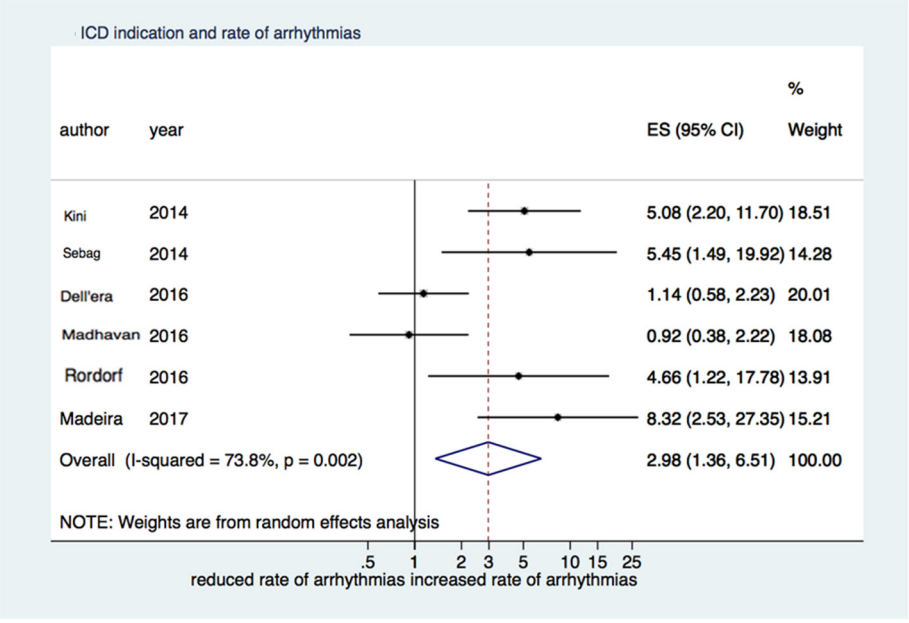


**Fig. 1.** Forrest plots for the analysis of the primary end-point in the whole population.

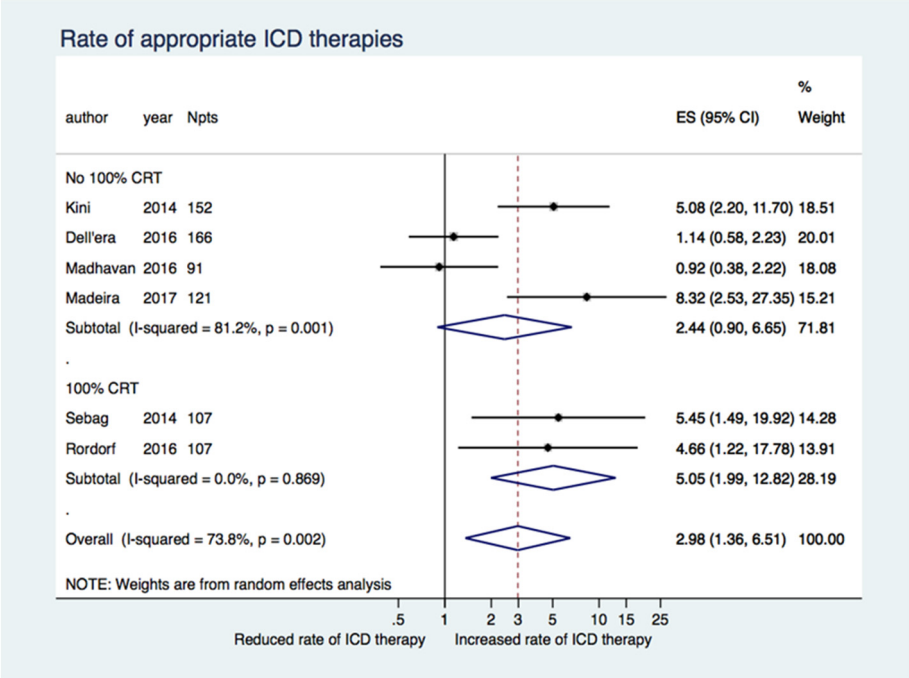


**Fig. 2.** Forrest plots for the analysis of the primary end-point in the whole population, in studies including 100% CRT patients and in remaining studies.

setting of ICD replacement. Indeed, patients stratified based on the assessment of LVEF at the time of generator replacement, and on the presence of ventricular arrhythmias during first ICD's life, showed significantly different arrhythmic risk during follow-up. An improvement in LVEF is associated with a reduced risk of ventricular arrhythmias as our studies demonstrated; nevertheless, the question is whether this risk reduction is sufficiently high to justify withholding ICD therapy [24]. The rate of appropriate ICD therapies in patients without a persistent ICD indication was 3.4/100-person-year, a risk above the general population with LVEF >35%, suggesting the need for further risk stratification not based solely on LVEF and history of previous arrhythmias. The degree of LVEF improvement is expected to be more important in CRT-D devices recipients [23,25], explaining the greater reduction of arrhythmic risk showed by the present analysis in this subpopulation. The concept that response to CRT is associated with a significant reduction in arrhythmic risk has been previously demonstrated [23]. Furthermore, the present study points to the importance of re-assessing the degree of response to CRT at the time of generator replacement, which is usually around 5 years later after initial implantation. A long-lasting response to CRT, defined as a positive left ventricular reverse remodeling persisting at the time of generator replacement, together with the absence of arrhythmias during first ICD's life, identify a subgroup of patients at very low subsequent arrhythmic risk (incidence of events <2.5/100 person-years). In this subgroup of patients, the need for a ICD generator replacement rather than downgrading to a CRT pacemaker should be considered [10,26].

When an ICD is implanted, usually, is viewed as a lifelong commitment, and when the ICD generator approaches to the end of his life the vast majority of the patients undergo an elective GR without any further investigation. The present study strongly suggest that this approach should be reviewed and that arrhythmic risk should be reassessed at the time of generator replacement. Accordingly, the latest guidelines on the management of patients with HF suggest re-evaluating the clinical need for an ICD before performing a generator replacement, based on several important considerations. First, generator replacement should not be considered a procedure without potential drawbacks: the rate of major complication rate is approximately 4% [9], and the occurrence of complications is associated with an increase in the risk of mortality [5,27]. In the REPLACE registry the infection rate after generator replacement was 1.4% for ICDs and 2.3% for CRT-D devices [28], and this risk was significantly higher in replacement procedures as compared to first implants [29]. Second, patients undergoing replacement procedures are foreseeable older than patients first receiving ICD therapy and potentially with more comorbidities, limiting life expectancy [3,30]. In this population the risk of a non-arrhythmic death is increased, and the potential benefit of ICD therapy present on the same patient at the time of the first implant may be significantly diminished. Lastly, the cost issue should also be taken into consideration: due to the aforementioned points, on major complications and potential limited efficacy of ICD therapy after replacement, the cost-efficacy of this therapy in this setting is very likely to be significantly diminished, although data on this issue are missing.

However, there is a paucity of data on this topic that significantly limits the ability of providers and patients to have an informed discussion. In clinical practice, the withdrawal of an ICD therapy, inactivating or not replacing the device, is generally considered only when the patient reaches a really critical state in disease progression, associated with a short-term poor prognosis.

According to our data we suggest to perform an accurate arrhythmic risk stratification, and to engage the patient and his relatives in the decision-making process, illustrating PROS and CONS, to reach a shared decision also at the time of elective generator replacement.

The results of our study support the algorithm recently proposed by Al-Khatib et al. [31] to help the decision making at the time of battery depletion for both single/dual-chamber ICD and for CRT-D devices. The proposed algorithm emphasizes the need to consider LVEF, previous arrhythmias and patients engagement in order to drive the decision.

## 5. Limitations

First and most important this meta-analysis does not include randomized studies comparing the occurrence of arrhythmic events in patients without persistent ICD indication randomized to continued vs. discontinued ICD therapy at the time of generator replacement. Such trial would definitely address the issue whether those patients might significantly benefit from ongoing ICD therapy. Moreover, only one of

the observational studies included in the meta-analysis reported estimates adjusted for confounding. Nevertheless, the results of the presented meta-analysis, coming from homogenous studies on the topic, add important information that could significantly help clinical decision making in this setting. Secondly, arrhythmic risk was defined based on the occurrence of appropriate ICD therapies only. Based on available data from the included studies it was not possible to distinguish between ventricular arrhythmias treated with anti-tachycardia pacing or shock. It is also well recognized that appropriate ICD therapies are not a surrogate of sudden death and limiting the analysis to appropriate ICD therapies could overestimate the efficacy of ICDs. It was impossible to extrapolate by the included studies if patients did not present an ICD indication at the time of GR because of a persistent LVEF <35% or for previous appropriate therapies before GR; therefore any specific analysis addressed to investigate the role of LVEF alone in predicting appropriate ICD therapies could not be performed. Thirdly, information on the rate of complications and of inappropriate therapies were not reported in analyzed studies, thus limiting the discussion on the potential drawbacks of continuing ICD therapy in those patients without persistent indication. Finally, only one of the included studies totally excluded CRT patients. When we performed our analysis excluding studies that enrolled only CRT patients there was still a 2-fold higher risk of subsequent arrhythmias in patients with persistent ICD indication. Nevertheless this effect could be partially driven by the presence of around 50% of patients with CRT in the remaining studies. More data in populations of non-CRT patients are needed to address the risk of arrhythmias after generator replacement in this setting.

## 6. Conclusion

Patients who no longer meet ICD implantation criteria at the time of generator replacement present a significantly lower risk of appropriate ICD therapies during the ICD's "second life", and this is true especially for CRT responder patients. The results of this meta-analysis underlines the importance of an accurate arrhythmic risk re-stratification at the time of generator replacement, based on the history of previous ventricular arrhythmias and LVEF assessment. Arrhythmic risk re-stratification, together with the clinical assessment of the patient status, should be taken into account in order to balance the risk-benefit ratio of replacing an ICD.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2018.12.068.

## Conflict of interest

The authors report no relationships that could be considered as a conflict of interest.

## References

[1] P. Ponikowski, A.A. Voors, S.D. Anker, H. Bueno, J.G.F. Cleland, A.J.S. Coats, V. Falk, J.R. González-Juanatey, V.-P. Harjola, E.A. Jankowska, M. Jessup, C. Linde, P. Nihoyannopoulos, J.T. Parissis, B. Pieske, J.P. Riley, G.M.C. Rosano, L.M. Ruilope, F. Ruschitzka, F.H. Rutten, P. van der Meer, G. Filippatos, J.J.V. McMurray, V. Aboyans, S. Achenbach, S. Agewall, N. Al-Attar, J.J. Atherton, J. Bauersachs, A. John Camm, S. Carerj, C. Ceconi, A. Coca, P. Elliott, Ç. Erol, J. Ezekowitz, C. Fernández-Golfín, D. Fitzsimons, M. Guazzi, M. Guenoun, G. Hasenfuss, G. Hindricks, A.W. Hoes, B. Iung, T. Jaarsma, P. Kirchhof, J. Knuuti, P. Kolh, S. Konstantinides, M. Lainscak, P. Lancellotti, G.Y.H. Lip, F. Maisano, C. Mueller, M.C. Petrie, M.F. Piepoli, S.G. Priori, A. Torbicki, H. Tsutsui, D.J. van Veldhuisen, S. Windecker, C. Yancy, J.L. Zamorano, J.L. Zamorano, V. Aboyans, S. Achenbach, S. Agewall, L. Badimon, G. Barón-Esquivias, H. Baumgartner, J.J. Bax, H. Bueno, S. Carerj, V. Dean, Ç. Erol, D. Fitzsimons, O. Gaemperli, P. Kirchhof, P. Kolh, P. Lancellotti, G.Y.H. Lip, P. Nihoyannopoulos, M.F. Piepoli, P. Ponikowski, M. Roffi, A. Torbicki, A. Vaz Carneiro, S. Windecker, H.S. Sisakian, E. Isayev, A. Kurlianskaya, W. Mullens, M. Tokmakova, P. Agathangelou, V. Melenovsky, H. Wiggers, M. Hassanein, T. Uuetoa, J. Lommi, E.S. Kostovska, Y. Juillière, A. Aladashvili, A. Luchner, C. Chrysohoou, N. Nyolczas, G. Thorgeirsson, J. Marc Weinstein, A. Di Lenarda, N. Aidargaliyeva, G. Bajraktari, M. Beishenkulov, G. Kamzola, T. Abdel-Massih, J. Celutkiene, S. Noppe, A. Cassar, E. Vataman, S. Abir-Khalil, P. van Pol, R. Mo, E. Straburzynska-Migaj, C. Fonseca, O. Chioncel, E. Shlyakhto, P. Otasevic, E. Goncalvesová, M. Lainscak, B. Díaz Molina, M. Schaufelberger, T. Suter, M.B. Yilmaz, L. Voronkov, C. Davies, 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure, Eur. Heart J. 37 (2016) 2129–2200.

[2] C.W. Yancy, M. Jessup, B. Bozkurt, J. Butler, D.E. Casey, M.H. Drazner, G.C. Fonarow, S.A. Geraci, T. Horwich, J.L. Januzzi, M.R. Johnson, E.K. Kasper, W.C. Levy, F.A. Masoudi, P.E. McBride, J.J.V. McMurray, J.E. Mitchell, P.N. Peterson, B. Riegel, F. Sam, L.W. Stevenson, W.H.W. Tang, E.J. Tsai, B.L. Wilkoff, 2013 ACCF/AHA guideline for the management of heart failure, J. Am. Coll. Cardiol. 62 (2013) e147–e239.

[3] D.B. Kramer, K.F. Kennedy, P.A. Noseworthy, A.E. Buxton, M.E. Josephson, S.-L. Normand, J.A. Spertus, P.J. Zimetbaum, M.R. Reynolds, S.L. Mitchell, Characteristics and outcomes of patients receiving new and replacement implantable cardioverter-defibrillators: results from the NCDR, Circ. Cardiovasc. Qual. Outcomes 6 (2013) 488–497.

[4] A.A. Alsheikh-Ali, M. Homer, P.V. Maddukuri, B. Kalsmith, N.A.M. Estes, M.S. Link, Time-dependence of appropriate implantable defibrillator therapy in patients with ischemic cardiomyopathy, J. Cardiovasc. Electrophysiol. 19 (2008) 784–789.

[5] G.H. Bardy, K.L. Lee, D.B. Mark, J.E. Poole, D.L. Packer, R. Boineau, M. Domanski, C. Troutman, J. Anderson, G. Johnson, S.E. McNulty, N. Clapp-Channing, L.D. Davidson-Ray, E.S. Fraulo, D.P. Fishbein, R.M. Luceri, J.H. Ip, Amiodarone or an implantable cardioverter–defibrillator for congestive heart failure, N. Engl. J. Med. 352 (2005) 225–237.

[6] A.J. Moss, W. Zareba, W.J. Hall, H. Klein, D.J. Wilber, D.S. Cannom, J.P. Daubert, S.L. Higgins, M.W. Brown, M.L. Andrews, Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction, N. Engl. J. Med. 346 (2002) 877–883.

[7] J.A. Manfredi, S.M. Al-Khatib, L.K. Shaw, L. Thomas, R.I. Fogel, B. Padanilam, D. Rardon, R. Vatthyam, L.W. Gemma, K. Golden, E.N. Prystowsky, Association between left ventricular ejection fraction post-cardiac resynchronization treatment and subsequent implantable cardioverter defibrillator therapy for sustained ventricular tachyarrhythmias, Circ. Arrhythm. Electrophysiol. 6 (2013) 257–264.

[8] D. Erkapic, J. Sperzel, S. Stiller, U. Meltendorf, J. Mermi, K. Wegscheider, B. Hügl, Long-term benefit of implantable cardioverter/defibrillator therapy after elective device replacement: results of the INcidence free SUrvival after ICD REplacement (INSURE) trial—a prospective multicentre study, Eur. Heart J. 34 (2013) 130–137.

[9] J.E. Poole, M.J. Gleva, T. Mela, M.K. Chung, D.Z. Uslan, R. Borge, V. Gottipaty, T. Shinn, D. Dan, L.A. Feldman, H. Seide, S.A. Winston, J.J. Gallagher, J.J. Langberg, K. Mitchell, R. Holcomb, for the R.R. REPLACE Registry Investigators, Complication rates associated with pacemaker or implantable cardioverter-defibrillator generator replacements and upgrade procedures: results from the REPLACE registry, Circulation 122 (2010) 1553–1561.

[10] M. Biffi, E. Menardi, M.L. Narducci, E. Ammendola, L. Messano, F. Giofrè, C. Baiocchi, D. Saporito, F. Lissoni, M. Bertini, A. Pierantozzi, G. Zingarini, M. Malacrida, M. Ziacchi, Manufacturer change and risk of system-related complications after implantable cardioverter defibrillator replacement: physicians' survey and data from the detect long-term complications after implantable cardioverter defibrillator replacement registry, J. Cardiovasc. Med. 18 (2017) 968–975.

[11] D. Moher, A. Liberati, J. Tetzlaff, D.G. Altman, T.P. Group, Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement, PLoS Med. 6 (2009), e1000097. https://doi.org/10.1371/journal.pmed.1000097.

[12] S. Taravelli, E. Rordorf, R. Vicentini, A. Petracci, B. Savastano, S. Sanzo, A. Raineri, C. Dusi, V. De Regibus, V. Sclesi, L. Ghio, S. Oltrona Visconti, L. De Servi, Cardiac resynchronization therapy defibrillator at the end of battery life; is time to discuss the need to re-implant a device with defibrillator back-up in all patients? Eur. Heart J. 37 (2016) 445–446.

[13] V. Kini, M.K. Soufi, R. Deo, A.E. Epstein, R. Bala, M. Riley, P.W. Groeneveld, A. Shalaby, S. Dixit, Appropriateness of primary prevention implantable cardioverter-defibrillators at the time of generator replacement: are indications still met? J. Am. Coll. Cardiol. 63 (2014) 2388–2394.

[14] F.A. Sebag, N. Lellouche, Z. Chen, A. Tritar, M.D. O'Neill, J. Gill, M. Wright, C. Lecler, C.A. Rinaldi, Positive response to cardiac resynchronization therapy reduces arrhythmic events after elective generator change in patients with primary prevention CRT-D, J. Cardiovasc. Electrophysiol. 25 (2014) 1368–1375.

[15] M. Madeira, N. António, J. Milner, M. Ventura, J. Cristóvão, M. Costa, J. Nascimento, L. Elvas, L. Gonçalves, G. Mariano Pego, Who still remains at risk of arrhythmic death at time of implantable cardioverter-defibrillator generator replacement? Pacing Clin. Electrophysiol. 40 (2017) 1129–1138.

[16] G. Dell'Era, A. Degiovanni, E. Occhetta, A. Magnani, M. Bortnik, G. Francalacci, L. Plebani, E. Prenna, S. Valsecchi, P. Marino, Persistence of ICD indication at the time of replacement in patients with initial implant for primary prevention indication: effect on subsequent ICD therapies, Indian Pacing Electrophysiol. J. 17 (2017) 29–33.

[17] M. Madhavan, J.W. Waks, P.A. Friedman, D.B. Kramer, A.E. Buxton, P.A. Noseworthy, R.A. Mehta, D.O. Hodge, A.Y. Higgins, T.L. Webster, C.M. Witt, Y.-M. Cha, B.J. Gersh, Outcomes after implantable cardioverter-defibrillator generator replacement for primary prevention of sudden cardiac death, Circ. Arrhythm. Electrophysiol. 9 (2016), e003283. https://doi.org/10.1161/CIRCEP.115.003283.

[18] J.E. Schliamser, A.H. Kadish, H. Subacius, A. Shalaby, A. Schaechter, J. Levine, J.J. Goldberger, Significance of follow-up left ventricular ejection fraction measurements in the defibrillators in non-ischemic cardiomyopathy treatment evaluation trial (DEFINITE), Heart Rhythm. 10 (2013) 838–846.

[19] N. Naksuk, A. Saab, J.-M. Li, V. Florea, M. Akkaya, I.S. Anand, D.G. Benditt, S. Adabag, Incidence of appropriate shock in implantable cardioverter-defibrillator patients with improved ejection fraction, J. Card. Fail. 19 (2013) 426–430.

[20] K.A. Ellenbogen, J.H. Levine, R.D. Berger, J.P. Daubert, S.L. Winters, E. Greenstein, A. Shalaby, A. Schaechter, H. Subacius, A. Kadish, Defibrillators in non-ischemic cardiomyopathy treatment evaluation (DEFINITE) investigators, are implantable

cardioverter defibrillator shocks a surrogate for sudden cardiac death in patients with nonischemic cardiomyopathy? Circulation 113 (2006) 776–782.
[21] Y. Zhang, E. Guallar, E. Blasco-Colmenares, B. Butcher, S. Norgard, V. Nauffal, J.E. Marine, Z. Eldadah, T. Dickfeld, K.A. Ellenbogen, G.F. Tomaselli, A. Cheng, Changes in follow-up left ventricular ejection fraction associated with outcomes in primary prevention implantable cardioverter-defibrillator and cardiac resynchronization therapy device recipients, J. Am. Coll. Cardiol. 66 (2015) 524–531.
[22] A.J. Moss, W. Zareba, W.J. Hall, H. Klein, D.J. Wilber, D.S. Cannom, J.P. Daubert, S.L. Higgins, M.W. Brown, M.L. Andrews, Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction, N. Engl. J. Med. 346 (2002) 877–883.
[23] J.A. Manfredi, S.M. Al-Khatib, L.K. Shaw, L. Thomas, R.I. Fogel, B. Padanilam, D. Rardon, R. Vatthyam, L.W. Gemma, K. Golden, E.N. Prystowsky, Association between left ventricular ejection fraction post-cardiac resynchronization treatment and subsequent implantable cardioverter defibrillator therapy for sustained ventricular tachyarrhythmias, Circ. Arrhythm. Electrophysiol. 6 (2013) 257–264.
[24] F.M. Merchant, T. Quest, A.R. Leon, M.F. El-Chami, Implantable cardioverter-defibrillators at end of battery life: opportunities for risk (Re)-stratification in ICD recipients, J. Am. Coll. Cardiol. 67 (2016) 435–444.
[25] M.H. Ruwald, S.D. Solomon, E. Foster, V. Kutyifa, A.-C. Ruwald, S. Sherazi, S. McNitt, C. Jons, A.J. Moss, W. Zareba, Left ventricular ejection fraction normalization in cardiac resynchronization therapy and risk of ventricular arrhythmias and clinical outcomes: results from the Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy (MADIT-CRT) trial, Circulation 130 (2014) 2278–2286.
[26] E.S. Nakou, E.N. Simantirakis, E.M. Kallergis, K.S. Nakos, P.E. Vardas, Cardiac resynchronization therapy (CRT) device replacement considerations: upgrade or downgrade? A complex decision in the current clinical setting, Eurospace 19 (2017) 705–711.
[27] A.D. Krahn, D.S. Lee, D. Birnie, J.S. Healey, E. Crystal, P. Dorian, C.S. Simpson, Y. Khaykin, D. Cameron, A. Janmohamed, R. Yee, P.C. Austin, Z. Chen, J. Hardy, J.V. Tu, Ontario ICD Database Investigators, Predictors of short-term complications after implantable cardioverter-defibrillator replacement: results from the Ontario ICD database, Circ. Arrhythm. Electrophysiol. 4 (2011) 136–142.
[28] D.Z. Uslan, M.J. Gleva, D.K. Warren, T. Mela, M.K. Chung, V. GottipatY, R. Borge, D. Dan, T. Shinn, K. Mitchell, R.G. Holcomb, J.E. Poole, Cardiovascular implantable electronic device replacement infections and prevention: results from the REPLACE registry, Pacing Clin. Electrophysiol. 35 (2012) 81–87.
[29] D. Klug, M. Balde, D. Pavin, F. Hidden-Lucet, J. Clementy, N. Sadoul, J.L. Rey, G. Lande, A. Lazarus, J. Victor, C. Barnay, B. Grandbastien, S. Kacet, PEOPLE Study Group, Risk factors related to infections of implanted pacemakers and cardioverter-defibrillators: results of a large prospective study, Circulation 116 (2007) 1349–1355.
[30] D.B. Kramer, K.F. Kennedy, J.A. Spertus, S.-L. Normand, P.A. Noseworthy, A.E. Buxton, M.E. Josephson, P.J. Zimetbaum, S.L. Mitchell, M.R. Reynolds, Mortality risk following replacement implantable cardioverter-defibrillator implantation at end of battery life: results from the NCDR®, Heart Rhythm. 11 (2014) 216–221.
[31] S.M. Al-Khatib, D.J. Friedman, G.D. Sanders, When is it safe not to reimplant an implantable cardioverter defibrillator at the time of battery depletion? Card. Electrophysiol. Clin. 10 (2018) 137–144.