**Favorable trend of Implantable Cardioverter-Defibrillators service-life in a large single-nation population. Insights from ten-year analysis of the Italian ICD Registry**

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Running Title: ICD service-life trends over ten years in Italy

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ABSTRACT

**Background** Implantable Cardioverter Defibrillators (ICD) are widely employed for the prevention of sudden cardiac death. Despite technological improvements, patients often need to undergo generator’s replacement which entails the risk of periprocedural complications. Our aim was to estimate the service-life of ICDs over a ten-year interval and to assess the main causes of replacement on the basis of data from the National ICD Registry of the Italian Society of Arrhythmology and Cardiac Pacing (AIAC).

**Methods and Results** AIAC registry includes data from over 400 hospitals in Italy. We included all patients who underwent device replacement from Calendar 2007 to Calendar 2016 years. The median service-life of the ICDs and its trend over the years was estimated across the three types of device (VR, DR, CRT-D) and the indication to implantation. The causes of replacement were also analyzed.We enrolled 29158 patients (80,9 % males; mean age at device replacement 65.8 ± 12.0 years old). The *median service-life of* the devices was 57,3 IQR 27.8 months. Over the years, device’s service-life showed an increasing trend. The majority of patients underwent elective replacement because of battery end of life and over the years there was a significant reduction of replacement for recalls, erosion/infections and CRT upgrading.

**Conclusions** Our data from a large single-nation population showed that the trend of ICD service-life, independently from ICD type, indication and settings, significantly improved over time. Moreover, there was a striking reduction of interventions for upgrading and infection/erosion. This favorable trend has important clinical, organizational and financial implications.

KEY WORDS:

* Implantable Cardioverter-Defibrillator
* Longevity
* Registry

INTRODUCTION

Implantable Cardioverter-Defibrillators (ICD) and Cardiac Resynchronization Therapy Defibrillators (CRT-D) have become a land-mark option for the prevention of sudden cardiac death in patients at risk of fatal ventricular arrhythmias.1,2 Registries from clinical practice have confirmed in larger scale the efficacy of ICD therapy in the setting of both primary and secondary prevention.3–5 The growing mismatch between the service-life of the devices and patients’ survival is an already well known issue. 6 Moreover, previous single and few-centers studies demonstrated highly variable ICD longevity according to device manufacturers. 7–11 Technology improvements, in particular on the front of battery longevity, have tried to solve the problem, but ICD and CRT-D service-life may still be shorter than patients’ average survival. This implies the need of generators’ replacements, which entails the risk of peri-procedural complications (damage of the leads, bleeding and infections) and negatively impacts on the cost-efficacy of the devices.12–16

The aim of this study was to estimate over a ten-year interval the trend of service-life of ICD and CRT-D generators, which also reflects device longevity, and to evaluate the main causes of replacement on the basis of data from the National ICD Registry of the Italian Society of Arrhythmology and Cardiac Pacing (AIAC), which regularly collects main technical and clinical information on all the ICD and CRT-D implantations performed in the vast majority of Italian Hospitals.

MATERIALS AND METHODS

We included all patients from the Italian National ICD Registry who underwent device replacement of the ICD/CRT-D from Calendar 2007 to Calendar 2016 years. Along all the period the main indications to replacement were explored according to the European Patient-Implantable Cardioverter/Defibrillator Identification Card (EURID) form.17–19

The mean duration from implantation to replacement was calculated subdividing the patients according to device characteristics (VR-ICD, DR-ICD or CRT-D), indications to implantation (primary or secondary prevention) and year of device replacement.

The Italian National ICD Registry is a centrally held database to which all participating centers (over 400 hospitals which perform about 95% of ICD/CRT-D implantations in Italy) voluntary provide clinical and technical data on every patient and device implanted. 17,19

Data are reported in the registry using EURID implant forms and retrieved by mail after implantation, replacement and explantation procedures. Validation of data is performed using a two-step protocol: first, at the time of data entry, data are checked for formal consistency, and then, at the time when the annual report is performed, data are evaluated for internal consistency. Of note, for internal policy the Italian National ICD registry does not publicly report data subdivided by devices’ manufacturer.

The causes of replacement were grouped in four categories: a) elective replacement for battery end of life; b) system recall according to specific manufacturer advisory or system malfunction detected at the follow-up center; c) upgrading to CRT device ; d) system infection or pocket erosion.

For the analysis IBM SPSS Statics Version 20 and R version 3.5.2 20powered by the rms package version 5.1-221 were employed. Data analysis included basic descriptive statistics, with categorical variables usually reported in frequencies (%) and absolute numbers, and continuous variables reported as mean ± standard deviation or median values and interquartile range (IQR), as appropriate. P-values have been calculated, whenever appropriate, using ANalysis Of VAriance (ANOVA) or Wilcoxon-Kruskal-Wallis test for continuous variables and Pearson chi-square test for categorical variables.The temporal trend of devices’ longevity was estimated using a general linear model with gamma distribution and log link function. The 95% Confidence Intervals for the estimations were evaluated by the estimation of 1000 bootstrap evaluations of the model, clustered at the subject level. [ Cribari-Neto, F., & Zarkos, S. G. (1999). Bootstrap methods for heteroskedastic regression models: evidence on estimation and testing. Econometric Reviews, 18(2), 211–228. doi:10.1080/07474939908800440 (https://doi.org/10.1080/07474939908800440)].

RESULTS  
In the decade 2007-2016 the Italian ICD Registry collected 29158 patients (80,9% males; mean age 65.2 ± 12.1 years old), whom underwent ICD/CRT-D device replacement. Among these patients, 18814 (64.5%; mean age at device replacement 66.2 ± 11.5 years) had received their first ICD/CRT-D for primary prevention and 10344 (35.5%; mean age at device replacement 64.1 ± 13.1 years) for secondary prevention.

Table 1 shows the distribution of patients according to the main clinical indication and the characteristics of the implanted device. Overall, the largest proportion of patients was implanted with a CRT-D (47.5%), but this distribution was strongly influenced by the larger subgroup of patients implanted for primary prevention; in fact, patients implanted for secondary prevention received the three ICD types (VR, DR, CRT-D) in substantially equally distributed percentages.

Table 2 shows the distribution of patients according to the underlying heart disease and device’s characteristics. Overall, the majority of patients suffered from ischemic cardiomyopathy and the second most represented etiology was non-ischemic cardiomyopathy; conversely, the last one was preponderant in the subgroup of patients implanted with a CRT-D. As expected, patients implanted for an idiopathic purely arrhythmic disease were more represented in the subgroup of patients implanted with an ICD-VR.

The *median service-life of* the replaced devices was 57.3 IQR 27.8 months. In detail, in those implanted for primary prevention median service-life was 56.8 IQR 27.0 months, whereas in those implanted for secondary prevention it was 58.0 IQR 29.4 months (p<0.001). The service-life of CRT-D devices was significantly lower than the service-life of ICD-VR and ICD-DR devices, independently from the indication to ICD implantation (Figure 1).

Over the years, device’s service-life showed an increasing trend which remains evident across the three types of ICD and across the two main indications to implantation. In particular, the median service-life of the ICD replaced in 2007 was 45.8 months (IQR 28.6 months), whereas the median service-life of the devices replaced in 2016 was 68.1 months (IQR 27.7 months; p<0,001) with a net increase of 22.3 months (relative increase 48.7%). According to ICD types, the net increase of longevity was respectively 32.6 months (relative increase 59%) in ICD-VR treated patients, 28.7 months (relative increase 59.4%) in ICD-DR treated patients, and 25.1 months (relative increase 68,9%) in CRT-D group (figure 2, figure 3 and supplementary table 1).

The main replacement causes are summarized in Table 3. The vast majority of patients underwent replacement because of battery end of life, in particular in the case of CRT-Ds (over 91% both in primary and secondary prevention). The proportion of replacements/explantations for recalls and infections/erosion was low and marginal. Conversely, the proportion of replacements for device’s CRT upgrading was important, in the range of around 10%, but was obviously limited to ICD-VR and ICD-DR systems.

Over the years there was a significant (p<0,001) reduction of replacement for recalls, erosion/infections and upgrading and, consequently, a relative increase of replacements for battery end of life was documented (Table 4).

DISCUSSION

Data from our large single-nation population, including more than 29000 replacements, showed that ICD service-life, independently from ICD type, indication and settings, significantly improved over ten-year period and that the causes of replacement evolved with a striking reduction of interventions for CRT upgrading and infection/erosion in favor of interventions for battery end of life. The relative increase in device longevity across the years was particularly evident for CRT-D, a subset of high-cost and more sophisticated devices with high technological evolution.

The importance of increasing the longevity of ICDs appears obvious both in the setting of purely electric diseases, a clinical condition where patients survival may be similar to the normal population, and in the cohort of patients with left ventricular dysfunction and heart failure, because long-term outcome of these patients has been recently improved with new pharmacologic agents and appropriate clinical management. Extension of devices’ longevity may reduce the mismatch that was demonstrated in the past between patient survival and ICD/CRT-D service-life.16 An increase of device longevity could be obtained by improved device technology (both hardware and software) and battery chemistry and determines both clinical and economic benefit, with important impact in reducing procedural complications and long-term cost of ICD therapy.13–15

The observed reduction of interventions for device system CRT upgrading could be explained in our experience by improvements in the initial choice of ICD type, which was probably induced by the evidence that periprocedural morbidity is higher in patients who undergo an upgrade compared to patients who undergo replacement of the generator.22 Conversely, in our Registry the reduction of explantations for erosion/infections could be justified by the improvement of surgical techniques and equipment, as well as by a more diffuse and increasing expertise across the implanting centers. ICD or CRT-D replacement for system recalls could have been reduced also by large implementation after the year 2012 of remote monitoring , which allows a stricter follow up permitting to postpone replacement.23–26 The reduction of the number of replacements has important clinical implications, related to a potential decrease in the risk of complications and specifically of device system infections that any replacement may imply according to a series of risk factors.27,28

The service-life of ICDs is determined by a multiplicity of factors and is difficult to be predicted a priori. Therefore, data from “real world” registries can be particularly helpful as they have already been shown to describe accurately the actual impact of ICD therapy on ordinary populations.3,4 In the last years several studies on ICD longevity have been published; most of them were single center or multicenter studies collecting data from less than 50 participating centers.8–10,29,30

With respect to previously published data, it must be noted that proper comparison of device service-life between different studies is difficult to be obtained due to inhomogeneity of patients included and data presentation. Thijssen et al.29 reported longevity as a mean value of 5.0 ± 0.1 years and included 4673 patients implanted with an ICD from calendar 1996 year to calendar 2011 year. Von Gunten et al. 9 showed that 69.8% of ICD were still operative after 5 years analyzing data from a population of 3436 patients from calendar year 1994 to calendar year 2004 and Zanon et al.30 estimated a median service-life of 5.9 IQR 2.0 years in VR and DR ICD and of 4.9 IQR 1.7 in CRT-D explanted from calendar March 2013 to calendar May 2015. Conversely, Manolis et al8 assessed ICD service-life over a 20 year period among 685 patients, the vast majority of them implanted with an ICD for secondary prevention; they estimated a mean service-life of 58.3±18.7 months. In another single-center study, the mean longevity of 1665 devices implanted in 1272 patients between calendar year 1998 and calendar year 2010 ranged from 5.2 to 5.7 years according to different manufactures.10 Device type and percentage of pacing, but not pacing output and ICD shocks, had an influence on battery longevity. 10

Data from Literature confirm our finding that longevity of CRT-D is shorter than that of VR and DR ICDs, which can be intuitively explained by the higher percentage of pacing, especially left-ventricular pacing, and by the device complexity.13,16,30

Battery end of life is the most frequent cause of device replacement interventions also in previous studies9,29,30. Only Thjissen et al.29 found higher percentages of substitution for erosion/infections and recalls, but their population included patients implanted with an ICD from calendar year 1996.

The trend toward a prolongation of service-life over the years, across all ICD types, has been highlighted in previous studies and is attributable to technology improvements. 9,29 The long-term effects of up-to-date ICD technology and programming should be evaluated in the future and compared with the longevity predicted by industry models.31

Since the cost of ICD therapy is typically characterized by the upfront cost of the device, at implant or replacement32, the positive trend in service-life that emerges in our analysis has important implications for the organization of care and for the financial resources spent for ICD therapy . The population across western countries is becoming older 33 and the lengthening of ICD service-life may allow to distribute the saved resources to a wider patient population.

**Study limitations**. The trend of service-life that we found could be explained by the characteristics of our “real –world” analyses, which includes the device replacements collected in a whole nation; it is plausible that a significative percentage of our patients received less device optimization if compared to patients enrolled in prospective studies and performed in selected centers. In particular, the Italian ICD registry did not consider the impact on service-life of large-scale implementation of up-to-date device programming, including long detection strategies and shock avoiding device settings.34–36 In addition, the effects on device longevity of the different pacing programming, percentage of atrial and ventricular pacing during the follow-up, number and type of ICD interventions (shock and/or ATP) were not analyzed in our study because not included in the queries of the Italian ICD Registry. Finally, we did not consider the ICD and CRT-D service-life according to the specific manufacturer because this type of analysis was not planned among the activities of the Italian ICD registry and could have been distorted by important technological inhomogeneities across a ten-year period. Similarly, other large and official ICD registries did not include in their reports a vendor analysis.37-38

CONCLUSIONS

The ten-year analysis from 2007 to 2016 of the National Italian ICD Registry showed that around 29 000 patients underwent ICD and CRT-D replacement and that the trend of ICD service-life, independently from ICD type, indication and settings, significantly improved over time. Moreover, the causes of replacement evolved over the ten-year period with a striking reduction of interventions required for CRT upgrading and infection/erosion in favor of battery end of life. The positive trend that emerged has important and favorable clinical, organizational and financial implications.

CONFLICT OF INTEREST  
GB reports speaker’s fees of small amount from Biotronik, Boehringer Ingelheim, Boston and Medtronic.

RPR reports minor consultancy fees by Medtronic, Boston Scientific and Dompé

ML reports modest speaker fees and modest advisory board grants from Boston Scientific, LivaNova and Medtronic.

SP, MZ, DF,MG, CL, DG and AP do not have any conflict of interest to disclose.

REFERENCES

1. Al-Khatib SM, Stevenson WG, Ackerman MJ, Bryant WJ, Callans DJ, Curtis AB, Deal BJ, Dickfeld T, Field ME, Fonarow GC, Gillis AM, Granger CB, Hammill SC, Hlatky MA, Joglar JA, Kay GN, Matlock DD, Myerburg RJ, Page RL. 2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *J Am Coll Cardiol*. 2018;72:e91–e220.

2. Priori SG, Blomström-Lundqvist C, Mazzanti A, Blom N, Borggrefe M, Camm J, Elliott PM, Fitzsimons D, Hatala R, Hindricks G, Kirchhof P, Kjeldsen K, Kuck K-H, Hernandez-Madrid A, Nikolaou N, Norekvål TM, Spaulding C, Van Veldhuisen DJ, ESC Scientific Document Group. 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;36:2793–2867.

3. Al-Khatib SM, Hellkamp A, Bardy GH, Hammill S, Hall WJ, Mark DB, Anstrom KJ, Curtis J, Al-Khalidi H, Curtis LH, Heidenreich P, Peterson ED, Sanders G, Clapp-Channing N, Lee KL, Moss AJ. Survival of Patients Receiving a Primary Prevention Implantable Cardioverter-Defibrillator in Clinical Practice vs Clinical Trials. *JAMA*. 2013;309:55.

4. Proclemer A, Muser D, Campana A, Zoni-Berisso M, Zecchin M, Locatelli A, Brieda M, Gramegna L, Santarone M, Chiodi L, Mazzone P, Rebellato L, Facchin D. Indication to cardioverter-defibrillator therapy and outcome in real world primary prevention. Data from the IRIDE [Italian registry of prophylactic implantation of defibrillators] study. *Int J Cardiol*. 2013;168:1416–1421.

5. Greenberg SM, Epstein AE, Deering T, Goldman DS, Ghidina M, Neason C, Proclemer A. A Comparison of ICD implantations in the United States versus Italy. *Pacing Clin Electrophysiol*. 2007;30 Suppl 1:S143-6.

6. Hauser RG. The growing mismatch between patient longevity and the service life of implantable cardioverter-defibrillators. *J Am Coll Cardiol*. 2005;45:2022–5.

7. Landolina M, Curnis A, Morani G, Vado A, Ammendola E, D’onofrio A, Stabile G, Crosato M, Petracci B, Ceriotti C, Bontempi L, Morosato M, Ballari GP, Gasparini M. Longevity of implantable cardioverter-defibrillators for cardiac resynchronization therapy in current clinical practice: an analysis according to influencing factors, device generation, and manufacturer. *Europace*. 2015;17:1251–1258.

8. Manolis AS, Maounis T, Koulouris S, Vassilikos V. “Real life” longevity of implantable cardioverter-defibrillator devices. *Clin Cardiol*. 2017;40:759–764.

9. von Gunten S, Schaer BA, Yap S-C, Szili-Torok T, Kühne M, Sticherling C, Osswald S, Theuns DAMJ. Longevity of implantable cardioverter defibrillators: a comparison among manufacturers and over time. *Europace*. 2016;18:710–717.

10. Seegers J, Expósito PM, Lüthje L, Fischer T, Lueken M, Wenk H, Sossalla ST, Hasenfuss G, Zabel M. Longevity of implantable cardioverter-defibrillators in a single-center population. *J Interv Card Electrophysiol*. 2015;44:179–86.

11. Shafat T, Baumfeld Y, Novack V, Konstantino Y, Amit G. Significant differences in the expected versus observed longevity of implantable cardioverter defibrillators (ICDs). *Clin Res Cardiol*. 2013;102:43–9.

12. Maisel WH. Pacemaker and ICD generator reliability: meta-analysis of device registries. *JAMA*. 2006;295:1929–34.

13. Landolina M, Morani G, Curnis A, Vado A, D’Onofrio A, Bianchi V, Stabile G, Crosato M, Petracci B, Ceriotti C, Bontempi L, Morosato M, Ballari GP, Gasparini M. The economic impact of battery longevity in implantable cardioverter-defibrillators for cardiac resynchronization therapy: the hospital and healthcare system perspectives. *Europace*. 2017;19:1349–1356.

14. Gadler F, Ding Y, Verin N, Bergius M, Miller JD, Lenhart GM, Russell MW. Economic impact of longer battery life of cardiac resynchronization therapy defibrillators in Sweden. *Clinicoecon Outcomes Res*. 2016;8:657–666.

15. Boriani G, Braunschweig F, Deharo JC, Leyva F, Lubiński A, Lazzaro C. Impact of extending device longevity on the long-term costs of implantable cardioverter-defibrillator therapy: a modelling study with a 15-year time horizon. *Europace*. 2013;15:1453–1462.

16. Boriani G, Merino J, Wright DJ, Gadler F, Schaer B, Landolina M. Battery longevity of implantable cardioverter-defibrillators and cardiac resynchronization therapy defibrillators: technical, clinical and economic aspects. An expert review paper from EHRA. *Europace*. 2018;20:1882–1897.

17. Proclemer A, Ghidina M, Gregori D, Facchin D, Rebellato L, Fioretti P, Brignole M. Impact of the main implantable cardioverter-defibrillator trials in clinical practice: data from the Italian ICD Registry for the years 2005-07. *Europace*. 2009;11:465–75.

18. Proclemer A, Ghidina M, Facchin D, Rebellato L, Corrado D, Gasparini M, Gregori D. Use of implantable cardioverter-defibrillator in inherited arrhythmogenic diseases: data from Italian ICD Registry for the years 2001-6. *Pacing Clin Electrophysiol*. 2009;32:434–45.

19. Proclemer A, Zecchin M, D’Onofrio A, Boriani G, Botto GL, Facchin D, Rebellato L, Ghidina M, Bianco G, Bernardelli E, Pucher E, Gregori D. [The Pacemaker and Implantable Cardioverter-Defibrillator Registry of the Italian Association of Arrhythmology and Cardiac Pacing - Annual report 2015]. *G Ital Cardiol*. 2017;18:67–79.

20. R Core Team. R: A language and environment for statistical computing. R Found. Stat. Comput. Vienna, Austria. 2018.

21. Harrell FE. rms: Regression Modeling Strategies. ﻿R package version 5.1-2. 2018.

22. Poole JE, Gleva MJ, Mela T, Chung MK, Uslan DZ, Borge R, Gottipaty V, Shinn T, Dan D, Feldman LA, Seide H, Winston SA, Gallagher JJ, Langberg JJ, Mitchell K, Holcomb R. Complication Rates Associated With Pacemaker or Implantable Cardioverter-Defibrillator Generator Replacements and Upgrade Procedures. *Circulation*. 2010;122:1553–1561.

23. Ricci R Pietro, Morichelli L, Varma N. Remote Monitoring for Follow-up of Patients with Cardiac Implantable Electronic Devices. *Arrhythmia Electrophysiol Rev*. 2014;3:123.

24. Varma N, Ricci R Pietro. Telemedicine and cardiac implants: what is the benefit? *Eur Heart J*. 2013;34:1885–95.

25. Varma N, Love CJ, Schweikert R, Moll P, Michalski J, Epstein AE, TRUST Investigators. Automatic remote monitoring utilizing daily transmissions: transmission reliability and implantable cardioverter defibrillator battery longevity in the TRUST trial. *Europace*. 2018;20:622–628.

26. Schmier JK, Lau EC, Patel JD, Klenk JA, Greenspon AJ. Effect of battery longevity on costs and health outcomes associated with cardiac implantable electronic devices: a Markov model-based Monte Carlo simulation. *J Interv Card Electrophysiol*. 2017;50:149–158.

27. Biffi M, Menardi E, Narducci ML, Ammendola E, Messano L, Giofrè F, Baiocchi C, Saporito D, Lissoni F, Bertini M, Pierantozzi A, Zingarini G, Malacrida M, Ziacchi M. Manufacturer change and risk of system-related complications after implantable cardioverter defibrillator replacement. *J Cardiovasc Med*. 2017;18:968–975.

28. Diemberger I, Biffi M, Martignani C, Boriani G. From lead management to implanted patient management: indications to lead extraction in pacemaker and cardioverter-defibrillator systems. *Expert Rev Med Devices*. 2011;8:235–55.

29. Thijssen J, Borleffs CJW, van Rees JB, Man S, de Bie MK, Venlet J, van der Velde ET, van Erven L, Schalij MJ. Implantable cardioverter-defibrillator longevity under clinical circumstances: An analysis according to device type, generation, and manufacturer. *Heart Rhythm*. 2012;9:513–519.

30. Zanon F, Martignani C, Ammendola E, Menardi E, Narducci ML, DE Filippo P, Santamaria M, Campana A, Stabile G, Potenza DR, Pastore G, Iori M, LA Rosa C, Biffi M. Device Longevity in a Contemporary Cohort of ICD/CRT-D Patients Undergoing Device Replacement. *J Cardiovasc Electrophysiol*. 2016;27:840–5.

31. Munawar DA, Mahajan R, Linz D, Wong GR, Khokhar KB, Thiyagarajah A, Kadhim K, Emami M, Mishima R, Elliott AD, Middeldorp ME, Roberts-Thompson KC, Young GD, Sanders P, Lau DH. Predicted longevity of contemporary cardiac implantable electronic devices: A call for industry-wide “standardized” reporting. *Heart Rhythm*. 2018;15:1756–1763.

32. Boriani G, Maniadakis N, Auricchio A, Müller-Riemenschneider F, Fattore G, Leyva F, Mantovani L, Siebert M, Willich SN, Vardas P, Kirchhof P. Health technology assessment in interventional electrophysiology and device therapy: a position paper of the European Heart Rhythm Association. *Eur Heart J*. 2013;34:1869–74.

33. Timmis A, Townsend N, Gale C, Grobbee R, Maniadakis N, Flather M, Wilkins E, Wright L, Vos R, Bax J, Blum M, Pinto F, Vardas P, ESC Scientific Document Group. European Society of Cardiology: Cardiovascular Disease Statistics 2017. *Eur Heart J*. 2018;39:508–579.

34. Moss AJ, Schuger C, Beck CA, Brown MW, Cannom DS, Daubert JP, Estes NAM, Greenberg H, Hall WJ, Huang DT, Kautzner J, Klein H, McNitt S, Olshansky B, Shoda M, Wilber D, Zareba W, MADIT-RIT Trial Investigators. Reduction in inappropriate therapy and mortality through ICD programming. *N Engl J Med*. 2012;367:2275–83.

35. Gasparini M, Proclemer A, Klersy C, Kloppe A, Lunati M, Ferrer JBM, Hersi A, Gulaj M, Wijfels MCEF, Santi E, Manotta L, Arenal A. Effect of long-detection interval vs standard-detection interval for implantable cardioverter-defibrillators on antitachycardia pacing and shock delivery: the ADVANCE III randomized clinical trial. *JAMA*. 2013;309:1903–11.

36. Saeed M, Hanna I, Robotis D, Styperek R, Polosajian L, Khan A, Alonso J, Nabutovsky Y, Neason C. Programming implantable cardioverter-defibrillators in patients with primary prevention indication to prolong time to first shock: results from the PROVIDE study. *J Cardiovasc Electrophysiol*. 2014;25:52–9.

37. Gupta N, Kiley ML, Anthony F, Young C, Brar S, Kwaku K. Multi-Center, Community-Based Cardiac Implantable Electronic Devices Registry: Population, Device Utilization, and Outcomes. *J Am Heart Assoc*. 2016;5:e002798.

38.Desai NR, Bourdillon PM, Parzynski CS, Brindis RG, Spatz ES, Masters C, Minges KE, Peterson P, Masoudi FA, Oetgen WJ, Buxton A, Zipes DP, Curtis JP. Association of the US Department of Justice Investigation of Implantable Cardioverter-Defibrillators and Devices Not Meeting the Medicare National Coverage Determination, 2007-2015. *JAMA*. 2018;320:63-71

Table 1. Distribution of patients who underwent ICD replacement in the period 2007-2016, according to the type of implanted device and indication to first ICD implantation. P<0,001. Data are expressed as count and percentage.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Primary Prevention** | **Secondary Prevention** | **Combined** |
| **ICD-VR** | 3797 (20.2%) | 3278 (31.7%) | 7075 (24.3%) |
| **ICD-DR** | 4733 (25.1%) | 3478 (33.6%) | 8211 (28.2%) |
| **CRT-D** | 10284 (54.7%) | 3588 (34.7%) | 13872 (47.5%) |
| **Combined** | 18814 (100%) | 10344 (100%) | 29158 (100%) |

Table 2. Demographic characteristics of the population and distribution of patients according to the underlying heart disease and device characteristics. Data are expressed as mean ± standard deviation or as count and percentage, as appropriate.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **ICD-VR** | **ICD-DR** | **CRT-D** | **COMBINED** |
| **Age (years)** | 61.3±14.4 | 64.3±12.6 | 67.7±9.7 | 65.2±12.1 |
| **Male Gender** | 5814  (82.2%) | 6849  (83.4%) | 10916  (78.7%) | 23579  (80.9%) |
| **Ischemic Cardiomyopathy** | 3797 (53.7%) | 4447 (54.2%) | 5836 (42.1%) | 14080 (48.3%) |
| **Non-Ischemic Cardiomyopathy** | 2157 (30.5%) | 2612 (31.8%) | 7393 (53.3%) | 12162 (41.7%) |
| **Hypertrophic Cardiomyopathy** | 185 (2.6%) | 296 (3.6%) | 80  (0.6%) | 561 (1.9%) |
| **Arrhythmogenic Ventricular**  **Cardiomyopathy.** | 125 (1.8%) | 118 (1.4%) | 30 (0.2%) | 273 (0.9%) |
| **Other Cardiomyopathies** | 241 (3.4%) | 304 (3.7%) | 284 (2.0%) | 829 (2.8%) |
| **Valvular Heart Disease** | 114 (1.6%) | 121 (1.5%) | 249 (1.8%) | 484 (1.7%) |
| **Long QT Syndrome** | 60 (0.8%) | 74 (0.9%) | 0 (0.0%) | 134 (0.5%) |
| **Idiopathic Arrhythmias** | 396 (5.6%) | 239 (2.9%) | 0 (0.0%) | 635 (2.2%) |

Table 3. Causes of replacement according to devices’ characteristics and indication to implantation. Data are expressed as count and percentage.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Primary Prevention**  **P<0,001** | | | **Secondary Prevention**  **P<0,001** | | | **Combined** |
| ICD-VR | ICD-DR | CRT-D | ICD-VR | ICD-DR | CRT-D |  |
| **Battery End of Life** | 2650 (69.8%) | 3502 (74.0%) | 9470 (92.1%) | 2297 (70.1%) | 2602 (74.8%) | 3302 (92.0%) | 23823  (81,7%) |
| **Recall/System Malfunction** | 35 (0.9%) | 59 (1.2%) | 120 (1.2%) | 53 (1.6%) | 51 (1.5%) | 36 (1.0%) | 354  (1.2%) |
| **CRT Upgrading** | 781 (20.6%) | 824 (17.4%) | 0  (0,0%) | 702 (21.4%) | 565 (16.2%) | 0  (0.0%) | 2872  (9.8%) |
| **Infection/Erosion** | 46 (1.2%) | 80 (1.7%) | 182 (1.8%) | 38 (1.2%) | 66 (1.9%) | 73 (2.0%) | 485  (1.6%) |
| **Not Available** | 285 (7.5%) | 268 (5.7%) | 512 (5.0%) | 188 (5.7%) | 194 (5.6%) | 177 (4.9%) | 1624  (5.6%) |

Table 4. Causes of replacement before and from calendar 2012 year. P<0,001. Data are expressed as count and percentage.

|  |  |  |
| --- | --- | --- |
|  | **Explantation before calendar 2012 year** | **Explantation from**  **calendar 2012 year** |
| **Battery End of Life** | 9424 (72.4%) | 13602 (84.2%) |
| **CRT Upgrading** | 2141 (16.5%) | 1528 (9.5%) |
| **Infection-Erosion** | 288 (2.2%) | 197 (1.2%) |
| **Recall/System malfunction** | 163 (1.3%) | 191 (1.2%) |
| **Not Available** | 997 (7.7%) | 627 (3.9%) |

Supplementary Table 1.Service life of the devices (months) subdivided per year of replacement and according to the ICD type and ICD indications. Data are expressed as median value with interquartile range (IQR).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Year of Explantation** | **ICD-VR** | **ICD-DR** | **CRT-D** | **Primary Prevention** | **Secondary Prevention** | **Combined** |
| **2007** | 55.0  IQR 29.7 | 48.3  IQR 21.6 | 36.4  IQR 19.3 | 42.2  IQR 28.1 | 48.7  IQR 27.9 | 45.8  IQR 28.6 |
| **2008** | 59.2  IQR 30.4 | 50.9  IQR 25.2 | 40.1  IQR 15.5 | 43.8  IQR 24.1 | 49.1  IQR 27.1 | 46.6  IQR 25.7 |
| **2009** | 57.9  IQR 32.4 | 53.7  IQR 22.0 | 44.1  IQR 16.6 | 47.2  IQR 21.2 | 51.4  IQR 24.6 | 48.7  IQR 23.3 |
| **2010** | 62.2  IQR 26.2 | 58.4  IQR 26.2 | 47.7  IQR 17.9 | 51.6  IQR 22.6 | 56.0  IQR 24.7 | 52.9  IQR 23.7 |
| **2011** | 64.1  IQR 26.9 | 63.2  IQR 27.2 | 48.8  IQR 17.9 | 53.7  IQR 24.6 | 57.4  IQR 27.4 | 54.7  IQR 25.6 |
| **2012** | 68.1  IQR 28.3 | 65.6  IQR 21.8 | 50.7  IQR 16.8 | 56.8  IQR 22.15 | 58.2  IQR 26.7 | 57.2  IQR 23.5 |
| **2013** | 71.6  IQR 31.6 | 68.4  IQR 21.4 | 53.9  IQR 19.8 | 59.7  IQR 24.8 | 63.7  IQR 27.8 | 60.6  IQR 25.6 |
| **2014** | 80.8  IQR 35.7 | 71.3  IQR 24.7 | 58.3  IQR 20.6 | 63.1  IQR 28.1 | 66.9  IQR 31.3 | 64.2  IQR 29.3 |
| **2015** | 89.8  IQR 27.6 | 70.6  IQR 24.3 | 59.2  IQR 20.4 | 64.8  IQR 27.0 | 67.3  IQR 30.8 | 65.4  IQR 27.7 |
| **2016** | 87.6  IQR 30.2 | 77.0  IQR 22.1 | 61.5  IQR 19.0 | 67.2  IQR 27.2 | 70.7  IQR 28.3 | 68.1  IQR 27.7 |
| **p for trend** | <0.001 | <0.001 | <0.001 | <0.001 | <0,001 | <0,001 |

FIGURES

Figure 1. Distribution of service-life (months) of ICD/CRT-D devices according to ICD indication and devices’ characteristics. Box borders represent the I and III quartile of the distribution, the segment inside the box represent the median value of the distribution, the vertical lines above and below the box extend up to 1.5 times the Inter-Quaritle Range (IQR, i.e., the heigth of the box), observations that excede 1.5 times the IQR are considered outliers and they are drawn as singular dots. Boxes are drawn with widths proportional to the square-roots of the number of observations in the groups.

In detail, the median service life was: a)Primary Prevention: ICD-VR 67.5 IQR 37.6 months, ICD-DR 64.6 IQR 28.0 months, CRT-D 51.9 IQR 20.5 months; b) Secondary Prevention: ICD-VR 66.2 IQR 33.6 months, ICD-DR 61.9 IQR 27.2 months, CRT-D 49.1 IQR 20.8 months.

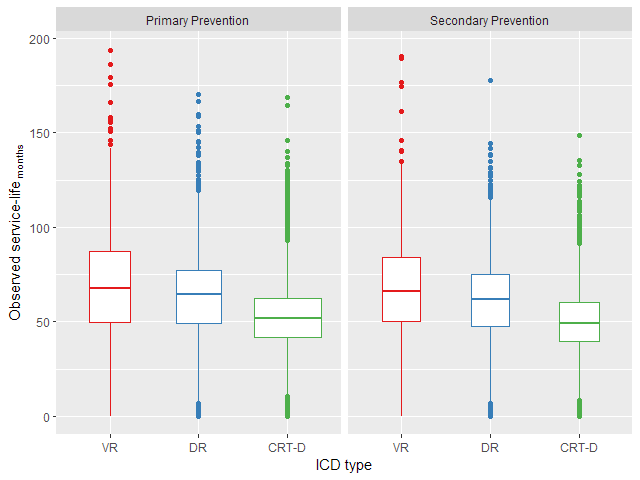


Figure 2. Trends of the ICD service-life’s distributions across the years according to ICD type.

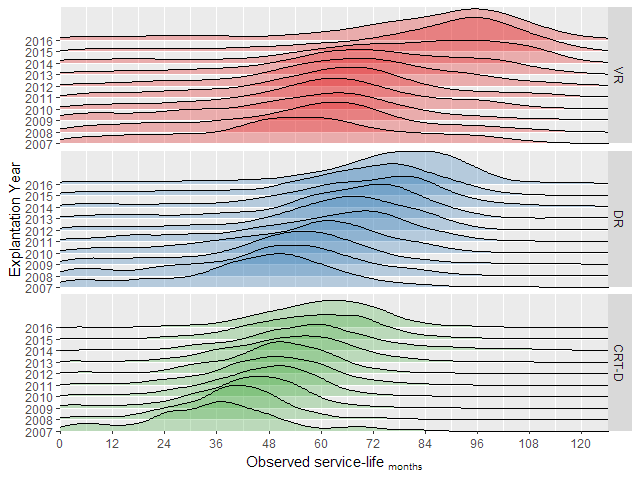


Figure 3. Model fitted by ICD type: trend of the expected service-life as modelled by the years.Vertical bars represent the original data. Shadows represent the 95% confidence interval for the drowned lines.

