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Practice Guidelines

Do all patients with implantable cardioverter defibrillator need a generator change? A health service evaluation of patients who underwent generator changes from a single tertiary center

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ABSTRACT

Background: The patient characteristics, therapy received and outcomes after one or more implantable cardioverter defibrillator (ICD) generator changes from contemporary practice is not well known.
Methods: We conducted a health service evaluation of patients who underwent ICD implantation and generator change. Patients who had generator changes from February 2016 to October 2019 were identified from our database and electronic records were reviewed for patient characteristics, number of generator changes, receipt of therapy and death.
Results: Our database included 88 patients with a generator change. A total of 22 patients (25.0%) received dual chamber ICD, 10 patients (11.4%) received single chamber ICD, 54 patients (61.3%) received cardiac resynchronization therapy defibrillator and 2 patients (2.3%) received subcutaneous ICD. A second generator change occurred in 18 patients and a third generator changes was performed in 6 patients. There were 29 deaths and a follow up period of 9.4 ± 2.9 years. From implant to initial generator change 39 patients had appropriate antitachycardia pacing (ATP), 6 patient had inappropriate ATP, 29 patients had appropriate shocks and 5 patients had an inappropriate shock. Between the 1st and 2nd generator change and the 2nd and 3rd there were no cases of inappropriate ATP or shock. Overall, 42 patients out of the 88 had appropriate therapy (47.7%) and 7 patients had inappropriate therapy (8.0%).
Conclusions: Most patients with ICDs do not receive therapy and a minority have inappropriate therapy which typically occur before the first generator change as we observed no inappropriate therapy beyond the first generator change.

1. Introduction

Implantable cardioverter defibrillators (ICD) are devices that are implanted in the body and used to treat ventricular arrhythmias. They are a life-saving therapy for patients at risk of sudden cardiac death which are indicated in cardiac arrest survivors with sustained ventricular tachycardia, patients with myocardial infarction/non-ischemic cardiomyopathy and severely impaired left ventricular (LV) function [1]. Currently, there are options in terms of ICD device to implant which include ICD-DR (dual chamber), ICD-VR (single chamber), cardiac resynchronization therapy (CRT) defibrillators and newer subcutaneous ICD devices. While manufacturers of ICD report a 5 to 9-year projected longevity, a study of 685 patients with ICD found that 238 patients required ICD pulse generator replacement and the mean ICD longevity was 4.9 years and 8% had premature battery depletion by 3 years [2]. In 2011, the average cost of a complete ICD system was estimated to be £9692 while a CRT-D system is estimated to be £12,293 [3].

Few studies have evaluated patients with box or generator changes after ICD implantation. Studies have been conducted that

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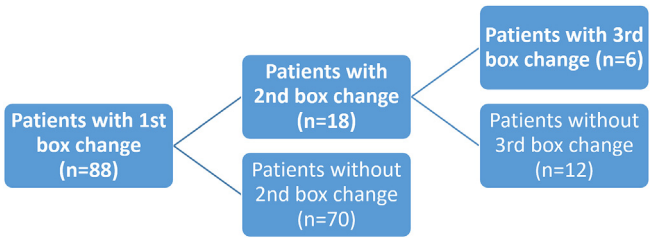

Fig. 1. Shows the flow diagram of generator or box changes. Of the 88 patients with a high-power device who underwent generator change out, a second generator change occurred in 18 patients and a third generator change was undertaken in 6 patients.

evaluate the cost-effectiveness of upgrade at time of generator change [4], infections [5], lead survival [6], generator longevity in CRT-D devices [7], appropriateness of generator replacement in Brugada syndrome [8] and arrhythmic events with CRT elective generator change [9] and complications with repeat ICD procedures [10]. The literature on patient characteristics, therapy received and outcomes after one or more ICD generator changes from contemporary practice is not well known. The question whether patients continue to need generator changes over long period of times remains unclear. Therefore, we conducted a health service evaluation of patients with ICD devices who underwent generator changes and evaluated therapies received, the appropriateness of the therapies and patient outcomes.

2. Methods

Royal Stoke Hospital is a tertiary cardiac center, serving a population of ~700,000. Annually, approximately 1600 cardiac implantable electronic devices are implanted of which 300 are ICD. We studied consecutive patients implanted with ICD in our database who underwent generator change out between February 2016 to February 2018. We reviewed electronic patient records as part of a health service evaluation on ICD generator changes and collected anonymized data on patient and procedural characteristics (type of device, indication, age, sex, electrocardiogram rhythm, QRS duration, LV function, smoking status, family history of heart disease, type of cardiomyopathy, hypertension, hypercholesterolemia, diabetes mellitus, adult congenital heart disease and medications. Additional data was collected on the number of generator changes, use of antitachycardia pacing (ATP) or shocks and the appropriateness of these therapies. Further data was collected on occurrence of ventricular tachycardia (VT) ablation, mortality and cause of death.

Statistical analysis was performed on Stata 15 (College Station, Texas, USA) and Microsoft Excel. Descriptive statistics and the number of ATP or shocks that were administered in the cohort were presented in Tables. A flow diagram was used to show the proportion of patients having generator changes. Other outcomes such as VT ablation and death were described narratively. In addition, we performed stratified analysis for appropriate and inappropriate ATP and shock according to primary prevention/secondary prevention, ICD/CRT-D and ischaemic/non-ischaemic cardiomyopathy. Multiple logistic regressions with adjustments for patient variables were used to determine the variables associated with ATP and shock.

3. Results

Our database of ICD devices with generator changes included 88 patients (Fig. 1). The baseline characteristics of these patients are shown in Table 1. At generator change-out, 22 patients (25.0%) received ICD-DR, 10 patients (11.4%) received ICD-VR, 54 patients (61.3%) received CRT-D and 2 patients (2.3%) received subcutaneous ICD. There were more patients secondary compared to primary prevention devices (55.7% vs 44.3%). The mean age of the participants was 71 years and a vast majority (81.8%) were male. The proportion of patients with atrial fibrillation and left bundle branch block were 25.0% and 55.7%, respectively and the QRS duration was prolonged in 64.8% of patients. For patients with CRT-D device, 47/52 (90.4%) had LBBB, 1/52 (1.9%) had IVCD, 1/52 had narrow QRS, 1/52 (1.9%) had RBBB and 2/52 (3.7%) patients had paced rhythms. More than two-thirds of patients had severely impaired left ventricular systolic function (68.2%) and majority of patients never smoked (78.4%). Considering normal as 60%, mild as 50%, moderate as 40% and severe as 30%, the mean LV ejection fraction for the cohort would be 36%. The left ventricular function at first generator replacement according to implantable cardioverter defibrillator or cardiac resynchronization therapy-defibrillator is shown in Supplementary Table 1. Majority of patients had ischemic cardiomyopathy (69.3%) while a smaller portion had dilated cardiomyopathy (21.6%). β-Blockers (89.8%), angiotensin converting enzyme inhibitors (76.1%), diuretics (55.7%) and spironolactone (35.2%)

Table 1
Characteristics of patients.

Variable	n (%)
Device implanted	
ICD-DR	22 (25.0%)
ICD-VR	10 (11.4%)
CRT-D	54 (61.3%)
S-ICD	2 (2.3%)
Indication	
Primary prevention	39 (44.3%)
Secondary prevention	49 (55.7%)
Mean age (years)	71 ± 12
Male	72 (81.8%)
Electrocardiogram	
Sinus rhythm	65 (73.9%)
Atrial fibrillation	22 (25.0%)
Atrial flutter	1 (1.1%)
Left bundle branch block	49 (55.7%)
Right bundle branch block	4 (4.5%)
QRS duration >120 ms	57 (64.8%)
Left ventricular function at device implant	
Normal	10 (11.4%)
Mildly impaired	8 (9.1%)
Moderately impaired	10 (11.4%)
Severely impaired	60 (68.2%)
Smoking status	
Never	69 (78.4%)
Ex-smoker	8 (9.1%)
Current smoker	11 (12.5%)
Family history of heart disease	11 (12.5%)
Ischemic cardiomyopathy	61 (69.3%)
Dilated cardiomyopathy	19 (21.6%)
Hypertension	40 (45.5%)
Hypercholesterolaemia	31 (35.2%)
Diabetes mellitus	22 (25.0%)
Adult congenital heart disease	1 (1.1%)
Medications	
Angiotensin converting enzyme inhibitor	67 (76.1%)
Angiotensin receptor blocker	16 (18.2%)
β-Blocker	79 (89.8%)
Digoxin	14 (15.9%)
Spironlactone	31 (35.2%)
Eplerenone	7 (8.0%)
Entresto	5 (5.7%)
Diuretics	49 (55.7%)
Hydralazine	2 (2.3%)
Nitrates	14 (15.9%)

ICD-DR = dual chamber implantable cardioverter defibrillator, ICD-VR = single chamber implantable cardioverter defibrillator, CRT-D = cardiac resynchronization therapy defibrillator, *S*-ICD = subcutaneous implantable cardioverter defibrillator.

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were the most common prescribed medications.

Between the study duration of February 24, 2016 to October 1, 2019 there were 29 deaths and a total follow up period of 9.4 ± 2.9 years (time of first implant to study period).

The breakdown of ATP and shocks between the periods up to generator change 1 between generator change 1 and 2 and between generator change 2 and 3 are shown in Table 2. Up to generator change 1 there were 39 patients with appropriate ATP and 6 patient with inappropriate ATP and there were 29 patients with appropriate shock and 5 patients with inappropriate shocks. Between the 1st and 2nd generator change and the 2nd and 3rd there were no cases of inappropriate ATP or shock.

Overall, 42 patients out of the 88 had appropriate therapy (47.7%) and 7 patients had inappropriate therapy (8.0%). During the follow up period 14 patients had underwent ventricular tachycardia ablations (15.9%).

The results for appropriate and inappropriate therapies stratified by primary prevention/secondary prevention, ICD/CRT-D and ischaemic/non-ischaemic cardiomyopathy are shown in Supplementary Table 2.

The significant variables associated with reduced odds of ATP were ischemic cardiomyopathy (OR 0.039 95%CI 0.003–0.542, $p = 0.016$), primary prevention (OR 0.058 95%CI 0.006–0.616, $p = 0.018$), diabetes (OR 0.066 95%CI 0.008–0.550, $p = 0.012$) and digoxin use (OR 0.018 95%CI 0.001–0.377, $p = 0.010$). Impaired left ventricular function that was mildly impaired (OR 69.33 95%CI 1.21–3965.05) and severely impaired (OR 267.97 95%CI 3.93–18,268.44) was associated with more ATP compared to normal left ventricular function. The only variable associated with a significant difference in shock was a reduction in odds of shock with primary prevention (OR 0.026 95%CI 0.002–0.297, $p = 0.003$).

There were 29 deaths among the 88 patients. Twenty-two patients died after the first generator change and the reasons they died were two for cancer, seven for heart failure, four for pneumonia, one for STEMI, three sudden cardiac arrest and five for unknown reasons. Four patients died after the second generator change because of heart failure, pneumonia and two patients with sudden cardiac arrest. Three patients died after the third generator change because of COPD, cancer and infective endocarditis.

4. Discussion

Our evaluation of ICD at a large tertiary cardiac center in the United Kingdom has several key findings. First, majority of patients are receiving CRT-D devices and the main pathology of patients is ischemic cardiomyopathy. Second, during a follow up of over 9 years - less than half (47.7%) of patients received appropriate therapy while 8.0% had inappropriate therapy. Third, observations from our practice suggest that most inappropriate therapy are delivered up to the first generator change and as there were no instances of inappropriate therapy after the first generator change. Finally, there were 33.3% deaths among the ICD/CRT-D examined in this evaluation.

Our evaluation adds to the existing literature on ICD generator changes. One decision tree study used previously published data to show that implanting low-risk patients with a resynchronization defibrillator at time of generator change was not cost-effective according the National Health Service Criteria in the United Kingdom [4]. One of the risks of generator change out is infection, which is higher compared to initial device implantation and primarily thought to be attributable to pocket colonization after repeat device procedures [5]. In addition, another large study for the National Cardiovascular Data Registry found that complication rates are higher for revision of a lead with our without extraction compared to pocket-only procedures such as generator changes [10]. However, another study of Brugada syndrome patients suggests that even though patients had no episodes of ICD therapy before generator change this could not guarantee a safe clinical course so ICD generator replacements should be considered in this group of patients [8]. In general, it is accepted that once a patient has an indication for high powered device the indication persists indefinitely. The question remains whether improvement in left ventricular function to near normal can predict low risk of future sudden cardiac death at the time of generator changes remains unclear in heart failure patients. The only other grounds for not performing the generator change would be poor life expectancy or significant frailty where a depleted battery may be deactivated and not replaced. Our evaluation adds to this literature by providing a description of patients who have generator changes while also highlighting what happens to patients in terms of appropriate and inappropriate therapies in contemporary practice.

Our findings may be explained by a few reasons. First, coronary heart disease is the is the most common cause of left ventricular dysfunction so it is not surprising that the main indication for ICD and CRT-D implantation was for ischemic cardiomyopathy. Second, most patients with these devices have appropriate therapy while a small proportion have inappropriate therapy. This may reflect better selection of patients that may benefit from these devices as well as better monitoring and adjustments of implanted devices in order to provide the least harm from inappropriate treatments in contemporary practice. This is supported by our observation that after the first generator change there were no episodes of inappropriate therapy which may suggest that cardiac physiologists have optimally programmed the devices to minimize adverse events. MADIT-RIT demonstrated that programming of ICD therapies for tachyarrhythmias of 200 beats per minute or higher or with a prolonged delay in therapy at 170 beats per minute or higher, as compared with conventional programming, was associated with reductions in inappropriate therapy and all-cause mortality during long-term follow-up [11]. Finally, the group of patients receiving ICD are, by their very nature, at high risk of mortality and in the current evaluation 33.3% of patients died over 9 years. This likely reflect the demographics of the population where there were more patients who had ICD for secondary prevention after severe impairment of LV function as oppose to patients with ventricular arrhythmias in the context of lesser degrees of LV dysfunction requiring secondary prevention ICD.

One key study worth discussing is the two center study of 253 patients by Madhavan et al. [12] In this study 26.9% of patients experienced appropriate therapy while in the current study 47.7%

Table 2
Antitachycardia pacing and shock in the cohort.

Variable	Up to 1st generator change (n = 88)	Between 1st and 2nd generator change (n = 18)	Between 2nd and 3rd generator change (n = 6)
Any appropriate ATP	39/88	9/18	5/6
Any inappropriate ATP	6/88	0/18	0/6
Any appropriate shock	29/88	7/18	2/6
Any inappropriate shock	5/88	0/18	0/6

ATP = antitachycardia pacing.

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of patients received appropriate therapy. In addition to our study being a more contemporary cohort, the major differences between Madhavan et al. and the current study is that Madhavan et al. excluded patients with CRT-D devices and only included patients under a primary prevention indication. Furthermore, the higher proportion of non-ischemic cardiomyopathy in the current cohort (33.0% vs 17.3%) and even among patients with non-CRT devices the proportion receiving appropriate therapy was 52.8%. We have also built on the findings of their study by considering second and third box changes. Their study found that low EF was predictive of appropriate ICD therapy after generator replacement (HR 1.96 95% CI 1.35–2.87, per 10% decrement) [12]. Our study shows similar findings as severe left ventricular function compared to normal left ventricular function was the strongest variable associated with appropriate shock therapy (OR 267.97 95%CI 3.93–18,268.44). In the current study the one third of patients (29/88, 33.0%) died which is similar to the rate reported by Madhavan et al. (90/253, 35.6%) [12]. Ultimately, the receipt of appropriate therapy and mortality rate likely depends on patient selection and their characteristics and some variation can be expected depending on the site where the study took place.

There are a few considerations regarding the findings of this evaluation. One of the issues with considering benefit in terms of appropriate therapy of ICD devices is the competing risk of death. As observed in our cohort the mortality rate over 2 years is high (33%) and patients that die will not benefit from having such therapy. Even though rates of mortality are high, our evaluation does not capture potential benefit in terms of symptoms of patients with the cardiac resynchronization therapy. As these high-power devices are more costly, the benefits of these devices should outweigh the cost or risks to patients. We also highlight that there are patients in contemporary practice that do well and have more than one generator change and there is a proportion that go onto have ventricular tachycardia ablation procedures. Furthermore, historically, transvenous systems were the only high-power devices available for clinical use, however our review included 2 patients with a subcutaneous ICD. While these systems offer defibrillation function similar to transvenous systems, they lack the pacing function of transvenous ICD devices and option of upgrading to cardiac resynchronization therapy so their role may be more limited in patients with heart failure [13].

The MADIT-II trial has shown that ICD therapy is associated with a significant reduction in risk of death during the early phase of follow up (up to 4 years) with continued life-saving benefit between 5 and 8 years [14]. In our study, we were able to follow up patients on average beyond 9 years and it is expected that patients will continue benefit from ICD therapy so there will be need continued need for generator change procedures as these devices have a 5- to 9- years projected longevity.

The challenge remains how to best risk stratify patients who did not have any ICD therapies at generator change in order to avoid generator changes due to risk of infections, shocks and cost. In our current analysis we are not able to answer this but it is important as we observed that more than half of patients in our cohort did not have any appropriate therapy during the follow-up period.

Our evaluation has several limitations. First, this retrospective audit was done at a single tertiary center so there is not a large sample size. Second, there was significant missing data for cause of death as only one-third of causes were available.

In conclusions, in contemporary practice, the most common ICD devices implanted are CRT-D devices for heart failure patients with ischemic cardiomyopathy. Most patients with ICD devices do not receive therapy and a minority have inappropriate therapy which typically occur before the first generator change as we observed no inappropriate therapy beyond the first generator change.

List of supports/grants information

None.

Declaration of competing interest

None.

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None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ipej.2020.08.003.

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