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A propensity matched case–control study comparing efficacy, safety and costs of the subcutaneous vs. transvenous implantable cardioverter defibrillator

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ABSTRACT

Background: Subcutaneous implantable cardioverter defibrillators (S-ICD) have become more widely available. However, comparisons with conventional transvenous ICDs (TV-ICD) are scarce.
Methods: We conducted a propensity matched case–control study including all patients that underwent S-ICD implantation over a five-year period in a single tertiary centre. Controls consisted of all TV-ICD implant patients over a contemporary time period excluding those with pacing indication, biventricular pacemakers and those with sustained monomorphic ventricular tachycardia requiring anti-tachycardia pacing. Data was collected on device-related complications and mortality rates. A cost efficacy analysis was performed.
Results: Sixty-nine S-ICD cases were propensity matched to 69 TV-ICD controls. During a mean follow-up of 31 ± 19 (S-ICD) and 32 ± 21 months (TV-ICD; p = 0.88) there was a higher rate of device-related complications in the TV-ICD group predominantly accounted for by lead failures (n = 20, 29% vs. n = 6, 9%; p = 0.004). The total mean cost for each group, including the complication-related costs was £9967 ± 4511 ($13,639 ± 6173) and £12,601 ± 1786 ($17,243 ± 2444) in the TV-ICD and S-ICD groups respectively (p = 0.0001). Even though more expensive S-ICD was associated with a relative risk reduction of device-related complication of 70% with a HR of 0.30 (95%CI 0.12–0.76; p = 0.01) compared to TV-ICDs.
Conclusions: TV-ICDs are associated with increased device-related complication rates compared to a propensity matched S-ICD group during a similar follow-up period. Despite the existing significant difference in unit cost of the S-ICD, overall S-ICD costs may be mitigated versus TV-ICDs over a longer follow-up period.

1. Introduction

The implantable cardioverter defibrillator (ICD) is a well-established treatment for the prevention of sudden cardiac death (SCD) [1–3]. Over 300,000 transvenous ICDs (TV-ICD) are implanted worldwide per annum [4]. However, these devices have been associated with early and long-term complications [5–10]. Device-related infection rates of between 0.67 and 1.49% have been reported over a three to 12 month follow-up period [5,6,8]. Overall pooled complication rates secondary mainly to lead displacement, hematoma, pneumothorax (excluding inappropriate shocks) of 9%, are reported in randomized controlled trials [11]. Long-term lead failure rates of up to 20% have been reported over a ten-year period [12]. These complications are recognized to have a financial impact [13,14].

Subcutaneous ICDs (S-ICDs) were introduced into clinical practice initially to treat those patients where venous access is not feasible due to their underlying anatomy, such as in congenital heart disease limiting the introduction of intracardiac leads, and young adults where lead longevity and the possible need of lead extraction in the future is a concern [15]. Preliminary results suggest that these devices are safe and effective [16–18].

As of yet there is minimal data available directly comparing S-ICDs and TV-ICDs in terms of complication rates [19,10]. From a cost-efficacy perspective S-ICDs are initially more expensive than conventional TV-ICDs at implant. However, the impact of potential differences in long-term complication rates on the overall cost has not yet been addressed.

We conducted a propensity matched case (S-ICD)-control (TV-ICD) study with the aims to i) compare the safety and efficacy during a long-term follow-up between these two groups ii) perform a cost efficacy analysis evaluating whether the initial implant costs are balanced by the long-term economic impact of device-related complications.

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2. Method

2.1. Sample characterization

We included all patients that underwent S-ICD implantation over a five-year period in a single tertiary center. These were defined as the cases. The controls used in the propensity match included all patients that underwent TV-ICD implantation over a contemporary period in the same centre. Patients who had a concomitant pacing indication, biventricular devices, documentation of sustained monomorphic ventricular tachycardia (VT) likely to require anti-tachycardia pacing (ATP), and advisory transvenous leads were excluded. Using electronic and paper records we collected data on baseline characteristics including age, gender, diabetes, hypertension, chronic kidney disease (defined as stage 4 or 5), and left ventricular ejection fraction (EF). Data was also collected on the underlying cardiac etiology and the indication of the ICD implant i.e. primary or secondary prevention. Propensity score matching employing the factors in Table 1 and with a 1:1 ratio was used to obtain a control group of TV-ICDs and assure that S-ICDs and their contemporary controls were similar in all baseline variables. Probabilities in the S-ICD group were matched 1:1 to the best TV-ICD corresponding patient. All procedures, in both groups, were performed by an electrophysiology consultant with greater than 10 years of experience in device implantation.

2.2. S-ICD procedure

Prior to S-ICD implantation all patients undergo electrocardiogram (ECG) screening to ensure suitability for a S-ICD through excluding those susceptible to T wave over-sensing. S-ICD implantation at our centre is performed under general anesthetic (GA).

2.3. Device programming

TV-ICDs were programmed either with one or two therapy zones based on the patient's age, underlying cardiac etiology and the presence of previous ventricular arrhythmia events. ATP and shocks were programmed in the VT and ventricular fibrillation (VF) zone in TV-ICDs. Subsequent adjustments to therapies and detection zones were performed during follow-up, or following the occurrence of arrhythmic events. Supraventricular tachycardia discriminators were switched on and high-rate timeout turned off.

2.4. Follow-up and outcomes

Analysis was performed on a time-to-event basis with incidence event rates and hazard ratios (HR) being calculated for the device-related complications encountered during follow-up in each group. Patients were censored once they experienced a device-related complication. The device-related complications included any early or late complications deemed to be related to the device. Early complications were implant-related complications i.e. those that occurred within 30 days of the first implant. Device-related infections were those necessitating removal of the ICD system and/or antibiotic treatment. Pocket hematoma were defined as those resulting in >2 g/dl haemoglobin loss and/or requiring evacuation. Lead failure was defined as those that resulted in inappropriate shocks secondary to lead noise and/or replacement of the lead.

Data from our local device clinic follow-up records and stored device electrograms (EGMs) during episodes of detected VT/VF, any therapy deliveries, and inappropriate shocks were analyzed by a cardiac physiologist specializing in electrophysiology, consultant electrophysiologist or senior electrophysiology fellow. Sustained VT episodes meeting criteria for appropriate ICD intervention were classified as either VT/VF, according to the rate and detection window where therapy was delivered. Non-sustained VT episodes that met detection criteria and terminated before therapy was delivered were not classified as VT/VF. Patients were classified as having had appropriate shocks, if a shock was delivered during a VT or VF event. Effective ATP therapy (for TV-ICDs) was defined as overdrive ventricular pacing able to restore sinus rhythm following a VT or VF episode. An appropriate ICD intervention was classified as the presence of either an appropriate shock or an effective ATP.

The incidence of inappropriate shocks delivered due to misdetection of tachycardia (either supra-ventricular tachycardia, sinus tachycardia, atrial fibrillation, T-wave oversensing, lead noise or artifact) was also compared between the two treatment groups.

Table 1
Shows the factors that were used in the propensity match.

Factors used in the propensity matching
Age
Gender
Diabetes
Hypertension
Chronic kidney disease
Left ventricular ejection fraction
Cardiac etiology
Indication i.e. primary or secondary prevention

Data regarding multiple arrhythmia episodes (either in the VT or VF zones), and appropriate ICD therapies (ATPs and appropriate shocks) in the same patient were collected, and the mean number was compared between the two groups. From 2011 onwards, home-monitoring systems (LATITUDE, CARELINK and MERLIN) became available in our institution and were also used for follow-up purposes.

We also collected data on mortality rates in both groups particularly if any deaths were device-related.

2.5. Cost-efficacy analysis

A cost efficacy analysis was performed where the initial implant costs and the costs of device-related complications in each group were determined and compared. For the device-related complications we took into account the costs of repeat procedure(s) including catheterization (cath) lab usage, GA cost, procedure-related equipment costs, and the cost of the new implant and hospital stay. We also took on board the cost of the investigations performed pre and post their repeat procedure i.e. ECGs, blood tests, blood cultures, chest x-ray, echocardiogram. As the mean procedure time and hospital stay for the initial TV-ICD and S-ICD procedure were not different in our cohort, the cost related directly to these was not taken into account when determining the cost difference between the two groups. As the S-ICDs were implanted under GA the cost related to GA was included in the implant cost. The UK Department of Health published costs for hospital stay are used by the centre in the costing of hospital stay for each patient and were thereby used in our cost calculations [20]. The cost of the device and procedure-related equipment was based on the cost of the centre paid directly to the manufacturer to purchase the products. The costs of the relevant investigations were obtained from the NICE guidelines on preoperative tests that are used by our centre in the costing of investigations [21].

2.6. Statistical analysis

A propensity score was obtained for all eligible participants undergoing ICD implantation through binary logistic regression: ICD modality (TV-ICD or S-ICD) was the binary outcome and all baseline variables (Table 1) were used as covariates for estimating a probability (the propensity score). Then, probabilities in the S-ICD group were matched 1:1 to the closest TV-ICD patient fulfilling inclusion criteria using the nearest neighbor matching approach. The propensity score was matched to 5 decimals whenever possible. If this was not possible, we subsequently attempted 4, 3 and then 2 decimal matching. If a S-ICD patient could not be matched to any TV-ICD subject on the second digit of the propensity score, then the S-ICD subject was discarded from the matched analysis.

Comparisons between S-ICD and TV-ICD were performed. Based on Stuart [22], analyses were performed using the groups as a whole, rather than using the individual matched pairs. Chi-square was used for the comparison of nominal variables. The student t-test, or its non-parametric equivalent, Mann–Whitney when appropriate, was used for comparison of continuous variables; the Levene's test was used in order to check the homogeneity of variance. Cox proportional regression model was used to calculate hazard ratios for each individual device-related complication. Results with $p < 0.05$ were regarded as significant.

Kaplan–Meier curves were traced for comparing survival free from device-related complications among the two treatment groups. For the purpose of time to event analysis only time to first event was considered, the patients were censored after their first event. SPSS (IBM SPSS Statistics, Version 20 IBM Corp, Armonk, NY, USA) was used for descriptive and inferential statistical analysis.

3. Results

A total of 69 patients underwent S-ICD implantation between 2010 and 2015. A total of 429 patients underwent TV-ICD implantation over a contemporary time period. Following propensity matching 69 of these were matched to the S-ICD group. Baseline characteristics of these two groups are demonstrated in Table 2.

3.1. Device programming

In the TV-ICD group 22 patients had a single VF zone programmed whilst the remaining 47 patients had an additional VT therapy zone. On average the VT therapy zone started at 176 ± 14 beats per min (bpm). S-ICDs were programmed with a SVT discriminator zone at 180-220 bpm and a VF therapy zone at >220 bpm.

3.2. Device therapy

In the TV-ICD group five patients had an appropriate ICD therapy (n = 4 ICD shocks for VT/VF and n = 1 ATP for VT). In the TV-ICD group the device failed to cardiovert VT in one patient and as a result they were externally cardioverted, followed by having the generator