The Efficacy of the Entirely Subcutaneous Implantable Cardioverter Defibrillator

Kelly Kurvers

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Abstract

Background: Sudden cardiac arrest (SCA) is the leading cause of death in the United States. The implantable cardioverter defibrillator (ICD) is widely used as an adjunct therapy for SCA and has been proven to be effective in terminating life-threatening arrhythmias, but the standard transvenous device is not without complications. The development of an entirely subcutaneous ICD (S-ICD) came about as a new approach to sudden cardiac death (SCD) prevention without the lead associated complications. The S-ICD has been commercially available in Europe and New Zealand since 2009 and was recently approved by the U.S. Food and Drug Administration. The purpose of this review is to evaluate the efficacy of the new entirely subcutaneous implantable cardioverter defibrillator.

Methods: An exhaustive medical literature search was conducted using Medline-OVID, CINAHL, and Web of Science using the keywords: ‘defibrillator, implantable’ and ‘subcutaneous.’ The additional keyword ‘efficacy’ was used with Web of Science for further specification. All relevant articles were reviewed for validity and then assessed for quality using the GRADE system.

Results: Five observational cohort studies were included in this systematic review. One of the articles demonstrated a direct comparison to the TV-ICD; all others focused solely on the efficacy of the S-ICD. The studies all had similar inclusion and exclusion criteria and the patients were prognostically similar, but the quality of evidence was limited due to the observational nature. The S-ICD showed excellent intraoperative defibrillation testing and appropriate shock therapy for life-threatening arrhythmias. There were a number of inappropriate shocks delivered and complications that arose due to the novelty of the device, but many of these adverse events were completely reversible with updates to the device.

Conclusion: The entirely subcutaneous implantable cardioverter defibrillator has been demonstrated to be a reliable alternative to the standard TV-ICD in prevention of sudden cardiac death in certain populations. However, longer-term randomized controlled trials would be of great value in further defining the efficacy of this new device.

Keywords: Defibrillator, implantable; Subcutaneous; Efficacy
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The Efficacy of the Entirely Subcutaneous Implantable Cardioverter
Defibrillator

Kelly Kurvers

A Clinical Graduate Project Submitted to the Faculty of the
School of Physician Assistant Studies
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For the Masters of Science Degree, August 10, 2013

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Clinical Graduate Project Coordinator: Annjanette Sommers, PA-C, MS
Abstract

**Background:** Sudden cardiac arrest (SCA) is the leading cause of death in the United States. The implantable cardioverter defibrillator (ICD) is widely used as an adjunct therapy for SCA and has been proven to be effective in terminating life-threatening arrhythmias, but the standard transvenous device is not without complications. The development of an entirely subcutaneous ICD (S-ICD) came about as a new approach to sudden cardiac death (SCD) prevention without the lead associated complications. The S-ICD has been commercially available in Europe and New Zealand since 2009 and was recently approved by the U.S. Food and Drug Administration. The purpose of this review is to evaluate the efficacy of the new entirely subcutaneous implantable cardioverter defibrillator.

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**Results:** Five observational cohort studies were included in this systematic review. One of the articles demonstrated a direct comparison to the TV-ICD; all others focused solely on the efficacy of the S-ICD. The studies all had similar inclusion and exclusion criteria and the patients were prognostically similar, but the quality of evidence was limited due to the observational nature. The S-ICD showed excellent intraoperative defibrillation testing and appropriate shock therapy for life-threatening arrhythmias. There were a number of inappropriate shocks delivered and complications that arose due to the novelty of the device, but many of these adverse events were completely reversible with updates to the device.

**Conclusion:** The entirely subcutaneous implantable cardioverter defibrillator has been demonstrated to be a reliable alternative to the standard TV-ICD in prevention of sudden cardiac death in certain populations. However, longer-term randomized controlled trials would be of great value in further defining the efficacy of this new device.

**Keywords:** Defibrillator, implantable; Subcutaneous; Efficacy
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List of Abbreviations

GRADE………. Grades of Recommendation, Assessment, Development and Evaluation
ICD………………………………………………………Implantable Cardioverter Defibrillator
IDE……………………………………….Investigational Device Exemption
LVEF………………………………………..Left Ventricular Ejection Fraction
S-ICD………………………………….Subcutaneous Implantable Cardioverter Defibrillator
SCA…………………………………………….Sudden Cardiac Arrest
SCD…………………………………………….Sudden Cardiac Death
TV-ICD…………………………….Transvenous Implantable Cardioverter Defibrillator
VT…………………………………………………..Ventricular Tachycardia
The Efficacy of the Entirely Subcutaneous Implantable Cardioverter Defibrillator

BACKGROUND

The approval of the new entirely subcutaneous implantable cardioverter defibrillator by the US Food and Drug Administration¹ in September 2012 has brought a lot of attention to the prevention of sudden cardiac death (SCD). Sudden cardiac arrest (SCA) is the leading cause of death in the United States. According to the American Heart Association, an estimate of 382,800 people experience SCA each year.² Unfortunately, 92% of those people do not survive.³ There are many causes of SCD, with coronary artery disease occurring in up to 80% of the instances, followed by nonischemic cardiomyopathy and valvular diseases.⁴ There are some genetic conditions, such as long QT syndrome or Brugada syndrome, that account for a lesser percentage of SCD. Often, the arrhythmia involved with SCD is ventricular fibrillation. The implantable cardioverter defibrillator (ICD) is widely used as an adjunct therapy for SCA and has been proven to be effective in terminating life-threatening arrhythmias. Results from a meta-analysis of 3 trials comparing ICD therapy versus amiodarone therapy for secondary prevention of SCD revealed a 28% reduction in the relative risk of death with the ICD.⁵ A pooled analysis of 10 primary prevention trials revealed that ICD implantation provides a 7.9% absolute mortality reduction in those at risk for SCD.⁶

The standard ICD consists of a generator that is implanted in a pocket usually below the left clavicle and transvenous leads that are inserted through a vein to the right ventricle and additional leads may be inserted in the right atrium or left ventricle.⁷ Implantation is usually performed under general anesthesia and with the use of fluoroscopy to verify proper positioning of leads. As stated previously, the transvenous
ICD (TV-ICD) has been proven to reduce mortality due to SCD, but it is not without complications. A study performed on 440 patients implanted with TV-ICDs concluded that 31% of patients experience complications related to their device within 4 years after implantation. Obtaining venous access can result in problems such as pneumothorax due to subclavian vein puncture, pericardial tamponade due to lead perforation, or thrombosis of the brachial, subclavian, or jugular veins. The study by Alter et al noted these perioperative venous complications in 2.2% of the patients. Implantation of the device has a 1-2% chance of infection requiring surgical explantation. The concern is that due to the direct connection of the leads to the heart, device infection can lead to endocarditis. In a study by Athan et al, endocarditis due to infection of cardiac device (pacemaker or ICD) occurred in 6.4% of their 2760 patients. Another known complication related to TV-ICDs are lead related problems, such as lead dislodgement, lead fracture, or lead insulation defects, all of which can lead to inappropriate shock delivery. Alter et al noted lead related complications in 52 of the 440 patients (12%). Another study by Daubert et al analyzed the frequency and outcome of inappropriate shocks of patients in the Multicenter Automatic Defibrillator Implantation Trial (MADIT) II. Daubert et al study revealed that one or more inappropriate shocks occurred in 11.5% of the total 719 MADIT II patients and were associated with a greater risk of all-cause mortality. Besides the obvious negative implications all of the mentioned complications have on the patient’s health, they also present a significant financial burden due to increased length of stay postoperatively or additional hospital visits.
The development of an entirely subcutaneous implantable cardioverter defibrillator (S-ICD) came about as a new approach to SCD prevention without the lead associated complications. Cameron Health Incorporated of San Clemente, California manufactures the S-ICD that recently passed FDA approval. It should be known that the S-ICD system has been commercially available in Europe and New Zealand since 2009 and has not been recalled for any reason. The device consists of a subcutaneous pulse generator that is placed in the area of the left 5th and 6th intercostal spaces between the midaxillary and anterior axillary lines. The generator is connected to an electrode that runs to the xiphoid and then vertically along the sternal border and is inserted in the subcutaneous tissue via 2 parasternal incisions (Figure 1). The implantation of the S-ICD can be performed using anatomic landmarks only, which eliminates the need for fluoroscopy thus reducing radiation exposure to the patient and physician. Boston Scientific, the company that acquired Cameron Health and the S-ICD system, claims on their website that some of the main benefits to the S-ICD is that there is no risk of vascular injury, there is a great reduction in the likelihood of systemic infections, and as stated, a reduction in radiation exposure due to the implantation technique without fluoroscopy. Due to the preservation of venous access, this device may be very beneficial for those with long-term indications, such as younger patients with channelopathies or cardiomyopathies, which is also the population that is likely to be more active and at risk for lead fractures with TV-ICDs. The S-ICD is contraindicated in patients in whom pacing is indicated, such as those with symptomatic bradycardia, persistent ventricular tachycardia (VT), or documented VT that is reliably terminated by anti-tachycardic pacing, as the S-ICD does not have pacing capabilities.
According to a large nationwide survey performed in 2009, over 300,000 TV-ICDs were implanted in a single year. The authors compared those numbers to a survey done in 2005, which revealed that there has been a significant rise in this number in almost every country surveyed, with the largest implanter being the United States. The S-ICD offers an alternative approach to SCD prevention without the lead associated complications. However, will the new entirely subcutaneous implantable cardioverter defibrillator prove to be efficacious?

METHODS

An exhaustive medical literature search was conducted using Medline-OVID, CINAHL, and Web of Science using the keywords: ‘defibrillator, implantable’ and ‘subcutaneous.’ The additional keyword ‘efficacy’ was used with Web of Science for further specification. The bibliographies of the articles were searched further for relevant sources. The titles and abstracts were screened for relevance and then full text articles with primary data evaluating the efficacy of S-ICD were formally reviewed. Articles were excluded if they were noted to be commentaries, had a population of children only, or if the study used a different configuration than the standard (i.e. right parasternal location). A search on the National Institute of Health was also conducted to reveal information of ongoing clinical trials.

All relevant articles were reviewed for validity using a standard critical appraisal form. The articles were then assessed using the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) system to analyze any methodology limitations, inconsistent results, indirectness of evidence, publication bias, or lack of
precision. The GRADE criterion was then applied to rate the overall quality of the study as high, moderate, low, or very low.

RESULTS

The initial search on the three previously mentioned databases revealed a total of 174 articles for review. Articles were screened for relevancy and primary data evaluating the efficacy of S-ICD. After screening, a total of 5 articles met inclusion criteria. The articles were all observational cohort studies, as there are no randomized controlled trials to date (see Table I). One of the articles demonstrated a direct comparison to the TV-ICD; all others focused solely on the efficacy of the S-ICD. All studies had the same general eligibility criteria for enrollment into the study. Inclusion criteria for all studies was Class I, IIa, or IIb ICD indications according to the current published guidelines at the time of the study. Patients were excluded from the studies if they required antibradycardic pacing, had a history of frequent VT, or documented VT that is reliably terminated by pacing, as the S-ICD does not have pacing capabilities. Any additional, study specific, inclusion or exclusion criteria are stated accordingly below.

Gold et al\textsuperscript{17} conducted the Subcutaneous versus Transvenous Arrhythmia Recognition Testing (START) study involving 64 patients that were implanted with the S-ICD in various centers. This study assessed the ability of S-ICD to accurately diagnose induced shockable versus nonshockable rhythms in comparison to 3 versions of single and dual chamber TV-ICDs. Baseline patient characteristics are displayed in Table II.

The results of the Gold et al study\textsuperscript{17} revealed a sensitivity of 100\% in the S-ICD’s detection of induced tachyarrhythmias and a specificity of 98\% in the response to ventricular and atrial arrhythmias. The S-ICD misclassified one of the induced atrial
arrhythmias. The authors listed the individual sensitivity and specificity values for each
TV-ICD, but overall TV-ICDs had a sensitivity of >99% and specificity of 76.7%. No
follow up data was collected in this study, so it was assumed that the devices respond to
spontaneous arrhythmias in the same way as induced arrhythmias.

Bardy et al\textsuperscript{18} conducted a clinical trial in New Zealand and Europe to evaluate the
efficacy of the S-ICD. They specifically looked at the ability of the device to detect
induced rhythms at implantation and then at a 10 month follow up, they analyzed the
device’s ability to detect and appropriately respond to spontaneous arrhythmias and also
any complications such as infection, lead problems, and inappropriate sensing. The study
consisted of 55 patients that were implanted with the S-ICD between the dates of
December 2008 and February 2009. Participants had to meet the above inclusion and
exclusion criteria with the addition of being excluded if they had a history of VT at rates
less than 170 beats per minute or an estimated glomerular filtration rate less than 30 ml
per minute. Baseline patient characteristics are displayed in Table II.

The results of the study by Bardy et al\textsuperscript{18} revealed 100% detection of induced
tachyarrhythmias and 98% successful conversion of 2 consecutive induced
tachyarrhythmias. Two patients were eliminated from this initial portion of the study
because defibrillation testing was not possible. One of the 53 patients had successful
conversion of the 1\textsuperscript{st} rhythm, but the 2\textsuperscript{nd} induced rhythm failed to convert to sinus
rhythm. This patient ultimately received a TV-ICD per protocol. At the 10-month follow
up, one patient died from renal failure, therefore the follow up data was based upon 54
patients. Three patients had a total of 12 episodes of spontaneous VT and 100% of these
were treated successfully. Zero patients experienced inappropriate shocks. Pocket
infection occurred in 2 patients, requiring pocket revision in one, while the other opted for discontinuation of ICD therapy. Lead migration or dislodgement occurred in 6 patients, requiring lead repositioning in 4. Oversensing or inappropriate sensing occurred in 4 patients, which was corrected by reprogramming the sensing vector and did not require surgery. Overall, the authors felt that the S-ICD was able to detect and treat induced and spontaneous arrhythmias successfully and that the complications that arose in this early study have been corrected now by modifications in the S-ICD system. They admit that further testing needs to be performed to analyze long-term benefits and complications, especially in comparison to the TV-ICD with large, randomized, multicenter, prospective clinical trials.

Dabiri et al\textsuperscript{19} performed a single center observational study of 31 patients in the Netherlands that assessed any surgical problems (lead migration, infection), inappropriate shocks, and the accuracy of detection and response to induced and spontaneous arrhythmias. Of note, the first 11 patients were included in the study above by Bardy et al.\textsuperscript{18} Baseline patient characteristics are displayed in Table II.

The study by Dabiri et al\textsuperscript{19} revealed 100% detection and conversion of induced tachyarrhythmias upon implantation of the S-ICD. Four patients had a total of 30 episodes of ventricular arrhythmias, which resulted in 100% successful treatment. Five patients had a total of 20 inappropriate shocks. Three episodes occurred in 2 patients due to myopotentials, which was corrected with lead repositioning in one and software upgrade in other. One episode occurred in one patient due to T-wave oversensing while coughing and another episode occurred in one patient due to double counting, both of which were corrected by selecting an alternate sensing vector. One patient was shocked
inappropriately 15 times due to T-wave oversensing after a newly developed right bundle branch block. This was corrected by making a new template according to the patient’s new electrocardiogram. Pocket infection occurred in one patient, however this patient had a known high infection risk but the device was deemed the best option despite the risk. Lead dislodgement occurred in 2 of the first 15 patients implanted, which was corrected by addition of an electrode suture sleeve at xyphoid level, which is now standard protocol.

Recall that 11 patients in the Dabiri et al study\textsuperscript{19} were also included in the Bardy et al study\textsuperscript{18} and without specific participant data, it is impossible to definitively discern which results overlap. The results of this study are limited by non-randomization and short, variable follow up, ranging from 30-638 days. Overall, the authors felt that the study revealed complications of the S-ICD that were largely reversible and that it proved reasonable efficacy for the given time frame. They agreed that larger, long-term trials would be beneficial.

Olde et al\textsuperscript{20} conducted a large multicenter retrospective study of 118 Dutch patients that were implanted with a S-ICD between the dates of December 2008 and April 2011. Of note, 40 patients were previously reported in the studies by Bardy et al\textsuperscript{18} and Dabiri et al.\textsuperscript{19} This study assessed the detection and appropriate response of the S-ICD to induced and spontaneous arrhythmias, inappropriate shocks, and clinically significant complications that required surgical correction or hospitalization. Baseline patient characteristics are displayed in Table II.

The results of Olde et al\textsuperscript{20} revealed 100\% detection and conversion of induced tachyarrhythmias. There were 45 episodes of spontaneous VT that occurred in 8 patients,
100% of which were successfully detected and 98% were successfully treated. One patient had an episode of VT that accelerated due to the shock instead of converting, however the rhythm spontaneously ceased with no further intervention. There were 15 patients that had a total of 33 inappropriate shocks. Eleven of these episodes occurred in 9 patients due to T-wave oversensing, which was solved by upgrading the software, changing the sensing vector, or making a new template during exercise testing. Fifteen episodes occurred in one patient due to T-wave oversensing after a newly developed right bundle branch block, as mentioned above. Another patient was inappropriately shocked due to excess noise sensing during transcutaneous electrical nerve stimulation therapy. Two episodes occurred in one patient due to atrial flutter with ventricular rates in the unconditional zone. Three patients had a total of 4 episodes due to myopotential sensing (caused by lead migration in 2 of 3 patients). The authors recognized that inappropriate shocks were more prevalent in the first 15 patients implanted per center (19% vs. 6.7%).

Complications that arose in the Olde et al study\textsuperscript{20} consisted of pocket infection in 7 patients, lead dislodgement in 3 patients, device dislodgment in 1 patient, skin erosion in 2 patients, and premature battery depletion in 2 patients. At least 3 of the 7 patients with infections had predisposing factors. All cases of lead dislodgement were corrected by the addition of the now standard electrode suture sleeve at xyphoid level. As with the inappropriate shocks, the authors noted that these complications were more prevalent in the first 15 patients implanted per center (17% vs. 10%). They speculated that these differences might likely be due to a learning curve of both the device and the physician implanting the device. They felt that despite the adverse events that occurred, the S-ICD
is a reasonable alternative to the TV-ICD for certain populations but that randomized trials comparing the two devices would be helpful.

Aydin et al.\textsuperscript{21} conducted a multicenter trial of 40 patients in Germany that were implanted with the S-ICD between the dates of June 2010 and July 2011 according to the inclusion and exclusion criteria stated above. This study assessed specifically shock efficacy (successful termination of arrhythmia) with a mean follow up of 229 days. The authors also addressed first shock efficacy, inappropriate shocks, and briefly any peri- and post-operative complications (e.g. infection and lead dislocation). Baseline patient characteristics are displayed in Table II. Of note, the majority of patients met ICD indication criteria for secondary prevention instead of primary and the main cause of cardiac disease was idiopathic ventricular arrhythmias instead of ischemic cardiomyopathy when compared to the other studies mentioned. The mean age of their participants was also younger than the other studies.

The results of the study by Aydin et al.\textsuperscript{21} revealed 98% detection and conversion of induced tachyarrhythmias, with 1 of 40 patients failing intraoperative defibrillation testing. Subsequent heart biopsy of that patient revealed subacute myocardial inflammation, therefore the S-ICD was explanted and the patient received a TV-ICD. Interestingly, the patient failed intraoperative testing with the TV-ICD as well, testing was finally successful 2 weeks post-op. In follow up of the remaining patients, only about 10% of participants experienced an event that tested shock efficacy. There were 25 episodes of spontaneous tachyarrhythmias, 21 of which were correctly identified and resulted in 28 shocks delivered by the S-ICD. Overall shock efficacy was calculated to be 96.4% and first shock efficacy was 57.9%. Two patients had a total of 2 inappropriate
shocks due to incorrect identification of sinus tachycardia. The authors concluded that despite successful conversion of induced rhythms, the S-ICD may still deliver ineffective shocks and therefore larger, long-term multicenter trials are needed to further define the safety and efficacy of the device.

DISCUSSION

The primary goal of this study is to provide a systematic review of the evidence thus far in the efficacy of the S-ICD system. These five initial studies\textsuperscript{17-21} covered a rather diverse population, given that the studies were conducted in Germany, the Netherlands, New Zealand, and the United States. It is important to note that two of the five studies reviewed, Bardy et al\textsuperscript{19} and Gold et al,\textsuperscript{17} have a likelihood of publication bias. The authors of those studies are either paid consultants or employees of Boston Scientific and/or Cameron Health. This is not surprising, given the novelty of the device, but should still be taken into consideration.

The FDA approval of the S-ICD in September 2012 was made based upon the results of these initial trials and the recent investigational device exemption (IDE) study,\textsuperscript{22} which is not yet published.\textsuperscript{1} According to the National Institute of Health, this study\textsuperscript{22} is a prospective, multicenter clinical trial conducted in U.S., Europe, and New Zealand. They enrolled 330 patients between the dates of January 2010 and May 2011 with the same inclusion and exclusion criteria as the studies reviewed in this article. The purpose of the study was to evaluate the safety and efficacy of the S-ICD by measuring the ability of the device to convert induced VF and by analyzing the rate of complications in a 180-day period.
Dr. Martin Burke presented results of the IDE study at the Heart Rhythm Society conference in May 2012. Nine participants withdrew from the study prior to implantation; implantation was then attempted in 321 patients and successful in 314. Of the 321 patients, the mean age of participants was 51.9 +/-15.5 and 74.1% were male. The mean LVEF 36% +/-16, with 79% of the participants meeting ICD criteria for primary prevention. The device was effective in converting all induced tachyarrhythmias upon successful implantation. During the 180-day follow up, there were a total of 78 spontaneous episodes of tachyarrhythmias in 21 patients, all of which either spontaneously converted on their own or were successfully converted by the device.

There were a total of 4 patients (1.3%) that had to undergo explantation of the device due to infection, but there were no cases of endocarditis or systemic blood stream infections. The researchers also noted that no infections requiring explantation occurred in the last 214 patients, implying again a possible learning curve. Inappropriate shocks occurred in 38 patients either due to oversensing or episodes of supraventricular tachycardia in the unconditional zone. The researchers felt that this rate of inappropriate shocks is comparable to that of the TV-ICD. Based upon these results, the FDA approved the device for use in patients with ICD indications that do not require pacing therapy, with the stipulation that the manufacturing company must conduct a postmarket study to evaluate the long-term safety and efficacy of the device and to assess any differences among various populations. The postmarket study will be conducted on 1616 patients with a 5-year follow up.

Overall, the S-ICD has proven to be very effective in rhythm detection and conversion of induced tachyarrhythmias. The only study comparing directly to TV-ICDs
showed promising data in the superiority of the specificity of the S-ICD in comparison to TV-ICDs.\textsuperscript{17} It should be noted that that study only analyzed the response to induced rhythms however, not spontaneous. One would speculate that the device would respond similarly regardless of the etiology of the rhythm, however one cannot be certain. Therefore a randomized trial assessing the sensitivity and specificity of the response to spontaneous tachyarrhythmias of TV-ICDs versus the S-ICD would be important. The remaining studies that did assess the response to spontaneous tachyarrhythmias revealed that the S-ICD is very effective in both detecting and responding appropriately to life-threatening arrhythmias. However, longer-term studies need to be conducted in a randomized controlled fashion to further define the shock efficacy in comparison to the TV-ICD.

Inappropriate shock delivery, as stated previously, has been shown to be associated with increased risk of all-cause mortality; therefore it is crucial that the S-ICD be comparable, if not superior, to the TV-ICD in this regard. At first glance, it may seem that the S-ICD had a high incidence of inappropriate shocks, especially considering that the ideal number would be zero. However, given that these are early clinical trials on a novel device, many of the instances were completely reversible by tweaking the device with software updates or altering the sensing vector. The investigators of the IDE study felt that the prevalence of inappropriate shocks with the S-ICD was comparable to that of the TV-ICD, however it would be very beneficial to conduct a randomized controlled trial assessing this incidence with a direct comparison of the two devices.

As with inappropriate shocks, many of the device-related complications that occurred in the trials appeared to decrease in prevalence as the device and physician
experience with the device evolved. Once again, longer-term trials will be important in evaluating these complications and randomized controlled trials will help determine whether the benefits of the S-ICD system outweigh the risks in comparison to the standard TV-ICD.

CONCLUSION

The entirely subcutaneous implantable cardioverter defibrillator has been demonstrated to be a reliable alternative to the standard TV-ICD in prevention of sudden cardiac death in patients not requiring pacing therapy. The early studies that were reviewed in this article revealed some complications that were easily reversible with revamping the design of either the device or the implantation procedure. The recent clinical trial revealed promising data as well, however longer-term randomized controlled trials would be of great value in further defining the efficacy of this new entirely subcutaneous device in comparison to the standard transvenous ICD.
References


Table I. GRADE Profile

<table>
<thead>
<tr>
<th>Design</th>
<th>Study</th>
<th>Limitations</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Inconsistency</th>
<th>Publication Bias</th>
<th>Quality</th>
<th>Overall Quality</th>
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<tr>
<td>Observational Cohort(^a)</td>
<td>Gold et al(^7)</td>
<td>No limitations</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No serious bias(^a)</td>
<td>Very Low</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bardy et al(^8)</td>
<td>No limitations</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No serious bias(^b)</td>
<td>Very Low</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dabiri et al(^9)</td>
<td>No serious limitations(^c)</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No bias</td>
<td>Very Low</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Olde et al(^10)</td>
<td>No limitations</td>
<td>No</td>
<td>No</td>
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<td>Low</td>
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<td>No serious limitations(^d)</td>
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<td>No</td>
<td>No bias</td>
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<td></td>
</tr>
</tbody>
</table>

\(^a\)Note, all observational studies automatically start at “low” quality
\(^b\)All authors are affiliated with Boston Scientific and/or Cameron Health
\(^c\)Supported by Cameron Health
\(^d\)Follow up was variable, ranging from 30-638 days. Anything less than 180 days is inadequate.
\(^e\)Follow up was inadequate, only 10% of patients experienced an event that tested shock efficacy

Table II. Baseline Patient Characteristics

<table>
<thead>
<tr>
<th>Study</th>
<th>Year/Location</th>
<th># of Patients</th>
<th>Mean age (years)</th>
<th>Sex</th>
<th>Mean LVEF (%)</th>
<th>ICD Indication</th>
<th>#1 Cause of Cardiac Disease</th>
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<tbody>
<tr>
<td>Gold et al(^7)</td>
<td>2011/multicenter (locations not specified)</td>
<td>64</td>
<td>60+/-12</td>
<td>78% male</td>
<td>31+/-14</td>
<td>79.7% Primary</td>
<td>Ischemic cardiomyopathy (53%)</td>
</tr>
<tr>
<td>Bardy et al(^8)</td>
<td>Dec 2008-Feb 2009/ Europe and New Zealand</td>
<td>55</td>
<td>56+/-13</td>
<td>80% male</td>
<td>34+/-13</td>
<td>78% Primary</td>
<td>Ischemic cardiomyopathy (67%)</td>
</tr>
<tr>
<td>Dabiri et al(^9)</td>
<td>2010/The Netherlands single center</td>
<td>31</td>
<td>53+/-16</td>
<td>77% male</td>
<td>38.8+/-15</td>
<td>67% Primary</td>
<td>Ischemic cardiomyopathy (58%)</td>
</tr>
<tr>
<td>Olde et al(^10)</td>
<td>Dec 2008-Apr 2011/ The Netherlands multicenter</td>
<td>118</td>
<td>50+/-14</td>
<td>75% male</td>
<td>41+/-14</td>
<td>60% Primary</td>
<td>Ischemic cardiomyopathy (38%)</td>
</tr>
<tr>
<td>Aydin et al(^11)</td>
<td>June 2010-July 2011/ Germany multicenter</td>
<td>40</td>
<td>42+/-15</td>
<td>70% male</td>
<td>47+/-15</td>
<td>57.5% Secondary</td>
<td>Idiopathic ventricular arrhythmia (30%)</td>
</tr>
</tbody>
</table>
Table III. Summary of Findings

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Study</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraoperative defibrillation testing</td>
<td>Gold et al(^\text{17})</td>
<td>S-ICD had a sensitivity of 100% in the detection of induced tachyarrhythmias and a specificity of 98% in the response to ventricular and atrial arrhythmias. Overall TV-ICDs had sensitivity of &gt;99% and specificity of 76.7%.</td>
</tr>
<tr>
<td></td>
<td>Bardy et al(^\text{18})</td>
<td>100% detection of induced tachyarrhythmias; 98% successful conversion of 2 consecutive induced tachyarrhythmias.</td>
</tr>
<tr>
<td></td>
<td>Dabiri et al(^\text{19})</td>
<td>100% detection and conversion of induced tachyarrhythmias</td>
</tr>
<tr>
<td></td>
<td>Olde et al(^\text{20})</td>
<td>100% detection and conversion of induced tachyarrhythmias</td>
</tr>
<tr>
<td></td>
<td>Aydin et al(^\text{21})</td>
<td>98% detection and conversion of induced tachyarrhythmias</td>
</tr>
<tr>
<td>Appropriate shock therapy</td>
<td>Bardy et al(^\text{18})</td>
<td>100% of ventricular arrhythmias were treated successfully (3 patients with a total of 12 episodes of spontaneous VT)</td>
</tr>
<tr>
<td></td>
<td>Dabiri(^\text{19})</td>
<td>100% of ventricular arrhythmias were treated successfully (4 patients with a total of 30 episodes)</td>
</tr>
<tr>
<td></td>
<td>Olde et al(^\text{20})</td>
<td>100% of ventricular arrhythmias were successfully detected (45 episodes in 8 patients); 98% of ventricular arrhythmias were successfully treated.</td>
</tr>
<tr>
<td></td>
<td>Aydin et al(^\text{21})</td>
<td>21 of 25 episodes were correctly identified, resulting in 28 shocks delivered. Overall shock efficacy was calculated to be 96.4%. 1st shock efficacy was 57.9%.</td>
</tr>
<tr>
<td>Inappropriate shock delivery</td>
<td>Bardy et al(^\text{18})</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Dabiri(^\text{19})</td>
<td>5 patients had a total of 20 inappropriate shocks.</td>
</tr>
<tr>
<td></td>
<td>Olde et al(^\text{20})</td>
<td>15 patients had a total of 33 inappropriate shocks.</td>
</tr>
<tr>
<td></td>
<td>Aydin et al(^\text{21})</td>
<td>2 patients had a total of 2 inappropriate shocks due to incorrect identification of sinus tachycardia</td>
</tr>
<tr>
<td>Complications</td>
<td>Bardy et al(^\text{18})</td>
<td>Pocket infection in 2 patients; Lead migration/dislodgement in 6 patients; Oversensing/inappropriate sensing in 4 patients</td>
</tr>
<tr>
<td></td>
<td>Dabiri(^\text{19})</td>
<td>Pocket infection in 1 patient; Lead dislodgement in 2 patients.</td>
</tr>
<tr>
<td></td>
<td>Olde et al(^\text{20})</td>
<td>Pocket infection in 7 patients; Lead dislodgement in 3 patients; Device dislodgment in 1 patient; Skin erosion in 2 patients; Premature battery depletion in 2 patients.</td>
</tr>
</tbody>
</table>

\(^{1}\)Of note, the first 11 patients were included in the study above by Bardy et al\(^\text{14}\).  
\(^{2}\)Note: 40 patients were previously reported in studies by Bardy et al and Dabiri et al.  
\(^{3}\)Of 53 patients had 1st rhythm successfully converted, but 2nd induced rhythm failed to convert to sinus rhythm. This patient ultimately received a TV-ICD per protocol.  
\(^{4}\)1 of 40 patients failed intraoperative defibrillation testing, subsequent heart biopsy revealed subacute myocardial inflammation. S-ICD was explanted and patient received TV-ICD. TV-ICD failed intraoperative testing as well, testing was finally successful 2 weeks post-op.  
\(^{5}\)1 patient had an episode of VT that accelerated due to the shock instead of converting, the rhythm spontaneously ceased with no further intervention  
\(^{6}\)5 episodes in 2 patients due to myopotentials (corrected with lead repositioning in 1 and software upgrade in other); 1 episode in 1 patient due to T-wave oversensing while coughing, 1 episode in 1 patient due to double counting (both corrected by selecting alternate vector); 15 episodes in 1 patient due to T-wave oversensing after newly developed right bundle branch block (corrected by making new template according to new ECG)  
\(^{7}\)1 patient had an episode of VT that accelerated due to the shock instead of converting, the rhythm spontaneously ceased with no further intervention  
\(^{8}\)Inappropriate shocks were more prevalent in the 1st 15 patients implanted per center (19% vs 6.7%). 11 episodes in 9 patients due to T-wave oversensing (solved by software upgrade, changing sensing vector during exercise testing, making a new template during exercise testing); 15 episodes in 1 patient due to T-wave oversensing after newly developed right bundle branch block (corrected by making new template according to new ECG); 1 episode in 1 patient due to noise sensing from transtcutaneous electrical nerve stimulation therapy; 2 episodes in 1 patient due to atrial flutter with ventricular rates in the unconditional zone; 4 episodes in 3 patients due to myopotential sensing (caused by lead migration in 2 of 3 patients)  
\(^{9}\)Infection occurred in patient with known high infection risk (implanted device despite risk because to allow revalidation and due to intolerance of life vest); Lead dislodgement occurred in 2 of the 1st 15 implanted, corrected by addition of electrode suture sleeve at xyphoid level, which is now standard protocol.  
\(^{10}\)Complications were more prevalent in 1st 15 patients implanted per center (17% vs 10%). At least 3 of the 7 patients with infections had predisposing factors. All cases of lead dislodgement were corrected by the addition of the now standard electrode suture sleeve at xyphoid level.
Figure I.

Locations of the Components of a Subcutaneous Implantable Cardioverter–Defibrillator In Situ.

The distal and proximal sensing electrodes (D and P, respectively) of the LGen-S8 device are shown, with the left lateral pulse generator and an 8-cm parasternal coil electrode (C).

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