

Editorial

Should the Subcutaneous Implantable Defibrillator Be the First Choice for Primary Prevention of Sudden Cardiac Death?



¿El desfibrilador subcutáneo debería ser la primera elección en la prevención primaria de la muerte súbita?

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Article history:

Available online 9 November 2016

*“Primum non nocere – First, do no harm”
Hippocrates*

The use of implantable cardioverter-defibrillators used to be limited to patients who survived cardiac arrest. However, due to improved stratification of patients at risk for this event, ICD use has been expanded to patients without a history of sustained ventricular arrhythmias. This latter group is often referred to as primary prevention patients and includes both ischemic and nonischemic cardiomyopathy patients with a reduced left ventricular ejection fraction.^{1,2} The survival benefit demonstrated in primary prevention trials was subsequently confirmed in real-world registry data.^{1–3} Because follow-up of the trials was short (16 to 48 months), it is likely that primary prevention ICDs will have an even greater impact on mortality in the long-term.

However, in the light of the fundamental principle of bioethics not to harm patients, there are some disquieting issues related to primary prevention ICDs. A minority of patients implanted with a primary prevention ICD will receive appropriate therapy, while all implanted patients are at risk for adverse events such as inappropriate shocks and device-related complications. Over the last decade, research has focused on reducing ICD harm by decreasing inappropriate shocks and complications. Multiple randomized studies have demonstrated that ICD programming strategies aimed at reducing nonessential therapy not only reduce the therapy burden for patients, but also significantly and consistently lower mortality.⁴ These findings are paramount because programming strategies can easily be implemented in routine care and are likely to decrease costs for health care systems due to fewer hospital admissions and unscheduled visits to the outpatient clinic. Further optimization of programming strategies may only have a limited effect because the absolute rates of both appropriate and inappropriate therapy are low.

Device-related complications are the other side of the coin. While there seems to be a quick fix for shocks, this is not the case for device-related complications. The complications rate is affected by the volume of centers performing ICD procedures, but even in

high-volume centers there are important implant-related complications such as lead dislodgement, cardiac perforation, (systemic) infection, hematoma, and pneumothorax.⁵ During long-term follow-up, complications related to chronic indwelling of transvenous leads occur, such as lead failure, venous obstruction, and bacteremia.

To reduce both the acute and chronic complications of transvenous leads, the subcutaneous ICD was introduced in 2008.⁶ The design of the subcutaneous ICD is radically different from that of the transvenous device, because it relies on a left lateral ‘hot’ can and an extrathoracic parasternal sensing and defibrillation lead. While the entirely subcutaneous position of the device results in a significantly higher defibrillation threshold and larger can, it eliminates a number of complications associated with transvenous leads. Pneumothorax, cardiac perforation, and venous obstruction are avoided because of the extrathoracic position of the lead and complications such as systemic infection, lead dislodgement, and lead failure are less likely than with transvenous ICDs.

The first head-to-head randomized comparison of transvenous and subcutaneous ICDs is currently underway, but publication of the main results will take another couple of years.⁷ The single-arm IDE trial and EFFORTLESS subcutaneous ICD registry have reported outcome data of the first-generation subcutaneous ICD in almost 900 patients and have made several interesting observations.⁸

First, these studies demonstrated much higher rates of inappropriate shocks than those reported by contemporary transvenous ICD trials such as MADIT-RIT and PREPARE. However, comparison of subcutaneous ICD and transvenous ICD inappropriate shock rates are hampered by the important differences in study design and patient demographics. MADIT-RIT included ICD and CRT-D patients aged 65 years and older with a mean ejection fraction of 26%, without atrial fibrillation, and fixed ICD programming. In contrast, the EFFORTLESS registry included younger patients (median age, 49 years) with a left ventricular ejection fraction of 42%, 17% of patients had a history of atrial fibrillation, and ICD programming was at physician discretion. The currently enrolling single-arm subcutaneous ICD trial (UNTOUCHED, NCT02433379) with similar inclusion criteria as MADIT-RIT and fixed ICD programming will put the inappropriate shock rate of the

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subcutaneous ICD into perspective. When the subcutaneous ICD inappropriate shock rates are placed in the context of transvenous ICD studies that did not have fixed programming, the 1-year rates seem to be in the same range.^{9,10} The most recent update of the discrimination algorithm may further reduce inappropriate shocks by the subcutaneous ICD, but this needs to be confirmed by prospective clinical data.

The second observation concerns the short-term device-related complications of the subcutaneous ICD. While there were no serious complications associated with subcutaneous lead insertion, such as cardiac perforation and systemic infection, the absolute complications rate was in the same range as that for transvenous devices.¹¹ An interesting and encouraging finding was that the number of complications was reduced by nearly 50% with greater individual implanter experience at the end of the learning curve.¹² In addition, a novel implantation technique, the 2-incision technique, was introduced in 2012; this technique omits the superior parasternal incision, which improves the esthetic appeal and may reduce the risk of infection.¹³

The premise of the subcutaneous ICD is that this device can eliminate long-term lead-related complications, among others. The Swedish ICD and pacemaker registry underscores the importance of reducing long-term complications, as the overall 10-year survival rate of ICD patients is 62%. The Leiden University Medical Center cohort is one of the few transvenous ICD cohorts with long-term follow-up and reported the occurrence of lead failure in 18% of patients at 12-years' follow-up.¹⁴ Long-term follow-up of the subcutaneous ICD is not yet available, as the first devices were implanted in 2008. To date, not a single spontaneous lead failure has been reported, while over 20 000 subcutaneous ICDs have been implanted since its introduction. Unlike transvenous ICDs, the lead of the subcutaneous ICD is not exposed to the approximate 100 000 daily cardiac contractions that pose repetitive mechanical stress on the lead, nor is it exposed to clavicular crush forces due to the left lateral position of the can. Therefore, truly long-term data up to 10 or more years is needed to determine whether the premise of reduction in lead-related complications can be translated into a benefit supported by clinical evidence.

The extrathoracic position of the subcutaneous ICD has several disadvantages. First, the defibrillation threshold is higher, which results in a larger can and shorter battery longevity. While the second-generation device is now 20% thinner and the longevity is projected at 7 years, this is still very different from modern transvenous ICDs, which are smaller and have better longevity.

The absence of pacing functionality is another important limitation of the subcutaneous ICD. Therefore, the device can obviously not be used in patients requiring bradycardia or resynchronization pacing. However, only a minority of patients with an ICD indication actually requires VVI or DDD pacing functionality. Of importance, only patients with symptomatic bradycardia have a pacemaker indication and there is no indication in the current guidelines for preventive pacemakers for patients who may develop conduction disease in the future. Unnecessary use of dual-chamber transvenous ICDs increases cost, prolongs the implant procedure, and adds to the complexity of the system, which results in more complications. Therefore, the use of dual-chamber ICDs should be limited to patients with a true bradycardia pacing indication.

The role of antitachycardia pacing (ATP) in the era of therapy reduction programming is not clear. Advocates of ATP will argue that patients should always have the option of painless arrhythmia termination. However, in the MADIT-RIT trial, very few patients received ATP in the high-rate and delayed-therapy arms. These findings raise the question of whether the potential benefit of ATP is outweighed by the risk of transvenous lead complications. In addition, recurrent ventricular tachycardia episodes should be treated with adequate medical therapy such as antiarrhythmic

drugs, ablation, or interventions to treat underlying ischemia, but not by only programming more ATP.

After subcutaneous ICD implantation, some patients may develop the need for ATP when they receive repeated shocks for monomorphic ventricular tachycardia that cannot be treated adequately by medication or ablation. Currently, a leadless cardiac pacemaker is under development that can be used as an add-on to the existing subcutaneous ICD, which has both VVI and ATP functionality. Through conductive wireless communication, the subcutaneous ICD functions as the mothership that commands the leadless pacemaker to perform up to 3 bursts of ATP.¹⁵ Having the option to add a leadless pacemaker to the subcutaneous ICD may stimulate the use of the subcutaneous ICD.

Other important barriers to the widespread adoption of the subcutaneous ICD are the currently recommended perioperative defibrillation testing and the desire of implanters to use general anesthesia during implantation. Both medical actions complicate the logistics in many catheter laboratories and operating rooms. The currently available registry data on perioperative defibrillation testing of the subcutaneous ICD demonstrates > 98% success rate and raises the question of whether the time has come to perform a trial to evaluate the safety of subcutaneous ICD implantation without defibrillation testing. A potential benefit of omitting defibrillation testing would be that implantation could be performed under a combination of conscious sedation and local anesthesia instead of general anesthesia.

Should the subcutaneous ICD be the first choice in primary prevention patients? From the patients' perspective, the subcutaneous ICD is likely to have eliminated the complications due to transvenous leads, although, as mentioned previously, definitive long-term comparison data are currently lacking. At this point, there is no evidence that the subcutaneous ICD outperforms the currently available transvenous ICDs. However, the shorter battery life will result in more replacement procedures over time. Therefore the choice of device type for patients with a primary prevention indication is not an easy one and the pros and cons should be discussed between the patient and physician. In our experience of using subcutaneous ICDs in more than 300 patients, the concept of the subcutaneous ICD appeals to patients. Despite its size and shorter longevity, patients often opt for the subcutaneous ICD when given a choice.

For physicians, particularly electrophysiologists, the subcutaneous ICD is a relatively simple device with few programming options compared with transvenous devices. However, virtually none of the features of modern transvenous ICDs have supporting evidence that outcomes (mortality or quality of life) are impacted in a meaningful way. The landmark primary prevention SCD-HeFT trial was performed with a 'shock box' type of device, similar to the subcutaneous ICD.

From a public health perspective, there is an urgent need for long-term head-to-head comparison data. The subcutaneous ICD is currently sold at a premium compared with single-chamber transvenous devices. Currently, both health care insurance institutions and hospitals demand that new technology is supported by substantial evidence and improved clinical outcomes at similar or lower prices. Given the current body of evidence, this premium cannot be justified (yet). This might explain why the adoption of the subcutaneous ICD has been slow, despite its revolutionary design.

The subcutaneous ICD is a radically different design that may offer long-term benefits by reducing lead-related complications. Long-term comparison data are urgently needed to establish its role among the various ICDs that are available today. From a cost-effectiveness standpoint, considering the available evidence, it is difficult to argue that the subcutaneous ICD must be the first choice in primary prevention patients. We do believe, however, that the subcutaneous ICD shows strong promise to be superior in the

long-term, which would make it the first choice for primary prevention of sudden cardiac death.

CONFLICTS OF INTEREST

R.E. Knops received personal fees and research grants from Boston Scientific, Medtronic and St. Jude Medical.

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