Combined use of S-ICD and absorbable antibacterial envelopes: a proof-of-concept study

Alessio Gasperetti[1], Marco Schiavone[1], Matteo Ziacchi[2], Simone Zanchi[3], Lombardi Leonida[1], Maurizio Viecca[1], Carmelo La Greca[3], Carlo Lavalle[4], Mauro Biffi[5], and Giovanni Forleo[1]

[1]Luigi Sacco University Hospital
[2]Ospedale S.Orsola-Malpighi
[3]Fondazione Poliambulanza Istituto Ospedaliero
[4]Umberto I Policlinico di Roma
[5]Universita degli Studi di Bologna Azienda Ospedaliera Sant'Orsola-Malpighi

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Abstract

Absorbable antibacterial envelopes (AAEs) are currently recommended in patients undergoing a transvenous ICD implantation in cases at high-risk of infection, who are indeed now preferably implanted with a subcutaneous ICD (S-ICD), whenever possible. Nevertheless, experiences using a combined approach with S-ICD and AAE have not been reported, therefore, aim of our study was to evaluate this strategy in patients at very high-risk of infection. Sixteen patients were implanted with the S-ICD+AAE using our combined approach, restricted to patients who would fit our decisional flow algorithm. Despite a very high-risk, only a single pocket infection was observed over the entire follow-up that was managed conservatively and solved with antibiotic therapy. The preliminary data of this proof-of-concept study show how a combined deployment of AAE and S-ICD in selected patients at very high-risk of infection is safe, feasible and may offer a true clinical benefit in specific clinical settings.

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Alessio Gasperetti[1,2*], MD; Marco Schiavone[1*], MD; Matteo Ziacchi[3], MD; Simone Zanchi[4], MD; Leonida Lombardi[1], MD; Maurizio Viecca[1], MD; Carmelo La Greca[4], MD; Carlo Lavalle[5], MD; Mauro Biffi[2], MD; Giovanni Battista Forleo[1],MD, PhD

Affiliations:

[1]Cardiology Unit, ASST-Fatebenefratelli-Sacco, Luigi Sacco University Hospital, Milan (IT)

[2]Division of Cardiology, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland (US)

[3]Cardiology department, Sant'Orsola Malpighi Hospital, Bologna, (IT)

[4]Cardiovascular department, Poliambulanza Institute Hospital Foundation, Brescia (IT)

[5]Cardiology department, Policlinico Umberto I – La Sapienza University, Rome (IT)

*shared first co-authorship

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Address for correspondence:

Marco Schiavone

ASST-Fatebenefratelli-Sacco, Luigi Sacco University Hospital

Viale G.B. Grassi 74, 20157, Milan, Italy

Email: marco.schiavone11@gmail.com

ABSTRACT

Absorbable antibacterial envelopes (AAEs) are currently recommended in patients undergoing a transvenous ICD implantation in cases at high-risk of infection, who are indeed now preferably implanted with a subcutaneous ICD (S-ICD), whenever possible. Nevertheless, experiences using a combined approach with S-ICD and AAE have not been reported, therefore, aim of our study was to evaluate this strategy in patients at very high-risk of infection. Sixteen patients were implanted with the S-ICD+AAE using our combined approach, restricted to patients who would fit our decisional flow algorithm. Despite a very high-risk, only a single pocket infection was observed over the entire follow-up that was managed conservatively and solved with antibiotic therapy. The preliminary data of this proof-of-concept study show how a combined deployment of AAE and S-ICD in selected patients at very high-risk of infection is safe, feasible and may offer a true clinical benefit in specific clinical settings.

Keywords: subcutaneous implantable cardioverter defibrillator; absorbable antibacterial envelope; Tyrx; device infection.

INTRODUCTION

In the last years, the subcutaneous implantable cardioverter defibrillator (S-ICD) has become an established option to prevent sudden cardiac death in patients showing high-risk of infection due to diabetes, chronic kidney disease (CKD), previous cardiac implantable electronic device (CIED) infections, mechanical heart valves, heart failure, immunological disorders, use of anticoagulants or immunosuppressant drugs[1,2]. Mostly in the same clinical scenario, absorbable antibacterial envelopes (AAE), as per International Guidelines[3], are recommended, although data on their use with S-ICDs are currently lacking and they have only been validated with transvenous (TV) ICDs. Although S-ICD related infectious complications resulting into device replacement or lead extraction can be managed easily when compared to TV-ICDs, S-ICDs have failed to show overall lower rates of infection and are indeed associated with a higher risk of pocket complications[4]. In the present manuscript we aimed to assess the feasibility of a combined deployment of AAEs and S-ICD in selected patients at very high-risk of infections and the infectious outcomes of this specific strategy.

METHODS

Consecutive patients who received the combination of an S-ICD (*Boston Scientific, Marlborough, Massachusetts, USA*) and an AAE (TYRX^{TM}, *Medtronic, Minneapolis, Minnesota, USA*) between March 2018 and May 2020 were included in this study. The inclusion period was set from the time of the first "combined" procedure (S-ICD+AAE, March 2018) to May 2020, in order to include only patients with at least 12 months of follow-up. Patients were enrolled from the ELISIR project (Experience from the Long-term Italian S-ICD registry; ClinicalTrials.gov Identifier NCT0473876), which is a multi-center, open-label, independent, and physician-initiated observational registry, whose characteristics and preliminary composition have been previously described[5]. This analysis has been approved by the institutional review board, and has been drafted in accordance with the tenets of the Helsinki Declaration.

Patient selection

All S-ICD placement indications in primary or secondary prevention were set as per the current ICD placement guidelines[6]. As per clinical practice in our centers, the combination of an S-ICD and an AAE is a procedure reserved for patients deemed at a very high-risk of infection. According to our routine, a very high-risk has been defined as the presence of at least 2 risk factors among the following: previous CIED

infection requiring device extraction; diabetes mellitus (either type 1 or type 2) requiring insulin treatment; chronic kidney disease requiring hemodialysis or peritoneal dialysis; active malignancy; chronic disease leading to immunodeficiency disorders (i.e. advance HIV infection, congenital immunodeficiencies); chronic use of anticoagulant or immunosuppressant drugs (i.e. post-transplantation anti-rejection medications). **Figure 1** presents the clinical algorithm used in our clinical practice. Even if no side effects or disadvantages for the patients have been reported with the use of the AAE have been reported so far, all patients were informed and educated about its placement and informed consent for the procedure was obtained in all cases.

Combined deployment technique

The entire combined procedure was performed in an electrophysiology laboratory, under sterile conditions and with the patient undergoing conscious sedation or local anesthesia. The first part of the S-ICD device system placement procedure was performed following the two-incision technique as first reported by Knops *et al.* [7]. Device pocket was created inter-muscularly, carefully separating the anterior surface of the serratus anterior and the posterior surface of the latissimus dorsi muscle.

Before device deployment, an AAE was retrieved. To allow fitting of the S-ICD device, the envelope was processed as follows: first, the envelope was dipped in a sterile bath of 0.9% saline. Then, using a surgical scissor, both lateral edges of the envelope were cut, to increase the envelope width span. As per manufacturer indication, the envelope was flipped inside out. The S-ICD device was then inserted into the wet, flipped, opened envelope. Through manual compression, envelope adhesion to the S-ICD was maximized. Three surgical knots, two anchoring the envelope to itself and one attached to the catheter port of the S-ICD device, were put in place, to guarantee envelope stability and fixation. Device was then placed in the intermuscular pocket and standard techniques to suture the pocket and the incision site were used. The steps used for envelope preparation and deployment are shown in**Figure 2** . At the end of the procedure, fluoroscopy was used to assess final system positioning. As per manufacturer indication, a 2-views chest radiography was obtained in the first post-operative day. All procedures were performed in high-volume centers by expert proceduralists (M.B., C.L.G., G.B.F.), with an extensive experience with the S-ICD system placement as well as with AAE.

Follow-up protocol

A home monitoring system (LATITUDE^{TM} NXT) was offered to all patients after device implantation. Patients were discharged on the second post-procedural day, as per standard ICD discharging practice in our country. As per our center outpatient clinic protocol, all patients were seen for an in-person standard device interrogation 1-month after discharge and every 6 months thereafter. At each follow-up visits, a clinical evaluation was performed, and patients were screened for appropriate/inappropriate shocks, infections, lead displacement and other adverse events. Complications were defined as device related events requiring medical or surgical intervention for resolution and/or device reprogramming.

RESULTS

Tventy-five patients (92% male, mean age 58.5±14.1 years) were implanted with the S-ICD device and the AAE using our combined approach. The most common high infective risk factors were diabetes requiring insulin treatment (80%) and CKD requiring hemodialysis (48%), with 7 (28%) patients presenting with more than 2 risk factors. More than half (56%) of the cohort had an underlying ischemic cardiomyopathy, with the overall left ventricular ejection fraction of the cohort resulting reduced (27.0 [25.0–35.0]). **Table 1** lists baseline characteristics of the study cohort. All procedures were successful in deploying the combined system. Peri-procedural characteristics of the cohort are listed in **Table 2**

Patients were followed-up for a median of 21 [14–29] months and all patients included in the study cohort completed at least 1 year follow-up. A single mild early post-operative hematoma was observed in the entire cohort (in an anticoagulated patient), that was managed conservatively, with a spontaneous resolution. No major device related infections were observed within the first 12 post-procedural months. Only a single pocket device infection was observed over the entire follow-up (at eighteen months of follow-up from device implant),

that was managed conservatively and solved with antibiotic therapy. All device reported correct function at all follow-up visits. During the entire follow-up, eight patients received appropriate S-ICD therapies. At last available follow-up, two inappropriate shocks were observed (n=1 T-wave oversensing; n=1 far field) and three patients died (n=2 terminal heart failure; n=1 active malignancy). Entire follow-up data were reported in **Table 3.**

DISCUSSION

This manuscript reports the combined implantation technique (S-ICD+AAE) that we have been using in a satisfactory manner at our centers in very high-risk patients over the last 2+ years. To our knowledge, this is the first report of the combined use of an AAE and S-ICD system in patients at very high-risk of infection. Although not being explicitly branded for the S-ICD system, the use of an AAE guarding a S-ICD device was completely feasible and safe in our cohort. Only little processing of the current commercially available AAE was needed, without difficult or lengthy maneuvers that may disrupt the routine or the normal workflow of a device laboratory. Procedural times and peri-procedural complication rates were not impacted by this practice, that does not have a learning curve for proceduralists accustomed by both components of this procedure. Albeit the cohort being at very high-risk of infection, no device related infections were observed at one-year and only a single, conservatively manageable, pocket infection was observed during the entire follow-up. These authors stand against a routine use of this combined procedure for all patients undergoing S-ICD placement. A careful patient selection and a patient-tailored assessment are needed to maximize the benefits associated with this approach. Nonetheless, it is our belief that this approach might benefit a niche of very high-risk of infection patients for which only limited data is available in the currently published major randomized trials[8,9].**Figure 1** reports the decisional flow algorithm we have been using at our institution to select patients potentially suitable for this combined approach.

A clinical and economical net benefit with the use of an AAE has been reported in selected patients with TV-ICD and, although previous reports failed to describe patients at a very high-risk of infection[9], data suggesting that AAE provides value for the healthcare system by reducing the incidence of CIED infection could be easily extended to the S-ICD[10]. If it is true that infective device-associated complications in patients implanted with an S-ICD system carry a lower mortality burden, being the management of those achieved with less invasive and less risky procedures, they cause patient discomfort and hospitalization for potential re-intervention is often required[11]. This may not pose a severe threat in a fit and young patient, but these patients at a very high-risk of infections are often frail, in a compromised systemic condition, and suffer from multiple sever comorbidities. Therefore, re-hospitalizations and re-interventions carry a different clinical impact in such a population, who often also shows a high arrhythmic burden (44% received an appropriate shock during follow-up) and cannot overlook the need for an ICD. This combined procedure is exactly aimed at minimizing re-hospitalizations in very high-risk patients, while helping to maximize the net benefit that the S-ICD may offer in specific clinical settings. Indeed, although re-hospitalization costs associated with the management of S-ICD related complications may be lower than what is observed in TV-ICDs, the device itself is currently much more expensive (currently billed around 2.5-3x times its TV-ICD counterpart in our country) and the deployment of an AAE may help avoiding expensive system replacement, reducing the overall costs for the healthcare system.

CONCLUSION

The combined deployment of AAEs and S-ICD in selected patients at very high-risk of infections is safe, feasible and may offer a true clinical benefit in specific clinical settings. None of the twenty-five patients implanted with a combination of AAE and S-ICD in this proof-of-concept study developed major device-related infectious complications in the first year of follow-up and only a single, conservatively manageable, pocket infection was experienced during in the entire cohort.

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Table 1: Patient population characteristics (n=25)

Age (years), mean±s.d
Male, n (%)
Hypertension, n (%)
BMI, mean±s.d
Diabetes, n (%) *Requiring insulin treatment*, n (%)
CKD, n (%) *Requiring hemodialysis*, n (%)
HF, n (%)
Arrhythmic substrate *Ischemic cardiomyopathy*, n (%) *Primitive dilatative cardiomyopathy*, n (%) *Valvular cardiomyopathy*,
AF, n (%)
LVEF (%), median [IQR]
Immunosuppressed state, n (%) *AIDS*, n (%) *Immunosuppressive medication*, n (%)
Active malignancy, n (%)
Type of Implant First ICD implant, n (%) Generator substitution, n (%) Conversion from TV device, n (%) Presence of aba
Patients on OAC, n (%)

Previous device related infections, n (%)	Precocious re-intervention, n (%)

Abbreviations: AIDS=acquired immunodeficiency syndrome; AF=atrial fibrillation; BMI=body mass index; CKD=chronic kidney disease; HF=heart failure; ICD=implantable cardioverter defibrillator; LVEF=left ventricular ejection fraction; OAC=oral anticoagulant; s.d.= standard deviation; TV=transvenous device; TWO=two wave oversensing; VF=ventricular fibrillation; VT=ventricular tachycardia.

Table 2: Procedural characteristics

Procedural time (mins), mean±s.d	53±11
DT performance, n (%)	16 (64)
Dual zone programming, n (%) *Monitoring zone (bpm),* mean±s.d *Shock zone (bpm),* mean±s.d	25 (100) 195±13 237±8
Standard shock polarity, n (%)	15 (94)
Sensing vector *Primary, n (%) Secondary, n (%) Alternative, n (%)*	*21 (84) 3 (12) 1 (4)*

Abbreviations: bpm= beats per minutes; DT=defibrillation testing, s.d.=standard deviation.

Table 3: Follow-up data

Follow-up time (months), mean±s.d	21 [12–29]
Appropriate shocks, n (%) *Sustained VT, n (%) VF, n (%)*	8 (32) *7 (28) 1 (4)*
Inappropriate shocks, n (%) *TWO, n (%) AF, n (%)*	2 (8) *1 (4) 1 (4)*
Device-related complication, n (%) *Pocket hematoma, n (%) Pocket infection, n (%)*	1 (4) *1 (4) 1 (4)*
Exitus, n (%) *Non cardiac exitus, n (%) Terminal HF, n (%)*	3 (12) 1 (4) 2 (8)

Abbreviations: AF=atrial fibrillation; HF=heart failure; TWO=two wave oversensing; VF=ventricular fibrillation; VT=ventricular tachycardia.

FIGURE LEGENDS

Figure 1. Decisional algorithm for combined S-ICD and absorbable antibacterial envelope used in our clinical practice[3,6].

Figure 2. Step by step procedure for absorbable antibacterial envelope deployment around an S-ICD device; A) Table setting; B) Opening of both sides of the envelope with a surgical scissor; C) Overturn inside-out the envelope; D) Deployment of the envelope around the S-ICD, with three external surgical knots for active fixation.

Figure 1

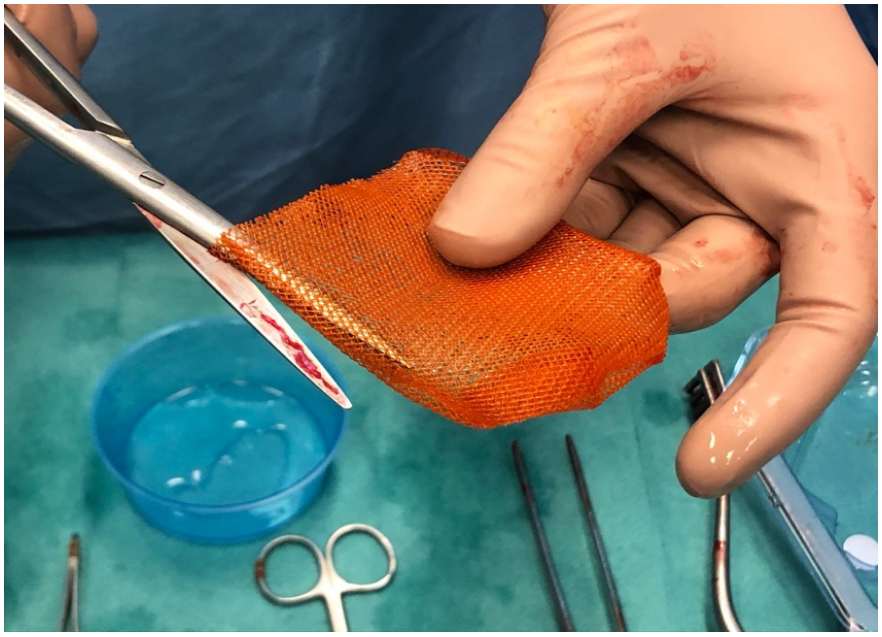

Figure 2