

Outcomes of Chlorhexidine Scrubbing without Capsulectomy vs. Complete Capsulectomy After Lead Extraction for the Treatment of Cardiac Implantable Device Infection

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Abstract

Introduction: Capsulectomy is recommended in patients with cardiac implantable electronic device (CIED) infection after transvenous lead extraction (TLE) but is time-consuming and requires extensive tissue debridement. In this study, we describe the outcomes of chlorhexidine gluconate (CHG) scrubbing in lieu of capsulectomy for the treatment of CIED infections. **Methods:** This retrospective observational study included patients who underwent TLE for CIED-related infections. In the capsulectomy group, complete capsulectomy was performed after hardware removal. In the CHG group, thorough scrubbing of the generator pocket with 20 cc of 2% CHG followed by irrigation with approximately 500 cc of sterile normal saline (SNS) was performed. The primary outcomes included reinfection and hematoma formation in the generator pocket. Secondary outcomes included any adverse reaction to chlorhexidine, the need for reintervention, infection-related mortality, and total procedural time. **Results:** A total of 102 patients (mean age 67.2 ± 13 years, 32.4% female) underwent CIED extraction with either total capsulectomy ($n=54$) or CHG ($n=48$) scrubbing. Hematoma formation was significantly higher in the capsulectomy group vs. the CHG group (13% vs. 0%, $p=0.014$), with no significant differences in the reinfection rate. Capsulectomy was associated with longer procedural time (133.7 ± 78.5 vs. 89.9 ± 51.8 minutes, $p=0.002$). No adverse reactions to CHG were found. Four patients (4.3%) died from worsening sepsis: 3 in the capsulectomy group and 1 in the CHG group ($p=0.346$). **Conclusions:** In patients with CIED infections, the use of CHG without capsulectomy resulted in a lower risk of hematoma formation and shorter procedural times without an increased risk of reinfection or adverse events associated with CHG use.

INTRODUCTION

The use of cardiac implantable electronic devices (CIEDs) has progressively increased over the past decades. This phenomenon can be attributed to technological advancements and accumulated procedural experience, enabling cardiac electrophysiologists to perform CIED placements on patients with complex clinical conditions. Unfortunately, the incidence of CIED infection is also rising, leading to increased morbidity, mortality, and healthcare costs.(1) Infection is undeniably the costliest device-related complication in patients receiving a pacemaker or defibrillator.(2) The clinical benefits of complete hardware removal are well-established in patients with CIED infections.(3) However, wound and pocket management is an area that has yet to receive

plenty of attention. After CIED implantation, wound healing results in fibrosis. The fibrotic avascular capsule inhibits antibiotic penetration and normal immune mechanisms and facilitates bacterial colonization.(4) Current guidelines recommend complete capsulectomy based on expert opinion and limited data, with no distinction between systemic infections (including persistent bacteremia/infective endocarditis) and localized pocket infections.(5) To adequately perform this procedure, significant operator experience is required, limiting its widespread adoption.

Furthermore, performing a capsulectomy is time-consuming, requires extensive tissue debridement, and increases the risk of bleeding and hematoma formation, mainly in patients with chronic oral anticoagulation.(6) Therefore, clinical practice varies widely, with recent surveys reporting that only 58-76% of physicians perform capsulectomy.(7,8)

Chlorhexidine is a positively charged molecule that binds to proteins and other negatively charged molecules on the bacterial cell wall causing instability, cellular membrane disruption, and eventually cellular death. It is a broad-spectrum biocide with bacteriostatic and bactericidal activity against fungi, and gram-positive and gram-negative bacteria. It has a very efficient microbiocidal rate (nearly 100% within 30 seconds of application) and prolonged activity due to its ability to bind to the tissues for up to 48 hours, which is not affected by blood or other bodily fluids.(9) These characteristics make it the drug of choice in several clinical scenarios, including skin and mucosal preparation for surgery, oral hygiene, prevention of ventilation-acquired pneumonia, and infection of intravascular catheters. Nevertheless, although preoperative chlorhexidine skin preparation is associated with a reduced risk of CIED infection(10) and has been suggested as a possible therapy after lead extraction,(11) outcomes related to its use in the treatment of CIED infection have not been described. We present the results of wound and device pocket scrubbing with chlorhexidine as an alternative to total capsulectomy after complete device removal in patients with CIED-related infections.

METHODS

Objective

We aimed to compare the effectiveness and safety of chlorhexidine gluconate (CHG) and saline pocket irrigation without capsulectomy versus capsulectomy after transvenous lead extraction (TLE) in the management of CIED-related infections.

Study design

This was a retrospective study of patients who underwent TLE as part of the treatment for CIED infection (including generator and/or lead extrusion, infective endocarditis [IE], persistent bacteremia, and pocket infection). Consecutive patients aged >18 years who had undergone TLE with complete capsulectomy (i.e., total removal of the anterior and posterior fibrous capsule) or CHG scrubbing without capsulectomy between July 2013 and September 2020 were included in the analysis. Patients who had partial capsulectomy were excluded. All patients signed a written informed consent authorizing the procedure.

Study procedures

Initially, subjects underwent a transesophageal echocardiogram and blood cultures to guide extraction and antibiotic therapy. Periprocedural anticoagulant management varied according to individual characteristics; in patients with mechanic mitral valves, warfarin was continued, and the procedure was performed with an INR 2-3, but patients on direct oral anticoagulants received the last dose at least 24 hours before the procedure. Oral anticoagulation was restarted 24 hours after the procedure if the patient did not develop a hematoma. All patients underwent complete hardware removal under general anesthesia using manual dilator sheaths (Sightrail® or Visisheath®, Spectranetics, Colorado Springs, CO, USA), mechanical rotating dilator sheaths (Tightrail®, Phillips Healthcare, Amsterdam, Netherlands), or laser-powered sheaths (Guidelight, Phillips Healthcare, Amsterdam, Netherlands) along with locking stylets (LLD, Phillips Healthcare, Amsterdam, Netherlands). Complete procedural success was defined as the removal of all targeted leads and material without permanently disabling complications or procedure-related death. Clinical success was defined as the retention of a small portion of a lead (<4 cm) that did not negatively impact the outcome goals

of the procedure.(12) Tissues extracted from the generator pocket and lead tips were sent for culture. In both groups, antibiotic irrigation was discouraged, as it has not shown any improvement in procedure-related infections.(13) All procedures were approved by the institutional review board.

Capsulectomy

After complete hardware removal, extensive tissue debridement aiming for complete capsule removal (both anterior and posterior capsule) was performed using cautery. Thereafter, pocket irrigation with 500 cc of SNS was performed. Proper hemostasis was achieved in all patients, and the wound was closed with an interrupted intradermal suture. Hemostatic fibrin products were not used since they are not approved for use in patients with infection. Pressure dressings were applied according to operator preference.

Chlorhexidine scrubbing (Figure 1)

Starting in 2017, institutional protocols for the management of CIED infection allowed CHG scrubbing in lieu of complete capsulectomy. This decision was based on the occurrence of hematomas requiring surgical drainage after capsulectomy, and previous reports on the safety of CHG use in wounds, even in delicate tissues such as the peritoneal membrane.(14-17) Moreover, capsule removal is frequently avoided in the treatment of infections in other sites where the extensive manipulation of adjacent tissues (i.e., liver or brain tissue) can lead to significant tissue damage.

After complete hardware removal, 20cc of 2% chlorhexidine soap was introduced into the generator pocket, and gentle manual scrubbing (using the index and middle fingers) of the entire cavity was performed for at least 1 minute. Subsequently, exhaustive irrigation with approximately 500 cc of SNS was performed, and manual scrubbing within the generator pocket was repeated. The pocket was dried using sterile gauze, and the wound was closed with an absorbable interrupted intradermal suture (with at least 1cm between suture points).

Management of pacemaker-dependent patients and follow-up

In patients without bacteremia who were pacemaker-dependent, contralateral implantation of a new CIED device was performed during the same procedure. In pacing-dependent patients with bacteremia or those considered at high risk of reinfection, contralateral implantation was performed once blood cultures were negative (with temporary pacing through a femoral or jugular temporary pacemaker). Antibiotics were given according to institutional protocols. The vast majority of patients had an initial follow-up six weeks after the procedure, but the long-term follow-up (every six months) was performed only in those patients who had the device reimplemented. At each in-office follow-up, wound sites were examined, and patients were interrogated for symptoms of CIED infection and chlorhexidine-related adverse events. We used electronic medical records and phone calls to patients and their relatives to ensure data completion.

Study Outcomes

The primary efficacy outcome was the recurrence of infection, defined as persistent infection, the presence of a pocket abscess with or without the need for surgical drainage or reintervention, or infection of a newly implanted device. The primary safety outcome was hematoma formation. Secondary outcomes included any adverse reaction to chlorhexidine (including allergic reactions and skin reactions), the need for reintervention (including surgical hematoma or abscess drainage), infection-related mortality, and total procedural time.

Statistical analysis

All statistical analyses were performed using SPSS Version 26 (IBM Corp., Armonk, NY). Quantitative data were expressed as mean \pm SD and were compared using a T-test. Categorical data were expressed as percentages and compared using the Chi-square test. For statistical tests, a $p < 0.05$ was considered statistically significant.

RESULTS

Patient characteristics

Between July 2013 and May 2022, a total of 102 patients (mean age 67.2±13 years, 32.4% female) underwent CIED extraction with either total capsulectomy (n=54) or CHG (n=48) scrubbing performed during the procedure. The mean follow-up was 638 days. The most frequently removed devices were single or dual-chamber pacemakers (n=44, 43.1%), cardiac resynchronization therapy and defibrillator devices (n=31, 30.4%); followed by implantable cardioverter-defibrillators (n=27, 26.5%). The extraction cause was equally distributed between bacteremia/infective endocarditis (50%) and device extrusion/pocket infection (50%), with no statistically significant differences between both groups. No significant differences in baseline characteristics between groups were found (**Table 1**). Bacteria were isolated from blood, pocket, or lead tip cultures in 67.6% of cases. Gram-positive bacteria, including methicillin-sensitive and methicillin-resistant *Staphylococcus aureus* (MSSA and MRSA, respectively), coagulase-negative staphylococcus (CoNS), and *Streptococcus* spp. were the most frequently found causative organisms. Complete procedural success was achieved in 84 patients (94.4%), and clinical success was achieved in 86 patients (96.6%) with no significant differences between groups. The length of stay was similar in the capsulectomy vs. CHG group (18.5±20.2days vs. 23.7±26.4 respectively, p=0.262). Fifty-six patients (54.9%) had a new device implanted, with no significant differences in the percentage of patients having a new implant between groups (53.7% vs. 56.3% in the capsulectomy vs. CHG, p=0.844). The mean for the reimplant procedure was 125.3±241.6 days in the capsulectomy group vs. 38.7±78.3 days in the CHG group (p=0.076); in the capsulectomy group 10 patients (34.5%) and 14 patients (51.9%) in the CHG had a new device implanted within a week from the extraction (p = 0.28). Regarding the type of placed device, 37.9% of patients in the capsulectomy group had a pacemaker (either single or dual chamber, or leadless), compared to 66.7% of patients in the CHG group. In the remaining patients in each group, the implanted device was related to underlying heart failure (i.e., an ICD or a CRT device). Procedural characteristics are shown presented in **Table 2**.

Outcomes

The primary effectiveness outcome (infection recurrence) occurred in 4 patients (4.3%) who died from worsening sepsis: 3 in the capsulectomy group and 1 in the CHG group (p=0.346). Individual characteristics of patients who died of sepsis are included in **Table 3**. There were no cases of reinfection of newly implanted devices or need for reintervention due to local infection. The primary safety outcome (hematoma formation) occurred in 7 patients (13%) in the capsulectomy group vs. none in the CHG group (p=0.014). There were no immediate or 30-day complications associated with chlorhexidine use. Consequently, post-procedural complications (i.e., hematoma or recurrent infection) were significantly more frequent in patients undergoing capsulectomy than in patients undergoing CHG scrubbing. The procedural time was significantly longer in patients undergoing capsulectomy (133.7±78.5vs. 89.9±51.8 minutes, p=0.002) (Central Illustration).

Outcomes in patients undergoing intervention for CIED pocket infection

We performed subgroup analysis to determine if capsulectomy was associated with meaningful benefits in patients with localized pocket infection. In this subgroup (n=51), capsulectomy was also associated with a significant risk of hematoma (6 vs. 0 cases, p=0.006) without significant differences in the risk of reinfection (p=0.596).

Discussion

Our study demonstrates the feasibility, efficacy, and safety of CHG scrubbing of the generator pocket while avoiding complete capsulectomy in the management of CIED infections. The main findings of our study are:

- Total capsulectomy is associated with a significant (13%) risk of hematoma formation.
- No significant adverse reactions were observed associated with CHG scrubbing.
- Avoiding capsulectomy when performing CHG irrigation is not associated with a higher risk of reinfection, even in patients undergoing early device implant (i.e., within the first week of extracting the infected CIED) or in patients undergoing extraction for pocket infection.
- Capsulectomy is associated with significantly longer procedural times than a more straightforward strategy involving CHG scrubbing.

Current rates of CIED infection have risen over the last several decades despite improved procedural techniques and prophylactic antibiotics, probably owing to a higher proportion of critically-ill patients being treated with implantable devices (particularly implantable cardiac defibrillators and resynchronization therapy devices). Several mechanisms have been proposed to explain device-related infections, including contamination during implantation, lead seeding during bacteremia episodes associated with distant infections, and skin erosion (which can be the cause or the consequence of a subclinical pocket infection). The risk of infection appears to be higher in patients undergoing generator replacement, lead or pocket revisions, device upgrades, and resynchronization device implantation. Given that 9% of patients presenting with a pocket infection have had a device-related infection in the past(18) and that a prior infection increases the risk of a future infection by 65%,(19) strategies to reduce the risk of infection recurrence are of paramount importance. Complete hardware removal undoubtedly plays a significant role in reducing this risk of reinfection and is recommended in current guidelines to achieve infection control.

Nevertheless, the appropriate management strategy for the generator pocket and the wound has yet to be established based on solid evidence.(5) This knowledge gap has led to many protocols, including the use of costly therapies with unproven clinical benefits.(20,21)

Total capsulectomy has been proposed to achieve resolution of the infection and is currently used by approximately 58-76% of centers, with no distinction made in current guidelines regarding the type of infection (i.e., pocket infection vs. bacteremia/endocarditis).(7,8) Furthermore, there is insufficient evidence to support its routine use, and capsulectomy is an arduous procedure associated with a significant risk of hematoma formation and the occasional need for pocket revision to control the bleeding.(6) The presence of post-procedural hematoma is associated with a substantial increase in the risk of infection (22) and could result in prolonged hospitalization and increased healthcare costs. Moreover, large hematomas frequently require OAC interruption, which is associated with significant stroke risks in patients with atrial fibrillation, the most frequent indication for OAC use. The hematoma formation rate in the present study is higher than that described in the MAKE IT CLEAN trial, which found hematoma formation in 6.1% of patients undergoing capsulectomy.(6) Interestingly, 6 out of the 7 hematomas were found in patients with a pocket infection, with only 1 in patients with infective endocarditis/bacteremia. As such, operators may perform more aggressive tissue debridement when managing pocket infections, thus explaining the higher rate of hematoma compared to the MAKE IT CLEAN trial.

Given the low cost, widespread availability, and low risk of adverse reactions associated with CHG, our current protocol is valuable by reporting the reduced risk of hematoma formation without increasing the risk of reinfection. To avoid adverse reactions associated with chlorhexidine, thorough washing of the pocket cavity is important, being careful not to exert excessive pressure during saline irrigation since high pressure can be associated with soft tissue damage. Moreover, allergic reactions to chlorhexidine are infrequent, with only 124 cases reported in the literature in over 40 years of use.(23)

As expected, the most frequently identified infectious organisms in our study were gram-positive bacteria (including MSSA, MRSA, and CoNS). Their presence explains this as normal skin flora in some patients and their ability to adhere to non-biological surfaces, creating biofilms. Biofilm mitigates antimicrobial effect, thus explaining the poor response to antibiotics to treat CIED infections if complete hardware removal is not performed. Notably, chlorhexidine can eradicate bacteria present in biofilm (and, possibly, on capsules),(9) which could explain our positive results.

Other protocols have been described to reduce the risk of recurrent infection in patients with CIED infection. Buckarma et al. described a protocol including surgical debridement, total capsulectomy, negative pressure, and surgical reevaluation 48 hours after the initial treatment.(24) Even though this protocol was associated with a reduction in the length of hospital stay, it failed to decrease the reinfection rates. Therefore, it is possible that many of the interventions applied in this protocol (including capsulectomy and negative pressure) are unnecessary and only increase procedural times and costs. Our reinfection rate is lower than previously published by Sohail et al., who described a 5% risk of recurrent/persistent infection.(25) These positive results are compelling, considering the high percentage of patients with pocket infection (50%) in

our series, given that a more “aggressive” approach (i.e., complete capsulectomy) would be preferred by most physicians in cases of pocket infection/device extrusion. Thereupon, contrary to what would be expected, the use of a “less aggressive” (i.e., CHG irrigation) approach in patients with pocket or device-related infections had similar outcomes to a “more aggressive” approach. Likewise, although 54.9% of patients received a new device, with patients in the CHG having a numerically shorter time to reimplant than patients in the capsulectomy group (albeit statistically non-significant), there were no significant differences in the rate of reinfection. Finally, CHG scrubbing was associated with a substantial reduction in procedural times, an important finding considering the rising importance of increasing lab efficiency. Although variations in individual procedural times may exist between different hospitals (as it is highly related to operator experience), a more straightforward procedure (i.e., CHG irrigation) is expected to be associated with reduced procedural times, particularly since during capsulectomy operators must constantly address and undertake different actions to control bleeding (e.g. identifying the site of bleeding and the use of cautery, manual pressure, or artery ligation).

Limitations

Our study has various limitations. First, the small number of patients included could impact our results, particularly in our lack of recurrent infection in both groups. However, to our knowledge, this is the largest trial evaluating the impact of capsulectomy on outcomes. Moreover, it is impossible to determine whether our favorable results are due to CHG scrubbing or if they can be achieved by saline irrigation only since wound irrigation removes debris and bacteria in experimental models and is associated with a reduction in the risk of surgical site infections.⁽²⁶⁾ Although both groups underwent saline irrigation, the volume of fluid used during saline irrigation differed between groups, as a larger volume was used in patients in the CHG group to thoroughly remove the CHG. However, it is implausible; that irrigation alone could explain our positive results since saline irrigation is frequently performed as a standard procedure for treating CIED infection. Finally, as this is a retrospective study, it is prone to confounding bias as there were significant differences in baseline characteristics of patient populations. As such, this study should be considered an observational study of a change in practice.

Conclusion

In this series of patients with CIED-related infections, CHG and saline pocket irrigation without capsulectomy was an excellent alternative to capsulectomy, with no cases of reinfection, even in patients with early device reimplantation and a significantly lower rate of hematoma formation. Furthermore, the use of CGH was not associated with any adverse reactions and was associated with a highly significant reduction in procedural times. Our results suggest that the use of CHG could be a safer and time-saving alternative to total capsulectomy in patients with CIED-related infection. In conclusion, our findings indicate that the use of CHG could be an alternative to total capsulectomy in patients with CIED-related infection, reducing procedural time and the risk of hematoma formation. Further randomized controlled trials are needed to determine the impact of CHG irrigation and capsulectomy in treating CIED infections.

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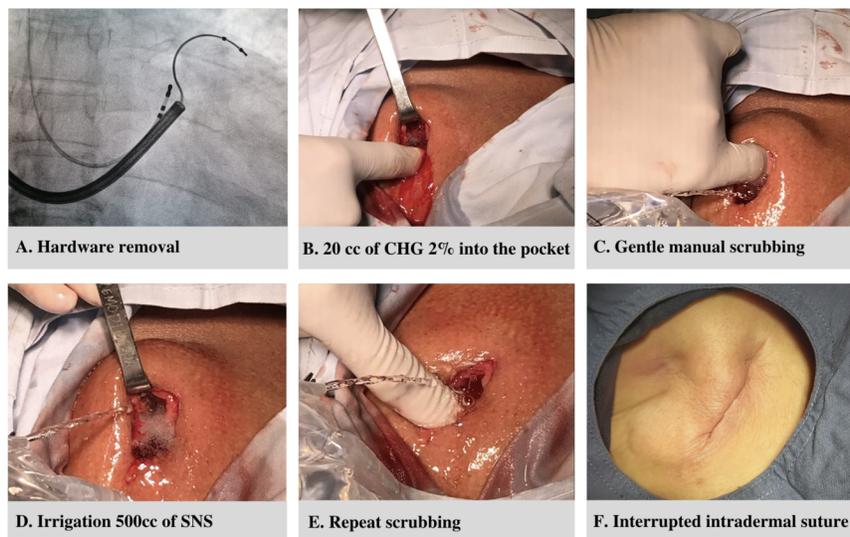


Figure 1. After complete device removal, patients in the CHG group underwent thorough scrubbing of the generator pocket with CHG, followed by saline irrigation of the generator pocket with additional scrubbing. In all cases, primary closure of the wound was performed with an absorbable suture, using an interrupted suturing technique. Abbreviations: CIED: cardiac implantable electronic device; SNS: sterile normal saline CHG: chlorhexidine gluconate.

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Central Illustration. Clinical outcomes associated with CHG irrigation vs. capsulectomy to treat CIED infections. Abbreviations: CHG: chlorhexidine gluconate.

Table 1. Baseline characteristics.

	All (n = 102)	Capsulectomy (n = 54)	CHG Irrigation (n = 48)	P value
Age (years)	67.2±13	66.9±14.4	67.6±11.3	0.795
Female sex (%)	33 (32.4%)	18 (33.3%)	15 (31.3%)	0.836
LVEF (%)	44.3±16	42.7±16.2	45.9±15.9	0.322
HTN	91 (89.2%)	50 (92.6%)	41 (85.4%)	0.34
DM	32 (31.4%)	18 (33.3%)	14 (29.2%)	0.675
CHF	54 (53.5%)	32 (59.3%)	22 (46.8%)	0.235
CAD	31 (30.7%)	18 (34%)	13 (27.1%)	0.52
CKD	13 (12.9%)	7 (13.2%)	6 (12.5%)	1.0
OAC	26 (25.5%)	12 (22.2%)	14 (29.2%)	0.497
Cause of extraction				
Device	51 (50%)	23 (42.6%)	28 (58.3%)	0.165
Extrusion/Pocket infection				
Bacteremia/IE	51 (50%)	31 (57.4%)	20 (41.7%)	0.165
Germ Gram	50 (49%)	24 (44.4%)	26 (54.2%)	0.428
positive Gram	19 (18.6%)	12 (22.2%)	7 (14.6%)	0.446
negative Gram	33 (32.4%)	18 (33.3%)	15 (31.3%)	0.836
Negative cultures				

Abbreviations: LVEF: left ventricular ejection fraction; HTN: hypertension; DM: diabetes mellitus; CHF: congestive heart failure; COPD: chronic obstructive pulmonary disease; CAD: coronary artery disease; CKD: chronic kidney disease; OAC: oral anticoagulant use; AP: antiplatelet therapy use; MRSA: methicillin-resistant *Staphylococcus aureus*; MSSA: methicillin-sensitive *Staphylococcus aureus*; IE: infective endocarditis.

Table 2. Procedural characteristics and outcomes.

	All (n = 102)	Capsulectomy (n = 54)	CHG Irrigation (n = 48)	P value
Complete Success	96 (94.1%)	52 (96.3%)	44 (91.7%)	0.416
Clinical Success	98 (96.1%)	52 (96.3%)	46 (95.8%)	1.0
Procedural time (min)	114.1±71	133.7±78.5	89.9±51.8	0.002
Total hospital length of stay	20.9±23.3	18.5±20.2	23.7±26.4	0.262
Post procedural length of stay	12.5±14.5	13±16.1	11.9±12.6	0.709
Reimplant	56 (54.9%)	29 (53.7%)	27 (56.3%)	0.844
Days after removal	83.6±185.6	125.3±241.6	38.7±78.3	0.076
Follow-up	638.1±604.7	541±550	747±648	0.086

	All (n = 102)	Capsulectomy (n = 54)	CHG Irrigation (n = 48)	P value
Post-procedural complications	7 (6.9%) 4 (3.3%) 21 (22.8%)	7 (13%) 3 (6.8%) 21 (22.8%)	0 1 (2.1%) 8 (16.7%)	0.014 0.346 0.111
Hematoma Formation				
Reinfection				
All-cause Mortality				

Values are given as mean \pm SD or n (%).

Table 3. Clinical characteristics of the 4 patients who died from worsening sepsis.

Three of the patients had infective endocarditis, while one patient had device extrusion. Abbreviations: M: male; F: Female; LVEF: left ventricular ejection fraction; IE: infective endocarditis; HTN: hypertension; DM: diabetes mellitus; CHF: congestive heart failure; CAD: coronary artery disease; CHG; chlorhexidine gluconate; COPD: chronic obstructive pulmonary disease; MRSA: methicillin-resistant *Staphylococcus aureus*.

Pt	Sex	Age	Type of infection	Germ	Underlying conditions	LVEF	Group	Procedural
1	M	84	Device extrusion	<i>S. epidermidis</i>	HTN, DM, CHF, CAD	19%	CHG	None
2	F	67	IE	<i>K. oxytoca</i>	HTN, COPD	70%	Capsulectomy	None
3	M	69	IE	<i>MRSA</i>	HTN, DM, CHF, Sarcoidosis	32%	Capsulectomy	None
4	M	49	IE	<i>S. epidermidis</i>	HTN, CHF	65%	Capsulectomy	None