1. Taurolidine containing antimicrobial wash to prevent cardiac implantable electronic device infection

Henke, J., et al., *Taurolidine containing antimicrobial wash to prevent cardiac implantable electronic device infection.* European Journal of Arrhythmia & Electrophysiology, 2022. **8**.

Background Cardiac implantable electronic device (CIED) infection has risen faster than the volume of procedures. Many measures against CIED infection have been tried, but only peri-operative antibiotics and an antibiotic eluting envelope have proved effective when tested in randomised clinical trials. Taurolidine is a long-established antimicrobial agent with a wide range of chemical activities and biological effects. The effectiveness of a taurolidine containing solution in preventing CIED infection was assessed in an observational study.
Methods All the hardware (leads, suture sleeves, pulse generator) was washed and the device pocket irrigated with an adjunct antimicrobial solution, which could be 3% hydrogen peroxide (H_2O_2), taurolidine in a galenic formulation or TauroPace™ (TP, Tauropharm, Bavaria, Germany), during any invasive procedure (new implantation, pulse generator replacement, lead repositioning or insertion, system upgrade or downgrade, revision) involving a CIED system at the authors' institute. Before 01/01/2020, the choice of antimicrobial solution was at the operator's discretion (retrospective). Afterwards, only TP was used (prospective). Patients were enrolled and followed consecutively in order of appearance. All CIED procedures performed at the author's institute between 01/01/2017 and 28/02/2022 were included for analysis. Patients who received the galenic taurolidine formulation were excluded from analysis. The primary end point was CIED infection according to the Novel 2019 international diagnostic criteria . The secondary end point was any adverse or serious adverse event (e.g. pneumothorax, allergy, etc.) possibly related to the use of the antimicrobial solution, the CIED or the procedure and all-cause mortality. The follow-up duration was standardised to 3 months as only acute and sub-acute infection post CIED procedure was of interest. The procedures and not the patients were the data units. Patients who underwent more than 1 procedure during the above-mentioned period were deemed to have been censored for the initial treatment group and re-classified as new data units (with or without cross-over to the other treatment group) at the time of the second procedure.
Results Between January 2017 and February 2022, 1417 invasive CIED procedures were conducted in one centre. 654 procedures were conducted with adjunct TP in 631 distinct patients, and 551 procedures with adjunct H2O2 in 532 distinct patients. The TP group had significantly more host risk factors (e.g. acute renal failure, anticoagulation) for infection than the H2O2 group ($p = 0.0058$), but similar device (e.g., CRT-D) and procedure (e.g., early revision) specific risk factors ($p=0.17$). Within three months post index procedure, CIED infection occurred in 0/654 (0.0%) in the TP group and 6/551 (1.09%) in the H2O2 group (95% CI: 0.5% to 2.36%, $p=0.0075$). Death occurred in 23/654 (3.5%) of the TP group and 14/551 (2.5%) in the H2O2 group (95%CI: – 2.98% to 1.05%, $p=0.33$). Non-infection related serious adverse events were rarer in the TP group than the H2O2 group (95%CI: – 4.79% to 0.26%, $p=0.0802$) (3.8% vs. 6.0%). The hazard ratio for major CIED infection was 0.40 (0.10 to 1.56) without adjustment and 0.37 (0.09 to 1.42) when adjusted for number of patient risk factors in a Cox regression using all follow-up (median 15 months).
Conclusions: Adjunctive use of TP during CIED procedures may have been a cause of a lower rate of acute and delayed major CIED infection without a higher incidence of complications compared to H2O2. The clinical utility of TP in reducing CIED infection will need to be further assessed in a randomised clinical trial.
Trial registration: ClinicalTrials.gov Identifier: NCT05576194

2. Use of Taurolidine in a Patient With a Cardiac Implantable Electronic Device Protrusion

Giudice M, et al., *Use of Taurolidine in a Patient With a Cardiac Implantable Electronic Device Protrusion. JACC: Case Reports*. 2023;14:101835.

Background: CIED components (pulse generator, anchor sleeves, leads) may protrude out of the device pocket if the lining tissues (typically skin and subcutaneous tissues) break down. The pocket breach

typically occurs through the tissues lining the edges rather than covering the surfaces of the pulse generator for several reasons. First, the edge lining tissues are more stretched than the surface lining tissues, becoming thinner and more at risk of pressure-induced necrosis. Second, the capillaries running through the edge lining tissues may be compressed, reducing their blood supply (ie, pressure-induced ischemia). Third, the edge lining tissues are more exposed to mechanical abrasion by any rubbing over the CIED pocket. Infection may contribute to the breakdown process by weakening the lining tissues from within and without. Once the lining tissues have been breached, the protruded CIED components will be colonized by bacteria. The current guidelines clearly recommend the extraction of all hardware in case of infection. However, in cases where patients are too frail to undergo extraction or object to the procedure itself only chronic antibiotic suppression and frequent dressing changes (i.e., palliation) is available.
Case presentation: We report the successful salvage of cardiac implantable electronic device pulse generator protrusion in a patient presenting 5 months after the last surgical revision, too frail to undergo extraction.
Conclusions: Although an externally exposed CIED system can be successfully salvaged, the circumstances leading to the adoption of this unconventional management strategy in this case are unusual and system salvage should not be regarded as a general substitute for the standard of care for CIED infection, which is complete hardware explantation. The risks and benefits of any treatment, particularly when deviating from guidelines, should be weighed carefully in the context of each individual patient. However, if the therapeutic objective is medium-term clinical freedom from infection without hardware removal, the salvage procedure described would be a valuable addition to the armamentarium of measures for dealing with CIED infection.

3. Pacemaker infection in fragile patients

Casorelli E, et al., *Pacemaker infection in fragile patients.* Herzschrittmachertherapie &Elektrophysiologie 2023.

Background: Complications associated with cardiac implantable electric devices (CIED) are manifold. They include lead dislocation, twiddler's syndrome, device malfunction, haematoma formation and infection. Infections can be divided into acute, subacute and late infections. Both the time of onset and the route of infection play a crucial role. The consequences of a CIED infection are devastating. The most modern treatment methods include the removal of all implanted implants. If complete removal is not followed in the event of infection, there is a high rate of infection recurrence. Open thoracic surgery to remove infected CIED hardware has been replaced by percutaneous lead extraction procedures. Lead extraction requires specialised equipment and expertise and may not be readily available or feasible for some patients. Any hardware removal comes with a risk of complications (e.g. damaging cardiac structures, haemothorax and pericardial effusion). For these reasons, the performance of such procedures should be limited to centres with adequate equipment and experience.
Case presentation: In our case, we report the successful salvage of an exposed generator in a frail patient treated more than 5 years after the last generator replacement.
Conclusions: A specific antimicrobial solution approved for the any CIED placement could be a safe and effective option and improve the clinical outcome in the CIED rescue procedure described here. At the same time, the risk of resistance is unlikely due to the main active ingredient, taurolidine.

4. Salvage of infected cardiac implantable electronic device with taurolidine—a case report.

Borov, S., et al., *Salvage of infected cardiac implantable electronic device with taurolidine—a case report.* The Cardiothoracic Surgeon, 2022. 30(1): p. 7.

Background: Cardiac implantable electronic devices (CIEDs) are commonly used to treat cardiac arrhythmias and prevent sudden cardiac death. Complications of CIED therapy include component malfunction, lead dislodgement, skin erosion and infection. Infection can result in significant morbidity and even mortality. The recommended treatment of CIED skin erosion and infection is urgent complete device extraction. When this is infeasible due to patient or resource factors, an attempt could be made to salvage the exposed or infected CIED system by debridement of all the infected necrotic tissues and

irrigation of the pocket and contaminated hardware with anti-septic/antibiotic solutions. Taurolidine, when dissolved in an aqueous solution, produces a broad spectrum of antimicrobial actions and may be used as a novel irrigation agent during CIED salvage.
Case presentation: This report describes the first use of a taurolidine-containing solution for pocket irrigation and in situ hardware sterilisation that resulted in the successful salvage of a CIED infected with multi-resistant Staphylococcus epidermidis.
Conclusions: A taurolidine-containing antimicrobial solution can be a safe and effective alternative to traditional antiseptic/antibiotic solutions for pocket irrigation and in situ hardware sterilisation during CIED salvage, and may produce better clinical outcomes by some unique mechanisms of action such as inhibition of biofilm formation and neutralization of endotoxins, with little risk of inducing and encountering resistance.

5. Salvage of Cardiac Implantable Electronic Device Pocket Infection with Skin Erosion in Frail 92-Year-Old.

Giaccardi, M., et al., *Salvage of Cardiac Implantable Electronic Device Pocket Infection with Skin Erosion in Frail 92-Year-Old.* Journal of Cardiovascular Development and Disease, 2022. **9**(3): p. 81.

Background: The incidence of cardiac implantable electronic device (CIED) infections has increased disproportionally in relation to the rise in surgical procedures related to CIEDs over the past decades. For CIED infection, both of the pocket and/or lead related endocarditis, state of the art treatment includes the removal of all indwelling hardware. Lacking adherence to complete system removal in case of infection comes with high rates of infection relapse. Open chest surgery for hardware removal has been superseded by percutaneous extraction procedures. Lead extraction requires special equipment and expertise and may not be readily available or infeasible for some patients. Any extract procedure is associated with a small risk of potentially fatal complications (e.g. cardiac avulsion, vascular avulsion, haemothorax and cardiac tamponade). For these reasons, the performance of such procedures should be limited to centres with adequate equipment and expertise. Alternative management options would be appealing in certain patients with CIED infection. Successful salvage of infected CIED systems with in situ sterilisation of the contaminated hardware has been reported.
Case presentation: In our case we report of a successful salvage of an exposed generator with polymicrobial contamination in a frail patient with taurolidine, presenting more than five months after the last generator substitution.
Conclusion: Our case demonstrates the feasibility of achieving mid-term freedom from clinical infection without hardware removal of a primarily or secondarily infected generator protruding through the skin in a frail patient.

6. Eradication of Ventricular Assist Device Driveline Infection in Paediatric Patients with Taurolidine.

Weichsel, J., et al., *Eradication of Ventricular Assist Device Driveline Infection in Paediatric Patients with Taurolidine.* Journal of Cardiovascular Development and Disease, 2022. **9**(1): p. 18.

Background: Ventricular assist devices (VADs) are used to provide mechanical circulatory support to patients with end-stage heart failure. The driveline connecting the external power source to the pump(s) of the intra-corporal VAD breaches the protective skin barrier and provides a track for microbes to invade the interior of the patient's body. Driveline infection constitutes a major and potentially fatal vulnerability of VAD therapy. Driveline infection cannot traditionally be salvaged and requires the extraction of the entire VAD system.
Case series: We report here the successful eradication of a series of VAD driveline infections with a taurolidine-containing antimicrobial solution used for preventing the infection of cardiac implantable electronic devices.
Conclusion: If replicated in more cases, the novel treatment concept described here may provide a valuable alternative management strategy of salvage rather than explantation for VAD driveline infection.