Infection remediation after septic device extractions - comparison of three treatment strategies including a one-year follow-up

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Abstract

Introduction: Treating patients with CIED infections is often challenging. In general, the infected device, including all leads, needs to be completely removed before a new CIED can be implanted. Especially in pacemaker-dependent patients, it is often impossible to have a device-free interval to treat the infection. In those cases, the question remains when to implant a new CIED and which bridging strategy to use. **Methods:** In this single-center retrospective analysis, we included 190 patients who received a complete CIED system extraction between 2013 and 2019 due to device-related infection. We compared three different treatment algorithms. Group 1 (SR) included 89 patients who received system removal only (and delayed re-implantation). Group 2 (EL) consisted of 28 patients who were treated with lead extraction and simultaneous epicardial lead implantation, while the 78 patients in Group 3 (SI) received lead removal with simultaneous contralateral implantation of a new device. We retrospectively analyzed the peri- and postoperative course and one-year follow-up. **Results:** Patients in the SR and EL groups were significantly older, had more comorbidities and a higher percentage of systemic infection compared to the SI group. We found a comparable high number of successful infection treatments in all groups, with complete lead removal in 95.5%, 96.4%, and 93.2% for the SR, EL, and SI groups, respectively. Lead vegetations were removed in 97.7%, 94.1%, and 100%. Device re-implantation was 100% in the EL and SI groups, whereas in the SR group, only 49.4% of patients received a device re-implantation. At one-year follow-up, the percentage of freedom from infection and pocket irritation was comparable between groups (94.7% SR and EL, 100% SI). We observed no procedure-related mortality, while one-year mortality was 3.4% in the SR, 21.4% in the EL and 4.1% in the SI group. **Conclusion:** We found comparable success rates regarding device removal, successful infection treatment and perioperative course between groups. However, most likely due to the sicker patient collective with a high number of systemic infections, the one-year mortality was significantly higher in the EL group. Treatment algorithm should be selected due to type, severity, location of infection and comorbidities of the patients.

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Results: Patients in the SR and EL groups were significantly older, had more comorbidities and a higher percentage of systemic infection compared to the SI group. We found a comparable high number of successful infection treatments in all groups, with complete lead removal in 95.5%, 96.4%, and 93.2% for the SR, EL, and SI groups, respectively. Lead vegetations were removed in 97.7%, 94.1%, and 100%. Device re-implantation was 100% in the EL and SI groups, whereas in the SR group, only 49.4% of patients received a device re-implantation. At one-year follow-up, the percentage of freedom from infection and pocket irritation was comparable between groups (94.7% SR and EL, 100% SI). We observed no procedure-related mortality, while one-year mortality was 3.4% in the SR, 21.4% in the EL and 4.1% in the SI group.

Conclusion: We found comparable success rates regarding device removal, successful infection treatment and perioperative course between groups. However, most likely due to the sicker patient collective with a high number of systemic infections, the one-year mortality was significantly higher in the EL group. Treatment algorithm should be selected due to type, severity, location of infection and comorbidities of the patients.

Article

Introduction

The use of cardiac implantable electronic devices (CIED) has been an essential and indispensable therapy option for patients with symptomatic cardiac arrhythmias or a high risk of sudden cardiac death (SCD) for over 60 years. Unfortunately, for most patients, the initial implantation of such a device implicates repeated revision procedures. Ideally, these should be limited to only pulse generator-replacement due to battery depletion. However, additional revision or correction surgeries do occur, originating in technical problems of the implanted systems or in infections. The predominant local infections are pocket infections, which often occur shortly after a device replacement, or those caused by percutaneous perforation of pulse generator or electrode components (1-3). Aside from local symptoms, like pain, swelling and tenderness, these infections pose a high risk for systemic seeding into the bloodstream. The transmission of the infection along the implanted electrodes is particularly feared, as it can lead to life-threatening endocarditis, which can be fatal in 35% of cases if left untreated (4,5). A similar vital threat can also arise from a primary hematogenous bacteremia with superinfection of the implanted device components. Biofilm-forming bacteria such as staphylococci, streptococci or pseudomonas are especially feared in this context (6). This often leads to septic vegetations on the intravascular parts of the leads, which can, on one hand trigger septic emboli and serve as a retreat for bacteria under a protective layer of biofilm during antibiotic therapy on the other. For these reasons, the timely and aggressive treatment of intracardiac infections is essential, as cardiac structures such as heart valves or myocardial tissue can be irreversibly destroyed if left untreated. Based on these findings, international and national professional societies recommend prompt and complete removal of intracardiac devices with a Class I recommendation in cases of proven infections. (11-15).

However, a CIED cannot always be easily removed. In addition to technical and anatomical imponderabilities, the further strategy must be carefully evaluated and planned, especially in pacemaker-dependent patients (16,17). In addition, there is still no uniform recommendation among experts regarding the timing of the re-implantation of a necessary system (12-19). Therefore, various approaches arise in clinical practice, which can be reduced to three established variants: The first and most commonly performed treatment option is system re-implantation after complete system removal (SR) with a time delay of 4-6 weeks under antibiotic therapy and after exclusion of an ongoing infection (18,19). This strategy is limited by the requirement of an adequate intrinsic cardiac rhythm. In case of pacemaker dependency, as a second option, simultaneous implantation of an epicardial pacing lead through an additional left lateral thoracotomy (system removal and implantation of an epicardial pacing lead - EL) can be performed during removal of the infected system. This is then connected to a subcutaneously implanted "sacrificial pacemaker" and ensures continued stimulation (18). Alternatively, temporary percutaneous transvenous "sacrificial electrodes" can also be placed (18,19). In both cases, implantation of a definitive system is performed in a second scheduled procedure after successful antibiotic therapy (18,19). The third and final therapeutic option is a simultaneous implantation of a permanent system from the contralateral side after removal of the infected system (System removal and contralateral implantation of a new device - SI). Thus, uninterrupted full device therapy is possible -

but with the remaining risk of re-infection, for example, via contact infections or continued hematogenous bacterial dissemination.

The decision for one of the described procedures is usually based on the clinical experience of the treating physicians, as there are no comparative studies or follow-up data on the outcome of these procedures in the currently available literature (13,19). For this reason, we retrospectively analyzed all patients treated in our hospital between 2013 and 2019 who received a CIED removal/extraction due to device infection. We searched for differences in the pre-existing conditions of the patient groups in a retrospective analysis of the treatment pathways in order to evaluate the clinical decisions made. We further analyzed whether peri- and postoperative differences in the treatment courses during the hospital stay could be shown. Finally, we investigated the one-year follow-up data of the 3 treatment strategies, in order to compare possible outcome differences between the treatment pathways.

Methods

The presented observation study is a retrospective analysis of all lead extractions performed in our center between 2013 and 2019. We identified 190 extraction procedures in patients with infectious indications, which were divided into the three treatment paths described above. This resulted in a total of 89 procedures in which the systems were removed exclusively (Exclusive System Removal = SR), 28 procedures in which the system was removed and an epicardial pacing lead was implanted simultaneously (System Removal and Implantation of an Epicardial Pacing Lead - EL), and 73 patients in whom a completely new and definitive device system was implanted on the contralateral side (System Removal and Contralateral Implantation of a new device - SI).

In addition to patient-specific data, cardiac pre-existing cardiac conditions or treatments and relevant comorbidities were recorded. Furthermore, the timing of the initial diagnosis, admission to our hospital, pre-operative antibiotic therapy, timing of the surgical procedure, and length of the treatment period were of interest. In particular, we also considered pre-operative infection parameters, previously identified pathogens, and the age of the implanted CIED components. Additionally, the indications for CIEDs and their implantation positions were recorded. During surgery, besides the group-specific method, the extraction techniques, number of removed electrodes, existing vegetation, pericardial effusion sizes, tricuspid valve function, and wound closure methods were documented along with the duration of the procedure, fluoroscopy, and laser times. In the post-operative course, the duration of the intensive care unit (ICU)- and overall hospital stay, further course of infection parameters (laboratory chemistry, pathogen detection), echocardiographic findings, and the discharge destination (home or another hospital) were recorded.

If a second surgery was required for re-implantation of a CIED, perioperative parameters and lead measurements were registered. At one-year follow-up we reassessed the completed healing of the CIED pockets, device function, laboratory parameters, current NYHA class, LV-EF, and lead-specific measurements. Fatal treatment courses were also recorded and distinguished between perioperative and post-discharge time points.

The collected data were obtained from the digital and analog patient records of our hospital and, in individual cases, were supplemented with additional information from treating colleagues. All data were digitalized and anonymized after the data collection was completed. Finally, the statistical analysis, tabular and graphical processing, and evaluation of the results were performed.

The investigations were carried out in accordance with the Declaration of Helsinki of the World Medical Association on the ethical principles for medical research involving human subjects and were approved by the Ethics Committee of the State Medical Association of Hessen/Germany (reference number: 2022-3185-evBO).

Statistical methods

All statistical analyses were performed with SPSS statistical software version 21.0 (IBM Corp, Somers, NY, USA). Continuous values are expressed as mean ± standard deviation or standard error of mean (SEM) as

indicated and were compared with Student's t-test after confirmation of normal distribution. Otherwise, the Mann-Whitney-U-test was used. Categorical variables are displayed as frequency and percentages and were compared using the Chi-square-test or Fisher's exact test in small sample sizes or when one or more of the cells had an expected frequency of five or less. Multi-group comparisons were performed using ANOVA test with Bonferroni post-hoc correction. For intra-group comparisons, a paired t-test was used. A p-value of less than 0.05 was considered to indicate statistical significance.

Results

1.) Preoperative comparison of patient characteristics

The analysis of the three groups (SR, EL, SI) showed significantly younger patients in the SR group, but in terms of gender and body dimensions, an equal distribution was observed throughout the entire patient population. The analysis of preprocedural parameters did not reveal any significant group-specific differences, but a detailed examination of the specific group data indicated tendencies. Patients in the SI group had the lowest New York Heart Association (NYHA) classification of 2.4 and American Society of Anesthesiologists (ASA) classification of 3.0 and the lowest proportion of patients with diabetes (23.2%). They also showed the lowest level of renal dysfunction (creatinine 1.3 mg/dl; glomerular filtration rate (GFR) 78.8 ml/min/1.7), had the lowest incidence of coronary heart disease (45.5%), and the least frequent percutaneous coronary interventions (PCI) (21.9%) prior to surgery. In contrast, patients in the EL group had a higher NYHA class (2.5), the highest ASA class (3.4), and the lowest GFR (62.1 ml/min/1.7) compared to the other groups. The highest percentage of arterial hypertension (82.1%) was also found in this group, as well as the highest incidence of coronary heart disease (64.3%), which was also reflected in the highest number of PCIs (39.3%) and cardiac surgeries (42.9%) prior to lead extraction. The SR group showed the highest NYHA class (2.6) and second-highest ASA class (3.3), the highest creatinine level (1.6mg/dl), the second-worst GFR value (66.6 ml/min/1.7), and the highest percentage of diabetics (34.8%). Unexpectedly, this group had the highest left ventricular ejection fraction (LV-EF) of all groups at 44.7% (Tab. 1).

2.) Group comparison of preoperative rhythm disorders and device data

Comparing the underlying rhythm disorders, it could be observed that in the EL group, there was a significantly higher proportion of atrio-ventricular (AV) blockages (69.2%), the highest proportion of primary prophylactic implantable cardioverter-defibrillator (ICD) patients (73.3%), and the highest proportion of cardiac resynchronization therapy (CRT) systems (54%). As expected, AV blockages were least common in the SR group with 28.2%. Conversely, the proportion of sinus node disorders as an indication for pacemaker implantation was highest in this group. Furthermore, considering the type of implanted devices, it can be seen that in the SR and EL groups, there was a comparable distribution between the implanted pacemaker (43.8% vs. 46.4%) and defibrillator systems (56.2% vs. 53.6%), while in the SI group there was a significantly higher proportion of implanted pacemakers (61.6%).

When looking at the age of the implanted leads, we found the oldest pacemaker electrodes (8.6 years) in the SR group, and the oldest defibrillator leads in the EL group (8.7 years). In contrast, the ICD- and pacemaker leads with the shortest implant duration were seen in the SI group (Tab. 1).

3.) Preoperative infection analysis

Of particular interest in the patient analysis was the preoperative infection status. While none of the patient cohorts showed an elevated body temperature under initiated antibiotic therapy, statistically significant differences were detected in the frequency of collected blood cultures and positive pathogen detections. In advance, the most common blood samples (92.9%) were taken in the EL group. In the SR cohort, this measure was carried out in 71.9%, while it was only performed in the SI group in 35.6% of cases. Pathogens were most commonly detected in the EL group (78.2%). Consistently, gram-positive, coagulase-positive cocci (66.7%/40.9%/50%) were predominantly found in all groups (SR/EL/SI), followed by gram-positive, coagulase-negative subspecies (26.7%/40.9%/38.9%). Gram-positive lactobacilli (11.1%/18.2%/11.1%) and gram-negative proteobacteria (2.2%/0%/11.1%) were also frequently detected in all groups, with slightly

higher frequencies in the SI group than in the other groups. Multiple pathogens were seen in all groups, with the highest frequency (11.1%) in the SI group. Finally, blood analyses showed the highest inflammatory parameters in the EL cohort (leukocytes: 11.2 Ts/µl, CRP: 6.3 mg/dl, PCT: 3.2 ng/dl), while the SI group showed the lowest signs of inflammation. Echocardiography was able to detect intracardiac lead vegetations most frequently in the EL group (60.7%).

Furthermore, different primary sources of infection were identified in the groups. Isolated pocket infections were significantly more frequent in patients of the SI group (74%), while bloodstream infections represented the dominant etiology in the other two groups (EL: 60.7%, SI: 41.6%) (Table 1).

4.) Peri- and post-operative findings

Perioperative data showed the highest proportion of patients requiring stimulation (75%) in the EL group, with a high proportion in the SI group, while no patient required stimulation in the SR group. Operating times varied depending on the surgical complexity, with the shortest operation times in the SR group. Extraction procedures in all groups relied on the use of specialized extraction devices such as the excimer laser (46.6-67.9%) or mechanical rotational extraction sheaths (7.1-12.3%) in more than 50% of cases. On average, between 2.3 and 2.6 electrodes were removed per patient, with 93.2 to 96.4% complete success rate. Existing lead vegetations were removed with an efficacy of 94.1% (EL) to 100% (SI). Approximately one-quarter of SR and EL patients received a wearable cardioverter defibrillator (WCD) for bridging until ICD re-implantation. A second operation to de novo implant or complete an epicardial pacing system was performed in 49.4% (SR) and 39.3% (EL) of cases. Here, transvenous leads were added in 100% of cases, and in the EL group, 90.9% of epicardial leads implanted at extraction could be re-used.

The necessary second implant procedure was performed in the SR group at a median of 26 days after extraction, significantly earlier than in the EL group (62 days). Most commonly, pacemaker and CRT-D systems were then implanted. Interestingly, 50.6% of SR patients did not receive a new device since there was no further indication for pacemaker/ICD device.

Surgical wounds could be primarily closed in 94.2% of all groups. Vacuum-assisted wound closure (VAC therapy) with the aim of secondary wound closure was used only in individual cases with the highest percentage in the SR group (7.9%). Overall, there was only one case of a perioperative complication where myocardial rupture with hemorrhage occurred during implantation of an epicardial LV electrode. However, the complication was successfully treated and had no further long-term consequences (Tab. 2).

5.) Procedure times and treatment endpoints required for therapy

The analysis of time intervals for diagnosis, initiation of therapy, hospital transfer, operative care, and post-operative treatment period showed that a considerable amount of time had lapsed until patients received final surgical treatment in all groups. It took a median of 14 (EL) to 19.5 (SR) days after diagnosis before patients were transferred to our hospital. Here, the process was expedited, and final surgical care could be provided after of 1 (SR) to 3 (EL) days. Postoperatively, none of the study groups had a prolonged intensive care unit stay (0 to 0.5 days), while the longest subsequent stay on regular ward was seen in the EL group with 14 days. Patients in the SI group were discharged home most frequently (84.9%), whereas only half of the other two groups were able to do so (SR: 48.3%; EL: 46.4%). All other patients had to be transferred to other hospitals for further treatment.

During the hospital stay, two patients (2.2%) in the SR group died from fulminant sepsis, which, in addition to terminal heart failure, developed into dialysis-dependent cardio-renal syndrome with right heart and liver failure and electrolyte imbalance. In the EL group, three patients died (10.7%) during in-hospital stay. One patient died due to a fulminant pneumogenic septic with dialysis-dependent anuria and multi-organ failure. Another patient developed a methicillin-resistant staphylococcus aureus (MRSA) mediastinitis and an enterococcus faecalis lead endoplastitis following a coronary artery bypass (CABG) and aortic valve operation. Despite the immediate removal of the foreign material, the septic process could not be averted and the patient died in fulminant septic shock. A third end-stage heart failure patient with a streptococcus

sanguis pocket infection died in terminal heart failure following a primarily uncomplicated CRT system extraction due to the postoperative lack of biventricular pacing. In the SI group, there was only one death (1.4%). This occurred in a stimulation-dependent patient with renal failure who experienced an unclear gastrointestinal complication with severe vomiting following the primary uneventful removal of the system and contralateral device implantation. This resulted in cardiac arrest due to electromechanical uncoupling, which led to death (Table 3).

6.) Patient outcome at one-year follow-up

One-year follow-up was available in 103 out of the total of 190 treated patients (54.2%). The follow up was conducted as part of CIED interrogations, which amounted to 51.7% of the SR (n=46), 67.9% of the EL (n=19) and 51.2% of the SI group (n=38). In this context, non-irritating wound conditions were found in 94.7% (EL, SR) and 100% (SR), and generator pockets were irritation-free in 100% of all cases. In the three cases of irritating wound healing, the previous generator pocket with keloid formation or a superficial wound irritation was identified as source of discomfort. However, in no case further surgical measures were required. The new device implants demonstrated adequate device function in 100% of cases in the EL and SI groups, whereas two uncomplicated RV electrode revisions were necessary in the SR group due to loss of sensing (4.9%). Overall, all groups showed excellent lead parameter measurements after one year (Tab. 3).

Of particular interest was the final assessment of the treatment courses. The laboratory inflammatory parameters, LV-EF, and current NYHA class were again determined. It was found that the infection treatments in all groups were comparably effective and successfully completed (Fig. 1, left). However, all patients showed a comparable improvement in NYHA classes and a recovered or improved LV-EF at the end of treatment (Fig. 1, right). It is noteworthy that the LV-EF initially decreased in the two groups (SR/EL) without immediate implantation of a final system, while the heart function of the SI group continuously improved from the start of the intervention until the end of observation (Fig. 2).

Finally, the question arose regarding the number of lethal treatment courses. Using the social data, we were able to supplement the time interval between hospital discharge and the one-year follow-up, although we could unfortunately only determine the date of death and not the exact circumstances of death. One death (1.1%) occurred in the 8th postoperative month in the SR group, three (10.7%) occurred after one month and two months in the EL group, and two (2.7%) occurred after one and six months in the SI group. The overall mortality rates at 1 year were 3.4% (SR), 21.4% (EL), and 4.1% (SI), with the EL group having the significantly highest mortality rate of all treated groups (Table 3).

Discussion

Device infections represent a relevant clinical problem with a significant proportion of patients affected, accounting for 10% (2020: 1,653) of the 18,000 revision procedures annually performed in Germany (20,21) and 1-2% of interventions worldwide (1). In this regard, international and national expert panels unanimously recommend immediate and complete removal of infected systems (11-15). Unfortunately, however, there is a lack of generally accepted strategies for the timing of subsequent reimplantation (1). For example, the EHRA "consensus document" (18) also states that there are currently no randomized trials on the appropriate timing of reimplantation. Therefore, the timing and indication of reimplantation should be determined on an individual basis and the indication be re-evaluated before reimplantation. Moreover, reimplantation should be performed no earlier than 72 hours after retrieval and blood culture-based exclusion of persistent infection. In contrast, Baddour et al. recommends reimplantation for proven valvular vegetations not earlier than 14 days after retrieval and confirmation of negative blood cultures (11). However, if patients require continued pacing, placement of a contralateral percutaneous "sacrificial electrode" or the implantation of an epicardial electrode should be performed at very high risk of reinfection. Nevertheless, in clinical practice, these recommendations are of limited use because a substantial proportion of infected patients require continued pacing therapy or uninterrupted CRT for heart failure support. Moreover, infections after percutaneous generator perforations may occur only locally in the pocket, as was the case in 74% of patients in our SI study group. These patients are usually pre-treated with antibiotics and may show only moderate laboratory

signs of inflammation or physical discomfort immediately before the surgical procedures, if any.

In our hospital, the respective treatment strategies were therefore decided in close cooperation of the interdisciplinary device team and the interdisciplinary endocarditis board. Decisions were based on the individual clinical assessment of symptoms, underlying arrhythmias and existing device dependencies, comorbidities, and especially the extent and location of the infection foci. The retrospective analysis of the decisions made revealed group-specific differences that tended to support our decision for one of the three treatment pathways described. For example, we found no pacing-dependent patients in the SR group but the highest number of implanted ICDs (56.2%). This group also had the preoperatively highest NYHA (2.6) and second-highest ASA class (3.3), indicating the clinical relevance of the current severe infection event. Likewise, the EL group had significant comorbidities in a very severe infectious event (NYHA class: 2.5; ASA class: 3.4; hypertensive patients: 82.1%; coronary artery disease: 62.1%; prior PCIs: 39.3%; prior cardiac surgery: 42.9%). Notably, however, it showed the highest pacing dependence (75%) und the lowest LV-EF (39.4%). Furthermore, we found that the highest number of blood cultures (92.9%) was taken here and the highest percentage of microbes (78.6%) was detected. Also, the laboratory results showed the most significant inflammatory parameters (leukocytes 11.2 Ts/µl, CRP 6.3 dl/ml, PCT 3.2 ng/dl) and the most frequent intracardiac vegetations (60.7%). These observations suggested that this was the most severely diseased group in our collective, followed by the SR group. And in our consideration, this also justified ex ante our aggressive and invasive treatment strategies. In contrast, the SI cohort appeared less severely ill, had the lowest NYHA (2.4) and ASA class (3.0) and showed the lowest comorbidities (creatinine: 1.3 mg/dl, diabetes mellitus: 23.3%, prior coronary artery disease: 45.2%, PCIs: 21.9%, cardiac surgery: 24.7%). In addition, the lead dwelling time was significantly shorter (HSM: 3.7 years, ICD: 2.5 years) and in 74% of cases, complaints were limited to the generator pocket. These facts presumably conditioned the blood cultures taken so infrequently and the few positive bacterial detections (24.7%). Thus, we concluded that this was the least severely diseased study group with the best prognosis.

In our study, the infected material was removed in all groups with a class 1/B indication according to the current expert recommendations (12-15). On average, 2.3 to 2.6 leads per patient were completely removed in 93.2% to 96.4%. Interestingly, existing lead vegetations could be removed with the extraction instruments in 94.1% to 100%, which may have had a positive effect on prognosis and treatment duration in our patient population.

Overall, there was only one periprocedural complication (EL group), representing 0.5% of the total cohort. However, a total of 6 deaths (3.2%) occurred during hospitalization. Thus, there were fewer complications and deaths than would have been expected on the basis of the GALLERY registry (total complication: 4.3%; MAE: 2.1%; in-hospital mortality: 3.6%) or the ELECTRa study (total complication: 2.4%-4.1%; MAE: 1.7%) (22,23). However, our study showed a slightly higher in-hospital mortality compared with the ELECTRa registry (ELECTRa: 1.2%-2.5%) (23). We attributed this mainly to significantly higher mortality in the EL group and low case numbers (SR: n=2 / 2.2%; EL: n=3 / 10.7%; SI: n=1 / 1.4%).

These findings raise the question of whether there are other, less invasive treatment options with good prognosis for stimulation-dependent patients. One possibility is the insertion of a temporary transvenous "sacrificial electrode" or, alternatively, the implantation of a leadless pacemaker (LP). Unfortunately, we could not include these options in our analysis because of the small number of cases. Nevertheless, it remains to report that the concept of the percutaneous "sacrificial pacemaker electrode" was initially criticized because of the risk of infection and dislocation (12, 18). However, publications reporting good results with this bridging method are now accumulating. Frausing et al. recently published the results of a nationwide Danish analysis on the incidence of infections after over 40,000 CIED implantations in which a temporary percutaneous pacing electrode was inserted for bridging. In the follow-up period of one year, there was no increased rate of all-cause CIED infections (24). Zhou et al. investigated the patient population of pacemaker-dependent CIED infections in the Temporary Pacing using Active Fixation Leads (TPAFL) study (25). In this study, a contralateral temporary stimulating electrode was implanted in 334 patients during removal of an infected CIED system. Afterwards, they received a new permanent system a median of 10

days later. There they observed a total of five adverse events (1.5%) and one infection (0.3%) in the entire cohort. Pecha et al. previously described comparable results in a smaller study in which there were even no reinfections or complications (26). Regarding the implantation of leadless devices, most current publications refer to an approximately 30-day delayed LP implantation after the extraction of an infected CIED system - i.e., non-pacemaker-dependent patients - and report low reinfection rates (27,28). In contrast, simultaneous implantation of an LP during an existing infection has been described only rarely and in small studies or individual case reports. For example, Chang et al. reported on 17 patients who received an LP for continued ventricular pacing during extraction of an infected device. Among these, no re-infection occurred after 143 days (29). Equally hopeful results were provided by case reports such as Wu et al. (30) or Jacobs et al. (31), who also found no reinfections after simultaneous implantation of an LP during extraction procedures. Nevertheless, with these methods it should be kept in mind that the introduction of new materials into the intravascular compartment may promote endocarditic processes by contact infection.

Furthermore, a comparison of our findings with those of the prospective Multicenter Electrophysiologic Device Infection Cohort (MEDIC) study by Boyle et al. (32) in 434 patients seems to be of interest. Of these, 381 underwent extraction treatment and 220 of them (57.7%) received new device systems after a median of 13 days. In comparison, significantly more patients (76.3%) received a new system in our overall collective. Only in the SR subgroup was the figure slightly lower (49.4%). However, Boyle's study did not focus on the outcome of different treatment strategies but rather on a possible correlation between the timing of device reimplantation after extraction and the frequency of re-infection. Six months after initial extraction procedure, an overall re-infection rate of 11.3% and an overall mortality of 26.4% were observed, which our numbers could not confirm even after one year of follow-up. Comparing similar groups in both studies, his cohort had 23 patients who, like our SI group (n=73), received a new permanent CIED system during the extraction procedure. Six months later, 69.6% of his patients remained free from re-infection. Additionally, there was one re-infection (4.3%) and four patients (17.4%) died. In our study, however, we observed no re-infection after one year and three deaths (4.1%). Comparing our one-year follow-up of the SR group (n=89, reimplantation 26 days after extraction) and our EL group (n=28, reimplantation 62 days after extraction) with Boyle's "reimplantation group" (n=42, reimplantation 21 days after extraction), we would have expected a mortality rate of 14.3%, 2.4% of re-infections, and uncomplicated healing in 83.3%. In contrast, we found no re-infections in our study cohort. In addition, our SR group performed significantly better with 100% uncomplicated wound healing and a mortality rate of 3.4% (n=3). However, our EL group had a high mortality rate of 21.4% (n=6) after one year, which we attributed to the proven severe illness and the more invasive treatment with the epicardial lead and secondary system upgrade. Overall, Boyle's group concluded that the risk of re-infection after complete removal of an infected system is very low regardless of the timing of reimplantation. We can confirm this statement with our retrospective data analysis. In addition, our long-term follow-up with a good detection rate (51.7% to 67.9%) showed that irritation-free wound conditions were found in 94.7% to 100% and properly functioning CIEDs in 95.1% to 100%.

Last but not least, the observations made in our study showed a significant decrease in inflammatory parameters (Figure 1) and improvement in NYHA classes and LV-EF (Figure 2) after one year in all groups, which we attribute to the healing of the infection. However, it was also shown that there was a transient decrease in LV EF in the EL group due to the higher operative trauma of a lateral thoracotomy on the one hand and in the SR group due to the lack of adequate pacing on the other hand. However, these increased again even above baseline levels after implantation of a final system and resolution of the infection. These courses suggest that the clinical decisions made regarding method selection were appropriate.

However, significant delays in patient transfer from 14 to 19.5 days after diagnosis were also evident in our study. This delay could be due to difficulties in diagnosis, blood culture analysis, or organizational issues that cannot always be resolved quickly. On the other hand, the suspicion remains that a repeated attempt at purely conservative treatment was made, which is contrary to international recommendations (12,32). Abandoning this approach could significantly improve outcomes. Upon arrival at the extraction center, the process accelerates, but still there was a delay of 1 to 3 days. This was mostly due to poor quality imaging or missing test results. To avoid these delays, we recommend that referring hospitals provide timely, up-to-date,

high-quality test results — because removing infected devices within three days of diagnosis can significantly reduce in-hospital mortality rates (33,34).

Conclusion

The study authors were able to confirm that in cases of severe bloodstream infections with generalized sepsis, complete removal of infected CIED systems should be performed according to international recommendations. In the absence of pacemaker dependency, our study showed a good long-term prognosis with low mortality after two-stage reimplantation.

On the other hand, in pacemaker-dependent patients, treatment strategies should be carefully considered, taking into account infection routes and localization, implant age, and existing comorbidities. For example, in localized, non-systemic pocket infections, simultaneous implantation of a contralaterally implanted CIED system can lead to rapid recovery with short hospital stay and low long-term mortality with good outcomes. Here, the authors found no significant differences in prognosis and reinfection rates between these two procedures. In contrast, for severe generalized bloodstream infections in pacemaker-dependent patients, implantation of an epicardial lead during extraction procedures to maintain pacing is a successful treatment option. However, mortality was significantly higher in this collective during hospitalization and at 1-year follow-up compared with other study groups - but the patients studied were also sicker. Whether the promising alternative of a temporarily implanted percutaneous pacing electrode or the implantation of a leadless pacemaker is a serious treatment option, on the other hand, remains to be clarified by further studies.

Limitations

The presented single-center study retrospectively analyzed patients from a clinical everyday population whose grouping was based solely on clinical assessment criteria. Thus, retrospective analysis looked for group-specific differences in collectives that were not fully comparable, which could result in a distorted picture. In addition, the fundamentally limited informative value of retrospective data analyses and observational studies should be pointed out, and last but not least, the small and unequal case numbers of the subgroups could cause a bias.

Tables:

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Figures:

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Fig. 1: Left: Course of leukocyte level in the course of infection treatment.

Right: Course of CRP level in the course of infection treatment.

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Fig. 2: Left: Evolution of NYHA class during the course of infection treatment.

Right: Development of LV-EF in the course of infection treatment.

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