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CLINICAL RESEARCH
Pacing and resynchronization therapy

Comparison of epicardial vs. endocardial reimplantation in pacemaker-dependent patients with device infection

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Aims Reimplantation of cardiac implantable electronic devices (CIEDs) after extraction due to device infection is a major issue in pacemaker-dependent patients. We compared in-hospital and long-term outcomes with two techniques: epicardial reimplantation (EPI) before CIED extraction and temporary pacing (TP) with a view to delayed endocardial reimplantation.

Methods and results Two cohorts of consecutive pacemaker-dependent patients who underwent transvenous lead extraction at our tertiary centre were included in this retrospective cohort study. According to successive policies, either the EPI or the TP approach was used. In-hospital complications occurred at similar rates in the EPI ($n = 59$) and TP ($n = 52$) cohorts (37.3% vs. 32.7%, respectively; $P = 0.61$). Thirteen (25.0%) patients in the TP cohort eventually were reimplanted epicardially, mainly because of infection of the temporary lead. Finally, 65 patients were discharged with an epicardial device and 37 with an endocardial device. Median follow-up was 41.7 (interquartile range 34.1–51.5) months. No difference was observed in long-term mortality according to the reimplantation strategy, but use of TP was associated with a reduced risk of late endocarditis and device reintervention (hazard ratio (HR) 0.25, 95% confidence interval (CI) 0.09–0.069, $P = 0.01$), whereas epicardial device reimplantation was associated with an increased risk (HR 3.62, 95% CI 1.07–12.21, $P = 0.04$).

Conclusion We observed similar in-hospital outcomes in our EPI and TP cohorts. Twenty-five percent of the patients initially paced by a TP strategy finally needed an epicardial device, mainly because of infection of their TP lead. Use of TP resulted in lower rates of late endocarditis and device reintervention.

Keywords Cardiac implantable electronic device infection • Epicardial reimplantation • Endocardial reimplantation • Lead extraction • Pacemaker-dependent patients • Temporary pacing.

Introduction

Implantation of cardiac implantable electronic devices (CIEDs) has increased dramatically recently due to improved recognition of the clinical need and broader indications.[1] Despite technological improvements and standardized protocols, the rate of CIED infections increases even out of proportion to the rate of new device implants.[2] CIED infections are associated with high morbidity, and an in-hospital mortality rate approaching 5% has been reported.[3]

Although there is clear evidence of the need for antibiotic therapy and complete CIED extraction in patients with an infected device,[4–7] major concerns remain regarding the modality and timing of reimplantation. The American Heart Association and the Heart Rhythm Society recommend postponing the definitive reimplantation of a

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What's new

- The implantation of an epicardial device before the extraction procedure and temporary pacing (TP) with a view to delayed definitive endocardial reimplantation have been proposed as alternative strategies for cardiac implantable electronic device (CIED) extraction in pacemaker-dependent patients with a CIED infection.
- The rate of in-hospital device-related complications was similar with both approaches.
- As many as 25% of our patients who had TP eventually received an epicardial device, mainly because of an infection of the temporary lead.
- We observed no difference in long-term mortality according to the reimplantation strategy.
- On the opposite, use of TP was associated with a fourfold-reduced risk of late endocarditis and device reintervention, whereas epicardial device reimplantation was associated with a more than threefold increased risk.

new CIED to allow blood cultures to remain negative for at least 72 h to 14 days, and to use an alternative lead access.[8,9] Similarly, guidelines for the management of infective endocarditis from the European Society of Cardiology stress the need to delay the definitive reimplantation to allow sufficient time for antibiotic treatment to work.[5] Clearly, the delay is especially challenging in pacemaker-dependent patients; the implantation of an epicardial device before extraction, or the use of a temporary pacemaker (TP) with a view to definitive delayed endocardial reimplantation, have been proposed as alternatives in such patients.[10] Nevertheless, there is paucity of data comparing these strategies, especially over the long term. We therefore performed a study to compare these two treatment options, to evaluate both in-hospital complications and device-related issues or death during long-term follow-up.

Methods

Until June 2011, we implanted an epicardial pacemaker (mainly single-chamber right ventricular devices) 1–2 days before CIED extraction in pacemaker-dependent patients with an infected device.[11] From July 2011, due to the results of our previous study,[3] and mainly for leaving the possibility of a delayed endocardial CIED reimplantation adapted to their clinical conditions,[8] these patients were primarily paced with a TP using a screwed-in pacing lead. In this study, we compared consecutive pacemaker-dependent patients with CIED infection who underwent transvenous lead extraction in our tertiary institution (treated between July 2011 and December 2014) with pacemaker-dependent patients included in a previous study from our institution (treated between February 2004 and December 2008).[3]

Pacemaker dependency was defined as a spontaneous ventricular escape rhythm <40 beats per minute on CIED interrogation the day before extraction. All types of infected CIED were considered, including resynchronization therapy (CRT) and implantable cardioverter-defibrillator (ICD) devices. The only exclusion criterion was a previous attempt at CIED extraction. Throughout both study periods, the clinical data were entered prospectively into dedicated databases.

The study complies with the ethical guidelines of the 1975 Declaration of Helsinki. The ethics committee of our academic hospital approved the study. All patients provided written informed consent.

Outcomes and follow-up

We compared the occurrence of in-hospital complications between the patients who had an epicardial device implanted before extraction of their infected CIED ('EPI cohort') with patients who were paced by a TP ('TP cohort'). Complications included events that occurred during the extraction or reimplantation procedures, and were associated with the TP system.

Over the longer term, we looked for predictors of mortality and of a composite outcome of device-related issues comprising late endocarditis (including infection of the new CIED), dysfunction of the reimplanted device, and need for revision or upgrade of the reimplanted device. Since some patients in the TP cohort eventually could not be reimplanted endocardially for medical reasons, we considered the long-term outcomes not only in light of the initial strategy [ITT (intention-to-treat): EPI vs. TP cohort), but also according to the final reimplantation strategy (AT (as treated): epicardial vs. endocardial].

All patients were followed in our combined cardiologist/infectiologist outpatient consultation at 1 month, 6 months, and annually after discharge from hospital. We contacted all patients, as well as their physicians, who relocated during follow-up or who could not attend follow-up consultations, to determine their medical status.

Diagnosis of cardiac implantable electronic devices infection

Our multidisciplinary approach for assessment of CIED infection has been described.[12] Briefly, CIED infections were categorized as 'pocket infection', if frank local inflammation was present or if hardware protruded though the skin, or as 'device-related endocarditis', according to the modified Duke criteria,[13] with assimilation of lead vegetations and clinical evidence of generator-pocket infection to major Duke criteria.[5,14] All patients underwent the recommended thorough baseline assessment before device extraction, including clinical, laboratory, and echocardiographic examinations.[5,8] Transthoracic echocardiography, completed eventually by transoesophageal echocardiography, was performed to detect vegetations or valvular damage. Cultures from blood, pocket, generator, and leads were taken for microbiological analysis in all patients. After taking at least two blood samples, antibiotic therapy was initiated and individualized by local infectious disease specialists according to current recommendations.[8,11]

Extraction

Complete extraction of all hardware was attempted in all patients. The primary approach consisted of transvenous lead extraction as described,[12,15] with surgical completion in the event of failed or complicated percutaneous intervention.

In the context of CIED infection, we defined complete procedural success radiologically as the extraction of all hardware without death or occurrence of permanently disabling complications.[9]

Reimplantation

EPI cohort

One or 2 days before extraction of the infected CIED, a cardiac surgeon implanted the new pacemaker device, with the patient under general anaesthesia. The patients had to be afebrile and under antibiotic therapy for at least 48 h before the operation. In the acute setting, priority was given to the antibradycardia function regardless of baseline indication for

the CIED or of underlying atrial rhythm, with delayed re-evaluation concerning the need for defibrillation or cardiac resynchronization functions. From that perspective, the reimplanted devices were principally single-chamber pacemakers, with the right ventricular lead inserted via a mini-subxyphoid incision and fixed on the anterior wall of the right ventricle. All epicardial leads were steroid-eluting. In the rare case of epicardial dual-chamber or CRT pacemaker reimplantation, the leads were placed by thoracotomy. The generator was finally implanted in a subcutaneous abdominal pocket.

TP cohort

At the beginning of the extraction procedure, a TP wire was placed into the apex of the right ventricle through the femoral vein, to provide backup pacing during the intervention. At the end of the extraction procedure, a right ventricular screwed-in lead (Tendril, St Jude, Saint Paul, Minnesota, USA) was introduced via an ipsilateral internal jugular or subclavian vein puncture. In case of venous thrombosis, we used a contralateral vein. The lead was then connected to a re-use pacemaker can programmed for bipolar pacing. The can was finally strapped to the skin and the patient transferred to a cardiology high-dependency unit for initial surveillance. In-hospital continuous electrocardiogram monitoring was provided until definitive reimplantation. The local endocarditis team (infectiologist, cardiologist, and rhythmologist) defined the delay until definitive reimplantation.[8] The electrophysiologist in charge of the patient adapted the type of device reimplanted to the condition of the patient according to current recommendations, including ICD and CRT functions.[16] The vascular access and the new device pocket were prepared contralateral to the initial infected CIED system. If judged medically indicated (e.g. in case of infection of the temporary lead) the treating physician could eventually reimplant patients with initial TP with an epicardial device.

Statistical analysis

Overall survival was computed from the date of extraction to the date of death (all-cause) or the date of last contact. The incidence of device-related issues was computed from the date of extraction to the date of the first event, or last contact, or death.

Device-related issues may be altered or prevented by death, creating a context of competing risks. The analysis was limited to the first event occurring in the competing risks framework using the following quantities commonly used to summarize outcomes by event type: (i) the cause-specific hazard function, which for device-related issues can heuristically be thought of as the probability of device-related issues in a short time interval, given that no death occurred before; and (ii) the cumulative incidence function, which for device-related issues corresponds to the probability of device-related issues in the presence of competing death.

A descriptive analysis was performed. Continuous variables are expressed as mean ± standard deviation and were compared with the Mann–Whitney test if non-normally distributed, or with Student's *t*-test if normally distributed. Categorical variables are expressed as count (percentage) and were compared using the χ^2 test or Fisher's exact test. Survival analysis was conducted using the Kaplan–Meier method and the Cox regression model to estimate hazard ratios (HRs) and their 95% confidence intervals (95%CIs). Regarding the analyses of device-related issues, subdistribution HRs and their 95% CIs were estimated using the Fine and Gray model. Univariate analyses were performed to identify prognostic factors, and all variables with $P < 0.20$ were included in the multivariable model. All multivariable models were systematically adjusted on reimplantation strategy. All of the tests were two-sided. $P < 0.05$ was considered to be significant. The analysis was performed using R Studio version 0.99.486 (RStudio 2015: Integrated Development for R. RStudio, Inc., Boston, MA URL; http://www.rstudio.com/). The R packages survival and cmprsk were used for survival and competing risk analyses, respectively (Bob Gray (2013), cmprsk: Subdistribution Analysis of Competing Risks. R package version 2.2-6; http://CRAN.R-project.org/package=cmprsk).

Results

From February 2004 to December 2008, 50 consecutive pacemaker-dependent patients underwent transvenous lead extraction at our centre. Two patients were excluded from the analysis, one of whom who was resident in another country and another who had undergone a previous attempt of CIED extraction in another hospital. The remaining 48 patients had an epicardial CIED reimplantation and were included in the EPI cohort.

From July 2011 to December 2014, 63 consecutive pacemaker-dependent patients underwent transvenous lead extraction at our centre. Eleven patients had primary reimplantation with an epicardial device before extraction, due to physician or patient choice, and were included in the EPI cohort for analysis. The remaining 52 patients had placement of an active fixation TP lead at the end of the extraction procedure with a view to a future endocardial reimplantation, and comprise the TP cohort. The patient flow chart is shown in *Figure 1*.

The baseline characteristics of the 111 patients are summarized in *Table 1*. There were no statistically significant differences between the cohorts in terms of age, sex, cardiac pathology, left ventricular systolic function, kidney function, CIED type, and type of infection.

Complications during available follow-up are summarized in *Table 2*.

In-hospital outcomes

Complete procedural success was achieved in 52 (88.1%) patients in the EPI cohort and 48 (92.3%) patients in the TP cohort ($P = 0.46$). Thirteen (11.7% of the overall population) patients showed a relevant increase in tricuspid insufficiency after lead removal, without a statistically significant difference between the two cohorts ($P = 0.07$). One patient in the EPI cohort had a pericardial effusion; the presence of the pericardial drain, inserted during implantation of the epicardial pacing system, prevented occurrence of cardiac tamponade. One patient in the EPI cohort died during extraction because of a cardiocirculatory shock, not associated with a pericardial effusion; and one patient in the TP cohort developed an unexplained persistent haemodynamic instability during lead extraction, which required prolonged use of vasoactive amines. Only one patient (in the EPI cohort) needed surgical completion of the extraction.

A screwed-in temporary lead was successfully secured to the right ventricle apex in all 52 patients in the TP cohort. The mean duration of temporary pacing was 11.1 ± 9.7 days. Eight (15.4%) patients developed vegetations on their temporary lead. One lead displacement with sudden loss of capture was reported, which was successfully treated by isoprenaline until lead repositioning.

A new CIED was reimplanted in 109 patients. Thirty-seven patients in the TP cohort were eventually reimplanted with an endocardial device after antibiotic therapy (including 2 patients with a small <4 cm-long lead tip remnant inside the right ventricle), and 13 patients were finally reimplanted with an epicardial device because of

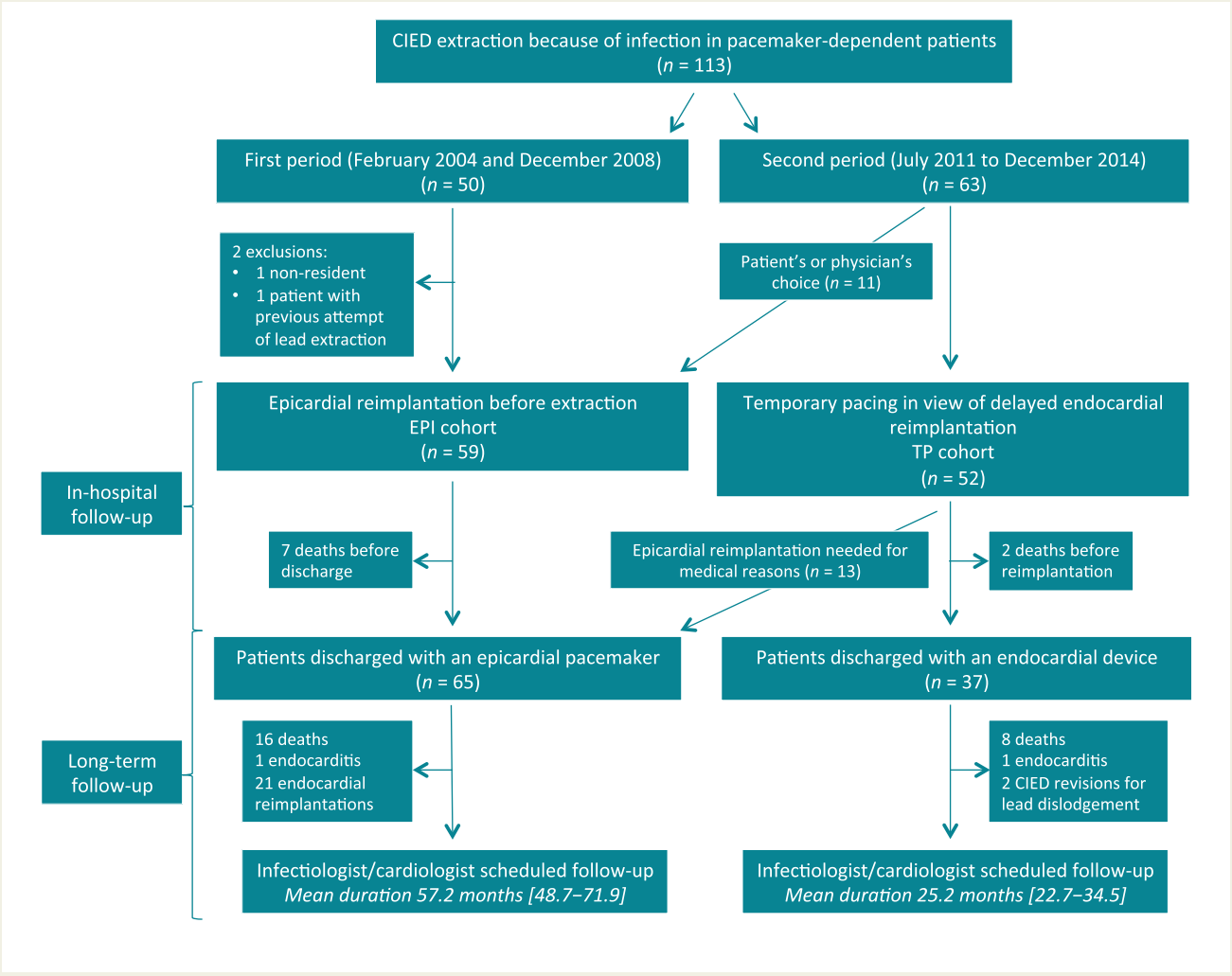

Figure 1 Patient flow-chart (presentation as treated). Please refer to Table 2 for details concerning the outcomes. CIED, cardiac implantable electronic device; EPI, epicardial reimplantation; TP, temporary pacing.

vegetations on their TP lead ($n = 6$), incomplete extraction of the infected device ($n = 2$), unclear persisting inflammatory syndrome ($n = 2$), lack of venous access from the contralateral side ($n = 1$), or a previous CIED-related endocarditis episode ($n = 2$). There was no device with ICD function reimplanted epicardially, and epicardial cardiac resynchronization was only implanted in seven patients. All patients with an endocardial device reimplantation who had had an ICD and/or CRT device explanted were reimplanted with a device with at least the same functions. The reimplantation procedures were uneventful in most patients. One patient with epicardial reimplantation and one with endocardial reimplantation developed a relevant haematoma at the pocket of the new CIED; both patients were managed conservatively. Finally, two patients had their epicardial reimplantation procedure complicated by a stroke and an aspiration pneumonia.

Seven (12.1%) patients in the EPI cohort died during hospitalization, including the patient who died during extraction. Two were found dead in their rooms without any explanation (1 and 7 days after extraction), one patient died because of progressive heart failure, and three died because of worsening sepsis. In the TP cohort, two (3.8%) patients died before definitive CIED reimplantation. The 1st died 7 days after the extraction procedure because of respiratory insufficiency and acute kidney injury due to septic shock. The 2nd patient died 29 days after the extraction procedure from a respiratory failure with tuberculosis suspicion. There was no evidence of vegetation on the TP lead on multiple echocardiographic controls in either patient. The rates of in-hospital death did not differ between the EPI and TP cohorts ($P = 0.17$). Taken together, there was no difference in the rate of in-hospital complications between the EPI and the TP cohorts (37.3% vs. 32.7%, $P = 0.61$).

Long-term outcomes

Information on follow-up after discharge was available in all but one of the patients, with a median follow-up duration of 41.7 (34.1–51.5) months (57.2 months [48.7–71.9] for patients with epicardial reimplantation and 25.2 months [22.7–34.5] for patients with endocardial reimplantation). At 1 year, 85 patients (76.6% of the initial 111 patients) were still alive, 21 (18.9%) had died, and 5 (4.5%) were lost

Table 1 Baseline characteristics of the pacemaker-dependent patients explanted because of a CIED infection

Baseline characteristics	EPI cohort ($n = 59$)	TP cohort ($n = 52$)
Age (years)	73.8 ± 12.5	77.2 ± 10.3
Men	47 (79.7)	45 (86.5)
Cardiac pathology		
None or hypertensive	24 (40.7)	27 (51.9)
Ischaemic, valvular, dilated, congenital	35 (59.3)	25 (48.1)
Left ventricular ejection fraction (%)	49.6 ± 11.9	48.1 ± 12.0
Diabetes mellitus	12 (20.3)	11 (21.2)
Serum creatinine (μmol/L)	126.2 ± 58.1	135.3 ± 93.9
Infected CIED		
Pacemaker	55 (93.2)	42 (80.8)[a]
Defibrillator	4 (6.8)	10 (19.3)[a]
Cardiac resynchronization	8 (13.6)	13 (25.0)
Number of leads (lead[s]/patient)	2.3 ± 0.7	2.6 ± 0.8
Age of the oldest lead (years)	9.8 ± 5.9	8.7 ± 6.6
Type of infection		
Pocket infection	20 (33.9)	24 (46.2)
Device-related endocarditis	39 (66.1)	28 (53.9)
Positive blood or material cultures	48 (81.4)	42 (80.7)

Data given as number (%) or mean ± SD.
M, mean; *n*, number; SD, standard deviation.
[a]Statistically significant difference between cohorts.

to follow-up. The mortality rate at 1 year was similar when considering the ITT cohorts (EPI (20.7%) or TP (18.0%), $P = 0.72$) or the AT reimplantation strategies (epicardial (21.7%) or endocardial (16.2%), $P = 0.50$). In addition to the in-hospital deaths, five patients died for non-cardiac reasons, four patients because of worsening heart failure, two for unknown reasons and one because of unexplained sudden death.

Figure 2 illustrates the overall survival according to the reimplantation strategy. Predictors of long-term overall mortality are detailed in *Table 3*. In multivariable analysis, advancing age, serum creatinine level >150 μmol/L, and left-ventricular ejection fraction <50% were independent predictors of mortality, whereas positive blood or material cultures were protective. The reimplantation strategy was not a predictor of all-cause mortality ($P = 0.94$ in ITT; $P = 0.85$ in AT).

Two late cases of endocarditis occurred during follow-up. One patient in the EPI cohort with chronic kidney disease developed a sepsis with positive blood cultures for *Staphylococcus aureus* 3 months after device reimplantation and died shortly thereafter. Another patient with endocardial CIED reimplantation developed a CIED reinfection after 21 months, but no complication on the TP lead was noted.

In addition to four patients with dysfunction of their epicardial lead (rising threshold or loss of capture), 17 (23.9%) of the patients discharged with an epicardial CIED needed an upgrade during follow-up, with an endocardial dual-chamber pacemaker ($n = 4$), ICD ($n = 4$), CRT-P ($n = 4$), and CRT-D ($n = 5$) devices. Two patients with an endocardial reimplantation needed a revision due to ventricular lead dislodgement, 1 and 4 days after reimplantation. None of the patients with initial endocardial CIED reimplantation needed an upgrade for defibrillator or resynchronization function.

Figure 3 illustrates the difference in the cumulative incidence of late endocarditis or device reintervention (considering the competitive risk of death) according to the reimplantation strategy. When considering the composite outcome, inclusion in the TP cohort was associated with a four-fold reduced risk of late complications ($P = 0.01$ in ITT) whereas epicardial device reimplantation was associated with a greater than threefold increased risk ($P = 0.04$ in AT) (*Table 4*). Reduced left ventricular ejection fraction was the only other independent risk factor.

Discussion

This retrospective, single-centre study is, to our knowledge, the first to compare in-hospital and long-term outcomes of endocardial vs. epicardial device reimplantation in unselected consecutive pacemaker-dependent patients who had their CIED—including ICD or CRT devices—explanted because of an infection. Specifically, we found no difference in long-term mortality between the strategies, but identified a statistically significantly reduced need for reintervention on the CIED in patients reimplanted with endocardial devices according to their clinical conditions. Despite the availability of multiple consensus documents and expert opinions,[8,17,18] the reimplantation strategy in pacemaker-dependent patients with infected CIED varies between tertiary centres.

Whereas temporary leads are associated with a fear of acute dislocation,[10] we observed a low risk of events with temporary pacing with screwed-in leads in our population, with no deaths and only one case of lead dislocation. This latter patient underwent continuous electrocardiogram monitoring while in hospital, and was rapidly stabilized with isoprenaline before replacement of the temporary lead. In general, one can expect that the rate of dislocation of active fixation temporary leads should be similar to that reported for definitive screwed-in pacing leads (1.4% in the study by Aggarwal *et al.*[19]). Surprisingly, despite the administration of guideline-recommended antibiotic therapy,[5] 15.4% of our patients with a TP developed vegetations on their temporary lead, indicating the complexity of initial infection control in such cases. However, we noted only one recurrence of CIED infection during follow-up in the patients with an endocardial reimplantation; importantly, this patient had no infectious issue during temporary pacing and was reimplanted with an endocardial device after 9 days of antibiotic therapy, slightly earlier than the recommended 14 days for valve vegetations.[8] To our knowledge, no previous report has addressed the development of vegetations on temporary leads, despite its obvious relevance to the infection control. Lever *et al.*[20] described localized infection at the exit site without evidence of systemic infection in 2/20 patients. The low rate of device reinfection of the definitive pacemaker after TP stimulation in our study is in accordance with reports by Lepillier *et al.*[21] (no reinfection in eight patients after a mean follow-up of 15 months) and by Amraoui *et al.*[17] (no reinfection in 80 patients during 1 year of follow-up).

The possibility of adapting immediately the type of device to the clinical condition of the patient is one of the main advantages of the TP strategy in terms of long-term cardiac prognosis, especially in patients with reduced left-ventricular systolic function. Although

Table 2 Complications during in-hospital and long-term follow-up

Baseline Cohort	EPI cohort	TP cohort	
Eventual reimplantation strategy	Epicardial	Epicardial	Endocardial
n	59	13	39
In-hospital complications			
Extraction procedure	10 Increase in TI 1 Death 1 Haemopericardium 1 Failed TLE needing a surgical approach	1 Increase in TI	2 Increase in TI 1 Unexplained severe haemodynamic instability
In-hospital	2 Sudden unexplained deaths 1 Death due to heart failure 3 Deaths due to worsening of sepsis	6 Vegetations on temporary lead	2 Vegetations on temporary lead 1 Torsade de pointe 1 Temporary lead dislocation 1 Death due to worsening of sepsis 1 Death due to respiratory failure
Reimplantation	1 Pocket haematoma 1 Stroke 1 Aspiration pneumonia		1 Pocket haematoma
Long-term complications			
Reinfection	1 Valve endocarditis		1 Lead endocarditis
Reintervention	15 Endovascular reimplantation for device upgrade 4 Endovascular reimplantations due to epicardial lead dysfunction	2 Endovascular reimplantation for device upgrade	2 Revisions for lead dislocation
Death	6 Non-cardiac 2 Due to heart failure 3 Unknown 1 Sudden unexplained death	2 Non-cardiac 1 Due to heart failure 1 Unknown	4 Non-cardiac 3 Due to heart failure 1 Unknown

n, number; TI, tricuspidal insufficiency; TLE, transvenous lead extraction.

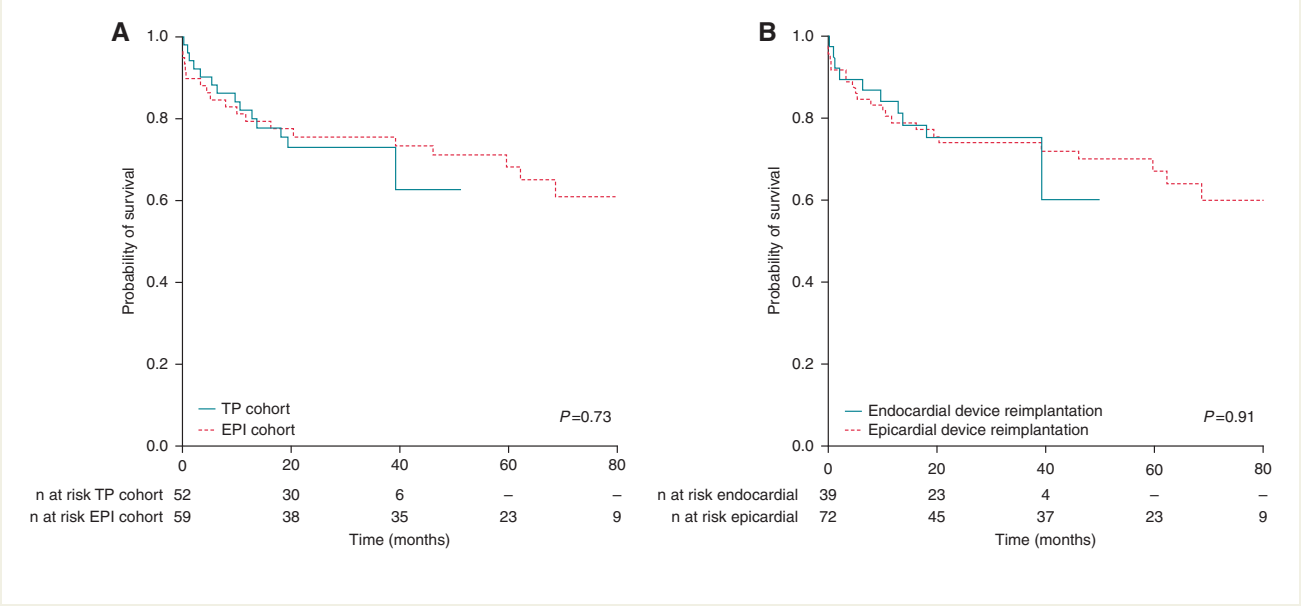

Figure 2 Kaplan–Meier survival curves considering initial cohort of inclusion (EPI vs. TP; *Panel A*) or effective reimplantation strategy (epicardial vs. endocardial *Panel B*).

Table 3 Univariate and multivariable predictors of long-term mortality

Patients characteristics	Univariate analysis		ITT multivariable analysis		AT multivariable analysis	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Female sex	1.29 (0.56–2.98)	0.55	–	–	–	–
Definite structural cardiopathy other than hypertensive	1.85 (0.89–3.81)	0.10	–	–	–	–
Diabetes mellitus	1.61 (0.75–3.49)	0.22	–	–	–	–
Type of explanted device: ICD	1.35 (0.52–3.49)	0.54	–	–	–	–
Type of infection: device-related endocarditis	1.10 (0.54–2.23)	0.80	–	–	–	–
Positive blood or material culture	0.52 (0.24–1.12)	0.09	0.43 (0.19–1.00)	0.05	0.43 (0.19–1.00)	0.05
Complete procedural success	0.62 (0.11–1.77)	0.37	–	–	–	–
Age, per 1-year increase	1.03 (0.99–1.06)	0.12	1.05 (1.00–1.10)	0.04	1.05 (1.00–1.10)	0.04
LVEF < 50%	2.07 (1.04–4.11)	0.04	2.40 (1.08–5.37)	0.03	2.47 (1.11–5.49)	0.03
Creatinine > 150 umol/L	3.36 (1.61–7.00)	<0.01	2.96 (1.41–6.20)	<0.01	2.94 (1.40–6.17)	< 0.01
Epicardial reimplantation	0.96 (0.44–2.07)	0.92	NA	NA	1.09 (0.46–2.57)	0.85
Temporary pacing	1.14 (0.55–2.37)	0.73	1.03 (0.45–2.35)	0.94	NA	NA

AT, as treated (according to effective reimplantation strategy, epicardial vs. endocardial); ICD, implantable cardioverter-defibrillator; ITT, intention-to-treat (according to initial cohort, TP vs. EPI); LVEF, left ventricular ejection fraction; NA, not available.

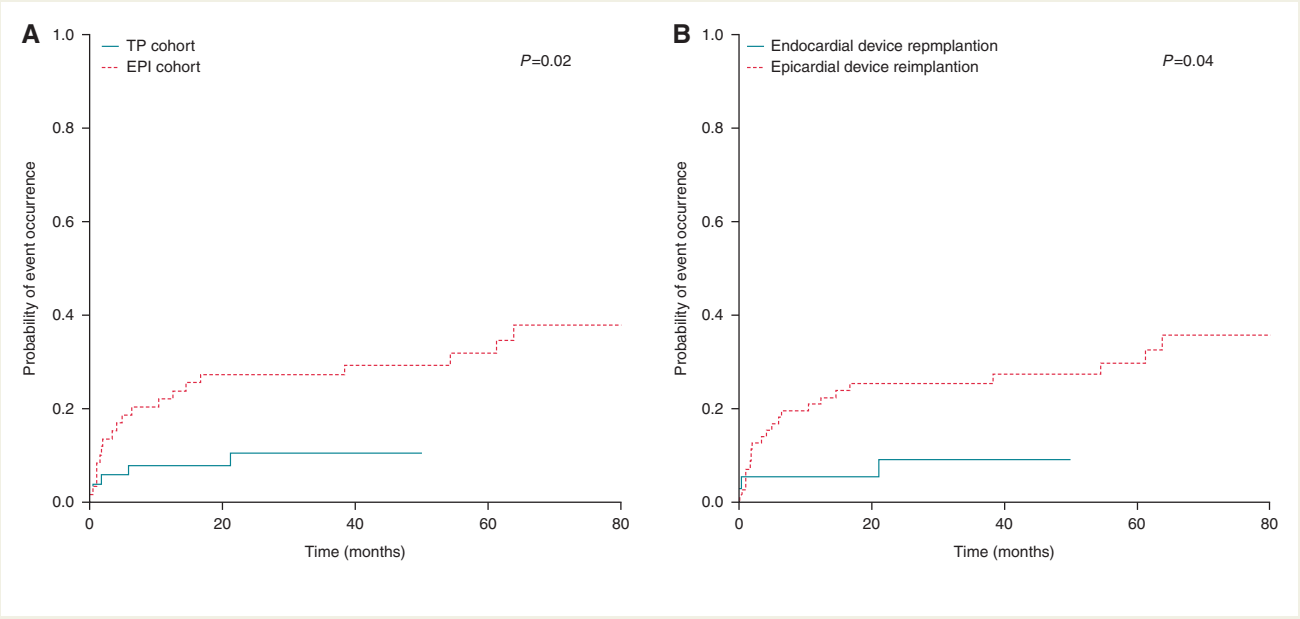

Figure 3 Cumulative incidence of late endocarditis or device reintervention (considering the competitive risk of death) according to initial cohort of inclusion (EPI vs. TP; *Panel A*) or effective reimplantation strategy (epicardial vs. endocardial *Panel B*).

epicardial atrioventricular sequential pacing or CRT remains possible with thoracotomy, cardioverter-defibrillator function requires, for most cases, an endocardial right-ventricular lead. Consequently, almost 25% of our patients with an epicardial CIED required reimplantation of an endocardial device during follow-up, mainly for cardiac resynchronization or anti-tachycardia protection. These endocardial reimplantations or upgrades during follow-up were decided after complete clinical re-evaluation and discussion in our institutional heart failure board. According to our multivariable analysis, the need for reintervention on the implanted device was more than three-fold higher in our patients with epicardial devices compared with endocardial ones. Obviously, these reinterventions significantly increase financial costs and morbidity burden of the treatment. This issue is particularly important regarding the change in life expectancy, with an increase in prevalence of pacemaker-dependency and heart failure to be expected in the future. Furthermore, the complications of epicardial reimplantation procedures have to be considered. In that view, despite the small size of our cohort, we noted one case of cerebrovascular insult and one severe pulmonary infection during epicardial reimplantation

The mortality of pacemaker-dependent patients who develop a CIED infection is poorly documented. Recently, Amraoui *et al.*[17]

Table 4 Univariate and multivariate predictors of long-term survival free of reinfection or reintervention on CIED, considering the competitive risk of death

	Univariate analysis		ITT multivariable analysis		AT multivariable analysis	
Patients characteristics	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***
Female sex	0.95 (0.32–2.77)	0.92	–	–	–	–
Definite structural cardiopathy other than hypertensive	3.04 (1.24–7.45)	0.02	–	–	–	–
Diabetes mellitus	1.35 (0.54–3.37)	0.53	–	–	–	–
Type of explanted device: ICD	2.08 (0.79–5.45)	0.14	–	–	–	–
Type of infection: device-related endocarditis	2.73 (1.02–7.30)	0.05	2.85 (1.0–8.11)	0.05	–	–
Positive blood or material culture	1.74 (0.53–5.72)	0.36	–	–	–	–
Complete procedural success	2.36 (0.31–18.05)	0.41	–	–	–	–
Age, per 1-year increase	0.98 (0.96–1.01)	0.15	1.0 (0.96–1.04)	0.93	0.98 (0.95–1.01)	0.27
LVEF < 50%	2.66 (1.23–5.74)	0.01	3.69 (1.55–8.81)	< 0.01	2.55 (1.15–5.65)	0.02
Creatinine > 150 umol/L	1.82 (0.78–4.28)	0.17	–	–	1.43 (0.56–3.65)	0.45
Epicardial reimplantation	3.63 (1.07–12.28)	0.04	NA	NA	3.62 (1.07–12.21)	0.04
Temporary pacing	0.31 (0.12–0.84)	0.02	0.25 (0.09–0.69)	0.01	NA	NA

AT, as treated (according to effective reimplantation strategy, epicardial vs. endocardial); ICD, implantable cardioverter-defibrillator; ITT, intention-to-treat (according to initial cohort, TP vs. EPI); LVEF, left ventricular ejection fraction; NA, not available.

reported a mortality rate at 1 year of only 5%. Interestingly, the mortality rate in our patients was much higher (18.9% at 1 year in our overall cohort), despite the patients having a similar mean age (75.4 years vs. 72.0 years, respectively) and left ventricular ejection fraction (48.9% vs. 48.0%, respectively). Whereas Amraoui *et al.*[17] excluded patients with CRT or ICD devices, 18.9% of our patients had CRTs and 12.6% had ICDs explanted, suggesting a more advanced cardiac disease and thus frail patients. Moreover, the mortality of our population concurs with that reported by Sandoe *et al.*[18] (2–15% in-hospital to 30-day mortality, 9–35% at 1 year, and 6–35% at ≥2 years), with renal dysfunction and reduced left-ventricular systolic function being independently predictive of death in our multivariable analysis.

Limitations

This study analysed prospective data from consecutive all-comer patients with infected CIED devices of any type, including ICD and CRT systems. However, the analysis remains retrospective. Second, we compared patients from two different periods. Consequently, despite the fact that treating physicians were advised to use the best possible medical treatments, one cannot exclude differences in treatment modalities. Third, we reimplanted mainly single-chamber right ventricular pacemakers in the patients being reimplanted epicardially, independently of the initial explanted device and of the underlying atrial rhythm. Consequently, our results mainly apply to this technique, which we favoured because of the simplicity of the procedure and despite the well-known advantages of multichamber pacemakers and ICD devices for some indications. That be, single-chamber pacing had been shown to be acceptable in high-grade atrioventricular block, especially in elderly.[22]

Conclusions

We observed similar in-hospital outcomes in our EPI and TP cohorts. 25% of the patients initially paced by a TP strategy finally needed an epicardial device, mainly because of infection of their TP lead. Use of the TP strategy resulted in lower rates of late endocarditis and device reintervention.

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