

Long-term outcomes following transvenous lead extraction: Data from a tertiary referral center

Gianmarco Arabia^{a,*}, Gianfranco Mitacchione^{a,1,2}, Angelica Cersosimo^a, Emiliano Calvi^a, Francesca Salghetti^a, Luca Bontempi^a, Daniele Giacomelli^{b,c}, Manuel Cerini^a, Antonio Curnis^a

^a Cardiology Department, Spedali Civili Hospital, University of Brescia, Italy

^b Clinical Unit, Biotronik Italia, Cologno Monzese (MI), Italy

^c Department of Cardiac, Thoracic, Vascular Sciences & Public Health, University of Padova, Italy

ARTICLE INFO

Keywords:

Transvenous lead extraction
Lead removal
Cardiac implantable electronic device
Infection
Long-term follow-up

ABSTRACT

Background: Transvenous lead extraction (TLE) has shown a safe and efficacy profile in the intraoperative and short-term setting; however, data on long-term outcomes are limited.

Objective: The purpose of this study was to assess long-term outcomes and prognostic factors in patients who underwent TLE.

Methods: Consecutive patients with cardiac implantable electronic device (CIED) who underwent TLE between 2014 and 2016 were retrospectively studied. The primary outcome was the composite endpoint of death and repeated TLE stratified by infective/non-infective indication. Individual components of the primary outcome were also evaluated.

Results: One hundred ninety-one patients were included in the analysis, 50% extracted for CIED-related infection. Complete procedural success was achieved in 189 patients (99%) with no major acute complications. After a median of 6.5 years, infection indication was associated with significantly lower event-free survival (67% vs. 83% non-infection group, adjusted hazard ratio [aHR] 1.97, 95% confidence interval [CI] 1.02–3.81, $p = 0.04$). All-cause mortality rate was higher in the TLE infection group (30% vs. 10%, $p < 0.01$). The rate of repeated TLE did not differ between groups (4% vs. 7%, $p = 0.62$). Among patients who had TLE for infection, the presence of vegetation (aHR 2.56; 95%CI 1.17–5.63, $p = 0.02$) and positive blood cultures (aHR 2.64; 95%CI 1.04–6.70, $p = 0.04$) were independently associated with the primary outcome.

Conclusion: Patients who underwent TLE for CIED-related infection exhibit a high mortality risk during long-term follow-up. Vegetation and positive blood cultures in patients with CIED-related infection are associated with a worse prognosis regardless of successful and uncomplicated TLE.

1. Introduction

Lead management for cardiac implantable electronic devices (CIEDs) is a serious issue due to the increasing rate of infection and the not negligible incidence of lead failures. [1,2] In the last decade, the increased awareness of indications, associated with the improved safety and efficacy of extraction procedures, has led to a significant growth in the number of transvenous lead extraction (TLE) procedures that account a central role in the lead management strategy. [3] Indeed,

although the high perceived risk, [4] TLE is reported to have a low intraoperative and short-term complication rate in high-volume extraction centers. [5,6]

To date, TLE is mandatory for patients with CIED-related infection; however, epidemiological data on post-extraction patients are still scarce and the recent expert consensus of the European Heart Rhythm Association (EHRA) strongly recommends conducting clinical research in this area. [3]

Ideally, post-extraction outcomes should be evaluated for much

Abbreviations: CIED, Cardiac implantable electronic device; TLE, Transvenous lead extraction; TEE, Transesophageal echocardiography.

* Corresponding author at: Cardiology Department, Spedali Civili Hospital, Piazzale Spedali Civili 1, 25123 Brescia, Italy.

E-mail address: gianmarcoarabia@gmail.com (G. Arabia).

¹ These authors share the first co-authorship.

² This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

<https://doi.org/10.1016/j.ijcard.2023.02.040>

Received 3 January 2023; Received in revised form 16 February 2023; Accepted 22 February 2023

Available online 24 February 2023

0167-5273/© 2023 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

longer time to understand if TLE could have long-term sequelae. The limited data available suggest a highest mortality rate during long-term follow-up despite uncomplicated extraction, particularly among patients with more comorbidities and different indications for TLE. [7–9] These data are important, as they should be taken into the decision-making and consent process for TLE, particularly in high-risk patients.

The aim of the present study was to assess long-term mortality and repeated extraction in patients who underwent TLE at a tertiary referral center, stratified by the presence of infective indication.

2. Methods

2.1. Study population

This is a retrospective cohort study. Consecutive patients with CIED who underwent TLE and subsequent device reimplantation from January 2014 to January 2016 were considered to receive a follow-up during 2022. All TLE procedures were performed by two experienced cardiac electrophysiologists at Spedali Civili Hospital (Brescia, Italy), which according to HRS guidelines is considered a high-volume center (>30 TLE procedures per year). [3]

Informed consent was obtained in all patients. This study has been drafted in accordance with the tenets of the Helsinki Declaration on human research and has been approved by the local institutional review boards. The study data are available from the corresponding author upon reasonable request.

2.2. Data collection

The clinical and demographic characteristics of the patients were retrospectively collected from electronic medical records. Chronic kidney disease (CKD) was defined by the presence of an estimated glomerular filtrate rate (eGFR) ≤ 60 mL/min/m², calculated with the CKD-EPI equation. TLE features including lead type, overall TLE duration and fluoroscopy time, number of leads removed, leads indwelling time (calculated as the oldest targeted lead *in situ* at the time of extraction), technical extraction information, tools used, and outcomes were also collected.

2.3. Transvenous lead extraction procedure

All TLEs were performed in accordance with the expert consensus document on transvenous lead extraction from the Heart Rhythm Society (HRS). [10] Indications for TLE were grouped as non-infection (lead dysfunction, venous access issues, access to magnetic resonance imaging, chronic pain, and several more unusual indications for TLE) and infection (bacteremia and/or endocarditis, pacemaker site swelling or erythema, skin erosion, or discharge from the pocket). TLE procedure undertaken at this center has been described in detail elsewhere. [11]

As for the center practice, a previous TLE risk stratification was assessed before the procedure through the LED and MB scoring systems to predict difficult procedures. [11] [12] These scoring systems account for the number of leads to be extracted, leads indwelling time, presence of high voltage lead, passive fixation lead, presence of infective vegetation.

A standard stepwise approach was adopted in all TLE procedures, which included a transition from simple to more complex strategies. Briefly, a direct manual traction was initially attempted to remove the lead. If unsuccessful, an appropriately sized locking stylet was inserted and a counter traction technique was used with the aid of manual dissecting sheaths. If lead removal was still not achieved, more advanced techniques were performed, which included the use of powered sheaths (mechanical and/or laser), and snares by femoral route for free-floating portion of leads. All procedures were performed by expert electrophysiologists with cardiac surgery backup available on site. Complete procedural success was defined as the removal of all targeted leads and

materials. All acute complications and procedural characteristics were also documented and traced. Major complications were defined according to the EHRA guidelines as those resulting in death, threatened life, significant surgical intervention, or causing persistent or significant disability. All other complications attributed to the extraction procedure were considered minor complications.

2.4. Device reimplantation

Blood tests and pocket cultures were assessed to decide the antibiotic course as well as reimplantation time, as for guideline recommendations. Transesophageal echocardiography (TEE) was performed in all CIED-related infection patients to assess the presence of vegetations.

The need and timing of CIED reimplantation was determined by electrophysiologists and infectivologists. Patients with infectious were generally reimplanted after negative blood cultures in absence of findings suggestive for intracardiac infective remnant persistence at TEE. In case of pacing-dependent patients, temporary pacing was used prior to delayed reimplantation, alternatively an immediate surgical epicardial pacing leads approach was adopted. For patients with non-infective indication for TLE, transvenous device reimplantation was assessed during the same procedure stage.

2.5. Follow-up

As for the standard of care of the enrolling center, patients were evaluated after discharge with an outpatient visit at 1-, 6, and 12-months, and every 12 or 6 months thereafter for reimplanted device assessment. During each visit, electrical parameters were tested and the adequacy of the programmed pacing parameters was confirmed. Moreover, the outpatient visit also aimed to evaluate TLE-related adverse events and the clinical status. Information on patients who did not receive the subsequent follow-up at enrolling institution was obtained from patient survey, the family practitioner, and from the referring institution. Data available by June 30, 2022, were considered for the analysis.

2.6. Cohort and outcomes definition

Patients were divided into two cohorts: 1) patients who underwent TLE for CIED infection 2) patients who underwent TLE for non-infective cause. The primary hazard outcome was a combine of all cause of death and a repeated TLE procedure. Individual components of the primary endpoint, analysis of the predictors of the primary endpoint, and subgroup analysis in patients with infectious indication were deemed secondary outcomes.

2.7. Statistical analysis

Data analysis was performed using STATA software, version 17.0 (StatCorp LP, College Station, TX, USA). All tests were two-tailed and a *p* value <0.05 was considered statistical significance. Continuous variables were reported as median [interquartile range, IQR] and compared between groups with the Mann-Whitney *U* test. Binary and categorical variables were expressed as absolute (relative) frequencies and analyzed with the Pearson's χ^2 or Fisher's exact test, as appropriate. Survival rates were calculated with the product-limit method, reported along with the 95% confidence interval (CI) and compared with the log-rank test. The association of independent variables with study outcomes was first estimated using univariable Cox proportional hazards regression models. Multivariable Cox analysis was then performed to identify predictors of poor prognosis including in the models all the relevant variables with a *p* value <0.10 in the univariate analysis considering the one-in-ten rule. Results were presented as hazard ratio (HR) with 95% CI and Kaplan-Meier survival curves.

3. Results

3.1. Baseline characteristics and TLE outcomes

A total of 249 patients who underwent a TLE procedure were screened. Of these, 191 patients had available follow-up data and were included in this analysis. Because our institution is a tertiary referral hospital for TLE, the remaining 58 patients were followed up at other hospitals after discharge. They had no major complications related to TLE but were excluded from the study due to lack of follow-up data. The characteristics of the excluded patients are reported in the Supplementary material (Table S1). Ninety-six out of 191 patients (50.3%) underwent a TLE procedure due to CIED-related infection (infection group), while 95 (49.7%) for a different reason (non-infection group). The baseline characteristics of the study cohort are summarized in

Table 1
Study population stratified according to infection and non-infection indication for transvenous lead extraction.

Variable	Overall (n = 191)	Infection (n = 96)	Non-infection (n = 95)	P-value
Gender male, N (%)	162 (84.8%)	83 (86.5%)	79 (83.2%)	0.66
Age (years), median [IQR]	70 (61–77)	74 (66–80)	66 (55–74)	<0.01
BMI (Kg/m ²), median [IQR]	25.8 (23.0–27.7)	25.9 (23.7–27.7)	25.6 (22.7–27.7)	0.30
Creatinine (mg/dL), median [IQR]	1.60 (1.34–1.80)	1.60 (1.30–1.80)	1.60 (1.45–1.89)	0.62
Comorbidities, N (%)				
Atrial fibrillation	65 (34.0%)	32 (33.3%)	33 (34.7%)	0.96
Chronic kidney disease	57 (29.8%)	35 (36.5%)	22 (23.2%)	0.06
Diabetes	41 (21.5%)	27 (28.1%)	14 (14.7%)	0.04
CABG	25 (13.1%)	10 (10.4%)	15 (15.8%)	0.39
Valvular prosthesis	13 (6.8%)	5 (5.2%)	8 (8.4%)	0.55
CAD	78 (40.8%)	40 (41.7%)	38 (40.0%)	0.88
DCM	40 (20.9%)	20 (20.8%)	20 (21.1%)	1.00
Congenital heart disease	10 (5.2%)	5 (5.2%)	5 (5.3%)	1.00
Device removed type, N (%)				0.01
PM	65 (34.0%)	36 (37.5%)	29 (30.5%)	
ICD	55 (28.8%)	18 (18.8%)	37 (39.0%)	
CRT-P/D	71 (37.2%)	42 (43.7%)	29 (30.5%)	
Indication for lead removal, N (%)				
Infection	96 (50.3%)	96 (100%)	0 (0%)	
Lead dysfunction	69 (36.1%)	0 (0%)	69 (72.6%)	
Device upgrade	18 (9.4%)	0 (0%)	18 (18.9%)	
Lead-related complications	10 (5.2%)	0 (0%)	10 (10.5%)	
Thrombosis/stenosis	4 (2.1%)	0 (0%)	4 (4.2%)	
Leads extracted, median (IQR)	2 (1–3)	2 (2–3)	1 (1–1)	<0.01
lead dwell years, median (IQR)	6.9 (3.7–9.3)	7.5 (3.7–12.6)	5.9 (3.2–8.4)	<0.01
Previous pocket revision, N (%)	49 (25.8%)	40 (41.7%)	9 (9.6%)	<0.01
Infection characteristics, N (%)				
Presence of vegetation	–	54 (56.8%)	–	–
Positive pocket cultures	–	25 (34.7%)	–	–
Positive blood cultures	–	14 (19.2%)	–	–
LED index ⁴	9 (6–12)	10 (7–14)	7 (5–10)	<0.01
MB score ⁵	4 (2–4)	4 (3–5)	3 (2–4)	<0.01

BMI: body mass index; CABG: coronary artery bypass graft; CAD: coronary artery disease; CRT-P/D: cardiac resynchronization therapy pacemaker/defibrillator; DCM: dilated cardiomyopathy; ICD: implantable cardiac defibrillator; IQR: interquartile range; PM: pacemaker.

Table 1. Compared to the non-infection group, patients in the infection group were older (74 [IQR 66–80] vs. 66 [IQR 55–74] years, $p < 0.01$), with a higher prevalence of diabetes (28.1% vs. 14.7%, $p = 0.04$) and chronic kidney disease (36.5% vs. 23.2%, $p = 0.06$). More complex TLE procedures were performed in the infection group; this translates into a higher number of leads removed (2 [IQR 2–3] vs. 1 [IQR 1–1], $p < 0.01$), longer leads indwelling time (7.5 [IQR 3.7–12.6] vs. 5.9 [IQR 3.2–8.4] years, $p < 0.01$), and higher risk stratification indexes (LED: 10 [IQR 7–14] vs. 7 [IQR 5–10], $p < 0.01$; MB: 4 [IQR 3–5] vs. 3 [IQR 2–4], $p < 0.01$).

Complete procedural success was achieved in 189 of 191 patients (99.0%) with no reported major complications. In the overall population, there were 9 minor complications (4.7%) without significant differences between the two groups. These latter included transient hypotension ($N = 7$, 3.7%), pericardial effusion that did not require invasive intervention ($N = 2$, 1.0%), and sustained ventricular tachycardia that required electrical cardioversion ($N = 2$, 1%). A temporary pacemaker was used in 62 patients (33.2%). The median fluoroscopy time was significantly longer in the infection group (11.0 min [4.2–17.4] vs. 6.0 min [2.7–10.4] in the non-infection group, $p < 0.01$); this observation can be largely explained by the different characteristics of the extracted systems in the two groups reported in **Table 1**. **Table S2** in the Supplementary material summarizes the procedural characteristics by study groups.

3.2. Long-term outcomes

During a median follow-up of 6.5 years [IQR 5.4–7.1], the primary outcome occurred in 31 patients (32.3%) in the infection group and 15 patients (15.8%) in the non-infection group (adjusted HR, 1.97; 95% CI 1.02 to 3.81, $p = 0.04$). The event-free survival rate in the non-infection group was 95.8% (95% CI: 89.2%–98.4%) vs. 78.1% (68.5%–85.2%) in the infection group after 3 years, and 82.9% (72.5%–89.7%) vs. 67.0% (56.4%–75.5%) after 7 years. The Kaplan-Meier curve for the primary analysis is plotted in **Fig. 1**, panel A. Among the variables considered (**Table 2**), obesity was associated with a >2-fold increase in the risk of the primary endpoint (adjusted HR, 2.26, 95% CI: 1.03–4.95, $p = 0.04$).

During the follow-up period, a higher number of all-cause deaths were found in the infection group ($N = 29$, 30.2%) compared to the non-infection group ($N = 9$, 9.5%, log-rank $p < 0.01$; **Fig. 1**, panel B). Details on the cause of death in the two groups are reported in **Table S3** in the Supplementary material.

The repeated TLE did not differ between the groups (4/96 [4.2%] vs. 7/95 [7.4%], log-rank $p = 0.62$), as shown in **Fig. 1**, panel C. In the infection group, a new TLE was due to a new device infection in 3 patients (3.1%), and to heart transplant in one patient (1.0%). In these patients, a second TLE procedure occurred after a median of 4.2 years [IQR 2.2–4.8]. In the non-infection group, seven patients underwent a new TLE after a median of 5.7 years [IQR 4.3–6.8]. A repeated TLE procedure was due to device pocket infection (4/95, 4.2%), lead dysfunction (2/95, 2.1%), and cardiac perforation during transvenous lead reimplantation (1/95, 1.1%).

3.3. Predictors of poor prognosis for patients with infective indication

The predictors of death / repeated TLE were evaluated within the group of patients who underwent TLE due to a CIED-related infection. Among all variables investigated, age, chronic kidney disease, presence of septic vegetation, and positive blood cultures were associated with the primary hazard endpoint in the univariate analysis (**Table 3**). Subsequently, two multivariate models were generated, including age and chronic kidney disease with the presence of vegetation (Model 1) and positive blood cultures (Model 2). Both were confirmed to be significantly associated with a poor prognosis (vegetation, adjusted HR, 2.56 [95% CI: 1.17–5.63], $p = 0.02$; positive blood cultures, adjusted HR, 2.64 [95% CI: 1.04–6.70], $p = 0.04$). The Kaplan-Meier survival curves

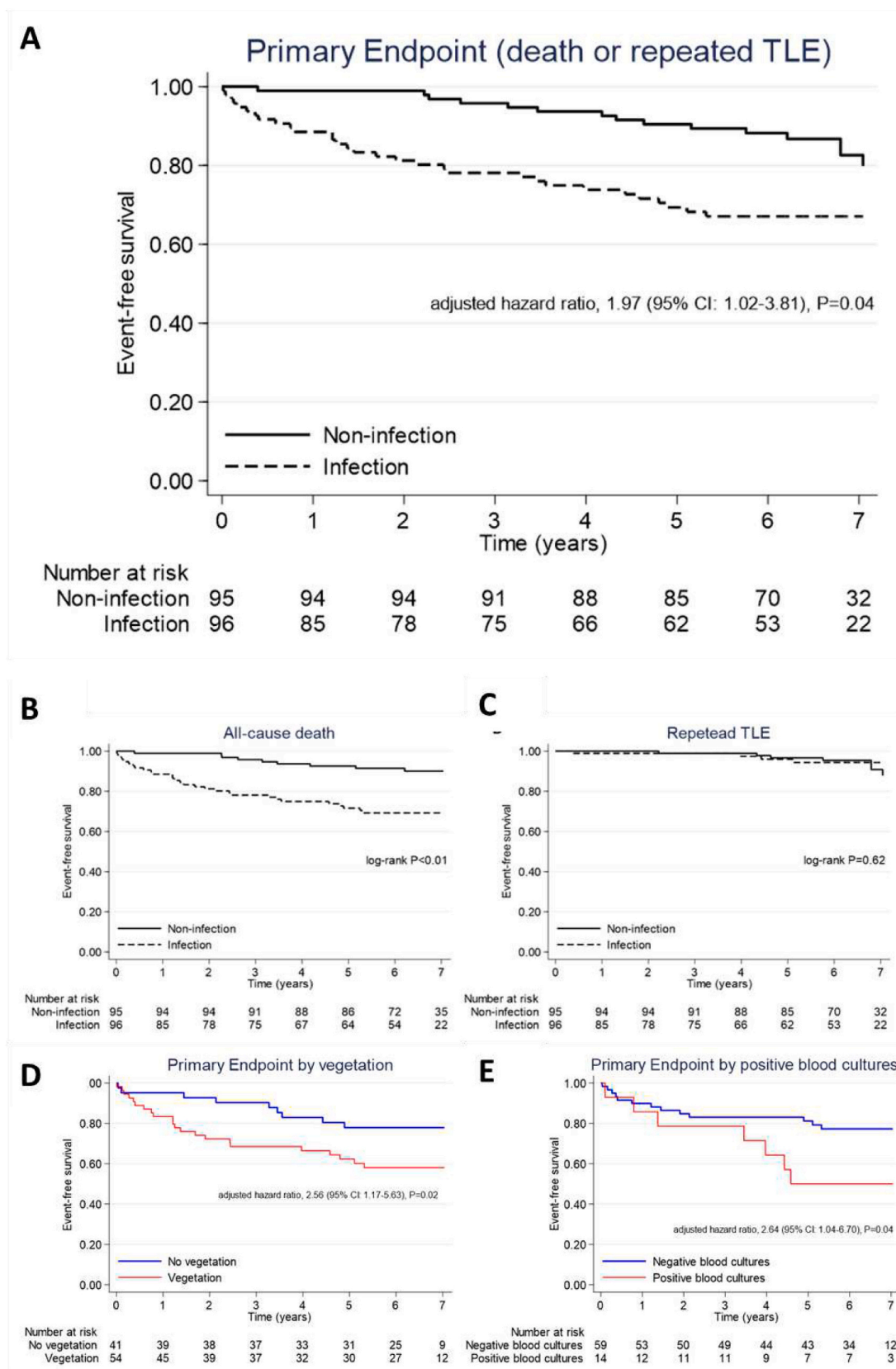


Fig. 1. Kaplan-Meier survival curves and analysis for the primary combined outcome by study group (A) and for the components of the primary endpoint, death from any cause (B) and repeated TLE procedure (C). Kaplan-Meier survival curves and analysis for the primary combined outcome among patients with infectious indication by the presence of vegetation (D) and positive blood cultures (E).

Table 2
Predictors of death or repeated TLE in all patients.

Variable	Univariate analysis			Multivariate analysis		
	HR	95% CI	P value	HR	95% CI	P value
Infective vs noninfective indication	2.47	1.33–4.57	<0.01	1.97	1.02–3.81	0.04
Patient features						
Age	1.03	1.01–1.06	0.01	1.02	0.99–1.05	0.13
Sex, male	1.23	0.52–2.90	0.64	–	–	–
Obese (BMI > 30 Kg/m ²)	2.25	1.05–4.82	0.04	2.26	1.03–4.95	0.04
Atrial fibrillation	1.59	0.88–2.86	0.12	–	–	–
Chronic kidney disease	2.14	1.19–3.84	0.01	1.70	0.91–3.19	0.10
Diabetes	1.44	0.75–2.79	0.27	–	–	–
Ischemic cardiomyopathy	1.26	0.71–2.26	0.43	–	–	–
Dilated cardiomyopathy	1.20	0.61–2.37	0.59	–	–	–
TLE features						
LED index	1.00	0.95–1.05	0.95	–	–	–
MB score	1.23	0.98–1.54	0.07	–	–	–
TLE-related acute complications	0.68	0.21–2.20	0.52	–	–	–

Univariate predictors with $P < 0.10$ were entered into multivariate Cox proportional hazard models to determine significant independent predictors. BMI: body mass index; TLE: transvenous lead extraction.

are shown in [Figs. 1](#), panels D and E.

4. Discussion

The main findings of our study can be summarized as follows:

1. Patients who underwent TLE with infective indication have a higher combined risk of death and repeated TLE compared to those with a different indication.
2. The worse outcome during follow-up is mainly due to a higher rate of all-cause mortality, while the rate of repeated TLE is low and similar between groups.
3. The characteristics of the CIED removed and the presence of intra-procedure TLE-related complications are not associated with long-term outcomes.

Table 3
Predictors of death or repeated TLE in patients with infective indication (n = 96).

Variable	Univariate analysis			Multivariate analysis (Model 1)			Multivariate analysis (Model 2)		
	HR	95% CI	P value	HR	95% CI	P value	HR	95% CI	P value
Patient-related									
Age	1.03	0.99–1.07	0.06	1.04	0.99–1.07	0.06	1.02	0.98–1.07	0.26
Sex, male	1.03	0.36–2.95	0.95	–	–	–	–	–	–
Obese (BMI > 30 Kg/m ²)	1.46	0.56–3.81	0.44	–	–	–	–	–	–
Atrial fibrillation	1.80	0.88–3.67	0.11	–	–	–	–	–	–
Chronic kidney disease	1.97	0.97–3.98	0.06	1.61	0.78–3.37	0.20	2.25	0.91–5.55	0.08
Diabetes	1.57	0.75–3.29	0.23	–	–	–	–	–	–
Ischemic cardiomyopathy	1.50	0.74–3.04	0.26	–	–	–	–	–	–
Dilated cardiomyopathy	0.92	0.38–2.25	0.86	–	–	–	–	–	–
Previous pocket revision	0.71	0.34–1.48	0.36	–	–	–	–	–	–
Presence of vegetation	2.22	1.02–4.82	0.04	2.56	1.17–5.63	0.02	–	–	–
Positive pocket cultures	0.90	0.34–2.40	0.84	–	–	–	–	–	–
Positive blood cultures	2.50	1.00–6.28	0.05	–	–	–	2.64	1.04–6.70	0.04
TLE-related									
LED index	0.97	0.91–1.03	0.32	–	–	–	–	–	–
MB score	1.12	0.81–1.54	0.50	–	–	–	–	–	–
TLE-related acute complications	1.14	0.16–8.38	0.90	–	–	–	–	–	–
Use of temporary pacemaker	0.93	0.45–1.92	0.85	–	–	–	–	–	–

4. Among patients with infective indication for TLE, the presence of septic vegetation and positive blood cultures are independent predictors of poor outcome regardless of event-free TLE and appropriate therapy.

4.1. Infective vs. non-infective indication

In our study, overall mortality after a median of 7 years since TLE was consistent (approximately 20%); moreover, the primary endpoint (a composite of death from any cause and repeated TLE) was significantly higher among patients who experienced TLE for CIED-related infection, with a nearly double HR compared with the non-infection patients. Univariate and multivariate analyses identified the infection indication for TLE, together with obesity, as the strongest predictors of mortality or repeated TLE.

Historical data shows that CIED-related local and systemic infection are well established risk factors for short- and long-term mortality. [13,14] In a series of 500 patients, *Polewczyk et al.* [7] showed a 29.3% mortality rated 3 years after TLE for endocarditis, which was similar to our data, with a worst outcome in the presence of large septic vegetation (>2 cm) or vegetation remnants respect to localized pocket infection. In a recent analysis on 1151 patients followed for a mean of 66.4 months, *Mehta et al.* [8] confirmed a higher long-term mortality rate in patients undergoing TLE for CIED-related infection (38.6% vs. 28.5% in non-infection; $p = 0.004$), without difference between local infection or systemic infection.

In contrast to the above-mentioned, recent data derived from large registries on leadless pacemaker implantation following TLE for infection, exhibit substantial safety and efficacy in this high-risk subset of patients, with a two-year all-cause mortality rate of 5.4% and no reinfection events [15,16].

Our study confirms the negative outcomes in patients who underwent TLE and reimplanted with transvenous devices ([Fig. 1](#)). This finding can partially be explained by an incomplete eradication of the vegetations with subsequent early infection recurrence.

When considering the independent contribution provided by both individual components included in the primary composite endpoint (death and repeated TLE procedure), no significant differences were found in the rate of repeated TLE between the groups. Although relatively rare (5.8%), the main indication for a repeated TLE procedure in both groups was the infection of the reimplanted system, whose occurrence was therefore independent of a preexisting infection. Consequently, the difference in the primary composite endpoint was primarily

driven by mortality and not by the rate of repeated TLE.

4.2. Systemic vs. local infection

Subgroup analysis according to lead infection, pocket infection, or pocket erosion as the primary indication for TLE showed the presence of vegetation (both on leads and valves) and positive blood cultures, associated with an increased risk of recurrence of the primary composite endpoint. Notably, no significant correlation was found between local infection with positive pocket swab culture and long-term mortality or repeated TLE. This finding may be explained by the greater efficacy that antibiotic therapy and pocket revision can obtain in terms of eradication of a localized pocket infection, in contrast to a systemic infection with persistent vegetation after TLE (which is more likely to cause severe complications such as sepsis and septic embolization [17]). Gould et al. [12] showed similar results showing a higher 30-day all-cause mortality in the systemic infection group compared to the local infection group (7.9% vs 2.1% respectively; $p = 0.003$), the difference being driven mainly by severe septic events. This high mortality rate among patients with endovascular infection was also confirmed after a longer follow-up (1 year).

These findings strengthen the recommendation of TLE in patients with lead infection and positive blood cultures suggesting that in the case of pocket infection/erosion an early TLE (associated with aggressive and prolonged antimicrobial therapy) may avoid the extension of the infection, thus preventing fatal septic complications.

4.3. Other risk factors

In addition to the impact of the device or lead infection on the primary outcome, other patient-related variables (i.e., obesity and chronic kidney disease) were identified as predictors of a poor prognosis in terms of death and repeated TLE. Specifically, the impact of chronic kidney disease on prognosis was statistically significant in the overall cohort and in the infection group. This finding is consistent with the current literature. [8,9,18] Brunner et al. [18] reported a 4.8-fold increase in mortality at 30 days for end-stage renal disease, with a cumulative impact on top of infective indication.

In our series, predictors of difficult TLE (LED index and MB score), neither intraoperative complications were found associated with long term outcomes, thus affecting hospital stay duration after TLE.

4.4. Study limitations

The findings of our study are mainly limited by the single-center design of the study. Due to the retrospective design of study, unmeasured significant confounders could not be excluded. The definition of infection indication was based on the presence of vegetations, positive blood cultures, or positive pocket cultures, thus excluding other parameters such as C-reactive protein levels that have previously been described to be correlated with mortality at 30 days. Finally, although the strength of a long follow-up, the study sample size was limited and our results should be confirmed in larger multicenter analyses.

5. Conclusions

Our data showed a higher long-term risk of combined death and repeated TLE in patients who underwent TLE for CIED-related infection when compared to different indications. This negative outcome is driven mainly by the mortality component. Infection indication for a TLE is further negatively affected in the presence of vegetations and positive blood cultures at the time of TLE. These high-risk patients should be considered for earlier TLE to limit the formation of vegetation and systemic infection spread.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Competing Interest

D.G. is employee of BIOTRONIK Italia. All the remaining authors have no conflicts of interest to disclose.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijcard.2023.02.040>.

References

- [1] A.J. Greenspon, J.D. Patel, E. Lau, J.A. Ochoa, D.R. Frisch, R.T. Ho, et al., 16-year trends in the infection burden for pacemakers and implantable cardioverter-defibrillators in the United States: 1993 to 2008, *J. Am. Coll. Cardiol.* 58 (10) (2011) 1001–1006.
- [2] D. Giacomelli, D. Azzolina, R.I. Comoretto, F. Quartieri, F. Rovaris, V. Schillaci, A. Gargaro, D. Giacomelli, Implantable cardioverter defibrillator lead performance: a systematic review and individual patient data Meta-analysis, *Int. J. Cardiol.* S0167-5273 (22) (2022), 01735–1.
- [3] F.M. Kusumoto, M.H. Schoenfeld, B.L. Wilkoff, C.I. Berul, U.M. Birgersdotter-Green, R. Carrillo, et al., 2017 HRS expert consensus statement on cardiovascular implantable electronic device lead management and extraction, *Heart Rhythm.* 14 (12) (2017) e503–e551.
- [4] M.G. Bongiorni, H. Burri, J.C. Deharo, C. Starck, C. Kennergren, L. Saghy, et al., 2018 EHRA expert consensus statement on lead extraction: recommendations on definitions, endpoints, research trial design, and data collection requirements for clinical scientific studies and registries: endorsed by APHRS/HRS/LAHRs, *Europace.* 20 (7) (2018) 1217.
- [5] J.A.T. Sandoe, G. Barlow, J.B. Chambers, M. Gammage, A. Guleri, P. Howard, et al., Guidelines for the diagnosis, prevention and management of implantable cardiac electronic device infection. Report of a joint working party project on behalf of the british society for antimicrobial chemotherapy (BSAC, host organization), *British Heart J.* 70 (2) (2015) 325–359.
- [6] M.G. Bongiorni, C. Kennergren, C. Butter, J.C. Deharo, A. Kutarski, C.A. Rinaldi, et al., The European Lead extraction ConTrolled (ELECTRa) study: a European heart rhythm association (EHRA) registry of Transvenous Lead extraction outcomes, *Eur. Heart J.* 38 (40) (2017) 2995–3005.
- [7] A. Polewczuk, W. Jacheć, A. Tomaszewski, W. Brzozowski, M. Czajkowski, G. Opolski, et al., Lead-related infective endocarditis: factors influencing early and long-term survival in patients undergoing transvenous lead extraction, *Heart Rhythm.* 14 (1) (2017) 43–49.
- [8] V.S. Mehta, M.K. Elliott, B.S. Sidhu, J. Gould, T. Kemp, V. Vergani, et al., Long-term survival following transvenous lead extraction: importance of indication and comorbidities, *Heart Rhythm.* 18 (9) (2021) 1566–1576.
- [9] R. Narui, I. Nakajima, C. Norton, B.B. Holmes, Z.T. Yoneda, N. Phillips, et al., Risk factors for repeat infection and mortality after extraction of infected cardiovascular implantable electronic devices, *JACC Clin. Electrophysiol.* 7 (9) (2021) 1182–1192.
- [10] B.L. Wilkoff, C.J. Love, C.L. Byrd, M.G. Bongiorni, R.G. Carrillo, G.H. Crossley 3rd, et al., Transvenous lead extraction: Heart Rhythm Society expert consensus on facilities, training, indications, and patient management: this document was endorsed by the American Heart Association (AHA), *Heart Rhythm.* 6 (7) (2009) 1085–1104.
- [11] L. Bontempi, A. Curnis, P. Della Bella, M. Cerini, A. Radinovic, L. Inama, et al., The MB score: a new risk stratification index to predict the need for advanced tools in lead extraction procedures, *Europace.* 22 (4) (2020) 613–621.
- [12] L. Bontempi, F. Vassanelli, M. Cerini, L. Inama, F. Salghetti, D. Giacomelli, et al., Predicting the difficulty of a transvenous lead extraction procedure: validation of the LED index, *J. Cardiovasc. Electrophysiol.* 28 (7) (2017) 811–818.
- [13] J. Gould, M. Klis, B. Porter, B.S. Sidhu, B.J. Sieniewicz, S.E. Williams, et al., Predictors of mortality and outcomes in transvenous lead extraction for systemic and local infection cohorts, *Pacing Clin. Electrophysiol.* 42 (1) (2019) 73–84.
- [14] T.D. Callahan, D.O. Martin, Quantifying risk after transvenous lead extraction, *J. Cardiovasc. Electrophysiol.* 31 (5) (2020) 1163–1165.
- [15] G. Mitacchione, G. Arabia, M. Schiavone, M. Cerini, A. Gasperetti, F. Salghetti, et al., Intraoperative sensing increase predicts long-term pacing threshold in leadless pacemakers, *J. Interv. Card. Electrophysiol.* 63 (3) (2022) 679–686.

- [16] G. Mitacchione, M. Schiavone, A. Gasperetti, G. Arabia, A. Breitenstein, M. Cerini, et al., Outcomes of leadless pacemaker implantation following transvenous lead extraction in high-volume referral centers: real-world data from a large international registry, *Heart Rhythm*. S1547-5271 (22) (2022), 02688–1.
- [17] L. Bontempi, G. Arabia, F. Salghetti, M. Cerini, A. Dell'Aquila, A. Milidoni, A. Ahmed, A. Cersosimo, D. Giapopelli, G. Mitacchione, A. Raweh, C. Muneretto, A. Curnis, Lead-related infective endocarditis with vegetations: prevalence and impact of pulmonary embolism in patients undergoing transvenous lead extraction, *J. Cardiovasc. Electrophysiol.* 33 (10) (2022) 2195–2201.
- [18] M.P. Brunner, E.M. Cronin, V.E. Duarte, C. Yu, K.G. Tarakji, D.O. Martin, et al., Clinical predictors of adverse patient outcomes in an experience of more than 5000 chronic endovascular pacemaker and defibrillator lead extractions, *Heart Rhythm*. 11 (5) (2014) 799–805.