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THE PRESENT AND FUTURE

JACC REVIEW TOPIC OF THE WEEK

Early Lead Extraction for Infected Implanted Cardiac Electronic Devices

JACC Review Topic of the Week

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ABSTRACT

Infection remains a serious complication associated with the cardiac implantable electronic devices (CIEDs), leading to substantial clinical and economic burden globally. This review assesses the burden of cardiac implantable electronic device infection (CIED-I), evidence for treatment recommendations, barriers to early diagnosis and appropriate therapy, and potential solutions. Multiple clinical practice guidelines recommended complete system and lead removal for CIED-I when appropriate. CIED extraction for infection has been consistently reported with high success, low complication, and very low mortality rates. Complete and early extraction was associated with significantly better clinical and economic outcome compared with no or late extraction. However, significant gaps in knowledge and poor recommendation compliance have been reported. Barriers to optimal management may include diagnostic delay, knowledge gaps, and limited access to expertise. A multipronged approach, including education of all stakeholders, a CIED-I alert system, and improving access to experts, could help bring paradigm shift in the treatment of this serious condition.

Cardiac implantable electronic devices (CIEDs) play an important role in the management of cardiac arrhythmias and the prevention of sudden cardiac death.[1] As the indications for primary prevention and cardiac resynchronization have expanded alongside an aging population, CIED implantation has increased worldwide over recent years.[2,3]

Although technological advances have improved both the devices and implantation procedures, cardiac implantable electronic device infections (CIED-Is) remain a significant problem.[4] These include pocket infection, systemic infection, and infective endocarditis, each of which can be life-threatening.[5-7] The Heart Rhythm Society and the European Heart Rhythm Association (EHRA) have published guidelines for the management of leads and devices, including recommending extraction for CIED-I.[5,8] Despite multiple recommendations on prevention, diagnosis, and management strategies,

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ABBREVIATIONS AND ACRONYMS

CIED = cardiac implantable electronic device

CIED-I = cardiac implantable electronic device infection

EHRA = European Heart Rhythm Association

discussions about barriers to optimal treatment and guideline adherence in clinical practice are limited.

The objective of this review is to summarize the literature to provide a comprehensive overview of CIED-Is and management. A structured literature review was performed in MEDLINE via the PubMed interface on October 21, 2020, for papers published in the last 15 years to inform this review. Titles and abstracts identified by the search were reviewed for eligibility based on inclusion criteria. Publications on CIED-I rates, outcomes of management strategies, associated clinical or economic burden such as health-related quality of life, and cost of infection were included. Furthermore, clinical practice guidelines on CIED-I management were captured in addition to papers discussing trends in clinical practice, adherence to guidelines, and/or barriers to optimal treatment. Search strategy and search results can be found in the Supplemental Appendix.

The review will systematically characterize the following: 1) the epidemiology and burden of CIED-Is; 2) clinical outcomes data on various treatment strategies and health care utilization research CIED-Is; 3) an overview of current guidelines on CIED-I treatment; 4) the adherence to consensus and guideline recommendations; and 5) potential barriers to the recommended treatment. We conclude the review with future directions and possible solutions to address barriers to optimal treatment.

HIGHLIGHTS

- Infection is a life-threatening complication of implanted CIEDs.
- Although clinical evidence and guidelines support extraction of infected CIED, adherence is limited.
- Educating stakeholders and optimizing use of technology can help address barriers to explanation of infected CIED.

CIED-I EPIDEMIOLOGY AND CLINICAL IMPACT

CIED-Is can lead to serious systemic complications. They can present either as a pocket infection in the chest, typically diagnosed clinically, or a systemic infection, which is confirmed with positive blood cultures. CIED-I rates across the world range from 0.8% to 4.2%.[4,9-19] Overall, CIED-I rates within a year of implantation range from 1.2% to 3.4%.[11-14] A U.S. cohort study using the National Inpatient Sample database found that 8,060 (4.2%) of 191,610 CIED implantations were admitted for CIED-Is in 2016.[18] Among a Danish CIED population (128,045 devices), the overall incidence of CIED-I was reported to be 1.43%.[16] A complete summary of infection rates can be found in **Table 1**.

The WRAP-IT (World-wide Randomized Antibiotic Envelope Infection Prevention trial) multicenter RCT evaluated the clinical and economic burden of CIED-I from the hospital, payer, and patient perspectives. Patients were found to have significantly reduced quality of life at the time of infection diagnosis vs baseline (0.83 ± 0.14 vs 0.75 ± 0.19; $P = 0.004$). Furthermore, patients with infection had a significant increased risk of death compared with the no infection group (risk-adjusted HR: 3.41; 95% CI: 1.81-6.41; $P < 0.001$).[20] Similarly, the Italian POINTED (Impact on Patient Outcome and health care utilization of cardiac ImplaNTable Electronic Device complications) Registry suggested that CIED-I is associated with poor survival compared with patients with other complications or those with none ($P < 0.001$).[17]

CIED-Is may be related to various patient, device and procedural factors (**Central Illustration**). Patient factors that may increase the risk of CIED-I include renal dysfunction, diabetes, and younger age.[13,14,16,19] Oral anticoagulation use and prior CIED-I have also been reported as risk factors.[14,16]

ECONOMIC BURDEN OF CIED-I

The economic burden of CIED-I varies depending on the region. A retrospective analysis of a large U.S. health insurer database showed that CIED-I increases the average annual medical costs by 2.4 times, with a 1-year adjusted incremental expenditure of $57,322 per patient (95% CI: $46,572-$70,484; per patient; $P < 0.001$).[13] The WRAP-IT trial further reported the mean payer costs per infection was $57,978 ± $29,431 for Medicare Advantage and $26,867 ± $14,893 for Medicare Fee For Service.[20] In Germany, a retrospective analysis of health claims data reported €15,822 higher costs in the year after CIED-I compared with the year prior to infection (excluding the cost of index device implantation).[14] The higher costs were approximately 98% driven by inpatient hospital care.[14] A Korean analysis of their National Health Insurance database found that the average cost per person associated with CIED-I was U.S.$17,105,[19] which was similar to the United Kingdom (£14,742).[21] Regional variations of infection costs per patient is shown in **Figure 1**.

TABLE 1 Summary of Globally Reported Infection Rates in Patients With CIEDs

First Author	Year	Region	Infection Rate, %	Details and Time Frame
Ahsan et al[9]	2014	United Kingdom	1.33	Of 1,798 device procedures performed between November 2004 and May 2009, 24 patients (1.33%) developed infections requiring device removal.
Chen et al[10]	2020	Taiwan	1.4	During a mean follow-up of 2.9 ± 1.7 y, 17 (1.4%) patients were diagnosed with a CIED infection episode.
Daneman et al[11]	2020	Canada	1.2	Among 17,584 patients, 215 (1.2%) developed a CIED-related infection during the year after implantation.
de Bie et al[12]	2012	Netherlands	1.1; 2.6	Of a total of 2,476 patients, the cumulative incidence of CIED after initial device implantation was 1.1% at 1 y and 2.6% at 3 y.
Eby et al[13]	2020	United States	1.28	The overall infection rate within the first year postimplant was 1.28%.
Ganesan et al[4]	2019	Australia	0.8	The incidence of CIED infection complication was 0.8% (244 patients [115 in public hospitals and 89 in private hospitals] of 32,364 patients).
Ludwig et al[14]	2018	Germany	3.4	There were 158 CIED infections in the 12 mo after implantation, an annual risk of 3.4%.
Nakajima and Taki[15]	2016	Japan	1.12-2.8	The overall infection rate was 1.12% (95% CI: 0.812%-1.505%); however, the rate was 2.77% at the sites with more experience with implantation.
Olsen et al[16]	2019	Denmark	1.43	The overall incidence of CIED infection between 1982 and 2018 was 1.43% (of 128,045 devices).
Palmisano et al[17]	2020	Italy	1.7	49 patients of 2,811 had devices infection at follow-up (median 56.8 mo).
Rennert-May et al[18]	2020	United States	4.2	8,060 infections (4.2%) were identified from 191,601 CIED implantations in 2016 via the Healthcare Cost and Utilization Project National Implant Sample database.
Yang et al[19]	2019	Korea	2.7	462 infections were reported for 16,908 at follow-up (mean 17.1 mo).

CIED = cardiac implantable electronic device.

CLINICAL OUTCOMES AND HEALTH CARE UTILIZATION FOR CIED EXTRACTION

Optimal CIED-I management includes device extraction and is a highly successful procedure. For safety and effectiveness, there were 16 studies reporting on outcomes for patients where the entire study cohort (100%) underwent extraction for the indication of CIED-I. Procedural success was consistently reported to be very high, with most studies reporting rates of >95% (Table 2). Also, procedural complication rates (range 0.0%-4.0%) and mortality rates (range 0.0%-1.0%) were consistently low across all studies[32-51] (Figure 2).

CIED extraction, when indicated, can be a potentially life-saving procedure. A retrospective study of CIED-I cases from a large academic center between 1991 and 2008 found that antimicrobial therapy without device extraction was associated with nearly a 7-fold higher 30-day mortality (HR: 6.97; 95% CI: 1.36-35.60).[38] Additionally, patients with CIED extraction for infection had a 1-year mortality rate of 13.3%, whereas those who were treated with antibiotics only (n = 23) had a 1-year mortality rate of 38.1%.[38] Similarly, in an international study examining endocarditis patients, there was an 18.3% difference in 1-year mortality between patients who had their device removed for CIED-I compared with those who did not (19.9% vs 38.2%; $P = 0.02$) (Figure 3).[52]

Timing of CIED extraction, early vs delayed extraction, after infection, also reveals significant differences in 1-year mortality (Figure 3). When extraction was conducted at the initial infection presentation (n = 370), 1-year mortality was significantly lower than those who had extraction after failure of antimicrobial therapy (n = 23) (11.4% vs 43.4%; $P < 0.001$).[38] A retrospective analysis of all consecutive CIED-I patients who underwent extraction at a single U.S. university hospital found similar results. For patients who had extraction within 10 days of diagnosis, a 1-year mortality of 16.9% was reported compared with 33.9% in patients who had extraction after 10 or more days ($P = 0.028$).[40] A 2020 study examining the impact of early vs delayed extraction with infected CIEDs found similar trends of significantly greater 12-month survival rate in patients with bacteremia ($P = 0.022$) and isolated pocket infections ($P = 0.027$) when CIED-I extraction occurred early (within 7 days from hospital admission).[53] Last, 4 studies reported on reinfection rates associated with complete vs incomplete extraction. Three large single-center studies (2 retrospective and 1 prospective) reported significantly lower rates of reinfection when complete extraction occurred for CIED-I (1.0% vs 50.0%; $P < 0.001$; 4.3% vs 20.8%; $P = 0.006$; 5.3% vs 21.4%; $P = 0.007$). One (retrospective) study failed to report statistical testing for significance.[39,54-56]

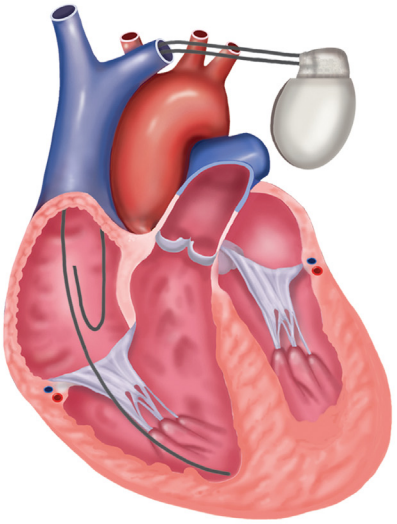
CENTRAL ILLUSTRATION **Cardiac Implantable Electronic Device Infection: Risk Factors, Clinical Presentation, and Addressing Barriers**

Risk Factors for CIED

Patient factors
- Renal dysfunction/hemodialysis
- Diabetes mellitus
- Heart disease/dysfunction
- Chronic corticosteroids
- Oral anticoagulation
- Immunocompromise-HIV, organ transplant, chemotherapy

Device factors
- >2 leads
- ICD/CRT
- Heart disease/dysfunction

Procedural factors
- Early reintervention
- Temporary pacing
- Fever ≤24 hours before implantation
- Unrecognized bacteremia or focus of infection
- Prolonged procedure duration



Key Stakeholders Involved in the ID/Diagnosis and Treatment of CIED Infections Include:
- Electrophysiologists
- Cardiologists
- Nephrologists
- Patients
- Cardiac surgeons
- Infectious disease specialists
- Device clinic staff
- Primary care physicians
- Hospitalists

Infection Type	Description	Signs/ Symptoms
Pocket infection	• Manifests as local occurrence where the device was implanted	• Skin redness • Pain/tenderness • Swelling/warmth • Drainage • Skin ulceration • Device erosion
Systemic infection	• >2 leads • ICD/CRT • Device revision or upgrade	• Fever/chills • Malaise • Nausea • Hypotension • Murmur on examination • Symptomatic HF

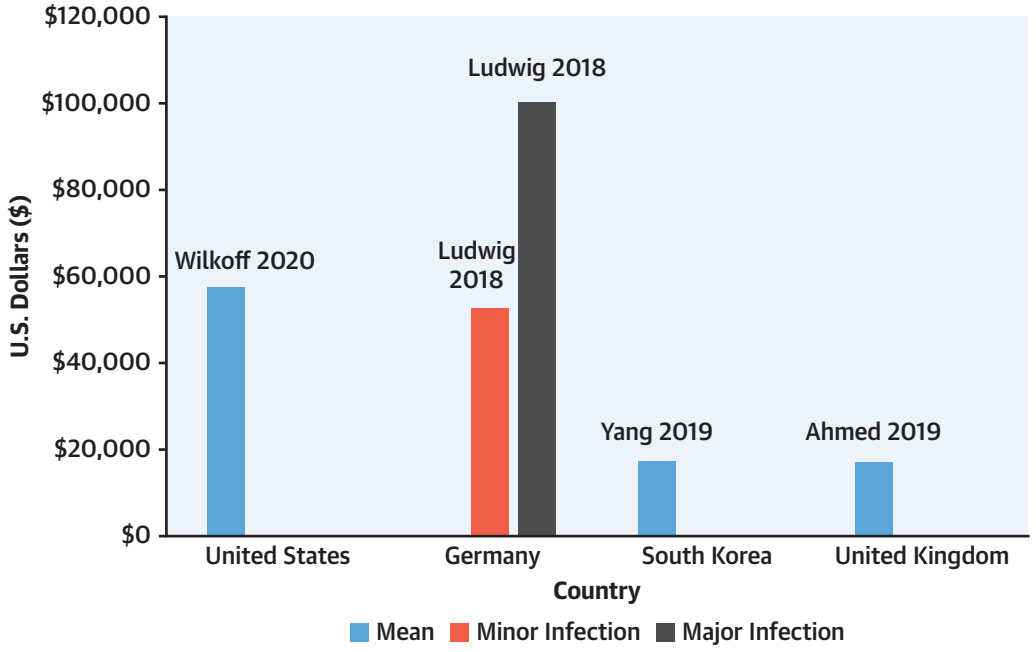
Barrier Type	Description	Recommendation
Identification	• Misdiagnosis with other infections and illnesses due to overlapping symptoms • Multidisciplinary issue with limited physician knowledge	• Integrate an electronic medical record alert (EMR) system
Referral	• Proximity/access to an extraction center • Fear of losing a patient to an extracting physician	• Creating a team structure to efficiently guide patients to appropriate experts including infectious disease specialists and device extraction specialists in a timely fashion
Extraction	• Patient age and comorbidities • Perceived complexity and high mortality risk of extraction procedure	• Educate key stakeholders about available evidence and guideline-directed therapy • Educate patients about extraction procedures as an option and potential complications if such a procedure is delayed • Build lead management teams

Lakkireddy DR, et al. J Am Coll Cardiol. 2023;81(13):1283–1295.

Cardiac implantable electronic device (CIED) infection may be related to various risk factors, and its clinical presentations can be highly variable. Key stakeholders in the diagnosis and management should be involved in all the steps of CIED infection management to address the barriers. CRT = cardiac resynchronization therapy; EMR = electronic medical record; ER = emergency room; ICD = implantable cardioverter defibrillator; ID = identification.

A recent analysis of a Medicare population from 2004 through 2019 provided updated information on device infection and all-cause mortality of these patients.[57] CIED-I incidence was 1.1% and only 25% (n = 2,814) of these patients had extraction.[57] Cumulative 1-year mortality was 32.4% for patients without extraction at 30 days, compared with 18.5% among patients with extraction within 6 days ($P < 0.001$).[57] Furthermore, any extraction was associated with lower mortality when compared with no

FIGURE 1 Regional Variations of Costs per Cardiac Implantable Electronic Device Infection



The global economic burden of cardiac implantable electronic device infection is significant and varies among different nations.

extraction (adj HR: 0.73; 95% CI: 0.67-0.81; $P < 0.001$); and extraction within 6 days was associated with even lower risk of mortality (adj HR: 0.59; 95% CI: 0.52-0.67; $P < 0.001$).[57] Although impactful, analysis from the Medicare database must be used with caution as there are limitations, including the retrospective nature of the data and underrepresentation of the number procedures.

In general, the evidence has demonstrated that prompt CIED extraction is associated with favorable health care resource utilization relative to alternatives. A large U.S. payer database analysis estimated that incremental health care expenditures for patients with an infection managed by inpatient admission with no extraction cost more than double the amount compared with infections managed by extraction in either an inpatient or outpatient setting ($104,077 vs $45,291).[58] Furthermore, Rungpradubvong et al[40] found that CIED-I patients with early removal (within 10 days of infection diagnosis) were associated with significantly shorter hospital stays compared with their delayed extraction counterparts (17.59 ± 12.64 days vs 43.77 ± 37.77 days; $P < 0.001$). In addition to shorter hospital stays, early extraction was associated with lower mean all-cause Medicare costs within 12 months postinfection, with extractions occurring on the same day as diagnosis costing an estimated $34,640 vs $76,836 for extractions occurring ≥180 days from infection diagnosis.[59]

Although the evidence presented supports timely CIED extraction, the context must be considered. Many of these studies are not randomized. Thus, delayed extraction cohorts are more likely to have older, frail patients, including those with end-stage diseases. CIED extraction is not without risk; associated major perioperative adverse events can include cardiac arrest/perforation, dissection, and pericardial tamponade. Also, studies are often limited to specific subgroups and may not be directly comparable. Furthermore, many of these studies may include outcomes from experienced centers with high extraction volumes. Although the positive outcomes reported provide confidence of the procedure, they fail to provide a comprehensive overview of extraction outcomes across all centers and individuals with varied experience.

GUIDELINE RECOMMENDATIONS AND REAL-WORLD CLINICAL PRACTICE PATTERNS

Five current guidelines from professional societies provide recommendations on CIED lead management and extraction: American Heart Association, British

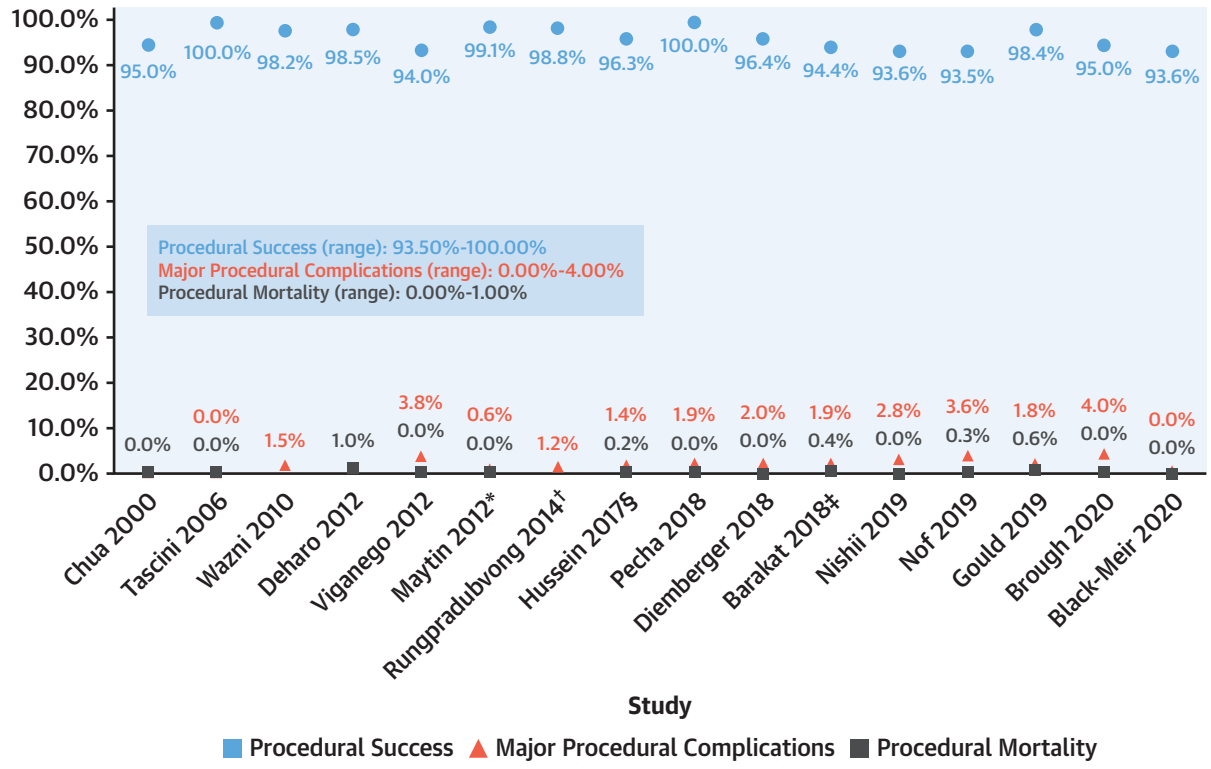
TABLE 2 Summary of Clinical Outcomes and Definitions Evaluating Extraction for CIED-I Indicated Only Patients

First Author	Year	Region	Study Design	Overall Sample Size	Reported Outcomes Definitions: Procedural Success, %	Major Complication, %	Procedural Mortality, %	Outcome Definitions
Chua et al[39]	2000	United States	Retrospective case series	123	95	NR	0	• Complete procedural success[a]
Tascini et al[35]	2006	Italy	Retrospective survey	121	100	0	0	• Complete procedural success[a]
Wazni et al[37]	2010	United States and Canada	Retrospective study	825	98.2[g]	1.5	NR	• Clinical success[b] • MAEs were defined as "any complication related to the procedure that required procedural intervention or transfusion to prevent death, threat to life, or any complication related to the procedure that resulted in death or serious harm to bodily function or structure"
Deharo et al[22]	2012	France	Matched cohort study	197	98.5	NR	1	• Complete procedural success[a]
Viganego et al[36]	2012	United States	Retrospective	52	94	3.8	0	• Complete procedural success[a] • Complications were classified according to published criteria
Maytin et al[23,c]	2012	United States	Retrospective cohort study	334	99.1	0.6	0	• Complete procedural success[a] • Major complications were defined as those that threaten life, require significant surgical intervention, cause persistent or significant disability, or result in death
Rungpradubvong et al[40,d]	2014	United States	Retrospective study	142	98.8	1.2	NR	• NR
Hussein et al[24,e]	2017	United States	Retrospective study	1063	96.3	1.4	0.2	• Complete procedural success[a] • Major complications were defined as complications that were life threatening, resulted in significant or permanent disability or death, or required surgical intervention
Pecha et al[34]	2018	Germany	Retrospective review	52	100	1.9	0	• NR
Diemberger et al[25]	2018	Italy	Prospective observational study	169	96.4[c]	2.0	0	• NR
Barakat et al[26,f]	2018	United States	Retrospective study	1159	94.4	1.9	0.4	• Complete procedural success[a]
Nishii et al[30]	2019	Japan	Retrospective review	109	93.6	2.8	0	• Complete procedure success[a]
Nof et al[31]	2019	Europe	Prospective registry review	1863	93.5	3.6	0.27	• Complete procedure success[a] • Major complications included: sepsis, multiorgan failure, tamponade, major vessel laceration, life-threatening arrhythmia, heart failure, acute myocardial infarction, acute massive valvular regurgitation, or any need for emergency surgery
Gould et al[27]	2019	United Kingdom	Prospective observational study	505	98.4	1.8	0.6	• Complete procedure success[a] • Major complication was defined as any outcome related to the procedure which was life threatening or resulted in death, an unexpected event that caused persistent or significant disability, or any event requiring significant surgical intervention to prevent any of these outcomes within 30 days of TLE
Brough et al[28]	2019	United Kingdom	Retrospective study	47	95[b]	4	0	• Complete clinical success[h] • Complications as defined by Wilkoff et al[29]
Black-Maier et al[30]	2020	United States	Retrospective study	27	93.6	0	0	• Complete procedure success[a]

[a]Complete procedural success defined as the ability to remove "all lead material from the vascular space," identified for each lead extracted. [b]Clinical success defined as achievement of "all clinical goals associated with the indication for lead removal," as identified only once for each procedure, according to NASPE 2000 Policy Statement.[31] [c]Results reported for the local infection cohort. [d]Results reported for the early extraction cohort. [e]Results reported for patients without abandoned leads. [f]Results reported for normal renal function group. [g]Reported as clinical success. [h]Reported a complete radiological success.

MAE = major adverse event; TLE = transvenous lead extraction.

FIGURE 2 Clinical Outcomes for Cardiac Implantable Electronic Device Extractions in Patients With Cardiac Implantable Electronic Device Infection



Extraction for cardiac implantable electronic device infection is associated with high procedural success (majority of studies showing rates of >95%), low major procedural complication (between 0% to 4%), and very low procedural mortality (0% to 1%). *Results reported for the local infection cohort. †Results reported for the early extraction cohort. ‡Results reported for the normal renal function group. §Results reported for patients without abandoned leads.

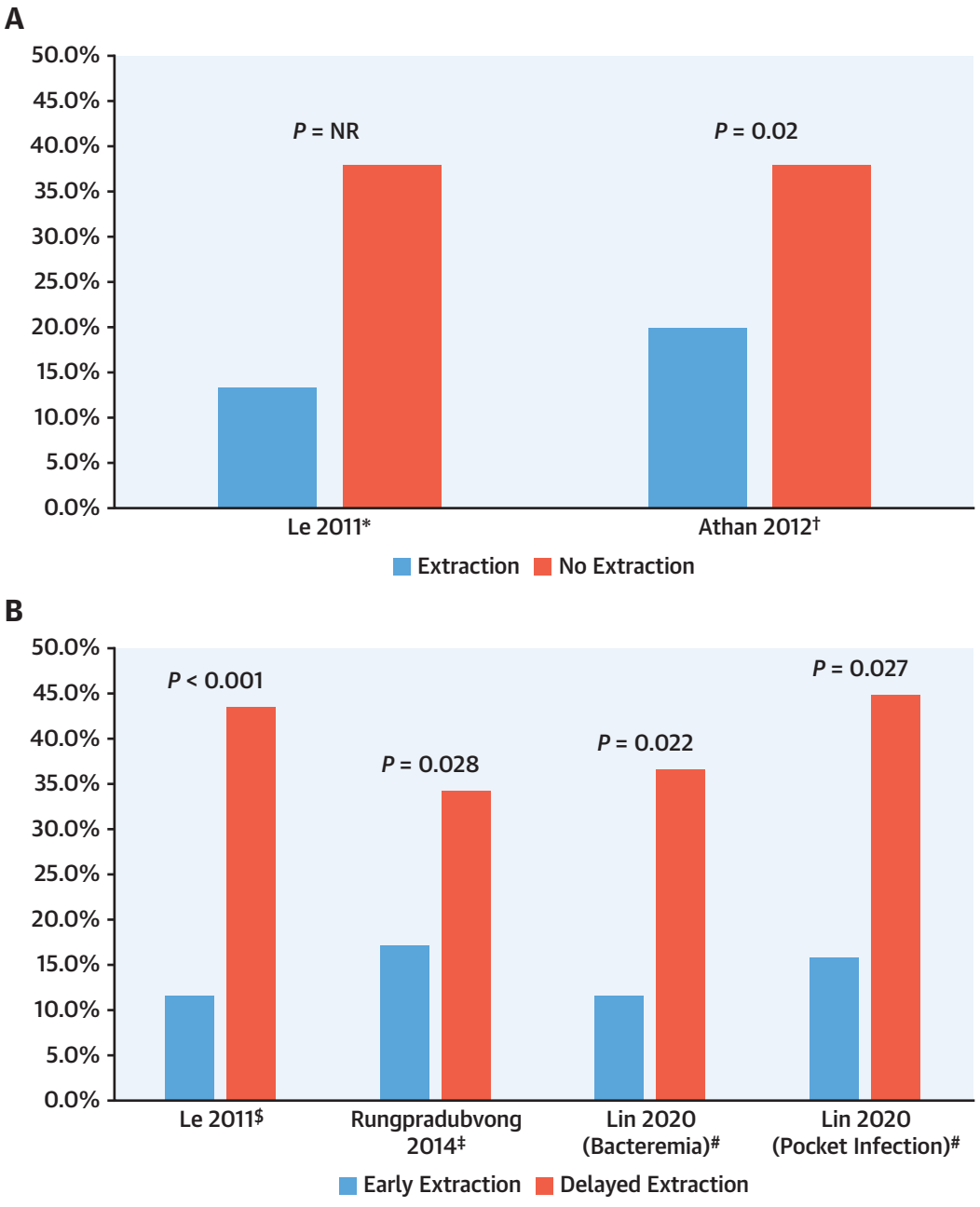
Heart Rhythm Society, European Society of Cardiology, Heart Rhythm Society, and EHRA. All report a Class I indication for complete system removal in patients with defined CIED-I (systemic, local, bacteremia, or infection endocarditis). Three of these guidelines explicitly recommended prompt and complete system removal for definite CIED-I.[5,7,8,60,61] A summary of the guideline recommendations for CIED-I can be found in **Table 3**.

Despite these guideline recommendations, a recent analysis of the U.S. Medicare database demonstrated that >8 of 10 patients were not treated according to Class I guidelines for CIED-I (full system extraction).[57] Additionally, a global survey of members of 7 arrhythmia societies found regional disparities in the clinical practices for the management of CIED-I. The survey revealed that all regions did not fully comply with current guidelines recommendations.[62] It found that only 62% of responders would manage CIED pocket infection with complete system removal and 13.7% would complete no action and wait until the next regular visit.[62] The European adherence rate (68.9%) was similar to a Germany single-center experience over 4 decades in which only 57% of CIED-Is were treated with system extraction.[56] Furthermore, the physician survey rate in the Asia/Pacific region (41.2%) aligned with 2 other Japanese surveys. One reported a 55.8% annual system removal rate in 2013, and a 2018 web-based survey of 155 Japanese cardiologists reported that 30% of CIED-I cases were treated by entire system removal.[15,63]

BARRIERS TO CIED GUIDELINE ADHERENCE

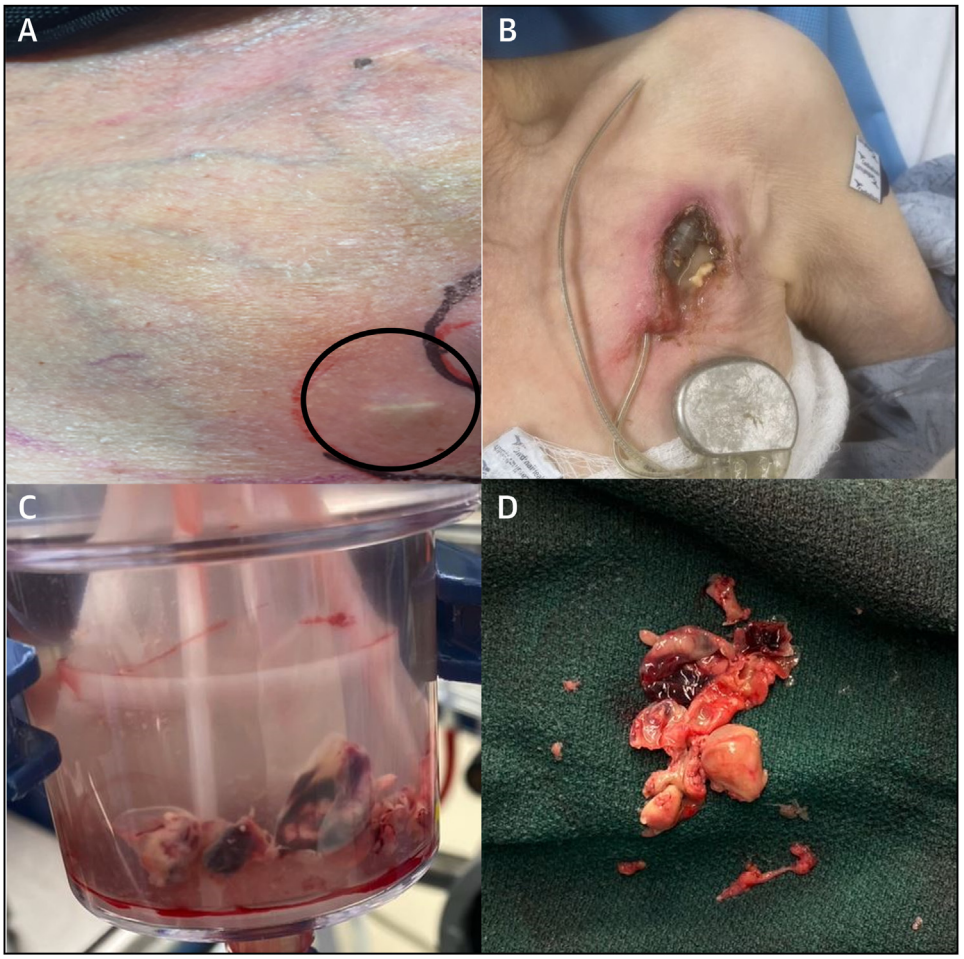
A 2020 physician education needs survey was conducted by the EHRA/European Society of Cardiology (ESC) to help assess guideline adherence and potential barriers in effective CIED-I management in clinical practice.[64] The 3 main barriers were as follows: 1) identification of the CIED-I; 2) prompt referral; and 3) access to extraction. *Identification barriers* often

FIGURE 3 1-Year Mortality for Cardiac Implantable Electronic Device Infection



(A) Extraction vs no extraction. Extraction for cardiac implantable electronic device infection is associated with lower 1-year mortality rates compared with no extraction. **(B)** Early vs delayed extraction. One-year mortality rates were significantly lower for patients who underwent early extraction compared with delayed extraction. *Antimicrobial therapy with complete device removal (n = 376) vs antimicrobial therapy only (n = 21). †CIED infective endocarditis patients with device removal (n = 141) vs no extraction (n = 34). ‡Early extraction (extraction within 10 days after indicated) (n = 83) vs delayed extraction (extraction performed >10 days after indicated) (n = 59). §Early extraction (extraction at initial presentation) (n = 370) vs delayed extraction (extraction after failure of antimicrobial therapy) (n = 23). #Early extraction (<7 days from hospital admission to extraction); bacteremia (n = 127), pocket infection (n = 106); 1-year mortality rates were extrapolated from the Kaplan-Meier curve in Lin et al.[53]

FIGURE 4 Examples of Cardiac Implantable Electronic Device Infection



(A) Localized pocket infection. **(B)** Device erosion with site inflammation **(C)** AngioVac filter filled with pieces of large vegetations. **(D)** Large lead vegetation removed with vacuum-assisted aspiration.

reflect gaps in physician knowledge and skills in CIED-I management (25% of extractors and more than 60% of nonextractors reported the need for improvement).[64] *Referral barriers* included factors such as proximity to an extraction center (reported by 18% of responders), ease of access to an extraction center (reported by 37% of responders), or fear of losing a patient to an extracting physician (reported by 14% of responders).[64] Other factors included bed constraints, cost, and perceived lack of a diagnosis. Additional factors associated with *extraction barriers* included patients' comorbidities, with 92% of responders reporting this affected their choice; age of the patients (reported by 83% of responders); and age of the lead (reported by 73% of responders). Responders were asked what factors may limit a patient from being considered for lead extraction: 77% reported a high risk of procedural mortality, and 44% reported the perceived difficulty or complexity of the procedure (**Table 4**).[64]

Barriers to identification may be caused by lack of optimal communication and coordination. These patients are often seen by specialties other than their implanting electrophysiologists (ie, hospitalists, primary care physicians, general cardiologists, and so on). Furthermore, symptoms of CIED-I can mimic other infections and illnesses and can be overlooked or misdiagnosed. Examples of CIED infection are shown in **Figure 4**. Referral barriers and patient factors seem to largely influence

TABLE 3 Summary of U.S. and European Guideline Recommendations for CIED Device Removal in Patients With Infection

Society, Year	Recommendations: Complete Extraction	Recommendations: Prompt Extraction	Details
AHA, 2010[61]	×	×	• Complete device and lead removal are recommended for all patients with definite CIED-I, CIED pocket infection, valvular endocarditis without definite involvement of the lead(s) and/or device, with occult staphylococcal bacteremia (Class I Indication) • Complete device removal should not be delayed, regardless of timing of imitation of antimicrobial therapy
BHRS, 2015[7]	×	×	• Complete and early (as soon as possible, but not more than 2 wks after diagnosis) removal of an infected CIED system (generator and all leads) combined with appropriate antimicrobial therapy is the most effective, safe, and efficient treatment option for pocket infections, CIED-LI, and CIED-IE
ESC, 2015[60]	×		• Prolonged (ie, before and after extraction) antibiotic therapy and complete hardware (device and leads) removal are recommended in definite CDRIE, as well as in presumably isolated pocket infection (Class I Indication)
HRS, 2017[8]	×	×	• Complete device and lead removal are recommended for all patients with definite CIED system infection, valvular endocarditis without definite involvement of the lead(s) and/or device, persistent or recurrent bacteremia or fungemia (Class I Indication) • Early diagnosis of CIED-I and performing lead extraction within 3 days of diagnosis is associated with lower in-hospital mortality
EHRA, 2020[5]	×	×	• Complete device removal is recommended (including abandoned leads, epicardial leads, and lead fragments) for patients with definite CIED-I (systemic and local), in cases of bacteremia, and infective endocarditis (Class I Indication) • Device removal should occur without unnecessary delay (ideally within 3 d)

AHA = American Heart Association; BHRS = British Heart Rhythm Society; CDRIE = cardiac device-related infective endocarditis; CIED = cardiac implantable electronic device; CIED-I = cardiac implantable electronic device infection; EHRA = European Heart Rhythm Association, ESC = European Society of Cardiology; HRS = Heart Rhythm Society; IE = infective endocarditis; LI = lead infection.

the decision of whether to use total device extraction.

ADDRESSING BARRIERS TO APPROPRIATE AND EFFECTIVE CIED-I MANAGEMENT

Because barriers to optimal treatment for CIED-Is are multifactorial, they may be addressed by various approaches and tools. Identification barriers largely stem from the lack of physician knowledge and awareness that can be mitigated with evidence and education. Another strategy is the incorporation of an electronic medical record alert system in which an automatic alert is sent to responsible physicians when a positive culture is registered in a CIED patient's medical record. An observational study examining

TABLE 4 Summary of Key Barriers to Extraction After CIED-I and Suggested Recommendations for Addressing Barriers

Barrier Category	Barrier Details	Discussion/Recommendation
Identification	• CIED-I symptoms often overlap with other infections and illnesses making diagnosis difficult[7] • 25% of extracting physicians and >60% of non-extracting physicians reported that their knowledge and skill in lead management need improvement[64]	• Integrate an EMR alert system • Educate stakeholders including hospital community members and patients
Referral	• 18% of survey responders reported proximity to an extraction center, whereas 37% reported ease of access to an extraction center are factors to referral[64] 14% of survey responders reported that the fear of losing a patient to an extracting physician is a barrier to referral[64] • Additional factors that affect delayed onward referral include: bed constraints, costs, and lack of a diagnosis[64]	• Untreated, inadequately treated (ie, with antibiotics), or delays in treatment for CIED-I can utilize more health care resources and costs, have negative consequences on patients such as increased mortality • Educate stakeholders including hospital community members and patients on the importance of early and complete extraction
Extraction	• 83% and 92% of survey responders reported that a patient's age and comorbidities affect the decision to perform extraction, respectively[64] • 77% of responders perceived a high risk of procedural mortality • 42% of survey responders believed the extraction procedure is difficult or complex[64]	• Across clinical studies (n = 16), procedural success rates were high (ie, >93%) whereas major procedural complications and procedural mortality remained low (ie, ≤4% and ≤1%, respectively) • A Japanese study reported high success rates and low complications despite being a midvolume center (compliant with the HRS 2017's recommendation of 20-30 extractions/y for clinical competency)[8,63]

EMR = electronic medical record; other abbreviations as in Table 3.

the impact of an electronic medical record alert system in individuals with CIED-I demonstrated positive trends in improvement in the time to evaluation and device removal compared with before implementation of the system.[65] Many of the cited referral barriers to extraction cannot be easily addressed with one solution, because they involve physicians' perceptions, preferences, and misconceptions. For example, it is unclear why patients diagnosed with CIED-I would be managed conservatively and why treating physicians are reluctant in seeking expert opinion and a more definite therapy. In many cases, CIED-Is are managed by teams that are not experts in CIED-I management. Creating a team structure that can accurately identify individuals with CIED-Is and efficiently channeling them to appropriate expert care that includes infectious disease specialists and device extraction specialists in a timely fashion could dramatically improve outcomes. For these patients, an explanation about the details of the extraction procedure as a therapy option and potential complications if such a procedure is delayed should be offered and adopted into standard clinical practice. To help address such barriers, a deeper understanding of how these reasons vary across setting, region, and physician type, as well as the relative dominance of such reasons, is key to building on education and resourcing platforms that can help to solve these gaps. It must be considered that untreated, inadequately treated, or delays in optimal treatment for CIED-Is can have consequences not only for the patient but also for the health care system in terms of resource and cost burden. This further supports the need to provide evidence and education to help inform physicians (and health care administrators) to prioritize early complete extraction for CIED-I as indicated by clinical guidelines. A quality initiative with a framework to increase guideline-driven care for patients with suspected CIED-I at hospitals may also address the gaps. Even though there is no existing concept of a center of excellence for lead extraction (ie, how many extractions should be performed), it is important that one must be created with established criteria. As with most implementation challenges, successful interventions need to be multifaceted to address the various barriers to optimal care. These interventions should be directed at the patient, physician, and system level.

CONCLUSIONS

CIED-I continues to be a serious and continued problem in clinical practice. Adherence to a guideline-based CIED-I management strategy including appropriate device extraction seems to be low. Barriers related to identification, referral, and perceptions around the extraction procedure are widely prevalent. Addressing knowledge gaps and overcoming the identified barriers in building effective CIED-I management teams and referral networks for timely and appropriate interventions including device extraction could improve the outcomes.

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APPENDIX For search strategy and search results, please see the online version of this paper.

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