ORIGINAL ARTICLE

Pol-CDRIE registry: 1-year observational data on patients hospitalized due to cardiac device–related infective endocarditis in Polish referential cardiology centers

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ABSTRACT

BACKGROUND The rate of cardiac device–related infective endocarditis (CDRIE) is increasing worldwide, but no detailed data are available for Poland.

AIMS We aimed to evaluate clinical, diagnostic, and therapeutic data of patients hospitalized due to CDRIE in 22 Polish referential cardiology centers from May 1, 2016 to May 1, 2017.

METHODS Participating cardiology departments were asked to fill in a questionnaire that included data on the number of hospitalized patients, number and types of implanted cardiac electrotherapy devices, and number of infective endocarditis cases. We also collected clinical data and data regarding the management of patients with CDRIE.

RESULTS Overall, 99 621 hospitalizations were reported. Infective endocarditis unrelated to cardiac device was the cause of 596 admissions (0.6%), and CDRIE, of 195 (0.2%). Pacemaker was implanted in 91 patients with CDRIE (47%); cardioverter-defibrillator, in 51 (26%); cardiac resynchronization therapy-

KEY WORDS
cardiac device–related infective endocarditis, cardiac resynchronization therapy, cardioverter-defibrillator, infective endocarditis, pacemaker

-defibrillator, in 48 (25%); and cardiac resynchronization therapy-pacemaker, in 5 (2.5%). The most common symptoms were malaise (62%), fever/chills (61%), cough (21%), chest pain (19.5%), and inflammation of the device pocket (5.6%). Cultures were positive in 77.5% of patients. The cardiac device was removed in 91% of patients. The percutaneous approach was most common for cardiac device removal. All patients received antibiotic therapy, and 3 patients underwent a heart valve procedure. Transesophageal echocardiography was performed in 80% of patients. The most common complication was heart failure (25% of patients).

CONCLUSIONS The clinical profile, pathogen types, and management strategies in Polish patients with CDRIE are consistent with similar data from other European countries. Transesophageal echocardiography was performed less frequently than recommended. The removal rate in the Polish population is consistent with the general rates observed for interventional treatment in patients with CDRIE.

WHAT'S NEW?

The present registry is the largest analysis of the issues regarding cardiac device–related infective endocarditis (CDRIE) in Poland. We report clinical, diagnostic, and therapeutic data of patients hospitalized due to CDRIE in Polish referential cardiology centers. The study showed that the clinical profile, pathogen types, and management strategies in patients with CDRIE from Polish tertiary care centers are consistent with similar data from other European countries. Moreover, the study revealed that patients are well treated in some fields of management, for example, percutaneous lead extraction was performed in the vast majority of patients. However, it shows that we should improve management in other fields, because, for example, transesophageal echocardiography was performed less frequently than it is recommended in the European Society of Cardiology guidelines.

INTRODUCTION Cardiac device–related infective endocarditis (CDRIE) is a life-threatening condition. The rate of CDRIE is increasing, which is attributed to, among others, implanting devices in older patients with more comorbidities and an increasing rate of high-energy device implantations (implantable cardioverter-defibrillator [ICD], cardiac resynchronization therapy defibrillator [CRT-D]). Data from the United States indicate that the rate of CDRIE among patients with implanted devices in 2008 was 2.41%, and it increased by 0.88% compared with 2004.[1] No detailed data on the rate of CDRIE are available for Poland. Based on an analysis of indications for device removal, nearly one-third of transvenous lead removals are due to infective endocarditis (IE).[2] According to a single-center registry that included 765 patients with a cardiac resynchronization therapy (CRT) device implanted, a diagnosis of CDRIE was made in nearly 1 in 20 patients within 3.5 years from implantation.[3] Data from the above registry indicate that outcomes of CDRIE in patients with CRT are particularly poor, with an in-hospital mortality rate of 50%.[3]

In the present study, we report data on CDRIE from 22 referential cardiology departments in Poland. The present publication is based on the first multicenter registry of CDRIE in our country. The aim of the study was to evaluate clinical, diagnostic, and therapeutic data of patients hospitalized due to CDRIE in Polish referential cardiology centers during the period of 1 year. We also assessed whether the management of these patients was consistent with the current European Society of Cardiology (ESC) guidelines.[4]

METHODS The study was conducted according to the project of the Clinical Initiatives Committee of the Polish Cardiac Society (in Polish, Komisja Inicjatyw Klinicznych ZG PTK). Data were collected retrospectively. Participating referential cardiology departments in Poland were asked to fill in a questionnaire that included data on the number of hospitalized patients, number and types of implanted cardiac electrotherapy devices, number of IE cases, as well as clinical, diagnostic, and therapeutic data on treatment of CDRIE. Data were collected from May 1, 2016, to May 1, 2017. Patients were diagnosed with CDRIE in accordance with the ESC definition of IE.[4] Only patients with a certain diagnosis of CDRIE were included in the registry. Only referential cardiology departments with extensive experience in cardiac electrotherapy, previously participating in multicenter studies, and certified in echocardiography were invited to participate in the study.

Statistical analysis Descriptive statistics on the frequency of analyzed variables were prepared using Microsoft Excel (Microsoft, Redmond, Washington, United States).

RESULTS **General data** During 12 months, overall 11 062 cardiac electrotherapy devices were implanted in 22 departments (from 183 per year to 1361 per year per department), including 6748 pacemakers (61%), 2655 ICDs (24%), and 1658 CRT devices (15%). The mean number of implanted devices per department per year was 503 (median, 386), including 306 pacemakers (median, 283), 121 ICDs (median, 74), and 76 CRT devices (median, 68).

Overall, 99 621 hospitalizations were reported in the participating departments during the study. Cardiac electrotherapy device

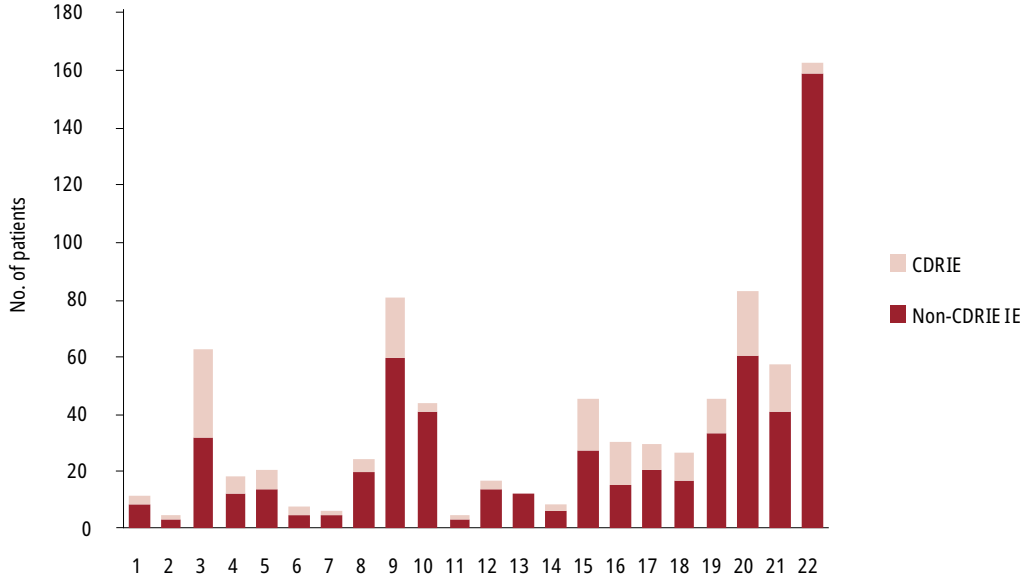

FIGURE 1 Number of patients with infective endocarditis (IE) without cardiac electrotherapy device and with cardiac device–related infective endocarditis (CDRIE) in the participating units

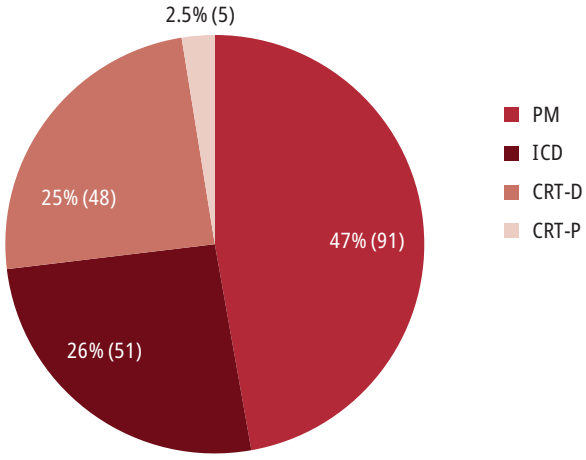

FIGURE 2 Types of cardiac electrotherapy device in patients with cardiac device–related infective endocarditis (n = 195)
Abbreviations: CRT-D, cardiac resynchronization therapy-defibrillator; CRT-P, cardiac resynchronization therapy-pacemaker; ICD, implantable cardioverter-defibrillator; PM, pacemaker

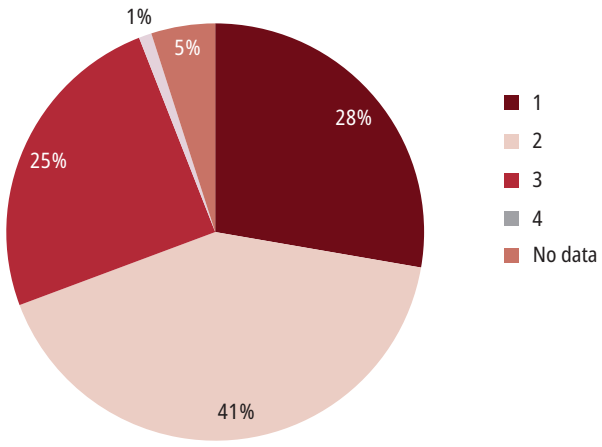

FIGURE 3 Percentage of implanted leads in patients with cardiac device–related infective endocarditis

implantation was the cause of 11 061 admissions (11%). Infective endocarditis unrelated to cardiac electrotherapy device was the cause of 596 admissions (0.6%), and CDRIE was the cause of 195 admissions (0.2%). Patients with CDRIE constituted 25% of all patients admitted due to IE. The mean number of patients with IE per department was 27, and of those with CDRIE, 9 (median, 16 and 6, respectively). The distribution of patients with IE and CDRIE in the participating departments is shown in FIGURE 1. Among patients with CDRIE, the median age was 69 years (range, 28–93 years), and 69% of patients were men. Hypertension was reported in 50% of patients; coronary artery disease, in 44%; diabetes mellitus, in 32%; atrial fibrillation, in 26%; and chronic kidney disease (defined as glomerular filtration rate <60 ml/min/1.73 m^2 using the Chronic Kidney Disease Epidemiology Collaboration formula), in 25%.

Clinical data The distribution of reported CDRIE cases in relation to the type of an implanted device and the number of implanted leads is shown in FIGURES 2 and 3. Among patients with CDRIE, 42% (n = 82) had 2 leads, 28% (n = 54) had 1 lead, 25% (n = 48) had 3 leads, and 1% (n = 2) had 4 leads implanted. The majority of the 195 patients with CDRIE had the device implanted on an elective basis (n = 109, 55.9%), 50 patients (25.6%) underwent urgent device implantation, and 9 patients (4.6%) required temporary transvenous lead insertion before the procedure. Data on the number of procedures performed within the device pocket (eg, device replacement) before the diagnosis of infection are shown in FIGURE 4.

Symptoms The most common symptoms reported by patients with CDRIE are listed in TABLE 1. The rates of involvement of various organs based

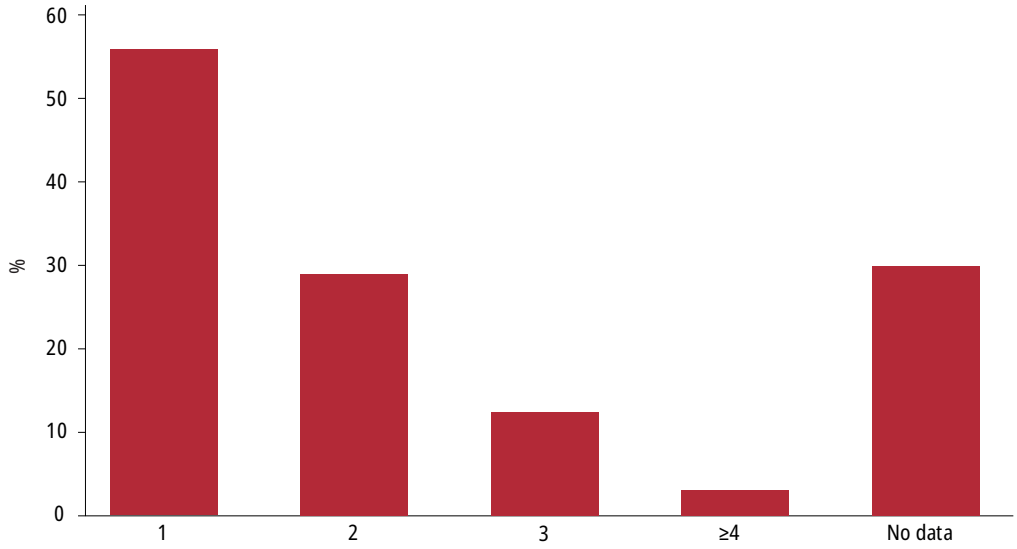

FIGURE 4 Percentage of procedures performed within the device pocket before the diagnosis of cardiac device–related infective endocarditis

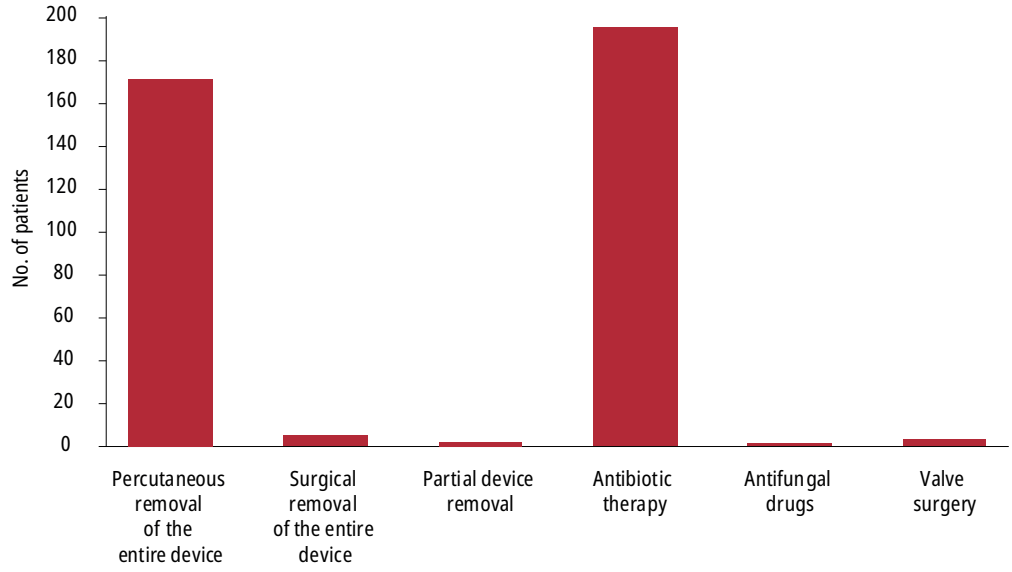

FIGURE 5 Management of cardiac device–related infective endocarditis (n = 195)

on cultures and visual assessment (including imaging studies) are shown in TABLE 2.

Investigations Blood cultures were performed in all patients with CDRIE (n = 195). In patients undergoing an intervention, samples obtained during the procedures were also cultured. Cultures were positive in 151 patients (77.5%) with the diagnosis of CDRIE. The identified microorganisms included staphylococci in 113 patients (58%), streptococci in 13 patients (6.7%), enterococci in 16 patients (8.2%), and HACEK organisms in 2 patients (1%).

Transthoracic echocardiography was performed in all patients with CDRIE, while transesophageal echocardiography (TEE), only in 156 patients (80%). Cardiac computed tomography (CT), positron emission tomography (PET), and tagged leukocyte single-photon emission computed tomography (SPECT-CT) were performed in 21 patients (10.8%), 18 patients (9.2%), and 1 patient (0.5%), respectively. None of the patients underwent cardiac magnetic resonance.

Management Cardiac device was removed completely or in part in 178 patients with CDRIE (91%), including 173 patients who underwent percutaneous extraction and 5 patients who underwent surgical extraction. All patients received antibiotic therapy, and 3 patients underwent a heart valve procedure (FIGURE 5).

Most patients (n = 89, 45.6%) were treated with antibiotics for 4 to 6 weeks, 58 (29.7%) were treated for 4 weeks, 26 (13.3%) were treated for 2 weeks, and 18 (9.2%) were treated for more than 6 weeks. No detailed data on the duration of antibiotic therapy were available in 4 patients (2%).

Complications In our registry, we noted a low mortality rate (6.2%) related to CDRIE. Due to the methodology of our registry, short-term

TABLE 1 Most common symptoms in patients with cardiac device–related infective endocarditis (n = 195)

Symptoms/clinical manifestations	Value, n (%)
Malaise	135 (69.2)
Fever and chills	119 (61)
Cough	42 (21.5)
Chest pain	38 (19.5)
Inflammation of the device pocket	11 (5.6)
Dyspnea	5 (2.6)
Shock	1 (0.5)

TABLE 2 Location of infection in patients with cardiac device–related infective endocarditis (n = 195) based on visual assessment (including imaging studies) and cultures

Location	Value, n (%)
Leads	133 (68.2)
Device pocket / generator	71 (40.5)
Native valve	23 (11.8)
Prosthetic valve	12 (6.2)

TABLE 3 Complications in patients with cardiac device–related infective endocarditis

Complications	Value, n (%)
Heart failure	49 (25.1)
Pulmonary	24 (12.3)
Valvular	21 (10.8)
Central nervous system involvement	6 (3.1)
Hepatic involvement	4 (2.1)
Rheumatologic	2 (1)
Spleen involvement	1 (0.5)
Acute coronary syndrome	1 (0.5)

in-hospital mortality data should not be compared with long-term observational data from tertiary centers.[3] Data on complications of CDRIE are shown in TABLE 3. Central nervous system complications included stroke, and hepatic complications were emboli or abscesses.

DISCUSSION **General data** The present registry is the largest analysis of the issues regarding CDRIE in Poland. The participating departments were tertiary care centers, including those providing cardiac device removal services. Based on the total number of admissions for cardiac device implantation and hospitalizations due to CDRIE, the latter accounted for 1.7% of all hospitalizations. In a Danish registry, CDRIE was reported in 1.2% of patients with a cardiac device.[5] When only patients with ICD and CDRIE related to ICD were considered, the rate was 1.9% and was slightly higher than the respective rate in the Danish registry (1.6%). For CRT, these rates were 3.1% in the POL-CDRIE registry and 1.7% in the Danish registry.[5] Based on these survey data on the number of implanted devices and CDRIE cases, it may be concluded that patients with CRT devices are at a higher risk of infective complications compared with those with pacemakers and ICDs. Available literature data indicate that the overall CDRIE rate among patients with cardiac devices is estimated at 0.5% to 2.2%, with higher rates for high-energy devices, higher number of leads, and more previous interventions within the device pocket.[6-8] Of note, the rate of CDRIE, especially in patients with CRT devices, is notably different between studies, which may result from heterogeneous study populations.[3,5,6] In the participating departments, patients with CDRIE accounted for 25% of all patients with IE. In an IE registry in California and New York State, patients with CDRIE accounted for 4.1% of all patients with IE in the years 2010 to 2013.[1] This difference is most likely related to the fact that the departments participating in the Pol-CDRIE registry are tertiary care centers that also manage CDRIE cases referred from other departments.

Symptoms Based on the registry data, the most common symptoms accompanying CDRIE were malaise and fever. Clinical evidence of inflammation of the device pocket was noted in only about 6% of patients. However, when culture results were also considered, the possible involvement of the device pocket or generator was identified in more than 40% of patients, although infection during device explantation cannot be excluded in these cases. Inflammation of the pocket was the most common presentation of CDRIE in a retrospective study from Mayo Clinic.[9] In that study, fever, chills, and malaise were present in more than 40% of patients.

Investigations Consistent with the literature data,[4-6,9] the most common microorganisms identified in patients with CDRIE were staphylococci. Transthoracic echocardiography was performed in all patients, while TEE was performed in only 80% of patients. The ESC guidelines recommend TEE in all patients with CDRIE regardless of transthoracic echocardiography findings.[4] In patients with CDRIE, TEE is characterized by superior sensitivity and specificity, allowing better evaluation of questionable lesions, better visualization of the leads, and better identification of perivalvular infection and left-sided cardiac involvement. For these reasons, TEE should be performed in all patients.[4]

Nearly 10% of patients in our registry also underwent leukocyte SPECT-CT or PET. According

to the ESC guidelines, these investigations may be considered in patients with an uncertain diagnosis of CDRIE.[4] British experts do not recommend routine PET scanning with ^{18}F-fluorodeoxyglucose in patients with CDRIE due to a lack of clear evidence of diagnostic benefits and a limited sensitivity for the detection of CDRIE.[6] However, they allow use of this modality in selected diagnostically difficult cases.[6]

Management Among CDRIE patients in our registry, the device was removed completely in 90% of patients and partially in 1% of patients. The ESC guidelines for the management of IE recommend complete device removal in case of CDRIE.[4] However, the joint guidelines of British societies for the diagnosis, prevention, and management of CDRIE, where this issue has been comprehensively discussed, indicate that in clinical practice, the device is not explanted in 3% to 15% of patients due to a lack of consent or a clinical condition precluding intervention.[6] In addition, partial device removal has been considered acceptable in these guidelines in some clinical scenarios, the discussion of which is beyond the scope of the present paper.[6] Thus, the removal rate (91%) in our registry is consistent with the general rates observed for interventional treatment, which cannot be applied in all patients with CDRIE (due to either lack of consent or in cases where the risk outweighs the benefit). Such an approach is in line with the European guidelines and the principles of good clinical practice.[4,6] A large majority of the devices were explanted percutaneously, which is also consistent with the European guidelines.[4,6] Of note, infectious indications for transvenous lead extraction are associated with worse long-term survival than noninfectious ones.[8]

All patients received antibiotic therapy. Most patients (>85%) with CDRIE were treated with antibiotics for 4 or more weeks. This is consistent with the ESC guidelines for the management of IE, which recommend extended antibiotic therapy in this patient group. However, 13.3% of patients were treated with antibiotics for 2 weeks. This duration of treatment is acceptable if the infection is limited to the generator and device pocket.[6] Reported practice of 2-week antibiotic therapy may by questionable considering the current standards, but this percentage includes patients who died in the first 2 weeks. On the other hand, in the Mayo Clinic study, a significant proportion of patients received antimicrobial treatment for 2 weeks after device explantation, particularly if coagulase-negative staphylococci were cultured.[9]

Complications In our registry, we noted a low mortality rate related to CDRIE, but some patients were transferred to other departments after device removal. In contrast, in the single-center registry that evaluated CDRIE cases in patients with CRT devices, in-hospital mortality was 50%.[3] Such a large discrepancy may be related to different study group characteristics. In our registry, nearly half of CDRIE cases occurred in patients with pacemakers, who usually have fewer comorbidities and thus a lower risk of complications related to antibiotic therapy and interventions. It may also be speculated that CDRIE contributes to an exacerbation of the underlying cardiac condition in patients with a CRT device implanted due to heart failure, which may contribute to worse outcomes in these patients. On the other hand, a higher New York Heart Association functional class itself is a risk factor for CDRIE in patients with a CRT device.[3] In a study by Sohail et al,[9] which included 189 patients with CDRIE related to pacemakers and ICDs, 7 deaths were noted during the index hospitalization and another 2 deaths due to recurrent infection, which is a similar rate to that observed in our registry.[9] Of the other complications included in the registry, the most common ones were related to pulmonary involvement, heart failure, or valve dysfunction, as expected, although the whole spectrum of other complications is also possible.

Study limitations Due to the fact that the participating tertiary care centers also manage referred CDRIE cases, the ratio of CDRIE cases to the overall number of implanted cardiac devices in the participating departments may be overestimated. Due to the registry design of our study, it was only possible to evaluate the number of CDRIE cases in relation to the number of device implantations over the period of 1 year. The mortality related to CDRIE could be underestimated because some of the patients were transferred to other departments after device removal. In our registry, however, we excluded patients without evidence for confirmed CDRIE. Therefore, patients admitted only for device explantation, and retransferred just after that procedure were not included. Nevertheless, some patients (included in the statistics) whose hospitalization was prolonged were transferred to other hospitals or transferred to intensive care units, and for those patients mortality data may not be complete. Reported mortality may be underestimated as clinical information after the transfer of patients to another department was not available.

The highest number of infections in patients with a dual lead system is most likely related to the large number of patients who had 2 leads implanted.

Transvenous lead extractions are performed in 39 hospitals in Poland. Although our registry is the largest analysis of the issues regarding CDRIE in Poland, it does not include all large cardiology centers.

Conclusions The clinical profile, pathogen types, and the management strategies in Polish patients with CDRIE are consistent with similar data from other European countries. Transesophageal echocardiography was performed less frequently than recommended in the ESC guidelines. The percutaneous approach was most commonly used for cardiac device removal, which is in line with the current knowledge and expert position statements. The removal rate in Polish patients is consistent with the general rates observed for interventional treatment in individuals with CDRIE.

ARTICLE INFORMATION

CONFLICT OF INTEREST None declared.

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