Cardiac device-related infective endocarditis in the Czech Republic: Prospective data from the ESC EORP EURO-ENDO registry

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Aim. Understanding cardiac electronic device infective endocarditis epidemiology is essential for the management of this serious complication. Only monocentric and limited data have been published regarding patients in the Czech republic so far. The aim of this study was to describe the current profile, microbiology and clinical characteristics of this population.

Patients and Methods. National data from the prospective ESC-EORP EURO-ENDO registry were collected. 57 consecutive patients with a diagnosis of cardiac device-related infective endocarditis (CDRIE) from 11 Czech centres were included.

Results. Staphylococcus spp. was responsible for 43.9% of isolates, whereas Culture negative endocarditis was documented in 26.3% episodes. The most frequent complications under therapy were acute renal failure (17.5%), septic shock and heart failure (both 10.5%). Extraction of device was performed in 75.4% of all patients, and the 1-year mortality was 22.5%.

Conclusions. The high proportion of culture-negative endocarditis is alarming and warrants further investigation. Cardiac device related infective endocarditis is a serious complication with a high 1-year mortality in a highly polymorbid spectrum of patients.

Key words: cardiac electronic device infective endocarditis, infective endocarditis, cardiac device complication

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INTRODUCTION

Contemporary, cardiac device-related infective endocarditis (CDRIE) is a serious public health problem. With the growing number of implanted devices, we also face a disproportionately growing incidence of CDRIE (ref.[1]). The treatment of infectious complications is both financially and time demanding; in the US, the treatment costs per patient and year exceed sixty-thousand dollars[2]. We can predict a surge in the incidence and prevalence of CDRIE owing to an ageing population, higher proportion of immunocompromised and polymorbid patients, as well as the increasing complexity of procedures. The morbidity and mortality is doubled in CDRIE compared to patients without infective complications and surprisingly , the increased mortality persists even after successful treatment of CDRIE (ref.[3]), and is comparable to mortality owing to infective endocarditis[4]. To date, there are no consistent multicentric data on the infective complications of this device therapy in the Czech Republic. In this study, we present a subanalysis of ESC-EORP EURO-ENDO registry of cardiac device related infective endocarditis in the Czech Republic, which includes consecutive patients from the majority of tertiary care cardiovascular centres in the country in a selected timeframe.

METHODS

Study design and data collection

All data were collected from the prospective multicentre ESC-EORP EURO-ENDO registry. The detailed methodology of EURO-ENDO has already been reported[4]. All consecutive patients aged ≥18 years with definite or possible IE were included, from April 2016 to March 2018. All participants signed informed consent. Patients from 11 main tertiary care cardiac centres in the Czech Republic were collected – Prague (Institute for Clinical and Experimental Medicine-IKEM, Faculty Hospital Kralovske Vinohrady, Faculty Hospital Motol, General Faculty Hospital), Faculty Hospital Brno Bohunice, Faculty Hospital Olomouc, Faculty Hospital Ostrava, Faculty Hospital Plzeň, Faculty Hospital Hradec Králové, Regional Hospital Liberec and Regional Hospital Zlín.

Baseline and follow-up data

Baseline data included clinical characteristics, biological and microbiological data, imaging data, treatment before admission and during hospitalization, complications under therapy, theoretical indication for surgery (as reported by responsible practitioners), in-hospital surgery/procedures performed (including both percutaneous and surgical procedures to remove infected intracardiac material), in-hospital mortality. 1-year follow-up data were obtained based on either a telephone call or a clinical examination.

Statistical analysis

Continuous data with normal distribution are presented as mean± SD (standard deviation), non-normally distributed variables as median (interquartile range - IQR). Categorical data are shown as frequencies and percentages. Between-group differences were tested using analysis of variance (ANOVA), Kruskal-Wallis, chi-square tests or Fisher exact test, as appropriate.

Calculations were done using SPSS version 21 (IBM SPSS Statistics, IBM Corporation, Armonk, New York). All statistical tests were 2-sided with a significance level of 0.05.

RESULTS

In total, 57 consecutive patients with discharge diagnosis of CDRIE have been enrolled. Baseline characteristics of patients and risk factors are summarized in Table 1. Median age of patients was 67 years, 22.8% of them were women. 50.8% of patients suffered from diabetes. Majority of patients (64.9%) were implantable cardioverter defibrillator (ICD) or cardiac resynchronization therapy defibrillator (CRT-D) recipients. Median time from symptoms onset to diagnosis reached 21 days (6-44).

Clinical presentation of patients and suspected source of infection are summarized in Table 2. Fever was present in 43 patients (75.4%), heart failure was the second most prevalent syndrome on admission. The most frequent complications on admission were embolic events, which occurred in 8 patients (14%) and conduction abnormalities (n=6, 10.5%).

Table 1. Patient demographics and characteristics.

Demographics	
Age (years) median	67 (60,71)
Females (%)	13 (22.8)
Type of implanted device	
Pacemaker (%)	20 (35.1)
ICD (%)	26 (45.6)
CRT-D (%)	11 (19.3)
History of CV disease	
Heart failure	31 (54.4)
Congenital heart disease	2 (3.5)
Ischemic heart disease	32 (56.1)
Atrial fibrillation	25 (43.9)
HOCM	1 (1.8)
Dilated cardiopathy	11 (19.3)
Known heart murmur	13 (22.8)
Previous IE (%)	2 (3.5)
Non-cardiac interventions (last 6 months)	
Dental procedure	1 (1.8)
GIT procedure	1 (1.8)
Risk factors	
Diabetes melitus	29 (50.9)
Previous stroke/TIA	9 (15.8)
Hypertension	39 (68.4)
COPD/asthma	9 (15.8)
Chronic renal failure	15 (26.3)
Haemodialysis	6 (10.5)
Chronic autoimmune disease	3 (5.3)
Cancer	2 (3.5)
Smoking	12 (21.1)
IVDA	0 (0)
Alcohol abuse	2 (3.5)
Immunosuppressive treatment	1 (1.8)
Long corticotherapy	3 (5.3)
Anticoagulant treatment	
VKA (%)	11 (19.3)
DOAC (%)	4 (7.0)
APA (%)	31 (54.4)
LMWH (%)	9 (15.8)
VKA/DOAC/LMWH + APA (%)	4 (7.0)

COPD, chronic obstructive pulmonary disease; HOCM, hypertrophic obstructive cardiomyopathy; ICD, implantable cardioverter defibrillator; IE, infective endocarditis; IVDA, intravenous drug abuse; PM, pacemaker; TIA, transient ischemic attack; VKA, vitamin K antagonist; DOAC, direct oral anticoagulation; APA, antiplatelet agents; LMWH, low molecular weight heparin

Basic microbiology results are displayed in Fig. 1. The most prevalent microorganisms were *Staphylococcus aureus* in 15 patients (26.3%) and Coagulase negative staphylococci in 10 patients (17.5%). No positive blood cultures were detected in 15 patients (26.3%).

Complications during therapy are summarized in Table 3. The most frequent complications were acute renal failure in 10 patients (17.5%), septic shock and heart failure (both in 10.5%).

Extraction of cardiac devices was performed during hospitalization in 43 (75.4%) patients, among them 30 (52.6%) were percutaneous, 12 (21.1%) surgical and a combination of both was indicated in 1 patient (1.8%). In 14 patients, neither percutaneous nor surgical extraction has been performed – in 4 patients due to refusal, in 7 because of exceedingly high surgical risk and in 3 because of death before procedure was reported.

In-hospital mortality was relatively low in patients with CDRIE, as only 4 patients deceased (7.1%), one patient was lost to follow-up. In contrast, one-year mortality reached 22.5% (9 patients) with 17 patients lost to follow-up.

DISCUSSION

This is, to our knowledge, the first multicentre registry of CDRIE in the Czech Republic. To date, only institutional, uni-center experience with CDRIE has been reported[5,6].

The incidence of CDRIE can be expected in a relatively wide range of 0.5-15 cases per 1000 patient years, and effects predominantly polymorbid patients[7,8]. We agree with that as more than half of our patients presented with history of diabetes, ischaemic heart disease and heart failure. Men are more frequently affected than women[9], in our cohort they represented 77.2% of all patients. Several risk factors for infection development have been described - such as the type of device, while ICDs having more than twice the risk of pacemakers[8], replacement or repeated procedures and patient related characteristics – age, diabetes, chronic obstructive pulmonary disease, steroid use, history of previous device infection, heart failure, renal insufficiency, or anticoagulant medication use[10]. In our study, most of patients had ICD or CRT-D implanted, showing an apparent discrepancy with population distribution of implanted devices, in which pacemakers are 4 times more prevalent than ICDs' (ref.[11]). Of note, no patient in our study was active intravenous drug abuser, which is an established risk factor for right sided endocarditis[12]. No significant link was found in relation to recent invasive procedures including dental ones, which further reinforces recommendation to consider patients with implantable devices as in low or intermediate risk for hematogenous spread of infection and thus no need for antibiotic prophylaxis before surgical procedures[13].

In principle, pathogen can reach an implanted device within days as a direct inoculation at the time of implantation or as a hematogenous spread of infection. The first way is much more common, which explains higher percentage of staphylococcus strain in device endocarditis specimens[14,15]. This was also our case with staphylococcus strain comprising almost half of positive findings – almost identically as in previous Czech retrospective series, which has not been limited only to CDRIE (ref.[16]). In 26% of cases no causative microorganism was found, which correspond to other published data[17]. There are several explanations for culture negative infective endocarditis, ranging from non-adequate blood and tissue cultures sampling, microorganism difficult to cultivate and empirical antibiotic therapy in time of blood sampling. Moreover in our study we have not performed lead tip tissue cultivation nor pocket tissue cultivation, techniques proven to be the most sensitive[18].

Serious complications unrelated to extraction procedure are rather uncommon in CDRIE. In contrast to left-sided endocarditis, in which we frequently see marked structural and systemic complications[4,19]. Even pulmonary embolism is fairly rare in CDRIE setting with only 3.5%

Table 2. Clinical presentation.

	CDRIE (n=57)
Signs and symptoms	
Fever	43 (75.4)
Cough	17 (29.8)
Dizziness	13 (22.8)
Cerebrovascular event	1 (1.8)
Syncope	1 (1.8)
Cardiac murmur	18 (31.6)
Congestive heart failure	21 (36.8)
Septic shock	1 (1.8)
Days from onset of symptoms to diagnosis	21 (6-42)
Complications on admission	
Abscess	4 (7.0)
Spondylitis	1 (1.8)
Conduction abnormality	6 (10.5)
Embolic events	8 (14)
Pulmonary	5 (8.8)
Cerebral	1 (1.8)
Splenic	1 (1.8)
Peripheral	1 (1.8)
Suspected source of Infection	
Health care associated IE	10 (17.5)
Nosocomial	5 (8.8)
Non-nosocomial	12 (21.1)
Community acquired	29 (50.9)

ICD, implantable cardioverter defibrillator; IE, infective endocarditis; PM, pacemaker

Table 3. Complications under therapy.

	CDRIE (n=57)
Embolic events	3 (5.3)
Pulmonary	2 (3.5)
Spleen	1 (1.8)
Spondylitis	1 (1.8)
CHF	6 (10.5)
Cardiogenic shock	4 (7.0)
Septic shock	6 (10.5)
Acute renal failure	10 (17.5)
Persistent fever	3 (5.3)
Positive blood cultures after 48 h	4 (7.0)
Increasing vegetation size	4 (7.0)
Thrombopenia (<10000)	1 (1.8)

CHF, congestive heart failure; ICD, implantable cardioverter defibrillator; PM, pacemaker

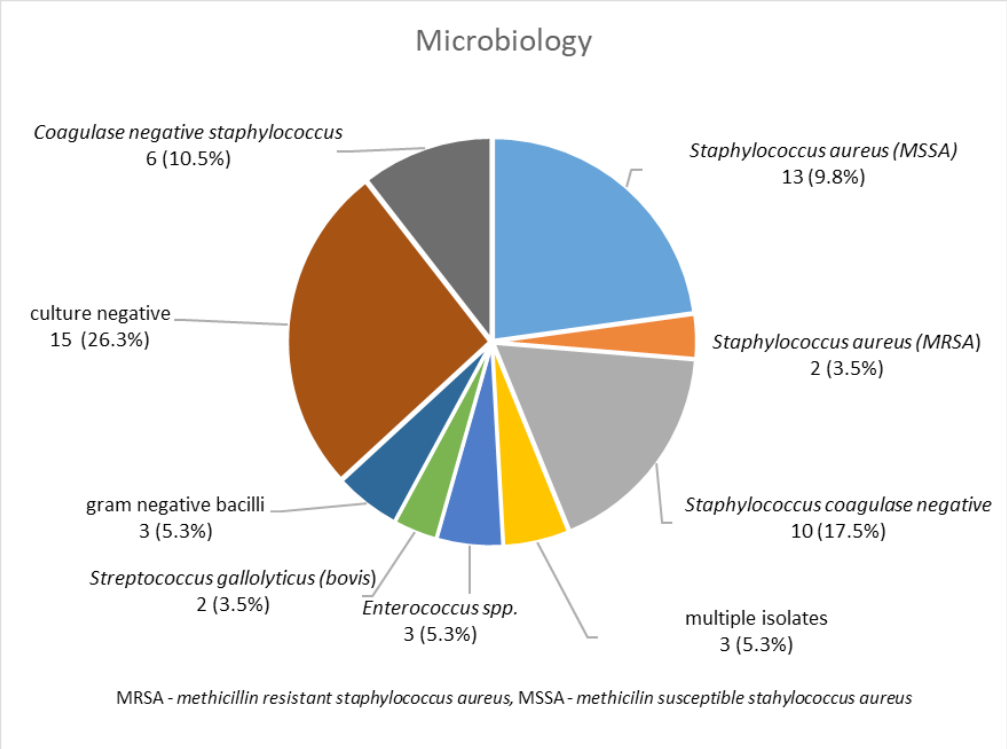

Fig. 1. Microbiology results.

percent of patients affected, which is in concordance with other series[20]. In our study 10.5% of patients suffered from septic shock, which also corresponds to results of EURO-ENDO study[4].

Complete extraction of whole device is essential for prognosis improvement and long-term infection control[21], especially when staphylococcus spp. is the causative microorganism. In our study no extraction has been performed in 14 patients (24.5%). Proportion is slightly higher than in comparable series[17], but lower than in EURO-ENDO whole population, in which up to 34.6% of patients did not undergo any procedure[4]. An analysis whether on site availability of either percutaneous extraction techniques or surgery has any impact on decision regarding extractions could be helpful, however in our case most (9 out of 11) centres have either cardiac surgery or extraction capability.

A relatively low in-hospital mortality was found in our cohort (7.1%), however 1-year mortality reached 22.5%, which is concordance with previously published Czech experience by Binova et al. (ref.[6]), demonstrating serious impact of CDRIE on a long-term survival of already highly polymorbid cohort of patients. Complete extraction of infected device is essential to tackle the high mortality of CDRIE, which was shown in previous studies[20,22,23], in contrast, patients treated conservatively exhibit the highest mortality[24].

CONCLUSIONS

Device infections remain one of the most dreadful complications of modern-era device therapy. High proportion of culture-negative endocarditis is alarming and warrants further investigation. CDRIE represents a serious complication with high 1-year mortality in already highly polymorbid spectrum of patients.

LIMITATIONS

We cannot guarantee that all centres really included all their patients consecutively and prospectively, since the study was based on the volunteer participation of each centre.

As most centres being tertiary referral centres with cardiac surgical programmes, thus the profile of the cases might have been affected by referral bias.

Marked proportion of patients, who lost to follow, which might have affected long term mortality outcomes.

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