## CLINICAL STUDY

# Characteristics, management, and outcome of infective endocarditis in the Czech Republic: prospective data from the ESC EORP EURO-ENDO registry

Pazdernik M<sup>1,2</sup>, Holicka M<sup>3</sup>, Pelouch R<sup>4</sup>, Precek J<sup>5</sup>, Widimsky J<sup>6</sup>, Pudich J<sup>7</sup>, Vancata R<sup>8</sup>, Siranec M<sup>9</sup>, Bohm A<sup>10</sup>, Blechova K<sup>11</sup>, Butta T<sup>12</sup>, Mikulcova M<sup>13</sup>, Mikulica M<sup>13</sup>, Wohlfahrt P<sup>14</sup>

Department of Cardiology, IKEM, Prague, Czech Republic. Michal.Pazdernik@email.cz

#### ABSTRACT

INTRODUCTION: Data describing contemporary profile of infective endocarditis (IE) in the Czech Republic are lacking. The aim of this study was to describe the current profile and outcomes of IE patients. METHODS: Prospectively collected data on consecutive patients admitted for IE diagnosis between April 2016 and March 2018 to 11 main tertiary care cardiac centers in the Czech Republic were used for this analysis.

RESULTS: Among 208 patients, 88 patients (42.3 %) had native valve IE (NVIE), 56 patients (26.9 %) had prosthetic valve IE (PVIE), and 57 patients (27.4 %) had intracardiac device-related IE (CDRIE). The mean age was 61.66±15.54 years. *Staphylococcus aureus* was the most common etiological agent of IE (27.4 %), whereas Culture negative IE was present in 26.4 % patients. Surgery was performed during hospitalization in 112 (53.8 %) patients. In-hospital death occurred in 21.2 % patients, while 1-year mortality was 40.3 %. In patients, who had an indication for surgery, but the procedure was not performed, mortality was significantly higher (p=0.002).

CONCLUSION: High proportion of culture negative IE and IE related to artificial intra-cardiac materials calls for action. Furthermore, we show that cardiac surgery should be more often contemplated, especially in the presence of risk factors as septic shock and congestive heart failure (*Tab. 6, Fig. 1, Ref. 32*). Text in PDF *www.elis.sk* 

KEY WORDS: infective endocarditis, mortality, surgery, Czech Republic.

<sup>1</sup>Department of Cardiology, IKEM, Prague, Czech Republic, <sup>2</sup>Department of Cardiology, 2nd Medical School, Charles University, University Hospital Motol, Prague, Czech Republic, <sup>3</sup>Department of Internal Medicine and Cardiology, University Hospital Brno, Brno, Czech Republic, <sup>4</sup>1st Department of Internal Medicine - Cardioangiology, Faculty Hospital in Hradec Kralove, Czech Republic, 5Department of Internal Medicine I - Cardiology, University Hospital Olomouc, Czech Republic, <sup>6</sup>Department of Cardiology, Regional Hospital Liberec, Liberec, Czech Republic, 7Department of Cardiovascular Diseases, University Hospital in Ostrava, Czech Republic, 8Internal Department II, University Hospital and Faculty of Medicine in Pilsen, Charles University, Pilsen, Czech Republic, 92nd Department of Internal Cardiovascular Medicine, First Faculty of Medicine, Charles University and General University Hospital in Prague, Czech Republic, 10National Institute of Cardiovascular Diseases, Bratislava, Slovakia, 11Cardiocenter, Third Faculty of Medicine, Charles University, Prague, Czech Republic, 12Department of Cardiology, Second Medical School, Charles University, Motol University Hospital, Prague, Czech Republic, 13Cardiovascular Center for Adults, Tomas Bata Regional Hospital, Zlin, Czech Republic, and 14Center for Cardiovascular Prevention of the First Faculty of Medicine, Charles University and Thomayer Hospital, Prague, Czech Republic.

Adress for correspondence: M. Pazdernik, MD, PhD, FESC, Institute for Clinical and Experimental Medicine (IKEM), CZ-140 21 Prague, Czech Republic.

Phone: +420 602 258544

## Introduction

Despite continuous advances in diagnostics and therapeutic management, infective endocarditis (IE) remains a life-threating disease (1). Based on findings from both individual institutional experiences and large, multi-centre studies, a considerable variability in the clinical features of infective endocarditis has been reported (2–6). Only limited data have been published on this topic with the aim to provide a current contemporary profile of the disease in the Czech Republic (6–8). Moreover, well-planned, representative IE epidemiological survey, including main tertiary care hospitals, has never been performed.

Several important factors garnered attention in the recent studies from the region, reporting an increasing incidence of the disease in elderly, change in the predisposing factors, marked shift in aetiology of IE (3, 6, 7). Nonetheless, these studies suffered from major limitations mainly due to retrospective analysis, small number of recruited patients, and most importantly representing only single or dual centre experience. Dzubova et al attempted to overcome these drawbacks, but including only small regional hospitals in their survey, hence excluding more 95-100

Tab. 1. Patient demographics and characteristics.

	Total (n=208)	Prosthesis+ Repair (n=56)	Native (n=88)	PM/ICD (n=57)	р
Age (years) median	61.70±15.44	65.88±13.24	57.00±17.34	64.72±12.72	0.001
Females (%)	55 (26.4)	14 (25.0)	26 (29.5)	13 (22.8)	0.64
History of CV disease					
Heart failure	76 (36.5)	27 (48.2)	16 (18.2)	31 (54.4)	0.00001
Congenital heart disease	30 (14.4)	4 (7.1)	22 (25)	2 (3.5)	0.0003
Ischemic heart disease	72 (34.6)	26 (46.4)	11 (12.5)	32 (56.1)	0.00001
Atrial fibrillation	77 (37.0)	29 (51.8)	18 (20.5)	25 (43.9)	0.0002
HOCM	3 (1.4)	0 (0)	2 (2.3)	1 (1.8)	0.54
Dilated cardiopathy	13 (6.3)	0 (0)	2 (2.3)	11 (19.3)	0.00002
Known heart murmur	66 (31.7)	29 (51.8)	22 (25)	13 (22.8)	0.001
Previous IE (%)	23 (11.1)	14 (25.0)	6 (6.8)	2 (3.5)	0.00001
Device therapy	79 (38.0)	12 (21.4)	3 (3.4)	57 (100)	0.00001
Non-cardiac interventions (la	st 6 months)				
Colonoscopy	6 (2.9)	3 (5.4)	3 (3.4)	0 (0)	0.54)
Dental procedure	6 (2.9)	1 (1.8)	4 (4.5)	1 (1.8)	0.787
GIT procedure	8 (3.8)	2 (3.6)	4 (4.5)	1 (1.8)	0.884
Urogenital procedure	7 (3.4)	3 (5.4)	4 (4.5)	0 (0)	0.514
Risk factors					
Previous stroke/TIA	29 (13.9)	13 (23.2)	6 (6.8)	9 (15.8)	0.019
Hypertension	131 (63.0)	42 (75.0)	46 (52.3)	39 (68.4)	0.014
COPD/asthma	33 (15.9)	12 (21.4)	11 (12.5)	9 (15.8)	0.361
Chronic renal failure	47 (22.6)	16 (28.6)	15 (17.0)	15 (26.3)	0.212
Haemodialysis	11 (5.3)	1 (1.8)	4 (4.5)	6 (10.5)	0.109
Chronic autoimmune disease	7 (3.4)	2 (3.6)	2 (2.4)	3 (5.3)	0.66
Cancer	13 (6.3)	5 (8.9)	4 (4.5)	2 (3.5)	0.394
Smoking	60 (28.8)	14 (25.0)	32 (37.6)	12 (21.1)	0.073
IVDA	13 (6.3)	4 (7.3)	9 (10.3)	0 (0)	0.047
Alcohol abuse	17 (8.2)	4 (7.1)	11 (12.9)	2 (3.5)	0.130
Immunosuppressive treatment	6 (2.9)	0(0)	4 (4.5)	1 (1.8)	0.213
Long corticotherapy	10 (4.8)	0 (0)	6 (6.8)	3 (5.3)	0.147

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

complicated cases of IE, a non-representative dataset was obtained (7).

Therefore, consecutive cases of IE seen over almost two year period, as part of the ESC EORP Euro-Endo registry (1), enrolled in the majority of main tertiary care referral centres in the Czech Republic were prospectively evaluated in order to provide a current profile of the disease.

# Methods

## Study design and data collection

All data were collected from the prospective multicentre ESC-EORP EURO-ENDO registry. The detailed methodology of EU-RO-ENDO has already been reported (9). All consecutive patients aged  $\geq$  18 years with a definite or possible IE were included from April 2016 to March 2018. All participants signed an 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 valvular surgery and 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 a normal distribution are presented as the mean  $\pm$  SD, non-normally distributed variables as median (interquartile range – IQR). Categorical data are shown as frequencies and percentages. Between-group differences were tested using the analysis of variance (ANOVA), Kruskal-Wallis, chi-square tests or Fisher exact test, as appropriate. Kaplan-Meier curves for time to all cause in hospital death were performed, with log rank test used to compare differences between groups. Univariate Cox regression for in

hospital death was used to identify the variables associated with mortality. Variables with a p < 0.1 in the univariate analysis were used as inputs for multivariate forward Cox regression. Multivariate logistic regression was used to identify clinical variables associated with 1-year mortality. 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

#### Patient demographics and characteristics

A total of 208 patients from 11 main tertiary care cardiac centres in the Czech Republic, admitted to the hospital between April 2016 and March 2018, were enrolled.

The main features of the cohort are illustrated in Table 1. Among 208 patients, 88 patients (42.3 %) had native valve IE (NVIE), 56 patients (26.9 %) had prosthetic valve IE (PVIE), and 57 patients (27.4 %) had intracardiac device-related IE (CD-RIE). The 7 remaining patients not categorized as PVIE, NVE, or CDRIE corresponded to the combined location of infection

#### Tab. 2. Clinical presentation.

	Total	Prosthesis+	Native	PM/ICD	
	(n=208)	repair (n=56)	(n=88)	(n=57)	р
Signs and symptoms					
Fever	149 (71.6)	39 (69.6)	64 (72.7)	43 (75.4)	0.787
Cough	52 (25.0)	11 (19.6)	23 (26.1)	17 (29.8)	0.451
Dizziness	48 (23.1)	13 (23.2)	22 (25)	13 (22.8)	0.946
Cerebrovascular event	13 (6.3)	7 (12.5)	5 (5.7)	1 (1.8)	0.062
Syncope	9 (4.3)	3 (5.4)	5 (5.7)	1 (1.8)	0.50
Cardiac murmur	126 (60.6)	42 (75)	64 (72.7)	18 (31.6)	< 0.00001
Congestive heart failure	73 (35.1)	18 (32.1)	31 (35.2)	21 (36.8)	0.867
Cardiogenic shock	5 (2.4)	0 (0)	5 (5.7)	0 (0)	0.037
Septic shock	18 (8.7)	6 (10.7)	9 (10.2)	1 (1.8)	0.123
Osler nodes	0 (0)	0 (0)	0 (0)	0 (0)	1.0
Janeway lesions	8 (3.8)	3 (5.4)	5 (5.7)	0 (0)	0.191
Roth spots	0 (0)	0 (0)	0 (0)	0 (0)	1.0
Days from onset of symptom	18 (6-40)	17 (6-33)	18 (5-40)	21 (6-42)	0.790
to diagnosis					
Complications on admission					
Abscess	37 (17.8)	16 (28.6)	15 (17.0)	4 (7.0)	0.01
Pseudo-aneurysm	3 (1.4)	1 (1.8)	2 (2.3)	0 (0)	0.532
Fistula	5 (2.4)	2 (3.6)	3 (3.4)	0 (0)	0.362
New prosthetic dehiscence	3 (1.5)	3 (5.4)	0 (0)	0 (0)	0.093
Perforation	10 (4.8)	0 (0)	10 (11.4)	0 (0)	0.001
Spondylitis	12 (5.8)	6 (10.7)	5 (5.7)	1 (1.8)	0.131
Conduction abnormality	36 (17.3)	12 (21.4)	15 (17.0)	6 (10.5)	0.288
Embolic events	46 (22.1)	17 (30.4)	19 (21.6)	8 (14)	0.11
Pulmonary	18 (8.7)	1 (1.8)	10 (11.4)	5 (8.8)	0.11
Cerebral	12 (5.8)	7 (12.5)	4 (4.5)	1 (1.8)	0.04
Splenic	12 (5.8)	8 (14.3)	3 (3.4)	1 (1.8)	0.008
Coronary	1 (0.5)	0 (0)	1 (1.1)	0 (0)	0.525
Renal	4 (1.9)	3 (5.4)	1 (1.1)	0 (0)	0.093
Hepatic	1 (0.5)	1 (1.8)	0 (0)	0 (0)	0.272
Peripheral	5 (2.4)	2 (3.6)	2 (2.3)	1 (1.8)	0.813
Haemorrhagic stroke	2 (1.0)	2 (3.6)	0 (0)	0 (0)	0.073
Suspected source of Infection					
Health care associated IE	29 (13.9)	10 (17.9)	8 (9.1)	10 (17.5)	0.217
Nosocomial	13 (6.3)	4 (7.1)	4 (4.5)	5 (8.8)	0.583
Non-nosocomial	45 (21.6)	9 (16.1)	20 (22.7)	12 (21.1)	0.620
Community acquired	94 (45.2)	19 (33.9)	41 (46.6)	29 (50.9)	0.163
Intravenous drug abuse associated	13 (6.3)	5 (8.9)	8 (9.1)	0 (0)	0.064

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

#### Tab. 3. Microbiology.

	Total (n=208)	Prosthesis+ repair (n=56)	Native (n=88)	PM/ICD (n=57)	р
Staphylococcus aureus (MSSA)	51 (24.5)	15 (26.8)	19 (21.6)	14 (24.6)	0.768
Staphylococcus aureus (MRSA)	8 (3.8)	2 (3.6)	3 (3.4)	2 (3.5)	0.999
Staph. Coagulase negative	32 (15.4)	8 (14.3)	10 (11.4)	12 (21.1)	0.275
Streptococcus viridans	15 (7.5)	2 (3.6)	12 (13.6)	1 (1.8)	0.012
Enterococcus	18 (8.7)	7 (12.5)	6 (6.8)	4 (7.0)	0.44
Streptococcus gallolyticus (bovis)	5 (2.4)	2 (3.6)	1(1.1)	2 (3.5)	0.555
G-bacillus	9 (4.3)	2 (3.6)	3 (3.4)	4 (7.0)	0.548
Culture negative	53 (25.5)	11 (19.6)	27 (30.7)	15 (26.3)	0.342
Coxiella burnetti	0 (0)	0 (0)	0 (0)	0 (0)	1.0

ICD - implantable cardioverter defibrillator, PM - pacemaker

(PVIE+CDRIE/NVIE+CDRIE). These patients were included to total analysis, but not to the groups comparisons analysis.

The mean age was  $61.66 \pm 15.54$  years, with NVE associated with younger age (p = 0.001). Females represented 26.4 % of the

cohort. IE considerably affected population with a previous heart disease – 36.8 % had a history of heart failure, 34.6 % had ischemic heart disease, and 13.9 % had a congenital heart disease. Previous IE was documented in 10.9 % of all the patients and was highly related to PVIE (p = 0.00001). There was a history of intravenous drug abuse (IVDA) in 6.5 % patients, none of them was documented in CDRIE.

### Clinical presentation

The location of IE was aortic in 107 (51.4 %) patients, mitral in 49 (23.6 %), tricuspid in 23 (11.1 %), and pulmonary in 2 (1.0 %). Infective endocarditis affected two or more valves in 7 (3.4 %) patients. The median time since the onset of symptoms and IE diagnosis was 18 (6-40) days.

The main characteristics of clinical presentation are displayed in Table 2. Fever occurred in 72.6 % of patients, cardiac murmur was audible in 61.7 % of patients. Congestive heart failure on admission was seen in 34.8 % of patients, equally distributed in all three main groups of the patients. Septic shock developed in 8 % of patients and was mainly related to NVIE and PVIE. Cardiac abscess was observed in 17.4 % of patients, significantly more likely seen in PVIE (p = 0.01). New conduction block occurred in 16.4 % of the patients. Embolic events were documented in 21.9 % of all cases, moreover, cerebral, and splenic embolisations were significantly associated with PVIE. Haemorrhagic strokes were seen solely in PVIE patients.

#### Microbiology

IE causative agents are displayed in Table 3. *Staphylococcus aureus (Staph. aureus)* was the most commonly seen etiological agent of IE (27.4 %), followed by Staph. Coagulase negative (14.9 %). Streptococci occurred in 10 %, mainly causing NVIE, whereas Enterococci were reported in 8.5 %. Culture negative IE cases were reported as high as in 26.4 % of all IE cases.

## Complications under therapy

Main events that occurred during hospitalization are illustrated in the Table 4. The most frequent complication during hospitalization in our cohort was an acute renal failure (18.9 %). Embolic events accompanied IE cases in 14.9 % and were less likely documented in CDRIE (p = 0.05). Septic

95-100

#### Tab. 4. Complications under therapy.

Total (n=208)	Prosthesis+ repair (n=56)	Native (n=88)	PM/ICD (n=57)	р
31 (14.9)	10 (17.9)	17 (19.3)	3 (5.3)	0.052
15 (7.2)	4 (7.1)	8 (9.1)	2 (3.5)	0.434
9 (4.3)	3 (5.4)	6(6.8)	0 (0)	0.142
0 (0)	0 (0)	0 (0)	0 (0)	1
6 (2.9)	2 (3.6)	4 (4.5)	0 (0)	0.278
8 (3.8)	5 (8.9)	2 (2.3)	1 (1.8)	0.082
1 (0.5)	0 (0)	1 (1.1)	0 (0)	0.525
3 (1.4)	2 (3.6)	1 (1.1)	0 (0)	0.274
1 (0.5)	1 (1.8)	0 (0)	0 (0)	0.272
2 (1.0)	1 (1.8)	1 (1.1)	0 (0)	0.623
2 (1.0)	1 (1.8)	1 (1.1)	0 (0)	0.623
12 (5.8)	6 (10.7)	5 (5.7)	1 (1.8)	0.131
24 (11.5)	4 (7.1)	13 (14.8)	6 (10.5)	0.36
21 (10.1)	6 (10.7)	11 (12.5)	4 (7.0)	0.572
33 (15.9)	10 (17.9)	15 (17.0)	6 (10.5)	0.477
0 (0)	0 (0)	0 (0)	0 (0)	1.0
38 (18.3)	8 (14.3)	20 (22.7)	10 (17.5)	0.430
14 (6.7)	7 (12.5)	4 (4.5)	3 (5.3)	0.157
17 (8.2)	3 (5.4)	8 (9.1)	4 (7.0)	0.700
16 (7.7)	7 (12.5)	2 (2.3)	4 (7.0)	0.051
18 (8.7)	13 (23.2)	5 (5.7)	0(0)	0.00003
9 (4.3)	3 (5.4)	5 (5.7)	0 (0)	0.191
15 (7.2)	6 (10.7)	6 (6.8)	1 (1.8)	0.151
	$\begin{array}{c} (n=208)\\ \hline 31 (14.9)\\ 15 (7.2)\\ 9 (4.3)\\ 0 (0)\\ 6 (2.9)\\ 8 (3.8)\\ 1 (0.5)\\ 3 (1.4)\\ 1 (0.5)\\ 3 (1.4)\\ 1 (0.5)\\ 2 (1.0)\\ 12 (5.8)\\ 24 (11.5)\\ 21 (10.1)\\ 33 (15.9)\\ 0 (0)\\ 38 (18.3)\\ 14 (6.7)\\ 17 (8.2)\\ 16 (7.7)\\ 18 (8.7)\\ 9 (4.3)\\ \end{array}$	Total (n=208)repair (n=56)31 (14.9)10 (17.9)15 (7.2)4 (7.1)9 (4.3)3 (5.4)0 (0)0 (0)6 (2.9)2 (3.6)8 (3.8)5 (8.9)1 (0.5)0 (0)3 (1.4)2 (3.6)1 (0.5)1 (1.8)2 (1.0)1 (1.8)2 (1.0)1 (1.8)12 (5.8)6 (10.7)24 (11.5)4 (7.1)21 (10.1)6 (10.7)33 (15.9)10 (17.9)0 (0)0 (0)38 (18.3)8 (14.3)14 (6.7)7 (12.5)17 (8.2)3 (5.4)16 (7.7)7 (12.5)18 (8.7)13 (23.2)9 (4.3)3 (5.4)	Iotal (n=208)repair (n=56)Native (n=88)31 (14.9)10 (17.9)17 (19.3)15 (7.2)4 (7.1)8 (9.1)9 (4.3)3 (5.4)6(6.8)0 (0)0 (0)0 (0)6 (2.9)2 (3.6)4 (4.5)8 (3.8)5 (8.9)2 (2.3)1 (0.5)0 (0)1 (1.1)3 (1.4)2 (3.6)1 (1.1)1 (0.5)1 (1.8)0 (0)2 (1.0)1 (1.8)1 (1.1)1 (0.5)1 (1.8)1 (1.1)2 (1.0)1 (1.8)1 (1.1)2 (1.0)1 (1.8)1 (1.1)2 (1.0)1 (1.8)1 (1.1)2 (1.0)1 (1.8)1 (1.1)3 (15.9)10 (17.9)15 (17.0)0 (0)0 (0)0 (0)33 (15.9)10 (17.9)15 (17.0)0 (0)0 (0)0 (0)38 (18.3)8 (14.3)20 (22.7)14 (6.7)7 (12.5)4 (4.5)17 (8.2)3 (5.4)8 (9.1)16 (7.7)7 (12.5)2 (2.3)18 (8.7)13 (23.2)5 (5.7)9 (4.3)3 (5.4)5 (5.7)	Iotal (n=208)repair (n=56)Native (n=88)PM/ICD (n=57)31 (14.9)10 (17.9)17 (19.3)3 (5.3)15 (7.2)4 (7.1)8 (9.1)2 (3.5)9 (4.3)3 (5.4)6(6.8)0 (0)0 (0)0 (0)0 (0)0 (0)6 (2.9)2 (3.6)4 (4.5)0 (0)8 (3.8)5 (8.9)2 (2.3)1 (1.8)1 (0.5)0 (0)1 (1.1)0 (0)3 (1.4)2 (3.6)1 (1.1)0 (0)2 (1.0)1 (1.8)1 (1.1)0 (0)2 (1.0)1 (1.8)1 (1.1)0 (0)2 (1.0)1 (1.8)1 (1.1)0 (0)2 (1.0)1 (1.8)1 (1.1)0 (0)2 (1.0)1 (1.8)1 (1.1)0 (0)3 (15.9)10 (17.9)15 (17.0)6 (10.5)21 (10.1)6 (10.7)15 (17.0)6 (10.5)0 (0)0 (0)0 (0)0 (0)33 (15.9)10 (17.9)15 (17.0)6 (10.5)0 (0)0 (0)0 (0)0 (0)38 (18.3)8 (14.3)20 (22.7)10 (17.5)14 (6.7)7 (12.5)4 (4.5)3 (5.3)17 (8.2)3 (5.4)8 (9.1)4 (7.0)18 (8.7)13 (23.2)5 (5.7)0 (0)9 (4.3)3 (5.4)5 (5.7)0 (0)

 $AV-atrioventricular \ block, \ CHF-congestive \ heart \ failure, \ ICD-implantable \ cardioverter \ defibrillator, \ PM-pacemaker, \ ICD-TIA-transient \ ischemic \ attack$ 

shock developed in 15.4 %, whereas a shock of cardiogenic origin appeared in 10.4 %. New cardiac abscess was documented in 9 %, predominantly affecting PVIE (p = 0.00003). Prosthetic valves were also prone for an increasing size of vegetation (p = 0.05).

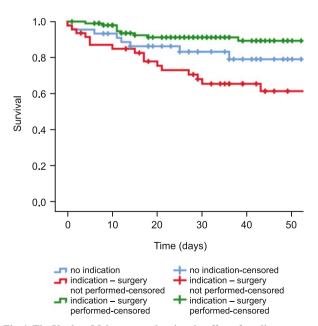


Fig. 1. The Kaplan–Meier curves showing the effect of cardiac surgery on in-hospital mortality.

# Cardiac surgery and mortality

Surgery was performed during hospitalization in 112 (53.8 %) patients. Following ESC guidelines, theoretical indication for cardiac surgery was reported in 162 (77.9 %) patients. Among them, surgery was finally performed in 26.8 % of PVIE, 54.5 % of NVE, and surgical or percutaneous extraction in 78.9 % of CDRIE.

In-hospital death occurred in 44 (21.2 %) patients. The risk of in-hospital mortality was lower (Bonferroni adjusted p < 0.05) in patients with CDRIE (7.1 %), as compared to both PVIE (30.9 %) and NVE (23.5 %), respectively. While taking into consideration the patients, who had an indication for surgery, but the procedure was not performed, mortality was significantly higher (p = 0.002) (Fig. 1). Predictors of in-hospital mortality by multivariable analysis were COPD/asthma, acute renal failure, septic shock, congestive heart failure and conservative treatment of IE episode (Tab. 5).

Overall, 159 patients had a complete 1-year follow up data. Of these, 64 (40.3 %) patients died.

Cardiogenic shock, septic shock, and history of haemodialysis were the independent predictors of increased 1-year mortality. In contrast, performed surgery during IE episode was the only protective factor of an increased 1-year mortality (Tab. 6).

# Discussion

The results of this EURO-ENDO registry provided a unique opportunity to characterize clinical presentation, therapeutic management and outcome of patients with IE in the Czech Republic. No similar extensive and complex descriptive study of this disease has ever been performed in this region.

The principal findings from this IE national registry can be summarized as follows: 1) IE affects predominantly men around 60 years of age, 2) Marked increase in PVIE and CDRIE was observed, representing more than half of IE cases, 3) *Staph. aureus* continues to be the main causative agent of IE, whereas a high incidence of Culture negative episodes needs further evaluation, 4) an individual thorough assessment towards a surgical treatment is crucial to affect the still high mortality of this disease.

Steadily increasing incidence of IE in older patients reflects progressively aging population in developed countries (10). Elderly people more often have previous cardiac and non-cardiac procedures, which predispose them for infections. The mean age of 61.7 years in our population represent a slightly higher age compared to data obtained from the recent EURO-ENDO registry (59.3 years) (1).

With regards to IE, an increasing trend over time differential with respect to sex has been reported in literature (11). Females represented 26.4% of the cohort, which is consistent with figures de-

Tab. 5. Multivariate Cox regression for all-cause in hospital mortality.

	HR	95.0		
	пк	Lower	Upper	- p
COPD/asthma	3.676	1.622	8.332	0.002
Acute renal failure	2.789	1.323	5.877	0.007
Septic shock	6.070	2.928	12.585	0.0001
Congestive heart failure	2.260	0.984	5.191	0.055
Surgery performed	0.401	0.190	0.848	0.017

CI – confidence interval, COPD – chronic obstructive pulmonary disease, HR – hazard ratio

Tab. 6. Multivariate logistic regression for all-cause one-year mortality.

	OR	95.0		
	UK	Lower	Upper	р
Cardiogenic shock	14.703	2.842	76.061	0.001
Septic shock	4.105	1.274	13.229	0.018
History of haemodialysis	14.170	1.927	153.018	0.011
Surgery performed	0.336	0.141	0.798	0.013

CI-confidence interval, OR-odds ratio

rived from dual-centre experience from Czech Republic spanning from 1998–2016, where the 25 % female incidence was reported (7).

The prevalence of *Staph. aureus* has been steadily increasing over recent years (12, 13). Institutional experience from Czech Republic demonstrated noteworthy finding that *Staph. aureus* accounted for almost one-third of the reported IE episodes in years 1998– 2006, and 2009–2016, respectively (14). Similarly, the results of our study, identifying *Staph. aureus* as a causative agent of IE in 27.4 % episodes, confirmed the previously reported heralded microbiological shift from Viridans group streptococci to *Staph. aureus* (6).

Cultures are negative in IE for three main reasons – previous administration of antibiotic treatment, inadequate microbiological techniques, and presence of infection with a highly fastidious bacteria or non-bacterial pathogens (15). The incidence of culture-negative IE varies by country, with a higher proportion of culture-negative IE in developing countries (up to 56 %) (16, 17). In contrast, studies from Western Europe identified Culture negative episodes of IE in 12–25 % (18, 19). 26.4 % incidence of Culture negative endocarditis in the current cohort represents a particularly high proportion, twice as much to previously reported data from the region (14), and warrants further investigations.

The incidence of the prosthetic IE has been increasing over recent years, PVIE represented in our series 26.9 %, which is comparable to 26 % of cases in the Euro Heart survey (20), and 25 % in the 2008 French registry (21). The use of intracardiac devices has also increased, and the incidence will likely continue to surge due to an aging population. Hence, this implies an increasing number of possible complications, including infections. The recent study in Spain demonstrated an increasing incidence of IE in pacemakers (22). CDRIE represented 27.4 % of all IE cases in our cohort, which is a substantially higher number compared to other reports from the European countries, including the overall results of EURO-ENDO registry (1, 23, 24). We may speculate, whether such high proportion of patients with CDRIE might have been affected by involvement of only tertiary care centres in our cohort, which 82 % (9/11) out of them possess Cardiac surgery department performing the most

complicated cases, including lead extractions. Thus, the profile of the cases was most likely affected by referral bias. Patients with CD-RIE have an increased short- and long-term morbidity and mortality (25, 26). Nevertheless, our results showed a better survival rates of patients with CDRIE compared to native/prosthetic valve IE cases.

Systemic embolism occurs in 22 % to 50 % of IE cases and represents the highest risk of major cardiovascular events, including death (2, 27). In our previous dual-centre experience from the Czech Republic, systemic embolism was documented in total of 36 % IE cases (7). In the recently published results from EURO-ENDO registry, embolism was already present on admission in 25.2 % patients, additionally, new episodes of embolism during hospitalization occurred as high as in 20.5 % (1). We documented a systemic embolism before and after admission in 22.1 %, and 14.9 %, respectively. Stratification of the embolic risk should be the indispensable corner stone of each patient assessment in the attempt to decrease the mortality of IE (28–28).

An increasing evidence with regards to the favourable impact of cardiac surgery, especially in cases of *Staph. aureus*, on survival of the patients with IE has been reported (1, 31, 32). Indication for surgery in our cohort was consistent with the major reports on the topic, as 53.8 % of the enrolled population underwent a surgical procedure. We agree with the results of the main EURO-ENDO registry analysis, which confirmed the essential role of surgery in patients with IE. In the patients, who had an indication for surgery, but the procedure was not performed, mortality was significantly higher (Fig. 1).

The important role of surgery in our cohort was further confirmed in multivariate survival analyses, as the performed surgery was the only protective factor of in-hospital and 1-year mortality (Tabs 5 and 6). COPD/asthma, acute renal failure, septic shock, and a congestive heart failure were the independent predictors of in-hospital mortality. On top of known risk factors of mortality of IE, haemodialyzed patients represented the most fragile cohort associated with an increased 1-year mortality (Tab. 6).

#### Conclusions

The results of this ESC EORP EURO-ENDO registry sub-study provided unique detailed data representing the current profile of IE in Central Europe. Reported heralded microbiological shift from viridans group streptococci to *Staph. aureus* has been confirmed. A marked increase in the incidence of Culture negative IE and IE related to artificial intra-cardiac materials has been observed. A significantly increased mortality of patients with IE in whom cardiac surgery is indicated, but not performed, warrants further focus.

## Limitations

1. 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

2.As most centres are tertiary referral centres with cardiac surgical programmes, thus the profile of the cases might have been affected by referral bias. 95-100

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