Decreasing number of valve-related infective endocarditis cases. An urgent call to action for improved diagnostic pathways: A retrospective tertiary center perspective (2015–2022)

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Decreasing number of valve-related infective endocarditis cases. An urgent call to action for improved diagnostic pathways: A retrospective tertiary center perspective (2015–2022)

Short title: Decreasing number of infective endocarditis cases 2015–2022: A call to action

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INTRODUCTION
Over the last few decades, the number of cases of infective endocarditis (IE) worldwide has been increasing [1] and has doubled over the last 20 years [2]. The widespread use of echocardiography should lead to early diagnosis and the implementation of more effective antibiotic therapy. Additionally, improvements in cardiac surgery and intensive care may potentially lower the mortality rate. We carried out an analysis to confirm this in a tertiary center serving IE cases in a stable population of 2.5 million inhabitants. The aim of the study was to analyze mortality and clinical predictors of death in hospitalized valve-related IE patients over the 2015–2022 period.

METHODS
From all hospitalizations in our facility, we selected cases of acute valve-related infective endocarditis admitted from January 2015 to the end of December 2022, qualified for both
surgical and conservative treatment. Transthoracic and transesophageal echocardiography were basic diagnostic tools for establishing the diagnosis of IE in all cases. We retrospectively analyzed the total number of cases, the number of fatal cases, and inhospital mortality. We defined preoperative death as occurring before the surgical procedure (including patients qualified for both conservative and surgical treatment) and perioperative death as occurring during or after the surgical treatment. We analyzed impact of multiple variables (including clinical features such as sex, IE localization, ethological factor and the presence of the artificial valve) on inhospital mortality in order to find predictors of deaths (also dived into overall, pre- and perioperative deaths).

Statistical analysis
Statistical analysis was performed using Statistica 13.1 software (Tibco, Palo Alto, CA, US) and R version 4.2.1. Nominal values are presented as both absolute values and percentages. Variables that did not follow normal distributions (as verified with Shapiro Wilk test) are presented as a median with interquartile range (IQR). In-hospital mortality is presented as a percentage value. Trends in the number of deaths during the analyzed period were assessed using the Mann-Kendall test (to determine the trend) with Sen’s slope evaluation (to find the trend positive/negative). Univariate binomial logistic regression was used to assess the impact of specific factors on mortality, divided into overall, pre- and perioperative mortality. A P-value <0.05 was considered statistically significant.

RESULTS AND DISCUSSION
Overall, we hospitalized 194 patients due to acute IE, and the majority of them were men (75.3%; n = 146). The results are presented in Supplementary material 1. The median of age of the studied group was 62 years, and patients between the ages of 58 and 68 were the most numerous group (n = 66). In cases with a confirmed etiological factor (n = 117), the most common causes of IE were Staphylococcus spp. (51.3%), Enterococcus spp. (22.2%), and Streptococcus spp. (15.4%). Left-sided IE was observed in the vast majority of cases (92.3%), as well as native valve-related IE (NV-IE, 72%). Surgical treatment was performed in 64.9% of patients. Overall, 27.8% (n = 54) of patients died during hospitalization (the preoperative mortality was 14.4%, n = 28). The general trend in the overall number of IE cases is significantly decreasing over the analyzed period (P = 0.046; Sen’s slope, −1.17; 95% confidence interval [CI], −3.0 to −0.001) (Figure 1), but we observed no change in the number of fatal cases and mortality (P = 0.618; Sen’s slope, −0.33; 95% CI, −1.5 to −1.8). In
2021, during the COVID-19 pandemic year, mortality reached a peak of 58% (n = 15), which probably interfered with the results. Fatal cases in 2021 were mostly preoperative (60%; n = 9; Supplementary material, Table S1). We also analyzed predictors of in-hospital mortality and found that an unidentified etiological factor in IE significantly increased the risk of death in cases of both preoperative and perioperative deaths (odds ratio [OR], 4.66; 95% CI, 1.07–20.23; \( P = 0.04 \)). Moreover, we found Staphylococcus spp. as a perioperative predictor of in-hospital death (OR, 0.16; 95% CI, 0.04–0.071; \( P = 0.02 \)), along with the number of infected valves (OR, 2.27; 95% CI, 1.19–6.23; \( P = 0.02 \)) and age as a preoperative predictor of death (OR, 1.04; 95% CI, 1.00–1.07; \( P = 0.03 \)).

Our results show a declining number of IE cases over the analyzed period, while the overall global incidence of IE is increasing [1]. The population we studied is similar to those reported from different European countries in the EURO-ENDO Registry [1] and the LEIOT [3]. The ICE Prospective Cohort Study, which contains data on over 5,000 patients with confirmed and suspected IE, also showed similar demographic results (men 69.4%; age 63.7 years; NV-IE 68.3%; Staphylococcus spp. as the main etiological factor) [4]. Furthermore, the above-mentioned study highlights a decreasing mortality rate over the last decades, despite an increasing complexity of IE cases. The most worrying result of our analysis, in contrast to global observations, is the decreasing trend in the number of confirmed IE cases. Consequently, the delay in establishing an IE diagnosis leads to higher mortality, which in our study was higher than reported in the EURO-ENDO Registry (17.1%) and ICE (19.3%). Healthcare authorities should conduct a careful analysis of the management of IE-suspected patients and the availability of diagnostic tools (such as echocardiography) in hospitals across the region.

The retrospective character of our work is the main limitations of this paper. Due to incomplete data, we were unable to analyze the impact of ‘time from diagnosis to cardiac surgery’ on in-hospital mortality. Additionally, the exclusion of device-related IE patients may have impacted our results. However, It is worth noting that our facility's human resources, technical base, and number of province inhabitants remained relatively consistent throughout the study period. Furthermore, the study period starts just before the publication of the current IE guidelines (September 2015). Although the diagnostic principles remain constant, we have decided to initiate our analysis from the beginning of 2015. The COVID-19 pandemic also had a significant impact on our study, as we had to pay special attention to patients with elevated body temperature or fever. This may have contributed to the higher number of confirmed IE cases in 2021. Furthermore, the time to diagnose IE was prolonged due to pandemic-related restrictions, which likely led to more complex cases and worse clinical conditions. There are
inconsistent worldwide data on reported IE cases during the COVID-19 pandemic. For example, Cabral et al. reported an increased number of IE patients during the first semester of 2020 [5], while a Danish study found no difference in IE incidence before and during lockdown. A study by XinPei et al. [6] from Beijing reported a lower number of IE patients admitted to their cardiac surgery department. The above-mentioned study from China also highlighted a higher surgical risk (EuroSCORE II) in admitted patients during the COVID-19 pandemic, although this was not associated with higher postoperative mortality. Similar observations were reported from Spain, where fewer IE incidences and fewer cardiac surgeries performed did not impact in-hospital mortality among IE patients [7].

In conclusion, our study shows a decreasing trend in the number of confirmed IE cases in our region, which is opposite to the global trends of increasing IE incidence. Further analysis is necessary to understand the reasons behind this observation and to improve the IE diagnostic pathways in the Lodz region. The impact of the COVID-19 pandemic on IE incidence and diagnosis should also be considered in future studies. These findings highlight the need for continuous monitoring and improvement of IE diagnosis and management to reduce mortality and improve patient outcomes.

Supplementary material
Supplementary material is available at https://journals.viamedica.pl/kardiologia_polska.

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References


Figure 1. The incidence of infective endocarditis over the analyzed period ($P = 0.046$; Sen’s slope: $-1.17$)