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Infective Endocarditis—Predictors of In-Hospital Mortality, 17 Years, Single-Center Experience in Bulgaria

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Abstract: Despite tremendous advances in medicine, infective endocarditis (IE) continues to be a challenge for physicians due to increasing morbidity and unchanged high mortality. Objectives: Our aim was to evaluate clinical outcomes in patients with IE and to identify predictors of in-hospital mortality. The study was retrospective, single-centered, and included 270 patients diagnosed with IE, for the period 2005-2021 (median age 65 (51–74), man 177 (65.6%). Native IE (NVIE) was found in 180 (66.7%), prosthetic IE (PVIE) in 88 (33.6%) and cardiac device-related IE (CDRIE) in 2 (0.7%), significantly more in the non-survivors group. Healthcare associated IE (HAIE) was 72 (26.7%), the most common pathogen were Staphylococci and the proportion of Gram-negative bacteria (GNB) non-HACEK were significantly higher in non-survivor's vs survivors (11 (15%) vs 9 (4.5%), p=0.004). Overall, early surgery was performed in 54 (20%) patients, with a significant difference between deceased/alive (3 (4.5%) vs 51 (25.1%, p=0.000). The all-cause in-hospital mortality rate was 24.8% (67). The risk factors identified that increased the risk of death were septic shock (OR – 83 1; 95% CI (17.0-405.2), p=0.000) and acute heart failure (OR –24.6; 95% CI (9.2-65.0), p=0.000). Early surgery (OR – 0.03, 95% CI (0.01-0.16), p=0.000) and low Charlson comorbidity index (OR – 0.85, 95% CI (0.74-0.98, p=0.026) in turn reduce this risk. We found that acute heart failure and septic shock are independent predictors of in-hospital mortality. Low Charlson comorbidity index and early surgery increased survival. Knowing the predictors of death would change the therapeutic approach to a more aggressive one and improve the near and long-term prognosis of patients with IE.

Keywords: infective endocarditis; in-hospital mortality; acute heart failure; septic shock; early surgery

1. Introduction

IE was first described 350 years ago [1], but it remains a major challenge for clinicians for several reasons. IE is a changing disease, and despite the availability of modern imaging and microbiological techniques, diagnosis is often difficult and delayed. The incidence of IE increased up to 13/100 000 worldwide [2]. Improvements in medical and surgical treatment in recent decades have not changed the mortality and serious complication rates [2,3].

The mortality rate in IE is still high, at 15-30% [2–4] and is linked to the changing profile of the disease. Patients are older with multiple comorbidities. High Charlson Comorbidity Index (>3), diabetes, kidney failure, prosthetic valve IE (PVIE) and hemodialysis associated with bad prognosis [4–8]. The incidence of PVIE has raised in recent decades [2,9,10]. The new type of IE - indwelling device-related IE and IE after TAVI (Transcatheter aortic valve implantation) is increasing as a result of scientific and technological advances in the field of medicine. They are difficult to treat and have an unfavorable outcome, as they generally occur in older patients with high comorbidity and very often require surgery [11–15]. Healthcare-associated IE (HAIE) accounts for almost a third of all cases and has been driven by medical progress, improved treatment and increased patient survival and is associated with an adverse outcome [16,17]. There has been a change in the microbiological spectrum of IE with the predominance of staphylococci and enterococci and the associated difficulties in treatment [10]. The most important predictors of mortality are complications - acute or worsening heart failure, septic shock, acute neurological events, acute kidney failure as a result of valvular dysfunction, embolisms and/or persistent infection [18]. These conditions are and the main indications

Early risk stratification for complications and death is of great importance. The timely identification of high-risk patients would change the therapeutic approach to a more aggressive one, especially when deciding on surgical treatment. Early surgery is associated with a reduction in in-hospital mortality and an improvement in the long-term prognosis of IE patients [9,10]. Knowledge of the predictors of death and complications would be helpful in our treatment decisions.

There is a lack of information on the predictors of in-hospital mortality in Bulgaria in the last few decades. We examined predictors of in-hospital death in patients with IE over 17 years.

2. Material and Method

This study is retrospective, single-centered, including 270 patients with a diagnosis of IE, according to the modified Duke criteria , treated at the University Hospital "St. Georgi", in the city of Plovdiv for the period January 2005–December 2021. The hospital capacity is 1500 beds, and the cardiology clinic is a reference center for the treatment of IE for a large part of southern Bulgaria. The medical records of treated patients with codes I33, I38, and I39 for the described period were used. Variables studied included demographics, risk group, presence of predisposing heart disease, comorbidities, Charlson comorbidity index (CCI) [19], entry gate, predictors for transient bacteremia, clinical, echocardiographic findings, causative organisms, complications, and clinical outcome.

2.1. Definition and Classification of IE

The diagnosis was defined as definite IE or possible IE according to the modified Duke criteria [20]. Surgical treatment of IE was defined as early when the surgery was performed during antibiotic treatment. Valvular involvement of IE is determined based on findings from echocardiography, other imaging studies, cardiac surgery, or in some cases by clinical presentation. Episodes of IE were categorized by mode of acquisition as: community-acquired IE (CAIE), healthcare-associated IE (HAIE), and intravenous-druguse-associated IE (IDUIE). These categories are mutually exclusive. IE was defined as HAIE according to the following criteria: (1) occurrence of IE > 48 h after hospital admission or within 6 months after hospital discharge for ≥ 2 days; (2) IE developed within 6 months after a significant invasive procedure performed during hospitalization or in an outpatient setting; (3) extensive outpatient healthcare contacts, defined as receiving wound care or intravenous treatment within 1 month before the onset of IE; or (4) stay in a clinic-home to receive similar care [12–15]. IE occurring on a prosthetic valve within 12 months of surgery is defined as prosthetic valve early endocarditis (PVIE) and is classified as HAIE. Patients with a recent (within 1 month) or longer history of intravenous drug use were classified as IDUIE. Patients with no medical history and no history of injecting drug use were classified as CAIE. IE following dental treatment is considered to be CAIE if there is no other healthcare contact. The presence of septic emboli and an extracardiac focus of infection was defined as a focus of infection detected by imaging or based on typical clinical presentation. Complications were diagnosed according to the established diagnostic criteria and recommendations.

2.2. Statistical Methods

Quantitative data are presented as arithmetic mean ± standard deviation (mean ± SD) or median and interquartile range (25–75 percentiles) according to the type of distribution of the variables (Kolmogorov–Smirnov test). Categorical variables were summarized using absolute (n) and relative (%) magnitudes. Mann–Whitney test for independent samples was used to compare quantitative

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variables between two groups. Z-test was used to compare the relative shares of categorical variables between the studied groups. Logistic regression was performed to determine the simultaneous influence of significant independent variables identified in the univariate analysis to predict belonging to one of two mutually exclusive categories (alive/dead) of the dependent variable output. To determine whether there were differences in the distribution of survival between patients who underwent early surgery and those who did not, a log rank test was performed. A p-value < 0.05 (two-tailed test) was considered statistically significant for all tests. A statistical analysis was performed using SPSS, version 26.0 (IBM Corp., Binghamton, NY, USA).

3. Results

Of all 270 patients, 205 (75.9%) had definite IE, with 133 (65%) of them having two major criteria and 72 (35%) having one major and three minor criteria. There were 65 (24.1%) diagnosed with possible IE, 62 (95%) of them with one major and one minor criterion and three with three minor criteria. The all-cause mortality rate was 24.8% (67). The patients' baseline characteristics are shown in Table 1. The median age was 65 (51–74), and the non-survivors were significantly older than survivors (67 (53–75) vs. 62 (44–73), p = 0.003). In the entire sample, man were 177 (65.6%), without distinction between survivors and non-survivors. The most patients presented with native valve IE 180 (66.7%) and 88 (33.6%) with prosthetic valve IE. We found CDRIE only in the non-survivors' group (2 (3%), p=0.013). No significant difference was identified between deceased and alive patients in terms of risk group, predisposing cardiac conditions, port of entry and type of IE according to mode of acquisition.

Table 1. Baseline characteristics.

Variables	Total IE cases 2005 – 2021 n=270	IE Non-Survivors n=67	IE Survivors n=203	p=value
Age in yrs., X ± SD *median (IQR)*	60.86±16.83 65 (51-74)	65.99±15.69 69 (59-78)	59.17±16.89 63 (46-73)	0.003†
Gender – male, n (%)	177 (65.6)	41 (61,2)	136 (67)	0.386*
Time symptoms-hospitalization, *median (IQR)*	30 (20-60)	30 (14-60)	30 (20-60)	0.188†
Risk groups, n (%)				
Low	136 (50.4)	36 (53.7)	100 (49.3)	0.532*
Moderate	44 (16.3)	10 (14.9)	34 (16.7)	0.729*
High	90 (33.3)	21 (31.3)	69 (34.0)	0.684*
Type of valves, n (%)				
Native IE	180 (66.7)	45 (67.2)	135 (66.5)	0.916
Prosthetic IE	88 (33.6)	20 (29.9)	68 (33.5)	0.586
Early prosthetic	9 (3.3)	1 (1.5)	8 (3.9)	0.341
Late prosthetic	79 (29.3)	19 (28.4)	60 (29.6)	0.852
CDRIE	2 (0.7)	2 (3.0)	0 (0.0)	0.013*
Entry door, n (%)				
Unknown	125 (46.3)	35 (52.2)	86 (42.4)	0.162
Non-dental manipulation/procedures	44 (16.3)	9 (13.4)	35 (17.2)	0.465
Dental	30 (11.1)	5 (7.5)	25 (12.3)	0.278
I.v. drug users	24 (8.9)	7 (10.4)	17 (8.4)	0.618
Hemodialysis	13 (4.8)	5 (7.5)	8 (3.9)	0.232
Skin	10 (3.7)	3 (4.50)	7 (3.4)	0.678
Urogenital	9 (3.3)	1 (1.5)	8 (3.9)	0.341
Gastrointestinal	5 (1.9)	1 (1.5)	8 (3.9)	0.341

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Respirators	5 (1.9)	0 (0.0)	5 (2.5)	0.191
Ear Nose Throat	4 (1.5)	1 (1.5)	3 (1.5)	1.000
Others	1 (0.4)	0 (0.0)	1 (0.5)	0.562
Predisposing heart conditions, n (%)				
Prosthetic valve	76 (28.2)	19 (28.3)	57 (28.0)	0.949
Past IE	20 (7.4)	6 (9.0)	14 (6.9)	0.569
Past IE prosthetic	14 (5.2)	3 (4.5)	11(5.4)	0.773
Past IE native valves	6 (2.2)	3 (4.5)	3 (1.5)	0.151
Rheumatic heart disease	11 (4.0)	1 (1.5)	10 (4.9)	0.221
Congenital heart disease	21 (7.8)	6 (9.0)	15 (7.5)	0.693
Bicuspid Ao valve	11 (4.1)	4 (6.0)	7 (3.5)	0.372
Mitral valve prolapse	8 (3.0)	1 (1.5)	7 (3.5)	0.406
Others	2 (0.7)	1 (1.5)	1 (0.5)	0.410
Degenerative valve	19 (7.0)	7 (10.5)	12 (5.9)	0.202
Intact valves	123 (45.6)	28 (41.7)	95 (46.8)	0.467
Type of acquisition				
Community acquired IE	173 (64.1)	43 (64.2)	130 (64.0)	0.976
Health care–associated IE	72 (26.7)	17 (25.4)	55 (27.1)	0.785
Intravenous drug use–related IE	25 (9.3)	7 (10.4)	18 (8.9)	0.714

* z-test; † Mann–Whitney U Test; CDRIE—cardiac device related IE.

Patients were presented with a wide range of comorbidity, the most common being arterial hypertension 171 (63.3%), chronic heart failure 124 (45.9%), previous cardiac surgery 95 (35.2%), chronic kidney failure 70 (25.9%), coronary artery disease 64 (23.7%), diabetes 51 (18.9%), atrial fibrillation 49 (18.1%) and more. We found a significant difference with more cases in the deceased vs alive for CCI (4 (3-6) vs 3 (1-5), p=0.000), chronic kidney disease (26 (38.8%) vs 44 (24.7%), p=0.006), atrial fibrillation (18 (26.9%) vs 31 (15.3%), (p=0.033) and previous stroke (15 (22.4%) vs 25 (12.3%), p=0.044). The most common clinical symptoms were fever 263 (97.4%), anemia 248 (92.5%) and heart murmur 178 (66.2%). Cases with splenomegaly 49 (8.1%) and skin changes 14 (5.5%) have decreased dramatically. There were significantly fewer febrile cases in the deceased group (63 (94%) vs 200 (98.5%), p=0.045). In terms of complications, we found that there were significantly more cases of acute heart failure (57 (85.1%), vs 71 (35%), p=0.000), septic shock (20 (29.9%) vs 3 (1.5%), p=0.000) and worsening kidney function (36 (53.7%) vs 75 (36.9%), p=0.015) in those who died compared with those who survived. Early surgery was performed overall in 54 (20%), but less frequency in non-survivors than in survivors (3 (4.5%) vs 51 (25.1%, p=0.000) (Table 2).

Table 2. Comorbidity, clinical symptoms and complications.

Variables	Total IE cases 2005 – 2021 n=270	IE Non-Survivors n=67	IE Survivors n=203	p=value
Comorbidity				
CCI, *median (IQR)*	3 (2-5)	4 (3-6)	3 (1-5)	0.000†
AH	171 (63,3)	43 (64.2)	128 (63.1)	0.860*
CHF	124 (45.9)	32 (47.8)	92 (45.3)	0.728*
Heart surgery	95 (35,2)	20 (29.9)	75 (36.9)	0.292*
CKD	70 (25.9)	26 (38.8)	44 (21.7)	0.006*
CAD	64 (23.7)	19 (28.4)	45 (22.2)	0.302*
Diabetes	51 (18.9)	11 (16.4)	40 (19.7)	0.551*
Atrial fibrillation	49 (18.1)	18 (26.9)	31 (15.3)	0.033*
Past stroke	40 (14.8)	15 (22.4)	25 (12.3)	0.044*
Gastrointestinal	32 (11.1)	6 (9.0)	26 (12.8)	0.580*

Malignancy	30 (11.1)	6 (9.0)	24 (11.8)	0.517*
COPD	21 (7.8)	5 (7.6)	16 (7.9)	0.936*
Hemodialysis	14 (5.2)	5 (7.5)	9 (4.4)	0.332*
Chronic liver disease	13 (4.8)	4 (6.0)	9 (4.4)	0.611*
Systemic disease	4 (1.5)	0 (2.0)	4 (2.0)	0.247*
Clinical symptoms				
Fever	263 (97.4)	63 (94)	200 (98.5)	0.045*
Anemia	248 (92.5)	61 (91)	107 (93)	0.590*
Cardiac murmur	178 (66.2)	46 (68.7)	132 (65.3)	0.620*
Splenomegaly	49 (8.1)	13 (19.4)	36 (17.7)	0.759*
Skin disorders	14 (5.5)	4 (6.0)	10 (4.9)	0.738*
Complications				
AHF	128 (47.5)	57 (85.1)	71 (35)	0.000*
Worsening kidney function	111 (41.1)	36 (53.7)	75 (36.9)	0.015*
Embolism	56 (20.7)	16 (23.9)	40 (19.7)	0.370*
Brain	29 (51.7)	8 (50.0)	21 (52.5)	0.866*
Lung	5 (8.9)	0 (0.0)	5 (12.5)	-
Spleen	10 (17.9)	5 (31.25)	5 (12.5)	0.098*
Skin	7 (12.5)	1 (6.25)	6 (15)	0.371*
Musculoskeletal	2 (3.6)	1 (6.25)	1 (2.5)	0.495
Combine	3 (5.4)	1 (6.25)	2 (5)	0.851*
Strock	30 (11.1)	9 (13.4)	21 (10.3)	0.486*
Septic shock	23 (8.5)	20 (29.9)	3 (1.5)	0.000*
Early surgery, n (%)	54 (20.0)	3 (4.5)	51 (25.1)	0.000*

*z-test; †Mann-Whitney U Test; CCI-Charlson comorbidity index; AH-arterial hypertension; CHF-chronic heart failure; CKD-chronic kidney diseases; CAD-coronary arterial diseases; COPD-chronic obstructive pulmonary diseases; AHF-acute heart failure.

The echocardiographic results are shown in Supplementary File S1. Transesophageal echocardiography (TOE) was performed more often in survivors than in deceased (86 (42.4%) vs 11(16.4%), p=0.000). We found that AV-TV involvement was significantly more common in the deceased group (3 (4.5%) vs 1 (0.5%, p=0.019) and ejection fraction was significantly lower in the same group (55 (51-66) vs 62 (55-68), p=0.001).

Hemoculture results were negative in 111 (41.1%) and the most common pathogens were Staphylococci in 89 (33%). Enterococci were more prevalent (25 (9.3%)) than streptococci (21 (7.8%)). The GNB non-HACEK were significantly more frequent in the deceased group (10 (14.9%) vs 9 (4.5%), p=0.004), especially for *Escherichia coli (5 (7.4%) vs 4 (2.0 %), p=0.030) and Serratia marcescens (3 (4.5%) vs 1 (0.5%) p=0.019)* (Supplementary File S2).

The predictors of in-hospital mortality from univariate analysis are summarized in Table 3.

Table 3. Predictors of in-hospital mortality - p value from univariate analysis.

Variables	Total IE cases 2005 – 2021 n=270	IE Non-Survivors n=67	IE Survivors n=203	p=value
Age in yrs., X ± SD, *median (IQR)*	60.86±16.83 65 (51-74)	65.99±15.69 69 (59-78)	59.17±16.89 63 (46-73)	0.003†
Carlson Comorbidity Index, *median (IQR)*	3 (2-5)	4 (3-6)	3 (1-5)	0.000†
AHF, n (%)	128 (47.5)	57 (85.1)	71 (35)	0.000*
AKF, n (%)	111 (41.1)	36 (53.7)	75 (36.9)	0.015*

Septic shock, n (%)	23 (8.5)	20 (29.9)	3 (1.5)	0.000*
Atrial fibrillation, n (%)	49 (18.1)	18 (26.9)	31 (15.3)	0.033*
CKD, n (%)	70 (25.9)	26 (38.8)	44 (21.7)	0.006*
Past stroke, n (%)	40 (14.8)	15 (22.4)	25 (12.3)	0.044*
AV-TV involvement, n (%)	4 (1.5)	3 (4.5)	1 (0.5)	0.019*
EF %. медиана (IQR)	60 (54-68)	55 (51-66)	62 (55-68)	0.001†
TR III ст, n (%)	12 (4.4)	6 (9.0)	6 (3.0)	0.040*
GNB non-HACEK, n (%),	19 (7.1)	11 (15)	9 (4.5)	0.004*
Escherichia coli, n (%)	9 (3.4)	5 (7.5)	4 (2.0)	0.030*
Serratia marcescens, n (%)	4 (1.5)	3 (4.5)	1 (0.5)	0.019*

*z-test; †Mann-Whitney U Test; AHF-Acute heart failure; AKF- Acute kidney failure; CKD-Chronic kidney diseases; AV-TV – Aortic valve-Tricuspid valve; EF-Ejection fraction; TR-Tricuspid regurgitation; *GNB non-HACEK-Gram negative bacteria non-HACEK- (Hemophilus species, Actinobacillus, Cardiobacterium, Eikenella, or Kingella).*

Logistic regression was performed to determine the simultaneous influence of significant independent variables identified in the univariate analysis to predict belonging to one of two mutually exclusive categories (alive/dead) of the dependent variable output. The logistic regression model was statistically significant, $\chi 2(4)=138.07$, p=0.000 and explained 59.4% (Nagelkerke R2) of the variation in outcome and correctly classified 86.3% of cases. The presence of septic shock increased the odds of death by a factor of 83.1 and the complication of acute heart failure (AHF) by a factor of 24.64. Early surgery and low CCI reduce this risk (Table 4).

Table 4. Logistic regression for periods.

Variable	B- coefficient	OR	95% CI	p	Nagelkerke R2
2005-2021					
Early surgery	-3.52	0.03	0.01-0.16	0.000	
Charlson comorbidity index	-0.16	0.85	0.74-0.98	0.026	59.4%
Septic shock	4.42	83.06	17.03-405.18	0.000	
Acute heart failure	3.20	24.64	9.20-65.98	0.000	

OR-odds ratio; CI- confidence interval;.

A log-rank survival analysis was performed to determine whether there was a difference in the survival distribution between patients indicated for early surgery who underwent surgery and those who did not. The result of the test was statistically significant, i.e. the survival distribution between the two groups was different – $\chi 2(1)=25.20$, p=0.000 (Figure 1). The Median time to event (death), with the estimated time to death being 6 days after hospitalization for the group of patients indicated for early surgery that was not performed. In addition, the 75% percentile of the data showed survival 3 days from hospitalization.

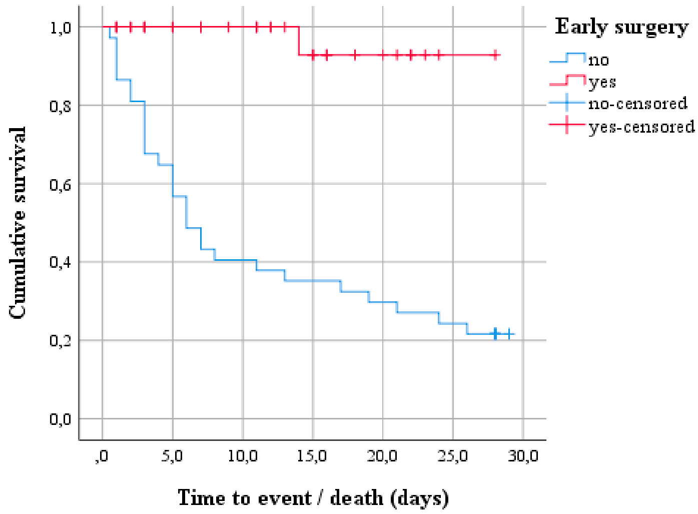

Figure 1. Survival function showing the difference in the distribution of survival between patients indicated for early surgery that underwent early surgery and those that didn't.

4. Discussion

The overall in-hospital mortality rate in our cohort was 24.4%. These data are consistent with those reported in the literature of 15-30% [2,3,21,22]. The data from the univariate analysis, which are associated with increased mortality (Table 3) can be summarized as follows:

1. Patient characteristics - age, high CCI >3, chronic kidney diseases, previous stroke, atrial fibrillation.

2. Complications occurred – acute heart failure, acute kidney failure, septic shock.

3. Echocardiographic data - low EF (%), severe tricuspid regurgitation, bivalve IE - aortic and tricuspid valve involvement. 4. Microbiological characteristics - *GNB non-HASEK* - *Escherichia coli* and *Serratia marcescens*. 5. Failure to perform early surgery when indicated.

Regarding the microbiological causative agent, gram-negative bacteria (GNB non HASEK) were significantly more frequently represented in the deceased group especially *Escherichia coli* and *Serratia marcescens.* Marco Falcone and author also found *Escherichia coli* as the most common cause of *GNB-IE* [23]. *GNB non HASEK-IE* is a rare infection, associated with high in-hospital mortalityi and characterized by the involvement of elderly patients with high comorbidity, nosocomial acquisition, and unfavorable outcome [24,25].

Acute heart failure and septic shock were strong predictors for in-hospital morality, while performed early surgery and low CCI were protective ones.

Acute heart failure is the most common complications of IE and the main indication for early surgery [9,10]. The frequency of heart failure in IE is reported in a wide range between 19-75% [26,27]. This complication is most commonly the result of leaflet perforation or rupture, mitral chordal rupture, valve dehiscence in PVIE and less frequently intracardiac fistula, valve obstruction, myocardial infarction due to embolization [10]. The severity of the manifestation depends on previous cardiac function and coexisting comorbidities. Heart failure in IE is a well-documented independent predictor of in-hospital and 1-year mortality. Surgery remains the only effective therapy linked to improved survival [26–28].

Septic shock is a life-threatening complication of IE and occurs in about 5 to 12% of patients [2,3,29–33]. It is well known independent predictor for in-hospital mortality. Risk factors for septic shock include S. aureus and gram-negative bacteria, nosocomial acquisition, acute renal failure, diabetes mellitus, central nervous system embolism [29]. Almost 2/3 of patients with septic shock die. In the context of persistent infection, septic shock is a main indication for early surgery. There is sufficient evidence that early surgical intervention reduces in-hospital and 1-year mortality in these patients [30].

Comorbidities are an important part of the IE patient profile and a predictor of disease outcome. We used the Charlson Comorbidity Index (CCI) [19], the most widely validated measure of the prognostic impact of multiple chronic diseases. Our data are similar to those of other studies for the CCI as an independent prognostic indicator in IE [34–36].

The independent predictors of death were found in our study are consistent with the literature. The most frequently reported predictors of death are heart failure, age >70 years [2,3,32,37]; Septic shock – [31,38,39], high CCI [2,40]. In other studies PVIE, Staphylococcus aureus IE, cerebrovascular complicatio ns, paravalvular abscess were reported as independent predictors of in-hospital death [3,21,32,37,41].

Early surgery is a protective indicator and failure to perform early surgery when indicated is a strong predictor of in-hospital death [2]. In our study, early surgery was performed in 20%, which is quite less compared to other countries 45-62% [2,3,21,41]. Data from the literature show that almost half of patients with IE are indicated for early surgery, but more than half of them do not receive it. The reasons are of a different nature. In EURO-ENDO, these are most often: high perioperative risk – 58.2%; death before surgery – 22.5%; patient refusal – 18.8%; neurological complications – 11.2%; lack of cardiac surgery in the medical facility – 6.2%; others – 20.7% [2]. Our data show the benefit of early surgery and the improvement in survival in IE. We found early surgery to be an independent predictor that reduced in-hospital mortality.

5. Limitations

This study is retrospective, and the data were based on the clinical database of a single center. Another limitation is the long study period and the changing recommendations and evidence, especially regarding early surgery, the use of new imaging techniques 18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) for diagnosis and new antibiotic molecules. Technological advances in echocardiography also have implications for echocardiographic data. Despite these limitations, our study is the only such study performed in Bulgaria in the last several decades, and it included a large number of patients over a long period of time (17 years).

6. Conclusions

Acute heart failure and septic shock are independent predictors of in-hospital mortality. Low Charlson comorbidity index and early surgery increased survival. Knowing the predictors of death would change the therapeutic approach to a more aggressive one and improve the near and long-term prognosis of patients with IE.

Institutional Review Board Statement: This study was conducted with the consent of the Local Ethics Committee (decision #2/09.03.2023) and in accordance with the principles of the Declaration of Helsinki.

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