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Risk of mortality in infective endocarditis — a single-centre experience

Czynniki ryzyka śmiertelności w infekcyjnym zapaleniu wsierdzia — doświadczenia jednego ośrodka

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Abstract

Introduction. Infective endocarditis (IE) is a disease associated with high morbidity and mortality. Multiple risk factors have been identified for mortality in IE.

Material and methods. 21 patients diagnosed with IE between January 2018 and January 2019 were retrospectively analysed. All data was expressed as mean ± standard error (SE). Variables were analysed with chi-square, Fisher's exact, and Mann-Whitney tests. A p-value < 0.05 was identified as statistically significant.

Results. Total mortality was 52.4% and in-hospital mortality was 28.6%. Patients who died in the course of IE were older compared to survivors (66.7 ± 19.8 years vs 70.8 ± 11.6). Staphylococci and Streptococci spp. were causative pathogens in 71.4% of cases of IE. Morphology was the most important feature that identified patients who died: white blood cells were higher in non-survivors (35.39 ± 14.36 vs 12.02 ± 4.67, p < 0.05); haemoglobin level was decreased (7.47 ± 0.96 vs 9.51 ± 1.33, p < 0.05); and thrombocytopenia (82.50 ± 45.85 vs 179.8 ± 56.13, p < 0.05) was characteristic for non-survivors. The plates-to-leucocytes ratio in patients who died during hospitalisation was 3.01 ± 2.89. For patients who survived hospitalisation it was 15.10 ± 10.86 (p = 0.0069). Similar results were achieved when comparing patients who died during hospitalisation 3.01 ± 2.89 vs patients who survived until 2019 16.94 ± 12.62 (p = 0.004662).

Conclusion. Morphology is recommended as the key diagnostic test in predicting mortality risk in patients with IE. The plates-to-leucocytes ratio is also a significant marker of mortality. Prompt identification and close monitoring of risk factors may prevent a higher mortality rate in IE.

Key words: infective endocarditis, risk factors of infective endocarditis, mortality in infective endocarditis

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Introduction

Infective endocarditis (IE) is a disease that is still associated with high morbidity and mortality. The most frequently indicated risk factors are: a prosthetic valve or prosthetic material used for cardiac valve repair, transcatheter-implanted prostheses and homografts, previous IE history, untreated cyanotic congenital heart disease (CHD), and

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CHD treated with palliative shunts, conduits or other prostheses [1]. Wallas et al. found in-hospital mortality of 18% and mortality at six months of 27%. The commonly indicated risk factors were not found to be predictors of adverse events in this study. Abnormal white cell count, serum albumin concentration, serum creatinine concentration, cardiac rhythm, the presence of two major Duke criteria, or visible vegetation were associated with a poor prognosis [2]. Alkhawam et al. [3] identified an overall mortality rate of 20.1% in patients with IE, and a readmission rate within 30 days of discharge of 21.5%. The most common organisms identified were Staphylococcus aureus (43.7%), viridans streptococci (17%), and Enterococcus (14.7%) [3]. Cresti et al. reported that in-hospital mortality was 24%. Independent predictors of mortality were older age, *S. aureus* infection, heart failure, septic shock, and persistent bacteremia. In an Egyptian population, the causes of mortality (38.7%) included congestive heart failure (CHF), sepsis, surgery-related stroke, cerebral haemorrhage, pulmonary embolism, sudden cardiac death, and hyperkalemia [4]. Differing experiences in IE and the diversity of markers of high mortality highlight the importance of identifying new risk factors, as well as of controlling and monitoring existing risk factors, for IE in the local population.

Material and methods

21 patients (10 male, 47.62%) who met the modified Duke criteria for definite infective endocarditis and who were hospitalised in the Cardiology Department between January 2018 and January 2019 were retrospectively analysed. Cardiovascular implantable electronic device-related IE concerned nine patients (42.9%), native valve-related IE concerned seven patients (33.3%), and prosthetic valve-related IE concerned seven patients (33.3%). In clinical characterisation, atrial fibrillation affected seven patients (33.3%), hypertension 17 patients (80.96%), coronary artery disease 10 patients (47.6%), myocardial infarction eight patients (38.1%), diabetes nine patients (42.9%), and chronic obstructive pulmonary disease 2 patients (9.52%). The clinical characteristics of the patients are set out in Table 1.

Statistical analysis

All data was expressed as mean ± standard error (SE). Variables were analysed with chi-square and Fisher's exact tests, and continuous variables with a Mann-Whitney test. A p-value < 0.05 was identified as statistically significant.

Table 1. Clinical characteristics of patients hospitalised because of infective endocarditis (IE)

Clinical characteristic	Patients who died during hospitalisation	Patients who died at home after hospitalisation	Patients who survived
CIED IE	2	3	4
Native valve IE	2	1	4
Prostethic valve IE	2	1	4
Hypertension	4	4	9
Diabetes mellitus	1	3	5
Mitral prosthesis	0	1	2
Aortic prosthesis	2	1	2
Biological prosthesis	1	0	4
Synthetic prosthesis	0	1	0
Mitral regurgitation	2	3	3
Tricuspid regurgitation	5	2	4
Atrial fibrillation	3	3	1
Coronary artery disease	3	3	4
Myocardial infarction in history	2	3	3
Sepsis in history	1	0	3
Dental caries	1	0	3
Abdominal surgery in history	2	0	6
COPD	0	0	2

CIED — cardiovascular implantable electronic device; COPD — chronic obstructive pulmonary disease

Results

In-hospital mortality was 28.6%, ambulatory mortality was 23.81%, and total mortality was 52.4%. Patients who survived IE were younger than those who died, both in hospital and at home (66.7 ± 19.8 vs 70.8 ± 11.6 vs 73 ± 13.8 respectively, p > 0.05). Heart failure was diagnosed in 14 patients (66.6%). Left ventricular ejection fraction was lowest in patients who died at home, 35 ± 22.9, compared to living patients 52.7 ± 10 and those who died during hospitalisation 43 ± 21.2 (p > 0.05). A pathogen was identified in 14 patients, including four who survived. The most common was *Staphyloccoci spp*. 6/14 (42.8%), followed by *Streptococci spp*. 4/14 (28.6%), *Klebsiella pneumonie* 3/14 (21.4%) and *Enterococcus fecalis* 2/14 (14.3%). In antibiotic therapy, vancomycine was the most frequently used (14/21; 66.6%) (Table 2). Transoesophageal echocardiography was performed in all patients: vegetation was visible in 10/21 (47.6%) who died, and in 8/21 (38.1%) who survived.

The most important feature that identified patients who died during hospitalisation was morphology, while C-reactive protein did not do so (Table 3) (p < 0.05). Plates-to-leucocytes ratio in patients who died during hospitalisation was 3.01 ± 2.89 compared to patients who survived hospitalisation 15.10 ± 10.86 (p = 0,0069). Similar results were achieved when we compared patients who died during hospitalisation 3.01 ± 2.89 vs patents who survived until 2019 16.94 ± 12.62 (p = 0.004662).

Discussion

Infective endocarditis is a disease difficult to diagnose in out-hospital settings and still results in high mortality. The analysis performed in our centre adds a relevant insight into IE.

In our study, total mortality was relatively high at 52.4%, as was in-hospital mortality at 28.6%. Delahaye et al. [5] indicated that the in-hospital death rate was 17% and was lower in operated patients (14.4% vs 19.3%, p > 0.05) [5]. Ternhag et al. [6] performed data analysis

Table 2. Antibiotic therapy in patients with infective endocarditis

Antibiotic	Patients who died during hospitalisation	Patients who died at home after hospitalisation	Patients who survived
Vancomycin	3	3	8
Gentamycin	4	2	3
Cilastatin + imipenem	1	0	2
Cloxacillin	2	4	1
Rifampicin	2	2	3
Ciprofloxacin	0	2	1
Ceftazidime	0	0	1
Ceftriaxone	1	2	3
Fluconazole	1	0	2
Teicoplanin	0	0	1
Meropenem	0	0	2
Sulfamethoxazole, trimethoprim	0	0	1
Piperacillin, tazobactam	0	1	1
Ampicillin	0	0	1

Table 3. Blood tests in patients with infective endocarditis

Blood test	Patients who died during hospitalisation	Patients who died at home after hospitalisation	Patients who survived	p-value
CRP [mg/L] medium	166.41 ± 122.71	143.02 ± 95.00	118.63 ± 95.14	0.205
WBC [thousand/μL]	35.39 ± 14.36	16.83 ± 13.25	12.02 ± 4.67	0.0068
Haemoglobin [g/dL]	7.47 ± 0.96	8.94 ± 2.37	9.51 ± 1.33	0.032
PLT [thousand/μL]	82.50 ± 45.85	155.4 ± 99.53	179.8 ± 6.13	0.025
eGFR [ml/min/1.73 m^2]	17.5 ± 5.75	21.2 ± 11.8	38.4 ± 28.5	0.033

CRP — C-reactive protein; WBC — white blood count; PLT — platelets; eGFR — estimated glomerular filtration rate

between 1997 and 2007. They found the 30 days all-cause crude mortality rate to be 10.4% and the standardised mortality ratio (SMR) was 33.7 (95% confidence interval [CI]: 31.0–36.6) [6]. In the literature, the early mortality has been found to be 14% to 31%, while late mortality rates after a five-year follow-up ranged from 25% to 60% [7].

Many risk factors of mortality in IE have been indicated. Delahaye et al. [5] found that a history of heart failure (odds ratio [OR]: 2.65), a history of immunosuppression (OR: 3.34), insulin-requiring diabetes mellitus (OR: 7.82), left-sided IE (OR: 1.97), heart failure (OR: 2.19), septic shock (OR: 4.33), lower Glasgow Coma Scale score (OR: 4.09), cerebral haemorrhage (OR: 9.46), and higher C-reactive protein level (OR: 2.60) were all risk factors of mortality in IE. In our study, none of these risk factors reached statistical significance [5].

Platelets play an important role in the pathogenesis of endocarditis and are sensitive monitors of the systemic host response to sepsis and the severity of thrombocytopenia and in predicting six-month mortality. Thrombocytopenia at day 8 indicated an impaired host response to sepsis and predicted increased mortality. Sy et al. [8, 9] recommended empirical antistaphylococcal therapy in patients with thrombocytopenia because of the strong association between baseline thrombocytopenia and *Staphylococcus aureus* infection [8, 9]. Experimentally induced thrombocytopenia has been associated with more severe disease in animal models [10]. In our study, the platelets count was significantly lower in non-survivors. The most frequently observed pathogens were *Staphylococcus spp*. and vanocomycine was mainly used in survivors, whereas cloxacillin was mainly used in non-survivors.

Rostagno et al. [11] identified that hospital mortality was closely related to age, clinical and laboratory evidence of advanced septic condition (temperature > 38°C, leukocytosis and creatinine > 2.0 mg/dL) and haemodynamic impairment [11]. In our study, white blood cells elevation and acute kidney failure with low estimated glomerular filtration rate (eGFR) was associated with both in-hospital and overall mortality rates in IE. We observed that leukocytosis was significantly higher in non-survivors, whereas haemoglobin level was severely decreased. We also evaluated whether plates-to-leucocytes ratios (PLRs) were significant markers of mortality. We identified PLRs as being strong risk factors of mortality in IE. Zencir et al. [12] showed that a higher PLR may predict in-hospital mortality in patients with IE, and that PLRs over 191.01 predicted in-hospital mortality with 56.3% sensitivity and 81.4% specificity [12].

The identification of risk factors, and close monitoring using simple parameters such as WBC, haemoglobin level, and platelets counts, may prevent a high mortality rate.

Conflict(s) of interest

The authors declare no conflict of interest.

Streszczenie

Wstęp. Infekcyjne zapalenie wsierdzia (IE) jest chorobą charakteryzującą się wysoką chorobowością i śmiertelnością. Zidentyfikowano liczne czynniki ryzyka śmiertelności w IE.

Materiał i metody. Dwudziestu jeden hospitalizowanych pacjentów z rozpoznanym IE w okresie od stycznia 2018 roku do stycznia 2019 poddano analizie retrospektywnej. Dane przedstawiono jako średnie z odchyleniem standardowym, wykonano testy: χ^2, Fishera i Mann-Whitneya. Współczynnik prawdopodobieństwa p poniżej 0, 05 uznano za statystycznie istotny.

Wyniki. Ogólna śmiertelność wynosiła 52,4%, natomiast wewnątrzszpitalna 28,6%. Pacjenci z IE, którzy zmarli, byli w starszym wieku w porównaniu z tymi, którzy przeżyli (66,7 ± 19,8 *v.* 70,8 ± 11,6). Gronkowce i paciorkowce były najczęstszymi patogenami u pacjentów z IE; stanowiły 71,4% przypadków. Najważniejszą cechą, która odróżniała pacjentów zmarłych w przebiegu IE, była morfologia krwi. Większa liczba białych krwinek (35,39 ± 14,36 *v.* 12,02 ± 4,67; p < 0,05), niższe stężenie hemoglobiny (7,47 ± 0,96 *v.* 9,51 ± 1,33; p < 0,05) i płytek krwi (82,50 ± 45,85 *v.* 179,8 ± 56,13; p < 0,05) były charakterystyczne dla osób, które zmarły w przebiegu IE. Stosunek trombocytów do leukocytów u pacjentów zmarłych podczas hospitalizacji wynosił 3,01 ± 2,89, w porównaniu z osobami, które przeżyły, u których wynosił 15,10 ± 10,86 (p = 0,0069). Podobne wyniki otrzymano, kiedy porównano pacjentów zmarłych w trakcie pobytu w szpitalu — 3,01 ± 2,89 z pacjentami, którzy przeżyli do 2019 roku — 16,94 ± 12,62 (p = 0,004662).

Podsumowanie. Morfologia okazała się kluczowym badaniem dodatkowym umożliwiającym prognozowanie ryzyka śmiertelności w grupie pacjentów z IE. Stosunek liczby trombocytów i leukocytów jest również ważnym markerem śmiertelności. Identyfikacja oraz uważne monitorowanie czynników ryzyka może się przyczynić do obniżenia wysokiego ryzyka śmiertelności w IE.

Słowa kluczowe: infekcyjne zapalenie wsierdzia, czynniki ryzyka infekcyjnego zapalenia wsierdzia, śmiertelność w infekcyjnym zapaleniu wsierdzia

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