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Iranian Registry of Infective Endocarditis (IRIE): Time to relook at the guideline, regarding to regional differences

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ABSTRACT

Aims: Infective endocarditis (IE) remained a potentially fatal disease with high rate of mortality and morbidity. The epidemiology and global burden of IE are largely different between the countries. We aimed to address the epidemiological aspects of IE in a tertiary hospital in Tehran, Iran.

Methods and Results: Between 2006–2018, all adults patients with diagnosis of IE were enrolled in the Iranian Registry of Infective Endocarditis (IRIE). The data were analyzed using the χ^2, Kolmogorov–Smirnov, and Mann–Whitney U tests. Overall, 602 patients, 407 (67.6%) men, mean age 46 ± 16 years were recruited. Positive blood culture found in 49%.The most common underlying heart diseases were: Congenital heart diseases (CHD) particularly bicuspid aortic valves (BAV) and ventricular septal defects (VSD) in 37%, followed by degenerative heart diseases :flail and mitral valve prolapse (16.3%), intravenous drug user in 12.6%, prosthetic valves in 11.1%, previous IE (8.9%), rheumatic heart diseases (RHD) in 8.4%. The most causative microorganisms were *Staphylococcus aureus*, *Enterococci*, coagulase-negative *staphylococci* and *Streptococcus viridans*. Cardiac or extra cardiac complications occurred in 56.6% of the patients.

Conclusions: Based on IRIE, IE occurs in the younger population in Iran with high rates of blood culture-negative IE. RHD are not the main cause of IE in Iran, CHD including BAV and VSDs, followed by prolaptic or flail mitral valve were the most common. These 2 groups can be considered a high-risk group for IE. More than half of the patients with IE had cardiac or extra cardiac complications.

1. Introduction

Infective endocarditis (IE) is a relatively rare and potentially fatal disease despite notable advances in medical and surgical treatment. The patterns of the disease in terms of its epidemiology, pathological basis, and antibiotic era vary considerably. The annual global incidence of IE has been estimated to be 3 to 10 per 100,000 people [1–3], similar in low-income and industrialized countries [4]. However, whereas rheumatic heart diseases (RHDs) have been suggested as the main key risk factor for IE in developing countries [5–7], degenerative valve diseases, prosthetic valves, intracardiac devices, and malignancies are increasingly associated with IE in developed countries [8]. Moreover, recent decades have witnessed a shift in the incidence of IE, from young adults to the elderly, reflecting medical and care advances in the control and prevention of IE [9].

The results of epidemiological studies vary with respect to the microbial pathogenicity of IE. Although the type of pathogen has not substantially changed over time—with *Streptococcus*, *Staphylococcus* and *Enterococcus* still accounting for more than 80% of all cases—the specific subtypes of microorganisms require a repartition of groups most at risk [10,11]. In conjunction with these issues, even with notable advances in diagnostic technology, improvements in antimicrobial selection, and formulation of new guidelines for the proper management of IE, the morbidity and mortality of the disease remain high inasmuch as 1 in 5 patients die during the initial hospital admission, which can be due to

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changes in the type and virulence of the infecting organisms and the changes in the population at risk of developing IE [12–14].

The considerable variations in the epidemiology, underlying heart diseases, pathogenic sources, and risk and prognostic factors of IE render the prompt identification of the clinical and epidemiological aspects of the disease with a view to devising the optimal management strategy and preventing the adverse consequences in any given society essential. Such assessment assumes even more significance in the context of countries like Iran, where there is a dearth of up-to-the-minute data in the face of evidence for significant changing patterns of IE [15,16].

Indeed, our exhaustive literature search of credible sources by employing main keywords yielded very little information on the epidemiological aspects of IE in our population. Hence, in the present study, conducted in a tertiary referral center, we sought to address the epidemiological aspects of IE vis-à-vis its etiology, underlying heart diseases, principal microbial pathogens, and prognosis.

2. Methods

2.1. Population

Between 2006 and 2018, all adult patients with a possible or definite diagnosis of IE based on the modified Duke criteria were enrolled in the Iranian Registry of Infective Endocarditis (IRIE) by an expert team.

Two groups of patients within 2 time periods were enrolled in the present study. Between 2006 and 2016, the medical records of 900 patients admitted to our tertiary referral center with a diagnosis of IE were reviewed. The exclusion criteria were comprised of age younger than 18 years, outpatient status, subsequent ruling-out of the IE diagnosis, and incomplete treatment. A total of 455 patients were, accordingly, excluded from the study and thereafter a retrospective review was conducted on 445 patients with a definite or possible diagnosis of IE. Afterward, between January 2016 and 2018, another 157 patients were prospectively enrolled (Fig. 1).

This study was approved by our local ethical committee according to the Helsinki Declaration of the World Medical Association (2000). All patients were informed and gave written consent before the study.

2.2. IE diagnosis

The diagnostic criteria for IE were based on the modified Duke criteria, requiring confirmation by pathology of the presence of vegetation or intracardiac abscesses and fulfillment of clinical criteria: 2 major, or 1 major plus 3 minor, or 5 minor criteria.

2.3. Blood culture

Blood samples for culture were drawn under sterile conditions and processed using BD BACTEC™ Blood Culture Media (Becton, Dickinson and Company, Franklin Lakes, NJ, USA). For each patient, the number of cultures, the positive or negative status of the culture, and the causative microorganism were recorded.

2.4. Echocardiographic assessment

The patients underwent transthoracic and transesophageal echocardiographic examinations for an assessment of the site and size of the vegetation, the extension of the abscess, and the leaflet movement.

2.5. Study variables and endpoints

The study population's demographic characteristics; history of cardiac diseases; history of IE; signs and symptoms; sites of infection; causative microorganisms; surgical treatments; antibiotic therapies; outcomes; complications; and clinical, laboratory, and echocardiographic features were recorded.

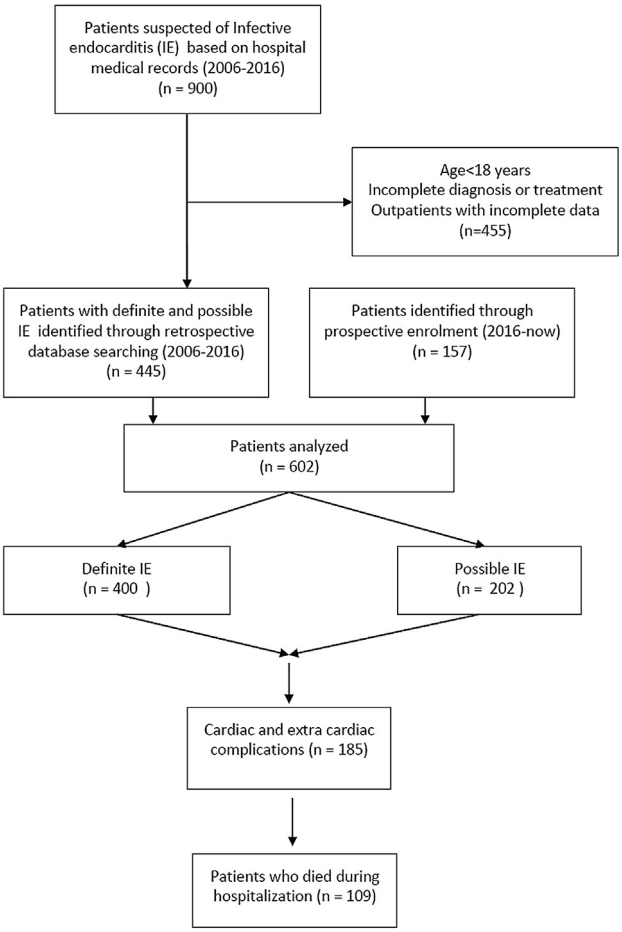

Fig. 1. Enrollment protocol of patients with definite or possible infective endocarditis.

Complications including embolic events (systemic or cerebral), heart failure, mycotic aneurysms, prosthetic valve dysfunction, acute renal failure, increasing vegetation size or new abscesses, septic shock, and persistent fever (>7 d) were recorded

The duration of follow-up was defined as the interval from the first day of hospitalization to the day of death or, if alive, up to the discharge day.

2.6. Statistics

The statistical analyses were performed with the SPSS software, version 16, for Windows (SPSS Inc, Chicago, Illinois). The results are presented as the mean ± the standard deviation (SD) for the quantitative variables and summarized by absolute frequencies and percentages for the categorical variables.

The one-sample Kolmogorov–Smirnov test was used to evaluate the distribution of the data, and the independent *t*-test or the Mann–Whitney *U* test was applied to compare the mean of the variables between the 2 groups. The qualitative data were compared using the χ^2 test or the Kruskal–Wallis test (ordinal variables). The logistic regression model was applied for multivariable analysis. A *P* value of less than 0.05 was considered statistically significant.

3. Results

The study population consisted of 602 patients, including 407 (67.6%) men, at a mean age of 46 ± 16.8 years. Based on the modified Duke criteria, 400 (66.4%) patients had definite and 202 (33.6%) had possible IE. Left-sided IE was reported in 535 patients: native valve

IE in 412 (68.4%) and left-sided prosthetic valve IE in 123 (20.4%). Right-sided IE was reported in 266 patients: native endocarditis in 245 (40.7%) and right-sided prosthetic endocarditis in 21 (3.5%).

3.1. Predisposing factors and symptoms

The study population's baseline characteristics, predisposing factors, signs and symptoms, and clinical examination and laboratory findings on admission are depicted in Table 1.

The most common underlying heart diseases for IE were CHDs (37%) and specifically, bicuspid aortic valves (BAVs) and ventricular septal defects (VSDs). Degenerative heart diseases (16.3%), including flail mitral valves and mitral valve prolapse (MVP), comprised the second most frequent underlying heart diseases for IE. In addition, intravenous drug use (12%), prosthetic valves (11%), previous IE (8%), RHDs (8%), and device-related IE (6%) accounted for the other predisposing factors for IE development (Fig. 2).

The most common chief complaint was fever (92%); additionally, cardiac murmurs were detected in 80% of the patients, loss of appetite in 25%, and splenomegaly in 24% (Table 1).

The mean of white blood cell (WBC) was 10269 ± 47, hemoglobin 10.3 ± 2, erythrocyte sedimentation rate was 56.4 ± 30, and the mean C-reactive protein level was 41.6 ± 48.3. An increased erythrocyte sedimentation rate (>20) was reported in 381 (63.3%) patients, an increased C-reactive protein level (>3) in 285 (47.3%), and a hemoglobin level of less than 12 g/100 mL in 473 (78.7%).

3.2. Causative microorganisms of IE

Two or more positive blood cultures with the same microorganism were reported in 296 (49%) patients. The most frequently isolated microorganism in the blood cultures was *Staphylococcus aureus* (*S. aureus*) (10%), followed by enterococci (9%), coagulase-negative staphylococci (8%), and *Streptococcus viridans* (*S. viridans*) (6%). *S. aureus*, enterococci, and coagulase-negative staphylococci were more prevalent in the patients with native valve endocarditis (including RHDs and degenerative heart diseases), but *S. viridans* was the leading cause of IE in those with CHDs.

Surgical interventions including valve replacement, residual defect repair, tricuspid valve excision without replacement, lead extraction, and large vegetation extraction were performed on 345 (57%) patients. The mean vegetation size was 3.12 ± 1.5 cm, and the most frequent sites of vegetation were the mitral valve (251 cases), the aortic valve (251 cases), the tricuspid valve (114 cases), and the pulmonary valve (22 cases).

Cardiac or extra-cardiac complications occurred in 56.6% of the study patients. Among the cardiac complications, heart failure was the most common (7%), followed by new abscesses (6%) and mitral-aortic intervalvular fibrosa pseudoaneurysms.

There was a significant relationship between the IE cardiac complications and *S. viridans* ($P = 0.04$), *Pseudomonas* ($P = 0.03$), and *Serratia marcescens* ($P = 0.005$). A significant relationship also existed between the extra-cardiac complications of IE and *S. aureus* ($P = 0.005$), enterococci ($P = 0.05$), *Klebsiella* ($P = 0.01$), and *S. saprophyticus* ($P = 0.01$).

Table 1
Predisposing factors, symptom and clinical examination and laboratory findings of patients with Infective Endocarditis.

	Patients with IE (n = 602)
Predisposing factors	
Congenital heart disease	223(37%)
Degenerative heart disease	98(16.3%)
Intravenous drug user	76(12.6%)
Prosthetic valve	67(11.1%)
Previous infective endocarditis	54(8.9%)
Chronic rheumatic heart disease	51(8.4%)
Device related IE	36(6.1%)
Symptoms and clinical examination	
Fever (chief complaint)	553(91.9%)
Cardiac Murmur	484(80.4%)
Loss of appetite	151(25.1%)
Splenomegaly	107(24.0%)

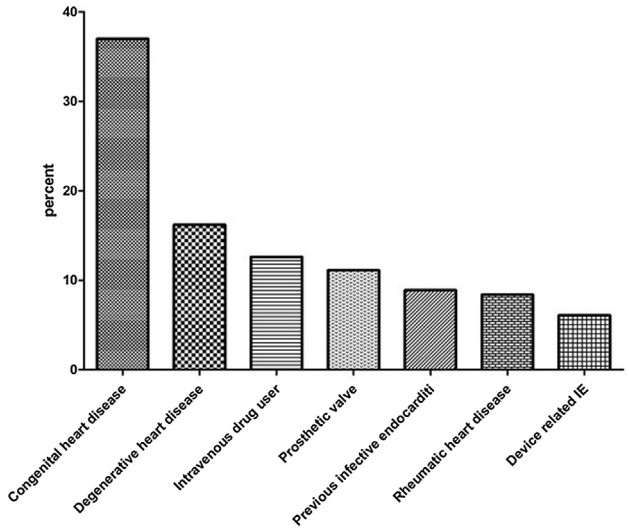

Fig. 2. Underlying heart disease in patients with infective endocarditis.

In-hospital mortality occurred in 109 (18%) patients, 45 of whom had surgical interventions. The relationship between mortality and surgical interventions was statistically significant in that the mortality rate was lower among the patients who underwent surgical interventions (63 patients with no surgery vs 45 patients with surgery) ($P < 0.001$).

In the multivariate analysis, the independent risk factors for mortality in the study population were age (95% CI: 1.004–1.048, $P = 0.02$) and *S. aureus* (95% CI: 1.973–11.187, $P < 0.001$).

A lower mortality rate in the study population was associated with *S. viridans*, degenerative heart diseases, CHDs, and cardiac surgical interventions (Table 2).

4. Discussion

The IRIE is the largest case-series study of patients with IE in Middle-Eastern countries (16).

The main findings of our study can be summarized as follows:

1. CHDs are the most common underlying heart diseases (37%) in patients presenting with IE in Iran.
2. The most frequent predisposing factors and underlying heart diseases for IE are CHDs (37%) and in particular, BAVs and VSDs. Degenerative heart diseases (16.3%), including flail mitral valves and MVP, comprise the second most common underlying heart diseases for IE. These 2 groups can be considered a high-risk group for IE. Our findings are contrary to previously reported data in developing countries identifying RHDs as the main cause of IE.
3. IE in Iran has a male predominance and occurs at a young age (mean age = 45 y), when the individual is expected to be at peak physical activity. Further, IE can cause high morbidity and mortality bearing in mind that more than 50% of patients with IE are liable to develop one form of cardiac or extra-cardiac complication.
4. Our data indicate a high burden of IE on community resources. More than half of our patients needed surgical interventions, along with prolonged hospitalization lengths and intensified needs for extensive antibiotic therapy and intensive care.
5. We found a high rate of blood culture-negative IE insofar as only 49% of our patients had typical positive blood cultures.
6. Despite diagnostic and therapeutic advances, IE continues to cause high mortality (18% in-hospital mortality) and morbidity rates. More than half of our patients with IE had cardiac or extra-cardiac complications.

Table 2
Baseline characteristics, predisposing factors, and clinical and laboratory findings of IE patients who died and those who survived.

	Univariate analysis			Multivariate analysis	
	Dead	Survived	p-value	Odds ratio (CI95%)	p-value
Age	54.90 ± 17.99	44.08 ± 15.90	P < 0.001	1.026 (1.004–1.048)	0.02
Sex (male)	72(66.1)	335(68)	0.70		
Device related IE	8(7.5)	28(5.8)	0.50		
Intravenous drug abuser	9(8.3)	67(13.6)	0.12		
Degenerative heart disease	10(9.2)	88(17.8)	0.02	0.884 (0.301–2.616)	0.82
Congenital heart disease	18(16.5)	208(41.6)	>0.001	0.987 (0.376–2.587)	0.97
Causative germ					
Staphylococcus aureus	25(22.9)	38(7.7)	>0.001	4.698 (1.97–11.18)	>0.001
Enterococci	13(11.9)	43(8.7)	0.29		
Coagulase negative staphylococci	15(13.8)	31(6.3)	0.008	1.723 (0.458–6.482)	0.42
Streplococcus viridans	0(0)	39(7.9)	0.002	0.001 (0.0001–0.009)	0.99
Cardiac surgical intervention	46 (42.2)	299(60.8)	>0.001	0.589 (0.290–1.195)	0.14
Cerebral embolic events on admission	36(39.6)	79(19.3)	>0.001	1.223 (0.570–2.622)	0.60

Although there is a global trend of increasing age among patients with IE, many studies have reported large epidemiological differences between the continents and even within a continent. The mean age of our patients was 45 years, which is very close to the mean age of 47 years among the patients in a study on IE in Turkey. The age of our study population is significantly lower than the pooled mean age for the occurrence of the disease reported in a systematic review of 160 studies on the epidemiological aspects of IE in 2013 (57.2 y) [17].

The existing literature contains a considerable number of studies on IE; still, there are remarkable differences between the studies concerning not only the underlying heart diseases but also the epidemiological, microbiological, and prognostic aspects of IE in each population. These disparities exist both between developed and developing countries and between Mediterranean and Middle Eastern countries. RHDs, suggested as the chief culprit for IE in developing countries, were not the main underlying heart disease in our study. Indeed, only 8.4% of our patients with IE suffered from RHDs, making them the sixth most common underlying cardiac disease in our study.

A recent study compared epidemiological data on IE in Mediterranean countries and reported remarkable differences with respect to the patients' age, causative microorganisms, and underlying heart diseases between these countries. Based on the classification in that study, patients with IE in northern Mediterranean countries were old (>50 y), *S. aureus* was the main causative microorganism, and prosthetic valves or intracardiac implanted devices were the major predisposing factors. Additionally, patients with IE in southern Mediterranean countries were young (<40 y), *S. viridans* was the prevalent etiological agent, and RHDs constituted the principal risk factors. Moreover, patients with IE in eastern Mediterranean countries were aged between 45 and 60 years, *S. viridans* was the main causative microorganism, and the incidence of RHDs varied between 8% and 66% [16,18].

One of the most interesting findings in the IRIE was the prevalence of the underlying heart diseases in the patients with IE insofar as CHDs (including BAVs and VSDs) and degenerative heart diseases (including MVP) accounted for more than half of the underlying cardiac diseases and were, thus, the major risk factors for IE. *S. viridans* was the leading cause of IE in the patients suffering from CHDs. Our data chime in with recently published data by Zhu and Zegri-Reiriz, who underlined the changing epidemiology and dominance of BAVs and MVP as the common cause of IE and flagged up BAVs and MVP as high-risk conditions for IE. Zhu and Zegri-Reiriz, having found higher rates of *S. viridans* in their patients with BAVs and MVP, recommended IE antibiotic prophylaxis.

BAVs and MVP, with corresponding prevalence rates of 1–2% and 2.0–3.0%, comprise the most common form of congenital cardiac abnormities and the most frequent predisposing cardiac conditions for IE in some countries, including Iran [16,19–23].

Unrepaired VSDs are another frequent congenital heart abnormality associated with IE. The overall incidence of IE in cases with unrepaired VSDs has been estimated to range between 1.5 and 2.4 per 1000 patient-years. The natural history of VSDs shows that the estimated lifetime risk for IE is 9.7% at age 30 years and 12% by the end of life [24–26].

We found that the frequency of causative microorganisms differed in tandem with the underlying heart disease. According to the IRIE, the most prevalent etiological agent was *S. aureus* (10%), followed by enterococci (9%), coagulase-negative staphylococci (8%), and *S. viridans* (6%).

S. aureus occurs predominantly in community-acquired and nosocomial cases of IE, as has been reported by recent series [10,11,27,28], whereas *S. viridans* was the prevailing etiological agent in previous decades and also in a few recent studies. What is deserving of special note, however, is that the causative microorganism is likely to differ based on the epidemiology of the country and the underlying heart diseases [6,29–31].

Our results showed an association between IE and high mortality (18% in-hospital mortality) and morbidity rates in Iran. Furthermore, the patients with IE who underwent surgical interventions had a lower mortality rate than their counterparts who did not, which is consistent with other published studies [32,33].

In respect of microbiological assessment, typical positive blood cultures were reported in 49% of the patients registered in the IRIE. According to a review of the literature published in developed countries, the presence of a positive blood culture varied from 83% to 96% [34–37]. Indeed, the high rate of blood culture-negative IE (no causative microorganism can be grown using the usual blood culture) in our study (51%) by comparison with the rates of 10–30% of blood culture-negative IE in the European studies and other centers studies make difficulties in antibiotic therapy. The diminished culture positivity rate in the current study can be explained partly by the fact that our tertiary referral hospital admits patients having already been placed on antibiotic treatment by peripheral hospitals.

4.1. Limitation

Our data gathering was heterogeneous on account of the fact that the information was obtained from medical records before the IRIE was established and the local data were prospectively obtained. Consistency was ensured through the use of similar data sheets for the comparison of the retrospective and prospective data. As contributors to the EURO-ENDO Registry, we received good feedback on data entering. The present study does not present data on the midterm follow-up and mortality of our patients; these data will, however, be presently published as a part of the EURO-ENDO Registry [38].

5. Conclusions

According to the IRIE, IE occurs in the younger population in Iran (mean age = 45 y) with high rates of blood culture-negative IE and different underlying heart diseases. CHDs (37%), including

BAVs and VSDs, followed by degenerative heart diseases (16.3%), including flail mitral valves and MVP, were the most common underlying heart diseases. These 2 groups can be considered a high-risk group for IE and in need of IE prophylaxis. More than half of our patients with IE had cardiac or extra-cardiac complications. The IRIE showed that in addition to the need for adherence to the European and American guidelines, the preventive and treatment policies for IE should be redefined in each country.

Declaration of Competing Interest

None.

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References

[1] D.R. Murdoch, G.R. Corey, B. Hoen, J.M. Miro, V.G. Fowler Jr., A.S. Bayer, A.W. Karchmer, L. Olaison, P.A. Pappas, P. Moreillon, S.T. Chambers, V.H. Chu, V. Falco, D.J. Holland, P. Jones, J.L. Klein, N.J. Raymond, K.M. Read, M.F. Tripodi, R. Utili, A. Wang, C.W. Woods, C.H. Cabell, Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century: the International Collaboration on Endocarditis-Prospective Cohort Study, Arch. Intern. Med. 169 (5) (2009) 463–473.

[2] X. Duval, F. Delahaye, F. Alla, P. Tattevin, J.F. Obadia, V. Le Moing, T. Doco-Lecompte, M. Celard, C. Poyart, C. Strady, C. Chirouze, M. Bes, E. Cambau, B. Iung, C. Selton-Suty, B. Hoen, Temporal trends in infective endocarditis in the context of prophylaxis guideline modifications: three successive population-based surveys, J. Am. Coll. Cardiol. 59 (22) (2012) 1968–1976.

[3] C. Selton-Suty, M. Celard, V. Le Moing, T. Doco-Lecompte, C. Chirouze, B. Iung, C. Strady, M. Revest, F. Vandenesch, A. Bouvet, F. Delahaye, F. Alla, X. Duval, B. Hoen, Preeminence of Staphylococcus aureus in infective endocarditis: a 1-year population-based survey, Clin. Inf. Dis.: Off. Publ. Inf. Dis. Soc. Am. 54 (9) (2012) 1230–1239.

[4] B. Hoen, F. Alla, C. Selton-Suty, I. Beguinot, A. Bouvet, S. Briancon, J.P. Casalta, N. Danchin, F. Delahaye, J. Etienne, V. Le Moing, C. Leport, J.L. Mainardi, R. Ruimy, F. Vandenesch, Changing profile of infective endocarditis: results of a 1-year survey in France, JAMA 288 (1) (2002) 75–81.

[5] J.R. Carapetis, A.C. Steer, E.K. Mulholland, M. Weber, The global burden of group A streptococcal diseases, Lancet. Infect. Dis. 5 (11) (2005) 685–694.

[6] E. Marijon, P. Ou, D.S. Celermajer, B. Ferreira, A.O. Mocumbi, D. Jani, C. Paquet, S. Jacob, D. Sidi, X. Jouven, Prevalence of rheumatic heart disease detected by echocardiographic screening, New England J. Med. 357 (5) (2007) 470–476.

[7] H.S. Yew, D.R. Murdoch, Global trends in infective endocarditis epidemiology, Curr. Inf. Dis. Reports 14 (4) (2012) 367–372.

[8] M.D. Seckeler, T.R. Hoke, The worldwide epidemiology of acute rheumatic fever and rheumatic heart disease, Clin. Epidemiol. 3 (2011) 67–84.

[9] D.D. Correa de Sa, I.M. Tleyjeh, N.S. Anavekar, J.C. Schultz, J.M. Thomas, B.D. Lahr, A. Bachuwar, M. Pazdernik, J.M. Steckelberg, W.R. Wilson, L.M. Baddour, Epidemiological trends of infective endocarditis: a population-based study in Olmsted County, Minnesota, Mayo Clinic Proc. 85 (5) (2010) 422–426.

[10] L.M. Baddour, W.R. Wilson, A.S. Bayer, V.G. Fowler Jr., A.F. Bolger, M.E. Levison, P. Ferrieri, M.A. Gerber, L.Y. Tani, M.H. Gewitz, D.C. Tong, J.M. Steckelberg, R.S. Baltimore, S.T. Shulman, J.C. Burns, D.A. Falace, J.W. Newburger, T.J. Pallasch, M. Takahashi, K.A. Taubert, Infective endocarditis: diagnosis, antimicrobial therapy, and management of complications: a statement for healthcare professionals from the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease in the Young, and the Councils on Clinical Cardiology, Stroke, and Cardiovascular Surgery and Anesthesia, American Heart Association: endorsed by the Infectious Diseases Society of America, Circulation 111 (23) (2005) e394–e434.

[11] V.G. Fowler Jr., J.M. Miro, B. Hoen, C.H. Cabell, E. Abrutyn, E. Rubinstein, G.R. Corey, D. Spelman, S.F. Bradley, B. Barsic, P.A. Pappas, K.J. Anstrom, D. Wray, C. Q. Fortes, I. Anguera, E. Athan, P. Jones, J.T. van der Meer, T.S. Elliott, D.P. Levine, A.S. Bayer, Staphylococcus aureus endocarditis: a consequence of medical progress, JAMA 293 (24) (2005) 3012–3021.

[12] A.J. Mansur, M. Grinberg, R.H. Cardoso, P.L. da Luz, G. Bellotti, F. Pileggi, Determinants of prognosis in 300 episodes of infective endocarditis, Thorac. Cardiovasc. Surg. 44 (1) (1996) 2–10.

[13] R.O. Netzer, E. Zollinger, C. Seiler, A. Cerny, Infective endocarditis: clinical spectrum, presentation and outcome. An analysis of 212 cases 1980–1995, Heart (British Cardiac Society) 84 (1) (2000) 25–30.

[14] G. Habib, P. Lancellotti, M.J. Antunes, M.G. Bongiorni, J.P. Casalta, F. Del Zotti, R. Dulgheru, G. El Khoury, P.A. Erba, B. Iung, J.M. Miro, B.J. Mulder, E. Plonska-Gosciniak, S. Price, J. Roos-Hesselink, U. Snygg-Martin, F. Thuny, P. Tornos Mas, I. Vilacosta, J.L. Zamorano, 2015 ESC Guidelines for the management of infective endocarditis: The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM), Europ. Heart J. 36 (44) (2015) 3075–3128.

[15] B. Hajihossainlou, M.A. Heidarnia, B. Sharif Kashani, Changing pattern of infective endocarditis in Iran: a 16 years survey, Pakistan J. Med. Sci. 29 (1) (2013) 85–90.

[16] F. Gouriet, H. Chaudet, P. Gautret, L. Pellegrin, V.P. de Santi, H. Savini, G. Texier, D. Raoult, P.E. Fournier, Endocarditis in the Mediterranean Basin, New Microbes New Infect. 26 (2018) S43–S51.

[17] L. Slipczuk, J.N. Codolosa, C.D. Davila, A. Romero-Corral, J. Yun, G.S. Pressman, V.M. Figueredo, Infective endocarditis epidemiology over five decades: a systematic review, PloS One 8 (12) (2013) e82665.

[18] S. Simsek-Yavuz, A. Sensoy, H. Kasikcioglu, S. Ceken, D. Deniz, A. Yavuz, F. Kocak, K. Midilli, M. Eren, I. Yekeler, Infective endocarditis in Turkey: aetiology, clinical features, and analysis of risk factors for mortality in 325 cases, Int. J. Infect. Dis.: IJID: Off. Publ. Int. Soc. Infect. Dis. 30 (2015) 106–114.

[19] R.P. Beynon, V.K. Bahl, B.D. Prendergast, Infective endocarditis, BMJ (Clinical Research Ed). 333 (7563) (2006) 334–339.

[20] T.J. Cahill, B.D. Prendergast, Infective endocarditis, Lancet (London, England) 387 (10021) (2016) 882–893.

[21] S.C. Siu, C.K. Silversides, Bicuspid aortic valve disease, J. Am. Coll. Cardiol. 55 (25) (2010) 2789–2800.

[22] I. Zegri-Reiriz, A. de Alarcon, P. Munoz, M. Martinez Selles, V. Gonzalez-Ramallo, J.M. Miro, C. Falces, C. Gonzalez Rico, X. Kortajarena Urkola, J.A. Lepe, R. Rodriguez Alvarez, J.M. Reguera Iglesias, E. Navas, F. Dominguez, P. Garcia-Pavia, Infective endocarditis in patients with bicuspid aortic valve or mitral valve prolapse, J. Am. Coll. Cardiol. 71 (24) (2018) 2731–2740.

[23] W. Zhu, Q. Zhang, J. Zhang, The changing epidemiology and clinical features of infective endocarditis: a retrospective study of 196 episodes in a teaching hospital in China, BMC Cardiovasc. Disorders 17 (1) (2017) 113.

[24] W.M. Gersony, C.J. Hayes, D.J. Driscoll, J.F. Keane, L. Kidd, W.M. O'Fallon, D.R. Pieroni, R.R. Wolfe, W.H. Weidman, Bacterial endocarditis in patients with aortic stenosis, pulmonary stenosis, or ventricular septal defect, Circulation 87 (2 Suppl) (1993) I121–I126.

[25] C.D. Morris, M.D. Reller, V.D. Menashe, Thirty-year incidence of infective endocarditis after surgery for congenital heart defect, JAMA 279 (8) (1998) 599–603.

[26] D.J. Penny, G.W. Vick 3rd., Ventricular septal defect, Lancet (London, England) 377 (9771) (2011) 1103–1112.

[27] S. Mouly, R. Ruimy, O. Launay, F. Arnoult, E. Brochet, J.L. Trouillet, C. Leport, M. Wolff, The changing clinical aspects of infective endocarditis: descriptive review of 90 episodes in a French teaching hospital and risk factors for death, J. Infect. 45 (4) (2002) 246–256.

[28] C.H. Cabell, E. Abrutyn, V.G. Fowler Jr., B. Hoen, J.M. Miro, G.R. Corey, L. Olaison, P. Pappas, K.J. Anstrom, J.A. Stafford, S. Eykyn, G. Habib, C.A. Mestres, A. Wang, Use of surgery in patients with native valve infective endocarditis: results from the International Collaboration on Endocarditis Merged Database, Am. Heart J. 150 (5) (2005) 1092–1098.

[29] E. Cecchi, D. Forno, M. Imazio, A. Migliardi, R. Gnavi, I. Dal Conte, R. Trinchero, New trends in the epidemiological and clinical features of infective endocarditis: results of a multicenter prospective study, Ital. Heart J.: Off. J. Ital. Fed. Cardiol. 5 (4) (2004) 249–256.

[30] S. Cicalini, V. Puro, C. Angeletti, P. Chinello, G. Macri, N. Petrosillo, Profile of infective endocarditis in a referral hospital over the last 24 years, J. Infect. 52 (2) (2006) 140–146.

[31] H. Nissen, P.F. Nielsen, M. Frederiksen, C. Helleberg, J.S. Nielsen, Native valve infective endocarditis in the general population: a 10-year survey of the clinical picture during the 1980s, Eur. Heart J. 13 (7) (1992) 872–877.

[32] J. Galvez-Acebal, M. Almendro-Delia, J. Ruiz, A. de Alarcon, F.J. Martinez-Marcos, J.M. Reguera, R. Ivanova-Georgieva, M. Noureddine, A. Plata, J.M. Lomas, J. de la Torre-Lima, C. Hidalgo-Tenorio, R. Luque, J. Rodriguez-Bano, Influence of early surgical treatment on the prognosis of left-sided infective endocarditis: a multicenter cohort study, Mayo Clin. Proc. 89 (10) (2014) 1397–1405.

[33] D.H. Kang, Y.J. Kim, S.H. Kim, B.J. Sun, D.H. Kim, S.C. Yun, J.M. Song, S.J. Choo, C.H. Chung, J.K. Song, J.W. Lee, D.W. Sohn, Early surgery versus conventional treatment for infective endocarditis, New England J. Med. 366 (26) (2012) 2466–2473.

[34] J. Fortun, T. Centella, P. Martin-Davila, M.J. Lamas, C. Perez-Caballero, L. Fernandez-Pineda, E. Otheo, J. Cobo, E. Navas, V. Pintado, E. Loza, S. Moreno, Infective endocarditis in congenital heart disease: a frequent community-acquired complication, Infection 41 (1) (2013) 167–174.

[35] T. Lalani, C.H. Cabell, D.K. Benjamin, O. Lasca, C. Naber, V.G. Fowler Jr., G.R. Corey, V.H. Chu, M. Fenely, O. Pachirat, R.S. Tan, R. Watkin, A. Ionac, A. Moreno, C.A. Mestres, J. Casabe, N. Chipigina, D.P. Eisen, D. Spelman, F. Delahaye, G. Peterson, L. Olaison, A. Wang, Analysis of the impact of early surgery on in-hospital mortality of native valve endocarditis: use of propensity score and instrumental variable methods to adjust for treatment-selection bias, Circulation 121 (8) (2010) 1005–1013.

[36] R.W. Sy, C. Chawantanpipat, D.R. Richmond, L. Kritharides, Development and validation of a time-dependent risk model for predicting mortality in infective endocarditis, Eur. Heart J. 32 (16) (2011) 2016–2026.

[37] M. Yoshinaga, K. Niwa, A. Niwa, N. Ishiwada, H. Takahashi, S. Echigo, M. Nakazawa, Risk factors for in-hospital mortality during infective endocarditis in patients with congenital heart disease, Am. J. Cardiol. 101 (1) (2008) 114–118.

[38] G. Habib, P. Lancellotti, P.A. Erba, A. Sadeghpour, M. Meshaal, A. Sambola, et al., Cohort profile The ESC-EORP EURO-ENDO (European Infective Endocarditis) registry, Eur. Heart J. Qual. Care Clin. Outcomes (2019), https://doi.org/10.1093/ehjqcco/qcz018, pii: qcz018.