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REVIEW

Staphylococcus aureus infective endocarditis at a tertiary Tunisian hospital. A changing profile?

Meriem Drissa *, Farah Amani, Habiba Drissa

Cardiology Department of La Rabta Hospital, Tunis, Tunisia

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Contents

1. Introduction

Despite all improvements in diagnostic imaging modalities, antibiotherapy regimens, and surgical methods, the frequency of *Staphylococcus aureus* infective endocarditis (SAIE) increases constantly and is associated with poor prognosis.

1.1. Aim of work

To update current knowledge on the epidemiology and the echocardiographic profile of SAIE in Tunisian hospital, and to determine the prognosis and predicting factors of mortality during this affectation.

2. Methods

This was a retrospective study which included 230 consecutive patients diagnosed with infective endocarditis (IE) and hospitalized in the cardiology department of Rabta hospital between 1996 and 2016. *SAIE* accounts for 30% of cases (70 patients). We included patients who were diagnosed with definite infective endocarditis based on the modified Ducke criteria.

Patients diagnosed with 'possible IE' based on these same criteria were excluded.

The patients were divided into two groups according to the date of diagnosis: group A (30 patients from January 1996 to June 2006) and group B (40 patients from June 2006 to December 2016). These groups were compared for epidemiologic factors, echocardiographic factors, and clinical outcome differences.

Data was extracted from the medical records of the patients. We analyzed the following informations: age, gender, comorbidities, conditions which predispose patients for IE, imaging assessment (transthoracic echocardiography (TTE) and/or

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* Corresponding author.
E-mail addresses: meriemdrissa@yahoo.fr (M. Drissa), akramhorizon@yahoo.fr (F. Amani).

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transesophageal echocardiography (TEE), cerebral tomography scan data), cardiac complications of SAIE, surgical treatment regimens, early outcome of IE, and in-hospital mortality data.

Tomography scan imaging was performed in 40% of cases: 8 patients in group A (28% of cases) and 20 patients in group B (50% of cases).

3. Statistical analysis

Quantitative variables are expressed as means ± the standard deviation. The normal distribution of variables was verified with the Shapiro-Wilk test.

Comparison between groups were carried out using Student's *t*-test or the Chi^2 test depending on the nature of quantitative or qualitative variables.

Single-variable then multivariate analyses were conducted in order to determine factors predicting mortality using a logistic regression model. A p-value under 0.05 was considered significant for all tests.

4. Results

The male-to-female ratio was 1.91. The mean age was 39 ± 10 years. SAIE involved prosthetic valve or surgical valve repair in 16 patients (23%) and a native valve in 54 patients (77%). Rheumatic heart disease was the most common predisposing factor for SAIE (95%). Four patients (5%) had degenerative valvular disease.

A debilitated clinical setting was observed in 32 patients (45%) of cases. Diabete (n = 17), cirrhosis (n = 6), and severe chronic renal failure (n = 9) were the most common ones. The means of entry was identified in 38 of cases (55%). Two of these were cutaneous (n = 36) and digestive (n = 2). *Staphylococcus aureus* was resistant to meticillin in 12 patients (17%). A combination of the two imaging modalities (TTE and TEE) demonstrated the presence of vegetation in 92% of patients, with an average size of 20 mm [05–35 mm]. Both valve abscess and valve mutilation were present in 14 patients (20%). A prosthetic valve dehiscence with severe regurgitation was observed in 7 patients (10%).

The most frequently reported complications were congestive heart failure (n = 35, 50% of cases), systemic embolism including central nervous systemic (CNS) and spleen location (n = 28, 40% of cases), neurological events (n = 26, 38% of cases), and sepsis (n = 21, 30% of cases). Thirty two patients (45%) underwent early surgery for valve replacement or valve repair. The average waiting time for surgery was 10 days with extremes ranging from 1 to 21 days. The rate of in-hospital mortality was 27% (n = 19).

Table 1
Predictive factors of mortality in univariate analysis.

	Death n: 18	Survival n: 52	p
Age	39 ± 3	37 ± 4	0.04
gender (H/F) 45/25	15/10	30/15	0.8
Cirrhosis	2 (11.1%)	4 (7%)	0.6
With Renal failure	3 (16%)	6 (11%)	0.7
Diabete	7 (38.33%)	10 (20%)	0.6
Prosthetic endocarditis	11 (68%)	5 (9%)	0.001
Heart failure	15 (83%)	20 (38%)	0.001
Severe sepsis	14 (77%)	7 (14%)	0.001
Systemic embolism	15 (83%)	13 (25%)	0.04
Neurological complications	12 (66%)	14 (27%)	0.001
Vegetation lenght	16 (88%)	48 (84%)	0.4
Abscess	11 (61%)	3 (5%)	<0.001
Mutilation	6 (33%)	8 (15%)	0.5
Prosthetic dehiscence with severe régurgitation	5 (27%)	2 (3%)	0.001
Meti R Staphylococcus	9 (50%)	3 (5%)	<0.001

Table 2
Predictor factors of mortality in multivariate analysis.

	OR	*CI*	*p*
AGE	1.2	[1–1.34]	0.8
prosthetic IE	2.2	[1.2–3.9]	0.006
abscess	1.7	[1.1–3.3]	0.03
Meti R Staphylococcus	1.5	[0.8–2.9]	0.2
Heart failure	5.2	[2–14.7]	**0.001**
sepsis	3.4	(1.8–5)	**0.004**
Systemic embolism	2.5	(1.1–7.5)	**0.04**
Neurological complications	0.76	(0.38–3)	0.25
Early surgery	0.4	(0.22–0.7)	**0.003**

Table 3
Patients characteristics: comparison between two groups A and B.

	Group A n : 30	Group B n :40	p
Age	35 ± 10	36 ± 9	0.8
Gender (M/F)	20/10	25/15	0.5
rheumatic valve disease	24 (80%)	27 (76)	0.6
Diabete	6 (20%)	11 (27.5%)	0.55
Cirrhosis	3 (10%)	3 (7.5%)	0.7
Severe renal failure	3 (10%)	6 (15%)	0.6
Prosthetic endocarditis	5 (17%)	11 (27%)	0.1
Abscess	3 (10%)	11 (28%)	0.680
Végétation	24 (80%)	40 (100%)	0.580
Perforation	5 (16%)	9 (22.5%)	0.7
Dehiscence of prosthetic	3 (30%)	4 (10%)	0.06
Meti R staphylococcus	3 (10%)	6 (15%)	0.4
Heart failure	15 (30%)	20 (50%)	0.06
Sepsis	13 (45%)	8 (20%)	0.04
Neurological complication	11 (37%)	15 (37.5%)	0.06
Systemic embolism	8 (28%)	20 (50%)	0.04
Early surgery	8 (26.66%)	24 (60%)	0.01
Hospital mortality (%)	13 (43%)	5 (13%)	0.04

Factors associated with in-hospital mortality through single-variable analysis (Table 1) were: age, prosthetic valve endocarditis, abscess, heart failure, severe sepsis, neurological complications, systemic embolic, and methicillin resistant (meti R) staphylococcus infection. Early surgery was associated with significantly lower hospital mortality.

Independent factors of hospital mortality during SAIE were: prosthetic valve endocarditis, abscess, septic complications, heart failure, and systemic embolism. Early surgery was significantly associated with lower hospital mortality (Table 2).

There was not a significant difference between the two periods of study concerning the age, sex, incidence of rheumatic valve disease, or the prosthestic EI associated with the patients (Table 3). Between the two period of study, there were no significant decreases in the proportions of annular abscess, vegetation, and valve perforation. Heart failure and neurological events rates were stable and similar in the two groups.

There was a significant decrease in the proportions of sepsis whereas the systemic embolism rate tended to increase over time. The early surgery rate increased significantly between the two consecutive periods. The in-hospital mortality is lower in group B (Table 3).

5. Discussion

The major findings of our study are as follows (1) Rheumatic valve disease was the predominant predisposing heart disease for SAIE, (2) the most common complication by far was heart failure (50%), (3) the global in-hospital mortality rate of SAIE continues to be high (27%), (4) independent factors of in-hospital mortality

are: prosthetic valve endocarditis, abscess, septic complications, heart failure, and systemic embolisms. Early surgery was significantly associated with lower in-hospital mortality, (5) comparison of the two periods revealed an increase in systemic embolism rate and a need for earlier surgery and a decrease in the rate of in-hospital mortality.

Staphylococcus aureus is the leading cause of infective endocarditis (IE) in many regions of the world.[1–3] It is a malignant disease which has now emerged as a dominant cause of IE.[4] The frequency of SAIE increases constantly and was recently estimated at between 25% and 50% of all cases of IE.[5,6] In our study, SAIE accounted for 30% of cases of IE.

SAIE occurs in a more debilitated clinical setting, including chronic renal failure, hemodialysis, diabetes mellitus, hematologic malignancy, and immunodepression.[1,7–9] This finding was also reported in 45% of cases in this study. SAIE remains a disease with high incidences of complications.[10–13] Cardiac failure may be present on admission or, more frequently, develops during hospitalization in 28–41% of patients with left-sided endocarditis.[14] In our study, a high frequency of heart failure cases was reported because we had included a prosthetic valve dehiscence cases that frequently developed heart failure signs.

Previous studies have noted a higher incidence of neurological events in patients with S. aureus[15–17] and estimate that 43.3% of patients with SAIE presented a neurological complication rate 2–3 times higher than that observed with other pathogens.[18] The high rate of 38% for neurological complications observed in our study corroborates the findings of other studies.

The true incidence of embolic events in our study may have been underestimated (40%) because of a less frequently-used imaging technique (scan tomography).

S. aureus is a malignant disease known to be responsible for severe sepsis[4,8] and poor prognosis.[19] In this study, we reported this complication in 20% of patients.

Early Surgery has become a necessity in the therapy of complicated IE.[2,20,21] It was performed in our study in 45% of patients, compared with 26.2% in published series on both right and left-sided native-valve SAIE.[10] This rate may be explained by the fact that we had included prosthetic endocarditis in our study.

Fiederspiel et al.[22] recently reported nearly a 60% increased risk of in-hospital mortality from SAIE compared with streptococcal and enterococcal endocarditis.

In-hospital mortality rates range between 30% and 71% according to various authors.[2,23] The in-hospital mortality rate in our study was 27%. Abdallh reported similar results[24] when including all types of SAIE (i.e. prosthetic valve, pacemaker, etc.), which ranged from 20% to 37%. The high in-hospital mortality rate reported in our study was due to the high frequency of complications.

Prosthetic infective endocarditis, abscess, severe sepsis, congestive heart failure, systemic embolism events, and the lack of early surgery were the risks factor of mortality. These same risk factors were also found in many series.[8,7,10]

S. aureus prosthetic valve infective endocarditis (SA PVIE) is a factor associated with high mortality rates reported in our study and several others.[25,26]

As previously reported in published series devoted to right and left-sided native-valve SAIE,[10] heart failure is a powerful predictor of in-hospital mortality.

Severe sepsis is a major prognostic predictor of in-hospital mortality and long-term mortality[8] because severe cases progress towards multiorgan dysfunction, disseminated intravascular coagulation, lactic acidosis, and death.[7,8,4,27,28]

Hoen and colleagues[2] suggested that the decrease in the rate of in-hospital mortality observed in a 10-year interval may have been related to a higher rate of cardiac surgery. Similarly, Lalani et al.[29] reported that patients with SAIE undergoing early surgery had a risk reduction of in-hospital mortality of 20.1% compared with patients treated medically. Similar results were found in this study.

The severe sepsis rate decreased significantly over time, which may be due to better management of antibiotics. The systemic embolism rate tended to increase because of an increased use of systemic tomography in group B (26% in group A, versus 50% in group B). The early surgery rate increased significantly between the two consecutive periods because of higher complications in groupe B. In-hospital mortality decreased over time thanks to better medical and surgical strategies within a multidisciplinary team.[30]

5.1. Limits of our study

- Our study is retrospective and therefore is inevitably subject to bias.
- The long period of the study was imposed by the rarety of this disease.
- The low number of patients despite the long period of study can also be explained by the strict selection criteria.
- Future prospective, multicenter studies are required to validate the results of our study

6. Conclusion

Despide therapeutic advances, SAIE is a still a potentially life-threatening infection associated with high mortality and morbidity rates. It is primarily associated with poor prognosis related to comorbidites, heart failure, as well as septic and embolic events due to the pathogen's aggressive destructive nature.

7. Abbreviation

- *Staphylococcus aureus* Infective Endocarditis (SAIE)
- Infective Endocarditis (IE)
- methicillin Resistant (meti R)
- Transthoracic Echocardiography (TTE)
- Transesophageal Echocardiography (TEE)
- Staphylococcus aureus Prosthetic Valve Infective Endocarditis (SA PVIE)

Conflicts of interest

The authors declare no conflict of interest.

Authors' contributions

All authors had contributed in writing this article.

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