

## Original Research Article

### **Infective endocarditis: experience of the Cardiology Department of the Mohammed VI University Hospital**

**Comment [a1]:** I guess the first letter should be capitalized.

#### **Abstract:**

**Introduction:** Infective endocarditis (IE) is a rare but potentially serious disease. It causes a high mortality and a high level of morbidity and complications. Its epidemiological, clinical and microbiological characteristics have changed in recent years.

**Comment [a2]:** The aim of the research should be mentioned here.

**Materials and methods:** Retrospective study including 110 patients hospitalized for a definite IE, according to the modified DUKE criteria, in the cardiology department of the Mohammed VI University Hospital over a period of 5 years and 10 months from January 2017 to October 2022.

**Comment [a3]:** The statistical method and package used should be mentioned here

**Results:** The average age of our patients was 43 years with a male predominance. The bacterial graft was on native valve in 80% with predominance of rheumatic origin (69%), on cardiac prosthesis in 10% of patients, on healthy heart (4%) and congenital heart disease (6%). The most frequent portal of entry was dental (30%). Blood cultures were positive only in 33% of patients, isolating a staphylococcus (16%), a streptococcus (14%) and a GNB (3%). Transthoracic echocardiography (TTE) showed vegetation in 108 cases, valve perforation in 7 cases, cord rupture in 1 patient and perivalvular abscess in 10 cases. Seventy-seven percent of patients had surgical treatment with a mean delay of 29 days. The overall mortality was 24% with heart failure ( $p < 0.001$ ), renal failure ( $p = 0.004$ ) and neurological complications ( $p = 0.002$ ) as predictive factors of mortality.

**Conclusion:** Infective endocarditis remains a real health problem with a consequent mortality and morbidity. The population is often young, revealing the IE by complications; its prevention is the best way to improve its prognosis.

**Key words:** Infective endocarditis- Entry portal- Echocardiography- Blood culture- Complications- Surgery - Prognosis.

#### **Introduction:**

Despite advances in the diagnosis and management, including surgery, of infective endocarditis (IE), this relatively rare disease remains potentially serious. It causes a high mortality and a high level of morbidity and complications. Its epidemiological, clinical and microbiological characteristics have changed in recent years. In industrialized countries, new risk groups have emerged: intravenous drug users, patients with degenerative valvulopathies linked to the ageing of the population, and the risk factors have changed with an ever-increasing share of infections on implanted devices.

**Comment [a4]:** The introduction section is too scanty without adequate background about infective endocarditis. Please make the introduction more captivating  
-Also, no citation whatsoever can be found in this section, please include citation

The aim of our work is to evaluate the current profile of infective endocarditis in Morocco and to compare it to the global profile.

**Comment [a5]:** The topic and study design didn't encompass the whole of Morocco, the topic focused on cardiology department of the Mohammed VI University Hospital Center, so this aim is inappropriate, author(s) should please take note

### **Materials and Methods:**

We conducted a retrospective study that included 110 patients hospitalized for definite IE, according to the modified DUKE criteria, in the cardiology department of the Mohammed VI University Hospital Center over a period of 5 years and 10 months from January 2017 to October 2022. All patients with infective endocarditis during this period are retained without exclusion criteria

All anamnestic, clinical, paraclinical and therapeutic data were collected from the medical records using an exploitation form.

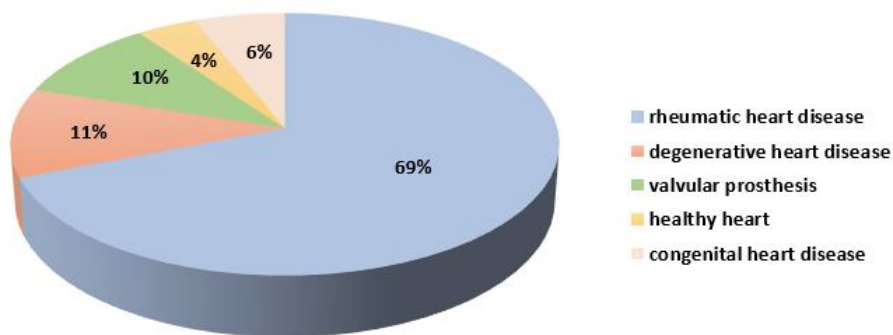
Results were entered and statistical data were analyzed using the SPSS 130 program.

After the hospital phase, most patients were lost to follow-up.

We calculated simple and relative frequencies for the categorical variables. We calculated means, medians and standard deviations and determined extreme values for quantitative values.

### **Results:**

The mean age of our study population was 43 years with a maximum of 75 years and a minimum of 16 years, with a male predominance (sex ratio: 1.8). IE was grafted on native valves in 89 patients (80%) with a predominance of rheumatic origin found in 76 patients (69%), Degenerative damage was observed in 11% of cases. In 10% of the cases, the bacterial graft was performed on a cardiac prosthesis. The heart was healthy in 4% of cases. Six per cent patients were followed for congenital heart disease (Figure 1).

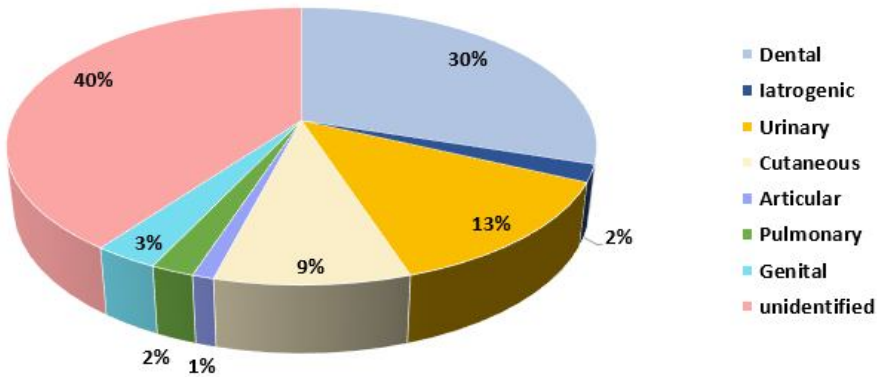


**Figure 1:** Distribution of heart disease underlying infective endocarditis

IE on aortic valves was most frequent in 48%, followed by mitral position 38%, multiple mitro-aortic location was present in 12%.

The portal of entry (POE) was identified in 66 patients (60%). Figure 2 illustrates the distribution of POE: with a dental origin in 33 patients (30%), iatrogenic 2% of cases, urinary in 13% of cases, cutaneous in 9% of cases, articular in 1% of cases, pulmonary in 2% of cases and genital in 3% of cases.

**Comment [a6]:** Material and Method should be sectioned into  
-study area  
-study population  
-study design  
-statistical analysis (which would state the level of significance adopted)

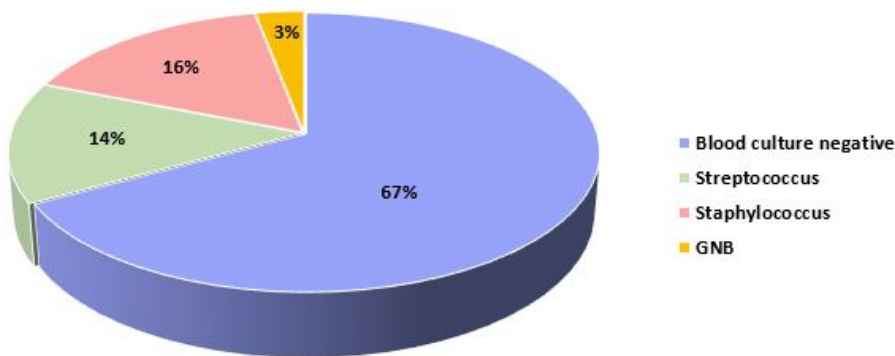


**Figure 2:** Distribution of patients according to portal of entry

The average time to consultation was 41.6 days. The onset of symptoms was progressive in the majority of cases (78%). The reasons for consultation were: fever in 96% of cases, asthenia and anorexia in 79% of our patients, dyspnea in 67% of cases and arthralgia (15%). Physical examination on admission showed a regurgitant murmur in 100 cases and signs of congestive heart failure in 42 patients (38%). Four patients had confusional consciousness on admission and 11 patients had hemiplegia (10%). Splenomegaly was palpated in 13 patients and cutaneous signs were found in 12 patients (11%). These were petechial purpura in 8 patients and erythematous Janeway's placard in 4 patients.

As for morbidity, we noted diabetes in 10% of patients and chronic renal failure in 8%.

Blood cultures were systematically performed in all patients and were positive in 37 cases (33%). The most frequently isolated germ was staphylococcus aureus in 17 cases and coagulase-negative in 1 case; followed by streptococcus, which was identified in 16 patients, including 3 beta hemolytic streptococci, 1 alpha hemolytic streptococci and 1 oral streptococci. Gram-negative bacilli (GNB) were identified in 3 cases, including enterobacter in 2 cases (Figure 3). The percentage of blood culture-negative IEs was high in our series (67%).



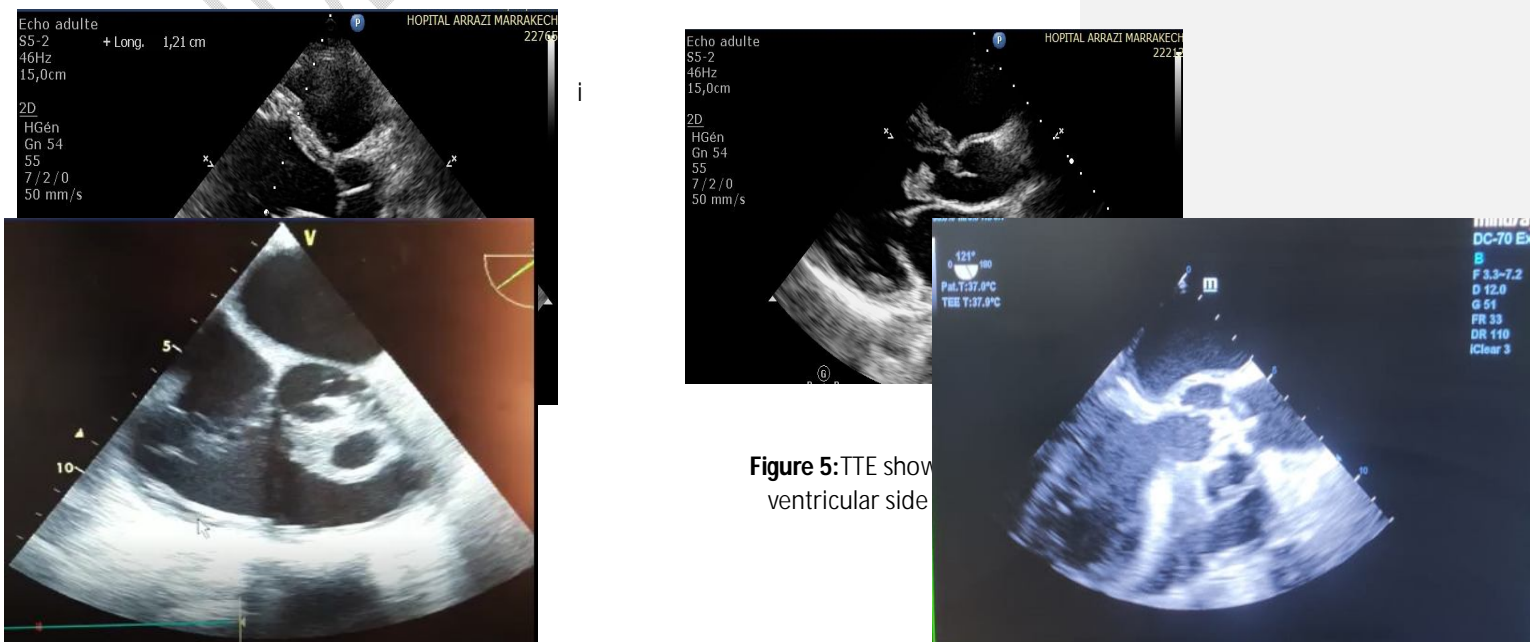
**Figure 3:** Distribution of patients by germ

The biological assessment on admission showed an elevated C-reactive protein level in 97% of our patients with a mean value of 130 mg/l. renal biological assessment had detected renal insufficiency in 9 patients (8%).

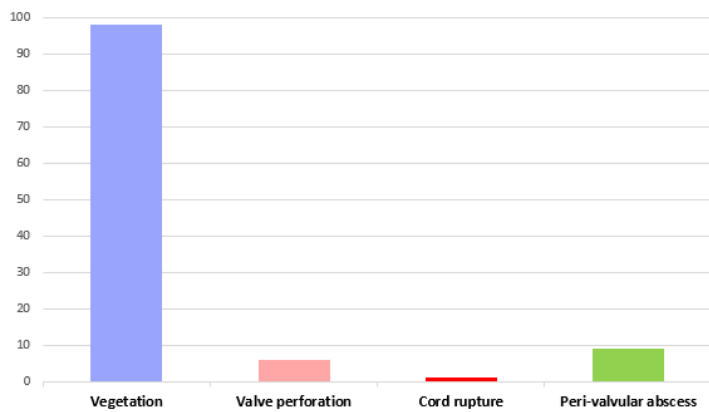
Transthoracic echocardiography is performed systematically in front of any suspicion of infective endocarditis. Transesophageal echocardiography (TEE) is systematically performed in case of IE on prosthesis. In our series, echocardiography offered a better evaluation of the lesions and a detection of complications. It is repeated when there is a bad evolution under medical treatment.

Transthoracic echocardiography (TTE) revealed vegetation in 108 cases (98%). (Figure 4,5). The location was aortic in 48 patients (43%) followed by mitral in 38 patients (34%), mitro-aortic in 12 patients (11%) and tricuspid in 3 patients (3%). The size of the vegetations was greater than 10 mm in 69 cases (62%). The mobile nature of the vegetations was noted in 89% of cases. Complications demonstrated by TTE were valve perforation in 7 cases (6%), cord rupture in 1 case and perivalvular abscess (Figure 6) in 10 cases (9%). (Figure 7).

Transesophageal echocardiography (TEE) was performed in 41 cases to confirm the findings on TTE.



**Figure 5:** TTE show ventricular side

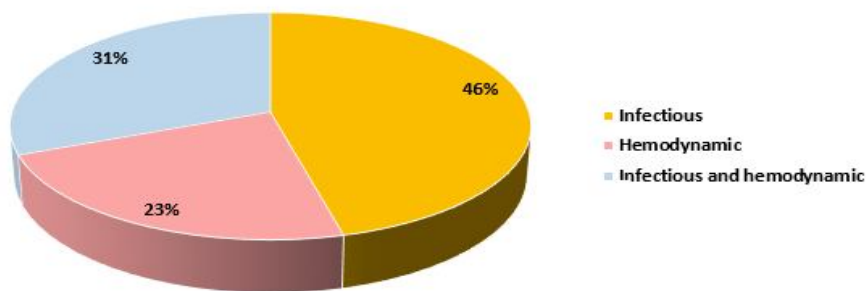


**Figure 7:** Distribution of echocardiographic signs on TTE

As for the forms of infective endocarditis on valve prosthesis, vegetations were noted in 9 patients. Paraprosthetic leakage was noted in 3 patients and prosthesis disinsertion was diagnosed in one patient.

All patients were put on medical treatment with a probabilistic antibiotic therapy initially. This antibiotic therapy was then modified in 31% of cases according to the antibiogram or in case of persistent fever.

The indication for surgery was given in 77% of patients. The average time to surgery was 29 days with extremes of 7 to 45 days. The operative indication was infectious in 46% of patients, hemodynamic in 23%, infectious and hemodynamic in 31% (Figure 8). Ten of the patients operated on had a prosthetic



valve. The operative procedure was a valve replacement by mechanical prosthesis in 83 patients.

**Comment [a7]:** No title for figure

Two patients had a vegetectomy. The in-hospital evolution was marked by the occurrence of complications in 63% of cases. Heart failure was by far the most frequent complication (54%), followed by Neurological complications were observed in 15% of cases: ischemic stroke (12 patients);

hemorrhagic stroke (2 patients), infectious meningitis (1 patient), and mycotic aneurysm (2 patients). Renal failure was observed in 11% of cases and embolic complications were observed in 12% of cases (Figure 9). In-hospital mortality was 24%. Predictive factors for mortality were heart failure ( $p<0.001$ ), renal failure ( $p=0.004$ ) and neurological complications ( $p=0.002$ ).

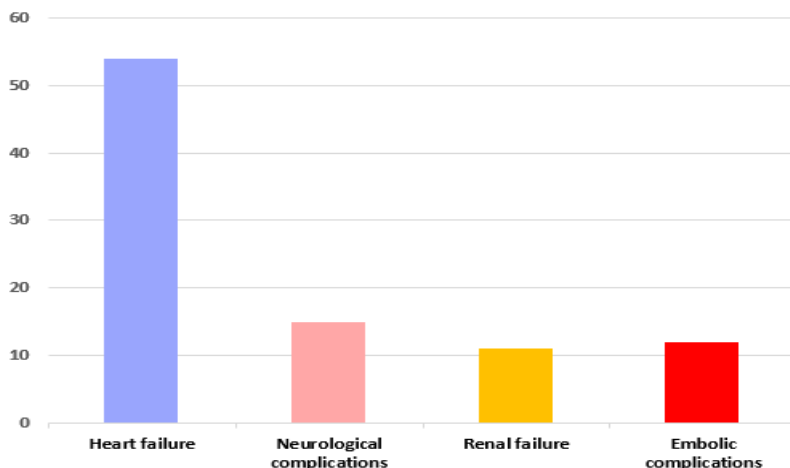


Figure 9: Distribution of complications

**Discussion:**

Infective endocarditis is a rare disease. The incidence of infective endocarditis varies between countries, ranging from 3-10 cases/100,000 people per year [1-2]. In Morocco, the lack of national registers does not allow us to have official figures on the incidence.

The epidemiological profile of IE is constantly changing. In the present work, we have tried to assess the situation in a sample of the Moroccan population (cardiology department at the CHU Mohamed VI in Marrakech) and to compare our data with other representative series from developing countries and Western countries.

The young mean age of our population (43 years) is comparable to that of a 2009-2015 Moroccan study conducted by Harrak S et al at the Department of Cardiology B, Ibn Sina University Hospital, Rabat [3] and concordant with three Tunisian studies [4,5,6] and an Algerian study [7]. This young age is explained by the high frequency of rheumatic heart disease in Morocco as well as in other developing countries [8]. In fact, in Western series, the profile of infective endocarditis has changed in the last decades [9,10]. Due to the increase in life expectancy, this condition often affects the elderly [9, 11]. The average age of patients is older, between 55 and 66 years.

Comment [a8]: Paragraphing is poor

Comment [a9]: Citation cannot start from discussion, it must start from introduction

Comment [a10]: Not needed, please adjust where applicable

There is a predominance of males, which is consistent with the data in the literature [4,6,8,12].

As for the underlying heart disease, rheumatic valve disease remains the most common underlying heart disease of IE in developing countries [13]. In our series, rheumatic valve disease accounted for 69% of underlying heart disease; a similar result was found in the Algerian study by Benatta NF et al.[7]

Comment [a11]: Same as above

In industrialized countries, other underlying cardiopathies have replaced rheumatic heart disease and predisposing factors are clearly increasing, such as degenerative heart disease, the practice of invasive procedures with a risk of bacteremia, the implantation of intracardiac prostheses, and toxic habits such as intravenous drug abuse. [14,15].

The frequency of endocarditis on prosthesis is estimated at 10% in our series, comparable to that found in the Moroccan study by Harrak S et al with a frequency of 12% [3].

The left heart remains the preferred site of IE. In our series, aortic valve endocarditis was predominant (48%), comparable to the results of the Moroccan study by Harrak S et al [3] and the French study by Capilla E et al [11]. While the damage is predominantly in the mitral location in the Tunisian series of Mzoughi K et al [5] and the Algerian series of Benatta NF et al [7] and distributed almost equally between aortic and mitral location in the other Tunisian [4,16] and French [1, 17] series.

The portal of entry was identified in only 60% of all our patients and the predominance of dental origin is preponderant in 30% of cases. A similar observation was made in developing countries [5,6,7]. In industrialized countries, the dental portal of entry is rarely found. It was observed in only 19% of patients in the Netzer series [18]. In an international study carried out between 2000 and 2003 [18] in 16 countries, the origin was nosocomial or care-related in 40% of cases [19]. Both iatrogenic and nosocomial entry points have increased during the 1990s [20]. This increase is probably related to the increase in invasive procedures.

The clinical data of our series show that fever was present in 88% of cases. Indeed, fever was almost always present in 90% of patients in the majority of European series.

Comment [a12]: Please provide reference to this claim

Infective endocarditis can be acute, subacute or chronic [22]. This difference is related to the nature of the microorganism responsible and the heart disease at risk (prosthetic material, valve prosthesis, etc.). According to the interrogation data, the acute form represents only 22% of the patients in our study series. In 78% of the cases, it is a subacute IE, or even a chronic IE because of the delay in diagnosis which is 41 days on average. These results are consistent with European series [1, 17, 18].

Non-specific symptoms as well as underestimation of symptoms by patients may delay diagnosis. Atypical clinical presentations have become more frequent and are related to the increasing age of onset on the one hand and immunocompromised subjects on the other hand [23].

In our series, fever remains the main symptom present in 96% of cases. However, we have noted new trends with a decrease in the frequency of cutaneous and immunological manifestations.

Blood cultures have a determining role in the identification of the germ and in testing its sensitivity. Blood cultures were positive in 33% of our patients. In contrast, in industrialized countries, the rate of negative blood cultures varies between 5 and 15% [24], and that of positive blood cultures is around 85% [25]. In our series, when the blood cultures were positive, the most frequently isolated germs, almost equally distributed, were streptococcus and staphylococcus.

In industrialized countries, *S. aureus* is responsible for an increasing rate of IE and is even the first germ in cause in recent studies [26,24].

Negative blood cultures account for 67%, a proportion of which is decapitated by antibiotic therapy before diagnosis. A proportion of these blood cultures is thought to be caused by unidentified streptococci. The search for germs with difficult growth as well as those with intracellular growth, by means of serologies, is not assured in our current practice. This fact also justifies the high proportion of negative blood cultures.

Positive diagnosis is facilitated by cardiac ultrasound. Vegetations were observed in 98% of our patients. This frequency is comparable to the Tunisian studies which is 93% for Trabelsi et al [27] and 82% for Mzoughi K et al [5], and that of the Algerian study of Benatta NF et al [7] which is 83% and the French survey of 2008 [2] estimated at 87.5%.

Cardiac abscesses were observed with a frequency of 9% in our patients, this frequency is comparable to that found in the Tunisian study [5] which is 5% and in the Algerian study [7] which is 18.9% and that in the French survey of 2008 [2] which is about 20.3% of cases. Prosthesis deinsertion was observed in only one patient among our patients with prosthesis.

Thanks to technological progress, echocardiography has made a considerable contribution to the positive diagnosis and to the diagnosis of complications, allowing better guidance of the treatment.

We were interested in the analysis of the complications of IE, which have a major impact on the prognosis of this pathology: in our series, heart failure was the most frequent cardiac complication (54%). It also remains the most frequent complication of IE in the Tunisian [5] and French surveys and the first cause of death [28].

Neurological complications come second (15%) in our series. This rate is comparable to that reported in the Tunisian study by Mzoughi K et al [5], estimated at 22%, and the Algerian study by Benatta NF et al [7], estimated at 27%, and that of Letaief at 20% [6], as well as to other European series [2, 29, 30]. The most frequent neurological complication in our series is ischemic stroke, observed in more than two thirds of all neurological complications.

Embolic complications constitute an evolving modality whose localization is polymorphic. It is a frequent complication whose real frequency is often underestimated by the clinical series because of its sometimes asymptomatic character [21].

In our series, renal failure represents 11% of complications. This complication is responsible for a significant mortality. This unfortunate prognostic significance has been confirmed by the study of Conlon et al showing a risk of fatal evolution multiplied by 5 compared to that observed in patients without renal failure.

The decision of surgical treatment in IE takes into account the risk factors of unfavorable evolution and the comorbidities of the patient [16]. In our series, 77% used surgical treatment; some series report the use of surgery in the acute phase of IE with a rate ranging from 25 to 45% [31,2,32]. In-hospital mortality in our study was 24%, the predictive factors were heart failure ( $p<0.001$ ), renal failure ( $p=0.004$ ) and neurological complications ( $p=0.002$ ), this has been found in other studies [1,2,5,7,31,33,34,35,36,37,38,39,40,29].

#### **Conclusion:**

Infectious endocarditis remains a real health problem with a consequent mortality and morbidity and this in spite of numerous diagnostic and therapeutic advances.

**Comment [a13]:** Too much and unnecessary

The epidemiology of infective endocarditis is complex to understand because of the diagnostic difficulties and the large impact of the reference bias on the characteristics of the populations studied.

The current profile of infective endocarditis in Morocco has not changed. This disease still affects young people and occurs in the context of rheumatic valve disease. During our study, we encountered several difficulties, namely: the diagnostic delay which is the source of multiple complications, the high proportion of unidentified entry points, the often negative blood cultures due to inadequate conditions of their realization and the lack of recourse to early surgery.

A multidisciplinary management must be applied for an optimal treatment and a better management of the patients in order to improve their survival and prognosis.

The improvement of the management and prognosis of IE is based on the reinforcement of preventive measures against rheumatic fever, the establishment of awareness campaigns for an earlier diagnosis and prophylaxis which remains an important link in the fight against this disease and which is essentially based on the eradication of any infectious focus in the general population and antibiotic prophylaxis for patients at risk.

#### **References:**

- [1] Hoen B, Alla F, Selton-Suty C, et al. Changing profile of infective endocarditis: results of a 1-year survey in France. *JAMA* 2002 ;288 :75–81.
- [2] Duval X, Hoen B. Evolution du profil épidémiologique des endocardites infectieuses. *J Anti Inf* 2011 ;13 :155–60.
- [3] Harrak S, Doghmi N, Fellat B, Zarzur J, Cherti M. L'endocardite infectieuse au Maroc à travers l'expérience d'un service hospitalier. *Annales de Cardiologie et d'Angéiologie* 68 (2019) 87–93
- [4] Hammami K, Kammoun S, Benjema M. 10èmes journées médico-chirurgicales de Sfax compte rendu de la table ronde « l'endocardite infectieuse ». *RevTuninfectiol.* 2007 ; 1 :32-4.
- [5] Mzoughi K, Zairi I, Jabeur M, Ben Moussa F, Kamoun S, Ben Said R, Souabni I, Fennira S, Kraiem S. Etude descriptive de l'endocardite infectieuse : données du Service de Cardiologie de l'Hôpital Habib Thameur. *Cardiologie Tunisienne - Volume 10 N°03 - 3 185 eTrimestre 2014 - 185-190*
- [6] Letaief A, Boughzala E, Kaabia N, et al. Epidemiology of infective endocarditis in Tunisia: a 10-year multicenter retrospective studying. *Int J Infect Dis* 2007 ;11 :430–3.
- [7] Benatta NF, et al. Endocardite infectieuse : expérience du service de cardiologie de l'établissement hospitalo-universitaire Oran. *Ann Cardiol Angeiol (Paris)* (2018).
- [8] Mylonakis E, Calderwood SB. Infective endocarditis in adults. *N Engl J Med* 2001; 345:1318–30.
- [9] Hoen B, Alla F, Selton-Suty C, Beguinot I, Bouvet A, Briancon S, et al. Changing profile of infective endocarditis: results of a 1-year survey in France. *JAMA* 2002; 288:75–81.
- [10] Cabell CH, Jollis JG, Peterson GE, et al. Changing patient characteristics and the effect on mortality in endocarditis. *Arch Intern Med* 2002 ;162 :90–4.
- [11] Capilla E, et al. Endocardite infectieuse : caractéristiques cliniques et pronostic entre 2004 et 2014 dans un hôpital non universitaire. *Ann Cardiol Angeiol (Paris)* (2016).
- [12] Goulet V, Etienne J, Fleurette J, Netter R. L'endocardite infectieuse en France. Caractéristiques épidémiologiques. *Presse Med* 1986 ;15(37) :1855–8.

- [13] Tleyjehi M, Abdel-Latif A, Rahbi H et al. A systematic review of population -based studies of infective endocarditis. *Chest* 2007; 132:1025-35.
- [14] Fowler Jr VG, Miro JM, Hoen B, Cabell CH, Abrutyn E, et al. Staphylococcus aureus endocarditis: a consequence of medical progress. *JAMA* 2005; 293:3012–21.
- [15] Slipczuk L, Codolosa JN, Davila CD, Romero-Corral A, Yun J, Press-man GS, et al. Infective endocarditis epidemiology over five decades: a systematic review. *PLoS One* 2013 ;8(12): e82665.
- [16] Hannachi n. Les endocardites infectieuses. Thèse de doctorat en médecine 1979. Faculté de médecine de Tunis.
- [17] Delahaye F, Goulet V, Lacassin F. Characteristics of infective endocarditis in France in 1991. A 1-Year surgery. *Eur Heart J*. 1995 ;16 :394-401.
- [18] Netzer R, Zollinger E, Seiler C, Cerny A. Infective endocarditis: clinical spectrum, presentation and outcome, analysis of 212 cases. *Heart* 2000 ; 3 :184–96.
- [19] Parize P, Mainardi JL. Les actualités dans l'endocardite infectieuse. *Rev Med int*. 2010 ;612-21.
- [20] Lagier JC, Letranchant L, Selton-study C, n loga J, Aissa n, Alauzet C et al. Bactériémies et endocardites à staphylococcus aureus. *Ann Cardiol Angeiol*. 2008 ;57 :71-7.
- [21] Que Y-A, oddo M, Liaudet i, Moreillon P. Endocardites infectieuses : mise au point. *Rev Med Suisse Romande*. 2004 ;124 :341-6.
- [22] Habib G, Lancellotti P, Antunes MJ, et al. ESC Guidelines for the management of infective endocarditis. The task force for the management of infective endocarditis of the European Society of Cardiology (ESC). *EurHeart J* 2015; 36:3075–128.
- [23] Perez de isla L, Zamorano J, Lennie V, Vazquez J, Ribera JM, Macaya C. negative blood culture infective endocarditis in the elderly: long-term follow-up. *gerontol*. 2007 ;53 :245-9.
- [24] Murdoch DR, Corey GR, Hoen B, Miró JM, Fowler Jr VG, Bayer AS, et al. Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century: the International Collaboration on Endocarditis-Prospective Cohort Study. *Arch Intern Med* 2009;169(5):463–73.
- [25] Habib G, Hoen B, Tornos P, et al. Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009). The Task Force on the Prevention, Diagnosis, and Treatment of Infective Endocarditis of the European Society of Cardiology (ESC). *EurHeart J* 2009 ;30 :2369–413.
- [26] Selton-Suty C, Célard M, Le Moing V, Doco-Lecompte T, Chirouze C, lung B, et al. Preeminence of Staphylococcus aureus in infective endocarditis: a 1-year population-based survey. *Clin Infect Dis* 2012;54(9):1230–9.
- [27] Trabelsi I, Rekik S, Znazen A, et al. Native valve infective endocarditis in a tertiary care center in a developing country (Tunisia). *Am J Cardiol* 2008 ;102 :1247–51.
- [28] Loire R, Tabib A. L'endocardite infectieuse mortelle aspects anatomiques actuels. A propos de 63 observations. *Sem Hop Paris*. 1985 ;62 :2463-6.
- [29] Heiro M, nikoskelainen J, Engblom E, et al. neurologic manifestations of infective endocarditis: a 17-year experience in a teaching hospital in Finland. *Arch intern Med* 2000; 160:2781-7.
- [30] Corral I, Martin-davila P, Fortun J, et al. Trends in neurological complications of endocarditis. *J neurol* 2007; 254:1253-9.
- [31] Tornos P, Gonzalez T, Thuny F, Habib G. Infective endocarditis: The European viewer point. *Curr Probl Cardiol* 2011; 36:175–222.

- [32] Mouly S, Ruimy R, Launay O, et al. The changing clinical aspects of infective endocarditis: descriptive review of 90 episodes in a French teaching hospital and risk factors of death. *J infect* 2002; 45:246–56.
- [33] Remadi JP, Habib G, Nadji G, Brahim A, Thuny F, Casalta JP, et al. Predictors of death and impact of surgery in *Staphylococcus aureus* infective endocarditis. *Ann Thorac Surg* 2007; 83:1295–302.
- [34] Duval X, Delaye F, Alla F, Tattevin P, Obadia JF, Le Moing V, et al. Temporal trends in infective endocarditis in the context of prophylaxis guideline modifications. *Am J Cardiol* 2012; 59(22):1968–76.
- [35] Thomas D, desruennes M, Jault F, Isnard R, Gandjbakhch I. Cardiac and extracardiac abscesses in bacterial endocarditis. *Arch Mal Coeur Vaiss* 1993; 86:1825-35.
- [36] Majumdar A, Chowdhary S, Ferreira MA, et al. Renal pathological findings in infective endocarditis. *nephrol dial Transplant* 2000; 15:1782-7.
- [37] Klein I, Lung B, Wolff M, et al. Silent T2 cerebral microbleeds: a potential new imaging clue in infective endocarditis. *neurology* 2007; 68:2043-52
- [38] Anderson DJ, Goldstein LB, Wilkinson WE, et al. Stroke location, characterization, severity, and outcome in mitral vs aortic valve endocarditis. *neurology* 2003; 61:1341-6.
- [39] Sonnevile R, Mirabel M, Hagege d, et al. Neurologic complications and outcomes of infective endocarditis in critically-ill patients: the EndoREA prospective multicenter study. *Crit Care Med* 2011;1-10.
- [40] Thuny F, Avierinos JF, Tribouilloy C, et al. Impact of cerebrovascular complications on mortality and neurologic outcome during infective endocarditis: a prospective multicentre study. *Eur Heart J* 2007; 28:1155-61.