

INFECTIOUS ENDOCARDITIS IN VALVE PROSTHESES: AN UPDATED REVIEW OF CLINICAL ASPECTS

Eduarda da Cunha Cavalini

<http://lattes.cnpq.br/3807305168218332>

Maria Clara Carvalho Gomes

<http://lattes.cnpq.br/5701126156519818>

Luíza Fricks Cabellino

<http://lattes.cnpq.br/7133148489662756>

Jhennifer Oliveira Vimercati

<http://lattes.cnpq.br/0382493739513032>

Júlia Bernardes Moreira

<http://lattes.cnpq.br/5063307291592639>

Karina Campanha

<http://lattes.cnpq.br/4066874277654419>

Júlia Gomes Geraldo

<http://lattes.cnpq.br/4195415447846831>

Júlio César Monteiro Carvalho

<http://lattes.cnpq.br/7179373154224997>

Sthefanie Sant'Anna de Almeida

<http://lattes.cnpq.br/3984967962875470>

Ruan Carlos Nogueira Santos

<http://lattes.cnpq.br/7311196427207534>

All content in this magazine is licensed under a Creative Commons Attribution License. Attribution-Non-Commercial-Non-Derivatives 4.0 International (CC BY-NC-ND 4.0).



Abstract: Introduction: The management carried out in patients with IE is very important for the outcome and prognosis. For this, a thorough history and physical examination are essential. Laboratory tests and echocardiography will contribute to better clinical reasoning and subsequently to appropriate treatment. **Objective:** Understand which group has a higher prevalence of presenting IE and what is the best treatment after a correct diagnosis. **Methodology:** This is a bibliographic review related to infectious endocarditis in valve prostheses. 10 articles were selected from the SciELO, PubMed and SOCESP Magazine (Society of Cardiology of the State of São Paulo). The following inclusion criteria were defined: articles in Portuguese and English, published between 2018 and 2023 and which addressed the themes proposed for this research, review-type studies, meta-analysis and observational studies. **Results:** Descriptions regarding the symptoms of IE are described as fever, heart murmurs, petechiae, anemia and embolic phenomena. It is important to highlight that IE is more common in elderly people aged between 50 and 60 years. **Conclusion:** It is concluded that elderly people with valve prostheses, vascular catheters, pacemakers and cardioverter defibrillators are more susceptible to infectious endocarditis. **Keywords:** Endocarditis. Prosthesis. Illness.

INTRODUCTION

The incidence of infective endocarditis (IE) varies from 3 to 15 cases per 100,000 people/year in population studies and is the eleventh cause of cardiovascular death in Brazil (SOUSA C, et al., 2021). It is defined as an infection of the cardiac endothelial surface that mainly affects the valves, but can also involve septal regions, chordae tendineae and endocardium. This condition can lead to valve incompetence, embolization, cerebrovascular

accident and heart failure. (FERNANDES JR, et al., 2022). IE can be caused by fungi or other microorganisms, but the most common etiology is bacterial. In developing countries, the majority of the affected population are young people 20 to 40 years old and the main etiological agent is Streptococcus. On the other hand, in developed countries, where life expectancy is higher, the elderly is the most involved and Staphylococcus is the main agent (MESQUITA CT, et al., 2023). The Duke criteria were created to assist in the diagnosis of IE, as it includes blood culture and echocardiography. The diagnostic hypothesis is determined when there is confirmation of a focus of infection in addition to a heart murmur or some other cardiac condition combined with fever, suspected embolism or acute or subacute heart failure. Other signs and symptoms may be observed, such as arthralgia, chills, myalgia, weight loss, night sweats, headache, among others. However, these criteria have their limitations, as they are not immediate and accuracy varies from 52% to 70%. (ACCORSI TAD, et al., 2023) Patients with cardiac structural changes, those with long-term devices and those exposed to conditions that can generate bacteremia, such as the dental treatments, invasive procedures in the genitourinary or intestinal tract, use of intravenous illicit drugs, piercings or tattoos are at greater risk of developing HEY. Furthermore, it is observed that the poor prognosis is directly related to the clinical conditions of the patients, as immunosuppressed patients have a worse disease progression. (PINHEIRO IL, et al., 2018) Despite technological advances, IE is increasingly related to patients with valve prostheses, catheters, pacemakers and cardioverter-defibrillators, with valve prostheses being the most serious form of endocarditis, with an incidence of 0.3 to 1.2% per patient/ year. It corresponds to 10 to 30%

of all cases of endocarditis, with an equal incidence in metallic or mitral prosthesis (SOBREIRO DI, et al., 2018).

Treatment varies according to time, since in acute IE, antibacterial treatment must be started immediately, while in subacute or late IE, the start of treatment can be delayed for a maximum of 48 hours, in an attempt to isolate the agent responsible. (MAIA JM, et al., 2020). Given this, it can be seen that a quick and accurate diagnosis is ideal for better patient intervention, while a late diagnosis can lead to serious complications and worse clinical results. (BIGNOTO Tiago, 2023).

LITERATURE REVIEW

According to Maia et al. (2020), the concept of bacterial endocarditis is as inflammation of the inner layer of the heart, mainly in the heart valves, although, in some cases, it occurs in the septum between the heart chambers (the mural endocardium) or in implantable cardiac devices, which with progression can lead to valve obstruction or insufficiency, myocardial abscess or mycotic aneurysm. The most affected valves are the mitral and aortic, while the occurrence of the disease in the tricuspid and pulmonary valves is lower, especially in the pulmonary valve. As main symptoms, the infection causes fever (most common symptom and present in more than 80% of cases), heart murmurs (second most frequent manifestation), petechiae, anemia and embolic phenomena. However, this pathology has had a notable change in its epidemiological characteristics in the last 30 years in Brazil, in which its incidence varies between 3 and 15 cases per 100,000 in population studies. (SOUSA et al., 2022).

Previously, the epidemiological age profile of IE was young adults with rheumatic valvular disease, however, with the evolution of treatment and prevention techniques, the panorama of the disease has changed,

which is currently more common in elderly people who have cardiac devices, as related to valve prosthesis holders, vascular catheters, implantable electronic devices, such as pacemakers and cardioverter defibrillators and new surgical devices, such as valve endoprostheses implanted by catheter (MAIA et al., 2020).

According to Sousa et al (2022) older patients are generally those most affected, with a median age between 50 (towards the end of the decade) and 60 years. Despite the advancement of antibiotic therapy and surgical techniques, the lethality of IE is still increasing, this change in the epidemiological profile highlights a strong relationship with risk factors and the susceptibility of patients, demystifying the virulence of microorganisms as the main cause. (FERNANDES et al., 2022).

The pathogenic mechanism occurs through changes in laminar blood flow, generating turbulence and resulting endothelial injuries; This forms a sterile thrombus that is a target for bacterial colonization. Furthermore, other independent factors can influence the development of IE, which when together potentiate the disease mechanism, including the alteration of the surface of the heart valve to produce a suitable site for bacterial attachment and colonization; bacteremia with an organism capable of attaching to and colonizing valve tissue; and creation of vegetation by the proliferating organism within a protective matrix of serum molecules (e.g., fibrin) and platelet (MAIA et al., 2020).

The infectious agents causing IE can be of direct origin, for example central venous access and surgical contamination, as well as of indirect origin such as distant infected sites. The main etiological microorganisms of early EPV (IE in valve prosthesis) are coagulase-negative staphylococci. Staphylococcusepidermidis represent the

majority of general cases of the pathology; other coagulase negatives related to IE include *S. hominis*, *S. hemolyticus*, *S. warnerii*, *S. cohnii*, and *S. saprophyticus*. The incidence of the age group and the causative agent also depend directly on the socioeconomic status of each region, as described by Mesquita et al. (2023) in developed countries, the most common pathogen is *Staphylococcus* sp., and according to research, the most affected patients are the elderly.

In developing countries, the causative agent with the highest incidence is *Streptococcus*, and the most affected patients are young people aged 20 to 40 years. Furthermore, according to a study carried out by Mesquita et al. (2023), patients with valve prostheses are subject to a greater risk of infectious endocarditis in the first year following their surgical insertion, with a mortality rate of 1.4% to 3% worldwide, being highest in the first three to six months post-operatively. surgery, with the main causative agents being hospital bacteria, *S. aureus* and coagulase-negative staphylococci. This rate gradually declines after this period, with the risk gradually decreasing to a low and stable rate in the subsequent years, until the sixth month, thus gradually reducing until reaching a relatively constant rate of 0.2% to 0.6%/year after the twelfth postoperative month. In these cases, the pathogen with the highest incidence are bacteria common to native valve endocarditis, such as viridans group streptococci. Eventually in developed countries, IE in valve prosthesis constitutes 10% to 30% of all cases of IE, consolidating itself as a serious cardiac surgical complication, despite the advances in diagnosis, treatment and prophylaxis that have been made nowadays. (FERNANDES et al., 2022).

Furthermore, EPV is classified as early, when the infection sets in within the first year after surgery, and late, which occurs

after this period. Usually, the period between bacteremia and symptomatic appearance in infective endocarditis is generally less than two weeks, however, in early EPV the incubation period can be longer, up to five months. (FERNANDES et al., 2022). **Diagnosis:** A priori, when infectious endocarditis is suspected, a thorough history and physical examination are essential, including previous pathological history, survey of risk factors and the detection of subjective clinical findings for IE that lead to the hypothesis of this disease. Therefore, it is necessary to carry out additional tests, such as: echocardiogram, blood culture, complete blood count, ESR, CRP and some biomarkers, procalcitonin and interleukin 6 (IL-6) to assess serum levels. (MESQUITA et al., 2023).

The gold standard test is blood culture, which must be collected at different periods of the disease, mainly before the use of antibiotics in order to sensitize the test. Positive blood culture results, especially if obtained from different collection sites, allow confirmation of a bacterial infection and identify its causative agent. Laboratory tests are also essential, as some results can contribute to the diagnosis and clinical reasoning, such as leukocytosis, anemia, increased ESR and CRP, indicating an active infectious process.

Another essential exam is echocardiography, which is available in two modalities, transthoracic (TTE) and transesophageal (TEE). TTE has a role as a first approach, with TEE being the most recommended due to its greater sensitivity and specificity, thus allowing a more detailed assessment. Transesophageal echocardiography is essential when IE is suspected in a cardiac valve prosthesis, due to better observation of valve hemodynamics, detection of vegetation, abscess or fistula. However, detection of vegetation can become difficult due to artifacts arising from the material used in the prostheses. However,

the sensitivity of TEE for EPV is still high, in the range of 82% to 96%, unlike TTE, in which sensitivity varies from 17% to 36% (MESQUITA et al., 2023). However, according to Fernandes et al. (2022), diagnostic criteria for IE were defined, taking into consideration, the diagnostic criteria of echocardiographic imaging, clinical and laboratory tests. This aggregate of assessments is called “Duke Criteria”, which are then divided into major criteria and minor criteria. (FERNANDES et al., 2022).

Minor criteria
IV drug use or presupposing heart disease Temperature > 38.0 degrees Celsius Vascular phenomenon: arterial embolism; pulmonary septic infarction, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhage, Janeway lesions
Immunological phenomenon, glomerulonephrite, Osler's nodules, Roth's spots or positive rheumatoid factor Microbiological evidence: positive blood culture by major criteria (excluding coagulase-negative staphylococcus in just a blood culture) or serological evidence of active infection by microorganism compatible with infective endocarditis
Defined endocardite
Presence of 2 major criteria, or 1 major, 3 minor ones, or 5 minor ones Intracardiac vegetation or abscess with histological evidence of active infective endocarditis or direct demonstration of microorganism in vegetation, abscess or embolus.
Possible endocardite – Presence of major and minor criteria, or 3 minor ones
Rejected endocardite
Clear diagnosis of another infectious focus or complete remission of two signals with less than 4 days of treatment or absence of anatomical pathological evidence of IE. in surgery or autopsy with less than 4 days of antibiotic treatment. It does not meet the above criteria.
Major criteria
Blood cultures
2 positive blood cultures for typical microorganisms: S. Viridans, S. Bovis, HACEK group bacteria, S. Aureus, or enterococci of community origin in the absence of a primary focus. Persistent bacteremia defined as 2 blood cultures collected > 12 hours apart, or positive in 3 blood cultures or a majority of 4 or more blood cultures (an interval greater than 1 hour between blood cultures) Positive culture for Coxiellaburnetiou, positive serology with Anti-phase titer > 1/800 Endocardial involvement

Positive echocardiogram (transeophageal echocardiogram is recommended in patients with valve prosthesis, patients classified as possible infective endocarditis by clinical criteria, or infective endocarditis with perivalvar abscess, transthoracic echocardiogram is recommended, as First option for other patients); intracardiac oscillating mass adhering to the valve, to the path of regurgitation jets to implantable material in the absence of another anatomical explanation or abscess or new dehiscence of a valve prosthesis.

Although the mainstays of the diagnosis of IE are blood cultures, echocardiography and laboratory tests, other complementary exams can be performed, such as chest tomography, abdominal ultrasound, and positron emission tomography- PET-CT (the latter with greater importance in EPV) help with the diagnosis.

Treatment: The treatment of IE has three general aspects: initial clinical stabilization, early obtaining of blood cultures and institution of definitive medication and/or surgical treatment. Initially, when the causative microorganism has been confirmed by blood culture, antibiotic treatment directed at this agent is established, thus avoiding empirical antibiotic therapy. However, when the clinical condition demands immediate intervention, even before isolating the pathogen through blood culture, therapy must be directed to the causative agents with the highest incidence. (FERNANDES et al., 2022).

According to Fernandes et al. (2022), to obtain good results in the treatment of Infectious Endocarditis, adequate antibiotic therapy is essential, with the ultimate objective of eradicating the pathogens contained in the vegetation. Medication with high microbicidal activity must be used intravenously, at doses and intervals that allow obtaining constant high serum levels for a prolonged period of time. For the treatment of PVE caused by Staphylococcus aureus, early valve replacement surgery is recommended and the use of a triple antibiotic drug regimen, oxacillin or vancomycin, with aminoglycoside, with rifampicin. Rifampicin has antistaphylococcal

capacity in prosthetic infections, however, if used alone, it has a high risk of emergence of resistant strains, hence the combination of vancomycin with aminoglycoside, reducing the possibility of emergence of staphylococcus resistance to rifampicin. Surgical indication in infective endocarditis is made through a broad assessment of cardiac and extra-cardiac complications, such as, for example, the patient's hemodynamic condition, clinical failure of antibiotic treatment, destruction of valve tissues with periannular extension (abscess or fistula), a new embolic event during antibiotic treatment and endocarditis caused by organisms that are difficult to treat and more virulent, such as *S. aureus* or fungi. The main objective of surgical treatment is to remove the infected tissue in order to restore valve function and correct the structural damage caused. Debridement of tissue necrosis and extensive reconstructions when necessary are responsible for the greater success in the surgical treatment of endocarditis, with an increase in the 12-month survival rate from 42% to 71% when comparing clinical treatment with surgical treatment. set. After removing the diseased valves or prostheses, all infected tissue is removed, with the in order to preserve the anatomical and functional integrity of the valve ring and cardiac chambers (FERNANDES et al., 2022).

CONCLUSION

It is concluded that infectious endocarditis is a bacterial inflammation in the inner layer of the heart, affecting mainly the heart valves, with the mitral and aortic valves being more recurrent, being mainly *Staphylococcus* sp (in developed countries) and *Streptococcus* (in developing) the most predominant infectious agents. The main clinical features are fever and heart murmur and the most prevalent age group are elderly people who have cardiac devices, for example the pacemaker. It is worth mentioning that despite advances in therapeutic resources (surgery and antibiotics) lethality is still very high, therefore, a good and rapid approach to the treatment of IE is crucial to guarantee the best assistance to patients suffering from this problem. Several factors play a fundamental role in determining the quality of this conduct, namely, the training of health professionals, the speed in identifying the disease by taking a good history and physical examination, in addition to accurate complementary measures, for example blood cultures at different periods. of the disease, echocardiogram and laboratory tests to also identify the causative microorganism and establish with greater specificity which antibiotic therapy to use. This article also addressed treatments for infective endocarditis, in addition to the use of antibiotics, such as rifampicin and oxacillin, a surgical approach, decided based on the assessment of possible complications, such as failure of drug treatment and destruction of valve tissues, in order to reestablish the valve function and rectify possible structural damage.

REFERENCES

- ACCORSI, Tarso Augusto Duenhas et al. Emergências Relacionadas à Doença Valvar Cardíaca: Uma Revisão Abrangente da Abordagem Inicial no Departamento de Emergência. **Arquivos Brasileiros de Cardiologia**, v. 120, p. e20220707, 2023.
- BIGNOTO, Tiago (Ed.). Endocardite Infecciosa: Novos Espectros, a Mesma Gravidade. **Arquivos Brasileiros de Cardiologia**, v. 120, n. 3, p. e20230117, 2023.
- FERNANDES, João Ricardo Cordeiro; LOPES, Mariana Pezzute; SICILIANO, Reinaldo Focaccia; VERONESE, Elinthon Tavares. Endocardite Infecciosa. Revista da Sociedade de Cardiologia do Estado de São Paulo, Revista da SOCESP, ano 2022, p. 183-194, 2022. DOI <https://dx.doi.org/10.29381/0103-8559/20223202183-94>. Disponível em: Revista SOCESP. Acesso em: 13 nov. 2023.
- GROSSMAN, Gabriel Blacher; CARREIRA, Lara Terra F. Papel do PET/CT no diagnóstico da endocardite infecciosa. **Artigo de Revisão Arq Bras Cardiol: Imagem Cardiovasc**, v. 32, n. 3, p. 209-13, 2019.
- MAIA, Jade Menezes et al. Tratamento da endocardite bacteriana causada pelo uso de prótese valvar e cateteres: uma revisão bibliográfica. **Revista Eletrônica Acervo Saúde**, v. 12, n. 11, p. e4856-e4856, 2020.
- MARQUES, Ana et al. Fatores de Risco para Mortalidade Hospitalar na Endocardite Infecciosa. **Arquivos Brasileiros de Cardiologia**, v. 114, p. 1-8, 2019.
- MESQUITA, Claudio Tinoco et al. Endocardite infecciosa: uma revisão narrativa. **Medicina, Ciência e Arte**, v. 2, n. 1, p. 73-84, 2023.
- PINHEIRO, Isabela Lima et al. Endocardite infecciosa em cirurgias valvares: avaliação ecocardiográfica e clínica como preditores de mortalidade em uma série de casos. **Revista da Sociedade Brasileira de Clínica Médica**, v. 16, n. 2, p. 113-115, 2018.
- SOBREIRO, Daniely Iadocico et al. Diagnóstico Precoce da Endocardite Infecciosa: Desafios para um Prognóstico Melhor. **Arquivos Brasileiros de Cardiologia**, v. 112, p. 201-203, 2019.
- SOUSA, Catarina; PINTO, Fausto J. Endocardite Infecciosa: Ainda mais Desafios que Certezas. **Arquivos Brasileiros de Cardiologia**, v. 118, p. 976-988, 2022.