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INFECTIOUS ENDOCARDITIS, ITS CHALLENGES AND UPDATING THE DUKE CRITERIA: A LITERATURE REVIEW

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Abstract
Infective endocarditis (IE) is an inflammatory process that occurs in the endocardium and also in implantable cardiac devices, the septum between the heart chambers, and in particular the heart valves, whether biological or prosthetic, this process comes from infection by some microorganism, especially bacteria. In 2023, the International Society of Cardiovascular Infectious Diseases (ISCVID) reformulated the diagnostic criteria, in particular those related to microbiological aspects. The aim of this study is to discuss the modified Duke criteria, therapeutic measures, and future challenges. The present study is a narrative bibliographical review that analyzed scientific production in online databases. Because it is a rare pathology, its annual incidence is between 3 and 10 cases per 100,000 people, and it is twice as common in males. Its treatment is complex, but its mainstay is antibiotic therapy and, when necessary, cardiac surgery. Empirical antibiotic treatment should be carried out as soon as possible after blood culture tests have been taken. In conclusion, IE is one of the most laborious and difficult medical conditions for physicians to practice, so it is important to employ a systemic approach based on scientific evidence for diagnostic investigation and therapeutic care for good results and patient well-being.

Keywords Infective endocarditis; treatment; modified Duke criteria; future challenges.

INTRODUCTION

Infective endocarditis (IE) is an inflammatory process that affects the endocardium and also in implantable cardiac devices, the septum between the heart chambers(MESQUITA, et al., 2023), and especially the heart valves, whether biological or prosthetic, this process proceeds from infection by some microorganism, especially bacteria(SILVA et al., 2023). Even though this pathology was first described more than 450 years ago by the French physician Jean François Fernel (FYE, 1997), it is still a complicated disease today (WILLIAMS, et al., 2021).

In the past, the group of individuals affected by IE was made up mainly of young patients with few comorbid conditions, such as those with congenital or rheumatic heart disease (SILVA et al., 2023). However, due to the spread and development of broad-spectrum antimicrobials with better bacterial characteristics, this patient profile has changed, giving prominence to elderly, clinically unstable individuals with multiple morbidities(SILVA et al., 2023). This has allowed Staphylococcus to replace Streptococcus as the most prevalent agent of IE(BIGNOTO T, 2023).

In general, all individuals can develop IE, however, some groups are more susceptible to being affected by pathogens that cause the disease (SILVA et al., 2023). For example, children with congenital heart disease, individuals who use injectable drugs, patients who have undergone surgery to replace a native valve with a prosthetic valve, those who have been exposed to invasive procedures and people with a previous history of endocarditis(CARVALHO LC, et al.m 2022).

The clinical manifestations of IE are extremely varied, including non-specific symptoms, isolated cardiac symptoms, and, in the most urgent cases, signs of shock(CHIRILLO F, 2020). At the same time, in some patients, IE can progress silently, only appearing when there is congestive heart failure in progress(SILVA et al., 2023). However, some patients may present extracardiac symptoms which, although uncommon, help to identify the condition, such as signs of cutaneous or conjunctival hemorrhage, subcutaneous Osler nodules, Janeway lesions, localized peritonitis and splenomegaly(YALLOWITZ AW and DECKER LC, 2023).

IE can be related to previous non-specific infections, such as following a urinary tract infection or dental procedures(SILVA et al., 2023). In addition, bacterial adhesion can occur through medical equipment, such as procedural instruments, valve prostheses, or implantations(SANTOS JM, et al., 2020). Another factor involved in the pathophysiology is the

interference of the coagulation cascade, which causes hypercoagulability, stimulated by inflammatory processes(DARGAINS RR, 2022). This is why vegetation formation occurs, due to the deposition of fibrin and platelets, associated with the inflammatory process(KAMDE SP and ANJANKAR A,2022).

In 2023, the International Society of Cardiovascular Infectious Diseases (ISCVID) reformulated the diagnostic criteria for IE, in particular those related to microbiological aspects. New microorganisms were added to the class of typical pathogens, these being the ones that most commonly cause endocarditis, so that a greater number of agents listed in the group of typical pathogens aims to increase the sensitivity of the Duke criteria for diagnosing the pathology at an early stage (SUNNERHAGEN T, et al., 2023).

The diagnosis of this infection is challenging, as it is common to find patients with a fever of unknown origin (MESQUITA et al., 2023). At the beginning of the infection, antibiotic therapy is the first choice, considering the epidemiological characteristics and the patient's clinical condition. However, when treatment with antimicrobial drugs is not effective, mainly due to the avascular vegetative presentation that makes it difficult to reach medications, surgical intervention is necessary. Surgery is recommended in cases of resistant infections, the development of abscesses and heart failure (SILVA et al., 2023). The aim of this study is therefore to discuss the modified Duke criteria, therapeutic measures and future challenges.

METHODOLOGY

This research is a narrative bibliographical review that looked at scientific production in an attempt to understand infective endocarditis and its challenges. To select the descriptors used, the Medical Subject Headings (Mesh) were consulted and the Boolean operators "AND" and "OR" were used to combine the terms. Articles written in English and Portuguese were selected from the following databases: Scielo, Lilacs, and Pubmed, using the descriptors "infective endocarditis", "endocarditis" and "bacterial endocarditis". As this was a literature review and used public domain databases, it was not necessary to submit the project to the Research Ethics Committee.

Initially, the titles and abstracts of the selected articles were read. The articles were then read in full in the first stage. The following aspects of the selected studies were assessed: the impact factor of the journal in which the article was published; the results obtained and the period of publication.

RESULTS

This is a rare pathology with an annual incidence of 3 to 10 cases per 100,000 people and is twice as common in males(art10). In addition, the most recent studies show that some conditions are more common in elderly individuals, such as artificial heart valve implantation, diabetes mellitus, acquired valve disease, and hemodialysis, favoring an increase in the average age to more than 65 years in individuals affected by IE(KHALEDI M, et al., 2022).

In Europe and the United States, 16% to 30% of cases are infections resulting from valve prostheses, and 25% to 35% of cases of native valve IE are infected within the hospital. In Brazil, valve disease as a result of rheumatic fever is still a significant risk factor for endocarditis, although in developed countries rheumatic disease is increasingly rare (MESQUITA et al., 2023; SOUSA, PINTO, 2022; CHEN et al., 2022).

The year 2021 had the highest number of cases and the highest mortality rate (de Melo, et al., 2021). As for the hospital mortality rate, according to EI-Dalati S, et al.(2019), it ranges between 15% and 20%. However, a 2019 study points out that in the first 30 days, the rate can reach 30%(HU,WANG,SU, 2019).

DISCUSSION

The Modified Duke Criteria, updated in 2023, are especially used in clinical practice and serve as an artifact for making choices about diagnosis and treatment quickly (MCDONALD EG, et al., 2023-art10). Initially suggested in 1994, these criteria for diagnosing IE were amended in 2000. However, the epidemiological characteristics, microbiological aspects and resources for diagnosing and treating this condition have changed significantly since the last update(FOWLER VG, et al., 2023). This is why, starting in 2021, ISCVID brought together a

working group made up of various experts from different continents and from areas such as cardiovascular surgery, cardiology, radiology, clinical microbiology, cardiovascular pathology and infectology, to point out updates to the criteria used(FOWLER VG, et al., 2023).

Since 1994, diagnostic imaging methods applied in medical practice have been evolving and becoming increasingly technological. This has brought benefits that have improved sensitivity and specificity rates compared to those of previous decades. Due to the adherence of these new technological resources in the most recent criteria, imaging modalities will be more prominent in the IE scenario. In addition, microbiological tests have also developed, but remain the same, with low specificity and high sensitivity (LINDBERG H, et al., 2023).

The recent update maintains the original model of the modified Duke criteria, including major imaging and microbiology criteria, which are complemented by minor criteria that may be correlated(LINDBERG H, et al., 2023). The new criteria, called the Duke-ISCVID 2023 criteria, are made up of major criteria that are divided into microbiological, imaging suggestive of IE, positive laboratory tests and surgical criteria, the last of which is new in the new adaptation(FOWLER VG, et al., 2023).

The microbiological criteria include positive blood cultures for the usual IE pathogens isolated in two or more blood cultures or positive blood cultures for microorganisms that rarely cause the disease isolated in three or more blood cultures (FOWLER VG, et al., 2023-art10). This criterion was one of the most important changes in the new update, as several pathogens were added to the typical group, such as Streptococcus dysgalactiae, Streptococcus agalactiae, Staphylococcus lugdunensis, Abiotrophia, Granulicatella and Gemella. This change has increased the sensitivity of the criteria, but decreased their specificity, which favors an increase in the probable classification of IE (SUNNERHAGEN T, et al., 2023).

Imaging criteria include: transesophageal or transthoracic echocardiogram, FDG PET/CT or CT scan showing cardiac involvement compatible with endocarditis. In addition to including new regurgitation on the echocardiogram, laboratory tests include: PCR or other nucleic acid-based method, positive for Bartonella species, Tropheryma whipplei or Coxiella burnetii ; or antibodies/ Indirect immunofluorescence for Bartonella. Due to this update, there is a new criterion, the surgical one, which is based on well-proven evidence of IE by intraoperative inspection during surgery, without major imaging criteria, microbiological or histological confirmation afterwards (FOWLER VG, et al., 2023).

Regarding the minor criteria, they deal with: (I) predisposition, previous episode of IE, congenital heart disease, previous history of valve intervention, hypertrophic cardiomyopathy or injection drug use; (II) immunological alterations, positive rheumatoid factor, glomerulonephritis, presence of Osler nodules or Roth spots; (III) vascular alterations, arterial embolism, conjunctival hemorrhage, mycotic aneurysm, splenic abscess or Janeway lesions ; (IV) microbiological phenomena, evidence that is not enough positive serology for pathogens that can generate IE, including PCR, metagenomic sequencing or amplicon; (V) imaging alteration, abnormal metabolic activity identified by FDG PET/CT within three months of ascending aortic graft, placement of intracardiac electrodes, valve prosthesis or other prosthetic material and (VI) fever greater than 38.0 degrees (FOWLER VG, et al. , 2023).

Therefore, considering the aforementioned criteria, the definitive diagnosis of IE is based on clinical or pathological criteria. The former assess the presence of pathological intracardiac lesions, whether abscesses or vegetations, which show active endocarditis on histology or identification of microorganisms according to histological analysis of cardiac tissue lesions or culture. The presence of one of the pathological criteria is acceptable for a definitive diagnosis. For a definitive clinical diagnosis, 1 major and 3 minor or 2 major and 5 minor clinical criteria are required. On the other hand, for a probable diagnosis of IE, the presence of 3 minor criteria or 1 minor and 1 major criterion is sufficient (FOWLER VG, et al., 2023).

The treatment of IE is complex, but its mainstay is antibiotic therapy and, when necessary, cardiac surgery(art9). According to Rezar R et al.(2021), empirical antibiotic treatment should be carried out as soon as possible after blood culture tests have been taken. Decisions on which antibiotic, form of therapy and timing depend on a number of factors, such as whether the affected valve is artificial or natural, and in the case of the latter, whether the surgery was recent or late. It is also necessary to consider whether the infection is community-acquired, nasocomial or of another type, as this affects the type of bacteria and possible resistance. When the pathogen is known, treatment should be targeted (CIMMINO G, et al., 2023). In any case, intravenous antibiotic therapy is indicated for around four to six weeks, which can be reduced to two weeks in stable patients, as long as the correct monitoring is maintained(ALMEIDA GMF, et al., 2023).

When drug therapy does not produce results, surgery is considered as the likely intervention. This therapy aims to remove damaged heart tissue and valve replacement in necessary cases(ARAÚJO KRS, et al., 2021-art10).However, this form of treatment should be advised before the end of the antibiotic treatment period in certain cases, for example when there is an uncontrolled infection, the need to prevent recurrence of embolism or refractory heart failure. In addition to these conditions, it is essential that the choice of surgery is based on an analysis of the patient's condition, possible contraindications and comorbidities that increase the risk of the procedure (CHIRILLO F, 2020). If infection occurs due to an implanted device, it should be removed, and if still necessary, rapid reimplantation should be avoided due to the risk of new infection(CIMMINO G, et al., 2023).

CONCLUSION

Infective endocarditis is one of the most laborious and difficult medical conditions for doctors in their clinical practice. Employing a systematic approach based on scientific evidence for diagnostic investigation and therapeutic care is extremely important for good results and patient well-being. Furthermore, when necessary, it is important to have discussions in multidisciplinary teams, detailed clinical assessment and new diagnostic techniques, as well as using the new Duke criteria in 2023, which aims to increase the tools available for investigating suspected patients and proposes standardization, aiding diagnosis and better outcomes in clinical management.

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