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Methods of diagnosing IE including nuclear imaging techniques - a review

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Abstract

Introduction and the purpose of work

IE is a disease diagnosed more and more often in recent years. Its treatment and diagnostics require a team of qualified specialists and are based on microbiological and imaging diagnostics. The purpose of this work is a summary and comparison of individual IE diagnostic methods, including their advantages and disadvantages.

State of knowledge: Diagnosis of infective endocarditis (IE) relies on positive blood cultures to identify the microorganism and its drug sensitivity. Advanced methods like MALDI-TOF MS and MIC are used for identification. The first-line imaging diagnostic method for IE is echocardiography, which assesses structural and functional heart damage. Variants include transthoracic (TTE), transesophageal (TOE), three-dimensional TOE, and intracardiac echocardiography. Echocardiography should be performed immediately when IE is suspected. Computed tomography (CT) is crucial for diagnosing infective endocarditis (IE), particularly perivalvular and periprosthetic complications. Whole-body CT, including the brain, detects distant lesions and sources of bacteremia. CT is more accessible in emergencies and effective in spotting ischemic and hemorrhagic complications. CT angiography identifies mycotic aneurysms in the vascular system. It also detects extracardiac sources of bacteremia, aiding treatment and pre-surgery planning. Nuclear imaging is also important in diagnosing IE, especially prosthetic valve endocarditis (PVE) when echocardiography is inconclusive. 18F-fluorodeoxyglucose-PET/CT and SPECT/CT with labeled leukocytes are recommended.

Conclusions: In addition to basic methods such as positive blood culture and echocardiography, there are more specialized methods that also allow for the assessment of treatment progress and prognosis.

Key words: infective endocarditis; echocardiography; blood cultures; computed tomography; nuclear imaging

Introduction

Infective endocarditis (IE) is a non-contagious infection of intracardiac structures that usually affects the valvular endocardium but may also affect devices implanted in the heart.

In 2019, the estimated incidence of IE was 13.8 cases per 100,000 people per year, and IE alone caused 66,300 deaths worldwide. (1) The incidence of IE has increased in recent years, which may be due to the increased use of more advanced diagnostic tools such as echocardiography in patients with positive blood cultures for microorganisms increasing the risk of IE (Enterococcus faecalis, Staphylococcus aureus, Streptococci) or computed tomography (CT) and nuclear imaging techniques especially among patients with prosthetic valves and implantable cardiac devices (2,3). Patients most often have non-specific symptoms that develop insidiously and may precede IE for several weeks or months. Despite advancements in diagnostics and treatment, the prognosis remains unfavorable, with increasing morbidity and hospital mortality underscoring the importance of rapid diagnosis for this disease which remains a big challenge for clinicians (4).In this work, we will focus on the entire diagnostic course of IE - from symptoms, through basic diagnostic methods such as echocardiography and blood cultures, to advanced imaging methods enabling effective and non-obvious diagnosis.

State of knowledge:

The etiological factors causing IE in over 90% of cases are bacteria (Staphylococci: Staphylococcus aureus, epidermidis and coagulase-negative, Streptococci: Streptococcus viridans - until recently the most common cause of IE on a natural valve, enterococci and Gram-negative bacteria, also from the HACEK group (5,6) Very rarely, IE is also caused by fungi, chlamydia, rickettsia and mycoplasmas. In people addicted to drugs, the etiology is often mixed. Factors of high risk contain a history of infective endocarditis (IE), prosthetic valves or cardiac repair materials, congenital heart disease (CHD), and ventricular assist devices. (7-10). Intermediate risk factors include rheumatic heart disease (RHD), non-rheumatic degenerative valve disease, congenital valve abnormalities such as bicuspid aortic valve disease, cardiovascular implanted electronic devices (CIEDs), and hypertrophic cardiomyopathy. (11)

Symptoms are nonspecific - high fever with chills or prolonged low-grade fever accompanied by sweating, malaise, weakness, joint and muscle pain, lack of appetite and weight loss,

headache, nausea.(12) If the left part of the heart is affected, murmurs of regurgitation of the damaged valve will be observed (~80% of patients), symptoms of heart failure, pulmonary edema, symptoms related to embolism to the CNS and arteries of the entire body. . If the right side of the heart is affected, the symptoms of pneumonia and pulmonary embolism predominate (cough and pleuritic chest pain). Vascular and immunological phenomena, such as splinter hemorrhages, Roth spots, and glomerulonephritis, continue to be common occurrences.(13). An atypical presentation frequently occurs in elderly or immunocompromised patients.

There are no specific laboratory tests to confirm or rule out EI. C-reactive protein and procalcitonin are used to monitor the course of the disease during antibiotic therapy. (14). The basis of diagnosis are positive blood cultures, which provide information about the type of microorganism and its sensitivity to drugs. Before administering antibiotics, a minimum of 3 sets of blood samples should be collected at 30-minute intervals and incubated in aerobic and anaerobic conditions. There is no need to wait for the fever to peak because bacteremia is almost constant in IE (15). Full identification is performed using new methods such as matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) or minimum inhibitory concentration (MIC), which is still the gold standard(16). If it is impossible to grow pathogenic microorganisms when using normal blood culture methods, this indicates the presence of infective endocarditis with negative blood cultures (BCNIE). The frequency of this phenomenon is variable and is most often associated with the administration of antibiotics before blood collection for culture (17). Systematic serological tests for Coxiella burnetii, Bartonella spp., Aspergillus spp., Mycoplasma pneumoniae, Brucella spp. and Legionella pneumophila should then be proposed as well as specific ones like polymerase chain reaction tests (PCR) towards Tropheryma whipplei, Bartonella spp. and fungi (Candida spp., Aspergillus spp.) from blood and collected tissues (18). In most laboratories, 16S and 18S rRNA sequencing from collected tissues can aid in diagnosing microorganisms in BCNIE. For patients with suspected BCNIE on an artificial valve, combining molecular imaging fluorescence in situ hybridization with 16S rRNA gene PCR and sequencing may improve pathogen identification. Future advancements in free next-generation sequencing of microbial DNA in plasma may enable quicker diagnosis of the cause of IE. (19) If all microbiological tests are negative, the diagnosis should be considered nonbacterial endocarditis and testing for antinuclear antibodies and antiphospholipid syndrome (APL) although these antibodies may also occur in patients with confirmed IE) (20).

The first-line diagnostic method for IE is echocardiography, which allows the assessment of both structural and functional damage to the heart. This test comes in several variants:

transthoracic echocardiography (TTE), transesophageal echocardiography (TOE), three-dimensional TOE and intracardiac echocardiography (21). Echocardiographic changes in the diagnosis and assessment of local complications of IE include: characteristics and size vegetation, perivalvular complications (abscess, pseudoaneurysm, new partial rupture of the valve prosthesis), intracardiac fistula and leaflet perforation. Echocardiography should be performed immediately when IE is suspected (22). Echocardiography more effectively detects common valvular lesions, especially small ones vegetation (<10 mm) which may not be visible in computed tomography, and flap perforations and fistulas. (23).

Computed tomography is also used in the diagnosis of IE and should be performed in accordance with recommendations for cardiac CT to maintain diagnostic accuracy. CT is more accurate than TOE in the diagnosis of perivalvular and periprosthetic complications (abscesses, pseudoaneurysms and fistulas). Computed tomography (CT) of the entire body, including the brain, is valuable for detecting distant lesions and sources of bacteremia in infective endocarditis (IE), such as septic emboli and mycotic aneurysms, and can assist in the diagnosis or exclusion of IE. (24,25) While MRI has some advantages in identifying neurological complications, CT is more accessible in emergencies and effective in detecting ischemic and hemorrhagic complications. CT angiography is useful for identifying mycotic aneurysms in the vascular system, including the CNS. (26) Additionally, CT can detect extracardiac sources of bacteremia, including early cancer lesions, which is important for patient treatment and planning before cardiac surgery. However, CT cannot replace specific diagnostic tests for non-cardiac sources of bacteremia, such as colonoscopy for colorectal cancer. Preoperative assessment includes coronary vessel angio-CT. If appropriate indications, CT is performed together with PET.

Nuclear imaging also plays an important role in the diagnosis of IE. 18F-fluorodeoxyglucose-PET/CT and SPECT/CT (single photon emission tomography/computed tomography) labeled with leukocytes (WBC, white blood cells) are recommended if PVE (prosthetic valve endocarditis) is suspected with inconclusive echocardiography results (27). SPECT/CT with labeled leukocytes is an alternative nuclear imaging technique in diagnostics IE when PET/CT is unavailable or there is insufficient experience with this technique. Imaging 99mTc-HMPAO (99mTechnetium-hexamethyl propylene amine oxime) SPECT/CT helped reduce the number of misdiagnosed IE cases classified in the "possible IE" category according to the modified Duke’s criteria. (28) Abnormal [18F]FDG uptake is not a necessary condition for the diagnosis of NVE (native valve endocarditis) due to the reduced inflammatory response and lower uptake of FDG and white blood cells (29). This method has low sensitivity, but is good at detecting

septic emboli. Whole body [18F]FDG-PET/CT imaging is also useful in identifying distant changes like mycotic aneurysms and sources of infection. Septic emboli are usually located in the spleen, lungs and kidneys and metastatic infections in intervertebral discs or the vertebrae, muscles, joints and in the liver (30, 31). Imaging FDG-PET/CT is less useful for detecting cerebral changes due to high physiological uptake of [18F]FDG in the brain.

Summary:

The diagnosis of infective endocarditis (IE) relies on clinical suspicion, supported by microbiological evidence and the identification of IE-related cardiac lesions through imaging. A key diagnostic criterion is the detection of involvement in native or prosthetic cardiac valves or prosthetic intracardiac material. Echocardiography is the primary imaging technique used, while CT, nuclear imaging, and MRI also play significant roles in diagnosing IE, assessing local and distant complications, and identifying the original source of bacteraemia. Additionally, imaging findings have prognostic value beyond just diagnosing IE.

Disclosure

Detailed author's contribution: conceptualization - Jagna Golemo and Małgorzata Miazga; methodology - Barbara Serkis; software - Zuzanna Bentkowska; checking - Julia Dębińska; formal analysis - Izabela Kałuża; investigation - Magdalena Ostojska, resources - Magdalena Górska; data storage - Magdalena Celichowska; letter - rough preparation - Jagna Golemo; writing - review and editing - Gabriela Dziuba, Magdalena Celichowska; visualization - Małgorzata Miazga; supervision - Barbara Serkis; project administration - Zuzanna Bentkowska, Gabriela Dziuba;

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