

Endocarditis diagnosis: Why the old rules no longer apply

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Infective endocarditis remains a diagnostic challenge, often presenting with non-specific symptoms and requiring a high index of suspicion. The previous diagnostic criteria, while foundational, sometimes struggled with atypical presentations or the nuances of modern diagnostic tools. The 2023 Duke-ISCVID criteria represent a significant evolution, aiming to provide a more precise and timely diagnosis for clinicians facing this complex condition, as detailed in their recent publication.

KEY TAKEAWAYS

- **The Pivot:** The 2023 Duke-ISCVID criteria integrate advanced imaging and microbiological methods, moving beyond the original Duke criteria's limitations.
- **The Data:** The revised criteria introduce new 'major' and 'minor' categories for imaging and microbiological evidence, enhancing diagnostic sensitivity and specificity.
- **The Action:** Clinicians should familiarize themselves with the updated definitions for echocardiographic findings, PET/CT, and molecular microbiological assays to apply the criteria effectively.

Diagnosing infective endocarditis (IE) has long relied on the modified Duke criteria, a framework that has served clinicians well since its inception. But medicine evolves, and with it, the tools available for detecting subtle signs of infection on heart valves. The original criteria, developed in an era predating widespread PET/CT and advanced molecular diagnostics, faced limitations in certain patient populations, particularly those with prosthetic valves or device-related infections. These cases often presented diagnostic ambiguities, leading to delays or misdiagnoses. The International Society of Cardiovascular Infectious Diseases (ISCVID) collaborated with Duke University to address these gaps, culminating in the 2023 Duke-ISCVID criteria.^{1,2,3} This revision aims to improve diagnostic accuracy by incorporating contemporary imaging modalities and microbiological techniques.^{1,2,3,4} The goal is a more robust and responsive diagnostic framework for a disease where early, accurate diagnosis can significantly impact patient outcomes.^{2,3,4} The Oxford Handbook of Infectious Diseases and Microbiology offers a concise overview of such diagnostic challenges.

Refining the Major and Minor Criteria

The core structure of major and minor criteria remains, but their definitions have been substantially updated. The 2023 criteria introduce new major imaging criteria that acknowledge the enhanced capabilities of modern diagnostics. For instance, evidence of active infection on 18F-FDG PET/CT in prosthetic valves or cardiac devices is now a major criterion.¹ This is a significant addition, as these infections are notoriously difficult to visualize with standard

echocardiography alone, and the ability to detect them early can prevent severe complications. Similarly, cardiac CT demonstrating perivalvular lesions, such as abscesses or pseudoaneurysms, also qualifies as a major imaging criterion. These changes reflect a pragmatic recognition that advanced imaging can provide definitive evidence of IE where echocardiography might be equivocal or negative.

Microbiological criteria also see significant revisions.¹ The definition of typical microorganisms has been expanded, and the role of molecular methods has been formalized.⁴ Positive blood cultures for typical IE organisms remain a major criterion, but now, positive results from culture-negative endocarditis panels, often employing PCR or metagenomic sequencing, can also fulfill a major microbiological criterion.^{1,4} This is particularly relevant for patients who have received prior antibiotic therapy, which can sterilize blood cultures but leave microbial DNA detectable. The inclusion of these advanced techniques acknowledges the increasing prevalence of culture-negative IE and provides a pathway for definitive diagnosis in these challenging cases.⁴ This shift aligns with broader trends in infectious disease diagnostics, as seen in discussions around Lyme disease diagnosis.

The Role of Imaging in the New Framework

Echocardiography, both transthoracic (TTE) and transesophageal (TEE), remains central to IE diagnosis. The 2023 criteria refine the echocardiographic major criteria, emphasizing specific findings like oscillating intracardiac mass on a valve or supporting structures, abscess, pseudoaneurysm, or new partial dehiscence of a prosthetic valve. But the real strength of the new criteria lies in their integration of other imaging modalities. PET/CT, particularly 18F-FDG PET/CT, is now explicitly recognized for its utility in prosthetic valve endocarditis (PVE) and cardiac implantable electronic device (CIED) infections.¹ A positive PET/CT scan showing increased uptake around a prosthetic valve or device is a major criterion, a significant upgrade from its previous ancillary role.¹ This acknowledges the superior sensitivity of PET/CT for detecting inflammation and infection in these complex anatomical sites.

Cardiac CT also gains prominence, with perivalvular lesions identified on CT now counting as a major imaging criterion. This is particularly useful when echocardiography is limited by acoustic windows or when better anatomical resolution is needed to characterize an abscess or pseudoaneurysm. The criteria also provide clearer guidance on what constitutes a 'new' regurgitation, moving away from subjective interpretation to more objective measures. This multi-modality imaging approach allows clinicians to leverage the strengths of different techniques, improving the overall diagnostic yield. The integration of advanced imaging parallels developments in other fields, such as the use of non-invasive markers for MASH diagnosis.

Microbiological Advancements and Clinical Context

The updated microbiological criteria are perhaps the most forward-looking aspect of the 2023 Duke-ISCVID revision.⁴ Beyond standard blood cultures, the criteria now explicitly incorporate molecular methods for pathogen identification.^{1,4} This includes PCR from excised valve tissue or emboli, as well as broad-range 16S rRNA gene sequencing. For patients with culture-negative endocarditis, a positive result from these molecular tests for a typical IE pathogen can now be a major criterion.⁴ This is a critical improvement, as a substantial proportion of IE cases are culture-negative, often due to prior antibiotic exposure or fastidious organisms.⁴

The minor criteria also see adjustments, with a greater emphasis on predisposing cardiac conditions and intravenous drug use. Fever (temperature $>38.0^{\circ}\text{C}$) remains a minor criterion, as do vascular phenomena (e.g., arterial emboli,

septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, Janeway lesions) and immunological phenomena (e.g., glomerulonephritis, Osler's nodes, Roth's spots, rheumatoid factor). The revised criteria also provide clearer definitions for these phenomena, reducing ambiguity. The careful consideration of clinical context alongside advanced diagnostics is paramount. For a broader understanding of diagnostic criteria in other conditions, one might review the 2023 criteria for Calcium Pyrophosphate Deposition Disease.

Applying the Criteria at the Bedside

For a definite diagnosis of IE, the 2023 Duke-ISCVID criteria require either two major criteria, one major and three minor criteria, or five minor criteria. A possible diagnosis is made with one major and one or two minor criteria, or three or four minor criteria. This tiered approach allows for flexibility while maintaining diagnostic rigor. The criteria also provide specific guidance for prosthetic valve endocarditis and device-related endocarditis, recognizing the unique challenges in these populations. For example, new major imaging criteria like PET/CT uptake are particularly impactful here.¹ The open-label nature of clinical application is the obvious caveat; these are diagnostic guidelines, not a randomized trial. Their utility depends on judicious application and the availability of advanced diagnostics.

The new criteria represent a significant step forward in IE diagnosis.^{2,3,4} They acknowledge the evolution of medical technology and provide a more comprehensive framework for clinicians.⁴ But the core challenge remains: recognizing the possibility of IE in a patient with non-specific symptoms. No diagnostic criteria, however refined, can replace clinical suspicion and a thorough patient evaluation. The criteria provide the tools, but the clinician must still wield them effectively. The next step will be to see how these criteria perform in real-world settings, particularly in resource-limited environments where advanced imaging may not be readily available.

CLINICAL IMPLICATIONS

The 2023 Duke-ISCVID criteria demand a shift in diagnostic thinking for infective endocarditis. Clinicians can no longer rely solely on echocardiography and blood cultures, especially in complex cases like prosthetic valve infections. Integrating advanced imaging, specifically PET/CT and cardiac CT, is now not just an option but a defined component of a major diagnostic criterion. This means a higher threshold for imaging referral and interpretation expertise.

The formal inclusion of molecular microbiological techniques for culture-negative endocarditis is a welcome, if overdue, development. It provides a clearer path to diagnosis for patients who have received antibiotics or are infected with fastidious organisms. But this also requires laboratories to be equipped for and clinicians to be aware of these specialized tests, which are not universally available or routinely ordered.

For general practitioners and specialists alike, understanding these updated criteria is critical. The revised definitions for major and minor criteria, particularly around imaging and microbiology, will influence how cases are investigated and managed. This is not merely an academic exercise; it directly impacts patient care, potentially reducing diagnostic delays and improving outcomes in a disease with high morbidity and mortality.

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