Duke-ISCVID 2023: What changed for endocarditis diagnosis at the bedside?

Written by The Life Science Feed Editorial Team · Edited by Mara Voss

> Infective endocarditis remains a formidable diagnostic challenge, often presenting with protean manifestations that can delay appropriate therapy. Early and accurate diagnosis is paramount for improving patient outcomes, but the traditional diagnostic criteria have faced limitations in capturing the full spectrum of the disease.
> The 2023 Duke-ISCVID criteria represent a significant evolution, aiming to enhance diagnostic precision by incorporating modern diagnostic tools and clinical insights.

KEY TAKEAWAYS

- The Pivot: The 2023 Duke-ISCVID criteria now integrate advanced imaging modalities and molecular microbiological techniques, moving beyond the limitations of earlier iterations.
- The Data: The updated criteria emphasize the role of PET/CT and cardiac CT, particularly for prosthetic valve endocarditis, alongside a refined approach to blood culture interpretation.
- The Action: Clinicians should be prepared to incorporate these advanced diagnostic tools earlier in the workup, especially in complex cases or when initial investigations are inconclusive, to avoid diagnostic delays.

Diagnosing infective endocarditis has historically relied on a combination of clinical, microbiological, and echocardiographic findings. The original Duke criteria, introduced in 1994 and modified in 2000, provided a structured framework that significantly improved diagnostic consistency. But the evolving market of medical interventions, particularly the increasing prevalence of prosthetic valves and intracardiac devices, exposed gaps in these earlier criteria. These devices present unique challenges for infection detection, often masking typical echocardiographic signs or yielding equivocal blood cultures.

The International Society of Cardiovascular Infectious Diseases (ISCVID) collaborated with Duke University to revise these criteria, culminating in the 2023 update. This revision addresses the limitations of prior guidelines by acknowledging the expanded diagnostic toolkit available to clinicians today. The goal was to create a more sensitive and specific diagnostic framework, particularly for challenging patient populations such as those with prosthetic valves or device-related infections. The revisions aim to reduce the number of 'possible' endocarditis diagnoses, pushing more cases into definitive or rejected categories.

Refining Major and Minor Criteria

The core structure of major and minor criteria persists in the 2023 Duke-ISCVID update, but with substantial modifications to their definitions and weighting. The major criteria for microbiological evidence now explicitly include

molecular techniques, such as PCR assays on excised valve tissue, alongside traditional blood cultures. This is an important addition, recognizing that many cases of endocarditis, particularly those involving fastidious organisms or prior antibiotic exposure, may yield negative standard blood cultures. A positive PCR from vegetation or embolus tissue can now contribute to a major criterion, offering a pathway to diagnosis where conventional methods fail. This shift reflects a broader trend in infectious disease diagnostics, where molecular methods are increasingly used to identify pathogens that are difficult to culture.

Echocardiographic major criteria have also seen refinement. While transesophageal echocardiography (TEE) remains the cornerstone for visualizing vegetations, abscesses, or new dehiscence of prosthetic valves, the updated criteria give more explicit guidance on what constitutes a definitive finding. The presence of new valvular regurgitation, previously a minor criterion, is now considered a major criterion if it is clearly attributable to endocarditis and not a pre-existing condition. This change acknowledges the significant prognostic implication of new or worsening regurgitation in the context of suspected endocarditis.

The Role of Advanced Imaging

Perhaps the most impactful change in the 2023 Duke-ISCVID criteria is the elevated role of advanced imaging modalities. Positron emission tomography/computed tomography (PET/CT) with 18F-FDG and cardiac computed tomography (CT) are now integrated as major criteria, particularly for prosthetic valve endocarditis (PVE) and intracardiac device-related endocarditis (ICD-E). For PVE, a positive 18F-FDG PET/CT scan showing abnormal uptake around the prosthetic valve, or a cardiac CT demonstrating perivalvular lesions, can now fulfill a major criterion. This is a significant departure from previous guidelines, which primarily relied on echocardiography.

The rationale for this inclusion is clear: prosthetic material often creates acoustic shadowing on echocardiography, making vegetations or abscesses difficult to visualize. PET/CT, by detecting metabolic activity associated with inflammation and infection, can pinpoint infected areas that might be missed by TEE. Similarly, cardiac CT offers superior anatomical detail for assessing perivalvular complications, such as pseudoaneurysms or fistulas, which are hallmarks of invasive endocarditis. These imaging techniques are particularly valuable in patients with suspected PVE or ICD-E who have inconclusive echocardiographic findings or persistent fever despite antibiotic therapy. General practitioners may find the Oxford Handbook of General Practice, 5th Edition a useful quick reference for initial assessment and referral pathways in such complex cases.

Microbiological Refinements

The microbiological criteria have also been sharpened. The definition of typical microorganisms consistent with infective endocarditis has been expanded, and the role of persistently positive blood cultures has been clarified. For instance, a single positive blood culture for Coxiella burnetii or Bartonella species can now satisfy a major criterion, reflecting their known association with culture-negative endocarditis. This is a pragmatic adjustment, recognizing that these organisms are notoriously difficult to isolate and often require specialized serological testing or molecular methods for diagnosis.

The criteria also provide more explicit guidance on how to interpret blood cultures in patients who have already received antibiotics, acknowledging that prior treatment can suppress bacterial growth and lead to false negatives.

The updated guidelines also emphasize the importance of identifying the specific pathogen, as this directly informs antibiotic selection and duration. For cases where blood cultures remain negative, but there is strong clinical suspicion,

the criteria now more clearly endorse the use of serological tests for atypical pathogens and molecular diagnostics on valve tissue or emboli. This comprehensive approach to microbiological diagnosis aims to reduce the incidence of 'culture-negative' endocarditis, a frustrating diagnostic category that often delays definitive treatment. Clinicians grappling with these complex diagnostic pathways might find our previous coverage on Lyme disease and missed early diagnosis relevant, as similar challenges with pathogen identification can arise.

Minor Criteria and Clinical Context

The minor criteria continue to play an important role in building a diagnostic picture, particularly when major criteria are not fully met. These include predisposing heart conditions or intravenous drug use, fever, vascular phenomena (e.g., arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, Janeway lesions), immunological phenomena (e.g., glomerulonephritis, Osler's nodes, Roth's spots, rheumatoid factor), and microbiological evidence not meeting a major criterion. The 2023 update refines the definitions of these phenomena, ensuring they are applied consistently. For example, the criteria now provide clearer guidance on what constitutes a 'predisposing heart condition,' focusing on conditions with a well-established link to endocarditis risk.

The overall framework still requires a combination of major and minor criteria for a definitive diagnosis (e.g., two major criteria, or one major and three minor criteria, or five minor criteria). This structured approach helps to balance sensitivity and specificity, ensuring that a diagnosis of endocarditis is not made lightly, given its severe implications for treatment and prognosis. The emphasis on clinical context remains paramount; the criteria are a tool to aid diagnosis, not a substitute for sound clinical judgment. The challenge often lies in integrating these diverse pieces of information, a skill honed through experience and supported by comprehensive resources like the Oxford Handbook of Infectious Diseases and Microbiology (3rd ed).

Implications for Clinical Practice

The 2023 Duke-ISCVID criteria represent a significant step forward in the diagnosis of infective endocarditis. For clinicians, this means a greater reliance on advanced imaging, particularly for prosthetic valve and device-related infections. It also necessitates a more precise approach to microbiological diagnosis, incorporating molecular techniques when traditional cultures are negative. The updated criteria should lead to earlier and more accurate diagnoses, potentially reducing the morbidity and mortality associated with this severe infection. But the availability and accessibility of these advanced diagnostic tools, such as PET/CT, will vary across healthcare systems, posing a practical challenge for widespread implementation. Our earlier piece on endocarditis and the team approach highlighted the importance of multidisciplinary collaboration, which becomes even more critical with these complex diagnostic pathways.

The criteria also highlight the importance of a high index of suspicion in at-risk patients. Clinicians should not hesitate to pursue advanced diagnostics when initial investigations are inconclusive, especially in the presence of persistent fever or new embolic events. The goal is to move beyond a 'possible' diagnosis to a 'definitive' one as quickly as possible, enabling timely initiation of appropriate antimicrobial therapy and, when indicated, surgical intervention. The revised criteria provide a clearer roadmap for achieving this, but their effective application will depend on clinician awareness and access to the necessary diagnostic infrastructure.

CLINICAL IMPLICATIONS

The 2023 Duke-ISCVID criteria are not merely an academic exercise; they demand a tangible shift in clinical practice. For clinicians, this means a greater comfort level with ordering and interpreting advanced imaging like PET/CT and cardiac CT, particularly in the context of prosthetic valves or intracardiac devices. Relying solely on echocardiography in these complex scenarios is now insufficient, and a 'wait and see' approach risks delaying definitive diagnosis and treatment.

The expanded microbiological criteria, incorporating molecular methods, should prompt a more aggressive pursuit of pathogen identification in culture-negative cases. This moves beyond the frustrating 'culture-negative endocarditis' label, offering a clearer path to targeted therapy. It also highlights the need for close collaboration with microbiology labs that can perform these specialized assays, ensuring that valuable tissue samples are processed appropriately.

For healthcare systems, the updated criteria highlight the need for equitable access to these advanced diagnostic modalities. If PET/CT is now a major criterion for PVE, then systems must ensure that patients, regardless of their location or socioeconomic status, can access these scans in a timely manner. This is not just about diagnostic accuracy; it is about reducing the significant morbidity and mortality associated with delayed endocarditis diagnosis, a burden that disproportionately affects vulnerable populations.

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