Caveats for Validating the Diagnostic Accuracy of Diagnostic or Classification Criteria for Infective Endocarditis

To the Editor—For the first time in 23 years, a proposal has been made to revise the Duke criteria for infective endocarditis (IE) [1], and I believe the revision is in line with the current situation, reflecting technological developments such as positron emission tomography–computed tomography and other imaging tests and nucleic acid–based microbiological tests. As the authors note, external validation remains to be performed. The authors state that the sensitivity should be examined in patients with pathologically confirmed IE, and the specificity should be examined in cases of valve histopathology that is denied by surgery or autopsy, or in patients with bacteremia who have negative imaging tests and can be treated with antimicrobial agents for a short period of time [1]. Such a validation of sensitivity and specificity is called a multiple-gate study or case-control study with multiple inclusion criteria, and is prone to overestimation due to bias because the disease spectrum tends to deviate from actual clinical practice [2, 3]. The classification criteria for rheumatoid arthritis and systemic lupus erythematosus have been validated for diagnostic accuracy by multiple expert panels or by using the clinical course of the disease as the "gold standard" [4, 5]. The diagnostic criteria for IE, which ought to be termed to as classification criteria, should likewise be validated by multiple experts who assess whether a patient with "suspected IE" actually has the condition based on the entire clinical course of the patient.

Note

Potential conflicts of interest. The author: No reported conflicts of interest. The author has submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

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Consequences of Excluding *Enterococcus faecium* as a Typical Endocarditis Pathogen in the Duke-ISCVID Criteria: Endocarditis Is Endocarditis Even if the Bacterium Is Uncommon

To the Editor—The 2023 Duke-ISCVID (International Society for Cardiovascular Infectious Diseases) criteria, recently published in your journal, provide many new important aspects to the diagnostic criteria for infective endocarditis (IE) [1]. The revised criteria keep the original format of the Duke criteria, including major imaging and major microbiology criteria, complemented with minor criteria [1–3]. Whereas methods for imaging have been revolutionized since the introduction of the Duke criteria in 1994 [2], the microbiological methods have developed but are still, in essence, the same. The more sophisticated imaging techniques have likely led to radically increased sensitivity and specificity as compared with the 1990s, whereas the sensitivity of the microbiological method remains high and the specificity remains low. This development should, in our opinion, result in a more pronounced emphasis on the imaging modalities in the diagnostic criteria for IE.

One of the changes in the 2023 Duke-ISCVID criteria is that *Enterococcus faecium* is no longer considered a "typical endocarditis pathogen" and thus 2 positive blood cultures with *E. faecium* are regarded as a minor criterion [1, 3]. In the previous version, nonnosocomial *E. faecium* bacteremia with unknown focus was considered as a typical endocarditis pathogen [3]. It is generally accepted that IE is rare in bacteremia with *E. faecium* [4, 5]. However, *E. faecium* can indeed cause IE and the consequence of the reclassification of the species is shown in Figure 1 with data from the Swedish Registry for Infective Endocarditis (SRIE) [6].

There were 7679 cases of patients treated for IE reported to the SRIE between 2008 and the present. Of these, 52 episodes (0.7%) were caused by *E. faecium*. Figure 1 demonstrates the consequences for the classification of these 52 cases by the proposed changes of the criteria. Importantly, in the 14 cases reclassified from definite IE to possible IE with the Duke-ISCVID criteria, 13 patients had vegetations demonstrated with echocardiography in conjunction with

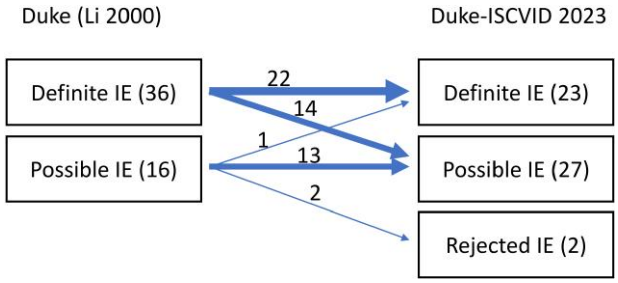

Figure 1. Consequence of the Dukes-ISCVID 2023 reclassification of *E.faecium on IE*, data from the Swedish Registry for Infective Endocarditis 2008–2023. Abbreviations: IE, infective endocarditis; ISCVID, International Society for Cardiovascular Infectious Diseases.

positive blood cultures with *E. faecium*. In 1 case, a patient with pacemaker vegetations was reclassified from possible to definite IE with the Duke-ISCVID criteria since pacemaker has been added as a minor criterion in the latter [1].

The sensitivity of the ISCVID-Duke criteria thus decreases when *E. faecium* is excluded from the "typical endocarditis pathogens." The Duke-ISCVID criteria chose to include nosocomially acquired *Enterococcus faecalis* bacteremia with known focus as a major criterion, although IE is known to be rare in this condition [7]. The argument for including *E. faecalis* was that the sensitivity of the criteria increased [8].

Our observations on *E. faecium* endocarditis point to the fact that it does not matter if a bacterium is a common or a rare cause of IE when the patient has IE as determined by echocardiography and concomitant bacteremia. We propose that the diagnostic criteria for IE could be revised so that patients fulfilling major imaging criteria and having significant bacteremia, irrespective of species, should be regarded as definite IE. In cases with negative imaging, the propensity of the bacterium to cause IE should be considered as well as other minor criteria.

Notes

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Microorganisms That Commonly Cause Infective Endocarditis: What About *Aerococcus* in the Duke–International Society for Cardiovascular Infectious Diseases Criteria?

To the Editor—International Society for Cardiovascular Infectious Diseases (ISCVID) criteria, recently published in *Clinical Infectious Diseases*, include important revisions to the microbiological aspects of the diagnostic criteria for infective endocarditis (IE) [1]. The revised criteria provide useful simplifications for the interpretation of blood culture results in relation to whether a bacteremia constitutes a major or a minor Duke–ISCVID criterion [1–3]. The most significant