**Evaluation of the Duke Criteria Versus the Beth Israel Criteria for the Diagnosis of Infective Endocarditis**

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New diagnostic criteria for infective endocarditis (IE) have been proposed by the Duke University Endocarditis Service (Durham, NC) to update the widely used Beth Israel (Boston) criteria. We compared the Duke criteria with the Beth Israel criteria in a series of 115 consecutive patients with suspected IE who were hospitalized in a referral center. The diagnosis of IE was histologically and/or bacteriologically confirmed for 27 operated patients. If surgery had not been performed on these 27 patients, 22 vs. 12 would have been classified as having “clinically definite” and “probable” IE by the Duke vs. the Beth Israel criteria, respectively, whereas 0 vs. 5 would have been “rejected” by the Duke vs. the Beth Israel criteria, respectively. The improvement in sensitivity of the criteria from 44% (Beth Israel) to 82% (Duke) was statistically significant \( P < .01 \). We confirm that the Duke criteria improve the sensitivity of diagnosis of IE. The specificity of these criteria should be further evaluated.

The diagnosis of infective endocarditis (IE) can be difficult in a high proportion of cases. In 1981, von Reyn and colleagues (Beth Israel Hospital, Boston) proposed diagnostic criteria based upon a strict case definition [1]. Four diagnostic categories with criteria for each were created: “definite,” “probable,” “possible,” and “rejected” (table 1). The Beth Israel criteria, also known as the von Reyn criteria, were rapidly accepted and widely used through the 1980s. However, they have been criticized in recent years for two main reasons: (1) they do not include the findings of echocardiography and (2) the “definite” category includes only cases proven by histologic examination of specimens obtained at surgery or autopsy, thereby limiting “definite” diagnoses to pathologically proven cases, which are a minority. These shortcomings result in most cases of IE being classified as “probable” or “possible” even when the diagnosis seems certain on clinical grounds [2], thus prompting clinical investigators to modify the Beth Israel criteria in various, often nonvalidated, ways [3–6]. New diagnostic criteria for IE developed by Durack et al. [7] from Duke University (Durham, NC) were designed to update the Beth Israel criteria [7]. The two case definitions, which are based upon conceptually different approaches [8, 9], can be differentiated from each other by their use of echocardiographic findings. These findings are emphasized in the Duke criteria, resulting in an improved sensitivity of clinical diagnosis of IE [7, 10].

The aim of this study was to independently evaluate the sensitivity of the Duke criteria as compared with that of the Beth Israel criteria for the diagnosis of IE.

**Patients and Methods**

**Hospital**

The Brabois University of Nancy Medical Center (Nancy, France) is a 1,100-bed hospital that serves as a tertiary referral center as well as a primary care center for the 300,000 people living in the Nancy area. It has two cardiovascular surgical wards, two cardiology wards, and one department of infectious diseases.

**Patient Population**

From January 1991 to December 1993, the data for all patients for whom IE was diagnosed who were hospitalized in either the cardiology ward or the infectious diseases department were prospectively recorded in a computerized database. The diagnosis of IE was obtained by consensus of a cardiologist (C.S.S.) and an internist from the department of infectious diseases (P.S.S.) and an internist from the department of infectious diseases (B.I.L.) on clinical, laboratory, and echocardiographic grounds. IE was defined as echocardiographically documented when a typical vegetation (defined as an oscillating intracardiac mass appended on a valve), a ring abscess, or a new partial prosthetic valve dehiscence could be demonstrated by either transthoracic or transesophageal echocardiography. All but two patients underwent both types of echocardiography. By the end of 1993, the records of 115 consecutive patients had been entered into the database. The suspicion of IE was such that all patients were given a full course of antibiotic therapy for 4–8 weeks.
Comparison of Diagnostic Criteria

We compared the Beth Israel criteria with the Duke criteria. Table 1 shows the original Beth Israel criteria. Table 2 lists the Duke criteria, and table 3 summarizes the definitions used in these Duke criteria.

The sensitivity of the Duke criteria was compared with that of the Beth Israel criteria in relation to our database population. The case population was separated into two subgroups: the first subgroup included all definite, histologically confirmed cases of IE, and the second subgroup included the remaining cases. In the first subgroup, each case was further reclassified on the basis of clinical, laboratory, and echocardiographic findings; histologic findings were excluded. In both subgroups, the three diagnostic categories of the Duke criteria (clinically definite, possible, and rejected) were cross-tabulated vs. the three diagnostic categories of the Beth Israel criteria (probable, possible, and rejected). The sensitivities of each set of criteria could only be calculated and compared in the first subgroup of cases since pathological proof was lacking in the second subgroup of cases.

Statistical Analysis

To compare the diagnostic sensitivities of the two sets of diagnostic criteria, the McNemar $\chi^2$ test was performed. Two-sided tests of significance were performed with an $\alpha$ of 0.05. Statistical analyses were performed using BMDP software (BMDP Statistical Software, Los Angeles).

Results

Patient Characteristics

Of the 115 patients for whom IE was diagnosed who were evaluated in this study, 75 (65%) were males and 40 (35%) were females; patients had a mean age of 53.7 ± 19.5 years. Fifty-one patients had previously diagnosed native valve disease, 28 patients had a prosthetic valve, and 36 patients had no previously known heart disease (5 of these 36 had intravenous drug addiction as their only risk factor for IE). The causative microorganisms were identified by cultures of blood and/or valve specimens from 94 patients (82%). These cultures yielded 57 streptococci (61%) (21 viridans streptococci, 16 Streptococcus bovis isolates, 9 enterococci, and 11 other streptococci), 29 staphylococci (31%), and 8 other pathogens (8%).

Table 1. Definition of IE according to the Beth Israel criteria.

<table>
<thead>
<tr>
<th>Category</th>
<th>Diagnostic Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite IE</td>
<td>Direct evidence of IE based on histologic evidence from surgery or autopsy or on bacteriologic evidence (gram stain or culture of valvular vegetation or peripheral embolus specimen)</td>
</tr>
<tr>
<td>Probable IE</td>
<td>Persistent positive blood cultures* plus one of the following: (1) new regurgitant murmur or (2) predisposing heart disease¹ and vascular phenomena²</td>
</tr>
<tr>
<td>Possible IE</td>
<td>Negative or intermittently positive blood cultures³ with all three of the following: fever, new regurgitant murmur, and vascular phenomena³</td>
</tr>
<tr>
<td>Rejected IE</td>
<td>Endocarditis unlikely, alternative diagnosis generally apparent</td>
</tr>
</tbody>
</table>

Table 2. Definition of infective endocarditis according to Duke criteria.

<table>
<thead>
<tr>
<th>Category</th>
<th>Diagnostic Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite IE</td>
<td>Pathologic criteria: (1) microorganism demonstrated by culture or histologic examination of a vegetation, or an intracardiac abscess specimen; or (2) pathologic lesions: vegetation or intracardiac abscess confirmed by histologic examination showing active endocarditis.</td>
</tr>
<tr>
<td>Probable IE</td>
<td>Clinical criteria*: (1) two major criteria, (2) one major and three minor criteria, or (3) five minor criteria.</td>
</tr>
<tr>
<td>Possible IE</td>
<td>Findings consistent with infective endocarditis that fall short of &quot;definite&quot; but are not &quot;rejected.&quot;</td>
</tr>
<tr>
<td>Rejected</td>
<td>(1) firm alternative diagnosis explaining evidence of infective endocarditis, (2) resolution of infective endocarditis syndrome (antibiotic therapy for ≤4 days), or (3) no pathologic evidence of infective endocarditis at surgery or autopsy (antibiotic therapy for ≤4 days).</td>
</tr>
</tbody>
</table>

* See table 3 for definitions of major and minor criteria.
Table 3. Definitions of terms used in the Duke criteria for the diagnosis of IE.

- Major criteria
  (1) Positive blood culture for IE
  A. Typical microorganism consistent with IE from two separate blood cultures as noted below:
     (i) viridans streptococci,* Streptococcus bovis, or HACEK group or
     (ii) community-acquired Staphylococcus aureus or enterococci, in the absence of a primary focus
  B. Microorganisms consistent with IE from persistently positive blood cultures defined as
     (i) at least two positive cultures of blood samples drawn >12 hours apart or
     (ii) all of three or a majority of four or more separate cultures of blood (with first and last sample drawn at least 1 hour apart)
  (2) Evidence of endocardial involvement
     A. Positive echocardiogram for IE defined as
        (i) oscillating intracardiac mass on valve or supporting structures, in the path of regurgitant jets, or on implanted material in the absence of an alternative anatomic explanation,
        (ii) abscess, or
        (iii) new partial dehiscence of prosthetic valve
     B. New valvular regurgitation (worsening or changing of preexisting murmur not sufficient)
- Minor criteria
  (1) Predisposition: predisposing heart condition or intravenous drug use
  (2) Fever: temperature, ≥38.0°C
  (3) Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, and Janeway’s lesions
  (4) Immunologic phenomena: glomerulonephritis, Osler’s nodes, Roth’s spots, and rheumatoid factor
  (5) Microbiological evidence: positive blood culture but does not meet a major criterion as noted in table 3 or serological evidence of active infection with organism consistent with IE
  (6) Echocardiographic findings: consistent with IE but do not meet a major criterion as noted in table 3

NOTE. HACEK = Haemophilus species, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella species, and Kingella kingae; IE = infective endocarditis.
* Excludes single positive cultures for coagulase-negative staphylococcus and organisms that do not cause endocarditis.
1 Excludes single positive cultures for coagulase-negative staphylococcus and organisms that do not cause endocarditis.

Twenty-one patients (18%) had culture-negative IE, two of whom had Coxiella burnetii endocarditis. All but three of the other 19 patients with culture-negative IE had received antibiotics before the first blood samples were taken for culture.

Comparison of Diagnostic Criteria

The diagnosis of IE was confirmed by autopsy for one non-operated patient and by surgery for 41 of 48 operated patients on the basis of macroscopic findings. However, because histologic examination was not done systematically, definite pathologic proof of IE could be obtained in only 27 cases (figure 1). There were seven patients without macroscopic evidence of IE at operation. Three of these patients had culture-proven, echocardiographically documented IE but were operated on >6 weeks after completion of antimicrobial therapy, at which time results of bacteriologic and histologic examinations of the removed valve were inconclusive. Two of the seven patients had echocardiographically documented staphylococcal tricuspid endocarditis associated with an endocardial pacemaker wire (which was withdrawn under extracorporeal circulation); no vegetation was observed and valve replacement was not performed at that time, so neither bacteriologic examination nor histologic examination could be performed. The final two patients had culture-negative, echocardiographically documented IE and an abnormal valve but did not have a vegetation or a ring abscess at operation; bacteriologic examination of the valve was negative, and histologic examination was either not done (one case) or inconclusive (one case).

When comparing the Duke criteria with the Beth Israel criteria, only the 27 histologically confirmed cases described above were considered pathologically definite and definite, respectively. If surgery or autopsy had not been performed on these 27 patients, 22 (82%) vs. 12 (44%) would have been classified as having clinically definite and probable IE by the Duke vs. the Beth Israel criteria, respectively, whereas 0 vs. 5 (19%) would have been rejected by the Duke vs. the Beth Israel criteria, respectively (table 4). The latter five cases rejected by the Beth Israel criteria included one clinically definite and four possible IE cases according to the Duke criteria. The one clinically definite case of IE was observed in a 65-year-old man with native valve disease who had endocarditis. He had no vascular phenomena, and 2 of 14 blood cultures yielded a coagulase-negative staphylococcus. Echocardiography showed a vegetation and a ring abscess, which were macroscopically and histologically confirmed at operation. Even without histologic confirmation, this case met one major (echocardiographic evidence) and three minor (predisposing heart condition, fever, and microbiological evidence) criteria that allowed it to be classified as clinically definite according to the Duke criteria. In the remaining four cases, patients had a previously known valve disease but no vascular phenomena, blood cultures were negative, and echocardiograms showed either typical vegetations or a ring abscess. The improvement in sensitivity from 44% to 82% with the Duke criteria was statistically significant (P < .01).

The remaining 88 patients for whom there was no histologic confirmation of IE were then classified by the Beth Israel and the Duke criteria. As shown in table 5, significantly more patients were classified as having clinically definite cases of IE by the Duke criteria than as having probable IE (a comparable category) by the Beth Israel criteria (75 of 88 vs. 40 of 88, respectively, P < .00000001). Only one of the 88 cases was rejected by the Duke criteria, whereas 14 were rejected by the Beth Israel criteria (P < .001). All of the seven cases defined
as clinically definite by the Duke criteria but that were rejected according to the Beth Israel criteria had typical vegetations on echocardiograms. In addition, three cases had no underlying valve disease but either positive blood cultures or vascular and/or immunologic phenomena, and four had negative blood cultures with both underlying valve disease and vascular and/or immunologic phenomena. The only case that was classified as rejected according to both the Beth Israel and the Duke criteria had underlying valve disease but no positive blood culture, a nondiagnostic echocardiogram, and neither vascular nor immunologic phenomena; when the patient was operated on, gross anatomic lesions were found that were consistent with the diagnosis of IE, but histologic examination was not done.

Discussion

As noted by Bayer et al. [10], it is important to have an accurate classification of IE in order to establish incidence statistics, to assess epidemiologic trends, and to design clinical trials for therapy and for prevention of IE. The Beth Israel criteria addressed these goals. However, because of a strict case definition that did not include echocardiographic data and because open heart surgery or autopsy was needed for IE to be considered definite, these criteria excluded a substantial number of cases from the definite category of IE. Durack et al. [7] showed that their new diagnostic criteria for IE had improved sensitivity, and these investigators assumed that they had maintained specificity. To date, Bayer et al. [10] have confirmed with an independent group of patients that the Duke criteria were indeed more sensitive than the Beth Israel criteria. Our validation study was performed on an independent sample of patients who were clearly different from the study population of Bayer et al. in that they included far fewer intravenous drug users. In addition, our series was remarkable for its high number of culture-negative cases of IE. There were 19 patients (16.5%) with IE in whom no causative microorganism was

<table>
<thead>
<tr>
<th>Duke criteria</th>
<th>Clinically definite</th>
<th>Possible</th>
<th>Rejected</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beth Israel criteria</td>
<td>Probable</td>
<td>12</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Possible</td>
<td>9</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Rejected</td>
<td>1</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Total (%)</td>
<td>22 (82)</td>
<td>5 (18)</td>
<td>0 ( . . )</td>
<td>27 (100)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Duke criteria</th>
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<th>Total (%)</th>
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<tbody>
<tr>
<td>Beth Israel criteria</td>
<td>Probable</td>
<td>39</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Possible</td>
<td>29</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Rejected</td>
<td>7</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Total (%)</td>
<td>75 (85)</td>
<td>12 (14)</td>
<td>1 (1)</td>
<td>88 (100)</td>
</tr>
</tbody>
</table>
identified, a number twice as high as that rate (8%) observed in a recent 1-year French survey [6]. The most relevant explanation for the high rate of culture-negative IE cases was that patients referred to our center often had received antibiotics prior to their transfer.

Finally, our patient population was biased towards the diagnosis of IE because all of the patients were treated as if they actually had this infection. One could hypothesize that for a population less highly biased towards the diagnosis of IE, the sensitivity of either the Duke or the Beth Israel criteria might be lower. However, as far as sensitivity is concerned, our findings are consistent with those of Durack et al. [7] and Bayer et al. [10], which was illustrated in different fashions. Only 1 of 115 cases was rejected by the Duke criteria, while 14 (not including the five operated cases, which were definite) would have been rejected by the Beth Israel criteria. Likewise, fewer cases were classified as possible IE with the Duke criteria than with the Beth Israel criteria. Of the 27 operated patients with histologically confirmed IE, 82% would have been classified as having clinically definite IE by the Duke criteria and 44% would have been classified as having probable IE by the Beth Israel criteria; this shows an almost twofold increase in sensitivity. Similar results were observed in the 88 nonoperated cases of suspected IE (85% clinically definite by Duke criteria vs. 45% probable by Beth Israel criteria), although these percentages cannot express a true sensitivity since pathological proof was lacking in these cases.

It is noteworthy that the improved sensitivity of the Duke criteria is mainly attributed to the use of echocardiographic findings. This was illustrated by the fact that in all the cases rejected by the Beth Israel criteria but classified as clinically definite or possible according to the Duke criteria, the echocardiogram was positive for typical vegetations and/or a valve ring abscess. Moreover, more than one-half of the cases rejected by the Beth Israel criteria were culture-negative, and the echocardiographic findings were essential to the ultimate clinical diagnosis of IE. This critical contribution of echocardiographic findings to the diagnosis of culture-negative IE in the Duke criteria has been illustrated in a previous study [5].

Whether or not the increased sensitivity of the Duke criteria might be counterbalanced by a decreased specificity, especially due to false-positive echocardiographic findings, should be evaluated. Future studies evaluating the Duke criteria should therefore be designed to assess this factor. If the Duke criteria are found to be highly specific while maintaining a high level of sensitivity, then there should be no reason not to substitute the Duke criteria for the Beth Israel criteria in the diagnosis of IE.

Acknowledgments

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References