Diagnosis of Infective Endocarditis

Sensitivity of the Duke vs von Reyn Criteria

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Background: Because of the highly variable clinical manifestations of infective endocarditis (IE), different sets of diagnostic criteria have been used to standardize case definitions of IE. We evaluated the validity of the recently proposed Duke criteria, as compared with the older von Reyn criteria, in patients with no history of injecting drug abuse.

Methods: A total of 243 consecutive episodes of suspected IE in 222 patients treated during the years 1980 through 1995 in a Finnish teaching hospital were retrospectively evaluated for the likelihood of IE by means of these 2 classification schemes.

Results: Of all disease episodes, 114 were designated as definite IE by the Duke criteria, as compared with 64 episodes so classified by the von Reyn criteria (P<.001; Fisher exact test). Moreover, as many as 115 disease episodes were rejected by the von Reyn criteria, whereas only 37 episodes were rejected by the Duke criteria (P<.001). Of the cases rejected by the von Reyn criteria, the Duke clinical criteria designated 6 (5%) as definite IE and 72 (63%) as possible IE. Among histopathologically verified episodes, 46 were designated as definite IE by the Duke clinical criteria, as compared with a diagnosis of probable IE by the von Reyn criteria in 33 episodes (P=.02). Moreover, 26 pathologically proved cases would have been rejected by the von Reyn criteria had surgery not been performed, as compared with none being rejected by the Duke criteria (P<.001).

Conclusions: Corroborating earlier findings, the higher sensitivity of the Duke criteria, as compared with the von Reyn criteria, was demonstrated in this study. These results confirm the validity of the Duke criteria in diagnosing IE in a non–drug-addict patient population.

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INFECTIOUS endocarditis (IE) is a serious disease, the diagnosis of which is often difficult. Because of the highly variable clinical manifestations of endocarditis, different sets of diagnostic criteria have been used to direct and standardize case definitions both in clinical practice and in scientific work. The first distinct case definition for IE was proposed by Pelletier and Petersdorf in 1977. A few years later, von Reyn et al presented a modification to this schema with the aim of improving the sensitivity and specificity of these diagnostic criteria. According to the von Reyn classification, histopathologic evidence is a prerequisite for a case to be diagnosed as definite IE, while the likelihood of IE is evaluated on the basis of blood culture findings, presence of fever and various heart conditions either predisposing to or indicative of IE, and occurrence of vascular manifestations. Evidently, these diagnostic criteria are most sensitive in diagnosing subacute endocarditis. During recent decades, however, the frequency of subacute IE has decreased, with a simultaneous increase in acute and prosthetic valve endocarditis. This epidemiologic trend accentuates the weaknesses of the von Reyn diagnostic criteria. Another major impediment is their failure to incorporate the results of modern echocardiography, despite their indisputable value in guiding clinical decisions.

A few years ago, Durack et al from Duke University, Durham, NC, introduced a new classification system, with the inclusion of certain echocardiographic findings and knowledge of predisposing injecting drug abuse as the main improvement on the older criteria. Moreover, according to the Duke classification, a case can also be designated as definite IE on the basis of clinical findings and echocardiographic results. The Duke diagnostic criteria have been independently validated in 2 patient populations, one treated in a municipal hospital in the United States and the other in a tertiary referral center in Sweden. Recently, Dodds et al showed that the negative predictive value of the Duke criteria for excluding the diagnosis of IE is at least 92%. In the present study, we retrospectively applied both the Duke and von Reyn diagnostic criteria in evaluating the likelihood of IE in patients treated for a suspicion of this dis-
PATIENTS AND METHODS

We reviewed the hospital files of 222 consecutive adult patients treated in the Department of Medicine, Turku University Central Hospital, Turku, Finland, during the years 1980 through 1993 for suspected or diagnosed IE. The hospital is a 1209-bed teaching facility with a cardiothoracic surgical department, serving as a tertiary referral center for the southwestern part of the country. Each suspected case was retrospectively evaluated for the likelihood of IE first by the Duke1 and then by the von Reyn2 diagnostic criteria. Sixteen patients had been treated for 2, 1 patient for 3, and 1 patient for 4 episodes of suspected IE. Thus, the total number of episodes analyzed was 243.

The clinical characteristics of these patients were assessed by reviewing their medical records. For each patient, the presence of predisposing heart conditions known to increase the risk for IE11 and the findings of echocardiographic examinations were evaluated. All patients had at least 1 transthoracic echocardiography (TTE) performed; in addition, 95 patients had transesophageal echocardiography (TEE) performed. Regarding physical examination, data were collected on the presence of a temperature of 38.0°C or more and recognition of new valvular regurgitant murmurs on heart auscultation or specific vascular and immunological manifestations suggesting IE.1,5 Furthermore, the patients were assessed for the findings of the blood cultures taken. For each blood culture, 10 mL of blood had been collected and cultured as follows. Early in the study (1980-1985), double bottles (Supplemented Peptone Broth Vacutainer, Becton Dickinson Co, Rutherford, NJ) for aerobic and anaerobic cultivation were used. Later (1986-1995), the lysis centrifugation method (Isolator, DuPont & Nemours Inc, Wilmington, Del) was used. Basic identification of bacteria was performed according to standard microbiological methods. In addition, histopathologic and microbiological findings of the tissue specimens were registered for those patients who had undergone surgery or autopsy. Finally, all patients were studied for history of injecting drug abuse.

DIAGNOSIS OF ENDOCARDITIS

The Duke Criteria

With the Duke classification, the disease episodes were categorized as either definite or possible IE, or were rejected. The classification schema is described in detail in Table 1 and Table 2. Briefly, evidence of endocardial involvement and typical blood culture are regarded as major criteria, while a predisposing cardiac condition or recent history of injecting drug abuse, the presence of temperature of 38.0°C or more, defined vascular and immunological phenomena, blood cultures intermittently positive for microorganisms, and echocardiographic findings consistent with IE but not meeting major criteria are regarded as minor criteria. The disease is designated as definite IE if a combination of (1) 2 major criteria, (2) 1 major and 3 minor criteria, or (3) 5 minor criteria is observed. The disease is also categorized as definite IE if histopathologic or microbiological evidence of IE is obtained at surgery or autopsy. Furthermore, an episode of suspected IE is rejected if (1) a firm alternate diagnosis is found, (2) the symptoms of the patient resolve with antimicrobial therapy for 4 days or less, or (3) surgery or autopsy is performed within 4 days after commencing antimicrobial therapy and no pathologic evidence of IE is obtained. Finally, the case is classified as possible if it can neither be rejected nor designated as definite IE.

The von Reyn Criteria

With the von Reyn classification, the disease episodes were categorized as definite, probable, or possible IE, or were rejected. By these criteria, the disease is classified as definite IE only on the basis of positive histopathologic or microbiological findings from the affected valve or peripheral embolus. Furthermore, a disease episode is classified as either probable or possible IE on the basis of criteria presented in Table 3. Briefly, an episode is designated as probable IE if the blood cultures of the patient were persistently positive for microorganisms in conjunction with a new regurgitant murmur or a predisposing heart condition combined with vascular phenomena. In case of negative or intermittently positive blood cultures, an episode is designated as probable IE if the patient has fever combined with a new regurgitant murmur and vascular phenomena. An episode is classified as possible IE if the patient's blood cultures are persistently positive for microorganisms and the patient has either a predisposing cardiac condition or vascular phenomena. In case of negative or intermittently positive blood cultures, a combination of a predisposing heart disease, fever, and vascular phenomena is needed for the episode to be designated as possible IE. For viridans streptococcal cases, an episode is designated as possible if the patient has fever and at least 2 blood cultures that are positive for microorganisms without an extracardiac source. Cases not fulfilling the above criteria are rejected as IE.

STATISTICAL ANALYSIS

Data were analyzed by the χ² test. A P value less than .05 was considered statistically significant.
Table 1. Definitions for the Diagnosis of Infective Endocarditis According to the Duke Criteria*

<table>
<thead>
<tr>
<th>Definite infective endocarditis</th>
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<tbody>
<tr>
<td>Pathologic criteria</td>
</tr>
<tr>
<td>Microorganisms: demonstrated by culture or histologic examination in a vegetation, or in a vegetation that has embolized, or in an intracardiac abscess, or Pathologic lesions: vegetation or intracardiac abscess present, confirmed by histological examination showing active endocarditis</td>
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<tr>
<td>Clinical criteria, using specific definitions listed in Table 2</td>
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<tr>
<td>2 Major criteria, or 1 Major and 3 minor criteria, or 5 Minor criteria</td>
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</table>

Possible infective endocarditis

Findings consistent with infective endocarditis that fall short of “definite” but are not “rejected”

Rejected

Firm alternate diagnosis for manifestations of endocarditis, or Resolution of manifestations of endocarditis, with antibiotic therapy for 4 days or less, or No pathologic evidence of infective endocarditis at surgery or autopsy, after antibiotic therapy for 4 days or less

*From Durack et al. 7

Definite IE

Among the 114 episodes designated as definite IE, the diagnosis relied on histopathologic evidence in 64 cases and on clinical criteria in 50 cases. Of the 64 histopathologically proved cases, 46 were designated as definite also by the Duke clinical criteria. Thus, the total number of cases designated as definite IE by the Duke clinical criteria was 96. Among them, 61 (64%) were classified as definite by 2 major criteria and 35 (36%) were so classified by 1 major and 3 minor criteria. Of the 46 cases classified as definite IE by both pathologic and clinical criteria, 37 affected native valves and 9 affected prosthetic valves. Echocardiography was abnormal during 43 of these episodes, with a major criterion met in 34. Blood cultures yielded growth during 42 episodes (91%). The remaining 18 histopathologically proved cases of IE were designated as possible by the Duke clinical criteria. Ten of them affected native valves and 8 affected prosthetic valves. Echocardiography was abnormal during 17 of these episodes, with 14 cases meeting major criteria. All but 1 episode were culture negative; in 9 culture-negative cases, the patient had received antimicrobial therapy before the admission.

Among all 114 definite cases, IE affected native valves in 91 episodes and prosthetic valves in 23 episodes, with the aortic valve most commonly involved in both types of IE. The relative contribution of the disease in different valves is shown in Table 4. A predisposing cardiac condition was present in 76 cases (67%), with a bicuspid aortic valve the most frequently recognized predisposing factor in native valve disease. A new regurgitant murmur was heard in association with 70 cases (61%) of definite IE.

Echocardiographic findings were normal in 8 cases (7%) and abnormal in 106 cases (93%), forming a major criterion for IE in 82 episodes and a minor criterion in 24 episodes. The most common echocardiographic finding was a valvular vegetation, visualized in

Table 2. Definitions of Terminology Used in the Duke Criteria*

<table>
<thead>
<tr>
<th>Major criteria</th>
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<tbody>
<tr>
<td>Positive blood culture for infective endocarditis</td>
</tr>
<tr>
<td>Typical microorganism for infective endocarditis from 2 separate blood cultures Viridans streptococci,† Streptococcus bovis, HACEK‡ group, or Community-acquired Staphylococcus aureus or enterococci, in the absence of a primary focus, or Persistently positive blood culture, defined as recovery of a microorganism consistent with infective endocarditis from: (1) Blood cultures drawn more than 12 hours apart, or (2) All of 3 or a majority of 4 or more separate blood cultures, with first and last drawn at least 1 hour apart</td>
</tr>
<tr>
<td>Evidence of endocardial involvement Positive echocardiogram for infective endocarditis (1) Oscillating intracardiac mass, on valve or supporting structures, or in the path of regurgitant jets, or on implanted material in the absence of an alternative anatomic explanation, or (2) Abscess, or (3) New partial dehiscence of prosthetic valve, or New valvular regurgitation (increase or change in preexisting murmur not sufficient)</td>
</tr>
<tr>
<td>Minor criteria</td>
</tr>
<tr>
<td>Predisposition: predisposing heart condition or intravenous drug use Fever: temperature at least 38.0°C (100.4°F) Vascular phenomena: major arterial emboli, septic pulmonary infarctions, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, Janeway lesions Immunological phenomena: glomerulonephritis, Osler nodes, Roth spots, rheumatoid factor Microbiological evidence: positive blood culture but not meeting major criterion as noted previously§ or serologic evidence of active infection with organism consistent with infective endocarditis Echocardiogram: consistent with infective endocarditis but not meeting major criterion as noted previously</td>
</tr>
</tbody>
</table>

*From Durack et al. 7
†Including nutritional variant strains.
‡HACEK indicates Haemophilus species, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella species, and Kingella kingae.
§Excluding single positive cultures for coagulase-negative staphylococci and organisms that do not cause endocarditis.

63 episodes. A new partial dehiscence of a prosthetic valve was detected in 12 cases and an intracardiac abscess in 9 cases. In addition to TTE, TEE was performed during 39 episodes of definite IE, of which a major echocardiographic finding would have been missed in 21 cases had only a transthoracic examination been made. Echocardiography was interpreted as normal during 8 episodes subsequently diagnosed as definite IE on the basis of histopathologic evidence. Four of them affected native valves and 4 affected prosthetic valves.

Blood cultures were positive for microorganisms in 91 cases (80%) of definite IE, with 70 (61%) meeting major criteria and 21 (18%) meeting minor criteria. The most frequently isolated organism was Staphylococcus aureus, followed by viridans streptococci (Table 5). Fever as a minor criterion was present in 93 cases (82%). Immunological phenomena were detected in 9 and vascular phenomena in 47 (41%) episodes of definite IE.

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Of the 92 episodes designated as possible IE, a predisposing cardiac condition was present in 66 cases (72%). Echocardiographic finding was abnormal during 41 (45%) of these episodes, forming a major criterion in 28 cases and a minor criterion in 13 cases. A new valvular regurgitant murmur was heard in association with 22 episodes of possible IE (24%). Blood cultures yielded growth during 22 episodes (24%), with a major criterion met in 10 cases and a minor criterion in 12 cases. Vascular manifestations suggesting IE were seen in 11 cases and an immunological manifestation in 1.

Possible IE

Of the 37 disease episodes rejected by the Duke criteria, a predisposing cardiac condition was present in 20 (54%) and blood cultures were positive for microorganisms in 9 (24%). Among the cases rejected, the following firm alternate diagnoses were seen: collagenosis (n=12), malignant neoplasm (n=5), pneumonia (n=4), pyelonephritis (n=4), sepsis of defined origin (n=2), rheumatic fever (n=1), infection of a permanent pacemaker (n=1), infection of an intravenous line (n=1), erysipelas (n=1), herpes zoster (n=1), and chronic rejection of a kidney transplant (n=1). In 4 patients, the clinical syndrome initially suspected to be IE resolved without antimicrobial therapy.

CLASSIFICATION BY THE VON REYN CRITERIA

With the von Reyn criteria, 64 disease episodes (26%) were classified as definite IE. In addition, 31 episodes (13%) were classified as probable and 33 episodes (14%) as possible IE. In 115 episodes (47%), the diagnosis of IE was rejected.

Definite IE

In the 64 episodes designated as definite IE, the diagnosis was based on histopathologic verification. A predisposing cardiac condition was observed in 48 (75%) of these episodes. The patient had blood cultures positive for microorganisms during 43 (67%), fever during 53 (83%), and vascular phenomena during 28 (44%) of the episodes of definite IE.
Probable IE

Of the 31 episodes designated as probable IE, a predisposing cardiac condition was observed in 12 episodes (39%) and a new valvular regurgitant murmur was heard in 28 episodes (90%). The patient had blood cultures positive for microorganisms during 27 episodes (87%) and vascular manifestations suggesting IE during 13 episodes (42%) of probable IE.

Possible IE

A predisposing heart disease was present in 28 (85%) of the 33 episodes designated as possible IE. In none of these patients was a new valvular regurgitant murmur heard. Blood cultures yielded growth during 24 episodes (73%), and vascular phenomena were detected during 13 episodes (39%) of possible IE.

IE Rejected

Among the 115 cases rejected by the von Reyn criteria, 74 (64%) had a predisposing cardiac condition. The patient had blood cultures positive for microorganisms during 28 (24%) and vascular phenomena were detected during 7 (6%) of the episodes rejected.

**COMPARISON BETWEEN THE DUKE AND VON REYN CRITERIA**

Categorization of all 243 episodes for the likelihood of IE by both the Duke and von Reyn criteria is shown in Table 6. Of all episodes, 114 were designated as definite IE by the Duke criteria, as compared with 64 episodes so classified by the von Reyn criteria (P<.001). Moreover, the number of cases designated as definite IE by the Duke criteria was nonsignificantly greater than the number of those designated as either definite or probable IE by the von Reyn criteria (114 vs 95 cases; P=1). Furthermore, as many as 115 disease episodes were rejected by the von Reyn criteria, whereas only 37 episodes were rejected by the Duke criteria (P<.001). Of the cases rejected by the von Reyn criteria, the Duke clinical criteria designated 72 (63%) as possible and 6 (5%) as definite IE. Blood cultures of all 6 of the definite IE patients were positive for microorganisms, and all 6 had a vegetation visualized on echocardiography, strongly supporting the diagnosis of IE. In addition, all of them had fever and 2 had, in addition, vascular manifestations suggesting IE. When the 243 episodes were reclassified on the basis of clinical and echocardiographic results after exclusion of all surgical and autopsy findings, 96 episodes were designated as definite IE by the Duke criteria, as compared with a diagnosis of probable IE in 64 episodes by the von Reyn criteria (P=.003).

The 64 episodes of histopathologically verified IE were then reclassified in the same manner; the clinical diagnoses are compared in Table 7. Among them, 46 cases were designated as definite IE by the Duke criteria, as compared with 33 episodes being designated as probable IE by the von Reyn criteria (P=.02). Moreover, 26 pathologically proved cases would have been rejected by the von Reyn criteria had surgery not been performed, as compared with none being rejected by the Duke criteria (P<.001). A total of 17 episodes of histopathologically proved IE occurred in recipients of prosthetic valves. After exclusion of pathologic findings, 13 (76%) of them were rejected by von Reyn criteria, as compared with none rejected by the Duke criteria (P<.001). The Duke clinical criteria designated 9 (53%) of these cases as definite and 8 (47%) as possible IE, while the von Reyn clinical criteria designated 3 cases (18%) as probable and 1 (6%) as possible IE.

Of the 179 episodes without histopathologic verification, 50 were designated as definite IE by the Duke criteria compared with a diagnosis of probable IE in 31 episodes by the von Reyn criteria (P=.02). Of the 121 culture-negative episodes analyzed, 86 (71%) were rejected by the von Reyn criteria and 28 (23%) by the Duke criteria (P<.001). The numbers of culture-negative cases designated as definite IE by these 2 sets of criteria were 21 (17%) and 23 (19%), respectively. Finally, the 33 cases rejected by the Duke criteria on account of a firm alternate diagnosis were reclassified after excluding the final diagnoses. The diagnosis of definite IE was correctly rejected in all.

The Duke and von Reyn criteria were then separately applied on episodes affecting native valves and those affecting prosthetic valves. Of the 182 episodes affecting native valves, the Duke criteria classified significantly more as definite IE than did the von Reyn criteria (91 vs 47 cases; P<.001). Similarly, significantly fewer cases were rejected by the Duke criteria than by the von Reyn criteria (28 vs 85 cases; P<.001). Among the 61 episodes affecting prosthetic valves, only 9 were rejected by the Duke criteria, while as many as 30 were rejected by the von Reyn criteria (P<.001). However, the number of cases designated as definite prosthetic valve IE by the Duke criteria was not significantly greater than the number of those so designated by the von Reyn classification (23 vs 17 cases; P=.33).

### Table 6. Categorization of 243 Episodes of Suspected or Diagnosed Infective Endocarditis (IE) for the Likelihood of IE by the Duke vs von Reyn Diagnostic Criteria

<table>
<thead>
<tr>
<th>Duke Criteria</th>
<th>Von Reyn Criteria, No. of Episodes (%)</th>
<th>Total, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Possible</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rejected</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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In the present investigation, a significantly higher proportion of all disease episodes were designated as definite IE, and significantly fewer episodes were rejected by the Duke criteria than by the von Reyn criteria. Moreover, reclassification of these episodes after excluding all pathologic findings showed that a significantly higher proportion were designated as definite IE by the Duke criteria, as compared with a diagnosis of probable IE by the von Reyn criteria. The Duke criteria also designated a significantly higher proportion of those episodes that were not pathologically proved as definite IE than were designated as probable IE when the von Reyn criteria were used. By illustrating higher sensitivity of the Duke criteria, these results are in agreement with previous findings. While first describing the Duke criteria, Durack et al.\(^7\) presented a series of 405 episodes of suspected IE and showed that application of their new criteria increased the number of definite diagnoses; the number of episodes designated as definite IE almost doubled among the cases without pathologic verification. Subsequently, Bayer et al.\(^8\) validated the Duke criteria in a cohort of 63 prospectively enrolled patients with suspected IE, of whom the presence of IE was histopathologically confirmed in 10 and excluded in 2. Of the remaining 51 patients who were not operated on, significantly more were classified as having definite IE by the Duke criteria than as having probable IE by the von Reyn criteria. Recently, Olaison and Hogevik\(^9\) reported corresponding findings on application of these 2 sets of criteria to retrospectively classify 161 consecutive episodes of suspected IE in patients treated at 1 Swedish institution during a 5-year period.

Furthermore, objective evidence of the significantly higher sensitivity of the Duke criteria was obtained by reclassifying all episodes with histopathologic verification of IE based on clinical and echocardiographic findings. In doing so, 46 of the 64 pathologically proved cases were designated as definite IE by the Duke clinical criteria, while 33 were classified as probable IE by the von Reyn criteria. Assuming the category “definite” of the Duke clinical criteria to be analogous to the category “probable” of the von Reyn criteria, the sensitivities of these 2 classification systems were 72% and 52%, respectively (\(P=.02\)). Our results are consistent with those reported by Durack et al.\(^7\) Also, in their study population, a significant difference was detected between the sensitivities of the Duke and von Reyn criteria to clinically classify cases with pathologic verification of IE, with the corresponding percentages of 80% vs 51%. In the series of Bayer et al.,\(^8\) all pathologically proved cases of IE were designated as definite by the Duke clinical criteria, while 50% of them were rejected by the von Reyn criteria. In this respect, the results reported by Olaison and Hogevik\(^9\) are different. Although a higher proportion of their histopathologically proved cases were designated as definite by the Duke criteria than classified as probable by the von Reyn criteria, this difference was not statistically significant.

In all 3 previous studies focusing on diagnosis of IE by the Duke vs von Reyn criteria,\(^7,8\) a lower proportion of the episodes of suspected IE, whether with or without pathologic verification, has been rejected by the Duke criteria. Consistently in the present study, the Duke criteria rejected only one third of the cases rejected by the von Reyn criteria. Moreover, as many as 26 histopathologically proved cases would have been rejected by the von Reyn criteria had surgery not been performed. Finally, 6 patients not operated on who were designated as having definite IE by the Duke criteria were rejected by the von Reyn criteria. Yet, on the basis of the clinical data presented above, we consider the likelihood that these patients had endocarditis to be high.

Admittedly, the von Reyn criteria were fundamentally not intended to guide therapeutic decisions, while the Duke criteria may often be useful in clinical practice. It is generally accepted that all cases designated as definite IE should receive appropriate antimicrobial treatment.\(^7\) The criteria for a case to be rejected as IE by the Duke classification are also well defined. Their clinical relevance is supported by the fact that not even 1 pathologically proved case has been rejected by these criteria in any patient population studied,\(^7,8\) including the present one. In contrast, the category “possible” of the Duke classification is complex. Decisions regarding the therapy in this group must always be made case by case on the basis of individual presentation.\(^7\) Of note, as many as 28% of the histopathologically proved cases even in this study fell into this category. The corresponding proportion in previous series has ranged between 20% and 27%).\(^7,9\)

Initially, the Duke criteria were severely criticized by other authorities\(^12,13\) for lending so much weight to the echocardiographic findings, despite their potential insensitivity and unspecificity. According to various reports, the sensitivity of TTE has varied between 42% and 56% in native valve endocarditis and between 12% and 33% in prosthetic valve disease.\(^14,15\) In recent years, the diagnostic accuracy has markedly improved by use of the transesophageal examination technique. In the laboratory of Mugg et al.,\(^16\) the detection rates for vegetation in a subgroup of patients with proved endocarditis were 58% and 90% for TTE and TEE, respectively; in other laboratories, the sensitivities have varied between 30% and 64% for TTE and between 82% and 94% for TEE.\(^17-20\) Furthermore, TEE is more sensitive in visualizing cardiac abscesses as well as in detecting prosthetic valve disease.\(^16,21\) Both echocardiographic techniques have proved highly specific.\(^18\) In our patients, echocardiography failed to visualize endocardial lesions during 8 episodes subsequently diagnosed as definite IE on the basis of histopathologic evidence. In 7 of them, echocardiography was performed as early as the beginning of the 1980s, and, in all cases, only

<table>
<thead>
<tr>
<th>Duke Criteria</th>
<th>Probable</th>
<th>Possible</th>
<th>Rejected</th>
<th>Total, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite</td>
<td>30</td>
<td>5</td>
<td>11</td>
<td>46 (72)</td>
</tr>
<tr>
<td>Possible</td>
<td>3</td>
<td>0</td>
<td>15</td>
<td>18 (28)</td>
</tr>
<tr>
<td>Rejected</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Total</td>
<td>33 (51)</td>
<td>5 (8)</td>
<td>26 (41)</td>
<td>64 (100)</td>
</tr>
</tbody>
</table>
a transthoracic examination was made. Although efforts are presently made to perform TEE in addition to TTE on all patients treated for suspected IE in our hospital, both of these examinations were performed during the study period in only 39 cases designated as definite IE by the Duke criteria. The finding that a major echocardiographic criterion would have been missed in 21 of these cases had only TTE been performed efficiently demonstrates the benefits afforded by TEE.

The diagnosis of IE is generally obvious if a patient’s blood cultures are repeatedly positive for microorganisms and characteristic valvular murmurs are heard; peripheral vascular manifestations sometimes further support the diagnosis. Visualization of endocardial involvement on echocardiography then confirms, although not definitely proves, the diagnosis. Since echocardiography presently constitutes a basic diagnostic tool in patients with suspected endocarditis, it seems logical to delineate certain echocardiographic findings as major diagnostic criteria. In the present investigation, an echocardiographic finding formed a major criterion of IE in 72% of all episodes designated as definite IE by the Duke criteria. Concurrently, a major echocardiographic criterion was encountered in 75% of all histopathologically proved cases. One can envision that in the future, if technical capacity and diagnostic skills further improve, the value of echocardiography in the evaluation of suspected IE may still increase.

Evidently, histopathologic verification is needed to unequivocally establish the diagnosis of IE. However, this is possible only in those patients with IE who undergo surgery or autopsy during the acute phase of their illness. Since the disease in these patients is obviously associated with an unusual severe presentation and fulminant course, they form a selected subgroup that is inadequately representative of all patients with IE. In this study, histopathologic verification of IE was obtained in 26% of all episodes and in 56% of the episodes designated as definite IE by the Duke clinical criteria. If only the pathologically proved cases were classified as definite IE, various epidemiologic and etiologic studies, as well as therapeutic trials, might be seriously flawed. Nevertheless, this relatively small set of patients is the only currently available group to be used as a criterion standard when the validity of different diagnostic clinical criteria is objectively evaluated.

In addition to the use of echocardiography, incorporation of the knowledge of injecting drug abuse into diagnostic criteria is commonly accepted as an important advantage of the Duke classification. In the series of Bayer et al., approximately half of the patients had a history of recent injecting drug abuse. In the Swedish series, drug abuse was a risk factor in 4% of the episodes of suspected IE, while none of the patients described herein used injected drugs. Together, these 2 Scandinavian studies validate the application of the Duke criteria also in patients with no or very uncommon drug abuse.

In our patient population, S. aureus was the most common causative microorganism of IE, while viridans streptococci were second. This was somewhat unexpected, since the present study involved patients with no injecting drug abuse. Yet the finding is in agreement with the general shift noted in the microbiological characteristics of IE during the past 30 years. Previously, staphylococci caused only about 15% of all cases of IE; in recent years, they have been etiologic agents in about 30% of cases in many studies. Illustratively, in the series of Watanakunakorn and Burkert, S. aureus was the major infecting organism, although most patients with staphylococcal endocarditis had acquired the infection in the community and were not users of the injected drugs. On the other hand, we regard it as possible that the high frequency of staphylococci in the present investigation may be partly explained by the fact that our hospital is a referral center for all severe cases of IE, whereas some subacute cases caused by viridans streptococci may also be treated in regional hospitals.

In conclusion, consistent with previous findings, the higher sensitivity of the Duke criteria, as compared with the older criteria to diagnose IE, was demonstrated in this study. Among the histopathologically proved episodes of IE, the sensitivity of the Duke criteria was 72%. None of the pathologically proved cases, whether native or prosthetic valve disease, were rejected in this study by the Duke clinical criteria. Supporting earlier studies, these results confirm the validity of the Duke criteria in diagnosing IE in patients with no injecting drug abuse.

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