INFORMATION AND OBJECTIVES. The present study was made to investigate the degree of discordance between the recommendations of clinical guidelines and actual practice in the care of patients with infectious endocarditis.

MATERIAL AND METHODS. Data was gathered on 34 patients that were admitted to our hospital for native valve infection over a 4-year period. The degree of discordance (%) was obtained by comparing each clinical history with a catalog of 15 specific actions recommended in the clinical guidelines for four consecutive phases: pre-diagnosis, hospital diagnosis, antibiotic treatment, and surgical treatment. A system was constructed, scoring each phase with the greatest detected error (on a severity scale of 0 to 8 points) and adding together the scores for the four phases.

RESULTS. The mean degree of discordance was 30.5% (range, 0-66%). Scores of more than six points were clearly associated with an unfavourable evolution.

CONCLUSIONS. The recommendations of clinical guidelines for infectious endocarditis are inadequately followed in practice, which can affect the course of the disease. It is necessary to increase adherence to clinical guidelines in practice, in order to improve the care of patients with this serious disease.


Full English text available at: www.revespcardiol.org

INTRODUCTION

There are many clinical guidelines\textsuperscript{1-7} that provide recommendations for the treatment of patients with infectious endocarditis (IE). Nevertheless, there is no information regarding the practical application of these recommendations; as far as we know, there is only 1 recent publication on this subject.\textsuperscript{8}

The purpose of this study is to investigate the possible discordance that exists between the established recommendations and actual treatment used in daily practice.
practice; which, for the purpose of simplification, we will call theoretical-practical discordance. Our hypothesis is that IE, having a low incidence rate and being subject, because of its clinical polymorphism, to the care of multiple specialists, constitutes a fertile field for the production of procedures that by their inclusion or omission falls far from the recommended standards. The secondary objective of this study is to see if the mistakes detected are related to end result of the disease.

MATERIAL AND METHODS

Patients and methods of analysis

With the help of a specific formulary containing a total of 90 parts, we reviewed the clinical histories of 34 non-addicted patients admitted for IE of a native valve over a period of 4 years (1996-1999). Twelve patients were from hospitals other than ours. The remaining patients were admitted through the emergency room (n=18) or after a consultation outside of our institution (n=4).

To evaluate the rate of discordance, we scrutinized a specific list of 15 potential errors divided into 4 consecutive phases (Table 1). The rate of discordance (%) was established by the ratio of the number of actions cataloged as erroneous to the total number of actions evaluated, multiplied by 100. As a corollary of the analysis, we constructed a scoring system each of the 4 phases, from the largest (1 only) of the errors detected (0=all right; 1=an error without consequences; 2=important error; 4=serious error; 8=very serious error). The sum of the points in each phase resulted in the final score that, consequently, ranged from 0 to 32.

The ramifications of the errors made were judged in accordance with the estimated probability of the patient being vitally compromised, rather than by the content of the error itself. For example, not instituting antibiotic prophylaxis before a dental extraction in a patient with mitral regurgitation could be formally considered a grave omission; nevertheless, under the category of vital risk it constitutes an important risk (2 points), but not a grave risk, as the patient can be cured with the appropriate treatment. Another example: a delay in the suspected diagnosis of more than 2 weeks is typically an important mistake (2 points), but becomes a grave mistake (4 points) if upon admission the patient already has serious intracardiac lesions. A very serious mistake would be unjustified dilatation during a complication that results in a NYHA Class I classification. There are many more examples, but suffice it to say that the analysis was performed by considering each case individually and reaching a consensus among the 3 authors. So that a grave error carried more weight than 4 errors, each scale index duplicated the previous one. In any case, this score had no other purpose than to note whether the treatment error, with
respect to the established standards, led to the end result of the illness.

Statistical analysis

The difference between continuous variables was evaluated by non-paired Student t test, and the percentages were evaluated by the exact Fisher test. For all tests, a value of \( P<0.05 \) was considered significant.

The marker, although translated into a number, is a mere ordinal value; in addition, a validated index is not involved. For this reason, the data were not subjected to parametric statistical treatment; they were only used to visualize the distribution on a scale with relation to patient course.

RESULTS

Patient and IE episode characteristics

Table 2 shows the basic patient characteristics. With respect to episodes of IE (Table 3), it is worth pointing out that upon admission 6 patients were in a grave state, that the causative microorganism was not identified in 5 patients, and that \textit{Staphylococcus aureus} was present in nearly one-quarter of the cases. It should also be noted that a total of 77 significant complications were detected among the patients. Twenty patients underwent surgery during their hospital stay and 3 additional patients underwent surgery during the 3 months after the infection was cured. There were a total of 10 deaths (29%), 7 following surgery.

Mistakes detected during the process

\textbf{Pre-diagnostic phase}

In only 2 patients was there a coincident septic risk—a subungueal abscess and a tooth extraction, respectively—with previous knowledge of valve involvement. These were ideal circumstances for preventative measures, but no measures were taken in either case.

In 18 patients, diagnosis was achieved in the first 2 weeks after symptoms began; in 6 patients, after 2 weeks but within the first month; in the 10 remaining patients, after the first month. The \textit{Staphylococcus} infections were diagnosed before the other infections (9±9 days versus 42±46 days; \( P=.044 \)), probably due to the higher suspicion caused by the virulence of the infection picture.

Nineteen patients received antibiotics before blood cultures were performed, while in 10 patients the dose was not productive; in 5 patients this circumstance could not be determined. In the non-\textit{Staphylococcus} group (n=23), we observed a tendency toward slower diagnosis when antibiotics had been administered before blood cultures were drawn (45±41 days versus 14±14 days; \( P=.070 \)). In the \textit{Staphylococcus} group, there was only 1 case of a patient who had not had prior antibiotic therapy, a finding present in 3 of the 5 patients with negative blood culture results.

\textbf{Diagnostic phase}

Beside the suspicion of IE, there was only 1 clinical error. This was a patient with slight aortic regurgitation who was admitted for a 4-day history of fever; blood cultures were negative and transthoracic echocardiogram (TTE) was inconclusive with respect to the existence of aortic microorganisms. Atypical chest pain and slight pericardial hemorrhage inclined the diagnosis toward acute idiopathic pericarditis that, after anti-inflammatory treatment, resulted in early discharge. The patient was readmitted 35 days later with acute pulmonary edema, serious regurgitation by infectious mutilation of the aortic and mitral valves and perivalvular mitral abscess. Fortunately, this resolved with surgical intervention.

No type 5 errors were committed: in all patients with a suspected clinical diagnosis and echocardiographic findings, whether suggestive or definitive with
Pacients who underwent surgery

Hospital course during the event

With at least 1 complication

With more than 1 complication

Patients who underwent surgery

During the same admission

During a later admission

Patient deaths

regard to IE, and negative blood cultures, serologic studies and tests for special microorganisms, such as those in the HACEK group or nutritionally-deficient Streptococcus, were performed.

We found that a type 6 error occurred—in—a transesophageal echocardiogram (TEE) when it was clearly indicated—in 3 cases in which perianular abscess pathways went undetected, 1 of which could have resulted in death by complete AV block, followed by unrecoverable aystolia. This was a patient with *Staphylococcus aureus* and grave but stable aortic regurgitation who was awaiting surgical intervention to treat an infection of a vascular hemodialysis prosthes-

Medical treatment

The source of infection was identified and treated correctly in all cases, except 1: the case mentioned above of a vascular hemodialysis prosthesis that was not removed as it should have been. The cases of *Staphylococcus viridans* were systematically investigated and treated, if they proceeded (n=5), from the dental point of view. As proposed by other authors, the maxillary sinuses were not investigated.

Only 9 patients received orthodox antibiotic therapy. The most frequent error (n=13) was too much treatment: the addition of an aminoglycoside to the treatment at 4 weeks with penicillin to eradicate a *Staphylococcus viridans* infection that was penicillin-sensitive (n=9); the addition over a prolonged period of time of an immunoglycoside to vancomycin to treat a vancomycin-sensitive *Staphylococcus aureus* (n=3); the addition of vancomycin to a regimen of ampicycline and gentamycin to combat an *Enterococcus* infection. One patient with *Staphylococcus viridans* and persistent fever on the tenth day of treatment was found to be still infected on antibiogram, as the germ was relatively resistant to penicillin. This error, attributable to poor communication, was resolved by substituting vancomycin for the penicillin. One of the 5 cases with negative blood cultures was treated with penicillin and gentamycin, instead of the recommended regimen of vancomycin and aminoglycoside.

An insufficient dose was found in only 1 case where the patient received 4 g/24 hours of ampicillin, together with gentamycin, to eradicate an *Enterococcus* infection; nevertheless, overdosage occurred with more frequency, especially with respect to the use of penicillin. Therefore, for example, of the 12 cases with insulinsensitive *Staphylococcus viridans*, 8 patients received the excessive dose of 24 millon U/24 hours, versus only 4 patients in whom the recommended dose (12-18 millons U/24 hours) was administered. If we add to this the fact that 12 patients received gentamycin, without the stipulated shortening of treatment to 2 weeks, we can conclude that these patient received excessive treatment.

With regard to the 3 patients with chronic renal insufficiency, 9 patients reached a creatinine level of ≥ 2.5 mg/dL during the course of the infection. Although the cause of this elevation of creatinine could be multifactorial, in 5 cases it was thought that the aminoglycoside used had an important effect. In general, monitoring the potential toxicity of antibiotics via determination of their level in the plasma was used relatively little; in this way, of the 30 patients who received potentially toxic antibiologic therapy, the concentration of the antibiotic in question was not determined in 10 patients.

The bactericide power of serum was determined in 13 of the 29 cases with positive blood cultures. In 4 of

**TABLE 3. Clinical profile of the 34 episodes of IE**

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Streptococcus viridans</em></td>
<td>13</td>
<td>38</td>
</tr>
<tr>
<td><em>Streptococcus agalactiae</em></td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td><em>Streptococcus fecalis</em></td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>8</td>
<td>23</td>
</tr>
<tr>
<td><em>Staphylococcus epidermidis</em></td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td><em>Candida albicans</em></td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Hemocult/negative serology</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

**Location**

<table>
<thead>
<tr>
<th></th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitral</td>
<td>13</td>
<td>38</td>
</tr>
<tr>
<td>Aortic</td>
<td>14</td>
<td>41</td>
</tr>
<tr>
<td>Mitral and aortic</td>
<td>7</td>
<td>21</td>
</tr>
</tbody>
</table>

**Complications detected**

<table>
<thead>
<tr>
<th></th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grave valve regurgitation</td>
<td>18</td>
<td>53</td>
</tr>
<tr>
<td>Grave cardiac insufficiency</td>
<td>13</td>
<td>38</td>
</tr>
<tr>
<td>Perivalvular abscess</td>
<td>10</td>
<td>29</td>
</tr>
<tr>
<td>Aortic pseudoaneurysm</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>10</td>
<td>29</td>
</tr>
<tr>
<td>Non-cerebral aneurysm</td>
<td>6</td>
<td>18</td>
</tr>
<tr>
<td>Myotic aneurysms</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Creatinine ≥ 2.5 mg/dLb</td>
<td>9</td>
<td>29</td>
</tr>
<tr>
<td>Conduction disturbance</td>
<td>5</td>
<td>15</td>
</tr>
<tr>
<td>Other neurological complications</td>
<td>3</td>
<td>9</td>
</tr>
</tbody>
</table>

**Hospital course during the event**

<table>
<thead>
<tr>
<th></th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Without complications</td>
<td>10</td>
<td>29</td>
</tr>
<tr>
<td>With at least 1 complication</td>
<td>6</td>
<td>18</td>
</tr>
<tr>
<td>With more than 1 complication</td>
<td>18</td>
<td>53</td>
</tr>
</tbody>
</table>

**Patients who underwent surgery**

<table>
<thead>
<tr>
<th></th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>During the same admission</td>
<td>20</td>
<td>56</td>
</tr>
<tr>
<td>During a later admission</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>Patient deaths</td>
<td>10</td>
<td>29</td>
</tr>
</tbody>
</table>

*aFistulized in 4 cases, 2 aortic and 2 mitral.
*bExcluding the 3 patients with chronic renal insufficiency.
the 12 cases in which the indication appeared to be clear (persistent fever after a week of apparently appropriate treatment), this test was not carried out.

Decision regarding surgery

Twenty patients underwent surgery before being discharged. In 19 of these, the indication for surgery was classification as NYHA class I, while for the other patient the decision was possibly incorrect, as the patient had serious cerebral damage with very little possibility of recovery (NYHA class III). There was no single isolated patient with NYHA class II disease, given that those patients in this class—for example, recurrent embolism in spite of appropriate treatment (NYHA class Iia; n=3) or mobile microorganism vegetation >10 mm (class Iib; n=3) were already classified as NYHA class I.

Fourteen patients did not undergo surgery, a decision that turned out to be appropriate in 9 patients. It was a matter of discussion with 1 patient, as the patient presented with a recidivant embolism (an indication of IIa). In another 2 patients, the indication for surgery was clear, but surgery was not performed, in 1 case because it was refused by the patient and in another case due to the patient’s advanced age and comorbidity. Not performing surgery in the other 2 cases was clearly an error. One was discharged and was to return for elective surgery, in spite of having acute serious aortic regurgitation, with tachycardia and early mitral valve prolapse; the patient returned in 4 days with pulmonary edema, and finally underwent a successful intervention. The other, who we referred to previously, had a Staphylococcus aureus infection and serious aortic regurgitation without cardiac insufficiency; the patient died suddenly due to complete A V block followed by unrecoverable asystolia, while awaiting surgery for an infection of a hemodialysis prosthesis.

These 2 last cases illustrate, dramatically in the second case, that the indication for surgery has to be correct not only with regard to form but with regard to timing. In this respect, in 7 of the 20 patients who underwent surgery, it was decided that the amount of time that had passed from the detection of a complication that resulted in a class I indication for surgery to the performance of the intervention was too long in relation to standards that have been published recently.12

Level of discordance and scoring system

Figure 1 shows the theoretical-practical discordance. The mean discordance level was 30.5% (range 0% to 66%). There were no differences between the 10 patients who died (28%) and the 24 who survived (31%), or between patients treated in the cardiology unit (31%) or in other hospital units (31%).

The 2 patients who died without undergoing surgery were deliberately excluded from the creation of the scoring system, given that intervention intrinsically constituted a potentially decisive act to achieve survival. For the rest, a score higher that 6 seems to be a clear indication of the patient course (Figure 2).

DISCUSSION

Our study shows that there is considerable discordance between what is recommended by the clinical guidelines and what occurs in daily practice with regard to IE patients. In a recent publication, the only
study we have seen on this subject, only 38% of patients were treated in accordance with the directives of the clinical guidelines, and an editorial that accompanied the article mentioned the possibility that the phenomenon was more frequent than previously suspected, and stated the need for studies to investigate this question.

We did not find any relationship between the level of discordance and the type of medical specialist who took care of the patient during hospitalization or to how the event ended. Nevertheless, qualitative analysis, via the use of an ordinal scale and its later translation into a numeric scoring system, underscored that not following the established standards may result in undesirable consequences (Figure 2). It seems advisable, therefore, to consider the origin and the context in which the discordances we found in our analysis occurred.

Prevention and suspected diagnosis

Both prevention and suspected diagnosis are tied to health education and the practice of general medicine. In only 2 cases of our series, when a procedure with a risk of bacteremia coincided with the knowledge of underlying valve disease, could the disease have theoretically been prevented. Finding only 2 cases in flagrant violation of the norms could suggest that the overall level of prophylaxis is adequate, but that risky procedures are probably being carried out, especially in the case of dental procedures, that do not appear as dangerous as they seem.

In this sense, we found a greater risk with regard to those aspects related to the host, such as general mouth-dental health, diabetes or renal insufficiency, and previous cutaneous infections, that in the case of procedures involving bacteremia risk only the administration of intravenous liquids was related to the risk of contracting IE, especially of the nosocomial type.

The panorama of early diagnosis is certainly a shadowy one. We are facing an uncommon disease (annual estimated incidence is 24 cases per 1 million inhabitants), and it is logical that it it not one of the primary concerns of physicians. It is true, however, that the old aphorism of «unexplained fever plus heart murmur equals IE, as long as pertinent blood cultures do not show this not to be the case» has fallen into disuse. Some patients with IE—especially of the nosocomial type—do not have clear auscultory semiology as they lack predisposing valve lesions, but, in others, the aphorism cannot be put into practice simply because the auscultation is not as carefully performed as it should be. To complicate matters even further, there is the terrible custom of using empirical antibiotic therapy even for those patients not diagnosed with a febrile syndrome.

Confirmation of diagnosis and medical treatment

Microbiology and echocardiography, in spite of being 2 very important diagnostic tools, do not have absolute sensitivity. For this reason, clinical judgment, and where appropriate, intense and sufficiently prolonged observation should not be neglected. Observation could probably have avoided 1 of the errors we found: that of the patient who was readmitted with ruptured valves 35 days after the diagnosis was discarded due to negative blood work and the absence of microorganism vegetation on TEE. Echocardiography, especially in its ET mode, is primordial in the detection of abscesses and other complications. The use of ETE is not clear, and its use is advisable when specific questions are not adequately answered by the initial TEE. The Spanish Society of Cardiology Guide for using ETE is when the periannular extension of the infection is suspected on TEE or ECG (new conduction disturbance), or simply following the suggestion of Vivancos et al, when faced with an episode of a high risk virulent germ, valve destruction, or an unfavorable clinical course. Clinical interest in the early detection of infectious periannular extension lies in the fact that very serious pathology is involved that requires surgical treatment in order to be cured. Pseudoaneurysm is a possible exception to this rule, as a favorable resolution has been reported without surgery.

The 2 principal deficiencies found with antibiotic therapy were: a) excessive treatment of cases of *Staphylococcus viridans*, and b) little vigilance of potentially toxic antibiotics. The great majority of *Staphylococcus viridans* infections that cause IE are very sensitive to penicillin and do not require the addition of an aminoglycoside; if this is added it is to shorten the treatment to 2 weeks, something that was never done in the cases we studied. The use of an aminoglycoside in this situation should be restricted to the 15% of *S. viridans* infections that are relatively resistant to penicillin, the group B nutritional variants and germs such as *S. agalactiae*, which are more virulent. When a potentially toxic antibiotic is used, it is important to determine its serum concentration. This was rarely done in our series, and it is possible that some important creatinine elevations had something to do with elevated levels of the aminoglycoside used.

In any case, the multifactorial character of renal insufficiency in IE makes retrospective evaluation of the problem difficult. With regard to the determination of bactercide activity in serum against the infective microorganism, it must be said that its clinical value is very limited.

Decision regarding surgery

The decision to operate or not operate on a patient with IE may be correct or incorrect. It is possible to
sin either on the side of being deficient or excessive in this regard. An example of the latter would be intervention in a patient without a grave endocardial lesion or other type of intracardiac complication (for example, an abscess) and a good clinical course from the point of view of infection. In this series there were no errors of this type. An error by default—not operating when the situation requires surgery—was identified in 1 case that, fortunately could be treated in time. We believe that this error was due to the conjunction of a misleading clinical stability and lack of knowing the significance of an early mitral valve prolapse. In any case, error by default most frequently was not related to the intention to operate but to the speed with which the operation was performed. In 1 case, «waiting for a hemodialysis vascular prosthesis to heal», dilatation, without removal of the prostesis, was abusive and probably caused the fatal ending. Without going to this extreme, in 35% of the patients on whom surgery was performed, it was judged in retrospect that too much time had elapsed between the moment when the intracardiac complication had been detected resulting in a NYHA Class I categorization and the moment when the surgery was performed.

**Study limits**

This study has 2 apparent limitations: its retrospective nature and the limited number of observations. With regard to the first of these, it is evident that a natural analysis could only be retrospective in nature. Concerning the second limitation, it is certain that a greater number of patients would have reinforced our findings; nevertheless, the sample was large enough to point out the importance of theoretical-practical discordance in the treatment of IE.

Without a doubt, the principal defect in our investigation consisted of the fact that we created a scoring system to track the errors. The fact that a skew could exist in the qualification of errors cannot be discarded, this attributing greater seriousness to the errors committed with regard to the patients who died.

**Clinical implications**

The fundamental result of this study is that we must rigorously improve theoretical-practical adequacy with regard to treating patients with IE. With regard to prevention, it seems difficult to go further than informing the patient regarding cardiopathic risk. The same is true with early diagnosis; it is more realistic that the patient at risk know that any fever that lasts more than 48 to 72 hours requires that blood work be performed. Obviously, patients who do not present with predisposing heart disease (or are unaware of it) cannot benefit from this strategy. For them, the only recourse is to invoke the auscultatory aphorism cited previously, accompanied, in addition by the concept that ordering blood work is never abusives abusiva, which is not the case with the use of an antibiotic to treat an unexplained fever. Nosocomial endocarditis should be in the mind of all physicians who work with patients at risk, for example nephrologists (hemodialysis) or oncologists and hematologists (immunosuppression). Given the cerebrovascular nature of the start of the clinical picture in some cases, some neurologists should also include IE in their diagnostic arsenal.

All patients admitted to the hospital with a well-founded suspicion of IE should be in expert hands; the discussion as to whether these should be the hands of a cardiologist or any other medical specialist appears banal to us. It would probably be more useful to create an «IE committee» in each hospital that would automatically become involved whenever necessary. An internist, infectiologist if there were one available, and a clinical cardiologist who work closely with cardiologists-echocardiologists, intensive care physicians, and cardiac surgeons, could consistute the core of this committee.

With regard to surgery, the adoption of a more decisive, less doubting, interventionist attitude including an anticipatory attitude with regard to complications when faced with very virulent germs such as *Staphylococcus aureus*, could be an important factor in achieving a cure in the most serious cases. To make this possible, we must pay understand that a good part of the indications in the field IE are code 0 or 1 of the classification jointly adopted by the Spanish Society of Cardiology and the Spanish Society of Cardiovascular Surgery, and that in order to treat these patients it is frequently necessary to change the always adjusted surgical program.

**REFERENCES**


