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A Critical Appraisal of the Quality of the Management of Infective Endocarditis

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OBJECTIVES The purpose of this study was to assess the quality of the management of infective endocarditis.

BACKGROUND Although many guidelines on the management of infective endocarditis exist, the quality of this management has not been evaluated.

METHODS We collected data on all patients (116) hospitalized with infective endocarditis over 1 year in all hospitals in the Rhône-Alpes region (France).

RESULTS Prophylactic antibiotics were not given before infective endocarditis to 8/11 cardiac patients at risk and who underwent an at risk procedure. Among the 55 cardiac patients at risk and with fever and who consulted a physician, blood cultures were not performed before antibiotic therapy was initiated for 32 patients. In-hospital antibiotic therapy was incorrect for 23 patients. The portal of entry was not treated for 16/61 patients with an accessible portal of entry. Among the 19 patients who had severe heart failure or fever persisting more than 2 weeks in spite of antibiotic therapy and who could have undergone early surgery, surgery was delayed for five, and not performed for three. Overall, the average score was 15/20.

CONCLUSIONS More information on the management of infective endocarditis should be widely disseminated to the physicians' and the dentists' communities and to the patients at risk. (J Am Coll Cardiol 1999;33:788–93) © 1999 by the American College of Cardiology

Numerous studies have reported the main characteristics of infective endocarditis, but most of these studies were retrospective, and the cases were collected over a period of several years (1–14). These studies have not shown dramatic changes in the incidence or in the profile of infective endocarditis despite the decreased incidence of rheumatic heart disease, marked advances in medical and surgical treatment and antibiotic prophylaxis recommendations (15–24). Its prognosis remains severe (25). Although many guidelines on the management of infective endocarditis exist, the management has not been evaluated. We thus collected data on all patients (n = 116) hospitalized with infective endocarditis between November 1, 1990 and October 31, 1991 in all hospitals (university, community or private) in the Rhône-Alpes region (France).

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METHODS

This study was part of a larger prospective study on the epidemiology of infective endocarditis which had been approved by the French National Commission on Computing and Freedom (25). The methods have been fully described elsewhere, and are briefly reported here (25).

For the present study, information was retrospectively collected on all patients living in the Rhône-Alpes region (France) and hospitalized for infective endocarditis between November 1, 1990 and October 31, 1991 in all public—university (n = 8) or community (n = 26)—or private (n = 10) hospitals located in the region (116 patients). The von Reyn et al. diagnostic criteria for infective endocarditis were modified to take into account echocardiographic findings and macroscopic observations made by cardiac surgeons (Table 1) (1).

For each patient the following information was recorded:

- Gender and age;
- History of heart disease, prosthetic valve, previous episode(s) of infective endocarditis;
- Current infective endocarditis: location, symptoms and physical signs, echocardiographic findings, number of positive blood cultures, causative microorganism, presumed portal of entry, surgical operation, lethality.

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Table 1. Criteria for Infective Endocarditis

Definite infective endocarditis
- Direct evidence of infective endocarditis based on macroscopy and/or histology from surgery or autopsy, and/or bacteriology (Gram stain or culture) of valvular vegetation or peripheral embolus

Probable infective endocarditis
- A. Persistently positive blood cultures* plus one of the following:
  1. New regurgitant murmur, or
  2. Predisposing heart disease and vascular phenomena† (at least two), or
  3. Predisposing heart disease and echocardiographic vegetation, or
  4. Vascular phenomena† (at least two) and echocardiographic vegetation
- B. Negative or intermittently positive blood cultures‡ plus one of the following:
  1. Fever and new regurgitant murmur and vascular phenomena† (at least two), or
  2. Fever and predisposing heart disease and vascular phenomena† (at least two) and echocardiographic vegetation

Possible infective endocarditis
- A. Persistently positive blood cultures* plus one of the following:
  1. Predisposing heart disease, or
  2. Vascular phenomena† (at least two)
- B. Negative or intermittently positive blood cultures‡ plus all three of the following:
  1. Fever,
  2. Predisposing heart disease, and
  3. Vascular phenomena† (at least two)

Rejected infective endocarditis
- A. Endocarditis unlikely, alternate diagnosis generally apparent
- B. Endocarditis likely, empiric antibiotic therapy warranted
- C. Culture-negative endocarditis diagnosed clinically, but excluded by surgery or postmortem

*At least two blood cultures performed, with 100% positive for two or three, or at least 70% positive if four or more. †Petechiae, splinter hemorrhages, conjunctival hemorrhages, Roth spots, Osler's nodes, Janeway lesions, aseptic meningitis, glomerulonephritis and pulmonary, central nervous system, coronary or peripheral emboli. ‡Any rate of blood culture positivity that does not meet the definition of persistently positive Nota bene; a serological assay can lead to bacteriological diagnosis (Rickettsia, Chlamydia and so forth).

All medical charts were reviewed by one of us (M.O.R.), and data were extracted using a specific form. Another investigator (F.D.) double-checked the data in a 10% random sample of the medical charts. There were fewer than 1% discrepancies, all minor.

The evaluation of the management of infective endocarditis was limited to the medical attitudes considered as having consensus in 1990, that is:

Quality of the antibiotic prophylaxis before the present episode of infective endocarditis: it was evaluated only in patients with a iatrogenic (i.e., due to a dental or a medical procedure) portal of entry and for whom the information was available; antibiotic prophylaxis was considered correct if it conformed with the recommendations issued by the French Federation of Cardiology in 1984 (26): type of cardiac disease, type of at risk procedure, dosage, route and type of antibiotics; it was considered incorrect if it did not conform with at least one of the cited features; no score was given since it is not quality of management of infective endocarditis stricto sensu, but quality of prophylaxis of infective endocarditis;

Prescription of blood cultures and/or hospitalization before prescribing antibiotics: it was evaluated only in patients with known valvular heart disease and fever and who went to a physician; the diagnostic process was considered correct (score = 1) when the physician prescribed one or more blood cultures and/or requested hospitalization before prescribing any antibiotics; it was considered incorrect (score = 0) when neither blood cultures nor hospitalization were performed before prescribing any antibiotics (27,28);

Quality of the management of the portal of entry: the portal of entry was considered certain when the same microorganism was found in that portal of entry and in the blood cultures; it was considered presumed:

- Either when a lesion was found and was compatible with the microorganism isolated in the blood cultures (e.g., an intestinal polyp and *Streptococcus bovis* in the blood cultures); or
- When there had been a dental or a medical procedure within 3 months before infective endocarditis and the microorganism isolated in the blood cultures was compatible with the location of the procedure (e.g., dental scaling and *Streptococcus sanguis* in the blood cultures);

Management of the found or presumed portal of entry was considered correct (score = 1) when the portal of entry was eradicated during the hospitalization (e.g., extraction of a tooth with an apical granuloma in a patient with IE due to *Streptococcus sanguis*); it was considered incorrect (score = 0):

- Either when the portal of entry was not searched for, although the microorganism had been isolated in the

blood cultures (e.g., no dental pantography performed in a patient with *Streptococcus sanguis* in the blood cultures); or

- When the found or presumed portal of entry was not eradicated during the hospitalization;

Quality of the antibiotic therapy of infective endocarditis during hospitalization: apyrexia was defined as a rectal temperature ≤37°C in the morning and ≤37.5°C in the evening; fever was defined as a rectal temperature >37°C in the morning or >37.5°C in the evening; antibiotic therapy was considered correct (score = 1) when it complied with published recommendations (29,30): antibiotics dosage, route, number, synergy and duration of treatment; it was considered incorrect (score = 0):

- Either when at least one of the cited features did not comply with these recommendations; or
- When the treatment had not been adapted (type, dosage, and so forth of antibiotics) to the course of the fever (fever persisting more than 1 week);

Cardiac surgical treatment during the acute (antibiotic therapy) phase of infective endocarditis: it was evaluated only in patients in whom the clinical status should have required cardiac surgery:

- Severe heart failure (Killip class 3 or 4) (31–35); and/or
- Persistence of fever more than 2 weeks after the beginning of correct antibiotic therapy and with no infectious metastatic location (28,32,35);

Surgical treatment was considered correct (score = 1) when patients requiring surgery were operated on; it was considered incorrect (score = 0) otherwise;

Surveillance during hospitalization: it was considered correct (score = 1) when, at discharge, the patient had had apyrexia for at least 1 week, and had no signs of congestive heart failure, and had stable or improved cardiac auscultation and echocardiography features; it was considered incorrect (score = 0) otherwise;

For each patient, a global quality score was calculated by dividing the figures found for the items applicable to that patient by the maximal possible score for that patient; a mean score was then calculated for the whole group.

RESULTS

The main characteristics of the population are presented in Table 2.

Table 2. Characteristics of 116 Patients With Infective Endocarditis

Characteristic	n	%
Whole treatment outside a university hospital	40	34
Initial admission, hospital		
University	41	35
Community	61	53
Private	14	12
Initial admission, department		
Cardiology	59	51
General internal medicine	21	18
Emergency	9	8
Infectious diseases	8	7
Intensive care	4	3
Other	15	13
Gender (men/women)	80/36	69/31
Age		
<51 years	39	33
51 to 67 years	38	33
>67 years	39	33
Known underlying heart disease	59	51
Valve prosthesis	15	13
History of infective endocarditis	8	7
Debilitated ground*	45	39
Diagnosis		
Certain	37	32
Probable	55	47
Possible	24	21
Location		
Mitral	47	41
Aortic	33	28
Mitral and aortic	13	11
Right heart	6	5
Right and left heart	4	3
Unknown	13	11
Microorganism		
Streptococcus	77	66
Staphylococcus	16	14
Other	10	9
Unknown	13	11
Certain or presumed portal of entry	77	66
Surgical intervention during the initial hospital stay	33	28
Surgical intervention while infective endocarditis bacteriologically active	19	16
Complications†	81	70
Heart failure	37	32

*Diabetes mellitus; cancer; chronic enolism; hepatic cirrhosis; chronic renal insufficiency; chronic respiratory insufficiency; immunosuppressive therapy; splenectomy; chronic hemopathy; intravenous drug abuse. †Heart failure; cardiogenic shock; septic shock; embolism; acute renal failure; infective spondylodiskitis; decompensated diabetes; decompensated cirrhosis.

Antibiotic prophylaxis before infective endocarditis. A portal of entry was found or presumed for 77 patients. Information about antibiotic prophylaxis was available for 17/19 patients with a iatrogenic (including dental procedures) portal of entry. Antibiotic prophylaxis was performed correctly for three patients. Rightly, six patients received no antibiotic prophylaxis: three patients had no known heart disease; three patients with known valvular heart disease underwent a procedure that was not considered to be at risk

(cardiac catheterization, central venous catheter and peripheral venous catheter). For eight patients, antibiotic prophylaxis was not used although it should have been (removal of an infected pacemaker: one patient; procedure at risk of infective endocarditis for patients with a heart disease at risk of infective endocarditis: seven patients).

Prescription of blood cultures and/or hospitalization before prescribing antibiotics. Among the 55 patients with known valvular heart disease and fever and who consulted a physician, 10 patients had blood cultures performed before antibiotic therapy was initiated and 10 other patients were immediately hospitalized. Blood cultures were not performed before antibiotic therapy was initiated for 32 patients (six of whom had prosthetic cardiac valves). For the remaining three patients blood cultures were performed, and these were positive, but the results were not well used (no hospitalization, no parenteral antibiotic therapy and no antibiotics at all).

Overall, 64% (35/55) of the patients in whom this feature was analyzable did not have a good quality of diagnosis.

Antibiotic therapy. Antibiotic therapy was incorrect for 23 of the 112 (20%) patients for whom all data were available: marked underdosage of beta-lactamins, for example, amoxicillin 3 g/day for a patient weighing 70 kg: seven patients; antibiotics not adapted to the microorganism or to the antibiogram: six patients; antibiotics not adapted to the course of the fever (no change of the dosage and/or of the antibiotic despite persistent fever for more than 1 week): six patients; insufficient length of antibiotic course: three patients; insufficient number of associated antibiotics: one patient.

Search for and treatment of portal of entry. The portal of entry was not at all searched for in two patients. The portal of entry was not treated before hospital discharge for 16 of the 61 patients (26%) with a curable portal of entry (intestinal polyps: seven patients; dental lesions: eight patients; polyps in the maxillary sinus: one patient).

Overall, 29% (18/63) of the patients in whom this feature was analyzable did not have a good quality of management of portal of entry.

Cardiac surgical treatment. Among the 19 patients who would have required surgery (severe heart failure: 10 patients; persistent fever for more than two weeks after the beginning of suitable antibiotic therapy: seven patients; both: two patients), eight received incorrect surgical treatment (42%). Surgery was unduly delayed for five patients: persistent fever; three patients; severe heart failure and persistent fever: two patients. Three patients were not operated on: one patient with severe heart failure was still alive at 2 years; two deceased patients may have benefited from surgery (one had fever for 5 months despite several changes in antibiotic therapy; one was operated on in emergency after having been discharged from hospital, although the fever had persisted for 5 weeks despite antibiotic therapy and four embolic episodes had occurred).

In-hospital surveillance. Among the 103 patients who left the hospital after the initial phase, seven (7%) were discharged in error: two had clinical and echocardiographic signs of prosthesis dehiscence, one had persisting fever, one had been apyretic for 5 days only, one had noncompensated cardiac failure, one had had a progressively increasing cardiac murmur and one had had progressively increasing dilation of the left ventricle. Four of these patients had a complication in the month following discharge (one relapse of infective endocarditis and three cases of severe heart failure necessitating surgery) and two during the first 6 months (one death due to cerebral hemorrhage and one severe heart failure necessitating surgery).

Overall. Globally, scores were obtainable in only 61% [(55 + 112 + 63 + 19 + 103)/(116·5)], mainly because an item was not applicable to some patients, sometimes because data were missing.

The mean overall score was 75%, that is, 15/20; on average, in a patient, 75% of the management of infective endocarditis was correct. Two patients were excluded because there was no applicable score. Among the remaining 114 patients, 44 (38%) had the maximal possible score (100%).

The score was not different according to the specialty of the medical ward the patients were first admitted to: cardiology: 15.0/20; general internal medicine: 15.2/20; intensive care: 15.0/20; infectious diseases: 14.9/20. Also, it was not different according to the type of hospital the patients were first admitted to: university hospitals: 15.9/20; community hospitals: 14.5/20; private hospitals: 14.5/20. Finally, the score was not different in patients alive at 2 years (15.0/20) and in those deceased at 2 years (14.7/20).

DISCUSSION

Although guidelines on the prevention and management of infective endocarditis exist, it seems from our results that compliance with these guidelines is poor.

Methodological quality of the study. Because the medical charts were reviewed by only one investigator, the data extraction form was very precise and complete. The double-checking of 10% of the medical charts disclosed less than 1% discrepancies, which were all minor. Thus, we are rather confident about the quality of our data.

Antibiotic prophylaxis of infective endocarditis. Although apparent failure of antibiotic prophylaxis has been reported (36), its efficacy has been reported at between 50% and 90% (37–39), and antibiotic prophylaxis has been reported to be cost-effective (40). Although on a country-wide scale, low efficacy prophylaxis has a little impact (between 60 and 120 events avoided for 1,500 patients treated per year in France [37]), for an individual patient it

is worthwhile, and its use for patients undergoing high risk dental procedures is not challenged. However, the absence of an overall consensus does not make the physicians' task easy, and compliance of dentists and physicians with recommendations for the prevention of infective endocarditis is low (15). In our study, for eight out of 11 patients with a iatrogenic portal of entry necessitating antibiotic prophylaxis, it was not administered. In agreement with our results, several studies in France, the USA and the U.K. showed that dentists and general practitioners varied in their knowledge of the risk factors for infective endocarditis and in their use of antibiotic prophylaxis, often despite knowing the recommendations in their countries (41–44).

Propositions for improving the quality of care of infective endocarditis. Can the compliance with guidelines be improved? The authors of a study in the U.K. suggested that general practitioners should be supplied with self-adhesive stickers to be placed at the front of the medical notes of all patients at risk (43). In France a summary of the recommendations of a consensus conference held in 1992 was sent to all dentists and general practitioners (45). In addition the French Federation of Cardiology is distributing a new prophylaxis card. A survey of the incidence of infective endocarditis is planned after this card has been in use for 5 years.

The unacceptably low rate of blood cultures before initiation of antibiotics (60% of the patients at risk in our series) needs to be improved. Regular reminders of the need for blood cultures in cardiac patients at risk before initiating a course of antibiotics should be sent to general practitioners. Also, similar to what is done for the surveillance of anticoagulant treatment, patients at risk of infective endocarditis could be given a prescription for blood cultures to be used when they have fever lasting more than 3 days without having to consult their physician.

The need for discussion between the clinician in charge of the patient and the microbiologist is highlighted by the high percentage of patients (20%) in our series who did not received the correct antibiotic therapy. Similarly, discussion between the cardiologist, the microbiologist and the cardiac surgeon is needed, because, although some indications for surgery are fully accepted, some are not (e.g., large vegetations, controlled heart failure, recent neurological complications). In our series 40% of the patients who could have been operated on early either had unduly delayed surgery or no surgery.

Although portals of entry may be more often found nowadays (25) than previously (46,47), a systematic search is not always performed. In a series of 53 patients with infective endocarditis due to *Streptococcus bovis* (48), the large bowel was not investigated in 19% of the patients. In addition, curable portals of entry are not always correctly treated. This was so for 19% of the patients in our series, and for five out of 27 patients with colonic tumors in the previously cited series (48).

Conclusions. The overall management of infective endocarditis was compliant with the guidelines for only 38% of our patients. These results demonstrate that better information for patients, dentists and physicians is needed. This information should be simple and rediffused at regular intervals. We believe that this study should be repeated in other health care settings.

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