Are blood and valve cultures predictive for long-term outcome following surgery for infective endocarditis?☆

Attilio Renzulli, Antonio Carozza, Claudio Marra, GianPaolo Romano, Gennaro Ismeno, Marisa De Feo, Alessandro Della Corte, Maurizio Cotrufo

Institute of Cardiac Surgery, Second University of Naples, V. Monaldi Hospital, Via L. Bianchi, Naples, Italy

Doctorate in Cardiology Sciences, Second University of Naples, Naples, Italy

1. Introduction

The dramatic reduction of incidence of rheumatic disease in the Western world has not led to a significant reduction of valvular heart disease requiring valve replacement [1]. Progresses in cardiac imaging techniques including echocardiography [2] and CT-scan allowed a more accurate diagnosis in patients with heart failure and in ageing people [3]. Moreover the incidence of infective endocarditis, in spite of antibiotic therapy and early diagnosis, does not appear to have declined in recent years, ranging from 10 to 50 cases/million inhabitants a year [4].

Therefore, infective endocarditis seems to be the most serious problem in valvular heart disease [5]; in spite of appropriate antibiotic treatment and improved surgical techniques, hospital mortality is higher than expected and the incidence of recurrence is still high [6,7].

Preoperative investigations in patients with infective endocarditis include echocardiography, abdominal CT-scan or ultrasound, brain CT-scan [8,9]. Moreover it is common practice to perform blood cultures [10] in patients with active endocarditis and to culture vegetations and infected valvular tissue in order to isolate the germs involved in the infection and to establish the appropriate postoperative antibiotic treatment. Bacteria isolation from valvular tissue is not always possible: healed endocarditis, broad-spectrum perioperative antibiotic therapy, systemic hypothermia, hemodilution and cold cardioplegia reduce the possibility of germ isolation from the infected tissue [11]. Nevertheless, it is still unclear whether bacteria isolation from the infected tissue and specific postoperative anti-

Keywords: Infective endocarditis; Blood culture; Valve culture

1010-7940/00/$ - see front matter © 2000 Elsevier Science B.V. All rights reserved.

PII: S1010-7940(00)00342-0
biotic therapy may improve long-term prognosis of infective endocarditis [12,13].

The objective of this retrospective study is to summarize our surgical experience with infective endocarditis during a 20-year period and to establish whether positive blood and valve cultures are predictors of early survival and better late outcome.

2. Materials and methods

Cases of infective endocarditis were classified retrospectively according to Duke criteria [14]. Moreover it has been our policy, since January 1980, to perform histology and microbiology examinations of all excised material at valvular surgery procedures, regardless of the etiology of valvular disease.

Blood cultures were performed routinely in all patients admitted to our Institution with valvular disease and fever. Blood cultures performed in the referring hospital were recorded as well.

For the definitions of active, healed, native, prosthetic and culture-negative endocarditis, modified Aranki’s criteria [12] were employed. Endocarditis was labeled ‘active’ if the patient had fever and/or leukocytosis at the time of surgery or required surgical treatment before completion of a standard course of antibiotic treatment. Endocarditis was labeled ‘healed’ if surgery was performed after completion of antibiotic treatment and no signs of active infection (fever, leukocytosis) were present.

Prosthetic valve endocarditis was defined as infection occurring on any type of tissue or mechanical valve device. ‘Early’ prosthetic valve endocarditis was present if recurrent or residual endocarditis occurred within 180 days after surgery. Prosthetic valve endocarditis occurring after 180 days was labeled ‘late’.

Culture-negative endocarditis was present when no microorganism could be identified either on serial blood cultures or on cultures from the explanted valvular tissue in patients presenting with the clinical picture of endocarditis, particularly in the presence of a new regurgitant murmur, congestive heart failure and/or vegetations on echocardiogram. These were confirmed at operation by presence of leaflet perforation, of vegetations, or valvular and perivalvular tissue destruction. The presence of acute or chronic inflammatory changes at microscopy confirmed the diagnosis of endocarditis.

Early mortality or morbidity was defined as death or complications occurring within 30 days or during the same hospital stay after surgery.

Late mortality and morbidity were classified according to Edmunds’ criteria [15].

Treatment failure was defined as the combinations of the following postoperative events: late mortality, reoperation, periprosthetic leak, recurrence of infection.

Patients were retrospectively classified into three groups according to the results of microbiology tests: Group A, patients with at least one positive blood culture but negative tissue cultures; Group B, patients with positive tissue cultures (regardless of blood cultures results); and Group C, patients with both negative blood and tissue cultures.

2.1. Patients’ characteristics

Between January 1978 and December 1998, 232 patients, 79 female (34.1%) and 153 male (65.9%), with an age ranging between 8 and 79 years (mean 44.95 ± 1.03 years) underwent surgery for infective endocarditis.

Several patients in our series had multiple indications to the surgical treatment; fever and/or persistence of infection were reported in 37.9%, cardiac failure in 47.8%, previous embolism in 26.3% others (renal failure, hemolysis, malaise, poor tolerance to antibiotic therapy) in 14.2%.

The infection involved a native valve (NVE) in 162 cases (69.8%) and a prosthetic valve (PVE) in 70 patients (30.2%).

As far as the site of infection is concerned, endocarditis involved the mitral valve in 66 cases (28.4%), the aortic valve in 118 cases (50.9%), the tricuspid valve in 13 cases (5.6 %) and the pulmonary valve in two cases (0.9%). Multiple valvular involvement was reported in the other 33 cases; the infection was localized on the mitral and the aortic valves in 27 cases (11.6%), on the mitral and the tricuspid valves in two cases (0.9%), on the aortic and the tricuspid valves in three cases (1.3%) and on the mitral, tricuspid and aortic valves in 1 case (0.4%).

2.2. Preoperative assessment

New York Heart Association status was evaluated in all patients: 103 patients (44.4%) were in NYHA class III and 57 (24.5%) in NYHA class IV, while 72 patients (31%) did not complain of dyspnea, being in NYHA class I or II.

To avoid embolization of vegetations and/or valvular tissue, cardiac catheterization was rarely performed (four cases), just to confirm through coronary angiography the clinical findings of an associated coronary artery disease.

B-mode transthoracic echocardiography was performed in all cases.

Since January 1989 either pre- or intraoperative color-Doppler echocardiography was routinely performed through the transesophageal approach in all patients. Echocardiographic investigation allowed the diagnosis of aortic regurgitation in 141 cases; mitral regurgitation was diagnosed in 70 cases.

Typical findings of infective endocarditis were recorded at echocardiography: periprosthetic leak was observed in 51 cases (22%), vegetations in 139 cases (59.9%), valvular tears in 60 cases (25.8%), periannular abscesses in 17 cases (7.3%) and chordal rupture in 13 cases (5.6%).

Preoperative investigations included brain CT-scan in 70 cases and abdominal ultrasound in 68 cases.
Blood cultures were performed routinely in all patients with fever or active infection.

2.3. Operative procedures

Surgical treatment was performed on elective basis in 84 cases (36.2%), on urgency basis (within 1 week from the hospital admission) in 121 cases (52.1%) and on emergency (<24 h after the hospital admission) in 27 cases (11.7%). Cardiopulmonary bypass, systemic hypothermia and moderate hemodilution were used in all cases. Myocardial protection was achieved with systemic and local hypothermia and with antegrade crystalloid cardioplegic infusion in all cases.

Mechanical and bioprosthetic valves were implanted with interrupted sutures. Homografts were inserted with an interrupted proximal suture line and a continuous distal suture line. Extensive debridement of vegetations and annular abscesses was always performed.

The aortic valve was replaced in 151 cases: with a tilting disc valve in 42 (27.6%) cases, with a bileaflet prosthesis in 66 cases (43.7%), with a bioprosthesis in 31 cases (20.5%), with a homograft in eight cases (5.3%) and with a stentless valve in three cases (2%). In one patient presenting with the third episode of a recurrent aortic endocarditis, the left ventricular outflow was closed and an apico-aortic conduit was implanted. Finally, three patients with aortic endocarditis underwent vegetectomy and valve repair.

The mitral valve was replaced in 99 cases: with a ball valve in 16 cases (16.2%), with a tilting disc valve in 30 cases (30.3%), with a bileaflet valve in 33 cases (33.3%) and with a bioprosthesis in 19 cases (19.2%). One patient with recurrent mitral endocarditis underwent reversed pulmonary homograft implantation (Top Hut technique).

Mitral repair was performed in two cases.

The tricuspid valve was replaced in 10 cases, with a mechanical valve in two and a bioprosthesis in eight. Tricuspid valve repair was performed in nine cases.

2.4. Postoperative treatment

All patients underwent i.v. antibiotic therapy for at least 4 weeks postoperatively. Culture-negative endocarditis was usually treated with combinations of broad-range antibiotics (Vancomycin–Tobramycin–Cephalosporins). Patients with positive cultures were treated according to susceptibility tests.

2.5. Follow-up

Data regarding hospitalization were obtained from the hospital records. Data on outcome after discharge and clinical status at follow-up were obtained from the Outpatient Department records or by telephone interviews either to the patients, or to the general practitioner or the referring physician. Follow-up was 97.9% complete. Follow-up time ranged from 4 to 239 months (mean 83.2 ± 14 months).

2.6. Statistical methods

All data were recorded on a dedicated software. Statistical analysis was performed with SPSS software. Categorical values were compared by $\chi^2$ analysis, whereas continuous data were compared by ANOVA and Bonferroni correction for post hoc comparisons. Late survival experiences of the different groups were compared by mean of the log-rank test and by constructing Kaplan–Meier survival curves.

All data were reported as mean ± standard error.

3. Results

Results of blood and tissue cultures are reported in Table 1.

The percentage of Staphylococcus strains was higher in valve cultures (68.6%) than in blood cultures (39.8%) ($P = 0.008$).

As far as age, male sex and incidence of preoperative embolic events were concerned no statistically significant differences were found between the three groups (Table 2). Incidences of preoperative fever, preoperative cardiac failure and native valve endocarditis were significantly higher in patients with positive blood cultures (Table 2). Hospital mortality was 12.5%. Causes of death were: low output syndrome in 16 cases, sepsis in six, ventricular fibrillation in two, ARDS in two, brain hemorrhage in two and multi-organ failure in one.

No differences ($P = 0.52$) were found between hospital mortality rates in the 3 Groups (Table 3). Late mortality was 8.37% (17/203) (8/74 in Group A, 5/32 in Group B and 4/97
in Group C). Causes of death were low cardiac output following reoperation in six cases, sudden death in three, cardiac failure in two, sepsis in two, cancer in two, chronic renal failure in one and stroke in one. Ten-year survival analysis, including hospital mortality did not reveal any differences ($P \leq 0.38$) between the three Groups (Table 3, Fig. 1).

As far as the incidence of reoperations is concerned, 12 patients required 21 reoperations. The most common cause of reoperation was periprosthetic leak (18 cases), followed by bioprosthesis degeneration (two cases) and malfunction of homograft in mitral position (one case). As far as 10-year freedom from reoperation is concerned, a higher incidence ($P \leq 0.003$) of reoperations in patients with perioperative positive tissue culture was found (Table 3, Fig. 2).

Analysis of late complications not requiring surgical treatment showed two cases of recurrent endocarditis and six cases of minor periprosthetic leak in Group A, no cases in group B, and ten cases of minor periprosthetic leak and four cases of recurrent endocarditis in Group C. Ten-year analysis of freedom from treatment failure showed no difference ($P = 0.46$) between the three Groups (Table 3, Fig. 3).

4. Discussion

Despite of improved antibiotic prophylaxis, the incidence of infective endocarditis has been increasing during the last two decades [4]. Improved care in patients with chronic diseases and with some degree of immunodepression [16], together with the expanding use of intracardiac devices such as pacemaker, defibrillators, catheters and prosthetic valves, have considerably increased the number of patients at risk for endocarditis [17]. Finally, i.v. drug addiction is another important risk factor for the development of infective endocarditis [18].

A significant contribution to the treatment of infective endocarditis is given by the microbiology team: blood cultures are routinely performed [5,19] in patients with active endocarditis and explanted material at surgical exploration (vegetations, leaflets, debris from abscesses, prosthetic valves) [11] is commonly cultured.

The incidence of negative blood cultures ranges in the medical literature between 20 and 60% [12,13,20] of cases who have undergone surgical treatment. Many factors, such as healed endocarditis, broad-range antibiotic therapy, low-virulence germs, and poor techniques of blood sampling and cultures may account for the lack of isolation of germs from the blood.

Incidence of positive cultures from vegetations and tissue retrieved at the operation is even lower. In our series we were able to identify the germs in 15.08% of cases. Failure in isolating germs from vegetations and explanted materials may be caused by healed endocarditis, broad-range preoperative antibiotic treatment, attitude to prime the oxygenator with crystalloid solution and antibiotics, and use of crystalloid cardioplegia that may cause an osmotic and physical shock to the bacteria still living in the vegetations [21,22]. Pre-treatment of vegetations [23] with ultrasound can improve bacterial growth and isolation from excised

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Postoperative data</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group</strong></td>
<td>A</td>
</tr>
<tr>
<td>Hospital mortality (%)</td>
<td>9 (10.8)</td>
</tr>
<tr>
<td>Survival (%)</td>
<td>62.7 ± 8</td>
</tr>
<tr>
<td>Freedom from reoperations (%)</td>
<td>85.2 ± 6</td>
</tr>
<tr>
<td>Freedom from treatment failure (%)</td>
<td>56.3 ± 8</td>
</tr>
</tbody>
</table>

* Not significant.
tissue at surgery. In our series we isolated germs from infected tissue in 16 cases with a preoperative negative blood culture. Targeted postoperative antibiotic treatment for more than 4 weeks carries a better prognosis according to recent reports [13,24].

Nevertheless, controversial observations about the prognostic impact of positive blood and tissue cultures are still issued. Aranki et al. [12] reported in a large series of aortic endocarditis a longer freedom from recurrence in patients with healed endocarditis compared to those with active endocarditis, even though in that series long-term survival was not influenced by activity of infection nor by the type (native or prosthetic) of endocarditis. Conversely, Dehler and Elert [13] reported a statistically significant worse prognosis at 1 and 5 years postoperatively in patients with positive ‘intraoperative’ cultures than in patients with negative ‘intraoperative’ cultures.

Our series shows no differences in terms of early and late survival between patients with positive cultures and those with negative bacteriological results. Moreover, the overall incidence of complications did not show any significant difference between patients with positive blood cultures, patients with positive tissue cultures and patients with negative cultures. Although no differences were found between the three groups as to recurrence of endocarditis, the incidence of late reoperations was higher in patients with positive cultures from vegetations. Such findings was associated to higher incidence of staphylococcal strains (58.6%) isolated from tissue cultures. Staphylococcal endocarditis causes annular disruption [25,26] increasing, in spite of complete cure of the infection, the risk of late aseptic periprosthetic leak due to annular weakness.

In conclusion, culture of vegetations allows bacterial identification in less than 25% of cases of bacterial endocarditis; nevertheless it can isolate germs undetected by blood cultures. Proper techniques of harvesting and culturing may improve the rate of success in bacterial identification. Positivity of cultures from the explanted tissue is higher in staphylococcal endocarditis and it is a determinant for late reoperation.

References


