

Infective Endocarditis. Surgical Therapy

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Objective - To assess the major causes of surgical morbidity and mortality in patients with infective endocarditis operated upon in a regional cardiology center.

Methods - Thirty-four patients underwent surgical treatment for infective endocarditis. Their ages ranged from 20 to 68 years (mean of 40.6) and 79% were males. Their NYHA functional classes were as follows: IV - 19 (55.8%) patients; III - 12 (35.2%) patients; II - 3 (8.8%) patients. Blood cultures were positive in only 32% of the cases. Eight patients had already undergone previous cardiac surgery, whose major indication (82.3%) was heart failure refractory to clinical treatment.

Results - Four (11.7%) patients died at the hospital. Follow-up was complete in 26 (86%) patients. Five (14.7%) patients died later, 12, 36, 48, 60, and 89 months after hospital discharge. Of the 21 patients being currently followed up, 1 is in NYHA functional class III, and 5 in NYHA functional class II.

Conclusion - A high degree of clinical suspicion, at an early diagnosis, and indication of surgical treatment prior to deterioration of left ventricular function and installation of generalized sepsis may improve prognosis.

Key words: endocarditis, valvular surgery, cardiac surgery

Despite all diagnostic and therapeutic advances, active intracardiac infection, so-called infective endocarditis, is still related to a high risk of morbidity and mortality in Brazil and in other countries¹⁻⁴. In a continental and heterogeneous country like ours, these advances frequently have a compromised application: patients initially managed in community hospitals with no laboratory resources or imaging techniques, such as ultrasonography, tomography, or magnetic resonance imaging, are frequently referred to specialized centers in an already advanced stage of the disease. In addition, regional centers, despite the increasing surgical demand, may still lack a large volume of surgeries, having, therefore, less experience in managing this type of patient. On the other hand, it would be impossible to imagine the entire national demand absorbed by 3 or 4 centers here considered to be excellent. Undoubtedly, early recognition, mainly stimulated by a high degree of suspicion of the disease and aggressive therapy, is the major factor for a successful strategy. Age, left ventricular function, presence of a cardiac valvular prosthesis, renal failure, diabetes, embolic complications, and the infecting agent are the major factors that determine the course of infective endocarditis⁵⁻⁷. In a retrospective study, we analyzed the major causes of morbidity and mortality in patients with infective endocarditis in a regional cardiology center and what can be done to improve the prognosis of this special group of patients.

Methods

From May 1986 to April 2001, 34 patients underwent cardiac surgery for infective endocarditis in the Service of Cardiothoracic Surgery of the Hospital São Vicente de Paulo, in the city of Passo Fundo, in the Brazilian state of Rio Grande do Sul. That is a university-affiliated general hospital with 640 beds, where 40 to 50 cardiac surgeries with extracorporeal circulation are performed every month. Its area of influence encompasses 300 municipalities in the states of Rio Grande do Sul and Santa Catarina, involving a population of 1,050,000 inhabitants. The hospital is located in the city of Passo Fundo (170 thousand inhabitants) in the

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northern region of the state of Rio Grande do Sul. Following a defined protocol, the medical records of those patients were reviewed and their clinical evolution analyzed.

The male sex prevailed, corresponding to 79.4% of the patients; their ages ranged from 20 to 68 years (mean age of 40.6 years). According to the NYHA functional class classification of heart failure, 19 (55.8%) patients were class IV; 12 (35.2%) were class III; and 3 (8.8%) were class II. Blood cultures were performed in all patients, and microorganisms were identified in only 11 (32.3%) patients. *Streptococcus viridans* (5 cases) and *Staphylococcus aureus* (3 cases) were the microorganisms most frequently found. *Klebsiella* and *Escherichia coli* were identified in 2 other patients. All cases were confirmed as infective endocarditis by surgical findings. The patients with negative blood cultures also had negative tissue cultures.

Clinical, laboratory, and radiological findings suggesting the diagnosis of infective endocarditis were in accordance with those of 2-dimensional Doppler echocardiography performed in all patients. In addition, 4 patients also underwent cine coronary angiography. Clinical signs compatible with cerebral embolism were identified in 2 patients. Their complementary study included computerized tomography of the brain in both patients and angiography of the internal carotid artery in 1 patient. In the latter, a cerebral abscess was drained and cardiac surgery was performed within 4 weeks. These patients neither underwent previous surgery nor were taking oral anticoagulant agents. Antibiotic therapy was performed from the beginning of the symptoms until the surgical procedure for a period ranging from 2 to 120 days (mean of 28.1 days). Eight patients had already undergone the following cardiac surgeries: 7 patients underwent aortic valve replacement (4 biological and 3 mechanical prostheses) and 1 underwent mitral valve replacement (mechanical prosthesis) (fig. 1a, 1b, 1c). In patients without previous surgical treatment, the following lesions were identified: mitral valve prolapse (4), mitral stenosis (1), congenital mitral insufficiency (1), and congenital aortic stenosis (1).

Of the patients undergoing surgical treatment, 19 (55.8%) had clinical signs of severe heart failure due to valvular lesions, but the systemic infection was considered under control. The remaining, in addition to the indication for valvular prosthesis implantation due to severe insufficiency, had their clinical picture impaired by the presence of sepsis, cardiogenic shock, abscess, aneurysm, or fistula. One patient was under mechanical ventilatory support. In 3 patients, the source of endocarditis was previous hemodialysis due to acute renal failure that developed after blood dyscrasia because of infection from lizard toxin (*Lonomia obliqua*). Hemodialysis due to chronic renal failure and aortic valve calcification were indications in 2 other patients.

All patients were operated upon with extracorporeal circulation in moderate systemic hypothermia (28°C), myocardial protection with topical cooling of the cardiac surface, and anterograde intracoronary infusion of a crystalloid

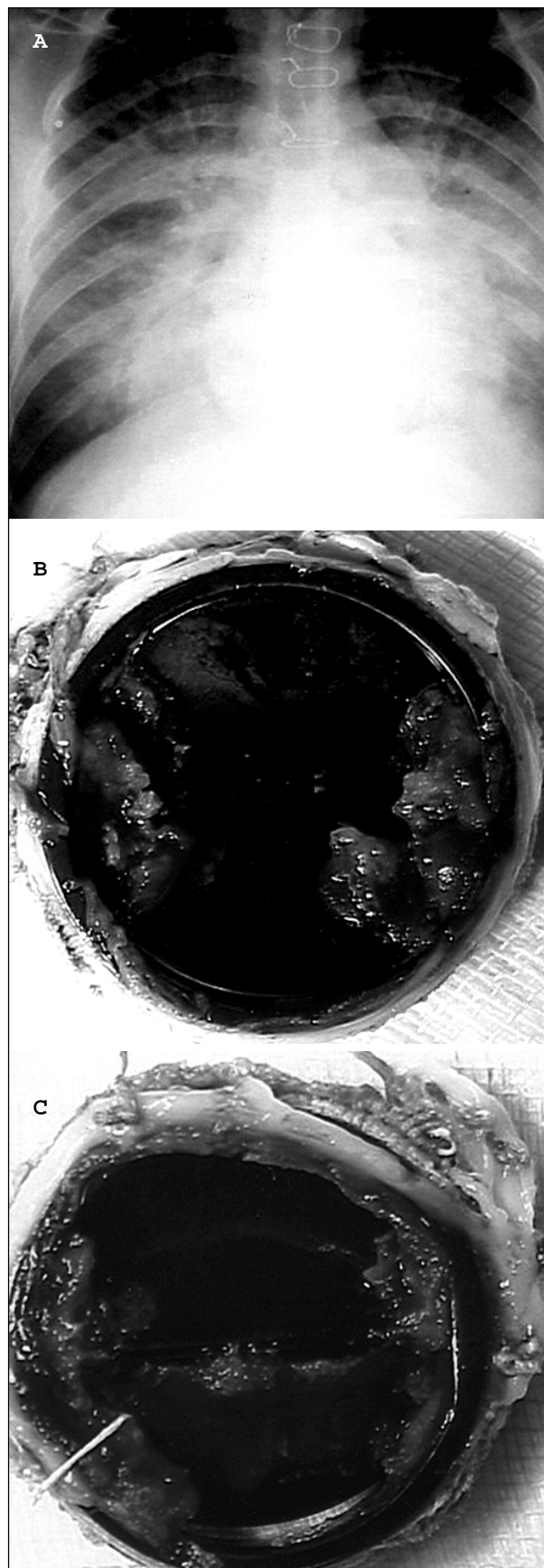


Fig. 1 – 1a) Implantation of double leaflet mitral prosthesis 14 months before. Active infective endocarditis; 1b) Atrial face of the prosthesis with vegetations; 1c) Ventricular face of the prosthesis blocked by vegetations.

cardioplegic solution. Due to annular fragility and aiming at strengthening the suture, the stitches were usually anchored in a Teflon pillow. When the aortic ring required widening or the fistulas required closing, a flap of bovine pericardium preserved in glutaraldehyde was used. The most frequently impaired valve was the aortic valve (17 patients - 50%), followed by the mitral valve (11 patients - 32.3%) (fig. 2 a, 2b), and the following associations: mitral-aortic in 3 (8.8%), mitral-tricuspid in 2 (5.8%), and aortic-tricuspid in 1 patient (3.4%). Two patients requiring mitral valve replacement by a mechanical prosthesis due to destruction of the valvular apparatus by infective endocarditis had a significant associated tricuspid insufficiency that required correction of the DeVega annuloplasty type, but no signs of infective endocarditis were observed in that valve. One patient (2.9%) had impairment of the tricuspid valve by infective endocarditis; the 4 patients treated with mitral valvuloplasty had vegetations characteristic of infective endocarditis in the valvular apparatus. Annuloplasty techniques⁸⁻¹⁰ with simple sutures (1) or placement of a Carpentier ring (3), partial resections of the impaired leaflets and repaired with direct sutures, when adequate (1), or repaired with bovine pericardium flap (3) were used in these patients. These conservative techniques were used only in situations in which the partial resection of the impaired leaflets did not prevent

complete resection of the vegetations. Five patients had total atrioventricular block at the time of the surgical decision. The surgical procedures are specified in table I.

Results

The major indication for surgery was the presence of refractory heart failure in 28 (82.3%) patients. Third-degree atrioventricular block, central embolism, and periannular aortic and mitral abscess with the formation of aortic/right atrium/left atrium fistula complete the remaining indications. Duration of aortic clamping ranged from 21 to 130 minutes (mean of 67.8 minutes). The mean length of stay in the intensive care unit was 5.2 days, and the mean postoperative hospital stay was 21 days. Of the 5 patients with total atrioventricular block at the time of surgery, 2 required definitive implants of artificial cardiac stimulation (1 epimyocardial and 1 endocardial). Two patients who had no conduction disorder detected in the preoperative period developed total atrioventricular block by the end of the surgical procedure, requiring a temporary pacemaker. One of these patients required the implantation of a definitive pacemaker, in which an epimyocardial electrode was used.

Four (11.7%) patients died during hospital stay as follows: 2 during surgery, 1 on the first postoperative day, and another on the ninth postoperative day. Of the patients dying in the operating room, 1 had staphylococcal endocarditis in the biological aortic prosthesis. This patient developed a dental abscess 20 days before and was being treated for congestive heart failure. As the patient did not improve, he was operated upon in total atrioventricular block, sepsis, and mechanical ventilation. On surgery, a periannular abscess of the biological aortic prosthesis and of the interventricular septum was identified. Even with the extensive surgical débridement and implantation of a new aortic prosthesis, the patient could not maintain sufficient cardiac output without extracorporeal circulation support and died in the operating room. The second patient, operated upon in a similar clinical condition, had his mitral valve destroyed by vegetations. Although the surgical treatment was considered adequate, the extracorporeal circulation support could not be removed, and the patient died with signs of right ventricular failure. The third patient, operated upon with cardiogenic shock (aortic and mitral insufficiency) and disseminated intravascular coagulation present, had to be reoperated on in the first 24

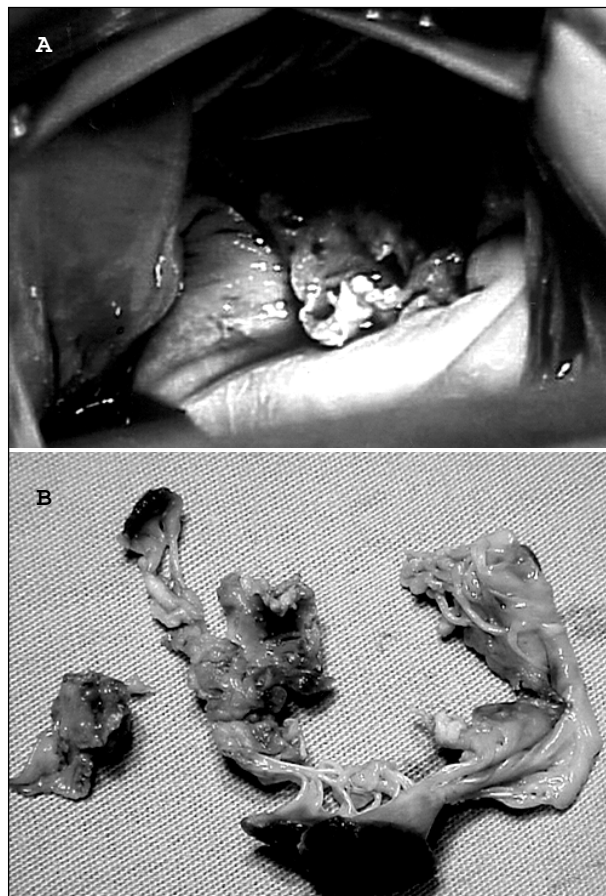


Fig. 2 - 2a) View of the mitral valve destroyed by vegetations during surgery; 2b) Excised mitral valve with alterations of infective endocarditis.

Table I - Procedures

Mechanical aortic prosthesis	11	Mechanical mitral prosthesis	5
Biological aortic prosthesis	4	Mitral valvuloplasty	2
Mechanical mitral prosthesis + tricuspid valvuloplasty	2	Mechanical aortic prosthesis + mitral valvuloplasty	2
Biological aortic + mitral prosthesis	1	Biological aortic + tricuspid prosthesis	1
Correction of aorta/RA/LA fistulas	2	Biological mitral prosthesis	4

hours because of persistent bleeding and cardiac tamponade. The patient was transferred to the intensive care unit in critical condition with maximal use of inotropic agents and died 7 days later because of the persistence of sepsis and multiple organ failure. The fourth patient, with tricuspid and aortic insufficiency, sepsis and cardiogenic shock, died on the first postoperative day because of cardiopulmonary failure. Table II shows these patients.

Five patients required more than 1 surgical intervention because of the recurrence of endocarditis or to its sequelae. One patient had to be reoperated on twice because of the recurrence of infection; the first episode was 2 years after the initial intervention and the second episode was after the third year. In the latter, destruction of the superior mitral ring was observed with formation of an abscess in the mitral-aortic continuity and loss of sustentation of the anterior mitral leaflet. Mitral valvuloplasty and implantation of a new aortic prosthesis were performed. This patient died after a 4-year follow-up due to a new return of the cardiac and systemic infection with consequent septicemia.

Another patient, initially with extensive aortic valvular destruction and aorta/right atrium fistula, required 3 surgical interventions to control infection and restore normal hemodynamics. Currently, the patient has a normal life, is asymptomatic, but a small residual aortic perivalvular fistula persists with no clinical repercussions.

Of the 30 patients discharged from the hospital, 4 were not followed up. Of the 26 patients with regular clinical follow-up, 5 died after 12, 36, 48, 60, and 89 months. These patients are described in table III.

Of the 19 patients operated upon in NYHA functional class IV, 5 died, 2 are being followed up, 7 evolved to class I, 4 to class II, and 1 to class III. Of the 12 patients operated upon in class III, 3 died, 2 are being followed up, 6 are in class I, and 1 is in class II. Of the 3 patients operated upon in class II, 1 died and 2 are in class I.

Table II – In-hospital deaths
Patient 1: Female, 26 years. Infective endocarditis in biological aortic prosthesis implanted 2 years before. Dental abscess for 20 days. Total atrioventricular block, sepsis, cardiogenic shock, under mechanical ventilation. <i>S. aureus</i> in the first blood culture 10 days before. Implantation of biological aortic and mitral prostheses on the day of transference to our service. Death in the operating room.
Patient 2: Female, 68 years. Cardiogenic shock and sepsis due to mitral valve destruction by vegetations. Negative culture. The patient underwent surgery on the day of transference to our service. Death in the operating room.
Patient 3: Male, 22 years. Cardiogenic shock, DIVC and sepsis due to aortic and mitral insufficiency. Culture positive for nonhemolytic <i>Streptococcus</i> 7 days before. Implantation of biological aortic and mitral prostheses. Reoperated upon in 24 hours due to cardiac tamponade. Death on the seventh postoperative day due to multiple organ failure and sepsis.
Patient 4: Male, 21 years. Drug addict. Under hemodialysis for 30 days. Tricuspid and aortic insufficiency. Sepsis, cardiogenic shock. Annular and subannular aortic abscess. Aortic and tricuspid vegetations. Death 24 hours after implantation of biological aortic and tricuspid prostheses due to cardiogenic shock and persistence of sepsis.

Discussion

Infective endocarditis has had a greater incidence since the 1980s, with reports of 5.9 and 11.6 episodes per 100,000 inhabitants in Sweden and Philadelphia, respectively^{11,12}. Approximately half of the cases reported in Philadelphia had a previous history of the use of injectable drugs. The incidence increases progressively after 30 years of age, exceeding 15 to 30 cases per 100,000 people/year between the sixth and eighth decade of life. Fifty-five to 75% of the patients with infective endocarditis in native valves have predisposing conditions, such as rheumatic disease, congenital disease, mitral valve prolapse, degenerative heart disease, asymmetric septal hypertrophy, or use of illegal intravenous drugs^{13,14}. Seven to 25% of the cases involve the presence of prostheses^{11,12}. In 25% of the cases, predisposing factors for infective endocarditis cannot be identified.

Signs and symptoms of infective endocarditis are frequently neglected and, when evident, normally reflect a complication and not an intracardiac infection per se. Clinical suspicion should be highly emphasized until diagnostic definition. Application of the criteria reported in the literature allows an approach with good sensitivity and specificity for the diagnosis of infective endocarditis^{3,16}. The use of echocardiography in patients with a clinical suspicion of infective endocarditis often allows morphological confirmation of infection and is of inestimable help in choosing the adequate approach in each case^{16,17}. Echocardiography should be performed mainly in patients with negative blood cultures³. Transesophageal echocardiography allows the visualization of small vegetations and adds resolution to the conventional transthoracic echocardiography with pulsed and continuous wave Doppler^{3,18}. Transthoracic echocardiography and its association with transe-

Table III – Late deaths

Preoperative period	Postoperative period
1) Male, 43 years old, aortic and mitral insufficiency, NYHA functional class IV. Aortic and mitral prosthesis	Death 12 months after surgery. Heart failure. Irregular and noncooperative treatment.
2) Male, 22 years old. Mitral insufficiency. NYHA functional class III. Mitral prosthesis.	Death 36 months after surgery. Heart failure.
3) Male, 63 years old. Endocarditis in the aortic valve prosthesis and native mitral valve. NYHA functional class III. Aortic prosthesis and mitral valvuloplasty.	Death 48 months after surgery. Heart failure due to perivalvular fistula.
4) Male, 40 years old. Mitral valve insufficiency. NYHA functional class II. Mechanical mitral prosthesis.	Death 60 months after surgery due to hemorrhagic stroke.
5) Male, 53 years old. NYHA functional class IV. Meningitis. Mitral prosthesis.	Death 89 months after surgery due to acute myocardial infarction. Prosthesis without alterations.

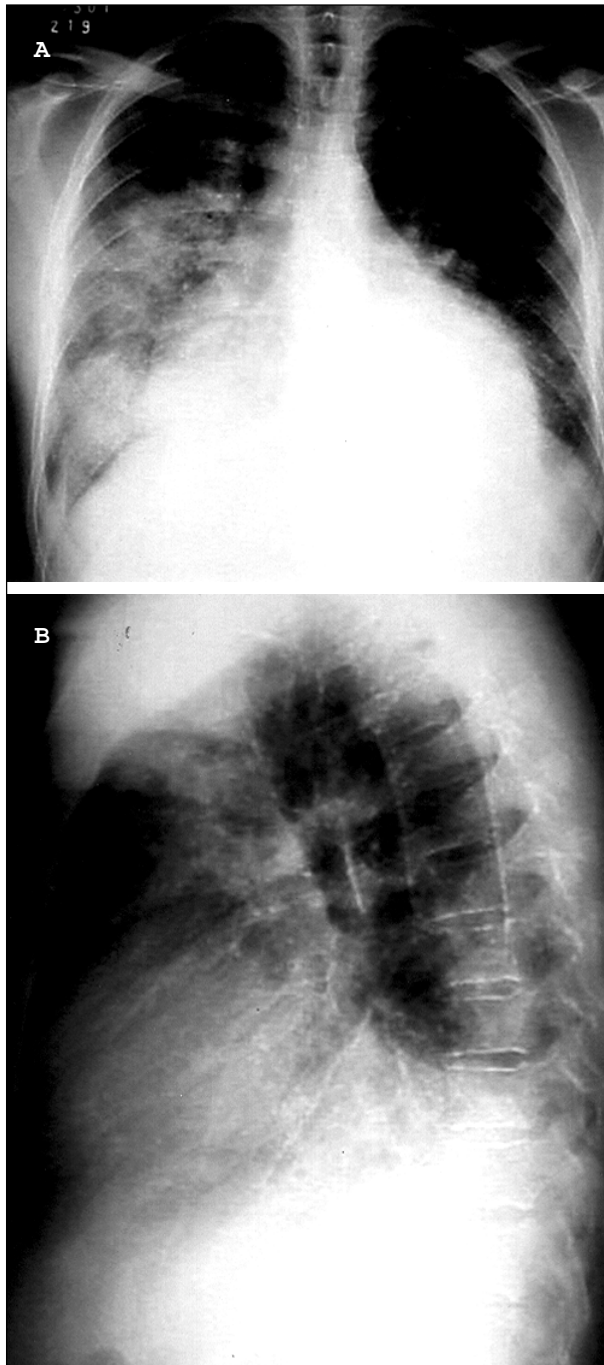


Fig. 3 – 3a, 3b) Active endocarditis in native aortic valve. Aortic insufficiency.

sophageal echocardiography, which have been used in our unit since 1991, were definitive for making surgical decisions. Transesophageal echocardiography has been used during surgery to search for residual fistulas while the extracorporeal circulation cannula is still installed in the patient.

The causal agent is identified through blood cultures. A positive blood culture is important for the diagnosis and management of the case, directly influencing the morbidity and mortality of these patients. In patients who had not previously taken antibiotics, positivity of the blood cultures should be expected in more than 95%. However, the

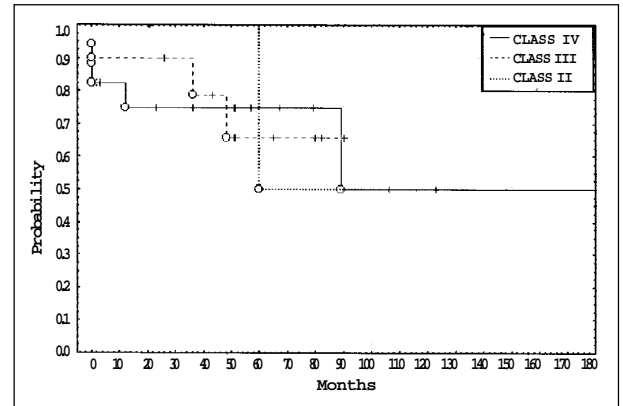


Fig. 4 – Patients' survival according to the Kaplan-Meier curve. Of the 26 patients under regular clinical follow-up, 5 died 12, 36, 48, 60, and 89 months after surgery.

indiscriminate use of antibiotics in the initial phase of symptoms is the major cause of lack of growth of microorganisms in culture in approximately 35% of the patients¹⁹. This is a common practice, and, in addition, several laboratories experience technical difficulties with cultures in an anaerobic medium. These facts may have accounted for the low rate of positivity in the cultures (32.3%) in our case series. The list of microorganisms causing infective endocarditis has increased due to the great number of uncommon pathogens that continue to be identified. Gram-positive microorganisms, particularly *Streptococcus* and *Staphylococcus*, still predominate. In patients using intravenous drugs and in immunocompromised patients, gram-negative and fungal infections have been reported. *Streptococcus viridans* accounts for 30 to 65% of the cases of endocarditis in native valves. Enterococci are responsible for 10 to 20% of the cases of infective endocarditis and may infect normal valvular tissue. *Staphylococcus aureus*, a common cause of infective endocarditis, is a highly virulent microorganism that usually has severe consequences for the patient. When present in the left cardiac chambers, *Staphylococcus aureus* is associated with a mortality of 35 to 40%, probably due to its ability to destroy normal and abnormal valvular tissue²⁰⁻²², causing frequent embolisms and metastatic infection. *Staphylococcus aureus* was identified in only 3 patients (32.3% of the positive cultures), 2 of whom died at the hospital, and, in the third patient, *Staphylococcus aureus* was the initial cause of infective endocarditis and 3 interventions were required because of the recurrence of the disease. In developed countries, epidemiological studies suggest that pros-

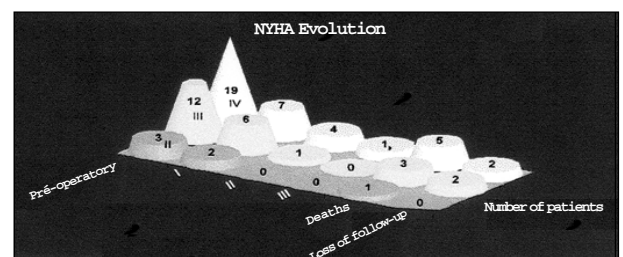


Fig. 5 – Evolution of pre- and postoperative functional classes.

thetic valve endocarditis (PVE) represents 10 to 30% of the cases of infective endocarditis²³. The major risk of developing infective endocarditis occurs in the first 6 months after surgery, mainly within the 5 and 6 initial weeks; the risk then declines, although some persists^{13,23}. Patients with previous endocarditis in the native valves, especially when operated upon in the active phase of the disease, are more prone to develop PVE^{13,24,25}. Prosthetic valve endocarditis occurs more often in the aortic position, and no statistical difference exists whether it is biological or mechanical. When the infected prosthesis is of the mechanical type, perivalvular destruction and presence of fistulas and abscesses are the most frequent findings, because no leaflet of organic material exists to be destroyed by the microorganisms. However, if the infection is early, the prosthesis may still be sterilized with early antibiotic therapy, which will avoid the need for a new surgery in the acute phase. Eight (23.5%) patients who underwent surgery here developed endocarditis in an implanted prosthesis; 7 (87.5%), like the report in the literature, were prostheses in the aortic position. One of the 4 in-hospital deaths occurred in this group with a biological aortic prosthesis, with extensive perivalvular necrosis and clinical findings of sepsis. General consensus exists about the unsatisfactory long-term results in PVE, despite adequate surgical techniques and good clinical management. Lytle et al²⁶ reported the recurrence of infection in 25% of their patients in a 5-year follow-up. In that study, 7 patients discharged from hospital after intervention for PVE were followed up. Two (28%) patients required new surgical interventions as follows: the first patient, after the second and third years, died from the recurrence of infection in the following year; the second patient, after the first and fifth years, had a small periaortic fistula without clinical repercussions and free of infection, and 9 years have already passed since the last surgical intervention. The microorganisms most frequently found in PVE are of the nosocomial and even community types. In the first 60 days after surgery, *Staphylococcus epidermidis*, *Staphylococcus aureus*, the gram-negative bacilli, diphtheroids, and fungi are the most common causes of PVE²⁶.

The indications for the surgical treatment of infective endocarditis reported in the literature^{27,28} are similar to those in our series and may be grouped as follows: severe and progressive heart failure refractory to clinical treatment; infection that could not be controlled with antimicrobial treatment; uncontrolled infection in a cardiac prosthesis, and systemic arterial embolisms. In regard to functional class, as reported by other authors²⁹⁻³¹, most patients were in NYHA functional classes III and IV. Of the indications for surgical treatment, heart failure and infection not controlled with adequate antibiotics are the most common^{30,31}. In our case series, those were responsible for approximately 91% of the surgical indications. Patients with mechanical prostheses under continuous use of coumarin anticoagulants (4) had their medication replaced by intravenous heparin, infusion of fresh plasma, and interruption of the infusion of heparin 4 hours prior to the surgical procedure.

The most common surgical procedure was valvular replacement with a biological or metallic prosthesis and homograft. Valvuloplasty was also possible with reconstruction techniques in select cases⁸⁻¹⁰.

The presence of total atrioventricular block in the clinical presentation of infective endocarditis and the need to implant a definitive pacemaker showed the severity and the extension of paravalvular tissue necrosis. The choice of endomyocardial electrodes will depend on the phase and the clinical situation in which these devices are implanted. Of the 3 patients receiving definitive pacemakers, the epicardial electrode was chosen for 2 patients, because definitive implantation was indicated early.

Perivalvular involvement with the formation of abscesses and fistulas represents a risk factor for recurrence of the disease³². Despite the extensive débridement and closure of the cavities and fistulas by using autologous or bovine pericardium, 5 patients required more than 1 surgical intervention due to a relapse of the endocarditis or its sequelae. Danchin et al³³ and Renzulli et al³⁴ did not find differences between the patients with and without perivalvular involvement, and, in a 10-year follow-up, reported a 58% rate of no relapse.

The in-hospital mortality of 11.7% (4 patients) here reported resulted from the delay in indicating surgery and consequent severe myocardial failure, to the present sepsis, and to the anatomic propagation with formation of intracavitary abscesses. Although 3 of the patients were young, which would be a factor favorable to survival, because they only experienced intervention in the final phase of the disease, they did not survive. A preoccupying fact in this and other surgical heart pathologies is the critical state at which surgery is considered for many of these patients. In this situation, integrity of the central nervous system was the major feature to be considered. If the central nervous system is considered suitable, with no irreversible injury, surgery is usually the option. However, 1 patient in our series was in a critical clinical situation and died in the operating room, although her neurologic condition was suitable when surgery was indicated. All 5 (14.7%) deaths after hospital discharge were the consequence of heart failure, except for 1 patient operated upon in class II, who died due to hemorrhagic stroke while using coumarin anticoagulants. This confirms the fact that even with the infection under control, ventricular dysfunction is a preponderant factor in the postoperative evolution of these patients. For us, the difficulty in the clinical follow-up of patients, who usually come from regions far from specialized centers, in addition to the inaccuracy in controlling the coumarin anticoagulants, is a reality that should be emphasized.

The current conception is that the surgical treatment of infective endocarditis should be instituted as soon as heart failure is identified. The major predictor of survival has been the presence of preoperative ventricular dysfunction. Surgery is usually necessary in the presence of PVE, because the extravalvular extension of the disease with abscesses and fistulas is common. In addition, the limitation

of the antibiotics in acting in the presence of an infected foreign body is well known.

Recent advances in the diagnosis of infective endocarditis, mainly transesophageal echocardiography, new antibiotic regimens, and adequate surgical techniques have provided early therapy and consequent improvement in the results. However, morbidity and mortality of infective endocarditis caused by microorganisms like *Staphylococcus aureus* and PVE still remain high in these patients. This study carried out in a regional cardiology center in the Brazilian state of Rio Grande do Sul shows that, in addition to those principles already internationally diffused, the early

diagnosis of infective endocarditis should be emphasized for the obtainment of greater positivity in blood cultures, that clinical and surgical treatment should be instituted as soon as possible and not when cardiogenic shock and sepsis had already occurred. On the other hand, new prospective research is required to answer several pending questions, ie, how to improve the management of complications and the indications of therapies in infective endocarditis.

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