The Surgical Approach to Infective Endocarditis: 10 Year Experience

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Key words: endocarditis, valve, surgery, repair, replacement

Abstract

Background: About 40% of patients with infective endocarditis will require surgical treatment. The guidelines for such treatment were formulated by the American College of Cardiology and American Heart Association in 1998.

Objectives: To examine our experience with surgical treatment of infective endocarditis in light of these guidelines.

Methods: Surgery was performed in 59 patients with infective endocarditis between 1990 and 1999. The patients' mean age was 48 years (range 13–80). The indications for surgery were hemodynamic instability, uncontrolled infection, and peripheral embolic events. The surgical treatment was based on elimination of infection foci and correction of the hemodynamic derangement. These objectives were met with valve replacement in the majority of patients. Whenever conservative surgery was possible, resection of vegetation and subsequent valve repair were performed and the native valve was preserved.

Results: Six patients (10%) died perioperatively from overwhelming sepsis (n = 3), low cardiac output (n = 2) and multiorgan failure (n = 1). The mean hospital stay was 15.6 days. Of 59 patients, 47 (80%) underwent valve replacement and in 11 (19%) the surgical treatment was based on valve repair. After 1 year of follow-up there was no re-infection.

Conclusion: The new guidelines for surgical treatment of infective endocarditis allow better selection of patients and timing of surgery for this aggressive disease, which consequently decreases the mortality rate. Valve repair is feasible and is preferred whenever possible. According to the new guidelines, patients with neurologic deficit in our series would not have been operated upon, potentially decreasing the operative mortality to 7%.

IMAJ 2003;5:641–645

Infective endocarditis still remains a challenge to cardiac surgeons. Prior to the antibiotic era, infected endocarditis was uniformly a fatal disease. Antimicrobial therapy as an integral component of treatment and adjunctive surgery in indicated cases resulted in a significant increase in survival rates [1]. Despite advancements in medical therapy, surgical techniques and intensive care of infective endocarditis, the morbidity and mortality rates are still considerable. The complexity of the clinical presentation along with the existence of concomitant conditions has raised many controversies concerning the type and timing of surgery in the management of patients with endocarditis.

Survival rates for surgery in infective endocarditis were higher when the operation was done earlier [2], the infected valve was repaired [3], special considerations were taken in patients with neurologic deficits [4], and in case of implantation of homografts [5,6]. Accordingly, a wide range of survival rates has been reported. Results of these studies have dictated the indications and guidelines for surgical treatment of patients with infective endocarditis.

The first stage in the infection of a valve is the formation of vegetations. When medical management has failed or is likely to fail, surgery is indicated. The infective process can occur on both a native and an already-replaced valve. The pathophysiologic mechanism in prosthetic valve endocarditis differs from that of native valve endocarditis. While the mortality in native valve endocarditis is between 7 and 10% [7], the overall mortality for non-surgically and surgically treated patients with prosthetic valve endocarditis was 65% and 45%, respectively [8]. Prosthetic valve infection may occur early (i.e., within 2 months of valve replacement) or late. High mortality rates have been reported in the early prosthetic valve endocarditis [9].

During the last decade, many studies focused on the indication for surgical intervention in infective endocarditis. The American College of Cardiology and the American Heart Association task force on practical guidelines for management of patients with valvular heart disease [10] published the updated guidelines for managing patients with infective endocarditis. In view of these recommendations, we present an analysis of our surgical experience with infective endocarditis patients.

Patients and Methods

The patient population was determined by a retrospective computerized review of patients who underwent cardiac surgical procedures as a treatment for infective endocarditis at the Hadassah University Hospital. Between January 1990 and December 1999, 59 patients underwent surgery for infective endocarditis. A total number of 844 patients underwent valve surgery for indications other than infective endocarditis during that period. All patients were reviewed at a peer review conference before being accepted for surgery.

All patients were treated by intravenous antibiotics during the perioperative period. Current practice includes a broad-spectrum combination of two antibiotics once the suspicion of infective endocarditis arises. Blood cultures then direct the specific antibiotic against the grown organism. In rare cases, when there is a clue of other infections like fungal and Q fever, medical treatment is broadened to include the specific pathogen.

The diagnosis of infective endocarditis was based on positive blood cultures for the same organism and a vegetation in a echocardiogram in a patient with a compatible clinical syndrome

that consisted of fever, new cardiac murmurs, peripheral embolic findings like petechiae, Osler nodes, Janeway lesions, Roth's spots, and histopathologic evidence of infective endocarditis in the surgical specimen. Infective endocarditis that was diagnosed within 60 days of operation was defined as early postoperative endocarditis, and those that occurred after 60 days were classified as late endocarditis.

The indications for surgery in native valve infective endocarditis were categorized into three groups according to the clinical consequences of infective endocarditis: a) hemodynamic instability and deterioration, b) overwhelmed infection or sepsis, and c) embolic events. However, in prosthetic valve endocarditis, hemodynamic and embolic sequelae of the endocarditis constituted the indication for surgical intervention.

Hospital records were reviewed retrospectively for patients' demographic characteristics, preoperative status and co-morbidities, intraoperative variables, and postoperative course. Surgery was considered urgent if the patient was treated with intravenous antibiotics until completion of assessment or refinement of antibacterial treatment. Emergent operation was defined as the condition that prompted immediate operation within 24 hours from diagnosis in order to minimize life risk or other major related complications in critically ill patients.

All patients were operated on using a standard cardiopulmonary bypass technique with mild to moderate hypothermia (32–28°C). Myocardial protection was achieved with antegrade and retrograde warm or cold blood cardioplegia. The mode of cardiopulmonary bypass and myocardial protection was the same during the study period. The surgical protocol for treatment was based on elimination of infection foci and correcting the hemodynamic derangement. For this purpose valve replacement was the most common surgical procedure in the majority of patients. Whenever these objectives were attained by conservative surgery, the vegetation was resected with subsequent valve repair when needed and the native valve was preserved. Whenever valve replacement was needed the decision regarding the type of the valve (mechanical/biological) was based on indications such as patient's age and compliance with anticoagulation administration and monitoring, and presence of contraindications to anticoagulation therapy. Age more than 65 years, low compliance and presence of a contraindication to anticoagulation favored replacement of the valve with a bioprosthetic valve. Homograft was implanted for the same indications but in a much younger age group and whenever a suitable size was available.

Results

Fifty-nine patients enrolled in the study during the follow-up period. Patients' mean age was 48.2 ± 15.6 years, ranging from 13 to 80 years. Male to female ratio was 34:25. The mean time from the diagnosis until surgery was 7 ± 4 days (median 6 days). The follow-up criteria for timing of surgery (from the time of diagnosis until the operation) were: clinical condition of the patient including severity of heart failure, septic status of the patient, and echocardiographic findings – mainly the changing size of the vegetations.

Table 1 demonstrates the patients' clinical findings. The most common clinical finding was preoperative signs and symptoms of heart failure. Before surgery, five patients had septic symptoms and two patients had to be mechanically ventilated due to respiratory failure. Embolic events were noted in nine patients, in three of whom the neurologic system was involved.

Table 1. Preoperative clinical findings

Heart failure	25 (42%)
Sepsis	5 (8%)
Respiratory failure	2 (3%)
Embolic events	9 (15%)

Table 2. Blood cultures

Pathogen	Native	Prosthetic	Number
Staphylococci	13	6	19 (49%)
Streptococci	12	1	13 (33%)
Enterobacter spp.	2	0	2 (5%)
Pseudomonas aeruginosa	1	0	1 (2.5%)
Haemophilus influenzae	1	0	1 (2.5%)
Acinetobacter	1	0	1 (2.5%)
Coxiella burnetii	1	0	1 (2.5%)
Candida	1	0	1 (2.5%)
Total no. of isolates	32	7	39

Echocardiographic assessment of patients played an important role in the diagnosis and decision-making for type and timing of surgery. Echocardiographic findings were acute valve incompetence, evidence of vegetation and abscess, and paravalvular leak. The discovery of vegetation was the most commonly reported. All patients underwent at least one preoperative echocardiographic evaluation. Trans-thoracic echocardiography was undertaken in 37 and trans-esophageal echocardiography in 38 of 59 patients. Positive findings for infective endocarditis were reported in 27 of 37 TTE tests (73%) and in 33 of 39 TEE tests (84%). TTE was the sole echocardiographic modality to diagnose infective endocarditis in eight patients.

The infective process involved the native valve in 43 patients (73%) and prosthetic valves in 12 patients (20%) (6 aortic, 5 mitral, and 1 aortic + mitral). However, in four patients (7%), vegetations of structures other than the valves were noted. The infective process involved the aortic valve in 20 patients, mitral valve in 15, tricuspid valve in 1, and more than a single valve in 21 patients. Prosthetic valve endocarditis involved the aortic valve in 4 patients, the mitral valve in 3, and more than one valve in 5 patients.

Of 59 patients, 39 had positive blood cultures (66%); 8 patients (13%) had culture-negative infective endocarditis. The serologic examinations in culture-negative patients were negative except for one patient with positive anticardiolipin antibodies. Data on blood culture were missing for 12 patients (20%) referred from other institutions. Table 2 summarizes the blood culture results. As shown, gram-positive cocci were the most common pathogens.

TTE = trans-thoracic echocardiography
TEE = trans-esophageal echocardiography

Indications for surgery in native valve infective endocarditis were as follows: 23 of 43 patients (53%) underwent surgery because of an uncontrolled infective process. The reason for surgery was hemodynamic instability in 12 patients (28%) and embolic events in 8 patients (19%). Regarding the indications for surgery in prosthetic valve infective endocarditis, of 12 patients with prosthetic infective endocarditis 5 were operated on because of hemodynamic changes, and 7 patients for infective involvement of extra-valvular structures.

The surgical procedure in 55 of the 59 patients (93%) included valve replacement or repair. In four patients (7%) the surgery was related to a cardiac structure other than a valve. Replacement of the aortic valve was performed in 18 patients (30%). Mitral valve replacement as a single procedure was done in 11 patients (19%). Fourteen patients underwent a combined replacement of aortic and mitral valves (24%). In 12 patients (20%), surgical treatment of infective endocarditis was performed by repair of the infected valve (11 mitral valves and 1 tricuspid valve).

Overall, 47 patients underwent valve replacement. Of 63 prosthetic valves implanted, 58 (92%) were mechanical valves and 5 were biological: 3 homografts and 2 xenografts. In all patients with a prosthetic valve endocarditis, the replaced valve was mechanical except for one who received a bioprosthetic valve in the aortic position. The mean age of patients with biological valve replacement (including homograft) was 60 $\pm$ 20 years ($P = 0.2$).

Cultures of surgical specimen grew gram-positive cocci, i.e., staphylococci and streptococci in 32 cases [Table 2]. Histopathologic evidence of infective endocarditis from excised tissue during surgery was found in 28 patients (47%).

Six patients (10%) died in hospital: three from sepsis, two from low cardiac output, and one from multiorgan failure. Three of 43 patients with native endocarditis and 3 of 12 patients with prosthetic endocarditis died. The postoperative complications are summarized in Table 3.

The mean hospital stay for patients who underwent surgery for infective endocarditis was 15.6 $\pm$ 11.5 days (range 6–42 days). All patients were treated with intravenous antibiotics for a mean period of 31 days. A long-term follow-up of patients revealed an actuarial survival of 90% at 6 months, 87% at 1 year, 74% at 5 years, and 64% at 7 years [Figure 1].

Table 3. Postoperative complications

Low output syndrome	6
Supraventricular arrhythmia	6
Sepsis	4
Bleeding	4
Conduction abnormality	4
Renal failure	3
Ventricular arrhythmia	3
Prosthetic valve dysfunction	1
Adult respiratory distress syndrome	1
Hepatic failure	1

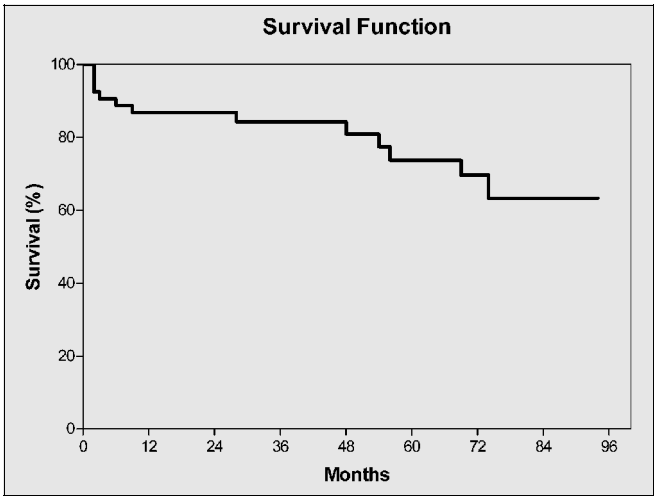

Figure 1. Kaplan-Meier analysis of patient's survival following surgery for infective endocarditis.

Discussion

Surgical treatment of patients with infective endocarditis is a necessary adjunct to medical therapy. Despite advancements in antibiotics, critical care, and surgical techniques, infective endocarditis is still considered a life-threatening disease with non-negligible mortality and morbidity rates.

Dramatic changes in the treatment of infective endocarditis have evolved over the last 50 years. Elimination of infected tissue and restoration of normal hemodynamics is the mainstay of surgical treatment [11,12]. Although this was considered the most safe and certain treatment policy, several researchers have introduced more diverse surgical methods for treatment of infective endocarditis, such as valve repair [3] and the use of homografts [5,6], with comparable long-term results and additional benefits.

Endocarditis is a complex condition with a wide range of clinical presentations. Often, systemic effects of sepsis, which are present, superimposed on an already compromised hemodynamic status caused by a variable degree of valvular incompetence, complicate decisions regarding the type and timing of surgery. Medical therapy alone is reserved for patients showing infection without evidence of significant valvular compromise. However, surgery is an indispensable part of treatment in conditions where uncontrollable infection is present with normal hemodynamics such as annular or myocardial abscesses [13–15]. The complexity of clinical features and concomitant conditions such as neurologic deficits in infective endocarditis are important factors determining the course and prognosis of the disease. Most surgical teams have attributed their success to strict criteria when selecting patients in the context of the above factors. Currently, improvements in treatment have focused on the timing of surgical intervention and the duration and efficacy of antimicrobial therapy [16,17].

The results of this study represent our experience in determining indications for surgical treatment with regard to three essential factors: timing of surgery, type of surgery, and concomitant neurologic deficits. In the present study, hospital mortality averaged 10%, a result that compares favorably with the experience of other investigators [18–20]. We determined the indications for the surgery as follows: a) infective/septic, b) hemodynamic

instability, and c) embolic. Three of the patients had neurologic complications prior to surgery. The presence of a neurologic deficit put these patients at higher risk for surgical treatment. Whether these complications preclude surgical treatment is an important question that needs to be addressed. The rationale for this hypothesis is the fact that anticoagulation therapy, hypotension, and edema associated with cardiopulmonary bypass may exacerbate neurologic injury.

When valve replacement was performed 5 days after acute nonhemorrhagic cardiogenic embolism, Maruyami and associates [21] noted severe neurologic deterioration in 4 of 14 patients (29%). They suggested that infective endocarditis, a large cerebral infarct, and a short interval between cerebral injury and cardiac operation predispose patients to hemorrhagic transformation and worse neurologic injury. Similarly, Matsushita and co-workers [22] reported that cardiac surgery for endocarditis performed within 5 days of a cerebral embolic event was frequently associated with neurologic deterioration. They concluded that an interval of at least 11 days between the cerebrovascular accident and valve replacement is advisable. They also recommended that this interval be extended to 4 weeks for embolic cerebrovascular accident with hemorrhage. In a series of patients suffering primarily from active endocarditis, Zisbrod and colleagues [23] performed valve replacement in 12 patients at an average of 12.7 days after the embolic cerebrovascular event. One patient died, and there were no new strokes.

According to the new guidelines of the American College of Cardiology and American Heart Association [10], the presence of neurologic deficits precludes surgery for infective endocarditis. In our study, three patients showed neurologic impairment before the surgery. Two of them died after the surgery. The mortality rate would have declined from 10% to 7% if these two patients had been excluded from the operation group, as suggested by the American College of Cardiology and American Heart Association guidelines.

In 12 patients (20%) a valve-repairing procedure was performed. The decision to perform valve repair instead of replacement was made in two separate instances: when the pathologic process of the valve was such that the function of the valve could be preserved with minimal manipulations and infection foci eliminated at the same time; the second when patients had absolute limitations or contraindications for anticoagulation therapy.

The mitral valve was the most commonly repaired valve followed by the tricuspid (n=11 and 1, respectively). The valve-repairing procedures included resection of the vegetations and restoring valve competence with implantation of a ring in most of the cases. All patients had good hemodynamics and favorable immediate results. No mortality was recorded in this group of patients and no recurrence of infection was observed. The short follow-up of these patients revealed no recurrence of infection. Echocardiographic follow-up for an average period of 1 month revealed favorable valve function.

The findings of our study demonstrate that valve repair results in excellent hospital survival, durability, and resistance to re-infection in patients with infective endocarditis. These results should put to rest the concern that mitral valve repair techniques are associated with high re-infection rates and poor durability [24,25]. The likely explanations for this excellent outcome are the avoidance of prosthetic material in the infected field and the preservation of left ventricular function associated with repairing mitral valves.

In conclusion, surgery remains the mainstay of treatment for infected endocarditis. Survival rates in patients treated surgically for infected endocarditis have risen in the past decade. Choosing the appropriate time and procedure might be the critical factor determining success in managing infected endocarditis. Repair of the infected valve may be a preferred procedure in selected patients with good results. In the new millennium, management of these patients is best when recommended guidelines are followed.

References

1. Verheul HA, van den Brink RB, van Vreeland T, Moulijn AC, Duren DR, Dunning AJ. Management of active infective endocarditis and outcome in a 25 year period. *Am J Cardiol* 1993;72:682–7.
2. Pelletier LC, Baillot R, Auger P, Dyrda I. Early valve replacement in active infective endocarditis. *Can J Surg* 1984;27:383–6.
3. Muehrcke DD, Cosgrove DM, Lytle BW, et al. Is there an advantage to repairing infected mitral valves? *Ann Thorac Surg* 1997;63:1718–24.
4. Gillinov AM, Shah RV, Curtis WE, et al. Valve replacement in patients with endocarditis and acute neurologic deficit. *Ann Thorac Surg* 1996;61:1125–9.
5. McGiffin DC, Galbraith AJ, McLachlan GJ, et al. Aortic valve infection. Risk factor for death and recurrent endocarditis after aortic valve replacement. *J Thorac Cardiovasc Surg* 1992;104:511–20.
6. Dossche KM, de la Riviere BA, Morshuis W, Schepens M, Ernst J. Aortic root replacement with human tissue valves in aortic valve endocarditis. *Eur J Cardiothorac Surg* 1997;12:47–55.
7. Miller DC. Determinants of outcome in surgically treated patients with native valve endocarditis. *J Cardiac Surg* 1989 4:331–9.
8. Kuyvenhoven JP, vanRijk-Zwikker GL, Hermans J. Prosthetic valve endocarditis: analysis of risk factors for mortality. *Eur J Cardiothorac Surg* 1994;8:420–4.
9. Petheram IS, Boyce JMH. Prosthetic valve endocarditis: a review of 24 cases. *Thorax* 1977;32:478–85.
10. Bonow RO, Carabello B, de Leon AC Jr, et al. ACC/AHA guidelines for the management of patients with valvular heart disease: executive summary. *Circulation* 1998;98:1949–84.
11. Haydock D, Barratt-Boyes B, Macedo T, Kirklin JW, Blackstone E. Aortic valve replacement for active infectious endocarditis in 108 patients. A comparison of freehand allograft valves with mechanical prosthesis and bioprostheses. *J Thorac Cardiovasc Surg* 1992;103:130–40.
12. Dreyfus G, Serraf A, Jebara VA, et al. Valve repair in acute endocarditis. *Ann Thorac Surg* 1990;49:706–11.
13. Aranki SF, Santini F, Adams DH, et al. Aortic endocarditis: determinants of early survival and late morbidity. *Circulation* 1994;90(Suppl 2):175–82.
14. Middlemost S, Wisenbaugh T, Meyerowitz C, et al. A case for early surgery in native left-sided endocarditis complicated by heart failure: results in 203 patients. *J Am Coll Cardiol* 1991;18:663–7.
15. Douglas JL, Dismukes WE. Surgical therapy of infective endocarditis on natural valves. In: Kaye D, ed. Infective Endocarditis. 2nd edn. New York: Raven, 1992:397–411.
16. Lantham RH. Medical therapy versus early surgical intervention in patients with endocarditis and vegetations seen on echocardiography. *South Med J* 1991;84:1347–51.
17. Bladassarre JS, Kaye D. Principles and overview of antibiotic therapy. In: Kaye D, ed. Infective Endocarditis. 2nd edn. New York: Raven, 1992:169–90.

18. Pompilio G, Brockmann C, Bruneau M, et al. Long-term survival after aortic valve replacement for native active infective endocarditis. *Cardiovasc Surg* 1998;6:126–32.
19. Bauerschmitt R, Jakob HG, Vahl CF, Lange R, Hagl S. Operation for infective endocarditis. *Ann Thorac Surg* 1998;65:359–64.
20. Sweeney MS, Reul GJ Jr, Cooley DA, et al. Comparison of bioprosthetic and mechanical valve replacement for active endocarditis. *J Thorac Cardiovasc Surg* 1985;90:676–80.
21. Maruyama M, Kuriyama Y, Sawada T, Yamaguchi T, Fujita T, Omae T. Brain damage after open heart surgery in patients with acute cardioembolic stroke. *Stroke* 1989;20:1305–10.
22. Matsushita K, Kuriyama Y, Sawada T, et al. Hemorrhagic and ischemic cerebrovascular complications of active infective endocarditis of native valve. *Eur Neurol* 1993;33:267–74.
23. Zisbrod Z, Rose DM, Jacobowitz IJ, Kramer M, Acinapura AJ, Cunningham JN. Results of open heart surgery in patients with recent cardiogenic embolic stroke and central nervous system dysfunction. *Circulation* 1987;76(Suppl 5):109–12.
24. Becker RM, Frishman W, Frater RWN. Surgery for mitral valve endocarditis. *Chest* 1979;75:314–19.
25. Hendren WG, Morris AS, Rosenkranz ER, et al. Mitral valve repair for bacterial endocarditis. *J Thorac Cardiovasc Surg* 1992;103:124–9.

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