# Early clinical course and long-term outcome of patients with infective endocarditis complicated by perivalvular abscess

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## Abstract

**Background:** Perivalvular abscess is an ominous development in patients with infective endocarditis. There is little information concerning the long-term outcome of these patients.

**Methods:** Patients admitted to a tertiary care centre in Ottawa between November 1987 and December 1995 because of infective endocarditis complicated by perivalvular abscess were identified by chart audit and by review of the transesophageal echocardiography database. The patients were followed for at least 4 years to determine cardiac complications, late cardiac surgery, long-term outcome and functional status.

**Results:** Forty-three consecutive patients with infective endocarditis and perivalvular abscess (32 men and 11 women; mean age 56 [standard deviation 16] years) were identified; 17 had native valve endocarditis and 26 had prosthetic valve endocarditis. Of the 43 patients, 31 had cardiac surgery during the hospital stay; 6 died in hospital, and 10 died during follow-up. Twelve patients received medical treatment alone; none died in hospital, and 8 died during follow-up. The medically treated patients had less severe heart failure than the surgically treated patients ($p = 0.12$), but the 2 groups were similar in age and infective organisms. After a mean of 4.5 years of follow-up, the cumulative death rate was 57%; survival was similar among the medically and surgically treated patients. The survivors were younger than the nonsurvivors ($p = 0.04$). Complications of perivalvular abscess, including pseudoaneurysms and fistulae, were common, occurring in all medically treated patients and in 10 of the 24 surgically treated patients who had follow-up transesophageal echocardiography.

**Interpretation:** Patients with infective endocarditis and perivalvular abscess had a high rate of death after hospital discharge and a high incidence of complications of perivalvular abscess, despite early surgical intervention in most patients. Lower age was the only predictor of long-term survival.

Despite advances in medical and surgical treatment, endocarditis remains a life-threatening disease, with high rates of in-hospital death and illness,[1,2] particularly among patients in whom perivalvular abscesses develop.[3–5] Early surgical intervention has been advocated to improve the outcome of these patients,[5–9] and the need for early surgery appears more compelling in patients with prosthetic valve endocarditis complicated by perivalvular abscess.[5,10–14] However, the optimal management of perivalvular abscess is unclear, since it is often diagnosed at surgery or autopsy and its presence is associated with other serious sequelae of endocarditis, such as valvular destruction and heart failure, which are indications for surgery independent of the presence or absence of perivalvular abscess.[5–9] Surgery in patients with active infection and perivalvular abscess carries a high risk of death and is associated with a significant risk of recurrent infection and periprosthetic leak.[11,13,15–17] The long-term outcome of these patients has not been well defined.[3–5] Cases of successful medical treatment of perivalvular abscess have been reported,[18–21] but there have been no series of consecutive patients and no comparison with surgically treated patients.

The purposes of this study were to describe the clinical features of patients with endocarditis and perivalvular abscess, to evaluate the evolutional changes of perivalvu-

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*This article has been peer reviewed.*

*CMAJ* 2002;167(1):19-24

ß See related article page 38

lar abscess on transesophageal echocardiography (TEE) and to assess the long-term outcome, including death, need for repeat surgery and complications of perivalvular abscess.

## Methods

At the University of Ottawa Heart Institute TEE has been an integral part of the investigation of endocarditis since November 1987. The clinical presentations and TEE findings of patients are recorded prospectively in a registry. I reviewed the registry to identify all patients with infective endocarditis and perivalvular abscess admitted to the institute between November 1987 and December 1995. I chose this study period to allow for at least 4 years of follow-up. The hospital records of these patients were examined to collect data on complications, whether cardiac surgery was performed and the type of surgery, reason for surgery, reason for not proceeding with surgery and whether the patient died. Follow-up of the survivors was performed by telephone interviews with the patients, their families or their primary physicians to determine their current functional state and, if they had died since discharge, the cause of death. To ensure that all patients with both endocarditis and perivalvular abscess were included, I performed an audit of all hospital admissions between November 1987 and December 1995 to identify patient records containing International Classification of Diseases (9th revision, clinical modification)[22] codes 421.0 to 421.9, 424.9 and 429.8. The study protocol was reviewed and approved by the Ottawa Civic Hospital Research Ethics Committee.

The criteria for the diagnosis of infective endocarditis were similar but not identical to the Duke criteria.[23] The condition was diagnosed when at least 2 of the following 3 criteria were present: echocardiographic evidence of vegetation or abscess; growth of the same organism on 2 or more blood cultures; and clinical findings such as fever, microvascular phenomena, and a new or changed heart murmur. The echocardiographic diagnosis of a vegetation was made if an abnormal echogenic mass (sessile or pedunculated) attaching to a leaflet or valve annulus was seen throughout the cardiac cycle.[3,24] Perivalvular abscess, diagnosed by means of TEE in all patients, was defined as a localized abnormal echolucent area within the perivalvular tissue without communication with the circulation, and a pseudoaneurysm was defined as an abnormal localized echo-free protrusion that communicated with a surrounding cardiac chamber.[3,21,24]

Echocardiography was performed using commercially available systems (Hewlett Packard 1000, 1500, 2000, 2500 and 5500 systems, Andover, Mass.) equipped with a 5-MHz TEE transducer. The TEE transducers used in this study included monoplane, biplane and multiplane probes. The details of the procedure have been previously described.[25] There were no procedural complications.

In the analysis, variables are expressed as percentages or means and standard deviations (SDs). The surgically treated and medically treated groups were compared using Student's *t*-test (2-tailed) for continuous variables and contingency tables with Fisher's exact test for discrete variables. A $p$ value of less than 0.05 was taken to signify statistical significance. Kaplan–Meier survival curves were plotted, and for this analysis heart transplantation was considered to be an event.

## Results

During the study period 43 patients (32 men and 11 women; mean age 56 [SD 16] years) were identified as having endocarditis complicated by perivalvular abscess. Of the 43, 17 had native valve endocarditis and 26 had prosthetic valve endocarditis. Severe valvular or perivalvular regurgitation was present on admission in 23 patients, and advanced heart failure was common, with 10 patients in New York Heart Association (NYHA)[26] functional class IV, 14 patients in class III and 19 patients in class II. *Staphylococcus aureus* and viridans streptococci were the common infecting organisms, accounting for 23 (53%) of the 43 cases. All but one patient were identified from the TEE registry. The additional case, revealed through the chart audit, was that of a 76-year-old man in whom fever developed while he was awaiting aortic valve replacement for symptomatic aortic stenosis; he did not undergo TEE. The periaortic abscess was not suspected clinically but was diagnosed at surgery.

Of the 43 patients, 31 underwent cardiac surgery during the same hospital stay; at the time of surgery, 9 were in NYHA class IV heart failure, 11 were in class III, and 11 were in class II. The perivalvular complications identified by TEE were confirmed at surgery in all cases. The 12 remaining patients were treated with medical therapy alone (Table 1). Two patients who had previously had valve replacement refused surgery. Three patients were not considered for surgery because of medical illnesses (renal failure while receiving dialysis, metastatic colon cancer and Behçet's disease [a form of diffuse vasculitis]). The 7 remaining patients, all of whom had previously had valve replacement, were not offered surgery because they were considered to be at prohibitively high surgical risk as a result of the extensive destructive infective process.

The characteristics of the patients who had surgical intervention and those who received medical treatment alone are shown in Table 2. The medically treated patients tended to be older than the surgically treated patients (mean age 62 [SD 15] years v. 54 [SD 16] years) ($p = 0.12$) and had less severe heart failure (fewer patients were in NYHA class III or IV) ($p = 0.12$). Nine of the 10 patients with NYHA class IV heart failure had surgery during the same hospital stay, versus 11 of the 19 patients in NYHA class II ($p = 0.18$). Six patients, all in the surgical intervention group, died in hospital.

### *Long-term outcome*

Only 1 patient (in the surgical intervention group) was lost to follow-up, because he had moved out of the country. Of the 42 patients with complete follow-up data, 24 (57%) died; 8 had been treated medically and 16 surgically (Table 3). Repeat cardiac surgery or late surgery after hospital discharge was performed in 5 survivors and 6 nonsurvivors. Other than age (mean 50 [SD 17] years for the survivors v. 60 [SD 14] years for the nonsurvivors; $p = 0.04$), the clinical profile was similar between the 2 groups. Of the 18 long-term survivors, 13 (72%) were free of cardiac symptoms.

The mean length of follow-up for the 36 patients who were discharged was 4.5 years (range 2 months to 10.5 years). The cumulative survival curves for the surgically and medically treated patients are shown in Fig. 1. Most of the deaths

**Table 1: Clinical characteristics and outcome of patients with infective endocarditis (IE) and perivalvular abscess who received medical treatment alone during hospital stay**

| Patient no. | Age/sex | Prosthetic valve | Predisposing condition | Infecting organism | NYHA class on admission | Findings onTEE | Course in hospital | Outcome |
|---|---|---|---|---|---|---|---|---|
| 1 | 51/M | No | Diabetes mellitus, renal failure during dialysis | *Staphylococcus aureus* | IV | Vegetations, severe MR and abscess at mitral–aortic intervalvular fibrosa | Permanent pacemaker insertion for complete heart block | Limited by CHF; died 2 mo after discharge |
| 2 | 74/M | No | Metastatic colon cancer | *S. aureus* | III | Severe AR and MR, perforated anterior mitral leaflet and mitral annular abscess extending to posterior aortic root | Infection was controlled, but remained in CHF | Discharged after 6 wk of treatment; died 2 wk later |
| 3 | 59/M | AVR(M) | – | *S. epidermidis* | II | Vegetation, mild AR and anterior root abscess | Infection responded to treatment | CHF controlled medically; died of cancer 6 yr after IE |
| 4 | 65/F | AVR(M) | Behçet's disease | Culture negative | II | Mild AR and posterior root abscess | Infection responded to treatment | Sudden death 19 mo after IE |
| 5 | 60/M | AVR(T) | – | Viridans streptococci | III | Vegetations, severe AR and large posterior root abscess | CHF and infection were controlled; discharged at 6 wk | Recurrent IE at 5 mo; AVR with plication of aortic root pseudoaneurysm at 7 mo; alive 10 yr after IE, NYHA I |
| 6 | 64/M | AVR(M) | – | *Corynebacterium* | II | Mild AR and large periaortic abscess involving two-thirds of aortic annulus | Infection was controlled; no CHF | Follow-up TEE showed progressive increase in AR; aortic root and valve were replaced by aortic allograft at 11 mo; alive 8 yr after IE, NYHA I |
| 7 | 72/M | AVR(T) | – | *S. aureus* | II | Moderate AR and anterior root abscess | CHF and infection responded to treatment | Moderate AR and MR on follow-up; died of cancer 30 mo after IE |
| 8 | 37/M | AVR(M) | – | *S. aureus* | II | Vegetations, moderate AR and posterior root abscess | Infection responded to treatment; no worsening CHF; small embolic right frontal lobe infarct; small apical left ventricular infarct | Follow-up TEE showed moderate PVR and large aortic root pseudoaneurysm; alive 6 yr after IE, NYHA I |
| 9 | 32/F | AVR(M) | – | *S. epidermidis* | II | No AR, large circumferential aortic root abscess | Infection responded to treatment | Repair of aortic root 16 mo after IE; postoperative course complicated by bleeding requiring reoperation; died intraoperatively 16 mo after IE |
| 10 | 73/M | AVR(M) | – | *Klebsiella* | II | Vegetations, mild AR and posterior aortic root abscess | Completed 6-week course of antibiotic therapy | Follow-up TEE showed aortic root pseudoaneurysm; died of cancer of larynx 40 mo after IE |
| 11 | 72/M | AVR(M) | Prior IE | Culture negative | II | Severe AR and large posterior aortic root abscess | Worsening CHF | Class III CHF on treatment; alive 56 mo after IE, NYHA III |
| 12 | 81/M | AVR (T) | Diabetes mellitus | Culture negative | III | Severe AR and posterior aortic root abscess | Development of anemia and renal failure | Follow-up TEE showed severe paravalvular AR; sudden death 39 mo after IE |

Note: NYHA = New York Heart Association, TEE = transesophageal echocardiography, MR = mitral regurgitation, CHF = congestive heart failure, AR = aortic regurgitation, AVR = aortic valve replacement, AVR(M) = mechanical aortic prosthetic valve, AVR(T) = tissue aortic prosthetic valve, PVR = paravalvular regurgitation.

were due to heart disease, but there were 5 noncardiac-related deaths: 2 in the surgical intervention group (1 from stroke and 1 from kidney failure) and 3 in the medical treatment group (all due to cancer [patients 3, 7 and 10]). Complete heart block requiring pacemaker insertion developed in 1 medically treated patient and 2 surgically treated patients.

**Table 2: Characteristics of patients with endocarditis and perivalvular abscess who received medical treatment alone and those who had surgery during the same hospital stay**

| Characteristic | Group; no. of patients* | |
|---|---|---|
| | Medically treated *n = 12* | Surgically treated *n = 31* |
| Mean age (and SD), yr | 62 (15) | 54 (16) |
| Female | 2 | 9 |
| Prosthetic valve endocarditis | 10† | 16‡ |
| Early-onset | 3 | 4 |
| Late-onset | 7 | 12 |
| Valve location | | |
| Aortic | 10 | 26 |
| Mitral | 1 | 2 |
| Both | 1 | 3 |
| Infecting organism | | |
| *S. aureus* | 4 | 12 |
| *S. epidermidis* | 2 | 1 |
| Viridans streptococci | 1 | 6 |
| Other | 2 | 8 |
| Culture negative | 3 | 4 |
| NYHA class III or IV | 4 | 20 |

Note: SD = standard deviation.
*Unless otherwise stated.
†7 mechanical, 3 tissue.
‡8 mechanical, 8 tissue.

**Table 3: Characteristics of the survivors and the nonsurvivors***

| Characteristic | Group; no. of patients† | |
|---|---|---|
| | Survivors *n = 18*‡ | Nonsurvivors *n = 24* |
| Mean age (and SD), yr§ | 50 (17) | 60 (14) |
| Female | 5 | 6 |
| Prosthetic valve endocarditis | 10 | 15 |
| Valve location | | |
| Aortic | 18 | 17 |
| Mitral | 0 | 3 |
| Both | 0 | 4 |
| Infecting organism | | |
| *S. aureus* | 7 | 9 |
| Viridans streptococci | 3 | 4 |
| Other | 6 | 6 |
| Culture negative | 2 | 5 |
| NYHA class III or IV | 11 | 12 |
| Valve surgery during same hospital stay | 14 | 16 |

*The data for 1 patient, who was lost to follow-up, are excluded.
†Unless otherwise stated.
‡Included 2 patients who underwent cardiac transplantation for severe heart failure.
§$p = 0.04$.

### *Cardiac surgery following discharge*

Three of the medically treated patients (patients 5, 6 and 9) had late cardiac surgery. Repeat cardiac surgery was performed in 8 of the surgically treated patients, for perivalvular leak in 3 and for persistent infection in 5. Severe heart failure requiring heart transplantation occurred in 2 of these 8 patients.

### *Transesophageal echocardiography*

Follow-up TEE was performed in all 12 medically treated patients. They had a mean of 5 (SD 3) TEE studies per patient (range 2–12), and the mean duration of TEE follow-up was 72 (SD 118) weeks (range 4–407 weeks). The first follow-up TEE examination was within 2 weeks after the diagnosis of perivalvular abscess in 5 patients and showed cavitation of the abscesses. Pseudoaneurysms with a thin wall were observed by the fourth week in 10 patients, with further expansion up to 6 to 8 weeks. The 2 remaining patients had pseudoaneurysms on their first follow-up TEE examination, in the eighth week; thereafter, no further expansion or rupture of the pseudoaneurysm was observed. The pseudoaneurysms communicated with the aortic root in 10 patients (Fig. 2) and with the left ventricle in 2 patients. These evolutional changes confirmed that the initial diagnosis of perivalvular abscess was appropriate.

Fistulae developed in 6 patients, communicating between the left ventricle and the left atrium in 2 patients, the left ventricle and the right ventricle in 2, and the left ventricle and the aorta in 2. Five of these patients had early surgery for severe heart failure.

Postoperative echocardiography was performed in all surgically treated patients who survived the initial surgical procedure, but follow-up TEE was performed in only 24 patients. Among the 24, significant paraprosthetic regurgitation was present in 10, aortoatrial fistula in 1 and pseudoaneurysms in 7 despite surgical obliteration of the abscess cavities.

## Interpretation

Perivalvular abscess is an ominous development in patients with endocarditis because it is associated with valvular and perivalvular destruction, leading to serious complications such as heart block, pericarditis and acute valvular insufficiency. The introduction of TEE enables us to arrive at an early diagnosis because of its high sensitivity in detecting vegetations and abscesses.[3,21,23]

In patients with endocarditis and perivalvular abscess, early surgery is advocated to achieve more rapid control of the infective process, to improve the chances of survival and to prevent the development of further perivalvular destruction.[5–14,27–31] However, the infection recurs in about 5% of pa-

tients,[7,15,16] and dehiscence of sutures in an area of acute inflammation is common, with postoperative perivalvular leak in up to 30% of patients with endocarditis and perivalvular abscess.[4,5,11,16] Some of these patients require a second and even a third operation to eradicate the perivalvular leak. On the other hand, when the active infection has subsided, the operation becomes easier, even when other forms of perivalvular complications, such as pseudoaneurysm, are present.[32–34] None the less, the practice at the University of Ottawa Heart Institute is to perform early surgery in these patients unless there are mitigating circumstances. Indeed, among the medically treated patients in this study, surgery was not performed largely because of prohibitive surgical risks or serious coexisting medical conditions. Thus, the prognosis of the medically treated patients was expected to be poor, and yet medical treatment alone was successful in at least a fourth of the cases. With a duration of follow-up of up to 10.5 years, survival appeared to be similar between the patients treated surgically and those treated medically, with cancer accounting for 3 of the late deaths in the latter group.

In most patients the abscess led to the development of an aortic pseudoaneurysm as a result of cavitation and drainage into the aorta with control of the infection.[21,35] The evolutional process was identical irrespective of the species of the infecting microorganism. Pseudoaneurysms occurred in some patients even after surgical intervention. Furthermore, pseudoaneurysms did not appear to undergo continuing enlargement beyond the acute phase, and no incident of rupture was encountered in this series. Less frequently, the abscess eroded into other adjacent structures, resulting in the formation of a fistula. Some of these patients had surgery several months later, after antibiotic treatment was completed and the active inflammation had settled down. Although the surgery was still complicated, with the need for reinforcement of the aortic root and obliteration of the pseudoaneurysm that was invariably present, the surgery could be performed successfully because the infective process was no longer active and postoperative perivalvular leak appeared less common.[32,33] In a retrospective study of 233 cases of perivalvular abscess from 42 French hospitals over a 5-year period, the medically treated patients, who made up 9% of the study population, had a survival rate similar to that among the surgically treated patients.[5] Furthermore, increasing patient age, staphylococcal infection and abscess fistulization predicted death, the rate of which was 41% at 27 months. In the current study, lower age was the only predictor of long-term survival. As in other studies,[4,5,11,16] valve surgery in the active phase of perivalvular abscess frequently resulted in perivalvular leak postoperatively.

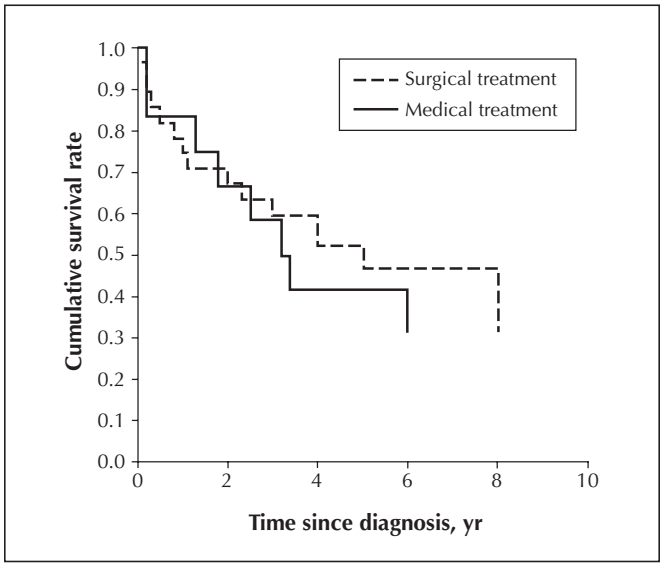


**Fig. 1: Kaplan–Meier survival curves from time of diagnosis for patients with endocarditis complicated by perivalvular abscess. Survival was similar for patients who received early surgical therapy (broken line) and those who received medical treatment alone (solid line).**

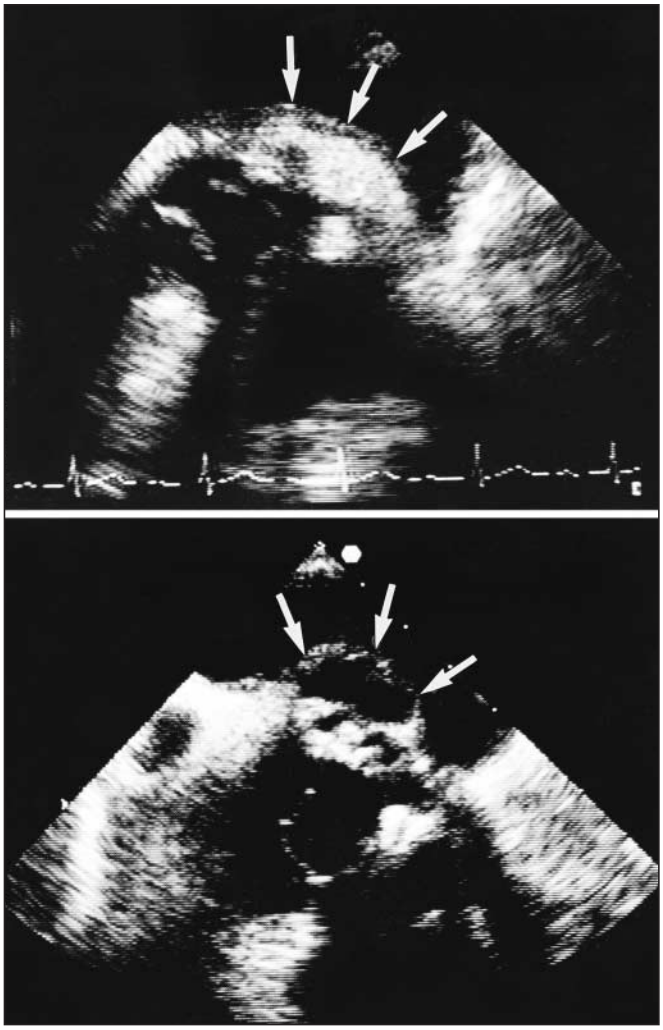

**Fig. 2: Transesophageal echocardiograms of aortic root in short axis, showing evolution of perivalvular abscess in patient with bioprosthetic aortic valve. Top: The abscess (arrows) was located in the posterior aortic root. Bottom: The abscess became a pseudoaneurysm (arrows) communicating with the aortic root on follow-up study.**

The findings of this study may have limited application to patients with perivalvular abscess complicating mitral valve endocarditis (present in only 7 patients in this study) and to intravenous drug users (none of the patients belonged to this risk group). The common infecting microorganisms were represented, but the size of the patient population did not allow me to entirely exclude the prognostic significance of specific microorganisms, such as *S. aureus*.

Although the data for this study were derived from a prospective registry, this was not a controlled trial. The patients were not randomly assigned to undergo either early surgery or no surgery, but they were consecutive patients from a single tertiary care centre. Infective endocarditis is a serious medical condition, and the management — particularly relating to the need for valve surgery — should be individualized. It is difficult, if not impossible, to perform a randomized study to assess the effect of early surgery in this population.

## Conclusion

Perivalvular abscess predicts a poor prognosis for patients with endocarditis. These patients also have a high incidence of perivalvular complications despite early surgical intervention. In view of the poor long-term outcome, these patients need to be closely monitored irrespective of whether they have early surgical intervention. The experience at the University of Ottawa Heart Institute indicates that TEE is the ideal tool for monitoring the evolutional changes of the perivalvular abscess.[3,24,35] The findings of this study suggest that the main impetus for surgery is severe heart failure despite medical treatment and that surgery may be deferred or avoided in patients whose heart failure is well controlled.[5] Lower age is the only predictor of long-term survival.

*Competing interests:* None declared.

*Acknowledgement:* This work was supported in part by the Heart and Stroke Foundation of Ontario.

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