Do all patients with prosthetic valve endocarditis need surgery?

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Abstract

A best evidence topic in cardiothoracic surgery was written according to a structured protocol. The question addressed was ‘do all patients with prosthetic valve endocarditis need surgery?’ Seventeen papers were found using the reported search that represented the best evidence to answer the clinical question. The authors, journal, date and country of publication, patient group studied, study type, relevant outcomes and results of these papers are tabulated. These studies compared the outcome and survival between surgically and non-surgically treated patients with prosthetic valve endocarditis. Of these studies, two were prospective observational studies and the rest were retrospective studies. The results of most of these papers were in accordance with the guidelines of the American College of Cardiology and American Heart association. These studies showed that unless a patient is not a surgical candidate, an operation is the treatment of choice in prosthetic valve endocarditis. Surgery should be performed as soon as possible, particularly in haemodynamically unstable patients and those who develop complications such as heart failure, valvular dysfunction, regurgitation/obstruction, dehiscence and annular abscess. In addition to the above indications and cardiac/valvular related complications of prosthetic valve endocarditis, infection with Staphylococcus aureus plays an important role in the outcome, and the presence of this micro-organism should be considered an urgent surgical indication in the treatment of prosthetic valve endocarditis. Surgery should be performed before the development of any cerebral or other complications. In contrast, in stable patients with other micro-organisms, particularly those with organisms sensitive to antibiotic treatment who have no structural valvular damage or cardiac complications, surgery can be postponed. The option of surgical intervention can also be revisited if there is a change in response to the treatment. This option is reserved for selected patients only and we conclude that as soon as the diagnosis of prosthetic valve endocarditis is made, cardiac surgeons should be involved.

Keywords: Review • Prosthetic valve • Endocarditis • Surgery

INTRODUCTION

A best evidence topic was constructed according to a structured protocol. This is fully described in the ICVTS [1].

THREE-PART QUESTION

In [patients with prosthetic valve endocarditis (PVE) (mechanical/biological)] does [surgical intervention/surgery] result in [better outcome/survival rate].

CLINICAL SCENARIO

A surgical review has been requested for a 73-year old man with diabetes, renal failure and a previous stroke who had a mechanical aortic valve replacement 15 years ago. The patient was admitted with septicaemia and investigations confirmed endocarditis of the mechanical prosthesis associated with moderate aortic regurgitation. He has been started on broad-spectrum antibiotics and surgical intervention needs to be considered. A redo aortic valve replacement is considered high risk and you decide to check the literature yourself before reaching a decision.

SEARCH STRATEGY


SEARCH OUTCOME

Seventeen papers that provided data to answer the question were found using the reported search. Non-English papers and those that did not compare surgery plus medical therapy with medical therapy alone were excluded. No randomized controlled trials were identified. There were only two prospective observational studies and the rest were retrospective reviews. These studies are presented in Table 1.
Table 1: Studies on prosthetic valve endocarditis

<table>
<thead>
<tr>
<th>Author, date, journal, country</th>
<th>Study type (level of evidence)</th>
<th>Patient group</th>
<th>Outcomes</th>
<th>Key results</th>
<th>Comments and limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calderwood et al. [3], 1986, J Thorac Cardiovasc Surg</td>
<td>Retrospective (level III)</td>
<td>PVE 116; 45 non-surgical, 71 surgical</td>
<td>In complicated PVE better outcome observed with surgical treatment</td>
<td>Outcome difference (P &lt;0.05)</td>
<td>Surgery was used mainly in complicated PVE and S. aureus infection</td>
</tr>
<tr>
<td>Yu et al. [4], 1994, Ann Thorac Surg</td>
<td>Prospective, observational, multi-centric (II)</td>
<td>PVE 74</td>
<td>Lower mortality with surgery compared with non-surgical treatment</td>
<td>Mortality (P &lt;0.05): • Non-surgical = 56% • Surgical = 23%</td>
<td>Survival was influenced by congestive cardiac failure</td>
</tr>
<tr>
<td>Otaki [5], 1994, ASAIO J</td>
<td>Retrospective (level III)</td>
<td>PVE 32; 7 non-surgical, 25 surgical</td>
<td>Non-surgical group all died Higher mortality with early onset PVE compared with late onset</td>
<td>In-hospital mortality (P &lt; 0.05): • Non-surgical = 100% • Surgical = 16%</td>
<td>Patients in non-surgical group were not surgical candidates due to cerebral complications or cardiogenic shock and all died subsequently</td>
</tr>
<tr>
<td>Wolf et al. [6], 1995, Chest</td>
<td>Retrospective (level III)</td>
<td>PVE 122; 57 non-surgical, 65 surgical</td>
<td>Overall mortality with antibiotics only was higher compared with surgery, however, this significance was due to S. aureus PVE</td>
<td>Mortality at 4 months (P &lt; 0.05): • Non-surgical = 48% • Surgical = 25% Mortality in S. aureus group (P &lt; 0.05) • Non-surgical = 100% • Surgical = 55% Mortality in non-S. aureus (P = NS) • Non-surgical = 81% • Surgical = 89%</td>
<td>S. aureus was the main predictor of death</td>
</tr>
<tr>
<td>Ho et al. [7], 2010, Asian Cardiovasc Thorac Ann</td>
<td>Retrospective (level III)</td>
<td>80 PVE; 46 non-surgical, 34 surgical</td>
<td>Surgery more beneficial in S. aureus and valve dysfunction</td>
<td>In-hospital mortality (P &lt; 0.05): • Non-surgical = 37% • Surgical = 15%</td>
<td>Surgery required more in early onset PVE</td>
</tr>
<tr>
<td>John et al. [8], 1997, Clin Infect Dis</td>
<td>Retrospective (level III)</td>
<td>33 PVE; (S. aureus) 9 non-surgical, 14 surgical</td>
<td>Surgical group with or without complications did better compared with the non-surgical group</td>
<td>In-hospital mortality (P &lt; 0.05): • Non-surgical = 63% • Surgical = 14%</td>
<td>All patients with S. aureus PVE benefit from surgery even without evidence of cardiac complications</td>
</tr>
<tr>
<td>Sohail et al. [9], 2006, Am J Med</td>
<td>Retrospective (level III)</td>
<td>55 PVE (S. aureus); non-surgical 23, surgical 32</td>
<td>Mortality was significantly higher in non-surgical group</td>
<td>In-hospital mortality (P &lt; 0.05): • Non-surgical = 48% • Surgical = 28%</td>
<td>Higher mortality with central nervous system involvement is seen and surgery was offered in one patient only</td>
</tr>
<tr>
<td>Gordon et al. [10], 2000, Ann Thorac Surg</td>
<td>Retrospective (level III)</td>
<td>77 PVE (early onset, within 12 months); 23 non-surgical, 54 surgical</td>
<td>Significantly better outcome with surgery in short- and long-term</td>
<td>PVE = 1% 30-day mortality (P &lt; 0.05) • Non-surgical = 35% • Surgical = 8% 1-year mortality (P &lt; 0.05) • Non-surgical = 60% • Surgical = 26% 2-year mortality (P &lt; 0.05)</td>
<td>Study population was collected for a 20-year period but no difference in the study outcome at the beginning and end of the study was found</td>
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| Akowuah et al. [11], 2003, Heart | Retrospective (level III) | 66 PVE, 28 non-surgical, 38 surgical | Better outcome with surgery but some selected patients can be treated with Abx alone | • Non-surgical = 63%  
• Surgical = 35%  
3-year mortality (P < 0.05)  
• Non-surgical = 67%  
• Surgical = 39%  
PVE Incidence = 4.5%  
In-hospital mortality (P < 0.05)  
• Non-surgical = 46%  
• Surgical = 24%  
10-year survival (P < 0.05)  
• Non-surgical = 28%  
• Surgical = 58%  
Freedom from endocarditis (P = NS)  
• Non-surgical = 65%  
• Surgical = 60%  
29% in Abx group required surgery later | Selection bias: some were too sick for surgery and died |
| Alonso-Valle et al. [12], 2010, J Thorac Cardiovasc Surg | Retrospective (level III) | 122 PVE, 26 non-surgical, 107 surgical | Better outcome with surgery after 1 year. Patients with perivalvular abscess have worse prognosis | PVE Incidence = 2.2%  
In-hospital mortality (P = NS)  
• Non-surgical = 42%  
• Surgical = 26%  
1-year survival (P < 0.05)  
• Non-surgical = 42%  
• Surgical = 71% | Small percentage of patients in non-surgical group were included |
| Habib et al. [13], 2005, Heart | Retrospective (level III) | 104 PVE, 53 non-surgical, 51 surgical | Less mortality and better survival in staph group and complicated group with surgery compared with non-surgical | PVE incidence = 2%  
All patients in-hospital mortality (P = NS)  
• Non-surgical = 17%  
• Surgical = 25%  
Significantly lower in complicated group | Early onset more common with mechanical valves |
| Kuyvenhoven et al. [14], 1994, Eur J Cardiothorac Surg | Retrospective (level III) | 70 PVE, 27 non-surgical, 43 surgical | Surgical group had better survival. Patients too ill for surgery were put in non-surgical group and all died | In-hospital mortality (P = NS)  
• Non-surgical = 30%  
• Surgical = 26% | Micro-organism and heart failure rather than other complications |
| López et al. [15], 2007, Eur Heart J | Observational (level II) | 66 PVE, 29 non-surgical, 37 surgical | No difference between surgical and non-surgical groups | In-hospital mortality (P = NS)  
• Non-surgical = 45%  
• Surgical = 32% | No long-term outcome |
| Chirouze et al. [16], 2004, Clin Infect Dis | Retrospective (multi-centric) (level III) | 61 PVE; (S. aureus) 40 non-surgical, 21 early surgery | More heart failure in surgical group. No difference in mortality | PVE = 2.8%  
Heart failure (P = NS)  
• Non-surgical = 30%,  
• Early surgery = 42%  
Difference in mortality (P = NS)  
Overall mortality = 47% | Stroke was the only prognostic factor |
| Tornos et al. [17], 1997, Clin Infect Dis | Late onset PVE 59; 42 non-surgical, 17 surgical | PVE can be managed medically unless severe valve dysfunction is present | Late PVE = 11%  
In-hospital mortality (P = NS)  
• Non-surgical = 24% | S. aureus PVE should undergo surgery |

Continued
RESULTS

PVE is a serious condition and several factors influence the outcome. Based on the guidelines of the American College of Cardiology/American Heart Association, surgery is indicated for PVE resulting in hemodynamic instability, heart failure or valvular complications such as valve dysfunction/dehiscence, valvular obstruction/regurgitation or abscess formation (Class I). In persistent bacteremia, relapsing infection and recurrent emboli, surgery is advisable (Class IIa). In cases of uncomplicated PVE with a sensitive organism, however, surgery is not indicated [2]. Our search showed that most studies published to date favour an aggressive approach to surgery for PVE.

In 1986, a study by Calderwood et al. [3] confirmed that patients with complicated PVE do significantly better with surgery compared with those treated with antibiotics alone. In that study, surgery was mainly used to treat complicated PVE associated with *Staphylococcus aureus* infection. Yu et al. [4] and Otaki [5] also showed better survival with surgery, however, the groups were not comparable and high-risk patients who were not surgical candidates were included in the antibiotic therapy group. Wolf et al. reported their results focusing on infection with *S. aureus*. Their analysis showed no difference with medical or surgical treatment of patients with PVE with non-staphylococcal organisms, whereas patients with *S. aureus* PVE had 100% mortality without surgery. They concluded that *S. aureus* PVE is the main predictor of outcome in PVE [6]. Similarly, Ho et al. [7] confirmed that surgery was more beneficial than medical therapy in *S. aureus* PVE. John et al. [8] and Sohail et al. [9] also reported the results of *S. aureus* PVE and showed significantly better outcome with surgery even in patients without valve-related complications.

In another study, 30-day, 1- and 3-year mortalities were shown to be significantly higher in a non-surgical group compared with those who had surgery, however, more than half of the patients in the non-surgical group were too ill to be operated on [10]. Ten-year survival was found to be significantly higher in the surgical group, but there was selection bias arising from the inclusion of non-surgical candidates in their analysis [11]. Other authors have shown better outcomes in these patients after 1 year when treated surgically, however, they failed to show any difference in the incidence of in-hospital mortality [12, 13]. In both of these studies, patients with valvular dysfunction were not included in the non-surgical category, and also conservative treatment was selected for patients with non-*S. aureus* PVE. Early onset of PVE was found to be more common with mechanical prostheses [12, 13]. Kuyvenhoven et al. [14] and López et al. [15] also showed no difference in the incidence of in-hospital mortality between treatment groups, but the type of micro-organism and the presence of heart failure were more important factors compared with other complications of PVE.

In contrast to the previous studies, Chirouze et al. showed that the overall mortality in *S. aureus* PVE was not different between the groups whether or not they had surgery. They included patients with heart failure in the surgical group and suggested that early surgery was only beneficial in patients with cardiac complications [16]. Tornos et al. studied late onset PVE and showed no difference between the groups with respect to in-hospital mortality, and 5- and 10-year survivals. They made a recommendation favouring early surgery for *S. aureus* PVE [17]. Truninger et al. also showed no difference in the mortality rate with or without surgery at mid- and long-term. His surgical group, however, included more patients with valvular complications whereas in his medical group, more patients with enterococcal PVE were included. He concluded that stable patients with non-staphylococcal PVE can be treated medically [18].

Only 1 of the 17 studies demonstrated a worse outcome with surgery, however, the difference did not reach statistical

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<tbody>
<tr>
<td>Truninger et al. [18], 1999, Heart</td>
<td>Retrospective (level III)</td>
<td>PVE 49; 10 non-surgical, 39 surgical</td>
<td>Haemodynamically stable patients with non-staphylococcal PVE can be treated with antibiotics</td>
<td>• Surgical = 29% Overall survival at 5-year (80%) and 10-years (63%) not different between groups (P = NS)</td>
<td>Early surgery before cerebral complications recommended in these cases</td>
</tr>
<tr>
<td>Rekik et al. [19], 2009, Neth Heart J</td>
<td>Retrospective (level III)</td>
<td>PVE 48; 28 non-surgical, 20 surgical</td>
<td>Higher mortality in surgical group but not statistically significant</td>
<td>In-hospital mortality (P = NS) • Non-surgical = 14% • Surgical = 14% Need for reoperation (P = NS) • Non-surgical = 19% • Surgical = 14%</td>
<td>More enterococcal in non-surgical group</td>
</tr>
</tbody>
</table>

PVE: prosthetic valve endocarditis; ASA: American Society of Anesthesia; *S. aureus*: *Staphylococcus aureus*; CNS: central nervous system.
significance. A longer delay in establishing the diagnosis and more heart failure in the surgical group were noted in this study as factors that negatively affect the outcome of surgery [19].

CLINICAL BOTTOM LINE

Unless a patient is not a surgical candidate, in PVE, surgery is the treatment of choice. This is particularly the case in patients who develop complications as a result of PVE. These complications include heart failure, valvular dysfunction, valvular regurgitation or obstruction, valve dehiscence and annular abscess. In these patients, early surgery also improves the outcome and increases the survival.

Injection with S. aureus should be considered an indication for surgery in PVE even without cardiac or valvular complications. These patients should undergo surgery as soon as possible before cerebral complications develop. In patients with other microorganisms, especially where the organism is sensitive to the particular antibiotic treatment regime and no structural damage or cardiac complications have occurred, surgery can be postponed or reconsidered if there is reason to the treatment. This option should be considered for selected patients only and cardiac surgeons should be involved from the early stages of the diagnosis.

Conflict of interest: none declared.

REFERENCES


eComment. Early surgery for patients with uncomplicated prosthetic valve endocarditis

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Attaran et al. [1] are to be commended for trying to answer an important question that recurrently arises in clinical practice: do all patients with prosthetic valve endocarditis (PVE) need surgery? The authors concluded after reviewing the relevant literature that redo surgery is warranted especially in case of complicated PVE, or when the culprit organism is Staphylococcus aureus. We entirely agree with their opinion and would like to add a brief comment concerning the timing of surgery in patients with uncomplicated PVE.

Despite advances in medical and surgical care interventions, PVE remains a diagnostic and therapeutic challenge. PVE accounts for 10–30% of all cases of infective endocarditis [2], with the International Collaboration on Endocarditis, the largest registry of patients with endocarditis, reporting a PVE incidence of 20% [3]. Furthermore, the proportion of infective endocarditis cases undergoing surgery ranges from 28-42% as shown in a recent meta-analysis [4]. Unfortunately, PVE still carries a high mortality risk ranging from 20-80% of affected patients [2]. Therapeutic strategies for PVE are not backed by evidence-based recommendations. Although several retrospective studies showed that surgical intervention is indicated in cases of PVE with severe prosthetic dysfunction, heart failure, abscess formation and early staphylococcal infection, no randomized trials have been performed to examine the role of valve surgery in the management of PVE.

There are no clear recommendations regarding the indication for surgery in PVE patients with uncomplicated large vegetations. Indeed, a recently published study tried to find an answer, albeit in patients with native valve endocarditis. The EASE study [Early Surgery versus Conventional Treatment in Infective Endocarditis] is a randomized control trial involving patients with native infective endocarditis, who were candidates for both early surgery and conventional treatment at two Korean medical centres [5]. They randomized 76 patients with vegetations larger than 10 mm, and severe valve dysfunction and assigned them to surgery within 48 hours after enrolment (early surgery) or to antibiotic therapy (conventional treatment). The primary end point was a composite of embolic events or death within 6 weeks after randomization. Early surgery prevented additional embolic events without increasing mortality, whereas 20% in the conventional treatment group had additional embolic events.

Postponing the surgery in this patient population on the assumption that operating on them is too risky and challenging, exposes these patients to the hazard of...