Acute infective endocarditis: early surgery versus conventional treatment

Background

Infective endocarditis (IE) refers to the inflammation of the inner layer of the heart, the endocardium, secondary to an infectious (most commonly bacterial) agent. It affects the left side of the heart more commonly than the right. IE has an estimated incidence of 1.4 to 6.2 per 100,000 persons in the developed countries, and is most commonly caused by *Staphylococcus aureus*, coagulase-negative staphylococcus, Viridans group streptococci and *Streptococcus bovis*. (1)

Although first described in the mid-16th century, IE remains a considerable cause of cardiovascular morbidity and mortality to date. (1) Over the past decades, IE has been extensively studied and reviewed in the published literature. Despite these efforts, however, mortality rates remain relatively unchanged for the past 25 years, with the current estimated one-year mortality close to 40%. (2)

The use of antibiotics has been the cornerstone of IE management. (3) However, advances in surgical treatment have expanded the role of surgery in managing IE patients. For example, the American Heart Association and the European Society of Cardiology now advocate for the surgical management of patients with certain IE-related complications. (4) Current indications for surgery include (4):

1. Development of heart failure.   2. Abscess formation.   3. Fungal IE.   4. Failure of antibiotic therapy.

Early surgery for IE (defined as valvular surgery within 1 to 7 days of hospital admission) has lately been theorised to confer superior outcomes compared to the current standard of care (i.e., antibiotics with or without delayed surgery.) (3) The aim of this poster is to review the evidence of whether early surgery is superior to conventional treatment for acute left-sided, native-valve IE.

OR

In-hospital mortality

In-hospital mortality is a vital outcome to measure, especially when comparing two life-saving treatments. A recent RCT compared the in-hospital mortality of early surgery vs. conventional treatment in a group of South Korean patients. One patient in the early surgery group (3%) and one patient in the conventional treatment group (3%) died within 6 weeks of hospitalisation (p = 1.00) (4) These results are in conjunction with data from previous observational studies. Funakoshi *et al* reported a similar in-hospital mortality (5% in both groups) between early surgery and conventional treatment (p = 0.58.) (5)

Current evidence supports

Neutral

Acute embolic events

This is defined as any systemic embolism (e.g., cerebral, cardiac, renal or splenic) that occurred secondary to IE within 6 weeks of hospital admission. Early surgery resulted in a significantly lower rates of acute embolism as compared to conventional treatment. A non-randomised trial found no embolic events (0%) compared to 14 (21%) in patients managed with early surgery and conventional treatment respectively (p < 0.001.) (6) Similar rates were reported in a recent RCT; no patients (0%) in the early surgery group compared to 9 (23%) in the conventional treatment group experienced embolic events (p < 0.03.) (4)

Current evidence supports

Early Surgery

Antibiotic regimen and course duration

All patients with IE are routinely given prolonged antibiotic therapy. Not only does this result in side-effects for patients, it also increases the emerging risk of antibiotic resistance. Therefore, it is important to assess whether early surgery changes the use of antibiotics (duration and/or regimen) in patients with IE.

A recent RCT found no difference in the median duration of antibiotic use between early surgery and conventional treatment (35 days for both groups; p = 0.93.) Patients in the conventional treatment group were more likely than the early surgery group to be put on multiple antibiotics (33% vs. 27% respectively.) However, this trend was not statistically significant (p = 0.62.) (4)

Current evidence supports

Neutral

All-cause mortality

In an RCT by Kang *et al*, all-cause mortality at 6 months was not statistically significant between patients managed by early surgery compared to conventional treatment (3% vs. 5% respectively; p = 0.59.) (4) Similar results were found in a number of observational studies. One retrospective study reported all-cause mortality at 7 years to be 16% in the early surgery group and 21% in the conventional treatment group (p = 0.61.) (5)

Current evidence supports

Neutral

Morbidity

Non-embolic post-IE complications include recurrence of IE and repeat hospitalisation. As well as worsening patient outcomes, complications and re-admissions pose a significant financial burden on the health care system.

In one study, patients' records were retrospectively reviewed over a 19-year period. Patients who received surgery within the first 7 days of admission were just as likely to be re-admitted or to have recurrent IE as those who received conventional treatment. (5)

Current evidence supports

Neutral

What does this mean for New Zealand?

Like anywhere else, IE remains a major cause of cardiovascular morbidity and mortality in New Zealand. During the period 1999 to 2007, there were 431 hospital admissions to Christchurch Public Hospital for IE or IE-related complications. (7) *Staphylococcus aureus* and Viridans group streptococci remain the two most common causative organisms in New Zealand. (8)

Treatment of IE remains largely dependant on antibiotics. Surgery is only performed for absolute indications such as development of heart failure, myocardial abscesses and fungal endocarditis. (9) Data from a 12-year surgical outcome series conducted in the South Island revealed extremely good prognosis for patients who underwent surgery, in spite of significant peri-operative morbidity and mortality. (9) Further studies are required to assess whether early surgery is a cost-effective treatment to introduce in New Zealand for patients with acute native-valve IE.

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Conclusion

Despite the recent interest in early surgery for managing IE patients, there is no good evidence currently to support its superiority over conventional treatment. Early surgery seems to decrease the risk of systemic embolism in patients with IE. However, there is still no sufficient evidence to support one management approach over the other in terms of in-hospital mortality, antibiotic duration and regimen, all-cause mortality or non-embolic post-IE complications.

Several considerations need to be taken into account when thinking of the role of early surgery in IE. Firstly, there does not appear to be a consensus on the definition of "early surgery." How early is *early*? The period set in this review (i.e., within one week of hospital admission) was an arbitrary one done to help focus the literature search and review. Secondly, the number of good-quality published research is very limited: a single RCT (the EASE trial) and two non-randomised trials. (4-6) This is mainly due to ethical, logistical and financial constraints, which hindre the ability to conduct good-quality, multicentre RCTs. Lastly, most of the published literature originates from Eastern Asian countries. Factors such as disease characteristics, surgical skills and patient demographics can all limit the generalisability of the results of these studies.

At the mean time, it is still difficult to delineate which patients would potentially benefit from early surgery. Therefore, early referral to medical centres with the appropriate cardiac surgical experience and resources is warranted for patients with IE. (4)

Future research efforts should focus on more robust and ethnically-diverse RCTs, comparing early surgery to conventional treatment for patients with acute native-valve IE. One such study is the ENDOVAL trial whose data are expected to be available late in 2012. (3)

References

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