Timing for surgery in patients with infective endocarditis and cerebrovascular complications—waiting may be best but results of early surgery are acceptable and improvements in neurology are common

Neil J. Howellab,* and Ian C. Wilsona

a Department of Cardiothoracic Surgery, University Hospital Birmingham, Edgbaston, Birmingham, UK
b School of Clinical and Experimental Medicine, University of Birmingham, Edgbaston, Birmingham, UK

* Corresponding author. Clinical Lecture in Cardiac Surgery, University of Birmingham, Edgbaston, Birmingham B152TT, UK. Tel: +44-0121-6272958; e-mail: neil.howell@uhb.nhs.uk (N.J. Howell).

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The timing of surgery for patients with infective endocarditis (IE) remains contentious, but over the last decade the number of patients operated on during the active phase has increased significantly [1, 2]. Cerebral complications associated with IE appear to be similar in both aortic or mitral infections. These cerebrovascular complications may be due to either embolic stroke affecting between 8 and 15% of patients, or cerebral haemorrhage affecting 2–3%. Of the total number embolic events associated with endocarditis 65% affect the central nervous system, the incidence of which has been reported as between 9 and 40% [3, 4]. This range may be due to the difference in preponderance of the causative organisms to embolize; Staphylococcus aureus and Streptococcus viridans have both been reported to be associated with an increased risk of neurological events [3–5].

Systemic heparinization and cardiopulmonary bypass in patients with cerebrovascular complications carry a risk of further neurological injury. Cerebral infarctions may be complicated by secondary haemorrhage, and haemorrhagic strokes may be extended. Periods of hypo-perfusion either during the period of cardiopulmonary bypass, or post-operatively during periods of low cardiac output may exacerbate any pre-existing neurological injury. The recognition of the risk that early surgery may propagate neurological damage led to the conclusion that delaying surgery in patients with embolic stroke for 2–4 weeks, and for those with haemorrhaging strokes for at least 4 weeks, may offer a lower exposure to risk by allowing time for maturation of any cerebral lesion, thereby reducing the risk of secondary haemorrhage. While this approach may reduce neurological complications, delayed surgery is not always feasible because of progressive heart failure, uncontrolled sepsis or ongoing embolic episodes. The results of such surgery are difficult to interpret; the numbers of patients are generally small, the patients pre-operative demographics and risk profile heterogeneous, and the surgery often complex.

In a retrospective multi-centre study by Eishi of 2523 patients with IE, 112 patients were identified with cerebral infarction and 34 with haemorrhagic stroke [3]. The operative mortality for those with an embolic stroke was 21.4%, and in those with a haemorrhagic stroke 17.6%. In this study, a significant correlation was demonstrated between the interval from neurological complication to surgery. Patients undergoing urgent surgery within 24 h had 66% mortality. In those undergoing surgery from 48 h until 7 days, mortality fell to 31%, and after this mortality continued to fall until, by 4 weeks, it was 7%. When examining the delay interval on neurological outcome in patients with embolic stroke, cerebral damage was exacerbated in 44% of patients undergoing surgery within 1 week gradually falling with time such that by 28 days it was 2.3%. The number of patients with haemorrhagic stroke was small and in this group there was no difference in neurological outcome in those who underwent early compared with those who underwent late surgery, suggesting that there is some risk of progression of cerebral damage irrespective of when surgery is undertaken. This study concluded that the risk of cerebral complications decreased to 10% in patients who underwent surgery after 2 weeks and to 2.3% in those who underwent surgery after 4 weeks.

Similar results were demonstrated in a recent single-centre review [5]. This identified only 13 patients over a 10-year period who had suffered a pre-operative neurological event, 10 embolic and 3 haemorrhagic. In the subgroup suffering embolic stroke, eight underwent surgery within 2 weeks of stroke due to complications of IE. Following surgery, two patients suffered additional neurological events and five experienced at least a partial improvement in their pre-operative neurological state. Only one patient with a haemorrhagic stroke underwent early surgery due...
to uncontrolled sepsis. This defect resolved postoperatively and the patient had no neurological deficit at late follow-up.

A propensity-matched analysis of the—Prospective Cohort Study registry was recently undertaken to examine the influence of early surgery on survival [6]. They identified 1552 patients of whom 720 (46%) underwent early surgery. Overall, they demonstrated that early surgery was associated with a significant reduction in mortality (12.1% with early surgery vs. 20.7% with delayed surgery). In subgroup analysis, early surgery was found to confer a survival benefit in a number of groups of patients including those with a pre-operative stroke or other embolic phenomenon. In the propensity-matched group of 100 patients with a pre-operative stroke undergoing early surgery compared with 100 patients undergoing delayed surgery, early surgery was associated with a 13% absolute risk reduction in in-hospital mortality. In the propensity-matched cohort of patients with other embolic phenomenon, early surgery was associated with a further 12.9% absolute risk reduction. It should be noted, however, that this study excluded illicit intravenous drug users and patients with prosthetic valve endocarditis; a group of patients that compromised 44% of patients in the registry, and study follow up was limited to the in-hospital episode. There was some criticism of the statistical methodology employed in the propensity-score matching performed in the International Collaboration on Endocarditis study [7], but in the absence of randomized data, this propensity-score matched study provides evidence that patients with prior cerebrovascular events do benefit from early surgery.

In an attempt to eliminate selection bias, a further single-centre propensity-score matched analysis was undertaken on 291 patients with native valve endocarditis [8]. Ninety-five patients who underwent surgery within the first week were compared with 196 patients who underwent later surgery. In the cohort as a whole, survival at 6 months was similar between groups, but the incidence of infective relapses resulting in valvular dysfunction was significantly higher in patients undergoing early surgery. In this study, the only propensity-matched groups in which surgery conferred a survival benefit were young patients, patients with S. aureus endocarditis, and patients with congestive heart failure and large vegetations.

The number of patients undergoing early surgery during the active phase of IE has risen due to a greater incidence of more virulent microorganisms and the development of surgical techniques that have demonstrated a beneficial effect in complicated endocarditis [8]. Although pre-operative cerebrovascular complications affect only a small proportion of patients with IE, it would seem that early surgery may be associated with a survival advantage in such patients, especially if they are young with con- gestive heart failure and large vegetations. Cardiac surgery does not appear to carry an unacceptable risk of further neurological damage, and neurological recovery is not uncommon. Patients with haemorrhagic stroke are at risk of further intra-cerebral bleeding even if surgery is delayed, and therefore such complications should not be a contraindication to early surgery. The major complication with early surgery remains the increased risk of recurrent infection resulting in early prosthetic valve endocarditis.

REFERENCES