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SCIENTIFIC EDITORIAL

Early surgery in infective endocarditis: Why should we wait?

Chirurgie précoce dans l'endocardite infectieuse : pourquoi devrions-nous attendre ?

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Abbreviations: ACC, American College of Cardiology; AHA, American Heart Association; ESC, European Society of Cardiology; ICH, Intracranial haemorrhage; IE, Infective endocarditis.

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MOTS CLÉS

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Background

Despite prevention and aggressive treatment, the incidence of infective endocarditis (IE) remains stable and the prognosis is poor (mortality of 30% at 1 year). This situation may be explained, in part, by the increasing number of cases of IE related to nosocomial virulent microorganisms and prosthetic valvular or intracardiac device material endocarditis. Therapeutic management relies on high doses of intravenous antibiotics and early cardiac surgery to treat or prevent heart failure, uncontrolled infection and cerebral embolism [1,2]. Recent studies report surgical interventions in about 50% of cases [3], and an absence of surgery in 25% of patients despite an appropriate indication [4].

Timing of cardiac surgery in recent guidelines

Guidelines from the European Society of Cardiology (ESC) [1] and the American Heart Association/American College of Cardiology (AHA/ACC) [2] both highlight the need to refer patients to expert centres with an “endocarditis team” for optimal medical and surgical management. One major role of the endocarditis team is to define the optimal timing of cardiac surgery. Then, these expert centres require facilitated access to cardiac surgery and specific imaging and bacteriological platforms. Unlike the 2014 AHA/ACC guidelines, the 2015 ESC guidelines provide an accurate staging of early surgery according to hemodynamic status: early surgery is graded as “emergency” for surgery performed within 24 hours, “urgent” for surgery performed in < 7 days, and “elective” when surgery is to be performed after at least 1–2 weeks of antibiotic therapy.

Early surgery in patients without cerebral complications

Most studies have defined early surgery as surgery performed between 48 hours and 4 weeks. The benefit of surgery performed during the initial hospitalisation period has been recently reported in a large cohort of non-selected patients with IE [5] and confirmed by a recent meta-analysis (of 21 studies) that reported a decrease in 1-year mortality of 20% when surgery was performed within 7 days [6]. However, no randomised trial exists and there are discrepancies in observational series evaluating the impact of early surgery, mainly because of differences in statistical methods [7]. Early surgery appears particularly beneficial in high-risk patients with heart failure symptoms, large vegetations and IE caused by *Staphylococcus aureus* [8].

Heart failure

Heart failure is the strongest predictor of poor outcome and the primary cause of early surgery. The acute heart failure observed in 50% of patients with left-side IE [4] is mainly caused by severe regurgitation and is rarely related to intracardiac fistulae or valvular obstruction. Cardiac surgery is the only option and should not be delayed. The 2015 ESC guidelines [1] recommend performing cardiac surgery as an emergency (within 24 hours) for patients with cardiogenic shock or persistent pulmonary oedema, and within 72 hours (urgent) in case of non-refractory heart failure. In patients with severe valvular regurgitation without heart failure, the timing of surgery is unclear, but early surgery may be a reasonable option in low-risk patients, especially when subclinical signs of poor hemodynamic tolerance are suspected on echocardiography.

Uncontrolled infection

Uncontrolled infection is the second cause of early surgery, and includes general and local uncontrolled infection. General uncontrolled infection is defined by unexplained persistent bacteremia after 1 week of adequate antibiotic treatment and is generally caused by virulent microorganisms (fungi, multiresistant organisms, *S. aureus* or non-HACEK [i.e. species other than *Haemophilus* species, *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens* or *Kingella*] gram-negative bacteria). Urgent surgery is recommended to prevent local and general complications: preventive for IE caused by virulent microorganisms; and curative for general uncontrolled infection.

Abscesses and increases in vegetation size under antibiotic therapy are also considered to be local uncontrolled infections. Antibiotic therapy has limited effect on these local complications and urgent surgery should be performed to prevent the risk of sudden cardiac death or an embolic event. An abscess complicated by a pseudo-aneurysm or a fistula may be challenging to identify on transesophageal echocardiography, and the ESC guidelines [1] highlight the importance of using multimodality imaging to improve diagnostic accuracy.

Embolic events

Embolic events are usually asymptomatic and frequent (30–50%) [9,10] but can be a life-threatening complication. The risk of an embolic event is major before the initiation of antibiotics [10] but decreases promptly after initiation of antibiotic therapy (8–12%) [10,11], especially after 2 weeks. The risk of embolism depends on several variables (age,

117 diabetes, atrial fibrillation, previous embolism before therapy, vegetation length and *S. aureus* infection) [12], but size and mobility are the main predictive factors for embolic events. Current ESC guidelines recommend urgent surgery for a large isolated vegetation (> 15 mm) and for a vegetation > 10 mm with a new embolic event despite adequate antibiotic treatment or with severe valvular disease [1]. The role of preventive surgery has been demonstrated in a randomised study conducted by Kang et al. [13], in which surgery performed within 48 hours in patients at low operative risk was associated with a lower rate of adverse events (death from any cause, embolic events or recurrence of IE).

130 Optimal delay in patients with cerebral complications

132 A systematic cerebral magnetic resonance imaging study demonstrated that asymptomatic cerebral complications are frequent (79%) in patients with confirmed IE [9]. The rate of symptomatic cerebral complications ranges between 20% and 50% [9,10], and they more frequently relate to a cerebral infarction than an intracranial haemorrhage (ICH). Management of these patients may be challenging and requires multidisciplinary expertise (an endocarditis team, including neurologists, neuroradiologists and neurosurgeons) to evaluate the risk of cerebral damage related to cardiopulmonary bypass [1,2].

143 Infective endocarditis with cerebral infarction

144 IE with cerebral infarction requires an aggressive therapy strategy to avoid embolism recurrence [1,2]. Several consistent studies have demonstrated that early cardiac surgery is superior to delayed surgery, with a low risk of cerebral complications (0–6%) and a good probability of complete neurological recovery. Okita et al. [14] reported a lower mortality rate in patients with IE-related cerebral infarction when surgery was performed within the first 7 days compared with delayed surgery. Piper et al. [15] showed that, after a stroke, very early surgery (within 72 hours) improved prognosis and did not increase the rate of haemorrhage conversion. In the absence of coma, cardiac surgery – when indicated – is best performed without delay in asymptomatic or symptomatic patients with cerebral infarction.

159 Infective endocarditis with intracranial haemorrhage

161 European guidelines are less aggressive in cases of ICH and recommend delaying surgery for at least 1 month. However, many patients with ICH have an urgent indication. This consensus is mainly based on one retrospective Japanese study that analysed, in detail, 181 patients with IE and cerebral complications [16]. Among them, 34 patients had a preoperative cerebral haemorrhage. One patient underwent cardiac surgery within 24 hours and died. Another patient with previous treatment for cerebral aneurysm was operated on day 5, with success. Five patients were operated

171 between day 15 and day 21, with a 20% mortality rate. Six patients were operated during the fourth week, with mortality rate of 0%, and 21 patients were operated after 1 month, with a mortality rate of 19%. No exacerbation of cerebral complications occurred in patients operated on within 28 days. In agreement with these results, Okita et al. [14] reported a low rate of hospital death (< 6%) when cardiac surgery was delayed to after the first week in patients with ICH. However, Garcia-Cabrera et al. [17] demonstrated conflicting results, with a higher mortality rate when surgery was performed within the first 3 weeks. Thus, early surgery (before 1 month) – when required because of hemodynamic instability – may be performed in patients with ICH after careful evaluation of the sizes and aetiologies of haemorrhagic lesions [18], and a multidisciplinary discussion.

186 Perspectives and conclusions

187 Overall, 75% of patients with IE have a surgical indication. Patients should be referred to an expert centre for rapid evaluation. Surgical indication and timing have to be defined by an endocarditis team. Early surgery is clearly beneficial in the absence of cerebral complications but also in patients with cerebral infarction without coma. Management of patients with ICH remains very complex but surgery may be performed within the first month after haemorrhagic stroke in selected patients, if there is a strong indication for early surgery.

197 Disclosure of interest

198 The authors declare that they have no competing interest.

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