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WHAT'S NEW IN INTENSIVE CARE

What's new in surgical treatment of infective endocarditis?

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Despite recent improvements (newer antibiotics, intensive care and surgical management), left-sided infective endocarditis (IE) is still associated with a significant in-hospital mortality and mid-term attrition rate [1, 2]. This is particularly true for patients admitted to intensive care unit (ICU) when endocarditis is due to methicillin-resistant *Staphylococcus aureus* and organ failures occur [3].

Optimal management of IE requires a broad range of expertise (infectious disease specialists, cardiologists, microbiologists, cardiac surgeons and intensivists). Given the low level of evidence available for the management of IE, international guidelines are particularly awaited and rather well implemented [4, 5].

This report summarizes newer information regarding indications and timing of surgery in the treatment of IE that reflect changes in the epidemiology (new antibiotics, resistant microorganisms, increased use of cardiovascular implants). They may help select the best treatment for the patients.

New evidence from systematic reviews and meta-analyses suggest that surgical treatment is clearly superior to conservative management. Recently, Anantha Narayan et al. published a meta-analysis on randomized trials, retrospective cohorts and prospective observational studies comparing outcomes between early surgery (<20 days or less) and conservative management [6]. In summary, early surgery is associated with significantly lower risk of mortality. Kang et al. compared early surgery to conservative treatment in patients with IE and large vegetations and found significantly reduced composite end points of death from any cause and a lower risk of systemic embolism with surgery [7]. Moreover, even in critically ill patients with multiorgan failure, surgery was reasonable in younger patients (<60 years), in those with predominant cardiac failure and/or with uncontrolled sepsis [8].

To facilitate decision-making, Wang et al. investigated the utility of risk scores on operative and long-term mortality. The best tool for post-operative stroke was EuroSCORE II, for ventilation >24 h the De Feo-Cotrufo Score while pre-operative inotropes, previous CABG and dialysis were independent predictors of operative and long-term mortality [9].

The main message of the ESC guidelines is clear: address patients with IE to an "Endocarditis Team" in tertiary care centres, facilitate early diagnosis using multimode imaging and promptly evaluate indications for surgery [10] (Table 1).

1. Failure to control pulmonary edema or cardiogenic shock or signs of progressive multiorgan failure within 24 h of maximal conservative therapy should prompt evaluation for immediate surgery.
2. Intracardiac destruction (abscess, severe valve regurgitation, fistula, conduction disturbances) requires surgery as soon as the complication is diagnosed.
3. Controversy (early versus delayed surgery) exists in the following situations:

   (a) Large or increasing vegetations and at least one embolic episode under adjusted antibiotic therapy.
   (b) IE caused by fungi or multiresistant organisms and specific situations where the risk of surgery is deemed to be too high. Early surgery may need to be reconsidered because of the availability of modern bactericidal antibiotics (daptomycin, ceftaroline and ceftobiprole and fungicidal substances like echinocandins) that may allow

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Table 1 Most important information regarding indications and timing of surgery in left-sided native and prosthetic valve endocarditis (from ESC Guidelines, 2015: [4])

Immediate (same day)	Emergency surgery must be performed irrespective of the status of infection, when patients are in persistent pulmonary oedema or cardiogenic shock despite medical therapy
Urgent (within days)	Severe valvular regurgitation or obstruction leading to heart failure Poor haemodynamic tolerance (high end-diastolic LV pressure, moderate to severe pulmonary artery hypertension) Uncontrolled infection leading to intracardiac destruction Increasing vegetation despite adequate antibiotic treatment. Persistent vegetations >10 mm after more than one embolic episode Endocarditis caused by fungi or multiresistant organisms (relative indication)
Delayed (within weeks)	Surgery should be considered depending on the tolerance of the valve lesion and according to the recommendations for the treatment of valve disease
Neurological complications	No delay following a silent embolism or transient ischaemic attack if indicated because of haemodynamic conditions or intracardiac destruction Interval of 3–4 weeks in case of haemorrhagic transformation of ischemic lesions No evidence of beneficial effect of angiographic coiling in case of unruptured septic cerebral pseudoaneurysms

successful medical treatment or widen the window of the optimal timing for surgery.

(c) Stroke.

Mihos et al. reviewed 14 studies that compared early versus delayed surgery for IE complicated by ischaemic stroke [11]. Early surgery meant an operation performed 3–14 days following stroke. Risk ratios were calculated for the outcomes of perioperative stroke, operative mortality and 1-year survival. Early surgery was associated with a significantly increased risk of operative mortality—regardless of surgery within the first 7 days after stroke—but with no observed benefit in 1-year survival.

In our institution, we adopt the following strategy:

1. Silent embolism (small MRI finding) or transient ischaemic attack: surgery is performed without delay, especially in case of haemodynamic deterioration and intracardiac destruction.
2. Haemorrhagic transformation of the ischaemic lesion: surgery is usually postponed for 3–4 weeks to avoid full heparinization for the extracorporeal circulation. Exceptionally, surgery is considered in cases of life-threatening cardiac and/or haemodynamic condition. A recent report confirmed that early surgery is safe in IE patients with cerebral infarction, while surgery within 7 days should be avoided in patients with intracranial haemorrhage [12].
3. Infection of cardiac devices.

The current incidence of implantable cardioverter-defibrillator (ICD) infection is unknown but more complex devices and procedures increase infection rates. Staphylococci cause the majority of infections. All-cause mortality ranges between 0 and 35 %. Failure to remove an infected device is associated with relapse and mortality. Complete and early (as soon as possible, but not more than 2 weeks after diagnosis) removal of an infected ICD system (generator and all leads) combined with appropriate antimicrobial therapy is the most effective and safe treatment option. Percutaneous removal is preferred for infected leads, combined with removal of the generator, while surgical removal should be considered for large lead-associated vegetations and when valve surgery is indicated [13].

Surgery for IE should attempt complete removal of the infected tissue and intracardiac reconstruction, including repair or replacement of the affected valve(s). Homografts are considered beneficial in root abscess and aorto-ventricular discontinuity.

In a prospective population-based survey, Iung et al. analysed the adherence to the guidelines regarding indications for surgery [14]. They found that surgery during acute IE was recommended in almost three out of four patients, but less than 50 % of the patients received surgery.

The best 1-year survival was observed in patients who had an indication for surgery and were operated on [14]. Chu et al. made a similar observation in 1296 prospectively recruited patients; surgical treatment was performed in 57 % but only in 76 % of patients with a surgical indication [15]. Patients who did not undergo surgical treatment were more likely to have medical comorbidities such as coronary artery disease, previous heart failure, diabetes and renal disease and to have infection caused by *S. aureus*. In-hospital and 6-month mortality rates were higher among patients who did not undergo surgery compared with those who did. In multivariate analysis, significant predictors of nonsurgical treatment were history of moderate/severe liver disease, stroke before surgical decision and *S. aureus* etiology. The most common reason for lack of surgery was having a poor

prognosis regardless of treatment (33.7 %) like haemodynamic instability, death before surgery, stroke and sepsis.

In patients with an indication for surgery, surgery was found to be associated with higher 6-month survival than no surgery. Patients with higher operative risk who underwent surgery had survival similar to patients with lower operative risk treated without surgery, whereas patients with higher operative risk who did not undergo surgery had very low survival [15].

In summary, patients with IE requiring ICU present special problems. Defining the optimal timing of surgery requires a close interdisciplinary communication between all specialists. Response to initial treatment of haemodynamics and infection, presence and risk of complications, and subtle changes in organ function should be taken into account to outweigh risk and benefits of early versus delayed surgical treatment.

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