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4 What's new in surgical treatment of infective endocarditis  
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30 Despite recent improvements (newer antibiotics, intensive care and surgical  
31 management), left-sided infective endocarditis (IE) is still associated with a significant in-  
32 hospital mortality and mid-term attrition rate (1,2). This is particularly true for patients  
33 admitted to intensive care unit (ICU) when endocarditis is due to methicillin-resistant S.  
34 aureus and organ failures occur (3).

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

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

43  
44 New evidence from systematic reviews and meta-analyses suggest that surgical  
45 treatment is clearly superior to conservative management. Recently, Narayan published  
46 a meta-analysis on randomized trials, retrospective cohorts and prospective  
47 observational studies comparing outcomes between early surgery (<20 days or less) and  
48 conservative management (6). In summary, early surgery is associated with significantly  
49 lower risk of mortality. Kang compared early surgery to conservative treatment in patients  
50 with IE and large vegetations and found significantly reduced composite end points of  
51 death from any cause and a lower risk of systemic embolism with surgery (7). Moreover,  
52 even in critically ill patients with multiorgan failure, surgery was reasonable in younger  
53 patients (< 60 yrs), in those with predominant cardiac failure and/or with uncontrolled  
54 sepsis (8).

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

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60 | The main message of the ESC guidelines is clear: address patients with IE to an  
61 "Endocarditis Team" in tertiary care centers, facilitate early diagnosis using multimode  
62 imaging and promptly evaluate indications for surgery (10).

63  
64 1. Failure to control pulmonary edema or cardiogenic shock or signs of progressive  
65 multiorgan failure within 24 hours of maximal conservative therapy should prompt  
66 evaluation for immediate surgery.

67  
68 2. Intracardiac destruction (abscess, severe valve regurgitation, fistula, conduction  
69 disturbances) requires surgery as soon as the complication is diagnosed.

70 3. Controversy (early versus delayed surgery) exists in following situations:

71 a. Large or increasing vegetations and at least one embolic episode under adjusted  
72 antibiotic therapy.

73  
74 b. IE caused by fungi or multiresistant organisms and specific situations where the risk  
75 of surgery is deemed to be too high. Early surgery may need to be reconsidered due  
76 to the availability of modern bactericidal antibiotics (daptomycin, ceftaroline and  
77 ceftabiprole and fungicidal substances like echinocandins) that may allow successful  
78 medical treatment or widen the window of the optimal timing for surgery.

79  
80 c. Stroke:  
81 Mihos published a review on 14 studies that compared early versus delayed surgery for  
82 IE complicated by ischemic stroke (11). Early surgery meant operation performed 3 to 14  
83 days following stroke. Risk ratios were calculated for the outcomes of perioperative  
84 stroke, operative mortality and 1-year survival. Early surgery was associated with a  
85 significantly increased risk of operative mortality - regardless of surgery within the first 7  
86 days after stroke - but with no observed benefit in 1-year survival.

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Formatiert: Englisch (USA)

87 In our institution, we adopt the following strategy :

88  
89 a) silent embolism (small MRI finding) or transient ischaemic attack: surgery is performed  
90 without delay, especially in case of haemodynamic deterioration and intracardiac  
91 destruction.

92

93 b) haemorrhagic transformation of the ischemic lesion: surgery is usually postponed  
94 for 3-4 weeks to avoid full heparinization for the extracorporeal circulation.  
95 Exceptionally, surgery is considered in cases of life-threatening cardiac and/or  
96 hemodynamic condition. A recent report confirmed that early surgery is safe in IE  
97 patients with cerebral infarction, while surgery within 7 days should be avoided in  
98 patients with intracranial hemorrhage (12).

Formatiert: Englisch (USA)

#### 100 d) Infection of cardiac devices

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

111 Surgery for IE, should attempt complete removal of the infected tissue and intracardiac  
112 reconstruction, including repair or replacement of the affected valve(s). Homografts are  
113 considered beneficial in root abscess and aorto-ventricular discontinuity.  
114 In a prospective population-based survey, lung analyzed the adherence to the guidelines  
115 regarding indications for surgery (14). He found that surgery during acute IE was  
116 recommended in almost three out of four patients, but less than 50% of the patients  
117 received surgery.

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118 The best 1-year survival was observed in patients who had an indication for surgery and  
119 were operated on (14). Chu made a similar observation in 1296 prospectively recruited  
120 patients, Surgical treatment was performed in 57% but only in 76% of patients with a  
121 surgical indication (15). Patients who did not undergo surgical treatment were  
122 more likely to have medical comorbidities such as coronary artery disease,  
123 previous heart failure, diabetes and renal disease and to have infection  
124 caused by S. aureus. In-hospital and 6 month-mortality were higher among  
125 patients who did not undergo surgery compared with those who did. In  
126 multivariate analysis, significant predictors of nonsurgical treatment were:

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127 history of moderate/ severe liver disease, stroke before surgical decision  
128 and S aureus etiology. The most common reason for lack of surgery was  
129 having a poor prognosis regardless of treatment (33.7%) like hemodynamic  
130 instability, death before surgery, stroke, and sepsis.

131 In patients with an indication for surgery, surgery was found to be  
132 associated with higher 6-month survival than no surgery. Patients with  
133 higher operative risk who underwent surgery had survival similar to  
134 patients with lower operative risk treated without surgery, whereas  
135 patients with higher operative risk who did not undergo surgery had very  
136 low survival (15).

137  
138 In summary, patients with IE requiring ICU present special problems. Defining the optimal  
139 timing of surgery requires a close interdisciplinary communication between all specialists.  
140 Response to initial treatment of hemodynamics and infection, presence and risk of  
141 complications, and subtle changes in organ function should be taken into account to  
142 outweigh risk and benefits of early versus delayed surgical treatment.

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223 Table

224 Most important informations regarding indications and timing of surgery in left-sided  
225 native and prosthetic valve endocarditis (from ESC Guidelines, 2015 - reference 4)

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227 Immediate 228 (same day) 229	Emergency surgery must be performed irrespective of the status of infection, when patients are in persistent pulmonary oedema or cardiogenic shock despite medical therapy.
230 231 Urgent 232 (within days) 233 234 235 236 237 238	<ul style="list-style-type: none"><li>- Severe valvular regurgitation or obstruction leading to heart failure</li><li>- Poor haemodynamic tolerance (high end-diastolic LV-pressure, moderate to severe pulmonary artery hypertension).</li><li>- Uncontrolled infection leading to intracardiac destruction.</li><li>- Increasing vegetation despite adequate antibiotic treatment.</li><li>- Persistent vegetations &gt; 10 mm after more than one embolic episode</li><li>- Endocarditis caused by fungi or multiresistant organisms (relative indication).</li></ul>
239 240 Delayed 241 (within weeks) 242 243	<ul style="list-style-type: none"><li>- Surgery should be considered depending on the tolerance of the valve lesion and according to the recommendations for the treatment of valve disease.</li></ul>
244 Neurological 245 complications 246 247 248 249 250 251	<ul style="list-style-type: none"><li>- no delay following a silent embolism or transient ischaemic attack if indicated because haemodynamic conditions or intracardiac destruction</li><li>- interval of 3-4 weeks in case of haemorrhagic transformation of ischemic lesions</li><li>- no evidence of beneficial effect of angiographic coiling in case of unruptured septic cerebral pseudoaneurysms</li></ul>

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