



## Editorial

# The different weight of indications for cardiac surgery in patients with infective endocarditis

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The optimal management of infective endocarditis (IE) relies on a close collaboration between a broad range of medical specialties, including cardiology, infectious diseases, internal medicine, neurology, intensive care, microbiology, and radiology. In addition, cardiac surgeons and anesthesiologists are involved in around 60–70% of cases - those who present theoretical indication(s) for cardiac surgery [1] - to evaluate the individual risk/benefit balance of this procedure. To confirm, or deny, cardiac surgery in patients with IE, is probably one of the most difficult medical decisions in modern medicine, as the benefits and the risks are often both elevated. Most of the times, the adequacy of the strategy that will be finally selected in agreement with colleagues, the patient, and his relatives, will be documented by survival, or death, the usual primary criteria in this decision-making process.

To assist these tricky medical decisions, clinicians may rely on international guidelines from Europe [2], and America [3]. The selection and the ponderation of indications for cardiac surgery are grossly similar in these two documents, as may be expected given their similar methods (i.e. systematic reviews of literature data, and experts advices), and timing (both guidelines were published during the fall of 2015). Indications for cardiac surgery have been categorized in three groups: heart failure, uncontrolled infection, and prevention of embolism. Risk stratification plays an important role for the selection of cases who will benefit from cardiac surgery, based on the estimates of the risks associated with an early surgical approach, as compared to a conservative

management. In addition, timing of cardiac surgery also plays an important role in the estimation of this risk/benefit balance. For instance, early surgery may be considered when a large vegetation is identified, for the prevention of embolism [1]. However, as the risk of embolism dramatically decreases following the start of appropriate antibiotics, the benefit of cardiac surgery will rapidly decrease, while the risks associated with cardiac surgery will remain grossly similar. Hence, the risk/benefit balance supports the indication of cardiac surgery for the prevention of embolism only if performed during the first days of medical treatment [1–3]. The situation is clearly different for the two other categories of indications for cardiac surgery in IE, i.e. heart failure, and uncontrolled infection, as these conditions usually tend to worsen with time, with a dismal prognosis in patients who cannot be operated. To take into account the time-dependent weight of the indication ‘prevention of embolism’, and the limited evidence supporting this indication, the European guidelines stated that ‘the decision to operate early to prevent embolism is always difficult’, and that, when indicated, ‘surgery must be performed very early, during the first few days following initiation of antimicrobial treatment’ [2]. The American guidelines used distinct wordings to express the strength of the indication, stating that early cardiac surgery ‘is indicated’ in patients with heart failure, or in case of annular or aortic abscess, while the words ‘is reasonable’, or ‘may be considered’ are used for indications related to the prevention of embolism [3].

The only randomized controlled trial that provides robust data on this decision-making process applies to a limited subset of patients with IE: young patients, with few or no comorbidities, and the combination of severe valvular regurgitation plus vegetation >10 mm [4]. The rest of the literature on this issue is based on observational studies, retrospective or prospective, all jeopardized by the following conundrum: among the large group of patients with theoretical indications for cardiac surgery, those who are finally operated are not the same as those who are denied (or who refused) cardiac surgery [5,6]. Unfortunately, even fancy statistical methods such as propensity-matched analysis are unable to erase potential biases, as illustrated by the major discrepancies found in the literature on this issue [7].

Colleagues from the Spanish Collaboration on Endocarditis, the ‘GAMES’ (*Grupo de Apoyo al Manejo de la Endocarditis en España*), brought an original brick in the wall, in this issue of International Journal of Cardiology [8]: Antonio Ramos et al. performed a large prospective multicentre cohort study of patients with IE managed in Spain during years 2008–2016, to analyze the relative weight of the 3 major indications for cardiac surgery, i.e. uncontrolled infection, heart failure, and

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prevention of embolism. Among the 538 patients of this cohort who had indications for cardiac surgery, but received medical treatment alone, the prognosis was better in patients with 'prevention of embolism' as the indication for surgery, with an in-hospital mortality of 54.7%, as compared to, respectively, 61.4%, and 75.6%, for those in whom cardiac surgery was theoretically indicated because of 'uncontrolled infection', or 'heart failure' ( $P < 0.05$ ). One year-mortality was also significantly lower when surgical indication was 'prevention of embolism', at 72.7%, vs. 76.7%, and 85.9%, respectively, when the indication was 'uncontrolled infection', or 'heart failure' ( $P = 0.016$ ). The reasons why surgery was not performed despite theoretically indicated were heterogeneous in this study, and most are also poor prognostic factors, whether or not surgery is performed: hemodynamic instability, neurological complications, and notable surgical difficulty being the top three.

Although this study suffers from potential biases inherent to its observational design, it provides original data in the field, that may be used as an additional tool in this complex decision-making process: depending on the nature of the indication(s) for cardiac surgery in IE patients, the prognosis of patients who are not operated significantly differs. This information may be of particular interest in the quite common borderline situations, when estimates of potential benefits, and risks of cardiac surgery, are close. The randomization of early cardiac surgery in clinical trials is particularly challenging, for obvious practical and ethical issues. Meanwhile, adequately designed observational studies, such as the one performed by Antonio Ramos and colleagues, will assist clinicians in the difficult decision of cardiac surgery in patients with IE.

#### Conflicts of interest

"The authors report no relationships that could be construed as a conflict of interest".

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