



## Infective endocarditis, is there a goal beyond antibiotics and surgery?

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In the vast majority of infectious diseases, the primary endpoint to evaluate an intervention relies on short terms variables and, when relevant, in-hospital mortality, or 28 days mortality. In most cases, these early targets are directly related to an intervention but could potentially fail to estimate a more global approach where other factors could modulate long-term prognosis. This problem was largely evaluated in sepsis survivors, although still largely debated, short prognosis has been related to corticoids [1], early goal-directed therapy [2], or delay in antibiotic administration [3–6]. Interestingly, in the past few years, several studies focused on late mortality in sepsis and identified a group of different factors associated with long-term mortality. These studies also included the evaluation of the quality of life, a key parameter to measure the consequences of an intervention at a population level. One of the first systematic reviews on the subject was published in 2010 and showed that patients with sepsis have ongoing mortality beyond short-term endpoints with a systematically impaired quality of life [7]. The authors suggested that future studies should include longer-term endpoints to understand the effect on targeted interventions. Similarly, the secondary analysis of 2 international randomized clinical trials in sepsis also focused on the evaluation of the quality of life [8]. Among the individuals who survived, one-third died and one-third did not return to an independent living by 6 months. These results were confirmed in other studies [9–11]. In a cohort of 94,748 adult sepsis survivors, several factors including comorbidities, prehospitalization dependencies were independently associated with long-term mortality [12]. More specifically, high body mass was associated with lower mortality at 28 days and even at 1-year; this phenomenon being known as “obesity paradox” [13,14]. All these studies suggest that all interventional trials should include extended follow-up care by primary physicians or dedicated teams [15].

Based on these principles, it seems obvious that in other specific infectious diseases, like endocarditis, a more global approach could also be proposed and makes sense. If we have a pretty clear idea of what is associated with short term prognosis [16–24], we miss data regarding long term survival in this category of patients. There is a strong rationale to explore this path; a Swedish cohort of 7817 episodes showed an

increased standardized mortality ratio from 1 to 5 years compared to the general population [25].

In a study including 212 patients, survival at 10 years was 50% and predicted mainly by early surgical treatment, age, and lack of congestive heart failure [26]. A prospective observational study with 193 patients showed that age, *Staphylococcus* spp, and contraindication to surgery predicted 6-month mortality [27]. An observational cohort with 328 patients who survived the active phase of endocarditis was followed for 5 years [19]. Compared with expected survival, this cohort had significantly worse outcomes with excess mortality observed in case of comorbidities, endocarditis recurrence, and history of aortic valve endocarditis in women.

In Spain, a multicenter prospective study collected 1804 consecutive cases of infectious endocarditis, the 1-year independent risks factors associated with mortality were age, neoplasia, renal insufficiency, and heart failure; surgery was protective [23]. Finally, a nationwide population-based study in Denmark analyzed 5576 patients treated medically or with surgery [28]. At 10 years, cardiovascular disease was the most frequent cause of death in both groups, surgery was also associated with a lower risk of dying of heart failure.

Globally, all these studies show that infective endocarditis patients compared to the general population have an increased long-term mortality, and most of the factors associated with this worse outcome cannot be controlled, like age, indication for early surgical treatment, or pathogen. In this issue of the European Journal of internal medicine, Durante-Mangoni et al. evaluated retrospectively 414 patients for a median of 39 months [29]. The multivariate analysis found peripheral arterial disease, hyperglycemia on admission, and a higher body mass index (BMI) to be independent predictors of long-term mortality (the last being completely the opposite of what was described in sepsis).

Identifying factors, like hyperglycemia and BMI, support, as stated by the authors, closer follow-up of cured endocarditis patients to improve long-term mortality. This personalized approach is beyond the treatment of the infectious episode and stands for an enlargement of the persons involved in multidisciplinary teams. International guidelines suggest that patients with complicated endocarditis should be evaluated

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by a multidisciplinary Endocarditis Team, including an infectious diseases specialist, a microbiologist, a cardiologist, imaging specialists, a cardiac surgeon, and, if needed, a specialist in congenital heart disease [30]. From this study and other diseases' experience, it seems urgent to set up a long-term follow-up with general practitioners and targeted specialists to improve the outcome of this disease. Gathering information on the long-term, implementing multidisciplinary approaches, networks between the hospital and the community represent the only option and challenge we are currently facing to improve the prognosis of these patients. This is probably one of the main gaps we will need to correct in the near future.

### Declaration of Competing Interest

The authors do not have any conflict of interest on the topic.

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