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EDITORIAL COMMENT

Enterococcus faecalis Bacteremia

Consider an Echocardiography, But Consult an Infectious Diseases Specialist*

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Enterococcus faecalis is the third most common etiology of infective endocarditis (IE) in industrialized countries, accounting for approximately 10% to 14% of cases in published studies (1,2). However, the perception of clinicians working in this field is that the incidence of *E. faecalis* IE has been increasing in recent years. In our experience, this has been accompanied by an increase in the median age of IE patients (**Figure 1**).

Enterococci are normal commensal bacteria in the gastrointestinal tract. They may be responsible for digestive or urinary tract infections, but they are also able to cause bacteremia by translocating through the intestine, gaining access to the lymphatics and bloodstream (3). *E. faecalis* IE usually affects elderly patients with comorbidities (4,5), a population of individuals who have an elevated risk of bacteremia originating from the digestive or urinary tract. Thus, it is not surprising that enterococci might be the first cause of IE after transcatheter aortic valve replacement (6).

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The clinical manifestations of *E. faecalis* IE are often nonspecific, and fever might be unnoticed until admission or even absent, so a high index of suspicion is needed to diagnose the infection. In this context, Dahl et al. (7), in this issue of the *Journal*, conducted a prospective multicenter study in which they performed echocardiography on 344 consecutive patients with *E. faecalis* bacteremia and found a 26% prevalence of definite IE after the IE team discussed every case. This percentage may seem very high compared with that of previous studies (4% to 12%) (8-10), but it is the first time that echocardiography has been performed systematically and highlights the need for active surveillance for IE in patients with *E. faecalis* bacteremia. However, although this finding is highly relevant, it is still unknown if it is generalizable to other populations. For example, we do not know if the Danish population is similar to Mediterranean populations. Second, it is possible that there is an effect of the center because community hospitals have different patient profiles than those of tertiary hospitals. It is possible that in the former, there is a greater proportion of patients with community-acquired *E. faecalis* bacteremia (who are at a higher risk of developing IE), while in the latter, there is a greater proportion of patients with nosocomial bacteremia associated with medical procedures. At Hospital Universitari Vall d'Hebron, a tertiary center including all medical and surgical specialties and serving a population of 500,000 inhabitants, every patient with bacteremia is prospectively evaluated by an infectious diseases (ID) specialist; 79 cases of *E. faecalis* bacteremia were detected in 2018 (50% more than in the Dahl study, proportionally), and IE was diagnosed in 11 cases (14%).

As occurs when cancer screening programs are initiated, if echocardiography is performed systematically, more cases are expected to be diagnosed. However, it is possible that in the case of small lesions, it is difficult to differentiate between IE and a degenerated valve. However, even eliminating the 23 patients with vegetations <5 mm, the prevalence of IE was still 20%. In any case, given the mortality

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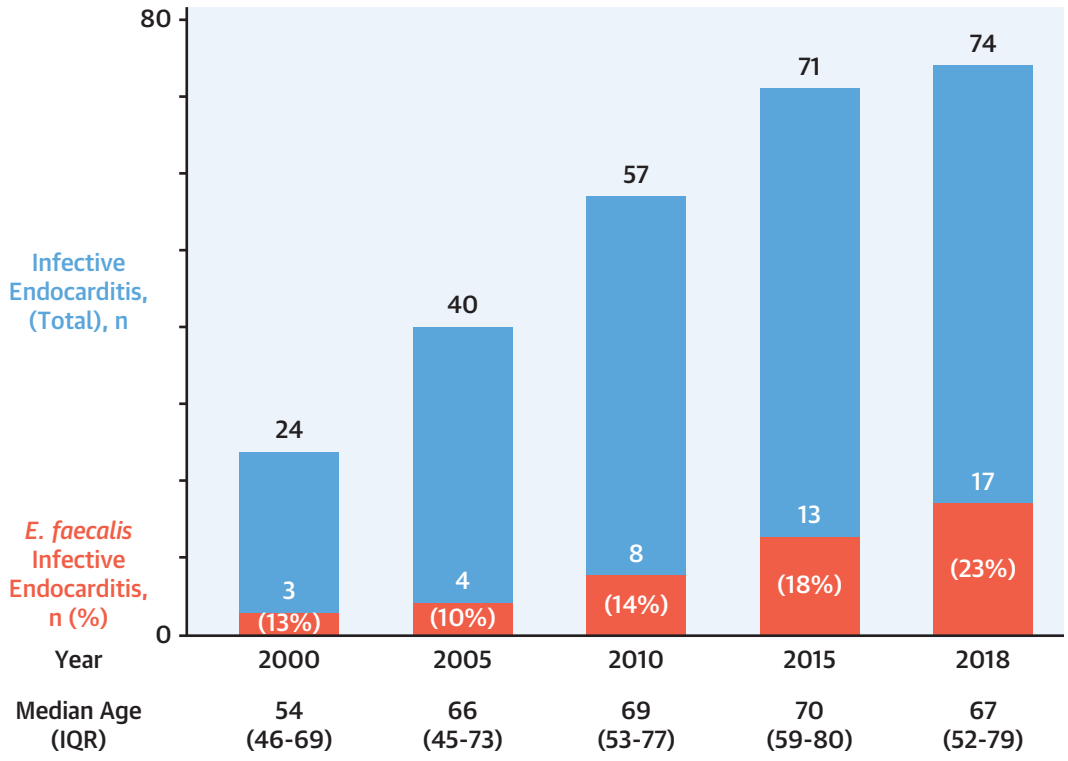
FIGURE 1 Rate of *Enterococcus faecalis* Infective Endocarditis at Hospital Universitari Vall d'Hebron



Percentage of patients with infective endocarditis caused by *E. faecalis* with respect to the total number of patients with infective endocarditis treated at Hospital Universitari Vall d'Hebron between 2000 and 2018 and the median age of infective endocarditis patients in the same period. IQR = interquartile range.

rate associated with untreated IE, we agree that it is better to overtreat than to fail to treat.

One of the strengths of the study is that the endpoint was very restrictive. As recommended by the 2015 ESC guidelines (11), all cases were discussed by an expert team, and any possible cases were not counted as cases of IE. As a result, the prevalence of IE could be even higher than that reported. The statistically insignificantly higher risk of recurrence in the group without IE than in the group with IE (7% vs. 4%) suggests that this may be the case. Unfortunately, control blood cultures were not mandatory after finishing antimicrobial therapy. Considering the low expressivity of some episodes of *E. faecalis* bacteremia/IE, this is an important limitation. On the other hand, the distinction between relapse and reinfection requires microbiological analysis of both strains to determine whether they are the same.

It was not the objective of the Dahl et al. (7) study to identify those patients who do not need to undergo echocardiography. However, 74% of patients with *E. faecalis* bacteremia did not have IE, and in patients with low (0 risk factors) and moderate levels of risk (1 to 2 risk factors), the prevalence of IE were 3% and 14%, respectively. Similar to what occurs in *Staphylococcus aureus* bacteremia (in which the risk of IE is elevated), an echocardiogram might not be recommended for all patients, and the decision to perform an echocardiogram should be individualized on a case-by-case basis (12–14). This decision is the one in which the ID specialist plays an important role.

The risk factors for *E. faecalis* IE identified in this study are not new. The same weight was assigned to each one, but in clinical practice this is not accurate. For instance, IE is an endovascular infection, so the demonstrated absence of continuous bacteremia has a very high negative predictive value. Likewise, polymicrobial bacteremia including *E. faecalis* suggests an abdominal focus. In our experience, true polymicrobial IE is very uncommon (4 out of 1,012 cases consecutively treated since 2000). Unfortunately, in

daily clinical practice, the evaluation of patients with *E. faecalis* bacteremia is challenging. *E. faecalis* bacteremia presents in so many varied forms that a considerable degree of expertise is needed when evaluating these patients. Thus, in our opinion, the decision to perform an echocardiogram is just another factor to consider in the clinical context. However, if the decision to perform an echocardiogram is made, it is important to bear in mind the low diagnostic performance of transthoracic echocardiogram in detecting vegetation.

Future studies should verify whether the percentage of endocarditis in *E. faecalis* bacteremia identified in this study is generalizable to different populations, and the NOVA and DENOVA scores (8–10) should be validated with the new available data (7). However, a score would never replace clinical judgment. As the complexity of the characteristics of our patients grows, teamwork and the multidisciplinary assessment of each case becomes more necessary.

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