

Bacteremia and sepsis

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Enterococcus spp. and *Streptococcus* spp. bloodstream infections: epidemiology and therapeutic approach

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ABSTRACT

Streptococcus spp. and *Enterococcus* spp. are frequent etiologies of bloodstream infection and endocarditis. In recent years, the incidence of *Enterococcus* spp. has been increasing, especially with nosocomial involvement, and with a high mortality rate. In this entity, the risk of endocarditis and its relationship with colorectal neoplastic pathology remains to be clarified, in order to establish indications for echocardiography and colonoscopy. In the case of *Streptococcus* spp., the risk of endocarditis depends on the species and the mortality rates are usually lower. Finally, in recent years, the treatment of endocarditis has been directed towards oral consolidation regimens and new long-term antibiotic treatments.

Keywords: Bacteremia, bloodstream infection, *Enterococcus faecalis*, *Streptococcus* spp. epidemiology, endocarditis

INTRODUCTION

Streptococcus spp. and *Enterococcus* spp. are a group of Gram-positive cocci that typically grow in chains or pairs. Both groups are commensal from human mucosa of the respiratory or the intestinal tract.

The genus *Streptococcus* spp. includes a wide variety of species that have been classically divided into six groups based on phylogenetic relationships. Currently, they are usually identified and classified by MALDI-TOF technique which has a high sensitivity and very low false positive rate.

The genus *Enterococcus* spp. was separated from *Streptococcus* in 1986.

EPIDEMIOLOGY OF BACTEREMIA AND INFECTIOUS ENDOCARDITIS

Enterococcus spp. bacteremia

Enterococcus spp. are the causative microorganism of 10% of all bloodstream infections (BSI) and constitute the third cause of Gram-positive BSI in Europe with a incidence of 7-19/100.000 person-years [1], after *E. coli* and *S. aureus*. This pathogen is more related to healthcare acquisition and it frequently affects elderly, fragile and immunocompromised patients [2].

More than two thirds of this bacteremia are caused by *E. faecalis* while *E. faecium* causes less than one third of them. The focus of the BSI is different depending of the aetiology: in *E. faecalis* a urinary infection is the most usual, while in *E. faecium* it is an abdominal or unknow focus, with more relationship with nosocomial infections [2]. Furthermore, endocarditis is also more frequent in *E. faecalis* bacteremia (90% of enterococcal endocarditis are due to *E. faecalis*) [3,4].

It is also important to notice the growing detection of vancomycin-resistant enterococci, much more frequent in *E. faecium*, especially among nosocomial infections [5].

In a percentage varying from 5-20%, enterococcal bacteremia can be associated to infectious endocarditis (IE), especially among older patients [2,4]. In recent years, these pathogens are becoming more common, and in last published series enterococcal IE is the third main cause of IE (15-30%) [2]. The indications of echocardiography in these patients have not been clarified at present. Scores such as NOVA and DENOVA scores which can predict the risk of endocarditis have been developed, and therefore, the indication of echocardiography [3]. However, further validations are needed to standardize these scores.

The mortality of these BSI and IE is around 20% [6], strongly influenced by risk factors of the patients. It is higher among *E. faecium* bacteremia, especially in vancomycin-resistant enterococci.

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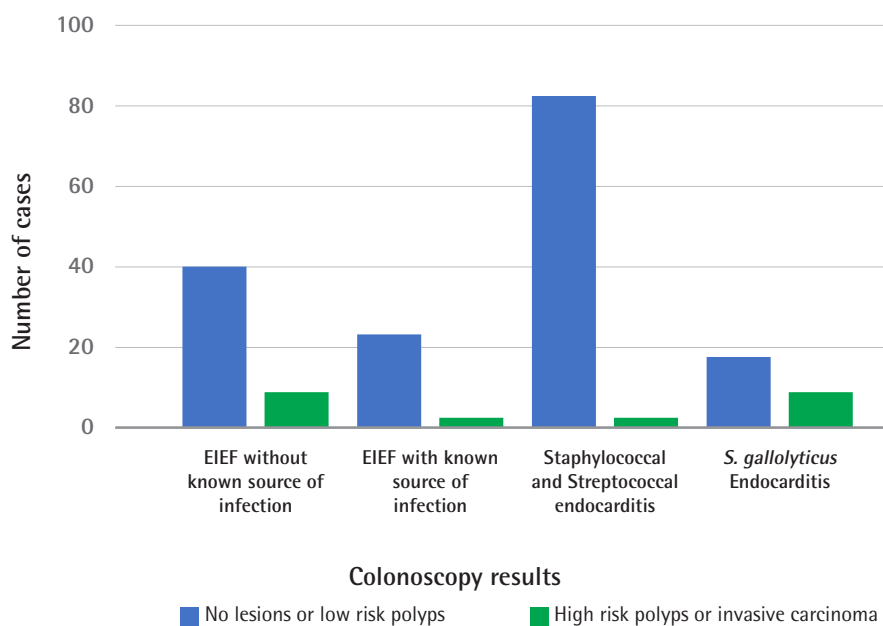


Figure 1 Data from retrospective study in Hospital Universitario y Politécnico La Fe, Valencia, 2010–2022

Streptococcus spp. bacteremia

Streptococcus spp. group is also a frequent microorganism involved in BSI. Bacteremia can be associated to IE in a different proportion depending on the specie, from 0–48% with an average of 7,1% [7]. IE is more probable in *S. mutans*, *S. gordonii*, *S. sanguinis* and *S. gallolyticus* (with a prevalence of more than 30%) and much less probable in *S. pyogenes* and *S. pneumoniae*. Recently, with the use of new diagnosis techniques for classification of streptococci, *S. tigurinus* has been described as a new species which has also frequently been related with IE [8].

It is also important to notice that bacteremia for *S. anginosus* is mostly related to abscesses and it is rarely a contaminant when isolated from blood cultures [9]. For this reason, if *S. anginosus* is detected in blood cultures, antibiotics for anaerobic bacteria should be considered.

The mortality rate of streptococcal BSI and IE depends also on the specie between 5–20% [6,7].

RISK OF COLORRECTAL PATHOLOGY

In the pathogenesis of BSI, the need to look for the source exists. It is mostly related to with intravenous catheters, but in some species, such as *S. gallolyticus* or *E. faecalis*, it can be related to colorectal lesions.

In the case of *S. gallolyticus*, this relationship was first described in 1974 and it has been widely studied [10]. For this reason, current American and European guidelines of IE indicate systematically colonoscopies when IE by this microorganism is diagnosed.

In the case of *E. faecalis*, this relationship has not been established clearly and doubts remain of when to indicate colonoscopies in these patients. In some recent studies it has been suggested that patients with an unknown focus of the infection have a higher probability of colorectal lesions than patients with known focus, most commonly urinary focus [11,12].

However, there is a need for further prospective studies to establish general recommendations.

TREATMENT

The initial management of BSI and IE must be intravenous. However, there are recent studies that support early switching to oral antibiotics with non-inferior results [13,14].

In *Streptococcus* spp. bacteremia there is a retrospective study which pleads for a short period of intravenous antibiotics (3–5 days) and early switching to oral antibiotics. However, the streptococci were mostly *S. pneumoniae* and pyogenic streptococci and bacteremia were non-complicated, so these results need further studies to be generalised.

On the other hand, the antibiotic management of IE has always been based on long periods of intravenous antibiotics (6 weeks). In the last few years, it has been suggested that IE could be managed with initial intravenous antibiotics followed by oral antibiotics if the evolution has been favourable. In this regard, the POET trial was first published in 2022 [13] with no difference in long follow-up with oral or intravenous antibiotics in IE patients.

Moreover, due to the increasing age of the patients who are being diagnosed with IE in the last few years, it is becoming more frequent for patients not to be candidates for surgical intervention, despite surgery is indicated. For this reason, long-term antibiotics have been proposed and some new long-action antibiotics are gaining importance in this matter. These antibiotics, dalbavancin and oritavancin have been studied mostly in consolidation of IE with good results. The doses have not yet been fully clarified and differ between different trials [15,16].

HIGHLIGHT POINTS

- IE prevalence among streptococcal bacteremia depends on the streptococci specie
- *E. faecalis* bacteremia is frequently associated with IE, it is necessary to establish clear indications of which patients should undergo an echocardiography
- *E. faecalis* IE seems to be associated with colorectal pathology, but less frequently than *S. gallolyticus*. It remains unclear when to indicate a colonoscopy and it may depend on the existence of a source of infection
- Treatment of IE is changing and there are recent studies which defend oral consolidation therapy
- The rise in average age of IE patients does not allow surgery in many cases, which forces them into a long-term antibiotic period. New long-action antibiotics will be a good option to the ambulatory management of these patients.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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