



Infective endocarditis in the 21st century

Infective endocarditis (IE) is a consequence of the localized or systemic diffusion of pathogens, generally bacteria or fungi, in the heart (1,2). Complications of heart valve endocarditis (HVE) develops in approximately from 1% to 43% of patients (3-5). Development of any degree of valve regurgitation in patients with LV dysfunction have a higher mortality risk than those without valve regurgitation (6). This fact alone remains the primary driver for surgery in patients with HVE.

The management of HVE in the 21st century has experienced considerable evolution in relation to the changing patients risk factor profile, demographic characteristics, and the etiology (1,7-9). Higher-risk patients currently include those requiring prosthetic valve replacement, hemodialysis, venous catheters or persons under immunosuppressive therapy as well as intravenous drug users. Moreover, another important concern is represented by the emerging field of cardiac implantable electronic devices (CIEDs) and the transcatheter valve procedure (1,2).

On the other side, the continuing improvement of diagnostic technologies is improving the management of HVE providing detailed information to rapidly take therapeutic decisions. Besides, echocardiography, new advancements in other imaging methods have proved effective in improving HVE management and guide surgical strategy. For example, MRI is useful because it allows to precisely locate abscess cavities especially if a prosthesis is already implanted while the CT imaging associated to metabolic imaging using 18-fluorodeoxyglucose positron emission tomography guarantees a diagnosis both for the embolic complications and the morphological characteristics of the lesion (10-15).

In high-income countries, IE occurs primarily in the population over 65 years of age and is sustained by virulent staphylococci. Staphylococcus species and coagulase-negative staphylococci (CoNS) (e.g., Staphylococcus epidermidis, Staphylococcus lugdunensis, and Staphylococcus capitis) have superseded the most common strains of penicillin-sensitive streptococci, typical of the 20th century. However, streptococci remained a pathogen still dangerous in low-income countries (7,16). The lack of randomized trials and the conflicts among European and American guidelines and professional societies recommendations regarding many aspects, such as surgery timing and valve substitutes (11,17), complicate the management of these worrisome infections.

Furthermore, staphylococcal contamination is increasingly characterizing nosocomial infection, which are additionally burdened by antibiotic multiresistance. These concerns have not been resolved by the introduction of 2 vaccines, which unfortunately have failed to show safety and effectiveness in Phase III clinical studies. The first vaccine showed unfavorable results in the prevention of *S aureus* bacteraemia in patients undergoing hemodialysis, while in the second has been associated to increased mortality in patients undergoing median sternotomy who had a postsurgical staphylococcal infection (18,19). Probably a more specific selection of high-risk patients could better assist preventative medicine research. Individuals most at risk of HVE are those who live more precarious socio-economic conditions and who do not have dental care, intravenous drugs users or alcohol abuser at risk for cardiovascular disease, and individuals with previous cardiac interventions for the treatment of congenital heart disease. It would be interesting to evaluate the effect of a new composite vaccine targeting 5 components of *S aureus* on these populations, considering the already promising results in preclinical models (20).

The increased use of long-term intravenous lines and invasive procedures for CIEDs has determined a significant rise in the rate of both left and right side endocarditis, according to the type of device used (21-23). The complications secondary to implantation of CIEDs have also increased and the cost of management of these complications is estimated at over \$15,000 per patient (24).

The opinion of the surgical community on the best timing to perform an operation for IE is not univocal. While some prefer to take advantage of a two-weeks “cool down” period with antibiotic treatment, others have shown no significant difference in 30-days and 1-year survival in patients undergoing early surgery (within 48 hours) compared with medical therapy (9,25), especially in case of prosthetic valve endocarditis (PVE) (26). The only contraindication to an early intervention is the presence of a neurological complication with potential cerebral hemorrhage (27).

From the surgical perspective several consideration should be made regarding the most adequate technique and valve substitutes to be used in different conditions. Infection localized to valve leaflet might benefit from isolated vegetectomy, while involvement of the valves and nearby structures would require more extensive tissue debridement and replacement with

prosthetic materials. In the case of significant involvement of the aorto-mitral continuity or periannular abscess, homograft could be used, especially in patients in which the risk of re-infection is a concern or in patients with contraindication to long-term anticoagulation (9,28).

For right sided endocarditis, the options of tricuspid repair or replacement are available. However, the staged procedure of valvectomy as bridge to replacement is an option in patients with persistent sepsis, abscess formation, ongoing drug use, and poor compliance to rehabilitation programs (29). This procedure could indeed represent an acceptable initial bridging therapy for tricuspid valve endocarditis giving time to identify candidates for staged valve replacement (30).

Nevertheless, the lack of specific randomized evidences in surgery for IE and the non-unanimous results from the currently available observational evidences still impede to reach definitive conclusions regarding the best management strategy and more investigations is required to clarify several aspects of IE treatment.

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