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Editorial

Reduced survival of young people with aortic stenosis after valve replacement

Menor supervivencia de los jóvenes con estenosis aórtica tras el recambio valvular

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Aortic valve replacement (AVR) is the only effective treatment for severe aortic stenosis (AS), and it might be expected that younger patients, who are normally at lower surgical risk than older patients, would have a survival rate similar to that of the general population. Nevertheless, recent studies have shown that this is not the case.[1] In one such study published recently in *Revista Española de Cardiología*, Hernández-Vaquero et al.[2] examined survival data collected over a period of approximately 20 years from almost 5000 severe AS patients aged 50 to 56 years who underwent AVR. The authors found that survival was lower than predicted for age and sex, with a 10% mortality rate linked to the underlying valve disease or related factors. The results in the whole study population were confirmed in a survival analysis of those patients without surgery-related complications, indicating that a satisfactory and complication-free intervention does not guarantee a life expectancy similar to that of the general population. While the cause is unknown, patients recovering from AVR surgery can have residual alterations related to their valve disease or to comorbidities, both of which can reduce life expectancy relative to the general population. The factors linked to long-term mortality risk in this study were female sex, age, atrial fibrillation, and comorbidities such as diabetes, kidney disease, and lung disease. Given the relatively young age of the study population, these findings are surprising; however, it may be that the risk factors underlying the appearance of AS also contributed to the lower than expected survival.

Although excess long-term mortality in a relatively young population surgically intervened for AS is surprising, a larger than expected reduction in survival among younger patients has been reported in other studies. For example, the SWEDEHEART study, with more than 23 000 patients, found a reduction in survival of more than 4 years in post-AVR patients younger than 50 years compared with a reduction of just 2.5 year among those older than 70 years.[1] The incidence of bicuspid valve in this and other studies was not reported; however, it is likely that a high proportion of patients had a bicuspid aortic valve, since stenosis in tricuspid aortic valves usually develops between the ages of 70 and 75 years. Diagnosis of bicuspid aortic valve can be difficult when the valve is highly calcified. Nevertheless, a study comparing AS patients with a bicuspid or tricuspid valve reported better postintervention outcome among those with a bicuspid valve, probably due to their younger age and their associated low incidence of comorbidities and risk factors.[3]

The higher mortality in the younger population might also be linked to complications arising from the implantation of the valve prosthesis. Although mortality in this group was higher among those patients fitted with a biological prosthesis, this was likely related to a worse baseline status or a higher number of comorbidities in these patients. Moreover, other studies have shown above-normal mortality among young adults receiving a mechanical prosthesis, with 8% of patients having prosthesis dysfunction.[4] Complications are not uncommon in patients fitted with a mechanical prosthetic valve and include thromboembolic phenomena, major bleeding, valve prosthesis thrombosis, structural deterioration, and reintervention, contributing to a 39% late mortality rate.[5] It is also likely that the smaller effective valve area of prosthetic valves compared with normally functioning native valves produces a mild left ventricular overload that could affect ventricular function over the mid-to-long term.

Several reports in recent years have demonstrated that AS is seldom an isolated valve disease and is frequently accompanied by systemic alterations such as arterial dysfunction and a high prevalence of hypertension and atherosclerosis.[6,7] Although valve replacement surgery substantially improves the prognosis of AS patients, uncertainty remains about the reversibility of AS-related left ventricular alterations, especially interstitial fibrosis, as well as other alterations such as left atrial dilatation and pulmonary hypertension. To take account of these issues, Généreux et al.[8] proposed a classification of cardiac involvement additional to the severity of the valve dysfunction. It would seem likely that the severity of cardiac involvement would determine whether valve replacement surgery could achieve complete or partial reversal of these alterations. However, Hernández-Vaquero et al. also detected a reduction in long-term survival among AS patients with no accompanying systemic alterations. The progressive obstruction of the aortic valve generates a pressure overload in the left ventricle, which triggers a hypertrophic response that acts to maintain wall stress and cardiac output over the years. Eventually, the ventricle decompensates through distinct phases, including myocardial fibrosis, myocardial injury, and cell death.

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There are 2 types of fibrosis: diffuse interstitial fibrosis, which is reversible after AVR, and focal replacement fibrosis, which develops later and is irreversible.[9] Histological and cardiac magnetic resonance studies have demonstrated that myocardial fibrosis is associated with higher total and cardiovascular mortality, post-AVR complications, and worse left ventricular remodeling.[10,11] Therefore, independently of other risk factors or comorbidities, each patient will likely have an individual predisposition to myocardial changes and the development of subclinical ventricular disease linked to poor long-term prognosis. Although current clinical practice recommendations are increasingly detailed, they are likely unable to identify this type of patient. The ongoing EVOLVED study is currently analyzing whether cardiac magnetic resonance-guided valve replacement can improve prognosis in asymptomatic patients undergoing this procedure.[12]

Thus, while the higher mortality rate in this nonelderly population may be attributable to comorbidities and complications arising directly from the prosthetic valve, it may also reflect cardiac involvement accumulating over years of unresolved severe AS. There is a clearly established indication for surgery in severe AS patients with symptoms or with left ventricular dysfunction. Current recommendations show a tendency to indicate ever-earlier intervention, and although the level of evidence is lower, current guidelines also recommend intervention in asymptomatic patients with low-flow AS or elevated biomarkers, especially if they are at low surgical risk.[13] Although AVR resolves severe valve dysfunction, secondary alterations due to cardiovascular involvement can persist after surgery. Moreover, being fitted with a valve prosthesis, whether mechanical or biological, is itself a minor complication that brings with it the risk of major complications related to the lower effective valve area, the risk of thrombosis, the risks associated with chronic anticoagulation, or the degeneration of biological prostheses. The study by Hernández-Vaquero et al. is limited by the lack of information on cause of death, but nevertheless provides important information on the outcome of AS patients after AVR, showing that prognosis does not always normalize to that of the general population. Future studies should analyze whether this survival deficit is attributable to prosthesis dysfunction, lifelong anticoagulation, or underlying factors related to the valve disease that persist after surgery.

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CONFLICTS OF INTEREST

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