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Editorial

Conduction Disorders and Transcatheter Aortic Valve. Clinically Relevant or Just a Mild Complication?

Trastornos de la conducción y válvula aórtica transcatéter. ¿Tienen relevancia clínica o son solo una leve complicación?

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INTRODUCTION

Ten years after the introduction of transcatheter aortic valve implantation (TAVI), an estimated 90 000 or more of these procedures have been performed around the world. This explosive growth of a new treatment can be explained by several factors: *a)* the large number of patients who are candidates for this approach, since aortic stenosis (AS) is the most common valve disease in adults and its incidence is rising; *b)* the advantage of resolving aortic valve stenosis without the need for surgery; and, finally, *c)* a favorable risk/benefit ratio.

Moreover, it is expected that TAVI will be used in the future to treat younger patients with fewer comorbidities. Doing so will require a reduction in the complications currently associated with the procedure, which include atrioventricular (AV) conduction disturbances (AVCD).

In this editorial, we discuss the available evidence on the frequency of new AVCD associated with TAVI, their causes and pathogenesis, the factors predictive of both AVCD and permanent pacemaker (PM) implantation, and the clinical consequences of these complications; finally, we discuss possible areas for improvement.

TYPES OF VALVES

Although new valves are being introduced,[1] nearly all the implantations performed to date–and hence the largest body of available information–involve 2 devices: the CoreValve® self-expanding device (Medtronic; Minneapolis, Minnesota, United States) and the SAPIEN® balloon-expandable valve (Edwards Life; Irvine, California, United States). The self-expanding prosthesis has a nitinol frame, is shaped like an hourglass, and measures between 52 mm and 55 mm. Its proximal portion is implanted into the left ventricular (LV) outflow tract, a technique that allows anchoring of the prosthesis. In contrast, the latest version of the SAPIEN® valve is made of cobalt chromium; it is cylindrical, its height ranges between 14 mm and 19 mm, and it is implanted at the level of the aortic annulus by means of an inflatable balloon.

INCIDENCE OF CONDUCTION DISTURBANCES

After the performance of TAVI, the most common conduction disturbance is left bundle branch block (LBBB), which occurs in 7% to 18% of patients with the SAPIEN® device and in 29% to 65% of patients with a CoreValve®.[2] In a series of patients who underwent CoreValve® implantation, Rubín et al.[3] found that 94% of the patients developed some type of AVCD. Among other factors, this variability is due to the different methods employed to evaluate the disorder, which range from a single electrocardiogram at the time of hospital discharge to continuous electrocardiographic and electrophysiological monitoring during prosthesis placement.

Unsurprisingly, the rate of permanent PM implantation also differs depending on the type of valve implanted: PM implantation ranges between 18% and 49% after CoreValve® placement and between 0% and 27% after SAPIEN® implantation. One noteworthy aspect is the significant variability in the rate of PM implantation even with the use of the same valve. For example, the mean frequency of PM placement in the Italian CoreValve® Registry was 19%; however, when participating centers were compared, the frequency ranged from 4% to 36%. This difference could be due to the diverse clinical characteristics of the patients, but there is also a possibility that the centers used different criteria to indicate this strategy. In fact, an analysis of decisions to perform PM implantation revealed that the indication was absolute in 66% of patients but was "prophylactic" in 34%.[4] Sudden complete AV block after TAVI has been identified as the cause of sudden deaths of uncertain origin occurring during follow-up. In accordance with clinical practice guidelines, this risk would justify PM implantation even in the absence of an absolute indication.

ETIOLOGY AND PATHOGENESIS

The AV node is located in the triangle of Koch in the interatrial septum; its lower portion penetrates the fibrous septum, becoming the bundle of His, and it emerges at the level of the aortic annulus between the noncoronary and right coronary leaflets. From there, it

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crosses the anterior fibrous trigone and divides into the right and left branches as it approaches the muscular septum. This position leaves it vulnerable to any mechanical injury produced from the interior of the aortic annulus, whether surgical or endovascular.

AVCD after aortic valve replacement surgery can be secondary to surgical injury during excision of the native valve, sutures in the region of the membranous septum, edema produced by surgical manipulation, or myocardial ischemia. In the case of TAVI, prolongation of the conduction times by the His-Purkinje system is mainly due to an intra-Hisian or infra-Hisian conduction disturbance.[5] This is consistent with a traumatic origin involving direct injury to the bundle of His as it passes through the aortic annulus. That is, the most probable mechanism of injury is the apposition of the metallic structure supporting the prosthetic valve on the bundle of His. This theory is corroborated by the high incidence of LBBB observed after implantation. Given that the fibers within the bundle of His itself can predetermine the configuration of the left or right branch, it is not surprising that the direct pressure exerted by the aortic annulus damages the fibers forming the left branch. The difference in the incidence of AVCD could be explained by the different features in the designs of the 2 prostheses, as well as their distinct sites of implantation (the CoreValve® penetrates further into the LV outflow tract and the SAPIEN® is limited to the aortic annulus).

PREDICTIVE FACTORS

Several reports have dealt with this subject and have identified a large number predictive factors, sometimes with markedly contradictory results, as is the case of septum thickness. Saia et al.[6] reported a very low rate of PM implantation (4%) with a septum thickness greater than 13 mm, whereas the rate was 44% with septa less than 13 mm thick. In contrast, demonstrated a relationship between an increased risk of PM implantation and a thicker septum.[7]

Other factors are thickening of the noncoronary leaflet, a small LV outflow tract, a smaller indexed effective orifice area following implantation, a large aortic annulus, mitral annular calcification, calcification at the level of the valve or in LV outflow tract, female sex, a reduced ejection fraction, and the presence of porcelain aorta.[8]

However, there are 3 factors on which the different published series appear to be in closest agreement: the previous existence of right bundle branch block (RBBB), the type of valve employed, and the depth of implantation of the prosthesis.

The existence of RBBB is one of the strongest predictors of new AVCD after implantation, and PM placement is required in more than 60% of these patients. This is unsurprising if we consider that the damage produced by the valve occurs at the level of the bundle of His, especially in the left branch, and that this is the only AV conduction pathway in the case of complete bundle branch block.

Assessment of predictive factors by the type of valve implanted is hampered by the absence of randomized studies comparing the SAPIEN® and CoreValve® devices. However, as previously stated, data from observational studies clearly demonstrate that the use of CoreValve® confers a greater risk for the development of new AVCD and for the need for PM implantation. As previously mentioned, this increased risk could be explained by design features and differences in the implantation technique.

Finally, although there is no definitive evidence of a causal relationship between the depth of the implant and the development of new AVCD, a number of studies indicate this association. Piazza et al.[9] found that the mean distance between the proximal end of the CoreValve® prosthesis and the lower edge of the noncoronary sinus was significantly shorter in patients who did not undergo PM implantation. These findings have been corroborated by other studies[2], both with the CoreValve® and SAPIENS® devices. Thus, when the lower edge of the prosthesis lay below the insertion of the mitral valve, 35% of the patients developed new onset LBBB compared with none of the patients with valve implantation above this point. In a study involving transesophageal echocardiography, Almería et al.[10] observed that the factors associated with the development of new AVCD were a prosthetic penetration into the LV outflow tract >12 mm and a contact surface between the prosthesis and the septum >90% in diastole. The introduction of technical changes in the delivery system for the CoreValve® prosthesis, allowing a reduction in the depth of device implantation within the LV outflow tract, has decreased the incidence of new AVCD.[11]

TIMING OF ONSET

Most AVCD occur during the procedure or within the following hours or days. In a study carried out in our center,[3] electrophysiological examination was performed before and immediately after CoreValve® implantation in 18 patients who underwent continuous monitoring of AV node conduction (AH interval) and infra-Hisian conduction (HV interval) during the entire procedure. The analysis demonstrated a prolongation of the AH and HV intervals, indicating an effect of the implant on both the AV node and the bundle of His. The majority of AVCD occur at 1 of 2 times: during valvuloplasty prior to device implantation or during device expansion.

It is equally–or even more–important to determine the maximum time at which an AVCD requiring PM implantation can occur, since the absence of AVCD immediately after TAVI does not rule out the possibility of the development of late disturbances. In contrast, some AVCD detected after TAVI are transient and disappear before hospital discharge in up to half of the patients treated with SAPIEN® and in one-third of those treated with CoreValve®. These findings suggest that the damage to the AV node and the bundle of His may be transient.

The majority of the AVCD occur within the first 6 days of implantation, but complete AV blocks have been reported to take place as late as 10 days after the procedure.[3] Therefore, identifying patients with a high probability of developing an AVCD and of requiring a PM is of the utmost importance. Mouillet et al.[12] analyzed "delayed" need for a PM (more than 24 h after TAVI) in patients without previous AVCD. The only independent predictor of the need for a PM was a prolonged QRS duration, and the authors concluded that patients with a QRS of less than 128 ms after TAVI have no risk of requiring a PM.

De Carlo et al.[13] have evaluated a conservative strategy in PM implantation. In a series of 275 patients who received a CoreValve® prosthesis, a PM was implanted only in those with persistent 3rd-degree AV block or other severe arrhythmias; in 14 patients with complete AV block immediately after TAVI that resolved spontaneously, no PM was implanted. After a 1-year follow-up, the authors concluded that this strategy had no negative effects on survival and, moreover, that in patients with new LBBB without severe bradycardia, prophylactic PM implantation to prevent sudden cardiac death is unnecessary.

CLINICAL CONSEQUENCES AND PROGNOSTIC IMPLICATIONS

The available information on the clinical consequences of the development of new AVCD following TAVI and PM implantation is limited and, in some cases, contradictory. In routine clinical practice, LBBB raises doubts as to whether it will progress toward

complete AV block requiring a PM or whether it will have a negative effect on ventricular function and prognosis. Houthuizen et al.[14] studied the impact of TAVI-induced LBBB on all-cause mortality during the follow-up of a cohort of 679 patients and found mortality to be higher among the patients with LBBB than in the remaining study population. However, in a series of 202 patients who underwent implantation of a SAPIEN® valve, Urena et al.,[15] showed that, although LBBB was associated with a significantly greater risk of AV block and PM implantation, it did not increase 1-year mortality. Importantly, there were no cases of sudden cardiac death during the follow-up period.

PM implantation is not free of complications, which increase with age, being recorded in 3.4% of patients older than 75 years and in 5.1% of those younger than 75 years. The most common complications are hemorrhages and hematomas, and both are favored by the dual antiplatelet therapy usually prescribed to these patients. It is for this reason that the timing of PM implantation and its relationship to the complications are so important. Schwerg et al.[16] analyzed this aspect and concluded that PM implantation on the same day as valve implantation is safe and does not increase the rate of complications compared with delayed PM placement.

Finally, Buellesfeld et al.[17] analyzed the possible impact of PM implantation on clinical outcomes. In a series of 353 patients who underwent TAVI, these authors compared the outcome in 3 groups: those who required a PM after implantation, those without PM, and those who had a PM prior to TAVI. After a 12-month study period, the mortality rate in the 3 groups was the same.

CONCLUSIONS

Transcatheter aortic valve implantation is frequently followed by the development of new AVCD and the need for PM implantation. The most probable cause is direct damage to the conduction system produced by the valve. The most robust predictive factors for the development of conduction disturbances are the existence of LBBB prior to TAVI, the implantation of a CoreValve® prosthesis, and the depth of the implantation within the LV outflow tract.

Although it was thought that there was risk of sudden cardiac death secondary to an AV block during follow-up, a belief that encouraged the practice of "prophylactic" PM implantation, this risk does not appear to have been confirmed, and a conservative approach to PM implantation does not have a negative impact on clinical outcome. Until further studies are carried out, it would seem reasonable to apply the indications for PM placement provided in the guidelines.

There is contradictory information on the clinical consequences of the conduction disturbances that develop after implantation. Thus, studies that shed light on this key unknown factor are necessary.

Future valves should be designed to minimize current limitations and avoid deep implantation, either through the structure of the prosthesis itself or through the introduction of delivery systems that allow implantation to be tightly controlled and, above all, enable the valve to be recaptured once it has been completely released and to be repositioned, if necessary. The technical features of the prosthesis, however, are only one of the possible areas for improvement. Other factors that would allow this technique to be used in a greater number of patients are better patient selection on the basis of clinical criteria, improved imaging techniques that would allow selection of the most suitable type and size of prosthesis in each patient, technical developments that would reduce vascular complications, and adjuvant techniques such as cerebral protection systems.

CONFLICTS OF INTEREST

Dr. Morís is a Proctor for implantation of the CoreValve® prosthesis and member of the Medtronic Advisory Board.

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