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As TAVI Population Expands, More Studies of Permanent Pacemaker Implantation Are Needed

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The occurrence of conduction disturbances and particularly high-degree atrioventricular block (HAVB) remains a frequent complication of transcatheter aortic valve implantation (TAVI) [1] and among the sub-optimal performances of the technique.

Despite the technological evolution of the new valves and the clinical experience acquired worldwide, the need for permanent pacemakers (PPM) implantation still occurs in more than 10% of cases. In particular, the rates of PPM after TAVI varied from 2% to 51% in 41 studies included in a recent meta-analysis [2], and PPM was the most common TAVI complication, with a pooled rate of 13%. Such events are obviously more relevant among younger patients, and as the indications to TAVI expand toward lower-risk and younger patients, the problem becomes more important.

The close proximity between the aortic valve and the conduction system explains the genesis of periprocedural conduction disturbances during TAVI. The left bundle branch's close relationship to the base of the interleaflet triangle separating the noncoronary and right coronary leaflets of the aortic valve and the great interindividual variability of the anteroposterior relationship of the atrioventricular node with respect to the apex of the triangle of Koch are the keys to understanding conduction disturbances after TAVI. Indeed, in the setting of TAVI, conduction disturbances result primarily from a direct mechanical insult to the conduction system associated with various degrees of edema, hematoma, and ischemia, as demonstrated by necropsy studies [3].

Some causes correlated to the damage to the conduction system have been identified, while in some cases this occurs in an unpredictable manner. Calcifications of the aortic valve, left ventricular outflow tract, and mitral annulus and the depth of prosthesis implantation have been associated with PPM after TAVI. Indeed, the mechanical damage to the conduction system created by the presence of the metallic components of the valve is one among the most commonly acknowledged explanations for the development of HAVB [4,5].

In this issue of *Cardiovascular Revascularization Medicine,* Oestreich et al. investigated the need for PPM implantation in a small consecutive series of relatively low-risk patients undergoing TAVI according to a previous exposure to corticosteroids, given for clinical reasons, independent of the TAVI procedure[6]. The authors reported on a single-center experience including 167 patients who were prospectively followed up to 30 days after valve replacement.

The authors have observed a protective effect among those patients under steroids (16, 10%) that suffered no interference between the conduction system and the valve after the implantation of the prosthesis, either balloon- or self-expandable. In fact, none of the patients who had received some active steroids, either by oral or endovenous means, in the previous days before TAVI needed a PPM implantation. Other patients, not exposed to this family of drugs, suffered major atrioventricular conduction disturbances in 18% of cases, and incidence that is perhaps higher than expected with the latest models of transcatheter valves. These data may simply reflect a very prudent behavior, as suggested by the implantation of PPM in some unclear cases, as such those where patients developed a new-onset persistent right and particularly left bundle branch block (LBBB) after TAVI, and the management remains highly controversial considering the current lack of specific guidelines.

New-onset LBBB occurs in 4%-65% of patients undergoing TAVI; 18%-65% with self-expandable CoreValve (Medtronic Inc, Minneapolis, MN) and 4%-30% with SAPIEN/SAPIEN XT valves (Edwards Lifescience LLC, Irvine, CA) [1].

In particular, the association of new-onset LBBB with the risk of HAVB or PPM at follow-up after TAVR has been evaluated in few studies, with a rate of patients with new-onset LBBB who developed HAVB ranging from approximately 8% in balloon-expandable valves [7] to 13% in self-expandable valves [8]. HAVB was reported as the indication for PPM in 47% to 95% of patients presenting new-onset LBBB after TAVR in different studies [7,9].

The authors, therefore, hypothesize a beneficial effect of corticosteroids in reducing the occurrence of HAVB due to the anti-

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inflammatory actions of the steroid drugs that are able to reduce the edema that follows to the traumatic tissue injury that the valve structures create to the cells around the conduction system.

Their hypothesis is supported by the well-known immediate and genome-mediated mid-term effects of the steroids and drives the attention toward an interesting therapeutic perspective that certainly deserves attention [10].

However, another small previous observation does not support the same conclusions, and the authors justify this discrepancy with the different time elapsed between the initiation of the steroid therapy and the valve implantation in their analysis compared to that of Havakuk et al. [11], which is actually not very different (more or less than one day before TAVI), but permits some room for speculation related to the late effects of the steroid therapy.

Apart from the possible or probable differences that a longer or shorter preventive therapy might introduce in the protection of the conduction system, it is, however, mandatory to underline that the series of patients reported in this article is certainly very small, and diluted in a quite long time frame, leaving a dominant role to the effect of chance as the most plausible explanation of these observations.

Another limitation of the present report is the relatively short length of the follow-up, limited to 30 days from the index procedure. In the recent MARE study [12], a multicenter collaboration implementing continuous cardiac monitoring for the detection of arrhythmic events, the investigators used implantable cardiac monitors for assessing the incidence of HAVB at 12-month follow-up. The study population consisted of 103 consecutive patients presenting with new-onset persistent LBBB following TAVI with either a balloon-expandable SAPIEN XT/3 (n=53) or self-expandable CoreValve/EvolutR (n=50). The authors found a high burden of arrhythmic events within 30 days post-TAVI. However, continuous ambulatory monitoring showed that approximately 40% of all arrhythmic events occurred between 30-day and 12-month follow-up, suggesting that such routine strategies are likely to fail in detecting a large proportion of arrhythmic episodes after discharge, which could potentially progress toward more dangerous conditions such as HAVB or severe bradycardia. Therefore, a longer follow-up is warranted to further investigate and characterize the potential long-term benefits of corticosteroids in patients undergoing TAVI.

Nevertheless, with these limitations in mind, the editors of the journal are to be commended for their provocative decision of publishing an article with weak bases but with strong potential for the development of future studies that, with practically no additional risk and cost, could investigate an alternative therapy with a logical rationale and an easy endpoint to test. This should serve as a stimulus for fueling new clinical research in a field that is rapidly reaching a large number of patients. Patients who due to the continuous technological advancement and team experience, have a longer life expectancy and, therefore, could be negatively affected by the artificial electrical stimulation of the heart that follows the permanent implantation of a PPM, an adverse effect that is worthy to minimize being by the technological improvements of the valve designs and implantation techniques, but also by an appropriate preventive and costless medical therapy.

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