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Prespective

Permanent Pacemaker Need after Transcatheter Aortic Valve Implantation: The Role of Cardiac Amyloidosis

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Abstract

Transcatheter Aortic Valve Implantation (TAVI) in patients with Aortic Stenosis (AS) and Cardiac Amyloidosis (CA) are discussed in this article. The aortic valve opening narrowing known as AS can cause reduced blood flow and, ultimately, left-sided heart failure. Patients who are at intermediate to high surgical risk can successfully treat AS with TAVI, a minimally invasive treatment. The development of conduction abnormalities, which may need the implantation of a Permanent Pacemaker (PPM), is one of the most common TAVI side effects. The article explores whether the existence of CA affects how frequently the need for PPM occurs after TAVI in patients with AS. Recent studies have demonstrated a considerable incidence of CA in individuals with AS. The discussion looks at how AS and amyloidosis are related, what causes conduction problems during TAVI, and how CA affects the prognosis of severe AS. The article might enhance our knowledge of the connection between CA and TAVI and, as a result, help us treat patients with these disorders more effectively.

Introduction

Aortic Stenosis (AS) is the narrowing of the aortic valve opening, causing restricted blood flow from the left ventricle to the aorta, which can eventually progress to left-sided heart failure. Transcatheter Aortic Valve Implantation (TAVI) is a minimally invasive procedure that can effectively treat AS in patients who are at intermediate to high surgical risk [1-3]. One of the most frequent TAVI complications is the formation of conduction disturbances, which may necessitate the implantation of a Permanent Pacemaker (PPM) [4,5]. Amyloidosis is a rare systemic disease caused by the extracellular accumulation of misfolded proteins in various organs [6]. Cardiac Amyloidosis (CA) is a subtype of amyloidosis characterized by the deposition of such proteins in heart muscles. Two main types responsible for CA are transthyretin amyloidosis (ATTR) and light chain Amyloidosis (AL) [7].

Recent studies that looked at patients who underwent TAVI and had Cardiac Amyloidosis and Aortic Stenosis (CA-AS) have shown a significant prevalence of CA in these patients [8], with reported prevalence rates ranging from 8.4% to 16% across different studies [9-11]. But among patients with paradoxical low-flow, low-gradient AS, it is thought that this number may be as high as 30% [12].

Given the high prevalence of CA in patients with AS, we aim to explore if the presence of CA increases the frequency of PPM after TAVI in AS. This article could help improve our understanding of the relationship between CA and TAVI, and ultimately lead to better management of patients with these conditions.

Discussion

Certain findings point to a connection between AS and amyloidosis. First, is that the prevalence of ATTR is known to be lower in noncardiac patients and tends to primarily affect older adult males [13], but the prevalence of AS-CA appears to be ten times higher, and it impacts both sexes almost equally [14]. Secondly, amyloidosis, which is detected by the findings of 99mTc-PYP imaging, are graded on a scale of 0 to 3, with 0 indicating no detectable amyloid and 3 indicating marked uptake. According to studies, AS-CA has a preference for grade 2/3 tracer uptake in AS, implying a causal link between AS and amyloidosis [14,15]. This may be due to significant shear stresses in AS that may contribute to increased TTR deposition through a mechano-enzymatic cleavage process [16]. The increased afterload brought on by AS may also prime the LV for amyloid deposition through increased extracellular matrix turnover, low-grade inflammation, chronic subendocardial ischemia, and ensuing cell death [16].

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With declining rates of complications over time, TAVI is a safe and efficient treatment for severe symptomatic aortic stenosis [17,18]. However, despite the use of some newer-generation transcatheter valves, the prevalence of conduction disturbances, such as high-degree atrioventricular block and new-onset left bundle-branch block, has not diminished and may even be rising [4,5,19,20].

During TAVI, the near proximity of the aortic valve to the conduction system may cause periprocedural conduction disturbances. The apex of the Koch triangle, which contains the atrioventricular node, is formed by the convergence of the Todaro's tendon, with the septal attachment of the tricuspid valve and the coronary sinus ostium making its base. The base of the interleaflet triangle that divides the noncoronary and right coronary leaflets of the aortic valve is connected to the conduction system, which emerges beneath the membranous septum on the left side [21-23]. According to necropsy studies, conduction disturbances in the context of TAVI are mainly caused by a direct mechanical insult to the conduction system that is accompanied by varying degrees of edema, hematoma, and ischemia [24]. Aortic stenosis has also been related to conduction disturbances caused by calcium deposition on the conduction system and left ventricular dysfunction, in addition to the mechanical interaction between the transcatheter valve and the conduction system described above [25]

Due to conduction abnormalities, PPM was the most prevalent TAVI complication, with a combined rate of 13% in an analysis combining 49 studies involving 16063 patients [26]. The rates of PPM after TAVI ranged from 2% to 51% in 41 studies analyzed in a recent meta-analysis [27]. The effects of CA on the prognosis of severe AS have been the subject of conflicting findings in earlier research. Initially, TAVI was believed to be risky in patients with ATTR-CA [28], but recent research has shown that it greatly improves outcomes, with post-TAVR survival rates comparable to those in patients with AS alone [14,29].

Disputed results on the frequency of PPM after TAVI in CA-AS vs AS alone are also seen. According to research on 204 patients, of the total number of patients undergoing TAVI, 28 needed pacemakers, with 19% of them being in the CA-AS group and 13% being in the AS alone group. The difference between the two categories was not significant [11]. Further, a meta-analysis including 4 studies including 735 patients and 113 PPM insertions, reported an odds ratio of 1.66 ($p<0.05$), which suggests that patients with both AS and CA are 1.66 times more likely to require pacemaker insertion after TAVI than patients with AS alone [30]. The pathophysiology of cardiac amyloidosis could be used to explain the observation that patients with both AS and CA had a higher incidence of pacemaker insertion. This disease directly impacts the heart's conduction system, causing degeneration and a higher risk of atrioventricular blocks, which may necessitate the implantation of a permanent pacemaker. Therefore, it is not surprising that patients having TAVI have a higher risk of pacemaker insertion when both AS and CA are present.

It is still unknown whether adopting new implantation methods, like the cusp overlap technique or using prostheses with lower radial forces and a supra-annular position, could lessen the risk of pacemaker implantation, and more research is needed to confirm this. Clinical trials that are currently underway, including the ATTRact-AS (NCT03029026) and AMYLOCARTESIAN (NCT02260466), will provide more information on the prevalence and prognostic consequences of CA for AS patients.

Conclusion

In conclusion, it should be noted that the presence of cardiac amyloidosis and aortic stenosis together is a frequent finding and is linked to a higher risk of conduction problems and future pacemaker insertion after TAVI. Although the pathophysiology of this connection is not fully understood, some potential contributing factors include increased mechanical stress, amyloid deposition in the conduction system as a result of high shear stresses and afterload in AS, as well as the direct mechanical insult during TAVI. To determine the best management approaches for patients with both illnesses, as well as to better understand the link between AS and CA, more study is required. The ultimate objective is to enhance the outcomes and quality of life for these patients through prompt diagnosis, suitable therapy, and careful observation of potential consequences.

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