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Bicuspid Aortic Valve - Current and Future Management Perspectives

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ABSTRACT

Bicuspid Aortic Valve (BAV) is the most common congenital heart defect, characterized by the presence of two cusps of the valve instead of three. This defect leads to hemodynamic disturbances, potentially resulting in serious health complications. BAV often remains asymptomatic for a long time, with symptoms eventually arising from valve degeneration along with the remodeling of the heart and aortic root, which are consequences of the initial condition. The aim of this study is to compile information regarding the defect, current treatment options, and potential new therapeutic directions. The classical approach for treatment is surgical aortic valve replacement (SAVR), which involves replacing the abnormal valve with either a mechanical or biological prosthesis through access via sternotomy. Mechanical valves are characterized by their longer lifespan but require ongoing anticoagulant therapy, whereas biological valves do not necessitate anticoagulation, although they tend to have a shorter durability. An alternative to SAVR is minimally invasive transcatheter aortic valve replacement (TAVR), which offers a shorter recovery time but limited long-term durability data restricts its use in younger patients. Other treatment options include the Ross procedure and valvuloplasty procedures, which may serve as viable solutions for pediatric patients. Despite the availability of different treatment methods, the selection of an appropriate therapeutic strategy remains a challenge, as each option carries distinct benefits and risks. Patient education plays a crucial role in the decision-making process, helping to alleviate anxiety and improve treatment outcomes. Emerging fields such as medical bioengineering might offer promising solutions in the future for patients with BAV.

KEYWORDS: bicuspid aortic valve, heart defect, cardiovascular surgery, valve prostheses

INTRODUCTION

Bicuspid aortic valve (BAV) is a congenital heart defect characterized by the presence of two cusps of the aortic valve instead of the usual three. It is the most common congenital heart defect(1). In this condition, the abnormal structure leads to hemodynamic and morphological disturbances that can result in serious health complications, including death. With modern imaging techniques, we are able to detect BAV at a very early stage of life, including prenatally (2). This allows for the identification of patients and monitoring of their condition, enabling timely interventions if necessary. Currently, there are numerous therapeutic options available. Each of these offers the patient a slightly different benefit profile, yet each is not without disadvantages. The therapeutic process itself can be associated with anxiousness in the patient, and this anxiety may be exacerbated by the necessity to make decisions regarding the type of procedure. Appropriate patient education can reduce this anxiety and its consequences, as demonstrated in studies (3–5). Inspired by above, the aim of this work is to summarize the knowledge regarding the treatment options for BAV, along with a general overview of the disease, as well as to consider potential future directions in its management.

EPIDEMIOLOGY

The prevalence of bicuspid aortic valve (BAV) is estimated to be between 0.5% and 2%, with a higher incidence in males (approximately 3:1 compared to females) (1). In females, BAV more frequently manifests as stenosis,

whereas in males, regurgitation is more common (6). Sex-related differences also pertain to various complications associated with the defect. BAV is associated with a 17-fold increased risk of endocarditis (6), with the incidence of endocarditis among patients with this anomaly being 4.5% in males and 2.5% in females (7). Aortic dissection is a rare yet serious complication linked to BAV, with male sex identified as a risk factor (8). Despite the low frequency of this complication, BAV increases the likelihood of dissection by up to 8 times compared to the general population (8).

CLASSIFICATION

There are several classifications of types of bicuspid aortic valve (BAV) (9). One of the most well-known classification systems was developed by Sievers and Schmidtke (10). This classification distinguishes three main types of BAV: type 0, type 1, and type 2. In type 0, there are two cusps with the absence of raphe. Type 1 is characterized by the presence of a single raphe, whereas type 2 features two raphae between the cusps. Depending on the location of the raphe (or the cusps themselves in type 0), subtypes are identified. Furthermore, the researchers proposed a third subclassification that defines the functionality of the valve. The above description of the classification is somewhat simplified, as the goal is merely to outline the complexity of the topic at hand. A schematic representation of the classification is presented in Figure 1. Based on the aforementioned classification and previous observations by researchers, it can be noted that the most commonly occurring type of BAV is type 1(11), with the raphe most frequently located between the left and right cusps (approximately 80%), considerably less often (17%) between the right and non-coronary cusps, and least frequently between the left and non-coronary cusps (2%) (12).

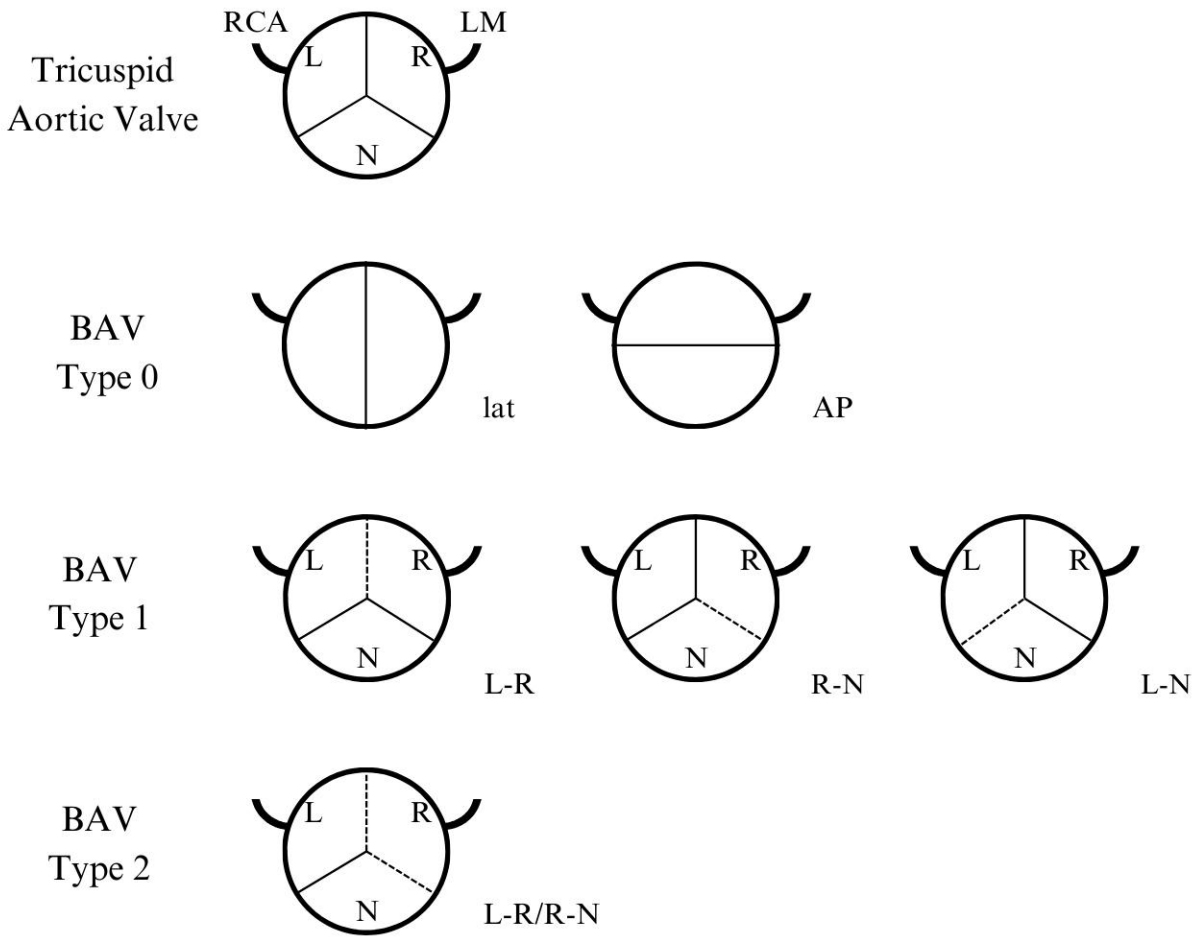

Figure 1. Schematic representation of Sievers and Schmidtke classification (10), including tricuspid aortic valve and three types of bicuspid aortic valves in the transverse plane. The solid line indicates the normal separation of cusps, while the dashed line corresponds to the presence of a raphe. Type 0 with vertical or horizontal cusp alignment is visible. Type 1 includes subtypes L-R, R-N, and L-N, indicating different raphe locations, and Type 2 features two raphes. AP, anterior-posterior; lat, lateral; L, left coronary leaflet; R, right coronary leaflet; N, non-coronary leaflet; RCA, right coronary artery; LM, left main (coronary artery).

CLINICAL PRESENTATION

A significant proportion of patients with bicuspid aortic valve (BAV) remain asymptomatic for a long period. It is estimated that 2 in 100 children present with clinically significant valve disease by adolescence (13). Over time, as valve degeneration progresses, symptoms such as anginal pain, syncope, and exertional dyspnea appear. These symptoms are often accompanied by complications such as dilation of the aortic root, which, according to reports, begins as early as childhood (14). These findings suggest that patients should remain under continuous cardiologic surveillance, as the risk of dissection increases with the enlargement of the aortic root (15). Therefore, asymptomatic patients, under specific morphological parameters seen in transthoracic echocardiography (TTE), should also undergo surgery (16). At this stage, patient education regarding the disease is crucial.

DIAGNOSTICS

Transthoracic echocardiography (TTE) is the preferred method for diagnosing and monitoring patients with bicuspid aortic valve. In some cases, extending the diagnostic process with magnetic resonance imaging (MRI) or CT angiography is recommended, as these methods can provide clinically relevant information, especially when TTE remains inconclusive (16). Currently, there are no laboratory markers for the disease in asymptomatic patients. Matrix metalloproteinases (MMPs) appear promising and are the subject of numerous studies (12,17,18). These proteins have been indicated as potential predictors of ascending aortic dilation in patients without significant valve dysfunction (12).

TREATMENT METHODS

Currently, the only form of treatment is surgical intervention. There are two main types of procedures: traditional and minimally invasive. In addition to the type of procedure, there is also a choice of materials to be used for the new valve.

Surgical Aortic Valve Replacement (SAVR)

SAVR is the traditional method of aortic valve replacement via median sternotomy. During the procedure, cardiopulmonary bypass is established using a machine for extracorporeal circulation. The heart is placed in a state of cardiac arrest, allowing the procedure to be performed safely and precisely. The next step is the replacement of the valve. Currently, two types of valves are used in SAVR procedures: bioprosthetic and mechanical valves. In the case of bioprosthetic valves, there is no need for long-term anticoagulants, unlike in mechanical valves. Unfortunately, bioprosthetic valves have lower durability, and over time, the risk of reoperation increases, which is higher compared to mechanical valve implantation (19). It is important to note—and patients should be made aware—that while mechanical valves have longer durability, reintervention may still be required in these cases, for example, due to perivalvular leakage (20). Because of the need for anticoagulants, the risk of stroke and major bleeding events is also higher with mechanical aortic valves. Anticoagulants also have embryotoxic effects, with warfarin embryopathy occurring in approximately 6.4% of live births (21). Interestingly, in terms of survival, a 15-year follow-up found no significant difference, despite a shorter reoperation-free interval in patients with bioprosthetic valves (22). Beyond mortality, a crucial factor in the choice of valve type is the quality of life of patients. Although one might assume that taking oral anticoagulants would decrease quality of life, certain studies show that quality of life does not significantly deteriorate after valve implantation, whether the valve is bioprosthetic or mechanical (23–26). Considering the advantages and disadvantages of different valve types, the decision is made by taking into account various factors, such as age, lifestyle, reproductive plans, and the patient's attitude toward anticoagulation therapy. An important consideration remains the potential for reoperation in the event of dysfunction of the newly implanted valve. In the case of a biological valve implantation, there is a physical possibility of subsequent transcatheter aortic valve implantation (TAVI), a minimally invasive procedure explained later in this article. During TAVI, the new valve is placed over the old, dysfunctional valve, which is pushed aside, thus creating space for the new structure. A mechanical valve is a structure that does not allow for such a procedure. Any potential

reintervention would require a more invasive procedure involving extracorporeal circulation. The implantation of a biological valve, with the potential for subsequent TAVI, may present an interesting alternative to mechanical valves, particularly for young, physically active individuals, where the risk of hemorrhagic incidents due to lifelong anticoagulation therapy could be a concern, especially in the case of injuries. Further comparative studies could yield interesting insights.

Transcatheter Aortic Valve Replacement (TAVR)

TAVR is, as mentioned above, a minimally invasive alternative to traditional SAVR. It is particularly appealing to patients due to its low invasiveness. The procedure involves placing a new valve using a catheter inserted into an artery, most commonly via a femoral approach (27). During TAVI, The catheter has a balloon at its distal end, which, when inflated, pushes aside the abnormal valve, and the created space is used to implant a new valve prosthesis. The entire procedure is performed under X-ray angiography control. Patients are usually administered local anesthesia during the procedure. In some centers, patients can be discharged as early as the next day after the procedure (28,29). There are reports suggesting that TAVR may provide similar early and mid-term outcomes compared to SAVR (30). However, concerns arise from the material used for the valve in this method and the fact that TAVR leaflets are thinner (due to the need for the device to be maneuvered into position), generating uncertainties regarding its long-term durability (31). There is a lack of long-term follow-up data (32), which is a significant limitation for its use in young adults, as this group is expected to have a long life expectancy. Nevertheless, due to the short-term outcomes being comparable to SAVR, TAVR is a good alternative for older patients and those disqualified from SAVR or for those who have previously undergone SAVR with a biological valve, which over time has degenerated.

Ross Procedure

In 1967, an article was published in *The Lancet* regarding the use of the pulmonary valve as a homograft for the aortic valve. The author of the paper was Donald N. Ross, whose name defines the mentioned procedure (33). Pulmonary autograft valves (PAV) represent a living structure that undergoes remodeling and adaptation (34). This is a significant feature for young, still-growing patients. These valves are not considered as foreign bodies, which means they do not require subsequent anticoagulant therapy. This presents an intriguing alternative to mechanical valves, which are most often chosen for younger patients (35). The Ross procedure appears particularly appealing for highly active individuals and young women with reproductive plans. It is also noteworthy that the quality of life after the Ross procedure might be higher than after the implantation of a mechanical valve (36). According to analyses, the main finding is that the Ross procedure is associated with improved freedom from all-cause mortality (37). Data show that this procedure can be performed with good outcomes as early as the second year of life (38). A limitation of this procedure is its considerable complexity compared to the straightforward implantation of a mechanical valve. The performance of the procedure requires an experienced team, which is why only a few centers worldwide undertake it. Importantly, it has been observed that among patients who undergo the procedure, dysfunction of the PAV may occur in nearly half of the patients within 20 years (39).

Surgical Aortic Valvuloplasty and Balloon Aortic Valvuloplasty

As mentioned earlier, in children, the majority of cases of BAV are asymptomatic. In some instances, symptoms may arise, most often due to the presence of aortic stenosis (40). In such situations, invasive procedures are considered, including surgical aortic valvuloplasty and balloon aortic valvuloplasty. Valvuloplasty in children is a more reliable procedure than typical cardiac surgeries in adults because, in the case of a growing heart, artificial valves may lose their function, which is associated with an increased risk of reoperation (the Ross procedure, as described above, is a separate topic). Valvuloplasty is proposed for various conditions in children associated with aortic stenosis, including BAV (41,42). In the case of the surgical method, commissurotomy is performed via median sternotomy. For the balloon method, a vascular access approach is chosen. Recently published studies have indicated the superiority of the surgical method of valvuloplasty over the balloon method in patients with BAV (43). These procedures have limited applicability in adult patients due to long-term event-free survival (44). Nevertheless, there are also data indicating that valve cusp repair may yield good results in adult patients, comparable to bioprosthetic valve replacement (45).

TISSUE-ENGINEERED HEART VALVES (TEHV)

In 1989, Dwight Emary Harken published an article in *The Annals of Thoracic Surgery* outlining the "ten commandments" for prosthetic valves (46). Despite the passage of time, no valve has yet been developed that meets all the criteria of an ideal valve. Promising advancements in this area appear to be related to the development of heart valves using biomedical engineering techniques (47,48). A particularly intriguing aspect in this field is the potential to create living material capable of regeneration (49). This field is rapidly evolving, and with modern 3D bioprinting techniques and computerization, it may yield surprising results in the future. Unfortunately, as of now, there have been no breakthroughs from the patient perspective, but progress in this area is being recognized by global cardiology societies (16), which underscores the importance of this phenomenon.

CONCLUSIONS

Bicuspid aortic valve is a complex condition. Although there are some recommendations and guidelines, clear algorithms for selecting the surgical technique or the material for the new valve are lacking. Each of these elements in the management of the condition presents various decision-making options, each offering a different profile of benefits and drawbacks. This illustrates the critical importance of education about the disease in the treatment process. Comprehensive patient awareness can reduce anxiety and aid in making appropriate therapeutic decisions. Efforts are ongoing to ensure that patients may not have to make this decision in the future. While we are still far from that scenario, it is worthwhile to observe the evolving new techniques, including tissue-engineered heart valves, in the hope of achieving a new ideal valve that meets all of the "ten commandments".

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