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JACC STATE-OF-THE-ART REVIEW

Semilunar Valve Interventions for Congenital Heart Disease

JACC State-of-the-Art Review

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ABSTRACT

Transcatheter balloon valvuloplasty for the treatment of aortic and pulmonary valve stenosis was first described nearly 40 years ago. Since that time, the technique has been refined in an effort to optimize acute outcomes while reducing the long-term need for reintervention and valve replacement. Balloon pulmonary valvuloplasty is considered first-line therapy for pulmonary valve stenosis and generally results in successful relief of valvar obstruction. Larger balloon to annulus (BAR) diameter ratios can increase the risk for significant valvar regurgitation. However, the development of regurgitation resulting in right ventricular dilation and dysfunction necessitating pulmonary valve replacement is uncommon in long-term follow-up. Balloon aortic valvuloplasty has generally been the first-line therapy for aortic valve stenosis, although some contemporary studies have documented improved outcomes following surgical valvuloplasty in a subset of patients who achieve tri-leaflet valve morphology following surgical repair. Over time, progressive aortic regurgitation is common and frequently results in the need for aortic valve replacement. Neonates with critical aortic valve stenosis remain a particularly high-risk group. More contemporary data suggest that acutely achieving an aortic valve gradient <35 mm Hg with mild aortic regurgitation may improve long-term valve performance and reduce the need for valve replacement. Continued study will help to further improve outcomes and reduce the need for future reinterventions. (J Am Coll Cardiol 2021;77:71–9)

Semilunar valve disease, specifically aortic valve stenosis (AS) and pulmonary valve stenosis (PS), occurs in isolation or in combination with a variety of congenital cardiovascular anomalies. The natural history of these diseases has been well described (1–3). For patients with severe valvular obstruction, surgical valvotomy was traditionally the first-line treatment. In the early 1980s, balloon valvuloplasty techniques were described as alternative, less invasive therapies (**Central Illustration**). There is now a significant body of medical research describing short-, intermediate-, and long-term outcomes of balloon valvuloplasty. This review focuses on isolated semilunar valve stenosis, the long-term outcomes of catheter-based therapy, and evolving strategies for transcatheter valve replacement.

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BALLOON PULMONARY VALVULOPLASTY

ACUTE PROCEDURAL RESULTS AND LONG-TERM FOLLOW-UP. Balloon pulmonary valvuloplasty (BPV) for PS was introduced in 1982 (4). A number of early studies demonstrated acute relief of right ventricular outflow tract (RVOT) obstruction with few complications in both pediatric and adult patients (5–9). In the current era, BPV has largely supplanted surgical pulmonary valvotomy as the first-choice therapy for PS. Although the tools have evolved

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ABBREVIATIONS AND ACRONYMS

AR = aortic valve regurgitation

AS = aortic valve stenosis

AVR = aortic valve replacement

BAR = balloon-to-annulus ratio

BAV = balloon aortic valvuloplasty

BPV = balloon pulmonary valvuloplasty

PR = pulmonary regurgitation

PS = pulmonary valve stenosis

PVR = pulmonary valve replacement

RV = right ventricular

RVEDVi = indexed right ventricular end-diastolic volume

RVOT = right ventricular outflow tract

SAV = surgical aortic valvuloplasty

TAVR = transcatheter aortic valve replacement

TOF = tetralogy of Fallot

with the introduction of low-profile sheaths and angioplasty balloon catheters, the technical aspects of the procedure are not much different now than they were during the development of this procedure.

Early in the experience with BPV, the focus was on the acute relief of RVOT obstruction and the factors that contributed to reintervention for residual PS. The multicenter VACA (Valvuloplasty and Angioplasty of Congenital Anomalies) registry identified younger age at initial BPV, a dysplastic pulmonary valve, smaller valve diameter, higher initial RVOT gradient, and a diagnosis of Noonan syndrome as risk factors for a suboptimal result with incomplete resolution of obstruction (10). RVOT obstruction in Noonan syndrome, as well as Williams-Beuren and Alagille syndromes, is often more supravalvular in nature, which is typically not amenable to BPV. If severe enough to require an intervention, surgical augmentation of the annulus, valve sinuses, and sinotubular junction is frequently necessary.

The typical metric for assessing the role of balloon sizing has been the ratio of balloon diameter to pulmonary valve annular diameter, or balloon-to-annulus ratio (BAR). The earliest clinical reports described the use of balloons with diameters equal to or less than that of the annulus (5). Studies of BPV in animal models demonstrated that significant balloon oversizing (BAR >1.5) could result in RVOT injury (11). This led to the early practice of using a BAR of 1.2 to 1.4 to improve gradient reduction and reduce the need for reintervention (12,13). However, more contemporary studies suggest that such an aggressive approach to balloon sizing is not necessary (14). Long-term follow-up studies showed that reintervention for residual PS following BPV is uncommon (10% to 15%), with similar risk factors for residual obstruction as seen in earlier studies (15,16). In the majority of cases, PS gradients in individual patients continue to decline over time following initial BPV (17,18).

The development of pulmonary regurgitation (PR) has emerged as a more common hemodynamic consequence of BPV than recurrent PS, and there are now a number of long-term studies that document the incidence and implications of PR in this population (15,16,18–20). Although published findings are mixed, contemporary studies suggest that aggressive balloon oversizing increases the long-term risk for PR (10,15,16,21,22). Pathak et al. (22) demonstrated that a more conservative balloon-sizing strategy (BAR ≤1.2) achieved similar gradient reduction while reducing the medium-term incidence of PR, and a BAR up to 1.2 to 1.25 has been proposed as a more appropriate target than the larger ratios advocated in earlier reports (14).

HIGHLIGHTS

- BPV is considered first-line therapy for congenital semilunar valve stenosis.
- Pulmonary valve regurgitation is common but usually mild following BPV.
- Neonates with critical AS remain at high risk for acute complications.
- Efforts to develop and enhance methods for transcatheter valve replacement are essential.

Estimates of the prevalence of moderate or severe PR have relied primarily on echocardiography and range from 30% to 60% (15,16,18,20). The progression of PR is time dependent, but even in studies with more than 2 decades of follow-up, severe right ventricular (RV) dilation and systolic dysfunction are uncommon (15,16,18). Significant PR after BPV has been related to younger age at BPV, higher initial RVOT gradient, and higher degree of immediate post-intervention PR (15,16,20).

LONG-TERM IMPACT OF PR. Investigations of the impact of chronic PR on RV size and function have focused largely on patients with repaired tetralogy of Fallot (TOF). Although the impact of chronic PR on the right ventricle following BPV has not been as well studied as in TOF, there are some data on the impact of chronic valve regurgitation on RV size and function in patients following BPV.

Harrild et al. (19) presented a cross-sectional view of patients following BPV to study the impact of chronic PR in patients treated for isolated PS. In patients studied a median of 13 years (range: 6.2 to 22.9 years) following BPV, the median PR fraction was 10%, while 34% had a PR fraction >15%. Younger age at BPV and higher BAR were associated with a higher PR fraction. The median indexed RV end-diastolic volume (RVEDVi) *z*-score was 1.8, and it was >2 in 40% of patients. PR fraction was positively correlated with RVEDVi and inversely with RV ejection fraction. Severe RV dilation (3% of patients) and dysfunction were uncommon. The investigators concluded that although PR following BPV was common, it was typically mild, and significant RV dysfunction was uncommon, which is largely in keeping with the

results of studies based on serial echocardiography in this population.

There has been some effort to understand how the impact of long-standing PR differs between patients with isolated PS and repaired TOF. Mercer-Rosa et al. (23) matched a small cohort of patients following BPV to a cohort of patients with repaired TOF on the basis of PR fraction and duration of PR in order to understand the relationship between PR and RV size and function in these 2 populations. Both groups were studied after an average duration of PR exposure of 14 years. In the BPV cohort, RVEDVi was normal on average, although 32% of patients had a dilated RV (RVEDVi *z*-score >2). The PR fraction was 19% on average and correlated positively with RVEDVi. BPV patients with moderate or greater PR had comparable RV function and aerobic capacity on exercise testing to patients with mild or less PR. A matched cohort of patients with repaired TOF had worse RV function, greater RV mass, and lower exercise capacity compared with BPV patients with similar duration and severity of PR.

These studies of long-term outcomes of BPV on the basis of magnetic resonance imaging–derived measures suggest that most patients develop mild PR and RV dilation, although risk factors such as a higher BAR may result in more significant long-term RV dilation. Significant RV dysfunction seems to be uncommon.

PULMONARY VALVE REPLACEMENT. The timing of pulmonary valve replacement (PVR) for chronic RVOT dysfunction is a widely debated topic that has focused largely on patients with repaired TOF (24). Published guidelines advocate for PVR in patients with severe PR, RV dilation, and symptoms of right heart failure. Management of asymptomatic patients is more controversial and has been based largely on magnetic resonance imaging–derived measures of RV volume and function (25). Many of these recommendations are based on studies of repaired TOF, and it is unclear if they should apply to patients with isolated valvular PS who have undergone BPV. On the basis of long-term imaging data, most patients following BPV probably do not meet the clinical criteria for PVR in patients with TOF. This is reflected in the long-term outcome studies, in which PVR is uncommon. Freedom from death or any reintervention 10 years after BPV has been reported to range from 83% to 87%, with only 2% to 3% of patients undergoing PVR (15,16,18).

Transcatheter PVR has become a common alternative to surgical PVR in patients with a stenotic or regurgitant conduit or bioprosthetic valve (26). However, the RVOT in patients with significant PR after BPV is often too large for available balloon-expandable transcatheter valves. In studies that evaluated the off-label implantation of balloon-expandable transcatheter pulmonary valves in patients with native RVOT dysfunction, approximately 12% to 13% of patients had an underlying diagnosis of valvular PS (27,28). Early outcomes in those series were favorable, but only a small fraction of patients who merit PVR after BPV will be eligible for current balloon-expandable valves.

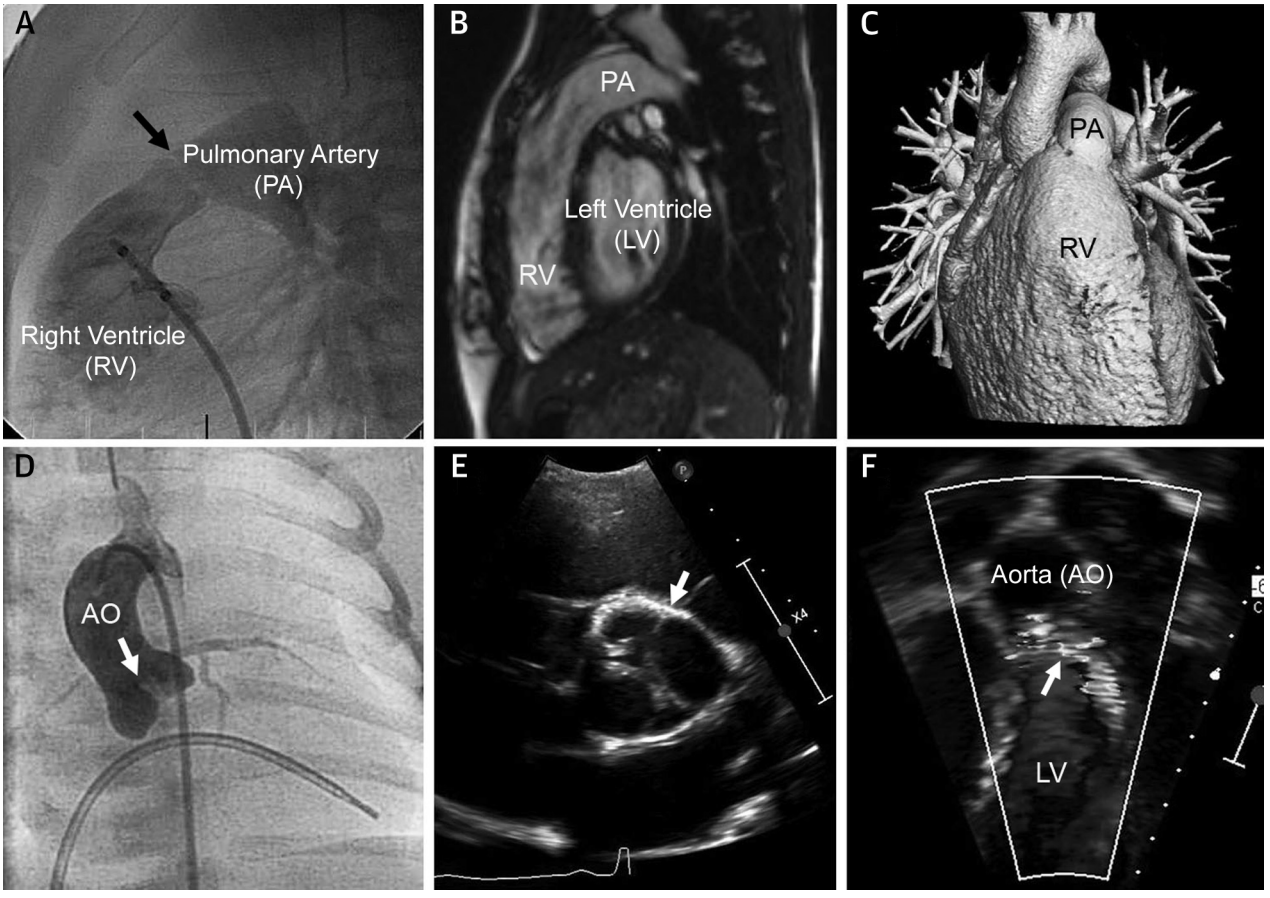
Self-expanding transcatheter valve frames have been developed specifically to target the large and variable RVOT anatomy commonly seen in patients with chronic PR. The first human implantation of a self-expanding transcatheter pulmonary valve was reported in 2010, and that valve design ultimately evolved into the Harmony transcatheter pulmonary valve (Medtronic, Minneapolis, Minnesota) (29). In addition to the Harmony valve, the Alterra Adaptive Prestent (Edwards Lifesciences, Irvine, California), Venus P-Valve (Venus MedTech, Hangzhou, China), Pulsta valve (TaeWoong Medical, Gyeonggi-do, South Korea), and Med-Zenith PT valve (Beijing Med-Zenith, Beijing, China) are self-expanding valve devices designed for PVR in large, native RVOT anatomy (30–33). Although principally designed to treat patients with TOF repaired with a transannular patch, these valves can also be used in patients with underlying PS and post-BPV PR who have suitable RVOT anatomy (**Figure 1**). One of 20 patients who received a valve in the Harmony early feasibility study had a dysplastic pulmonary valve without an outflow tract patch (34).

The progression of PR and RV dilation is a well correlated, time-dependent phenomenon. Accordingly, as with repaired TOF, it is likely that patients meeting indications for valve replacement after BPV will continue to increase with ongoing follow-up. In addition to a wider range of valve options, advanced imaging of the RVOT continues to improve, and as more patients with post-BPV PR reach criteria for PVR, it is increasingly likely that either a balloon-expandable or self-expanding transcatheter pulmonary valve will be the first choice for valve replacement.

BALLOON AORTIC VALVULOPLASTY

ACUTE PROCEDURAL RESULTS AND ADVERSE EVENTS. Prior to the development of transcatheter balloon aortic valvuloplasty (BAV), surgical valvotomy was the primary treatment for congenital AS (35–37). BAV was first described in 1984, and this

CENTRAL ILLUSTRATION **Examples of Long-Term Follow-Up of Balloon Aortic and Pulmonary Valvuloplasty**



Morray, B.H. et al. J Am Coll Cardiol. 2021;77(1):71-9.

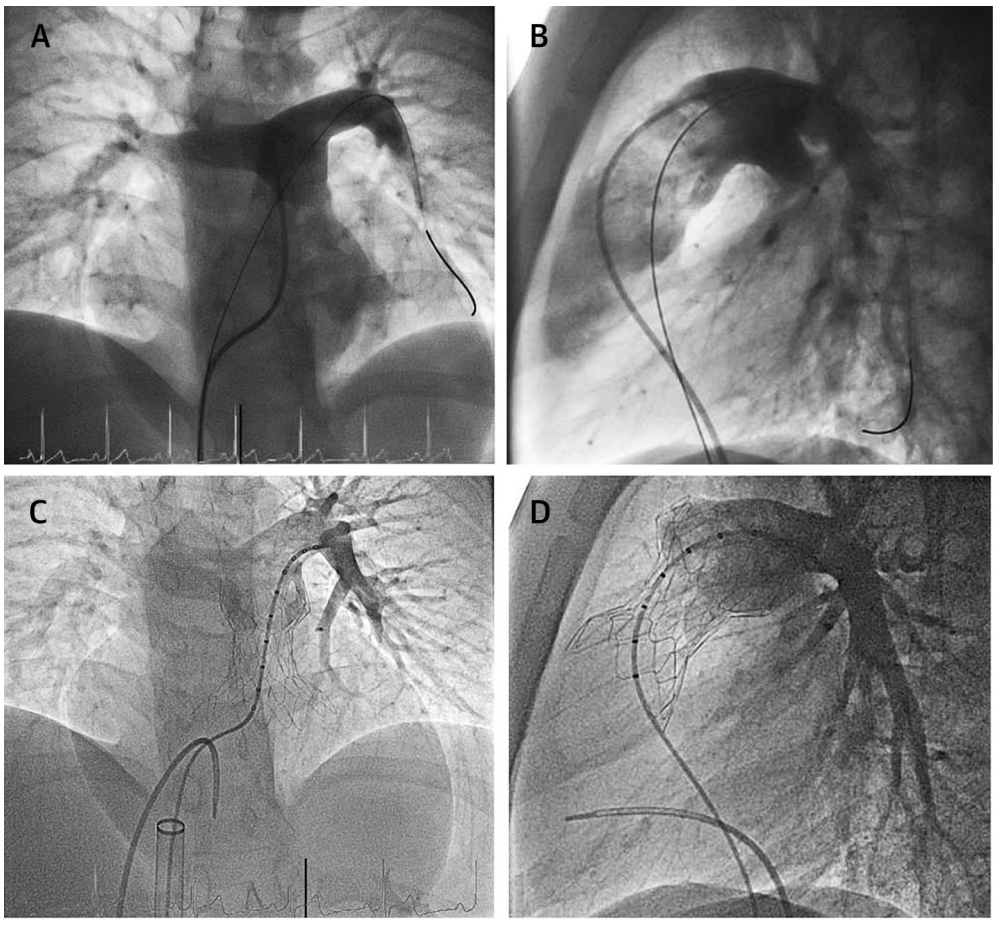
(A) This angiogram shows the pulmonary valve **(arrow)** in a neonate with critical pulmonary valve stenosis who underwent balloon pulmonary valvuloplasty (BPV). **(B)** Magnetic resonance imaging 18 years following BPV demonstrates right ventricular dilation and pulmonary valve insufficiency. **(C)** A 3-dimensional computed tomographic reconstruction in the same patient demonstrates intact valve sinuses and a dilated main pulmonary artery. **(D)** This ascending aortic angiogram shows the thickened aortic valve **(arrow)** prior to intervention in a neonate with critical aortic valve stenosis who underwent balloon aortic valvuloplasty (BAV). **(E)** This echocardiogram in the same patient shows a bicuspid aortic valve with fusion of the intercoronary commissure **(arrow)**. **(F)** On echocardiography 16 years after BAV, there was moderate aortic regurgitation **(arrow)** with mild left ventricular dilation.

report was followed by a number of single-center case series (38-42). These studies demonstrated significant aortic valve gradient reduction with the initial dilation (43,44). At most centers, BAV is typically considered the first-line therapy for patients with aortic valve obstruction significant enough to warrant intervention.

Early animal and human studies sought to define the patient and procedure-related factors that contributed to successful intervention and to adverse events and mortality, with particular focus on the impact of balloon sizing and aortic valve morphology. In early animal studies, a BAR >1.2 was associated with significant valve injury, and in early human studies, a BAR >1.1 was associated with greater risk for important acute aortic valve regurgitation (AR) (40,41). The majority of patients experienced significant reductions in the peak systolic ejection gradient with development of some degree of AR, although moderate to severe AR was uncommon (45).

The first large, multicenter study to examine factors associated with acute outcomes after BAV was from the VACA registry (46). That study defined a suboptimal outcome as a residual peak gradient

FIGURE 1 Transcatheter Pulmonary Valve Replacement Following Balloon Pulmonary Valvuloplasty



Images from an 18-year-old man who was diagnosed with severe pulmonary valve stenosis and underwent balloon pulmonary valvuloplasty as a neonate. He developed severe pulmonary valve insufficiency with a dilated right ventricle with preserved ventricular function. **(A,B)** Angiography demonstrated a severely dilated main pulmonary artery with severe pulmonary valve regurgitation. **(C,D)** The patient underwent successful implantation of a Harmony transcatheter pulmonary valve (Medtronic) as part of a multicenter, prospective trial.

>60 mm Hg, which occurred in 17% of patients. Risk factors for suboptimal outcome included higher pre-BAV gradient, neonatal AS, and a BAR <0.9. The development of severe AR was associated with pre-existing AR, a larger valve annular size, and a larger BAR. Mortality was 9.6% in neonates, and patients <3 months of age were more likely to experience suboptimal outcomes and major morbidity than older patients. The registry did not examine relationships between valve morphology and outcome. In other early studies, neonatal mortality was between 9% and 12%, similar to the VACA registry, but survival improved over time (44,46,47). In more contemporary studies, 30-day mortality for noncritical AS was <1%, although it was higher (6.3%) in neonates with critical AS (48). Older children were more likely to have adequate outcomes, with a lower rate of procedure-related or hospital mortality (45).

Criteria for defining the therapeutic adequacy of BAV have evolved over time on the basis of a combination of consensus opinion and long-term outcomes regarding the need for aortic valve reintervention (48–51). Currently, procedural success is typically defined as a residual peak systolic ejection gradient <35 mm Hg and a mild or less degree of AR. From 2 large cohorts, procedural success using these criteria was 70%, with >80% of patients achieving residual gradients <35 mm Hg (49,50). There was no procedural mortality. A successful outcome was less likely in patients with critical AS, histories of prior valve intervention, or higher grade AR prior to intervention. Despite these improvements, neonates

with severe and critical AS remain at higher risk for in-hospital mortality and morbidity, particularly vascular complications (49,50).

LONG-TERM RESULTS. In studies of long-term outcomes following BAV, overall survival was 80% to 90% at 20 years (51,52). Reintervention was common, particularly in neonates and patients with more severe AS (51). Studies have reported repeat BAV for recurrent stenosis in a substantial number of patients, with freedom from repeat BAV at 10 years ranging from 46% to 70% (44,51). The prevalence and severity of AR increases over time, and 10-year freedom from significant AR as low as 49% has been reported (52). The risk for progressive moderate to severe AR during long-term follow-up has been described in both neonates and older patients (51,53,54).

A number of studies have identified important associations between acute BAV outcomes, long-term development of AR, and need for aortic valve reintervention and aortic valve replacement (AVR). Specifically, higher acute residual gradients and degree of post-BAV AR were associated with a greater risk for AVR (51,53). In the VACA registry, a suboptimal outcome was defined, in part, as a residual left ventricular outflow tract gradient >60 mm Hg. In more contemporary studies, composite outcomes that include residual gradient and acute AR severity have been created to guide understanding of what constitutes an acceptable or optimal outcome (48–50). This was based, in part, on a study by Brown et al. (51), which demonstrated that patients with residual left ventricular outflow tract gradients <35 mm Hg and less than trivial AR were significantly less likely to require AVR during follow-up compared with other composite outcomes. The investigators concluded that acute gradient reduction was more important than the development of mild or greater AR in reducing the risk for AVR. Not all studies have agreed with this finding. A single-center study by Sullivan et al. (53) showed that patients who achieved acute gradient reductions <30 mm Hg at the expense of moderate to severe AR had a greater long-term risk for AVR compared with those with higher residual gradients and less AR (53). The hope is that by standardizing outcome criteria, we will achieve more consistent and durable results and reduce the need for reintervention and AVR (48).

Referral for surgical AVR after BAV is driven predominantly by progressive AR and mixed aortic valve disease (52). The development of moderate to severe AR is strongly associated with the need for subsequent AVR. In one single-center study, only 13% of patients were estimated to remain free from AVR 15 years after the onset of moderate to severe AR, and the average time from the development of moderate to severe AR to AVR was only 2.2 years (53). Indications for AVR in the setting of severe post-BAV AR include symptoms or, in the absence of symptoms, severe left ventricular dilation or systolic dysfunction (55).

AORTIC VALVE MORPHOLOGY. Several studies have focused on the relationship between aortic valve morphology and long-term outcomes, including the need for reintervention and AVR. Bicuspid aortic valves are the most common configuration encountered in studies of BAV. It has been documented that in patients with bicuspid aortic valves, fusion of the right and noncoronary commissures is associated with a more rapid progression of stenosis and regurgitation and a shorter time to valve intervention (56). Not surprisingly, the presence of a functional or true unicuspid aortic valve is associated with a greater risk for repeat intervention, AVR, death, or heart transplantation compared to patients with a bicuspid valve (57).

SURGICAL AORTIC VALVOTOMY VERSUS BAV. There are relatively few published studies that directly compare BAV and surgical aortic valvotomy (SAV). Past studies comparing SAV with BAV tended to demonstrate equivalent outcomes in terms of survival and need for aortic valve reintervention (58). A more recent meta-analysis demonstrated no difference in acute outcomes, survival, or AVR between BAV and SAV, but did identify a higher rate of reintervention in patients following initial BAV (59). For this reason, at most centers, BAV is favored as the first-line therapy given its less invasive nature. However, with advancements in surgical valve repair, a small number of contemporary studies reported that the need for repeat aortic valve intervention may be reduced in patients following SAV, particularly if a trileaflet valve morphology can be achieved following repair (60,61).

Attempts to conduct retrospective cohort studies comparing these 2 techniques are fraught with difficulty, and there are no randomized studies upon which we can rely. The retrospective nature of these studies makes it difficult to control for variables such as the clinical status of the patient at time of intervention and the morphology of the valve. Moreover, the overall rate of reintervention can be a complicated outcome metric, as interventionalists may take a cautious approach to BAV in neonates, erring on the side of reintervention rather than more severe acute AR. The decision to reintervene is also dependent on sometimes variable thresholds and criteria. As is

often the case, patient selection is important. There are likely patients for whom SAV will offer the least risk for future reintervention, and as surgical techniques for valve repair continue to improve, we will have more data to draw upon.

AVR. In adults with severe AS, surgical AVR and transcatheter AVR (TAVR) are considered first-line therapies. The choice of a surgical or transcatheter approach is based on the assessment of surgical risk and the patient's predicted life expectancy. On the basis of current guidelines, patients with severe stenosis who are at high risk for surgical AVR and have predicted post-TAVR survival >12 months are recommended to undergo TAVR (62). However, this field continues to evolve as TAVR is studied in progressively lower risk populations. BAV can play a role in the management of AS in adults as a palliative measure as well as a bridge to AVR in symptomatic patients with severe stenosis who are high-risk surgical candidates (63).

A barrier to the application of existing TAVR technology in pediatric patients is the effectiveness of BAV for congenital AS (which is not true for acquired calcific AS), and predominance of AR or mixed aortic valve disease in this population, often following BAV or associated with other congenital or post-operative pathology. The majority of experience with TAVR has been in adults with calcific AS. However, with improving technology and experience, TAVR is beginning to extend to patients in whom AR is the predominant lesion (64,65). Currently available transcatheter aortic valves are not approved for use in pediatric patients and are often not suited to the anatomy or size of the patient. As a result, the application of TAVR in pediatric or young adult patients with aortic valve disease (either in isolation or in conjunction with other forms of congenital heart disease) is limited. There are a few case reports and small case series that describe off-label use of the Melody valve (Medtronic) or Sapien valves (Edwards Lifesciences) for TAVR in pediatric and congenital patients (66–68). These reports describe valve modifications and delivery techniques that are specific to this unique population. However, the number of patients reported is small, and follow-up is short.

Despite the limited experience with TAVR in young patients with congenital or acquired aortic valve disease, it is likely that advances in technology and clinical experience will ultimately lead to expanded application of transcatheter therapies in these populations. It is important that congenital centers leverage the experience of, and partner with, adult structural cardiologists and institutions to help guide patient selection, pre-procedural imaging, and procedural performance. Such collaboration will help ensure optimal outcomes as the experience with TAVR grows in younger patients.

CONCLUSIONS

Transcatheter techniques for the management of aortic and pulmonic valve stenosis have been extensively described over the past 40 years. Important modifications in technique, such as improved understanding of appropriate balloon sizing, have occurred as we have learned more about the impact that acute outcomes have on long-term survival and reintervention. The early focus on acute gradient reduction at the expense of valvular regurgitation has shifted to achieving a balance between gradient reduction and the development of regurgitation. Particularly for patients with AS, the probability of developing hemodynamically significant AR is great and increases over time. Careful analysis of long-term follow-up data has facilitated a better understanding of appropriate hemodynamic results of BAV. Despite this, contemporary data from multicenter registries suggest that we are achieving desired outcomes in only 70% of cases. Additionally, smaller and younger patients and those with more severe AS remain at higher risk for morbidity and mortality than older patients with less severe disease. Contemporary studies of surgical aortic valve repair suggest improved rates of reintervention compared with BAV, particularly when a trileaflet valve morphology is achieved. Careful pre-procedural analysis of valve morphology and the progression of surgical techniques may push some patients toward surgical repair.

The thoughtful analysis of patients with TOF has greatly enhanced our understanding of the long-term consequences of chronic PR. On the basis of the most contemporary data, most patients do not develop more than mild PR and RV dilation following BPV. The probability of developing significant RV dilation and dysfunction appears to be relatively low. However, with ongoing follow-up, there may be a greater burden of valve regurgitation and resultant ventricular dilation. The recognition of the impact of chronic PR on morbidity and reintervention has tempered the tendency for balloon oversizing during BPV in an effort to maintain valve competency and reduce the long-term risk for reintervention. More information on the rate of PVR following BPV is necessary to further validate this approach.

Currently, transcatheter PVR in pediatric and adult congenital patients is far more common than

TAVR. Progress is actively being made on the development of novel, self-expanding transcatheter valve devices intended for the large native or patched RVOT that will further expand our ability to restore pulmonary valve function in the catheterization laboratory. TAVR is well studied in adults with acquired AS but has not yet found a foothold in the congenital population. As the portfolio of valve types expands and operators gain experience managing AR or mixed aortic valve disease in patients with a bicuspid or unicuspid valve, we will likely see TAVR extend into younger patients. This will provide opportunities to offer transcatheter options to the growing number of patients living with congenital aortic valve disease.

Although balloon valvuloplasty has been performed for nearly 4 decades, it is important to continue innovating in this space. Reviewing the landscape of published research demonstrates that there are still improvements that can be made to improve outcomes and reduce the need for valve replacement. Additionally, there is more work to be done to ensure that transcatheter valve replacement options can be offered to all patients who may come to need a new pulmonary or aortic valve.

AUTHOR DISCLOSURES

Dr. Morray is a consultant for Medtronic. Dr. McElhinney serves as a proctor and consultant for Medtronic.

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REFERENCES

1. Nadas AS. Report from the Joint Study on the Natural History of Congenital Heart Defects. I. General introduction. Circulation 1977;56:I3–4.

2. Hayes CJ, Gersony WM, Driscoll DJ, et al. Second natural history study of congenital heart defects. Results of treatment of patients with pulmonary valvar stenosis. Circulation 1993;87:I28–37.

3. Keane JF, Driscoll DJ, Gersony WM, et al. Second natural history study of congenital heart defects. Results of treatment of patients with aortic valvar stenosis. Circulation 1993;87:I16–27.

4. Kan JS, White RI Jr., Mitchell SE, Gardner TJ. Percutaneous balloon valvuloplasty: a new method for treating congenital pulmonary-valve stenosis. N Engl J Med 1982;307:540–2.

5. Kan JS, White RI Jr., Mitchell SE, Anderson JH, Gardner TJ. Percutaneous transluminal balloon valvuloplasty for pulmonary valve stenosis. Circulation 1984;69:554–60.

6. Lababidi Z, Wu JR. Percutaneous balloon pulmonary valvuloplasty. Am J Cardiol 1983;52:560–2.

7. O'Connor BK, Beekman RH, Lindauer A, Rocchini A. Intermediate-term outcome after pulmonary balloon valvuloplasty: comparison with a matched surgical control group. J Am Coll Cardiol 1992;20:169–73.

8. Ananthakrishna A, Balasubramonium VR, Thazhath HK, et al. Balloon pulmonary valvuloplasty in adults: immediate and long-term outcomes. J Heart Valve Dis 2014;23:511–5.

9. Taggart NW, Cetta F, Cabalka AK, Hagler DJ. Outcomes for balloon pulmonary valvuloplasty in adults: comparison with a concurrent pediatric cohort. Catheter Cardiovasc Interv 2013;82:811–5.

10. McCrindle BW. for the Valvuloplasty and Angioplasty of Congenital Anomalies (VACA) Registry Investigators. Independent predictors of long-term results after balloon pulmonary valvuloplasty. Circulation 1994;89:1751–9.

11. Ring JC, Kulik TJ, Burke BA, Lock JE. Morphologic changes induced by dilation of the pulmonary valve anulus with overlarge balloons in normal newborn lambs. Am J Cardiol 1985;55:210–4.

12. Radtke W, Keane JF, Fellows KE, Lang P, Lock JE. Percutaneous balloon valvotomy of congenital pulmonary stenosis using oversized balloons. J Am Coll Cardiol 1986;8:909–15.

13. Qureshi SA, Ladusans EJ, Martin RP. Dilatation with progressively larger balloons for severe stenosis of the pulmonary valve presenting in the late neonatal period and early infancy. Br Heart J 1989;62:311–4.

14. Rao PS. Percutaneous balloon pulmonary valvuloplasty: state of the art. Catheter Cardiovasc Interv 2007;69:747–63.

15. Hansen RL, Naimi I, Wang H, et al. Long-term outcomes up to 25 years following balloon pulmonary valvuloplasty: a multicenter study. Congenit Heart Dis 2019;14:1037–45.

16. Devanagondi R, Peck D, Sagi J, et al. Long-term outcomes of balloon valvuloplasty for isolated pulmonary valve stenosis. Pediatr Cardiol 2017;38:247–54.

17. Karagoz T, Asoh K, Hickey E, et al. Balloon dilation of pulmonary valve stenosis in infants less than 3 kg: a 20-year experience. Catheter Cardiovasc Interv 2009;74:753–61.

18. Merino-Ingelmo R, Santos-de Soto J, Coserria-Sanchez F, Descalzo-Senoran A, Valverde-Perez I. Long-term results of percutaneous balloon valvuloplasty in pulmonary valve stenosis in the pediatric population. Rev Esp Cardiol (Engl Ed) 2014;67:374–9.

19. Harrild DM, Powell AJ, Tran TX, et al. Long-term pulmonary regurgitation following balloon valvuloplasty for pulmonary stenosis risk factors and relationship to exercise capacity and ventricular volume and function. J Am Coll Cardiol 2010;55:1041–7.

20. Poon LK, Menahem S. Pulmonary regurgitation after percutaneous balloon valvoplasty for isolated pulmonary valvar stenosis in childhood. Cardiol Young 2003;13:444–50.

21. Berman W Jr., Fripp RR, Raisher BD, Yabek SM. Significant pulmonary valve incompetence following oversize balloon pulmonary valveplasty in small infants: a long-term follow-up study. Catheter Cardiovasc Interv 1999;48:61–5.

22. Pathak SJ, Pockett CR, Moore JW, El-Said HG. Effect of balloon:annulus ratio on incidence of pulmonary insufficiency following valvuloplasty. Congenit Heart Dis 2016;11:415–9.

23. Mercer-Rosa L, Ingall E, Zhang X, et al. The impact of pulmonary insufficiency on the right ventricle: a comparison of isolated valvar pulmonary stenosis and tetralogy of Fallot. Pediatr Cardiol 2015;36:796–801.

24. Weinberg CR, McElhinney DB. Pulmonary valve replacement in tetralogy of Fallot. Circulation 2014;130:795–8.

25. Stout KK, Daniels CJ, Aboulhosn JA, et al. 2018 AHA/ACC guideline for the management of adults with congenital heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2019;73:1494–563.

26. Cabalka AK, Hellenbrand WE, Eicken A, et al. Relationships among conduit type, pre-stenting, and outcomes in patients undergoing transcatheter pulmonary valve replacement in the prospective North American and European Melody valve trials. J Am Coll Cardiol Intv 2017;10:1746–59.

27. Martin MH, Meadows J, McElhinney DB, et al. Safety and feasibility of melody transcatheter pulmonary valve replacement in the native right ventricular outflow tract: a multicenter Pediatric Heart Network Scholar Study. J Am Coll Cardiol Intv 2018;11:1642–50.

28. Sinha S, Aboulhosn J, Asnes J, et al. Initial results from the off-label use of the SAPIEN S3 valve for percutaneous transcatheter pulmonary valve replacement: A multi-institutional experience. Catheter Cardiovasc Interv 2019;93:455–63.

29. Schievano S, Taylor AM, Capelli C, et al. First-in-man implantation of a novel percutaneous valve: a new approach to medical device development. EuroIntervention 2010;5:745–50.

30. Zahn EM, Chang JC, Armer D, Garg R. First human implant of the Alterra Adaptive Prestent™: a new self-expanding device designed to remodel the right ventricular outflow tract. Catheter Cardiovasc Interv 2018;91:1125–9.

31. Promphan W, Prachasilchai P, Siripornpitak S, Qureshi SA, Layangool T. Percutaneous pulmonary valve implantation with the Venus P-Valve: clinical experience and early results. Cardiol Young 2016;26:698–710.

32. Kim GB, Song MK, Bae EJ, et al. Successful feasibility human trial of a new self-expandable percutaneous pulmonary valve (Pulsta valve) implantation using knitted Nitinol wire backbone and trileaflet alpha-gal-free porcine pericardial valve in the native right ventricular outflow tract. Circ Cardiovasc Interv 2018;11:e006494.

33. Shang X, Chen S, Zhang C, et al. First-in-man implantation of Med-Zenith PT-Valve in right ventricular outflow tract for pulmonary regurgitation. J Am Coll Cardiol Intv 2019;12:1989–90.

34. Bergersen L, Benson LN, Gillespie MJ, et al. Harmony feasibility trial: acute and short-term outcomes with a self-expanding transcatheter pulmonary valve. J Am Coll Cardiol Intv 2017;10:1763–73.

35. Sandor GG, Olley PM, Trusler GA, Williams WG, Rowe RD, Morch JE. Long-term follow-up of patients after valvotomy for congenital valvular aortic stenosis in children: a clinical and actuarial follow-up. J Thorac Cardiovasc Surg 1980;80:171–6.

36. Tveter KJ, Foker JE, Moller JH, Ring WS, Lillehei CW, Varco RL. Long-term evaluation of aortic valvotomy for congenital aortic stenosis. Ann Surg 1987;206:496–503.

37. Brown JW, Stevens LS, Holly S, et al. Surgical spectrum of aortic stenosis in children: a thirty-year experience with 257 children. Ann Thorac Surg 1988;45:393–403.

38. Lababidi Z, Wu JR, Walls JT. Percutaneous balloon aortic valvuloplasty: results in 23 patients. Am J Cardiol 1984;53:194–7.

39. Rao PS, Thapar MK, Wilson AD, Levy JM, Chopra PS. Intermediate-term follow-up results of balloon aortic valvuloplasty in infants and children with special reference to causes of restenosis. Am J Cardiol 1989;64:1356–60.

40. Sholler GF, Keane JF, Perry SB, Sanders SP, Lock JE. Balloon dilation of congenital aortic valve stenosis. Results and influence of technical and morphological features on outcome. Circulation 1988;78:351–60.

41. Helgason H, Keane JF, Fellows KE, Kulik TJ, Lock JE. Balloon dilation of the aortic valve: studies in normal lambs and in children with aortic stenosis. J Am Coll Cardiol 1987;9:816–22.

42. Vogel M, Benson LN, Burrows P, Smallhorn JF, Freedom RM. Balloon dilatation of congenital aortic valve stenosis in infants and children: short term and intermediate results. Br Heart J 1989;62:148–53.

43. Reich O, Tax P, Marek J, et al. Long term results of percutaneous balloon valvoplasty of congenital aortic stenosis: independent predictors of outcome. Heart 2004;90:70–6.

44. McElhinney DB, Lock JE, Keane JF, Moran AM, Colan SD. Left heart growth, function, and reintervention after balloon aortic valvuloplasty for neonatal aortic stenosis. Circulation 2005;111:451–8.

45. Moore P, Egito E, Mowrey H, Perry SB, Lock JE, Keane JF. Midterm results of balloon dilation of congenital aortic stenosis: predictors of success. J Am Coll Cardiol 1996;27:1257–63.

46. McCrindle BW. Valvuloplasty and Angioplasty of Congenital Anomalies (VACA) Registry Investigators. Independent predictors of immediate results of percutaneous balloon aortic valvotomy in children. Am J Cardiol 1996;77:286–93.

47. Egito ES, Moore P, O'Sullivan J, et al. Transvascular balloon dilation for neonatal critical aortic stenosis: early and midterm results. J Am Coll Cardiol 1997;29:442–7.

48. Porras D, Brown DW, Rathod R, et al. Acute outcomes after introduction of a standardized clinical assessment and management plan (SCAMP) for balloon aortic valvuloplasty in congenital aortic stenosis. Congenit Heart Dis 2014;9:316–25.

49. Boe BA, Zampi JD, Kennedy KF, et al. Acute success of balloon aortic valvuloplasty in the current era: a National Cardiovascular Data Registry study. J Am Coll Cardiol Intv 2017;10:1717–26.

50. Torres A, Vincent JA, Everett A, et al. Balloon valvuloplasty for congenital aortic stenosis: multicenter safety and efficacy outcome assessment. Catheter Cardiovasc Interv 2015;86:808–20.

51. Brown DW, Dipilato AE, Chong EC, Lock JE, McElhinney DB. Aortic valve reinterventions after balloon aortic valvuloplasty for congenital aortic stenosis intermediate and late follow-up. J Am Coll Cardiol 2010;56:1740–9.

52. Maskatia SA, Ing FF, Justino H, et al. Twenty-five year experience with balloon aortic valvuloplasty for congenital aortic stenosis. Am J Cardiol 2011;108:1024–8.

53. Sullivan PM, Rubio AE, Johnston TA, Jones TK. Long-term outcomes and re-interventions following balloon aortic valvuloplasty in pediatric patients with congenital aortic stenosis: A single-center study. Catheter Cardiovasc Interv 2017;89:288–96.

54. Balmer C, Beghetti M, Fasnacht M, Friedli B, Arbenz U. Balloon aortic valvoplasty in paediatric patients: progressive aortic regurgitation is common. Heart 2004;90:77–81.

55. Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 2014;129:e521–643.

56. Fernandes SM, Khairy P, Sanders SP, Colan SD. Bicuspid aortic valve morphology and interventions in the young. J Am Coll Cardiol 2007;49:2211–4.

57. Maskatia SA, Justino H, Ing FF, Crystal MA, Mattamal RJ, Petit CJ. Aortic valve morphology is associated with outcomes following balloon valvuloplasty for congenital aortic stenosis. Catheter Cardiovasc Interv 2013;81:90–5.

58. McCrindle BW, Blackstone EH, Williams WG, et al. Are outcomes of surgical versus transcatheter balloon valvotomy equivalent in neonatal critical aortic stenosis? Circulation 2001;104:I152–8.

59. Hill GD, Ginde S, Rios R, Frommelt PC, Hill KD. Surgical valvotomy versus balloon valvuloplasty for congenital aortic valve stenosis: a systematic review and meta-analysis. J Am Heart Assoc 2016;5:e003931.

60. Vergnat M, Asfour B, Arenz C, et al. Aortic stenosis of the neonate: a single-center experience. J Thorac Cardiovasc Surg 2019;157:318–26.e1.

61. Siddiqui J, Brizard CP, Konstantinov IE, et al. Outcomes after operations for bicuspid aortic valve disease in the pediatric population. Ann Thorac Surg 2013;96:2175–83.

62. Nishimura RA, Otto CM, Bonow RO, et al. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2017;70:252–89.

63. Bonow RO, Brown AS, et al. ACC/AATS/AHA/ASE/EACTS/HVS/SCA/SCAI/SCCT/SCMR/STS 2017 appropriate use criteria for the treatment of patients with severe aortic stenosis. J Am Coll Cardiol 2017;70:2566–98.

64. Yoon SH, Schmidt T, Bleiziffer S, et al. Transcatheter aortic valve replacement in pure native aortic valve regurgitation. J Am Coll Cardiol 2017;70:2752–63.

65. Stachon P, Kaier K, Heidt T, et al. Nationwide outcomes of aortic valve replacement for pure aortic regurgitation in Germany 2008–2015. Catheter Cardiovasc Interv 2020;95:810–6.

66. Hasan BS, McElhinney DB, Brown DW, et al. Short-term performance of the transcatheter Melody valve in high-pressure hemodynamic environments in the pulmonary and systemic circulations. Circ Cardiovasc Interv 2011;4:615–20.

67. Martin MH, Gruber PJ, Gray RG. Transcatheter neoaortic valve replacement utilizing the Melody valve in hypoplastic left heart syndrome. Catheter Cardiovasc Interv 2015;85:615–9.

68. Sinha S, Khan A, Qureshi AM, et al. Application of transcatheter valves for aortic valve replacement in pediatric patients: a case series. Catheter Cardiovasc Interv 2020;95:253–61.

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