Aortic Valve Repair: From Concept to Future Targets

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Aortic valve repair has become an important treatment alternative to patients with aortic insufficiency. In this paper, we review refinements and advances in the understanding of core concepts of aortic valve anatomy and pathophysiology which have enhanced our approach to aortic valve preservation and repair. With these improvements in understanding and techniques, the outcome for aortic valve repair continues to improve. We also review current challenges in the field and explore potential areas of innovation and future study including timing of surgical intervention for aortic insufficiency, comparisons between aortic valve repair and replacement in randomized trials, and development of personalized surgical management plan based on patient-specific pathologies. These advances will further establish the role of aortic valve repair in the management of aortic valve and aortic disease.

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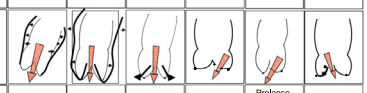
AI Class	Type I Normal cusp motion with FAA dilatation or cusp perforation				Type II	Type III
	Ia	Ib	Ic	Id	Cusp Prolapse	Cusp Restriction
Mechanism						
Repair Technique (*Primary*)	STJ remodeling *Ascending aortic graft*	Aortic Valve sparing: *Reimplantation or remodeling with VAJ annuloplasty*	VAJ annuloplasty	Patch Repair *Autologous or bovine pericardium*	Prolapse Repair • *Free margin plication* • *Triangular resection* • *Free margin resuspension* • *Patch*	Leaflet Repair • *Shaving* • *Decalcification* • *Patch*
(*Secondary*)	VAJ annuloplasty		STJ annuloplasty	VAJ annuloplasty	VAJ annuloplasty	VAJ annuloplasty

Updated repair-oriented functional classification of aortic insufficiency with description of disease mechanisms and repair techniques used.

Central Message

Current opportunities include defining timing of surgery, comparisons between repair and replacement in trials, and development of personalized surgical plans based on specific pathologies.

INTRODUCTION

Aortic valve (AV) repair has evolved to become an important treatment alternative to AV replacement (AVR) for patients with aortic insufficiency (AI). Patients with AVR incur cumulative risks of bleeding and thromboembolic events for mechanical valves, and valve deterioration for bioprosthetic valves. Conceptually, by preserving native valve tissue, AV repair obviates the need for anticoagulation and prosthesis-related complications. In this paper, we review the core concepts of AV repair, new understanding of AV anatomy, mechanisms of AV insufficiency, current evidence for AV repair, and areas for future development.

FUNCTIONAL ANATOMY OF THE AV

Although the anatomy of the AV has been well known for many decades, several recent investigations have highlighted certain nuances that are particularly relevant for AV repair. The normal function of the AV involves a complex interaction between the AV cusps, and the functional aortic annulus (FAA).[1]

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The anatomy and function of each AV cusp is defined by 3 important geometric characteristics: the free margin length, the effective height, and the geometric height. The free margin is the border of the aortic cusp that participates in coaptation and is often elongated and prolapsed in chronic AI as a result of constant stress from turbulent flow. The average normal free margin length is approximately 32–34 mm.[2] While the length of the free margin has been difficult to measure intraoperatively, a free margin length sizer is currently under development.

The effective height is the distance between the central free margin and the aortic insertion line in diastole and is significantly shortened in a prolapsed cusp. The normal effective height has been shown to be approximately 7–12 mm.[3] The development of a caliper for effective height measurement has allowed for systematic intraoperative assessment of effective height, which significantly decreased the incidence of AV reintervention and recurrent AI after AV repair.[4] It has been proposed in multiple studies that an effective height of <9 mm is a risk factor for AV reintervention.[5–7]

The geometric height is the largest distance between the nadir of the cusp to the center of the free margin, and it is correlated with the height of the patient. A shortened geometric height may be due to cusp retraction. Based on 621 patients undergoing AV preserving or repair procedures, Schafers et al defined cusp retraction as geometric height ≤16 mm for TAVs and ≤19 mm for

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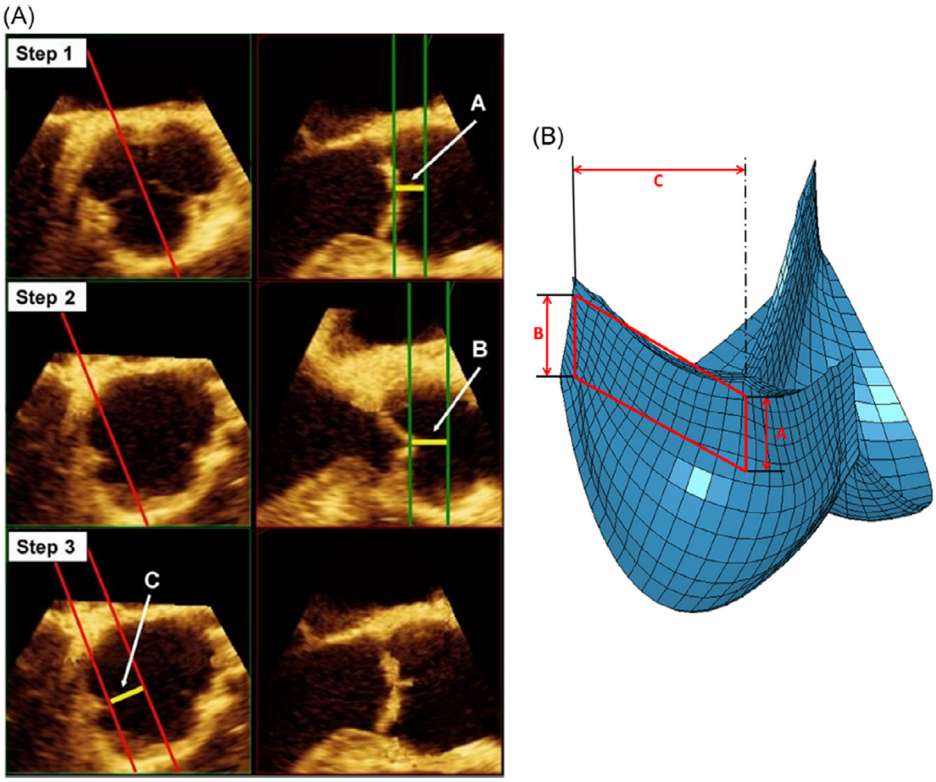

Figure 1. (A) Images of a normal AV from multiple plan reconstruction of the AV; (B) trapezoidal shape of the AV coaptation surface area.[11] Reproduced with permission from the authors.

nonconjoint cusp of BAVs.[8] Although cusp restriction has been an established risk factor for reduced repair durability, quantitative parameters may assist in intraoperative decision-making.[9]

The FAA is further divided into 3 components: (1) the sinotubular junction (STJ), connecting the aortic root to the ascending aorta; (2) the crown-shaped aortic annulus, which serves as the insertion point for AV cusps; and (3) the ventriculo-aortic junction (VAJ), which connects the aortic root and the left ventricle (LV) in a curvilinear fashion.[10] Pathology at every level of the aortic root may reduce cusp coaptation and lead to AI. There is increasing appreciation of the VAJ dilatation, particularly in the muscular portion of the annulus, as the primary cause of aortic insufficiency in a number of patients. This is frequently associated with prolapse of the anterior cusp, both in BAVs and TAVs.

Ultimately, a competent AV requires cusp surface area corresponds appropriately to annular area and results in coaptation. Recent investigations have demonstrated the ability to evaluate this using 3D echocardiography to visualize and quantify cusp coaptation area, which, if it can be reproducibly measured, may emerge as an important predictor of repair durability (Fig. 1).[11]

CLASSIFICATION OF MECHANISMS OF AORTIC INSUFFICIENCY

A repaired-oriented classification of AI based on pathologies of the FAA and the aortic cusp has provided a framework for a systematic approach for AI (Fig. 2). Pathologies of the FAA, including dilatation of isolated STJ (Type 1a), STJ and VAJ (Type 1b), or isolated VAJ (Type 1c) are managed with valve-sparing root replacement (VSRR) with either the reimplantation technique or remodeling technique.[12–14] For Type 1b and 1c where VAJ is dilated, a circumferential annuloplasty is indicated for further stabilization of the subvalvular apparatus.[9,15,16]

Pathologies of the aortic cusps are divided into those with perforation and normal leaflet motion (Type 1d), cusp prolapse (Type II), or cusp restriction from calcification, thickening, or fibrosis (Type III). Type 1d is managed with primary repair or repair with pericardial patch, Type II is repaired with free margin plication or free margin resuspension,[12] and Type III can be managed with shaving/decalcification.[9]

In addition to understanding the mechanism of AI, there is increasing appreciation of the impact of commissural orientation on the repair techniques used for bicuspid AVs. Building on the system above, we propose the addition of commissural orientation to the repair-oriented classification of AI. The commissural angle would be classified into 4 categories: TAV at 120°/120°/120°, ≤140°/220° BAV, ≥140°/220° BAV, and symmetrical BAV at 180°/180°. The incorporation of commissural orientation allows for the integration of BAV into the current classification of AI and has important implication in repair strategy. For patients with a commissural orientation of ≤140°/220° BAV, the repair should aim at restoring the commissural angle toward 120°/120°/120°; on the other hand, for patients with

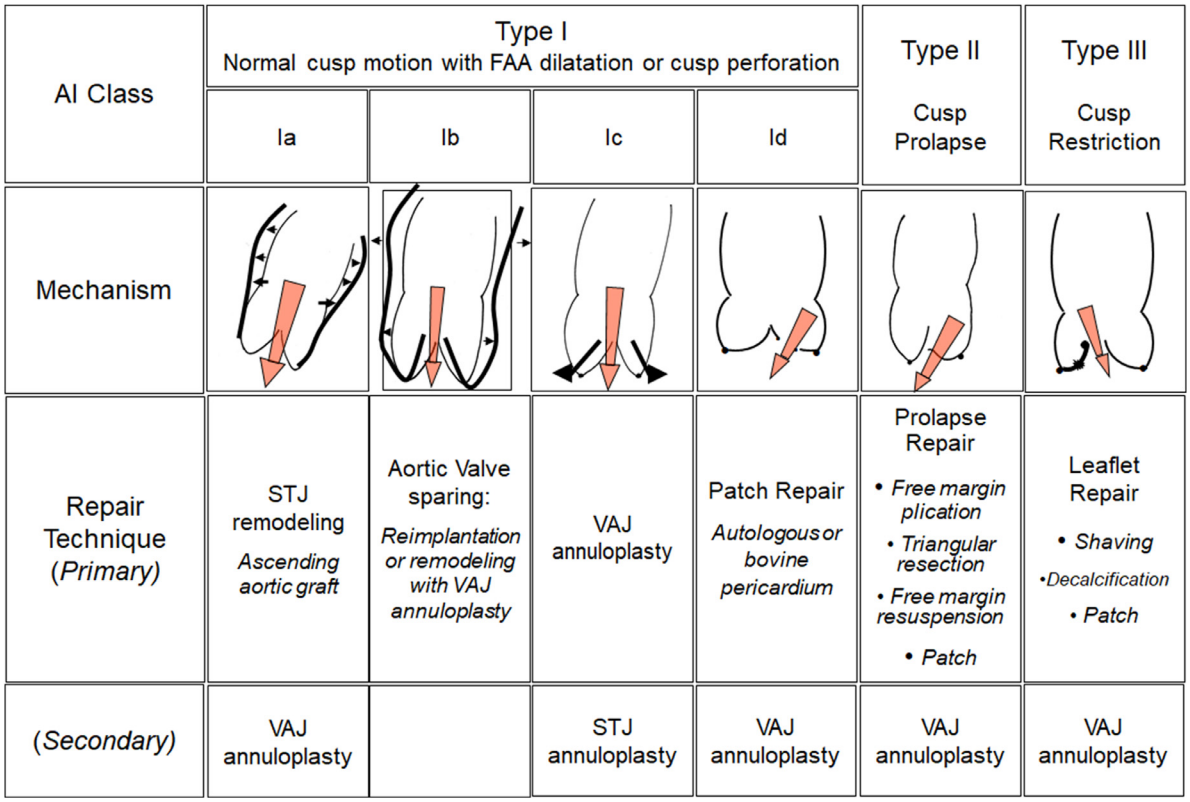

Figure 2. Updated repair-oriented functional classification of aortic insufficiency with description of disease mechanisms and repair techniques used; the main update involves the replacement of SCA with VAJ annuloplasty due to the superior stability of the latter.[9] FAA, functional aortic annulus; SCA, subcommissural annuloplasty; STJ, sinotubular junction; VAJ, ventriculo-aortic junction. Reproduced and modified with permission from the authors.

commissural angle ≥140°/220°, a postrepair commissural orientation of 180°/180° is often targeted.[17,18]

PREDICTORS OF AV REPAIR FAILURE

Multiple studies have identified risk factors that increase the risk of early and late valve repair failure. Based on the current best available evidence, the surgeon should aim for a repair with the following characteristics to minimize recurrent AI and need for AV reintervention:

1. Minimal residual AI; particularly avoid any eccentric AI[19]
2. A level of coaptation above the aortic annulus (ie, no leaflet prolapse)[19]
3. A coaptation length of ≥4 mm[19]
4. An effective height of ≥9 mm[5–7]
5. VAJ ≤25 mm (achieved using reimplantation technique or other methods of circumferential annuloplasty if preoperative VAJ ≥25 mm)[5,19–23]
6. Avoid leaflet augmentation with pericardial patches[5,18]

FUTURE DIRECTIONS

A number of important challenges and opportunities lie ahead of the field of AV repair.

Define Optimal Timing for Intervention

The optimal timing for intervention for patients with AI is not well established. The current indication for surgery for AI is determined by symptoms, reduced LV ejection fraction (LVEF), and dilated LV end-diastolic and end-systolic dimensions (LVEDD and LVESD).[24] However, decrease in LVEF and dilatation of LVESD may already represent advanced sequelae of AI, and evidence from large retrospective studies have suggested that patients with normal LVEF and smaller than currently indicated LVESD also experienced a survival benefit from AVR or AV repair.[25–27] When AI was managed with AVR, delayed intervention may be beneficial to delay prosthetic valve-related complications. However, as AV repair techniques continue to evolve and produce favorable short- and long-term outcomes, there may be a role for an earlier surgical threshold to achieve maximal LV preservation. In an institutional series of 331 patients, Sharma et al found that at 15 years, patients with preoperative LVEF of <50% had 3.5-fold greater risk of late mortality (hazard ratio [HR] 3.46; 95% confidence interval [CI] 2.05–5.82), and patients with a preoperative LVESD of >50 mm had 2-fold greater risk of late mortality (HR 2.08; 95% CI 1.05–4.12). In addition, compared to an age- and gender-matched control cohort, the survival of patients with LVESD >50 mm and LVEF <50% was significantly worse ($P < 0.01$).[28] Further investigation in the impact of earlier

repair for patients with chronic AI is therefore supported and needed.

In recent years, biomarkers such as N-terminal pro B-type natriuretic peptide and new methods to assess myocardial function such as speckle tracking or tissue Doppler involving the measurement of global longitudinal strain have shown promising results as markers to be used to predict early LV remodeling from aortic regurgitation.[29–31] Further studies using novel diagnostic techniques could identify early LV changes in AI and refine the optimal stage for surgical intervention.

Lack of Randomized Controlled Studies Comparing AV Repair to AVR

The short- and long-term outcome of AV repair has been well described in the literature; however, there is a lack of studies comparing AV repair to replacement for the management of AI. Saczkowski et al conducted a meta-analysis of studies on AV repair prior to 2013 and looked at 17 studies with a total of 2891 patients and a median age of 54 years old. The reported in-hospital mortality was 2.6%, and 2% of patients required early AV reintervention due to repair failure. Freedom from AV reintervention was 92% at 5 years; rate of thromboembolic events was 0.5%/patient-year, and incidence of late mortality was 1.3%/patient-year.[32] In a meta-analysis of VSRR prior to 2015, 31 studies with a total of 4777 patients and a mean age of 51 years old were included. In-hospital mortality was 2%, and the linearized rate of thromboembolism, hemorrhage, and AV reintervention were 0.41%/patient-year, 0.23%/patient-year, and 1.32%/patient-year, respectively.[33] These results confirmed the low operative risk of selected patients undergoing AV repair in specialized centers; however, comparison to AVR in a similar group of patients was not conducted in these studies.

Multiple retrospective studies compared institutional experiences with VSRR and composite valve graft replacement (CVG) with mechanical or bioprosthetic valves or allografts. However, in addition to the limitations of single center, nonrandomized, retrospective studies, most studies comparing VSRR and CVG included patients who underwent replacement for indications such as aortic stenosis, potentially introducing multiple important confounders. Furthermore, the benefit of VSRR when compared to mechanical CVG in an era of lower INR threshold has not been well established. In a series of 370 patients, VSRR had the highest 5-year survival at 95.2%, with no differences in 5-year freedom from AV reintervention and lower bleeding risk at 5 years as compared to mechanical CVG.[34] On the other hand, in another propensity-matched cohort, the need for AV reintervention was significantly higher in VSRR (7.3%) as compared to mechanical CVG, driven mainly by the use of remodeling technique.[35] In the largest institutional series addressing this question, Svensson et al compared 957 patients who underwent VSRR to bioprosthetic or mechanical CVG, as well as allograft root replacement. VSRR patients experienced no in-hospital mortality, but had a significantly higher incidence of early AV reintervention, driven mainly by BAV patients who underwent remodeling VSRR, and mechanical CVG had the lowest need for early and late AV reintervention and incidence of recurrent AI.[36] It is important to note that many of the studies included patients who underwent VSRR and AV repair prior to the use of aortic annuloplasty and precise measurement tools for intraoperative assessment. Therefore, the benefit of contemporary AV repair techniques over AVR, as well as patient-specific factors that influence outcome, need to be better characterized.

Personalized Repair Based on Patient-Specific Modeling

Recent developments in patient-specific computational modeling have allowed for preoperative simulation and evaluation of patient-specific valve anatomy and pathology. A finite-element model of the AV has been developed to model various AV pathology and simulate outcome after application of different leaflet repair techniques.[37] This could be valuable in preoperative surgical planning as a tool to predict postoperative valve performance, giving another measure of certainty over surgical intuition.

Management of VAJ Dilatation

Last, components of the aortic root should be individually characterized, and combinations of surgical techniques should be tailored to patient-specific pathology. One of the developing areas is the management of VAJ dilatation. Although the remodeling technique has the theoretical benefit of preserving root dynamic, in patients with VAJ dilatation and SoV or STJ dilatation, the remodeling technique did not provide sufficient annular stability.[5,19–23] On the other hand, for patients with aortic regurgitation as a result of isolated VAJ dilatation, VSRR by the reimplantation technique may be too aggressive.[38] Traditionally, isolated VAJ dilatation has been managed with subcommissural annuloplasty; however, there is accumulating evidence suggesting that subcommissural annuloplasty is not sufficient; in fact, the application of subcommissural annuloplasty in VAJ dilatation is a risk factor for recurrent AI.

Over the past decade, multiple techniques have developed to address this problem. The CAVIAAR study compared the use of an expansible subvalvular aortic ring with remodeling technique to CVG for patients with an aortic root aneurysm and aortic regurgitation. Two hundred sixty-one patients were prospectively recruited from 20 participating centers, with 131 patients in the CVG group and 130 in the repair group, a mean age of 56.1 years old, and 44.7% BAV. The 30-day mortality was 3.8% for both groups; 96.8% of patients in the repair group had ≤grade 1 AI. After propensity match, there was no significant difference in 30-day mortality, reoperation, thromboembolic, hemorrhagic, infectious events, heart failure, or major adverse valve-related events. In addition, subvalvular aortic ring was found to result in more VAJ reduction when compared to subcommissural annuloplasty.[15]

In some patients, the limit of external dissection of the aortic root prevents the placement of the ring at the level of the true VAJ. Schneider et al compared the use of external suture annuloplasty in addition to BAV repair in 164 patients with 104 patients who underwent BAV repair without suture annuloplasty. Thirty-seven patients underwent suture annuloplasty with braided

polyester and 127 patients with polytetrafluoroethylene (PTFE). With suture annuloplasty, 5-year freedom from reoperation was significantly improved from 73.2% to 92.6% ($P < 0.01$); furthermore, suture annuloplasty with PTFE had a significantly higher incidence of freedom from reoperation as compared to suture annuloplasty with braided polyester (96.7% vs 83.5%, respectively).[39] On the other hand, internal annuloplasty systems have also been developed. However, experience is limited and there is concern regarding the rigidity of the devices available and their interaction with valve cusps. Similar to external suture annuloplasty, an internal ring annuloplasty could negate the need for deep external dissection.[40]

CONCLUSION

AV repair has established itself as a promising alternative treatment for young patients with AI, with low early and long-term adverse events. Further studies are required to set appropriate surgical intervention threshold for AI, characterize benefit of AV repair in patients with AI over AVR, understand patient-specific risk factors that may influence the outcome of repair, and continue to improve on operative techniques, tailoring appropriate surgical strategy to individual patients to achieve the best outcome.

REFERENCES

1. Loukas M, Bilinsky E, Bilinsky S, et al: The anatomy of the aortic root. Clin Anat 27:748–756, 2014
2. De Kerchove L, Momeni M, Aphram G, et al: Free margin length and coaptation surface area in normal tricuspid aortic valve: An anatomical study. Eur J Cardiothorac Surg 53:1040–1048, 2018
3. Bierbach BO, Aicher D, Issa OA, et al: Aortic root and cusp configuration determine aortic valve function. Eur J Cardiothorac Surg 38:400–406, 2010
4. Lansac E, Di Centa I, Sleilaty G, et al: Long-term results of external aortic ring annuloplasty for aortic valve repair. Eur J Cardiothorac Surg 50:350–360, 2016
5. Aicher D, Kunihara T, Abou Issa O, et al: Valve configuration determines long-term results after repair of the bicuspid aortic valve. Circulation 123:178–185, 2011
6. Kunihara T, Aicher D, Rodionycheva S, et al: Preoperative aortic root geometry and postoperative cusp configuration primarily determine long-term outcome after valve-preserving aortic root repair. J Thorac Cardiovasc Surg 143:1389–1395, 2012
7. Marom G, Haj-Ali R, Rosenfeld M, et al: Aortic root numeric model: Annulus diameter prediction of effective height and coaptation in post-aortic valve repair. J Thorac Cardiovasc Surg 145:406–411.e1, 2013
8. Schafers HJ, Schmied W, Marom G, et al: Cusp height in aortic valves. J Thorac Cardiovasc Surg 146:269–274, 2013
9. Boodhwani M, de Kerchove L, Glineur D, et al: Repair-oriented classification of aortic insufficiency: Impact on surgical techniques and clinical outcomes. J Thorac Cardiovasc Surg 137:286–294, 2009
10. Underwood MJ, El Khoury G, Deronck D, et al: The aortic root: Structure, function, and surgical reconstruction. Heart 83:376–380, 2000
11. Sohmer B, Jafar R, Patel P, et al: Aortic valve cusp coaptation surface area using 3-dimensional transesophageal echocardiography correlates with severity of aortic valve insufficiency. J Cardiothorac Vasc Anesth 32:344–351, 2018
12. Boodhwani M, El Khoury G: Aortic valve repair. Op Tech Thorac Cardiovasc Surg 14:266–280, 2009
13. David TE: Aortic valve sparing in different aortic valve and aortic root conditions. J Am Coll Cardiol 68:654–664, 2016
14. Sarsam MA, Yacoub M: Remodeling of the aortic valve annulus. J Thorac Cardiovasc Surg 105:435–438, 1993
15. Lansac E, Bouchot O, Arnaud Crozat E, et al: Standardized approach to valve repair using an expansible aortic ring versus mechanical Bentall: Early outcomes of the CAVIAAR multicentric prospective cohort study. J Thorac Cardiovasc Surg 149:S37–S45, 2015
16. Schneider U, Aicher D, Miura Y, et al: Suture annuloplasty in aortic valve repair. Ann Thorac Surg 101:783–785, 2016
17. Aicher D, Bewarder M, Kindermann M, et al: Aortic valve function after bicuspidization of the unicuspid aortic valve. Ann Thorac Surg 95:1545–1550, 2013
18. Schneider U, Feldner SK, Hofmann C, et al: Two decades of experience with root remodeling and valve repair for bicuspid aortic valves. J Thorac Cardiovasc Surg 153:S65–S71, 2017
19. le Polain de Waroux JB, Pouleur AC, Robert A, et al: Mechanisms of recurrent aortic regurgitation after aortic valve repair: Predictive value of intraoperative transesophageal echocardiography. JACC Cardiovasc Imaging 2:931–939, 2009
20. Navarra E, El Khoury G, Glineur D, et al: Effect of annulus dimension and annuloplasty on bicuspid aortic valve repair. Eur J Cardiothorac Surg 44:316–322, 2013. discussion 22–23
21. de Kerchove L, Mastrobuoni S, Boodhwani M, et al: The role of annular dimension and annuloplasty in tricuspid aortic valve repair. Eur J Cardiothorac Surg 49:428–437, 2016. discussion 37–38
22. Habertheuer A, Milewski RK, Bavaria JE, et al: Predictors of recurrent aortic insufficiency in type I bicuspid aortic valve repair. Ann Thorac Surg 106:1316–1324, 2018
23. de Kerchove L, Boodhwani M, Glineur D, et al: Valve sparing-root replacement with the reimplantation technique to increase the durability of bicuspid aortic valve repair. J Thorac Cardiovasc Surg 142:1430–1438, 2011
24. 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. J Thorac Cardiovasc Surg 148:e1–e132, 2014
25. Chaliki HP, Mohty D, Avierinos JF, et al: Outcomes after aortic valve replacement in patients with severe aortic regurgitation and markedly reduced left ventricular function. Circulation 106:2687–2693, 2002
26. Klodas E, Enriquez-Sarano M, Tajik AJ, et al: Aortic regurgitation complicated by extreme left ventricular dilation: Long-term outcome after surgical correction. J Am Coll Cardiol 27:670–677, 1996
27. Mentias A, Feng K, Alashi A, et al: Long-term outcomes in patients with aortic regurgitation and preserved left ventricular ejection fraction. J Am Coll Cardiol 68:2144–2153, 2016
28. Sharma V, Suri RM, Dearani JA, et al: Expanding relevance of aortic valve repair—Is earlier operation indicated? J Thorac Cardiovasc Surg 147:100–107, 2014
29. Pizarro R, Bazzino OO, Oberti PF, et al: Prospective validation of the prognostic usefulness of B-type natriuretic peptide in asymptomatic patients with chronic severe aortic regurgitation. J Am Coll Cardiol 58:1705–1714, 2011
30. Olsen NT, Sogaard P, Larsson HB, et al: Speckle-tracking echocardiography for predicting outcome in chronic aortic regurgitation during conservative management and after surgery. JACC Cardiovasc Imaging 4:223–230, 2011
31. Alashi A, Mentias A, Abdallah A, et al: Incremental prognostic utility of left ventricular global longitudinal strain in asymptomatic patients with significant chronic aortic regurgitation and preserved left ventricular ejection fraction. JACC Cardiovasc Imaging 11:673–682, 2018
32. Saczkowski R, Malas T, de Kerchove L, et al: Systematic review of aortic valve preservation and repair. Ann Cardiothorac Surg 2:3–9, 2013
33. Arabkhani B, Mookhoek A, Di Centa I, et al: Reported outcome after valve-sparing aortic root replacement for aortic root aneurysm: A systematic review and meta-analysis. Ann Thorac Surg 100:1126–1131, 2015

34. Badiu CC, Deutsch MA, Sideris C, et al: Aortic root replacement: Comparison of clinical outcome between different surgical techniques. Eur J Cardiothorac Surg 46:685–692, 2014. discussion 92
35. Gaudino M, Lau C, Munjal M, et al: Contemporary outcomes of surgery for aortic root aneurysms: A propensity-matched comparison of valve-sparing and composite valve graft replacement. J Thorac Cardiovasc Surg 150:1120–1129.e1, 2015
36. Svensson LG, Pillai ST, Rajeswaran J, et al: Long-term survival, valve durability, and reoperation for 4 aortic root procedures combined with ascending aorta replacement. J Thorac Cardiovasc Surg 151:764–774.e4, 2016
37. Labrosse MR, Boodhwani M, Sohmer B, et al: Modeling leaflet correction techniques in aortic valve repair: A finite element study. J Biomech 44:2292–2298, 2011
38. Al-Atassi T, Boodhwani M: Aortic valve insufficiency in aortic root aneurysms: Consider every valve for repair. J Vis Surg 4:60, 2018
39. Schneider U, Hofmann C, Aicher D, et al: Suture annuloplasty significantly improves the durability of bicuspid aortic valve repair. Ann Thorac Surg 103:504–510, 2017
40. Mazzitelli D, Pfeiffer S, Rankin JS, et al: A regulated trial of bicuspid aortic valve repair supported by geometric ring annuloplasty. Ann Thorac Surg 99:2010–2016, 2015