Aortic Valve and Ascending Aorta Guidelines for Management and Quality Measures

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1. Introduction and Methodology

The question may be asked why another Guideline manuscript is needed. The reasons are fivefold: (1) to outline pros and cons of treatment options; (2) to outline areas where further research is needed, potentially from updated Society of Thoracic Surgeons (STS) data collection variables as there are few randomized trials that give more absolute answers to questions; (3) to provide technical guidelines for aortic valve and aortic surgery; (4) to provide background for recommended quality measures and suggest quality measures; and (5) to present the new STS valve data collection variables that address issues related to the preoperative testing and technical aspects of aortic valve surgery (Appendix 1).

The evaluation of aortic valve procedures suffers from a dearth of prospective randomized trials that have shown definitive superiority of one procedure over others, although this has been attempted (eg, mechanical versus biological valves, and homografts versus Ross procedure, etc) [2–18]. Indeed, when valve devices are compared for survival (homograft, biological valves, mechanical valves or Ross procedure) and the only adjustment made is for age, there is no difference at all in late survival and thus the debate revolves more around valve durability and anticoagulation [14] (Figs 1 to 3).

Hence, the guidelines rely primarily on nonrandomized trials, observational studies, registries, propensity analyses, and consensus statements of experts. Clearly, these may require revision over time, particularly related to the new transcatheter aortic valve replacement (TAVR) procedures. The application of class of recommendation and level of evidence characterization is according to those recommended by ACCF/AHA (Table 1).

The guidelines address only the adult population and not the pediatric population. When needed, the guidelines draw heavily from the previously published 2010

The Society of Thoracic Surgeons Clinical Practice Guidelines are intended to assist physicians and other health care providers in clinical decision making by describing a range of generally acceptable approaches for the diagnosis, management, or prevention of specific diseases or conditions. These guidelines should not be considered inclusive of all proper methods of care or exclusive of other methods of care reasonably directed at obtaining the same results. Moreover, these guidelines are subject to change over time, without notice. The ultimate judgment regarding the care of a particular patient must be made by the physician in light of the individual circumstances presented by the patient.

For the full text of this and other STS Practice Guidelines, visit http://www.sts.org/resources-publications on the official STS Web site (www.sts.org).

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For authors' disclosure of industry relationships, see Appendix 2.

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Abbreviations and Acronyms

ABP = antegrade brain perfusion
ACE = angiotensin-converting enzyme
AR = aortic regurgitation
AS = aortic stenosis
AVA = aortic valve area
AVR = aortic valve replacement
BAV = balloon aortic valvuloplasty
BSA = body surface area
CABG = coronary artery bypass graft
CAD = coronary artery disease
CT = computed tomography
DLCO = diffusing capacity of lung for carbon monoxide
ECG = electrocardiogram
EF = ejection fraction
EOA = effective orifice area
FDA = Food and Drug Administration
HCA = hypothermic circulatory arrest
IMH = intramural hematoma
INR = international normalized ratio
IVUS = intravascular ultrasound
LV = left ventricular
MRI = magnetic resonance imaging
PFT = pulmonary function test
PPM = patient-prosthetic mismatch
PROM = preoperative risk of mortality
RBP = retrograde brain perfusion
RVOT = right ventricular outflow tract
SVD = structural valve deterioration
TAVR = transcatheter aortic valve replacement
TEE = transesophageal echocardiogram
TTE = transthoracic echocardiogram

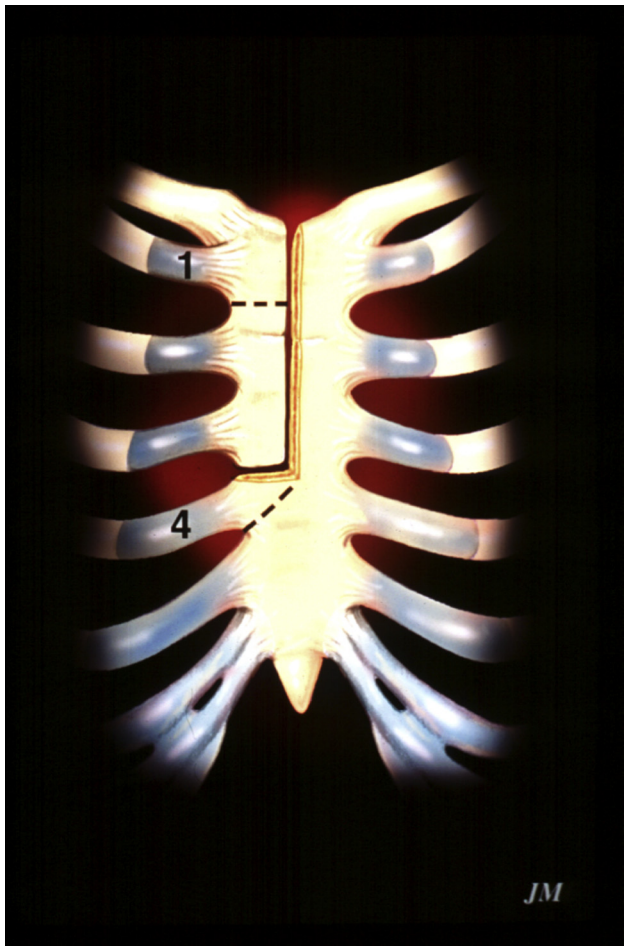

Fig 1. Options for minimally invasive J incision.

ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guideline for the diagnosis and management of patients with thoracic aortic disease. Hence, indications for surgery are not covered in detail, except where new evidence suggests an update is needed. The previous guidelines for severity of disease and the management of outcomes for patients with asymptomatic disease are summarized and covered in detail in the 2010 document [1, 19, 20]. For cardiologists and cardiac surgeons, there have been few options and no guidelines on how to manage the high risk, previously inoperable, patients. The TAVR technology and particularly the pivotal Placement of Aortic Transcatheter (PARTNER) trials and the ongoing CoreValve trial have further focused efforts on managing this population. Previous studies have suggested that between 38% of patients (Europe) and two thirds of patients (southern California) with severe aortic valve stenosis go untreated [21, 22]. With the advent of TAVR both the traditionally open aortic valve replacement (AVR) procedures and balloon aortic valvuloplasty (BAV) have also pari passu evolved. Hence, these aspects are discussed. The field is rapidly developing, and undoubtedly later guidelines will need to update recommendations based on new iterations.

Literature searches were conducted using standardized MeSH terms from the National Library of Medicine PUBMED database list of search terms. Section authors then drafted their recommendations, using prior published guidelines as a reference when available, and circulated to the entire writing committee as drafts. Revisions were made until consensus was reached on class, level of evidence, references, and language. Finally, the full document was submitted for approval by the STS Workforce on Evidence Based Surgery before publication. The guidelines were posted on the STS website for an open comment period. The guidelines then were also submitted to the STS Council on Quality, Research, and Patient Safety Operating Board and the STS Executive Committee before submission for publication.

1.1. Evaluation of a Valve Procedure

Paramount to evaluating a valve procedure is (1) ease of procedure; (2) safety; (3) efficacy (hemodynamic performance, effective orifice area, and energy loss); (4) durability, measured as freedom from structural valve deterioration; and (5) event-free survival.

For aortic valves this would entail (1) ease of prosthetic aortic valve insertion or valve repair; (2) safety of the

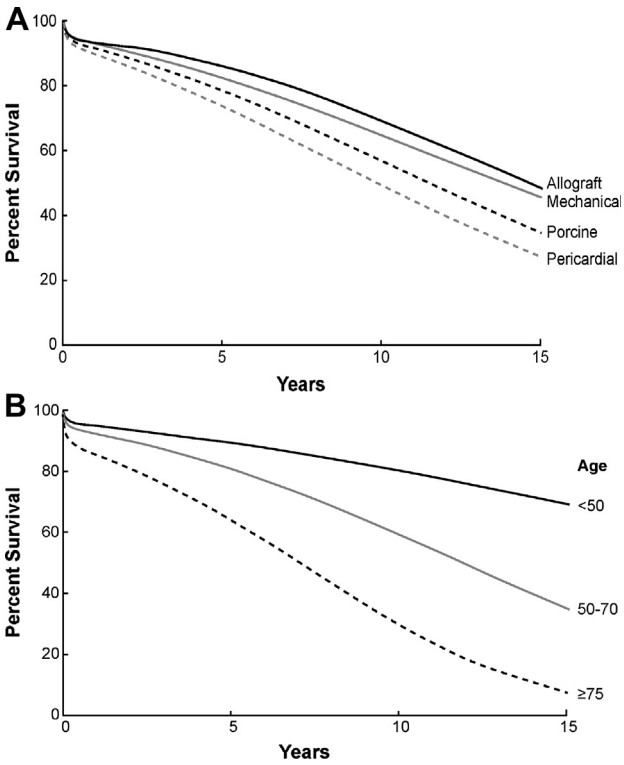

Fig 2. (A) Relationship of late survival to years after aortic valve insertion in 13,258 patients, divided by aortic valve prosthesis. (B) Survival by age.

operation; (3) effective orifice area (EOA) including gradients and energy loss; and (4) long-term durability, with no difference in survival compared with other devices, but better than the untreated population.

Clearly, there are few, if any medical procedures that are as effective in relieving symptoms, improving quality of life, and also increasing long-term survival as much as AVR for aortic stenosis (AS) or aortic regurgitation (AR), but for perhaps the exception of heart transplantation, but the latter adds the problem of managing new medications and increased monitoring. Recent data from 3,600 Medicare patients show that there is a reduced hospital readmission rate and increased survival among high-risk Medicare patients (aged ≥65 years) treated with AVR for severe AS, despite the extra cost. Of note, open AVR does not reduce the cost when compared with medical management despite the multiple readmissions for heart failure in the latter.

The potential population needing AVR for severe AS is estimated at 350,000 and increasing. The exact number of aortic valve procedures, including repairs and replacements, is unknown. A number of 48,000 has been reported [23]; however, a number of 95,000 Medicare patients was reported in a recent publication [24] (Tables 2 and 3). Table 2 shows the number of valves sold to hospitals for one year (92,514). The STS Adult Cardiac Surgery Database (ACSD) does not capture the number as only patients who undergo single valve or valve plus coronary bypass are tracked. Double valve, AVR plus aorta, and so forth, are not tracked. Nevertheless, the STS data show

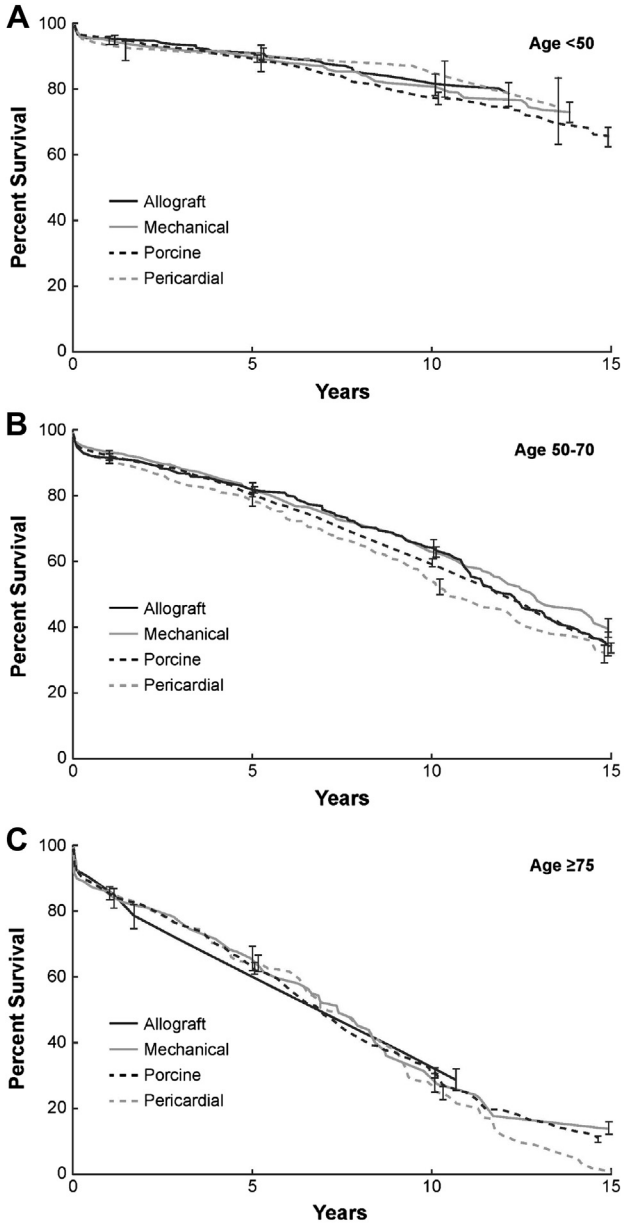

Fig 3. Survival by age groups: (A) younger patients; (B) middle-aged patients; (C) elderly patients. Note that differences disappear.

AVR is increasing, probably because of the aging population and increasing awareness of good results, and the option of TAVR. Despite this, on average an STS site does 23 isolated aortic valves and on average a cardiac surgeon only does 8 AVR per annum (Fig 4). Figures 5 through 18 show some important trends.

The new STS valve data 2.73 module adds various variables that members of the writing committee and the STS Workforce on National Databases considered would be important information for future studies, and that would allow for further research to improve both the process of an aortic valve insertion as well as the procedure quality of care. Clearly this will raise new questions that will result in the evolution and iteration of newer guidelines based on

Table 1. ACCF/AHA Classification of Recommendations and Level of Evidence

SIZE OF TREATMENT EFFECT

ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT	CLASS I *Benefit >>> Risk* **Procedure/Treatment SHOULD be performed/ administered**	CLASS IIa *Benefit >> Risk* *Additional studies with focused objectives needed* **IT IS REASONABLE to perform procedure/administer treatment**	CLASS IIb *Benefit ≥ Risk* *Additional studies with broad objectives needed; additional registry data would be helpful* **Procedure/Treatment MAY BE CONSIDERED**	CLASS III *No Benefit* or CLASS III *Harm* Procedure/Test / Treatment COR III: No benefit — Not Helpful / No Proven Benefit COR III: Harm — Excess Cost w/o Benefit or Harmful / Harmful to Patients
LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Sufficient evidence from multiple randomized trials or meta-analyses
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is useful/effective ■ Evidence from single randomized trial or nonrandomized studies	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Evidence from single randomized trial or nonrandomized studies
LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard of care	■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard of care
Suggested phrases for writing recommendations	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	COR III: No Benefit: is not recommended; is not indicated; should not be done; is not useful/ beneficial/ effective COR III: Harm: potentially harmful; causes harm; associated with excess morbidity/mortality; should not be done
Comparative effectiveness phrases†	treatment/strategy A is recommended/indicated in preference to treatment B treatment A should be chosen over treatment B	treatment/strategy A is probably recommended/indicated in preference to treatment B it is reasonable to choose treatment A over treatment B		

*Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as gender, age, history of diabetes, history of prior myocardial infarction, history of heart failure, and prior aspirin use. A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Even though randomized trials are not available, there may be a very clear clinical consensus that a particular test or therapy is useful or effective. †For comparative effectiveness recommendations (Class I and IIa; Level of Evidence A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated. Reprinted with permission from Ref. 24a [Jacobs AK, et al. Circulation. 2013;127:268–310. ©2013 American Heart Association, Inc.]

the data collected by the STS database. Online in Appendix 1 are the new fields specific to valve procedures. See the comments relevant to specific fields referenced. In this document we have avoided reference to company names and models as there are 368 models of biological valves alone that are available for implantation.

2. Summary and Update of ACCF/AHA Guidelines for Indications and Timing of Surgery

Major advances in the evaluation and management of patients with valvular heart disease during the past several decades have resulted in substantial improvement in the outcomes of patients in terms of survival and quality of life. These advances include the development of imaging modalities (most notably cardiac ultrasonography) that have yielded essential data on natural history and the predictors of outcome after operative intervention. At that same time, the steady and significant advances in cardiac surgery have expanded operative windows to include surgery on both older patients with severe comorbidities and younger patients earlier in the natural history of the disease, even those who are asymptomatic.

Table 2. Valves Sold in the United States for the Year Ending June 2011

Valve	Number
Mechanical	
All (conduits 11%)	16,780
Tissue	
All	75,734
ATS	216
Carbomedics	5,290
Edwards	39,367
Medtronic	18,688
St. Jude	11,666
Total	92,514
Tissue valve costs:	All, $435,716,947.00

These advances, coupled with the growing prevalence of diseases of heart valves in an aging population and the impact on quality of life, health care resources and need for quality improvement, stimulated the ACCF/AHA Task Force on Practice Guidelines to establish a writing committee to formulate guidelines for the management of patients with valvular heart disease. The ACCF/AHA guidelines for the management of patients with valvular heart disease were first published in 1998 [25], extensively revised in 2006 [20], and updated in 2008 [19]. The knowledge base summarized in the guidelines is channeled into a large number of specific recommendations supported by the literature to assist clinicians in their care of patients across the wide spectrum of valvular heart disease, including diagnosis, medical management and indications for surgical intervention. Comparable guidelines from the European Society of Cardiology have been published in 2007 [26].

Although the ACCF/AHA guideline recommendations represent a major step forward in improving and standardizing quality of care, there are fundamental weaknesses in the underpinnings of these guidelines. Unlike many other areas of cardiovascular disease, such as secondary prevention, acute coronary syndromes and heart failure, there is a major scarcity of large-scale multicenter trials addressing the diagnosis and treatment of patients with valvular disease from which to derive the definitive evidence base required for firm recommendations. The available data in the literature represent primarily the experiences reported by single institutions in relatively small numbers of patients. In the absence of an authoritative database, management issues in many situations remain controversial or uncertain.

Thus, virtually all of the recommendations in the ACCF/AHA document are based on expert consensus (level of evidence C) rather than on prospective multicenter randomized trials (level of evidence A). In fact, in the 2006 document, only 1 of 320 recommendations (0.3%) was based on level of evidence A data [27]. In this context, it is noteworthy that the consensus-driven recommendations in the ACCF/AHA document are remarkably similar to those in the European Society of Cardiology guidelines on the management of valvular heart disease [26]. This underscores the collective experience that has accumulated over the past several decades on both sides of the Atlantic. Nonetheless, implementation of prospective randomized trials is necessary to move the field forward.

Classification of Recommendations

The ACCF/AHA guidelines for the management of patients with valvular heart disease recommendations follow the standard format established for other ACCF/AHA recommendations (Table 1):

- Class I: conditions for which there is evidence for and/or general agreement that the procedure or treatment is beneficial, useful, and effective
- Class II: conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment
- Class IIa: weight of evidence/opinion is in favor of usefulness/efficacy
- Class IIb: usefulness/efficacy is less well established by evidence/opinion
- Class III: conditions for which there is evidence and/or general agreement that the procedure/treatment is not useful/effective and in some cases may be harmful

Table 3. Trends in Hospital Volumes of Medicare Patients and the Proportion of Medicare Patients Who Underwent Aortic Valve Replacement Operations in High-Volume Hospitals From 1999 through 2008. Note this is for two-year data

	Variable Period				
	1999–2000	2001–2002	2003–2004	2005–2006	2007–2008
AVR					
No. of hospitals	1,013	1,064	1,105	1,139	1,161
No. of patients	74,541	80,223	85,556	87,421	95,033
Hospital volume					
Median	53	54	57	53	60
Interquartile range	28–99	29–105	30–104	29–102	31–108

Patient number is for 2-year periods. Hospital volume is per year.

AVR = aortic valve replacement.

Table 4. Valve Academic Research Consortium Criteria for Successful Valve Insertion and Composite Endpoints

Device success

1. Successful vascular access, delivery and deployment of the device, and successful retrieval of the delivery system
2. Correct position of the device in the proper anatomical location
3. Intended performance of the prosthetic heart valve (aortic valve area $\leq$1.2 cm^2 and mean aortic valve gradient $\geq$20 mm Hg or peak velocity $\geq$3 m/s, without moderate or severe prosthetic valve aortic regurgitation)
4. Only one valve implanted in the proper anatomical location

Combined safety endpoint (at 30 days)

1. All-cause mortality
2. Major stroke
3. Life-threatening (or disabling) bleeding
4. Acute kidney injury—stage 3 (including renal replacement therapy)
5. Periprocedural myocardial infarction
6. Major vascular complication
7. Repeat procedure for valve-related dysfunction (surgical or interventional therapy)

Combined efficacy endpoint, at 1 year or longer

1. All-cause mortality (after 30 days)
2. Failure of current therapy for aortic stenosis, requiring hospitalization for symptoms of valve-related or cardiac decompensation
3. Prosthetic heart valve dysfunction (aortic valve area $\leq$1.2 cm^2 and mean aortic valve gradient $\geq$20 mm Hg or peak velocity $\geq$3 m/s, or moderate or severe prosthetic valve aortic regurgitation)

2.1. Indications for Aortic Valve Surgery

2.1.1. AORTIC STENOSIS—RECOMMENDATIONS

Class I

1. AVR is recommended in patients with severe AS at the onset of symptoms of dyspnea, angina, or light-headedness or syncope (Fig 1) [28–36]. (Level of evidence B)
2. AVR is recommended, regardless of symptoms, with the identification of left ventricular (LV) systolic dysfunction (ejection fraction [EF] <50%). (Level of evidence C)
3. AVR is recommended in patients with severe AS who are scheduled to undergo coronary artery bypass graft surgery (CABG), surgery on other cardiac valves, or surgery on the aortic root or ascending aorta. (Level of evidence C)

Class IIa

1. AVR is reasonable in patients with moderate AS undergoing CABG or surgery on the aorta or other heart valves [37–40]. (Level of evidence B)

Class IIb

1. Exercise testing in asymptomatic patients with AS to determine the need for AVR may be considered to elicit exercise-induced symptoms and abnormal blood pressure responses [41–43]. (Level of evidence B)
2. AVR may be considered for asymptomatic patients with severe AS and abnormal response to exercise (eg, asymptomatic hypotension). (Level of evidence C)
3. AVR may be considered for adults with severe asymptomatic AS if there is a high likelihood of rapid progression (age, calcification, and CAD) or if surgery might be delayed at the time of symptom onset. (Level of evidence C)

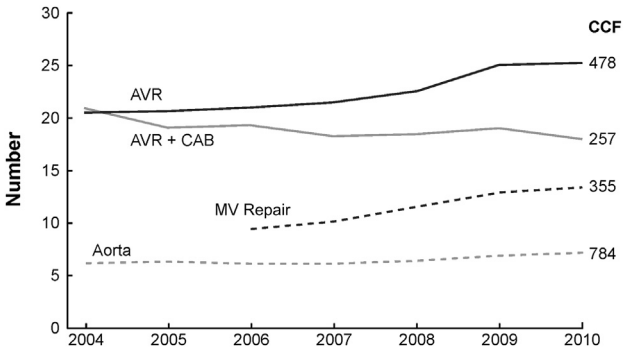

Fig 4. Average annual valve procedures for STS sites (left axis) and busy practice (right axis) over time. (AVR = aortic valve replacement; CAB = coronary artery bypass; CCF = Cleveland Clinic Foundation; MV = mitral valve repair.)

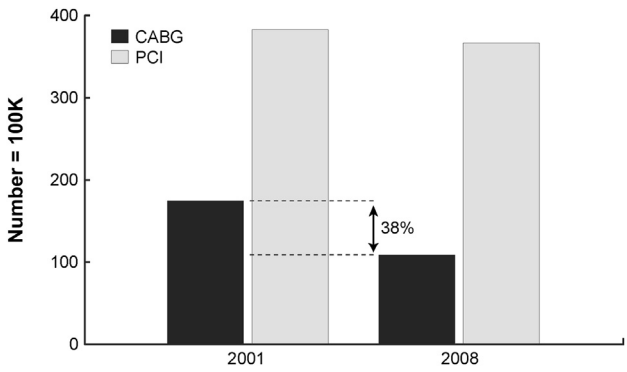

Fig 5. Coronary artery bypass and percutaneous coronary intervention volume trends.

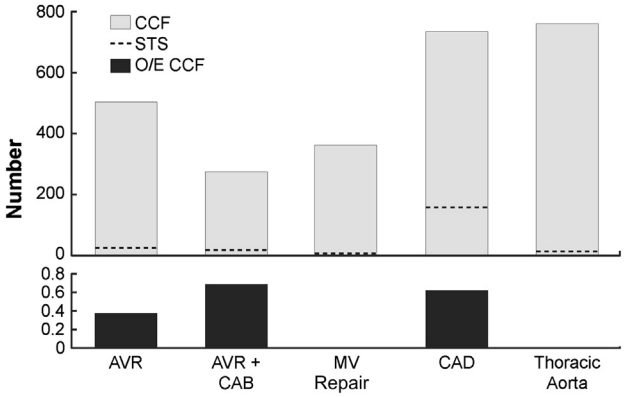

Fig 6. Trends in volume for STS sites and a large center with increasing valve and thoracic aorta numbers. (AVR = aortic valve replacement; CAB = coronary artery bypass; CAD = coronary artery disease; CCF = Cleveland Clinic Foundation; MV = mitral valve; O/E = observed to expected mortality ratio at CCF.)

4. AVR may be considered in patients undergoing CABG who have mild AS when there is evidence, such as moderate to severe valve calcification, that progression may be rapid. (Level of evidence C)
5. AVR may be considered for asymptomatic patients with extremely severe AS (aortic valve area [AVA] <0.6 cm^2, mean gradient >60 mm Hg, and jet velocity >5.0 m/s) when the patient's expected operative mortality is less than 1%. (Level of evidence C)

Class III

1. AVR is not useful for the prevention of sudden death in asymptomatic patients with AS who have normal LV systolic function [44]. (Level of evidence B)

The guideline recommendations for AVR in patients with AS pertain only to those with severe AS (Fig 19). No intervention is recommended in patients with mild or moderate AS unless there are indications for other forms of cardiac surgery. However, it is understood that establishing the diagnosis of severe AS is not always straightforward. For purposes of the guidelines recommendations, severe AS in patients with normal LV systolic function is defined as (1) a peak aortic jet velocity by Doppler echocardiography more than 4 m/s; (2) a mean aortic valve gradient more than 40 mm Hg; and (3) a calculated AVA less than 1.0 cm^2 or valve area index less than 0.6 cm^2/m^2 [20]. Critical aortic valve stenosis has been defined as less than 0.8 cm^2.

World	2011E	2012E	2013E	2014E	2015E
Market (B)	$4.6	$4.7	$4.9	$5.1	5.3
N = Sold	28,146	43,481	59,870	78,281	95,184
Penetration	16%	23%	30%	37%	44%
Revenue (M)	$669	$1,036	$1,449	$1,898	$2,305

Fig 7. Predicted global trends for transcatheter aortic valve replacement (TAVR).

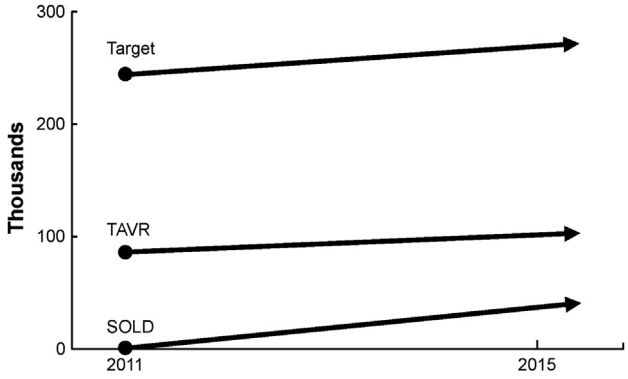

Fig 8. Predicted trends for transcatheter aortic valve replacement (TAVR) in the United States.

Additional class IIb indications in the ACCF/AHA guidelines that may be used to consider AVR include asymptomatic patients with severe AS in whom there is a high likelihood of rapid progression (such as severe valvular calcification), in whom surgery might be delayed at the time of symptom onset, or in whom the AS is extremely severe (AVA <0.6 cm^2, mean gradient >60 mm Hg, and jet velocity >5.0 m/s). However, surgery is considered reasonable in an asymptomatic patient only in a center in which the anticipated operative mortality is 1.0% or less [19].

2.1.2. AORTIC REGURGITATION—RECOMMENDATIONS

Class I

1. AVR or repair is indicated for symptomatic patients with severe AR irrespective of LV systolic function (Fig 2) [45–51]. (Level of evidence B)
2. AVR or repair is recommended for asymptomatic patients with chronic severe AR and LV systolic dysfunction (EF $\leq$50%) at rest [45–61]. (Level of evidence B)
3. AVR or repair is recommended in patients with chronic severe AR who are undergoing CABG or surgery on the aorta or other heart valves. (Level of evidence C)

US	2011E	2012E	2013E	2014E	2015E
Target AVR	242,967	249,691	256,601	263,703	271,000
High Risk	5%	5%	5%	5%	5%
Un-operated	30%	31%	32%	32%	33%
TAVR%	35%	36%	37%	37%	38%
N=TAVR	85,038	89,264	93,708	98,379	103,290
Device Price (K)	$27	$26	$25	$26	$25
U.S. TAVR Market (B)	$2.2	$2.3	$2.4	$2.5	$2.6
N = Sold	1,077	8,936	18,928	29,939	41,463
Penetration	1%	10%	20%	30%	40%
Revenue (M)	$29	$238	$496	$773	$1,054

Fig 9. Targeted market and likely population of transcatheter aortic valve replacement (TAVR).

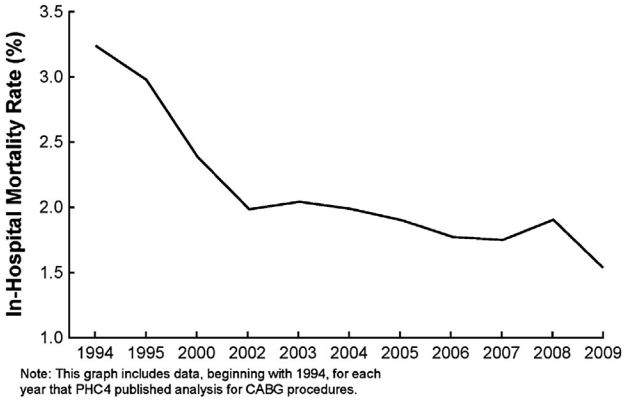

Fig 10. Trends for in-hospital mortality for coronary artery bypass graft surgery (CABG) in Pennsylvania. Note the decline. Source: Cardiac Surgery in Pennsylvania 2008–2009. Used with permission of PA Health Care Cost Containment Council.

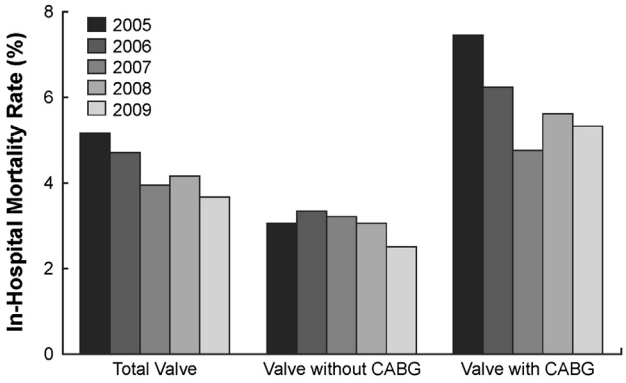

Fig 11. Trends for in-hospital mortality for valve procedures in Pennsylvania. Note the decline. Source: Cardiac Surgery in Pennsylvania 2008–2009. Used with permission of PA Health Care Cost Containment Council.

Class IIa

1. AVR or repair is reasonable for asymptomatic patients with severe AR with normal LV systolic function (EF >50%) but with severe LV dilation (end-diastolic dimension >75 mm or end-systolic dimension >55 mm) [46, 47, 51–55, 57–60, 62]. (Level of evidence B)

Class IIb

1. AVR or repair may be considered in patients with moderate AR who are undergoing CABG or surgery on the aorta or other heart valves. (Level of evidence C)
2. AVR or repair may be considered for asymptomatic patients with severe AR and normal LV systolic function at rest (EF >50%) when the degree of LV dilation exceeds an end-diastolic dimension of 70 mm or end-systolic dimension of 50 mm, when there is evidence of progressive LV dilation, declining exercise tolerance, or abnormal hemodynamic responses to exercise. (Level of evidence C)

Class III

1. AVR is not indicated for asymptomatic patients with mild, moderate, or severe AR and normal LV systolic function at rest (EF >50%) when the degree of LV dilation is not moderate or severe (Fig 20) [63–67]. (Level of evidence B)

As with AS, surgical intervention in patients with AR is recommended only for those with severe AR, and there are no recommendations for surgery in those with mild or moderate AR unless patients are undergoing other forms of cardiac surgery. Determining severity of AR, however, is inherently less precise than assessing AS severity. The ACCF/AHA guidelines adopted the definitions of severity of AR promulgated by the American Society of Echocardiography [68] in an attempt to emphasize the need to use quantitative rather than simply qualitative, visual assessments. Severe AR, using Doppler echocardiography methods, is defined as a vena contracta width more than 0.6 cm, a regurgitant volume greater than 60 mL per beat, a regurgitant fraction more than 60%, and an effective regurgitant orifice area more than 0.30 cm^2 [20, 68]. Severe AR should also be accompanied by evidence of a volume load on the left ventricle, with an elevated LV end-diastolic volume or increased LV end-diastolic diameter. The management strategies are summarized in Figures 5 through 7.

2.1.3. AORTIC ROOT DISEASE Dilation of the ascending aorta and/or aortic root is among the most common causes of isolated AR and in some patients, the severity of aortic

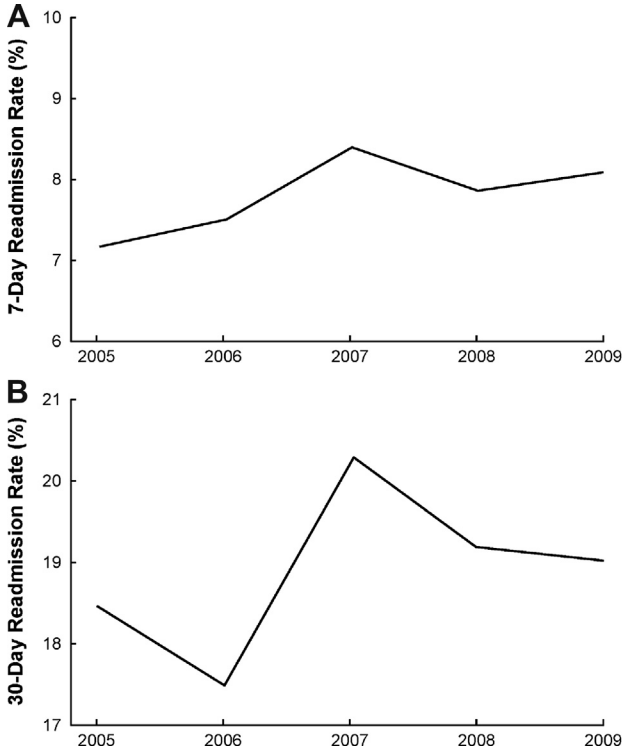

Fig 12. (A) Seven-day readmission after valve surgery (note increasing trend) for Pennsylvania. (B) Thirty-day readmission after valve surgery. Source: Cardiac Surgery in Pennsylvania 2008–2009. Used with permission of PA Health Care Cost Containment Council.

Reporting Group	Patients Readmitted within 30 Days		For patients readmitted within 30 days, the readmissions were associated with . . .					
	Number	Percent	Mortality Percent	Average Length of Stay	Total Days	Average Hospital Charge[1]	Estimated Medicare Payment[2] Average	Estimated Medicare Payment[2] Total
Total	2,042	15.1%	3.1%	6.1	12,542	$48,203	$9,310	$7,377,161
CABG without Valve	1,117	12.8%	2.1%	5.7	6,402	$47,338	$8,552	$3,446,323
Valve without CABG	486	17.1%	3.7%	6.1	2,980	$44,713	$9,507	$1,853,930
Valve with CABG	439	21.8%	5.0%	7.2	3,160	$54,269	$10,651	$2,076,908
Total Valve	925	19.0%	4.3%	6.6	6,140	$49,248	$10,100	$3,930,838

[1] In almost all cases, hospitals do not receive full reimbursement of charges; hospitals typically receive actual payments that are considerably less than the listed charge.
[2] The estimated Medicare payments were calculated by applying the 2008 fee-for-service Medicare payment data (the most recent data available to PHC4) to the fee-for-service Medicare patients who underwent a CABG and/or valve procedure in 2009 and were readmitted within 30 days.

Fig 13. Readmission costs and Medicare payments for Pennsylvania. (CABG = coronary artery bypass graft surgery.) Source: Cardiac Surgery in Pennsylvania 2008–2009. Used with permission of PA Health Care Cost Containment Council.

enlargement becomes the principal indication for surgery. This is particularly the case in patients with bicuspid aortic valves. The ACCF/AHA guidelines on valvular heart disease discuss aortic root disease only in the context of bicuspid aortic valves [20], with emphasis on obtaining measurements by computed tomography (CT) or magnetic resonance imaging (MRI) in addition to echocardiography. The guidelines also emphasize that a number of factors must be considered regarding surgical indications, including the patient's age, the relative size of the aorta and aortic root, the structure and function of the aortic valve, and the experience of the surgical team.

The guidelines recommend that patients with bicuspid valves undergo elective repair of the aortic root or replacement of the ascending aorta if the diameter of these structures exceeds 5.0 cm (Class I, level of evidence C) and should be performed by a surgical team with established expertise in these procedures [69, 70]. Others have recommended a value of more than 2.5 cm/m^2 or greater as the indication for surgery [71] or a cross-sectional area to height ratio of more than 10 [1, 14]. Surgery is also recommended if the rate of increase in aortic dilation is $\geq$0.5 cm per year or more (Class I, level of evidence C). If patients with bicuspid valves and associated aortic root enlargement have indications for AVR because of severe AS or AR, it is recommended that repair of the aortic root or replacement of the ascending aorta be performed if the diameter of these structures is more than 4.5 cm (Class I, level of evidence C) [72]. Similar indications for aortic surgery in patients with bicuspid aortic valves were recommended in the 2010 ACCF/AHA guidelines for the diagnosis and management of patients with thoracic aortic disease [1].

The thoracic aortic disease guidelines also provide recommendations for surgery in other conditions associated with aortic root disease [1]. Surgery is indicated at lower size thresholds in patients with certain genetic syndromes (Class IIa, level of evidence C). Examples include a threshold of 4.5 cm to 5.0 cm for Marfan syndrome and 4.2 cm for Loeys-Dietz syndrome or a confirmed TGFBR1 or TGFBR2 mutation. Specific Class IIa (level of evidence C) recommendations are also made for women with Marfan syndrome contemplating pregnancy, in whom one might consider elective aortic surgery when the diameter exceeds 4.0 cm, and in patients with Marfan syndrome in whom the ratio of the maximal

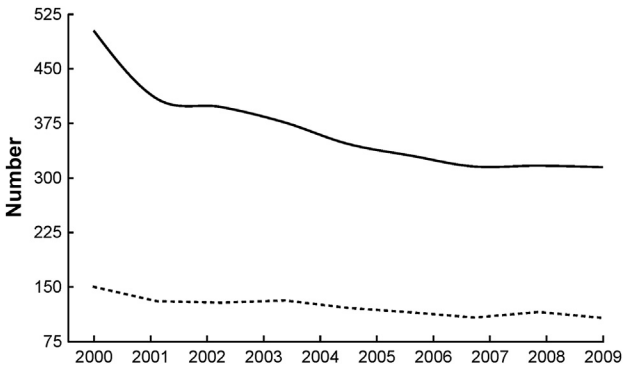

Fig 14. Average number of heart procedures performed by Pennsylvania hospitals (solid line) and surgeons (stippled line). Source: Cardiac Surgery in Pennsylvania 2008–2009. Used with permission of PA Health Care Cost Containment Council.

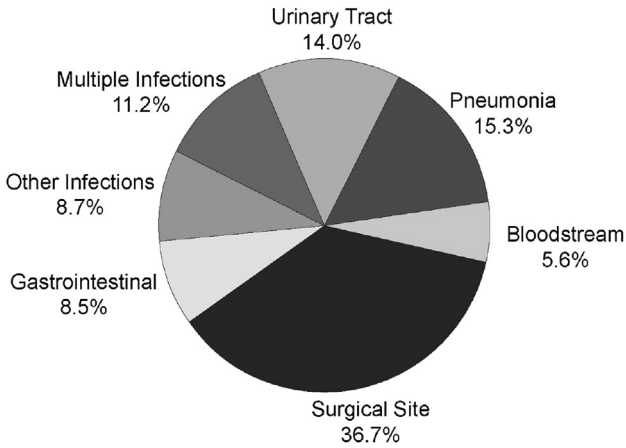

Fig 15. Hospital infections after cardiac surgery in Pennsylvania. Note the 37% at surgical site. Source: Cardiac Surgery in Pennsylvania 2008–2009. Used with permission of PA Health Care Cost Containment Council.

Fig 16. Outcomes after hospital infections, increase in cost, and estimated Medicare reimbursement. (CABG = coronary artery bypass graft surgery; HAI = hospital acquired infection.) Source: Cardiac Surgery in Pennsylvania 2008–2009. Used with permission of PA Health Care Cost Containment Council.

	Mortality Percent		Readmissions Percent		Average Post-Surgical Length of Stay	Average Hospital Charge[1]	Estimated Average Medicare Payment[2]
	In-Hospital	30-Day	7-Day	30-Day			
All Cardiac Surgery Patients							
With an HAI	9.0%	10.7%	14.9%	41.8%	18.0	$338,179	$63,986
Without an HAI	2.0%	2.5%	5.9%	13.7%	7.2	$154,548	$35,868
CABG without Valve Patients							
With an HAI	6.2%	7.5%	14.3%	43.6%	15.2	$268,231	$47,623
Without an HAI	1.3%	1.8%	5.0%	11.4%	6.5	$137,367	$29,677
Total Valve Patients							
With an HAI	12.8%	15.1%	16.0%	38.9%	21.9	$432,619	$76,922
Without an HAI	3.0%	3.8%	7.6%	17.9%	8.4	$183,631	$44,776

cross-sectional area in square centimeters of the ascending aorta or root to the patient's height in meters exceeds 10 [1]. In the absence of a bicuspid valve or genetic/familial cause of aortic enlargement, the threshold recommended for elective surgery is an aortic diameter of 5.5 cm for patients with degenerative thoracic aneurysms, chronic aortic dissections, intramural hematomas (IMH), penetrating atherosclerotic ulcers, mycotic aneurysms, or pseudoaneurysms (Class I, level of evidence C) [1].

2.1.4. AORTIC VALVE ENDOCARDITIS—RECOMMENDATIONS

Class I

1. AVR is recommended in patients with aortic valve infective endocarditis and severe heart failure or cardiogenic shock due to aortic valve dysfunction when there is a reasonable likelihood of recovery with satisfactory quality of life after surgery [20, 73–76]. (Level of evidence B)
2. Surgery is recommended in patients with annular or aortic abscesses, heart block, infections resistant to antibiotic therapy, and fungal endocarditis [73–77]. (Level of evidence B)

Class IIa

1. Surgery is reasonable in patients with infective endocarditis who present with recurrent emboli and persistent vegetations despite appropriate antibiotic therapy. (Level of evidence C)

Class IIb

1. Surgery to prevent embolization might be considered for patients with large vegetation size (>1.5 cm),

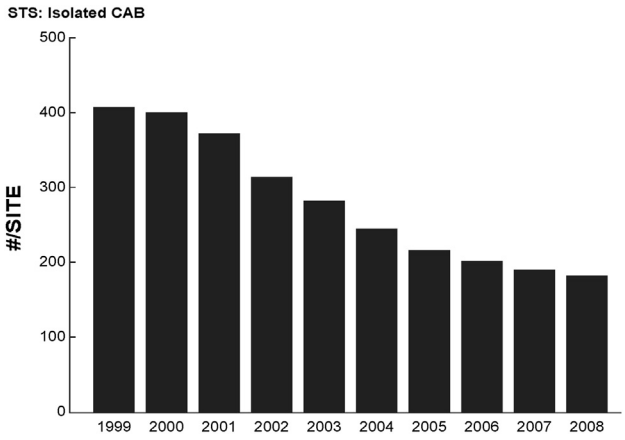

Fig 17. Material decline in coronary artery bypass surgery (CAB) by STS sites from an average of approximately 400 cases per annum.

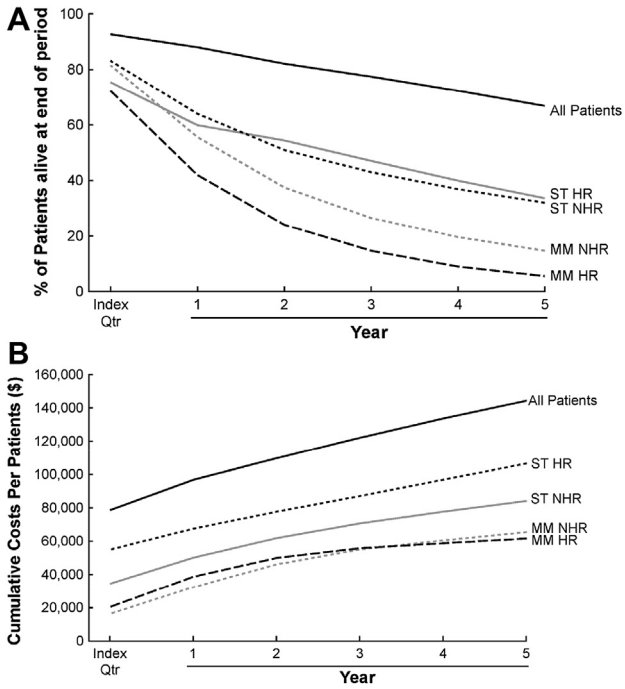

Fig 18. (A) Survival for 3,624 Medicare patients treated in 2003 for isolated aortic valve stenosis. The 5% random sample showed 31% were treated medically, 651 were categorized as high-risk medically treated. The associated variables in the 651 medically treated high-risk patients were central nervous system or psychiatric disease 53%, unstable angina 43%, prior surgery 40%, peripheral vascular disease 28%, chronic pulmonary disease 22%, pulmonary hypertension 20%, and cancer 18%. These variable likely influenced the decision not to operate. The curves show the 5-years survivals. (HR = high risk; MM = medically managed; NHR = not high risk; ST = surgical treatment.) (B) Cost of care over 5 years for those operated on or treated in 2003. Costs are Medicare payments for Parts A, B, and schedule beneficiary cost sharing.

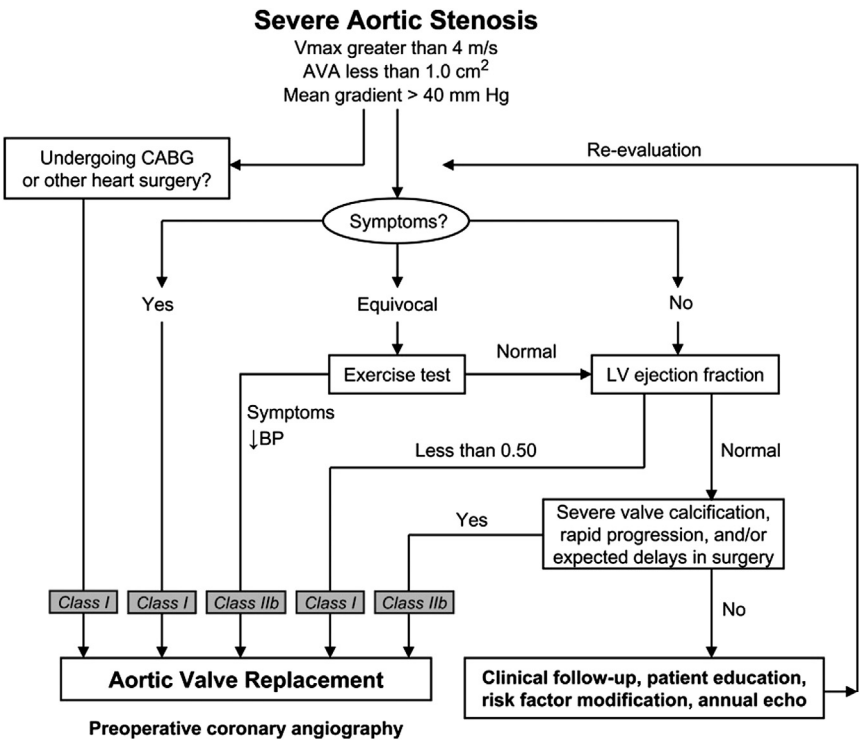

Fig 19. Management strategy for severe aortic stenosis. Preoperative coronary angiography should be performed routinely as determined by age, symptoms, and coronary risk factors. Cardiac catheterization and angiography may also be helpful when there is discordance between clinical findings and echocardiography. (AVA = aortic valve area; BP = blood pressure; CABG = coronary artery bypass graft; LV = left ventricular; Vmax = maximal velocity across aortic valve by Doppler echocardiography.) Reprinted with permission from Ref. 19 [Bonow RO, et al. Circulation. 2008;118:e523–e661. ©2008 American Heart Association, Inc.]

especially if other relative indications for surgery are present (eg, severe AR) and the surgical risk is low [78, 79]. (Level of evidence C)

Surgery should not be delayed in the setting of active infective endocarditis when heart failure intervenes. However, surgery is not indicated if complications (severe embolic brain damage) or comorbid conditions make the prospect of recovery remote. The indications for surgery for infective endocarditis in patients with stable hemodynamics are less clear.

3. Preoperative Testing and Assessment of Comorbid Disease and Frailty

As a disease, the natural history of unoperated on AS has largely remained unchanged for half a century. The mean survival of patients with symptomatic severe AS has been reported to be 23 ± 5 months, with 1-year and 5-year probability of survival 50% and 18%, respectively. In light of the poor prognostic fate of patients symptomatic from severe AS, the majority of clinicians believe that the risk-benefit analysis of surgical AVR should always err on the side of surgery. This has led to many innovations in surgical technique to the point where AVR can often be performed minimally invasively with outstanding results, even in higher risk cohorts. In-hospital mortality for high-risk AVR remains between 3% and 10% using standard cardiac surgery methods, although there is evidence that a minimally invasive J incision may benefit some high-risk patients, particularly with severe chronic pulmonary disease [14, 80]. Indeed, less than 1% mortality has been reported for minimally invasive J incision operations [14]. However, some patients remain poor surgical candidates under any circumstance and have heretofore been left with no option other than medical therapy alone. As recently highlighted from the results of the PARTNER trial, cohort B, medical therapy alone for this "too high risk" population carries a 50% mortality at 12 months; a higher risk than most advanced cases [81]. With the introduction of TAVR, more emphasis on a quantitative assessment of comorbidity of the patient with severe AS is performed.

Unfortunately, many high-risk AS patients are not considered for surgery at many institutions [21, 22]. Freed and associates [21] found that in a large academic medical center only 31% of patients with severe AS were referred for AVR including almost half the patients who had already manifested symptoms. Much of this lack of surgical referral was attributable to physicians not recognizing symptoms and overestimating operative risk. This lack of referral is an important issue that must be revisited [21]. In the age of TAVR the decision regarding which patients should forego aortic valve surgery secondary to prohibitively high risk should no longer be made in a surgical vacuum. In particular, the risk assessment of the aged and frail subpopulation should involve a multidisciplinary consultation with cardiologists, surgeons, imaging specialists, and anesthesiologists. Ideally, an interested and qualified "heart team" should discuss each case individually. Although each patient must undergo comprehensive objective testing and evaluation regardless of intervention, it is imperative to keep in mind that due to lack of convincing randomized data at this time, the key element in the preoperative assessment of the patient with aortic valve disease is

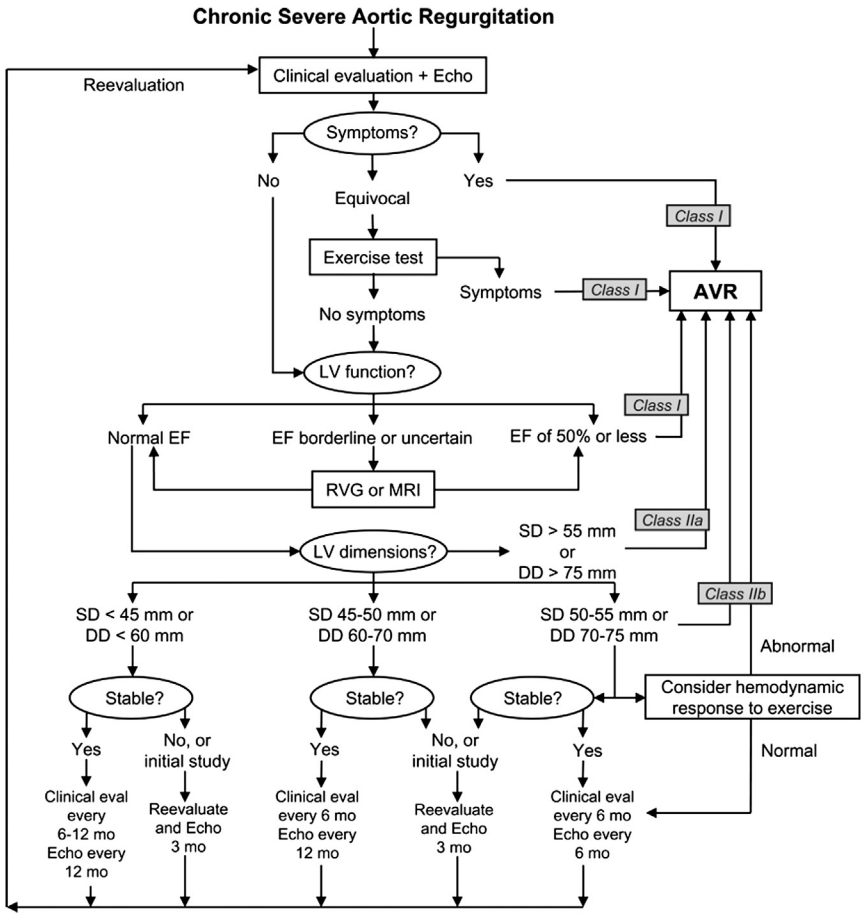

Fig 20. Management strategy with chronic severe aortic regurgitation. Preoperative coronary angiography should be performed routinely as determined by age, symptoms, and coronary risk factors. Cardiac catheterization and angiography may also be helpful when there is discordance between clinical findings and echocardiography. "Stable" refers to stable echocardiographic measurements. In some centers, serial follow-up may be performed with radionuclide ventriculography (RVG) or magnetic resonance imaging (MRI) rather than echocardiography to assess left ventricular (LV) volume and systolic function. (AVR = aortic valve replacement; DD = end-diastolic dimension; Echo = echocardiography; EF = ejection fraction; SD = end-systolic dimension. Reprinted with permission from Ref. 19 [Bonow RO, et al. Circulation. 2008;118:e523–e661. ©2008 American Heart Association, Inc.]

whether he or she is too high risk for intervention, either AVR or TAVR. This assessment is still highly dependent on clinical judgment, and should be used in association with quantitative evaluation [82].

The preoperative assessment of patients with aortic valve disease should include verification of disease severity, evaluation of LV function, detection and characterization of coronary artery disease (CAD) in at-risk persons, and delineation of major comorbidities, including functional status and frailty. In addition to a focused history and physical examination, minimal routine testing comprises an electrocardiogram (ECG), transthoracic echocardiogram (TTE), chest radiograph, complete blood count, comprehensive metabolic panel, and coagulation function. Coronary angiography is performed in patients with known or suspected CAD and/or multiple atherosclerotic risk factors. Assessment of the extent of ascending aortic calcification, when indicated, can be obtained with noncontrast chest CT. A surgical risk score (eg, STS-Preoperative Risk of Mortality [PROM] or the European System for Cardiac Operative Risk Evaluation [EuroSCORE]) and frailty index should complete the assessment and help guide counseling. The latter may require carefully supervised exercise testing (ie, 6-minute or 5-meter walk test).

With regard to functional capacity and constitutional make-up, establishing an accurate measure of an individual patient's resilience defined roughly as ones ability to withstand a surgical procedure or intervention and return to a reasonable quality of life after hospital discharge is paramount. Resilience includes the ability to cope with stress of surgery and regain health by learning and adaptation, a well-known capacity of the human mind [83]. With the increasingly frail population of older adults, the line between tolerating a procedure with successful return to activities of daily living or death has never been finer. Thus, a measurement of frailty along with selective use of objective functional testing such as dobutamine stress and exercise testing is required in every high-risk patient's workup before aortic valve intervention.

Attempts have been made at risk modeling that account for preoperative patient factors that may impact outcomes. The STS uses such risk models to create risk-adjusted performance reports for participants in the STS ACSD. Although risk models were initially developed for CABG surgery, similar models have now been developed for use with heart valve surgery, particularly as the proportion of such procedures has increased [84]. The last published STS model for isolated valve surgery was based on data from 2002 to 2006 models and includes several nonfatal complications in addition to mortality. At this time, TAVR has not yet been incorporated into

the risk scoring process leaving individual centers to extrapolate calculated PROM based on parameters and data for surgical AVR, but the new STS data collection module 2.73 will include more information that will make the latter possible.

As one assesses patients for aortic valve intervention, either surgical AVR or TAVR, it is important to keep in mind that there is a new and yet to be fully defined population of aortic valve patients who are too high risk for AVR, but are suitable for TAVR. An elderly patient with a hostile mediastinum from prior surgery or the presence of a porcelain aorta would be examples of this population. In addition, there is also an "ultra-high risk Group C" population that is not suitable for either intervention. This latter population is analogous to terminal cancer patients both in quality of life and prognosis. The goal of the preoperative assessment should then be to sort out which patients can be treated with intervention, surgical AVR versus TAVR and which are best left to medical therapy and palliation, possibly with the judicious use of BAV.

After confirming the diagnosis, an extensive review of systems and comorbidities should be undertaken with particular attention to those preexisting conditions that have been shown to negatively affect outcome in the surgical patient. These conditions include but are not limited to CAD, heart failure, peripheral arterial and cerebral vascular disease, diabetes mellitus, renal insufficiency, chronic pulmonary disease, immunocompromised states, radiation heart disease, liver or other organ dysfunction [80, 84, 85]. After performing initial functional studies, the preoperative testing and assessment becomes more straightforward and involves objective testing mainly related to anatomical considerations. The caveat here is that once a patient is directed to a particular intervention, surgical AVR versus TAVR, the needed objective prospective data can differ slightly for each group. For example, in surgical AVR an evaluation of the aortoiliac system is generally unwarranted, yet the entire feasibility of TAVR options depends upon its extensive characterization by multislice CT scan of the chest, abdomen, pelvis, and intravascular ultrasound (IVUS) and/or aortoiliac angiography.

3.1. Surgical Risk Scores—Recommendations

CLASS IIA

1. Performing risk score analysis is reasonable to evaluate patients undergoing surgical AVR or TAVR to quantitate PROM [81, 84, 86]. (Level of evidence B)

CLASS IIB

1. Performing risk score analysis may be reasonable to aid in determining which patients should undergo AVR, TAVR or medical therapy alone in high-risk patients. (Level of evidence C)

Surgical risk scores such as the logistic EuroSCORE and the STS-PROM are commonly used to identify high-risk surgical or "inoperable" patients for TAVR (Fig 21) [87]. Using STS data from 2002 to 2006, isolated valve surgery

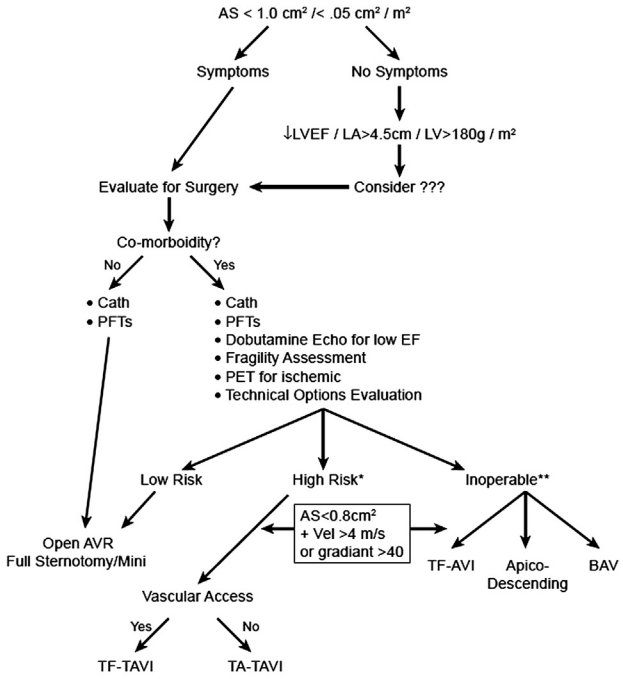

Fig 21. Surgical evaluation of patients for aortic valve replacement (AVR) or transcatheter aortic valve replacement (TAVR). (AS = aortic stenosis; AVI = aortic valve implantation; BAV = balloon aortic valvuloplasty; Cath = catheterization; LA = left atrium; LVEF = left ventricular ejection fraction; LV = left ventricle; PET = positron emission tomography; PFTs = pulmonary function tests; TA = transapical; TAVI = transcatheter aortic valve implantation; TF = transfemoral; Vel = velocity.)

risk models were developed for operative mortality, permanent stroke, renal failure, prolonged ventilation (more than 24 hours), deep sternal wound infection, reoperation for any reason, a major morbidity or mortality composite endpoint, prolonged postoperative length of stay, and short postoperative length of stay.

The STS study population consisted of adult patients who underwent one of three types of valve surgery: isolated AVR (n = 67,292), isolated mitral valve replacement (n = 21,229), or isolated mitral valve repair (n = 21,238). The population was divided into a 60% development sample and a 40% validation sample. After an initial empirical investigation, the three surgery groups were combined into a single logistic regression model with numerous interactions to allow the covariate effects to differ across these groups. Variables were selected based on a combination of automated stepwise selection and expert panel review. Unadjusted operative mortality (in-hospital regardless of timing, and 30-day regardless of venue) for all isolated valve procedures was 3.2%, and unadjusted in-hospital morbidity rates ranged from 0.3% for deep sternal wound infection to 11.8% for prolonged ventilation. The number of predictors in each model ranged from 10 covariates in the sternal infection model

to 24 covariates in the composite mortality plus morbidity model. Discrimination as measured by the c-index ranged from 0.639 for reoperation to 0.799 for mortality. When patients in the validation sample were grouped into 10 categories based on deciles of predicted risk, the average absolute difference between observed versus predicted events within these groups ranged from 0.06% for deep sternal wound infection to 1.06% for prolonged postoperative stay [84].

The EuroSCORE was also developed with similar goal in mind to stratify risk of cardiac surgery; however, several studies have shown that the STS score, although more reliable in predicting outcomes still often overestimates mortality, but not as much as the EuroSCORE, which may overestimate by up to three times as much [88, 89]. The STS score appears to be a powerful tool for predicting long-term outcome and for selecting patients who may benefit from early surgery. Hence, risk-scoring using the STS score should be routinely performed in high-risk patients with AS to support the clinical decision-making process [90].

3.2. Frailty Assessment

The assessment of frailty has become increasingly useful as a tool for predicting how an individual patient will respond or tolerate surgical intervention. Several groups have begun to systematically quantify frailty as a predictive measure of risk in the preoperative assessment [91-94]. Fried and colleagues [95] initially provided a potential standardized definition for frailty in community-dwelling older adults and offered concurrent and predictive validity for the definition. This study involving 5,317 men and women aged more than 65 years found that there is an intermediate stage identifying those at high risk of frailty and provided evidence that frailty is not synonymous with either comorbidity or disability, but comorbidity is an etiologic risk factor for, and disability is an outcome of, frailty. Frailty was defined as a clinical syndrome in which three or more of the following criteria were present: unintentional weight loss (10 lbs in the past year), self-reported exhaustion, weakness (grip strength), slow walking speed, and low physical activity [95].

To date, frailty as a specific measure associated with a patient's ability to undergo surgical AVR or TAVR has not been studied in a randomized fashion. Columbia University has developed the Columbia Frailty Index, which may become as a useful quantitative measure for frailty to be used in preoperative decision-making. Currently, many centers are adopting at minimum the 6-minute walk test, as required by the Food and Drug Administration (FDA) TAVR studies, or a gait speed determination in the assessment of frailty. In a study when rate of death, myocardial infarction, or stroke by EuroSCORE risk was stratified by 6-minute walking distance, the 6-minute walk test added prognostic information [93]. In a Cox regression analysis, 6-minute walk test distance was the only variable retained as an independent predictor of the composite outcome of death, myocardial infarction or stroke at 12 months (hazard ratio 0.28, 95% confidence interval: 0.09 to 0.85, $p = 0.025$). The investigators concluded that the 6-minute walk test is safe and feasible to carry out in patients with severe AS before AVR, and provides potentially important functional and prognostic additional information to clinical assessment and the risk score [93].

Alfilalo and colleagues [91] studied a multicenter prospective cohort of elderly patients undergoing cardiac surgery at four tertiary care hospitals between 2008 and 2009. Patients were eligible if they were aged 70 years or more and were scheduled for CABG or valve replacement or repair, or both. The primary predictor was slow gait speed, defined as the time taken to walk 5 meters in more than 6 seconds. The primary endpoint was a composite of in-hospital postoperative mortality or major morbidity. The cohort consisted of 131 patients with a mean age of 75.8 $\pm$ 4.4 years; 34% were female. Sixty patients (46%) were classified as slow walkers before cardiac surgery. Slow walkers were more likely to be female (43% versus 25%, $p = 0.03$) and diabetic (50% versus 28%, $p = 0.01$). Thirty patients (23%) experienced the primary composite endpoint of mortality or major morbidity after cardiac surgery. Slow gait speed was an independent predictor of the composite endpoint after adjusting for the STS risk score (odds ratio 3.05, 95% confidence interval: 1.23 to 7.54) [91]. Using a comprehensive assessment of frailty test, Sunderman and colleagues [94] studied 400 patients aged 74 years or more who were admitted to a single center between September 2008 and January 2010 [94]. For comparison, the STS score and the EuroSCORE were calculated. The primary endpoint was the correlation of frailty score to 30-day mortality. The study involved 206 female and 194 male patients. There were low-to-moderate albeit significant correlations of frailty score with STS score and EuroSCORE ($p < 0.05$). There was also a significant correlation between frailty score and observed 30-day mortality ($p < 0.05$) [94]. Consideration should also be given to a "mini-mental" evaluation of borderline elderly patients.

3.3. Physical Examination

Aortic stenosis typically is first suspected on the basis of the finding of a systolic ejection murmur on cardiac auscultation; however, physical examination findings are specific but not sensitive for the diagnosis of AS severity [96]. The classic findings of a loud (grade 3 to 4/6), basal, mid-to-late peaking systolic murmur that radiates to the carotids, a single or paradoxically split second heart sound, and delayed and diminished carotid upstroke confirm the presence of severe AS. However, in the elderly, the carotid upstroke may be normal because of the effects of aging on the vasculature. In other settings, the murmur may be soft (especially if LV systolic function is impaired) or may radiate to the apex (Galavardin effect). The only physical examination finding that is reliable in excluding the possibility of severe AS is a normally split second heart sound [96]. Echocardiography is indicated when there is a systolic murmur that is grade 3/6 or greater, a single S2, or symptoms that might be due to AS. Chronic AR is associated with a decrescendo diastolic murmur along the left or right sternal border, a wide pulse pressure, and bounding pulses. The normal difference between systolic leg and arm pressures is accentuated.

Transthoracic echocardiography is indicated for evaluation of any diastolic murmur.

3.4. Chest Radiography

Posteroanterior and lateral chest roentgenograms often yield qualitative information on cardiac chamber size, pulmonary blood flow, pulmonary and systemic venous pressure, chronic pulmonary disease, and aortic calcifications. Although cardiac size is often normal in patients with AS, occasionally rounding of the LV border and apex due to the LV hypertrophy is apparent. Cardiomegaly is a late feature in patients with AS and warrants careful echocardiographic analysis. In cases of advanced heart failure, the right atrium and right ventricle may also be enlarged. The lung fields should also be checked for tumors, emphysema, interstitial disease, and fluid collections [97]. With right-side heart failure, the lungs become unusually radiolucent because of decreased pulmonary blood flow. Conversely, significant failure on the left side of the heart is characterized by the presence of pulmonary edema or a cephalic blood-flow pattern. Aortic valve and aortic root calcification are best appreciated in the lateral projections or on fluoroscopy.

3.5. Pulmonary Function Testing

The variables that are conventionally measured to assess lung function before heart surgery include forced expiratory volume in 1 second, forced vital capacity, forced expiratory flow between 25% and 75%, diffusing capacity of lung for carbon monoxide (DLCO), and arterial blood gases. The STS has defined mild, moderate, and severe chronic obstructive pulmonary disease. Although few papers exist specifically regarding preoperative pulmonary function tests (PFTs) in predicting outcomes after AVR, it has been well defined that severe airway obstruction carries significant surgical risk, leading to an increased expectation of difficult weaning from the ventilator and the possibility of tracheostomy [98]. Generally, preoperative hypercarbia (pCO_2 >50 mm Hg), forced expiratory volume in 1 second less than 30% predicted, forced expiratory flow between 25% and 75% less than 25%, or DLCO less than 50% carries risk for postoperative complications and prolonged intensive care unit stay. Data from Adabag and associates [98] show that a DLCO less than 50% of predicted on preoperative pulmonary function testing is an independent risk factor increasing the risk of mortality more than threefold after adjusting for a validated mortality risk estimate. Furthermore, the risk conferred by reduced DLCO was additive to that brought by airway obstruction, increasing mortality risk by 10 times among patients with both airway obstruction and reduced DLCO [98].

Nevertheless, it remains critically important to ascertain the reasons for poor PFT such that every attempt at determining the etiology of dyspnea before intervention should be made. Pleural effusions should be drained before performance of PFTs. Similarly, bronchitis or pneumonia should be treated before pulmonary testing. Kyphosis is an important factor to consider even in the absence of restrictive or obstructive spirometry values, because the sternotomy may compromise cough and the ability to clear secretions. It is plausible that replacement of the aortic valve in some patients with dyspnea largely attributable to pulmonary disease may prolong life, but not necessarily improve quality of life. In this scenario, BAV can be performed as an initial procedure to evaluate the improvement of the dyspnea. Improvement in shortness of breath and repeat PFTs may indicate a more robust and predictable success of AVR. When the contribution of chronic pulmonary disease to the overall pattern of heart failure, particularly dyspnea, is uncertain, BAV maybe a physiologic "test" that better determines the pulmonary contribution. A marked improvement would suggest that AS is a major contributing factor.

In terms of TAVR with the transfemoral approach, the strict adherence to the traditional guidelines can be relaxed somewhat with many centers proficient in TAVR allowing patients to qualify for treatment with PFTs in an approximately 25% predicted lower range. This again depends on analysis of each individual case and origin of symptoms. It also should be noted that as the new generation devices become available more centers will push to perform TAVR in the nonintubated patient with worse PFTs. As for transapical TAVR, this still requires mandatory intubation and a minithoracotomy. Direct aortic approaches also require intubation and minithoracotomy or J mini sternotomy approaches. At this time, it is best to remain rigid in the requirement to meet the standard PFT guidelines for patients undergoing thoracotomy or sternotomy for transapical or direct aortic approaches. Regardless of the approach, surgical AVR or TAVR should be considered in patients with severe chronic pulmonary disease if life expectancy of more than 1 year is anticipated; otherwise BAV may be a more reasonable palliative approach.

Various approaches and incisions have been used for doing procedures on the aortic valve. A median sternotomy is the traditional approach however minimal invasive approaches such as a paramedian incision, hemisternotomy J incision and right mini thoracotomy have been used with varying success. However, the J incision appears to have a benefit in patients with chronic pulmonary disease [1, 99–106]. The newer approach of TAVR will be reviewed separately.

3.6. Electrocardiography

The typical finding on ECG in patients with severe AS is LV hypertrophy, often with secondary repolarization abnormalities. Left atrial enlargement, as indicated by a P-wave abnormality (P 0.12 s), or LV hypertrophy, or conduction delay is present in more than 80% of severe AS patients. Conduction abnormalities may include left or right bundle branch block with left or right axis deviation, or occasionally, isolated right bundle branch block. That may be due to extension of the calcification into the surrounding conduction system. Atrial fibrillation can also develop, particularly in older patients and those with hypertension [97].

3.7. Echocardiography—Recommendations

CLASS I [107]

1. TTE is recommended for the diagnosis and assessment of AS or AR severity. (Level of evidence B)
2. Echocardiography is recommended in patients with AS or AR for the assessment of LV wall thickness, size, and function. (Level of evidence B)
3. TTE is recommended for reevaluation of patients with known AS or AR and changing symptoms or signs. (Level of evidence B)
4. TTE is recommended for the assessment of changes in hemodynamic severity and LV function in patients with known AS or AR during pregnancy. (Level of evidence B)
5. TTE is recommended for reevaluation of asymptomatic patients: every 6 months for severe AS or AR, every 1 to 2 years for moderate AS or AR, and every 3 to 5 years for mild AS or AR. (Level of evidence B)
6. Intraoperative TEE is recommended to check repairs or replacements. (Level of evidence B)

Transthoracic echocardiography is the imaging modality of choice for diagnosis and assessment of AS or AR. Moreover, TTE is valuable for determining the LV response to pressure overload, detecting other associated valve lesions, and in estimating pulmonary artery pressures. In nearly all patients, the severity of the stenotic lesion can be defined with Doppler measurements of maximum jet velocity, mean transvalvular pressure gradient, and continuity equation valve area, as discussed in the 2003 ACC/AHA/ASE guidelines for the clinical application of echocardiography [108].

Transthoracic echocardiography demonstrates the morphology of the aortic valve and can often delineate if it is trileaflet or bicuspid. The spectrum of calcific aortic valve disease ranges from aortic sclerosis without obstruction to severe AS. Aortic sclerosis is common and is often seen in people aged more than 65 years. On TTE, it is characterized by focal areas of valve thickening, typically located in the leaflet center with commissural sparing and normal leaflet mobility. Diffuse leaflet thickening is not characteristic of aortic sclerosis; instead, it suggests normal aging changes, a different valvular pathology, or an imaging artifact. With aortic sclerosis, valvular hemodynamics are within normal limits, with an aortic valve velocity of less than 2.5 m/s and a aortic valve opening of 1.6 cm to 2.6 cm [109]. In patients with severe AS and normal LV systolic function, TTE parameters include a jet velocity more than 4.0 m/s, mean aortic valve gradient more than 40 mm Hg, AVA less than 1.0 cm^2, or a valve area index less than 0.6 cm^2/m^2 [19].

In patients with AS, the aortic valve leaflets are usually thickened and calcified, with limited excursion and a reduced AVA. Doming of the aortic leaflets due to asymmetry and restriction is often seen in young patients with bicuspid aortic valves. The ascending aorta should also be evaluated and measured to detect associated aortic aneurysms, which are particularly common in patients with bicuspid valves. In the absence of heart failure, the LV cavity is usually of normal size or small. Left ventricular hypertrophy is often present, as is left atrial enlargement; LV systolic function is usually normal. If heart failure has developed, the left ventricle may be enlarged and systolic function depressed [97].

As the AVA decreases with time, the velocity of forward flow across the valve increases. Assessing the severity of AS using Doppler criteria is dependent not only on the severity of AS, but also on the aortic flow. In patients with low cardiac output, such as patients with LV dysfunction, the calculated gradients and AVA may not be representative of the true severity of stenosis. In such cases of "low output, low gradient" AS, the administration of low-dose dobutamine may be needed to truly assess the severity of AS and to differentiate patients with anatomically severe AS from those with "pseudo" AS [97, 110, 111].

Severe AR is defined as a vena contracta width more than 0.6 cm, regurgitation volume more than 60 mL per beat, regurgitation fraction more than 60%, and effective regurgitation orifice more than 0.3 cm^2 [20, 68].

3.8. Exercise Testing—Recommendations

CLASS IIB

1. Exercise testing in asymptomatic patients with AS or AR may be considered to elicit exercise-induced symptoms and abnormal blood pressure responses. (Level of evidence B)

CLASS III

1. Exercise testing should not be performed in symptomatic patients with AS or AR. (*Level of evidence B)*

Exercise testing can provide valuable information in patients with valvular heart disease, either AS or AR, especially in those whose symptoms are difficult to assess. It can be combined with echocardiography, radionuclide angiography, and cardiac catheterization. It has a proven track record of safety, even among asymptomatic patients with severe AS or AR. Exercise testing has generally been underutilized in this patient population and should constitute an important component of the evaluation process.

Many patients with AS or AR do not recognize symptoms that may develop gradually and cannot differentiate fatigue and dyspnea from aging and physical deconditioning. Other patients modify their lifestyle to prevent symptoms from occurring. In apparently asymptomatic patients with severe AS or AR, exercise testing may have a role in eliciting symptoms or an abnormal blood pressure response to exercise. Such testing should be performed with close physician supervision and should not be performed on patients with symptoms [19, 111].

Exercise testing in adults with AS has poor diagnostic accuracy for evaluation of concurrent CAD. Presumably, this is due to the presence of an abnormal baseline ECG, LV hypertrophy, and limited coronary flow reserve. Electrocardiographic ST-segment depression during exercise occurs in 80% of adults with asymptomatic AS and has no known prognostic significance.

Exercise testing should not be performed in symptomatic patients owing to a high risk of complications. However, in asymptomatic patients, exercise testing is relatively safe and may provide information that is not uncovered during the initial clinical evaluation [41–43, 96, 112, 113]. When the medical history is unclear, exercise testing can identify a limited exercise capacity, abnormal blood pressure responses, or even exercise-induced symptoms [41–43]. In one series, patients manifesting symptoms, abnormal blood pressure (<20 mm Hg increase), or ST-segment abnormalities with exercise had a symptom-free survival at 2 years of only 19% compared with 85% symptom-free survival for patients who had none of these findings with exercise [42]. Four patients died during the course of this study (1.2% annual mortality rate); all had an AVA less than 0.7 cm^2 and an abnormal exercise test. In another series, exercise testing brought out symptoms in 29% of patients who were considered asymptomatic before testing; in these patients, spontaneous symptoms developed in 51% over the next year compared with only 11% of patients who had no symptoms on exercise testing [43]. An abnormal hemodynamic response (eg, hypotension or failure to increase blood pressure with exercise) in a patient with severe AS is considered a poor prognostic finding [42, 114]. Finally, in selected patients, the observations made during exercise may provide a basis for advice about physical activity. Exercise testing in asymptomatic patients should be performed only under the supervision of an experienced physician with close monitoring of blood pressure and the ECG.

3.9. Dobutamine Stress Echocardiography and Cardiac Catheterization for Low-Flow/Low-Gradient Aortic Stenosis—Recommendations

CLASS IIA

1. Dobutamine stress echocardiography is reasonable to evaluate patients with low-flow/low gradient AS and LV dysfunction for possible AVR or TAVR [81, 113, 115–122]. (Level of evidence B)
2. Cardiac catheterization for hemodynamic measurements with infusion of dobutamine can be useful for evaluation of patients with low-flow/low-gradient AS and LV dysfunction. (Level of evidence C)

Patients with severe AS and low cardiac output often present with a relatively low transvalvular pressure gradient (ie, mean gradient <30 mm Hg). Such patients can be difficult to distinguish from those with low cardiac output and only mild to moderate AS. In the former (true anatomically severe AS), the stenotic lesion contributes to an elevated afterload, decreased EF, and low stroke volume. In the latter, primary contractile dysfunction is responsible for the decreased EF and low stroke volume; the problem is further complicated by reduced valve opening forces that contribute to limited valve mobility and apparent stenosis. In both situations, the low-flow state and low-pressure gradient contribute to a calculated effective valve area that can meet criteria for severe AS.

Alternate measures of AS severity have been proposed as being less flow dependent than gradients or valve area. These include valve resistance and stroke work loss. However, all of these measures are flow dependent, have not been shown to predict clinical outcome, and have not gained widespread clinical use [123]. In selected patients with low-flow/low-gradient AS and LV dysfunction, it may be useful to determine the transvalvular pressure gradient and to calculate valve area during a baseline state and again during exercise or low-dose pharmacologic (ie, dobutamine infusion) stress, with the goal of determining whether stenosis is severe or only moderate in severity [113, 115–119, 121, 122]. Such studies can be performed in the echocardiography laboratory or in the cardiac catheterization laboratory. This approach is based on the notion that patients who do not have true anatomically severe stenosis will exhibit an increase in the valve area and little change in gradient during an increase in stroke volume [115, 117]. Thus, if a dobutamine infusion produces an increment in stroke volume and an increase in valve area more than 0.2 cm^2 and little change in gradient, it is likely that baseline evaluation overestimated the severity of stenosis. In contrast, patients with severe AS will have a fixed valve area with an increase in stroke volume and an increase in gradient. These patients are likely to respond favorably to surgery. Patients who fail to show an increase in stroke volume with dobutamine (<20%), referred to as "lack of contractile reserve," appear to have a very poor prognosis with either medical or surgical therapy [108, 120]. Dobutamine stress testing in patients with AS should be performed only in centers with experience in pharmacologic stress testing and with a cardiologist in attendance.

The clinical approach to the patient with low-output AS relies on integration of numerous sources of data. In addition to measurement of Doppler velocity, gradient, and valve area, the extent of valve calcification should be assessed. Severe calcification and minimal leaflet movement suggests that AVR may be beneficial. When transthoracic images are suboptimal, transesophageal imaging or fluoroscopy may be used to assess the degree of valve calcification and orifice area. The risks of surgery and patient comorbidities also are taken into account. Although patients with low-output severe AS have a poor prognosis, in those with contractile reserve, outcome is still better with AVR than with medical therapy [120]. Some patients without contractile reserve may also benefit from AVR, but decisions in these high-risk patients must be individualized because there are few data indicating who will have a better outcome with surgery.

3.10. Computed Tomography

Traditional use of a CT scan in the assessment of the patient with aortic valve disease has been reserved as a secondary testing modality to further elucidate unusual anatomy, quantitate the calcium burden, and assess risks of reoperation. Both electron beam and multislice cardiac CT can provide quantitative assessment of valve

calcification and have been shown to correlate with echocardiographic assessment and clinical outcome [124]. The role of CT in clinical management of AS is not yet well defined, but CT has an established role in evaluating the presence and severity of aortic root and ascending aortic dilation in patients with associated aortic aneurysms [97]. In TAVR, however, accurate preoperative assessment of potential leaflet calcium obstructing the coronary ostia and the aortic annulus diameter is critical for correct valve sizing to minimize the potential for paravalvular AR or device migration. However, a gold standard has not yet been established [125]. Compared with fluoroscopy and standard echocardiography, limited by their two-dimensionality, multislice CT can provide three-dimensional data sets with a high spatial resolution [126]. The utility and cost effectiveness of TTE, TEE, and CT scan has not fully been evaluated for TAVR, and there are some data suggesting that TEE may be all that is needed for preoperative assessment. One study involving 187 patients referred for TAVR dual-source CT and TTE could not definitely predict TEE measurements. The TEE measurements showed good intraobserver and interobserver variability, which is more satisfactory than that for dual-source CT measurements [127]. The researchers concluded that taking TEE annulus measurements as decisive parameter for the implantation is safe with a low rate of complications such as necessity of valve-in-valve implantation, severe paravalvular leak, or valve migration.

Another important component in the assessment for TAVR entails evaluation of the aortoiliac system [128]. That can be done by way of at least three different imaging modalities: angiogram, IVUS, or CT scan [129, 130]. The aortoiliac angiogram is usually performed at the completion of the cardiac catheterization and adds little to no morbidity to the procedure in the patient with normal renal function [131]. In patients with concomitant renal disease where dye load is of concern, IVUS is an excellent option for analyzing calcium and plaque burden, and vessel size. IVUS does not, however, impart critical information related to tortuosity. Multislice CT scan with contrast is being used alone or in combination with the other modalities in most ongoing TAVR clinical trials including with a catheter leaflet in the distal aorta at the time of catheterization [81]. Again, in patients with renal issues, contrast can be forgone but delivers suboptimal imaging, and these patients are probably bettered served by having a minimal contrast aortoiliac angiogram with complimentary IVUS.

3.11. Cardiac Catheterization—Recommendations

CLASS I

1. Coronary angiography is recommended before AVR in patients with AS or AR at risk for CAD. (Level of evidence B)
2. Patients aged more than 45 years undergoing a valve procedure should undergo coronary imaging. (Level of evidence C)
3. Cardiac catheterization for hemodynamic measurements is recommended for assessment of severity of AS or AR in symptomatic patients when noninvasive tests are inconclusive or when there is a discrepancy between noninvasive tests and clinical findings. (Level of evidence C)
4. Coronary imaging is recommended before AVR in patients with AS or AR for whom a pulmonary autograft (Ross procedure) or root procedure is contemplated and if the origin of the coronary arteries were not identified by noninvasive technique. (Level of evidence C)

CLASS IIB

1. For patients aged less than 45 years, CT coronary angiography may be considered. (Level of evidence C)

CLASS III

1. Cardiac catheterization for hemodynamic measurements is not recommended for the assessment of severity of AS before AVR when noninvasive tests are adequate and concordant with clinical findings. (Level of evidence C)
2. Cardiac catheterization for hemodynamic measurements is not recommended for the assessment of LV function and severity of AS or AR in asymptomatic patients. (Level of evidence C)

Because of the accuracy of echocardiographic assessment of the severity of AS or AR, cardiac catheterization is currently used most often to identify the presence of associated CAD rather than to define hemodynamic abnormalities. However, invasive hemodynamic measurements are helpful in patients in whom the noninvasive tests are inconclusive or provide discrepant results regarding the severity of AS or AR. This is performed by measuring simultaneous LV and ascending aortic pressures and measuring cardiac output by either the Fick principle or the indicator-dilution technique. The AVA can be calculated and considered severe when the valve area is 1.0 cm^2 or less, or the AVA index is 0.6 cm^2/m^2 or less. Coronary arteriography is recommended before AVR for all patients aged 35 years or more and for patients aged less than 35 years if they have LV systolic dysfunction, possible symptoms or signs suggesting CAD, or two or more risk factors for premature CAD [97].

For patients with AS or AR, the indications for cardiac catheterization and angiography are essentially the same as for other conditions, namely, to assess the coronary circulation and confirm or clarify the clinical diagnosis. In preparation for AVR, coronary angiography is indicated for patients suspected of having CAD. If the clinical and echocardiographic data are typical of severe isolated AS or AR, coronary angiography may be all that is needed before AVR. A complete left-side and right-side heart catheterization may be necessary to assess the hemodynamic severity of the AS if there is a discrepancy between clinical and echocardiographic data or a patient has a history of radiation heart disease. The pressure gradient across a stenotic valve is related to the valve orifice area and the transvalvular flow [132]. Thus, in the presence of depressed cardiac output, relatively low pressure

gradients may be obtained in patients with severe AS. Conversely, during exercise or other high-flow states, significant pressure gradients can be measured in minimally stenotic valves. For these reasons, complete assessment of AS requires the following: measurement of transvalvular flow; determination of the mean transvalvular pressure gradient; and calculation of the effective valve area.

Attention to detail with accurate measurements of pressure and flow is important, especially in patients with low cardiac output or a low transvalvular pressure gradient [19].

In patients with associated extensive CAD and poor LV function, the contribution of the individual components of valve disease or CAD to poor function can be difficult to assess. In this scenario, the use of either PET scanning or cardiac MRI may help in differentiating the etiology and as to whether a patient may potentially improve with AVR or TAVR.

The STS data collection form, version 2.73, can be found online (Web address provided in Appendix 1). Perusal of it will show that members of the writing committee, and other contributors, added new fields that particularly gather data on sicker patients, especially for TAVR. The new fields gather information related to patient frailty including nutritional and functional reserve. Clearly, as more patients undergo TAVR, the number of patients with frailty and limited reserve or very high risk that undergo conventional surgery will decline. Thus, some of the fields may not be part of global predictive models, such as radiation heart disease or cirrhosis, but for subgroup analysis, these data would be useful. The fields also incorporate data that is relevant to TAVR.

4. Cannulation Options for Aortic Valve and Root Surgery—Recommendations

Class I

1. For most patients requiring a simple aortic valve procedure without ascending aortic disease, the distal ascending aorta is recommended as the site for cannulation [14]. (Level of evidence B)
2. For complex repairs involving the arch or a calcified aorta or porcelain aorta, use of the axillary artery with a side graft is recommended [14]. (Level of evidence B)

The site of cannulation for aortic valve procedures, with or without ancillary procedures, has been found to influence stroke and survival. Arterial cannulation for procedures involving the aortic valve through the ascending aorta can be tailored for each patient's specific pathology. These guidelines address the most commonly utilized, but not all, of these options for cannulation with regard to valve and proximal aortic abnormalities. The sites of cannulation discussed here will include the ascending aorta, the aortic arch, the LV apex, the left axillary or subclavian artery, and the femoral arteries. These options will be discussed in relation to "simple" AVR, the porcelain aorta, redo sternotomies, and procedures involving the aortic arch. The advantages and disadvantages of each site are discussed relative to the specific pathologies.

Although related to the cannulation site, approaches to brain protection will not be discussed in detail in this section. For further information on brain protection, reference should be made of the recently completed guidelines on thoracic aortic disease [1]. Principles of brain protection will be referred to, but not discussed directly outside of the cannulation options. The advantages, disadvantages and some of the data for each approach will be discussed.

4.1. Ascending Aorta

The ascending aorta remains the most commonly utilized site of arterial cannulation for cardiac surgery, including aortic valve surgery. The main advantage of the ascending aorta is proximity as it is exposed during exposure of the heart in creating the pericardial well. In cases limited to the aortic valve or root, there is sufficient distance to isolate the proximal ascending aorta with a cross clamp and distal perfusion. Further, the cannulation is probably the most straightforward, with direct cannulation within one or two pursestrings. For isolated aortic valve and root procedures without a calcified aorta, few would argue that this is not the optimal site of cannulation.

However, the drawbacks mainly deal with the abnormal ascending aorta, whether it is thin, aneurysmal or dissected. Although some surgeons do cannulate aneurysms or dissections directly, many others prefer alternate sites to avoid complications of the cannulation including dissection, rupture, and the need to cannulate again after resection of the ascending aorta. These complications can occur to any access site, but in this case the dissection would require ascending aortic replacement [133–135]. Another aortic abnormality that may preclude ascending aortic replacement is the presence of intraluminal abnormalities that can embolize. Atheroma or atherosclerotic disease of the aorta can embolize anywhere in the arterial tree resulting in stroke, bowel infarct, or other end organ malperfusion.

The Cleveland Clinic and Baylor both published large studies demonstrating the safety of ascending aortic cannulation for cardiopulmonary bypass [136, 137]. The complication rates were minimal including rates of stroke and dissection. Cannulation of the ascending aorta has been described in even Type A dissection repair in selected patients with good results in small single center cohorts [138, 139]. Epiaortic echocardiographic scanning may aid in decision making.

4.2. Aortic Arch

Cannulation of the arch has the advantage of being distal to ascending aortic pathologies. The cross-clamp can be placed up to the base of the innominate artery. The extra length can be particular helpful in not only ascending aortic pathology, but also in circumstances where aortic domain can be compromised because of vein graft proximal anastomosis and even because of outflow grafts for

ventricular assist devices. In many patients, the arch tissue may be more robust than the ascending aorta.

The disadvantages of arch cannulation can be the depth and angulation of the arch. Moreover, cannulation complications of this site can be difficult to repair when complications do occur. It provides no benefit for arch operations except for speed of cannulation as the site will be resected, and it provides no access for selective antegrade perfusion during the open arch.

The data on distal arch cannulation are limited, but Borger and associates [140] demonstrated fewer embolic events during CABG by transcranial Doppler. They found no clinical correlates of stroke or neuropsychological impairment to these emboli, but the study was small [141]. Importantly, these studies demonstrated no right sided malperfusion with this technique demonstrating it can be safe for cases with loss of ascending aortic domain from previous operations or a fragile ascending aorta. Early studies have shown adequate perfusion to the brain with arch cannulation confirmed by electroencephalogram and fewer strokes compared with peripheral cannulation [142]. No study directly compares ascending to arch cannulation, but few data exist suggesting that arch cannulation is not safe.

4.3. Right Axillary or Subclavian Artery

The right axillary or subclavian artery started being utilized because of the anatomy of the innominate artery. By cannulating the right axillary, the right side of the brain can be perfused by occlusion of the innominate. Using this site, the transition from full body perfusion to selective antegrade brain perfusion (ABP) is easy. Further, it may facilitate the de-airing of the arch once the open portion is complete by allowing pressurization of the brachiocephalic vessels before reapplication of the cross-clamp and returning to full body reperfusion. Additionally, this site is an excellent choice for the difficult redo sternotomy. If the heart or great vessels are attached to the posterior sternum and potential injury during entry is likely, axillary artery cannulation can be a safe approach to secure arterial access before sternal division.

The disadvantage to axillary cannulation is that it takes time to sew on a graft. While some centers will directly cannulate the artery, overwhelmingly an 8-mm Dacron graft is sewn on for access since this is associated with less strokes and brachial plexus nerve injury. This facilitates closure later and allows continued right arm perfusion. The proximity of the brachial plexus and the axillary vein can put these structures at risk for injury and can cause chronic pain in some patients. While the peripheral positioning of this site may be its most significant advantage, it can also be a drawback. For instance, the needle holes from this graft can bleed throughout the heparinization which tends to drain away from the pericardial well. If the area is not draped properly to catch this bleeding or a pump suction basket placed in the well, a significant amount of blood can be lost during long bypass periods.

The data regarding this site are limited to single institutional studies, but most suggests a stroke benefit with use of axillary perfusion including when using selective ABP. The Cleveland Clinic demonstrated that direct cannulation may have more complications than sewing on a side arm, and that this approach may limit the stroke incidence in arch and circulatory arrest cases [143, 144]. More retrospective evidence has arisen from Halkos and colleagues that axillary cannulation during proximal aortic procedures can reduce resource utilization through reduced pulmonary and renal complications [145]. The data regarding the optimal cannulation for arch operations are mainly retrospective and single institution, but the majority of arch surgeons utilize this cannulation site for selective antegrade brain protection during the open arch. Of note, Merkkola and colleagues [146, 147] suggested that selective ABP through the axillary alone would not fully perfuse the left hemisphere of the brain which is why some advocate multiple sites of antegrade perfusion during hypothermic circulatory arrest (HCA). The clinical significance of this is still not known although in approximately 14% of patients the circle of Willis is not complete, endangering brain perfusion.

4.4. Femoral Artery

Femoral artery cannulation may be the easiest and fastest site of cannulation in emergency. Both open and percutaneous exposures are relatively uncomplicated in most patients. The access can be further facilitated by accessing the artery with a wire or arterial line, especially in cases where hasty arterial access may be anticipated. Before the popularization of axillary artery cannulation, the femoral approach was very commonly utilized in aortic dissections with success. In almost all cases, one femoral artery or the other is spared from the dissection and mostly the right is spared 80% of the time. Additionally, the femoral arteries are commonly utilized for minimally invasive surgery. The arterial cannulation is completely separate from the operative field and therefore out of the way.

The drawbacks of the femoral artery are essentially related to size and to atherosclerotic disease. The femoral artery of some patients may be too small to achieve an appropriate cardiac index on bypass. Atherosclerotic disease can complicate both cannulation and cannulation complications may arise, such as retrograde brain embolization. Distal limb perfusion may also be compromised and hence some surgeons advocate a second smaller distal cannula or use of a side graft. Clearly for transfemoral TAVR, distal limb ischemia may be a problem for long procedures. Preoperative CT scanning or TEE screening for atherosclerotic disease may reduce the risk of stroke, particularly for minimally invasive procedures, including robotic procedures. Diminished femoral pulses can make identification and wiring of the vessel more difficult, particularly in obese patients or for reoperation [148]. Further, opening diseased vessels can lead to further stenosis of the artery at the cannulation site with repair as well as lead to potential retrograde embolization with the initiation of bypass [149, 150]. For aortic dissections, retrograde flow on bypass can even extend the dissection proximally or distally. Despite these potential drawbacks,

femoral cannulation with retrograde corporal perfusion remains widely used with a reasonable safety profile [151].

4.5. Left Ventricular Apex

Cannulation of the apex of the heart remains an option when other possibilities are exhausted. The cannula can be placed through an apical purse string with passage of the cannula out through the aortic valve. This can be particularly valuable in cases where the aorta cannot be safely manipulated such as dissection or porcelain aorta [152, 153].

Although this can be a valuable bailout, other strategies are preferred because this site requires manipulation of the apex of the heart which is not well tolerated in most patients. Further, the outflow of the cannula must be distal to the aortic valve to avoid ventricular distension. Distension can also be caused by aortic insufficiency from the cannula crossing the valve. A LV vent is suggested for both potential removal of air and prevention of ventricular distension. While in theory the apical cannulation could affect the ventricular function, this small change in shape with closure of this access site does not appear to cause any clinically evident decrease in function. However, the scar created by this repair could potentially lead to aberrant ventricular electrical conduction, clot formation, or an apical aneurysm.

Studies have shown the feasibility of transapical cannulation during dissection. Recently Sosnowski and coworkers [154] reported their preferred technique of cannulation for aortic dissection requiring TEE guidance to insure appropriate true lumen perfusion. This approach has been utilized for various types of procedures for cardiopulmonary bypass, but may be more of a bailout than a preferred approach for arterial cannulation with the majority of publications referring to aortic dissection repair [153, 155].

4.6. Further Research

The optimal approach to cannulation of straightforward cases is probably the ascending aorta. However, the optimal approach to cannulation for cases involving the ascending aorta and arch will be dependent on the optimal approach to brain protection during the open arch surgery. This research would require a multicenter comparison of neurocognitive outcomes using selective antegrade perfusion with perfusion of the right carotid, both carotids, or all three brachiocephalic vessels compared with retrograde brain perfusion (RBP) and HCA. To complicate the evaluation, patient factors such as atherosclerotic burden and distribution can play a significant role in this decision and evaluation. Only then can the optimal cannulation site for these cases be narrowed down.

4.7. Quality Measures

The Achilles heel to cannulation continues to be embolization. Quality measures need to be focused on the most crippling of embolization: cerebrovascular accidents. Postoperative delirium can also be a significant measure to follow as small emboli or air embolization may cause significant perioperative confusion. At this time, consequences of high-intensity transcranial Doppler signals or MRI-related defects are poorly understood in the absence of frank stroke. Other considerations would be iatrogenic dissection or rupture secondary to cannulation. However, the interdependence of cannulation with the type of brain protection may not muddy the picture sufficiently that cannulation strategy alone becomes a covariable. Thus, we do not believe a specific cannulation site is an absolute essential.

4.8. Conclusions

The optimal site for cannulation remains a surgeon preference. No perfect site exists and probably needs to be tailored to the specific patient anatomy, the perfusion requirements of the procedure, and the surgeon's preference for potential brain protection. For the overwhelming majority of cases the cannulation of the ascending aorta is preferred, but the choice of arterial cannulation site can be tailored with thoughtful consideration of both the patient's anatomy and the procedure being performed.

5. Mechanical Aortic Valves—Recommendations

Class I

1. Before mechanical AVR, all patients who have known CAD, have had a prior myocardial infarction, have angina pectoris as a symptom, or are greater than age 45, should have preoperative screening of their coronary arteries, either by direct coronary angiography. (Level of evidence C)
2. All patients undergoing mechanical AVR should receive perioperative prophylactic antibiotics to cover both gram positive and negative organisms. (Level of evidence C)
3. All patients receiving a mechanical aortic valve should receive postoperative anticoagulation, beginning after valve implantation. (Level of evidence C)
4. All patients with mechanical aortic valve prostheses should receive prophylactic antibiotics for all dental or surgical procedures to prevent prosthetic endocarditis. (Level of evidence C)

Class IIa

1. Nasal mupirocin is probably indicated for methicillin resistant organism or routinely before and after operations. (Level of evidence C)
2. Preoperative chlorhexidine showers and mouth washes should be considered. (Level of evidence C)

Quality Measures

1. All patients receiving a mechanical aortic valve should receive indefinite postoperative anticoagulation therapy. Controversy exists over the exact target international normalized ratio (INR) levels for mechanical aortic valve prostheses. Appropriate levels of therapeutic INR vary according to concomitant patient risk factors [156]. The safety of lower levels of anticoagulation is improved with patient-controlled anticoagulation [157].

2. All patients with mechanical aortic valve prostheses should receive prophylactic antibiotics for all dental or surgical procedures to prevent prosthetic endocarditis.
3. Angiotensin-converting enzyme (ACE) inhibitor therapy should be considered in patients with low EF postoperatively.

Pros

Currently available mechanical aortic valve prostheses have several advantages, including ease of insertion, safety, durability, excellent hemodynamics and long-term track record of performance. Mechanical aortic valves are all relatively easy for cardiac surgeons to implant. There are often different types of cloth sewing rings available to adjust for annular differences. In addition, all current mechanical valves have a low profile, making implantation much easier. The potential for obstruction of the coronary ostia during implantation is minimal. Care must be taken, however, to insure that the tails left on implanting sutures cannot impinge between the disc and valve housing during valve closure.

Structural dysfunction of currently approved mechanical heart valves is extremely rare but not zero. Because most mechanical prosthetic occluders are constructed of some form of pyrolytic carbon, they are susceptible to some degree to chipping or fracture that can be induced by trauma at the time of insertion, such as metal-induced scratches, or cavitation erosion. For all intents and purposes, however, current mechanical aortic prostheses have endured accelerated bench testing without destruction for the equivalent of several patient lifetimes. For younger patients who want to minimize the risk of reoperation, mechanical aortic valves are the best option.

All mechanical aortic valves currently available in the United States are of some type of bileaflet design, since Medtronic, Inc, withdrew its single tilting disc prosthesis from the market in late 2009. Generally speaking, the hemodynamic performance of bileaflet aortic prostheses is excellent with efficacious orifice-to-annulus ratios and thus EOAs. Whereas all mechanical valves have some intentionally designed regurgitation, this is rarely of clinical significance.

Several models of currently available mechanical aortic valves have been in clinical use for more than 30 years. Thus, excellent long-term data on large numbers of patients with mechanical aortic valves are available to prove their low incidence of structural dysfunction, nonstructural dysfunction, and prosthetic endocarditis, and also to define anticoagulation strategies that minimize thromboembolic events while limiting anticoagulant-related bleeding complications.

Cons

All valve prostheses have their disadvantages, some of which are common to all prostheses and some of which are specific to different types or designs. As with all prostheses, mechanical aortic valves have a thromboembolic potential, risk of prosthetic endocarditis, tissue ingrowth, and risk for nonstructural dysfunction, including paravalvular leak and hemolysis [158]. The thromboembolic potential of mechanical aortic prostheses is substantially greater than that of bioprosthesis, and all mechanical valves require some type of anticoagulation. The gold standard for anticoagulation of mechanical valves has been warfarin. The suggested target levels of therapeutic INR for mechanical valves vary more according to associated patient risk factors than to the individual commercial models. Higher target levels of INR are associated with significantly increased risk of anticoagulant-related bleeding. Lower risks of thromboembolism and anticoagulant-related bleeding have been achieved with patient-monitored anticoagulation. As with all anticoagulation strategies, the risks of thromboembolism and anticoagulant-related bleeding are essentially two sides of the same coin. One can often lower the risk of one but only by increasing the risk of the other. Thus, the composite thromboembolism and bleeding index is the most accurate assessment of the combined risk [159]. The ongoing and cumulative risks of thromboembolism and bleeding have led most patients in recent years to opt for bioprosthesis, accepting the probable need for reoperation.

Considerable controversy exists concerning the efficacy of adding antiplatelet agents, usually aspirin, to warfarin for anticoagulation of mechanical aortic valves. Several studies have suggested lower rates of thromboembolism, particularly in patients with concomitant CAD, while most studies have shown a significantly increased incidence of gastrointestinal bleeding with the combined therapy. Nevertheless, in patients who, for example develop amaurosis fugax, particularly with composite mechanical valves, the addition of aspirin may alleviate the problem.

Several trials of using only antiplatelet therapy for mechanical heart valves are in process with no clear proof of the safety of that strategy. One future hope for anticoagulation therapy lies with direct thrombin inhibitors, which might obviate many of the complications associated with warfarin.

The risk of prosthetic endocarditis accrues to all prosthetic heart valve designs. Although the risk is quite low and probably unrelated to differences in commercial designs, the potential mandates antibiotic coverage of all patients with mechanical aortic valves during operative and dental procedures.

Nonstructural dysfunction of mechanical aortic valves usually presents in one of two ways, predominantly paravalvular leak or less frequently hemolysis. The incidence of paravalvular leak relates more to patient factors such as heavily calcified aortic annulus or technical factors at the time of insertion than it does to differences in commercial designs. There are various types of cloth sewing rings available for some mechanical aortic valves that may contribute to lowering the risk of paravalvular leak.

Hemolysis due to mechanical aortic valves is probably present at a low, but clinically insignificant, level in all patients. Occasionally individual mechanical valves can be associated with clinically significant hemolysis, rarely necessitating valve replacement. Hemolysis in a patient with a mechanical aortic prosthesis may not be due to the

valve itself, as there are obviously other medical causes of hemolysis.

There are some hemodynamic issues with aortic bileaflet designs that are of some hypothetic, if not clinical, concern. There is no orientation of a bileaflet prosthesis in the aortic annulus that is not associated with at least some turbulence during systolic flow. The orientation that places the axis of the two leaflets in the middle of the noncoronary cusp yields the least turbulence.

Bileaflet mechanical valves also have some intentional, built-in regurgitation during diastole, meant to wash away microthrombi. Different commercial models of bileaflet mechanical aortic valves all have different hinge designs, some of which theoretically wash better during diastole. In large prostheses this regurgitant fraction is not insignificant. Theoretically the combination of turbulence during systole and regurgitation during diastole contributes to energy loss for the left ventricle.

There are some disadvantageous features of mechanical valves that are unique to their design, as compared with bioprosthesis. When forced into a tight-fitting annulus, the leaflets may not function normally. Another is patient-sensed noise. In occasional patients mechanical prostheses are associated with audible or sensed sounds during virtually every heart beat. Some patients find this unnerving and completely unacceptable, whereas other patients have found it to be reassuring.

Results

Primary, isolated AVR should be able to be performed with certainly less than 5% mortality; in purely elective situations, this should be 1% or less.

Retrospective literature review [158] suggests that the linearized rates of valve-related complications for mechanical aortic valve prostheses should be in the following ranges:

- Structural deterioration, 0% to 0.2% per patient-year
- Nonstructural dysfunction, 0.2% to 0.5% per patient-year
- Thromboembolism, 1.2% to 2.5% per patient-year
- Anticoagulant-related bleeding, 1.0% to 2.5% per patient-year
- Composite thromboembolism and bleeding, 4.0% to 4.5% per patient-year
- Prosthetic endocarditis, 0.4% to 1.0% per patient-year

6. Biological Valves—Recommendations

Class I

1. A bioprosthesis is recommended for AVR in patients of any age who will not take anticoagulation, either warfarin or the direct factor Xa or thrombin inhibitors or who have major medical contraindications to anticoagulation [20]. (Level of evidence C)
2. A bioprosthesis is recommended for AVR in patients aged 65 years or more without risk factors for thromboembolism [20]. (Level of evidence C)

Class IIa

1. Patient preference is a reasonable consideration in the selection of aortic valve prosthesis if appropriate surgical counseling is carried out.

Class IIb

1. A bioprosthesis may be considered for AVR in a woman of childbearing age who desires to have children [20]. (Level of evidence C)
2. A bioprosthesis may be reasonable for AVR in patients aged less than 65 years who elect to receive this valve for lifestyle considerations after detailed discussions of the risks of anticoagulation versus the likelihood that AVR may be necessary in the future [20]. (Level of evidence C)

Quality Measures

1. All patients should receive both gram-positive and gram-negative prophylactic antibiotics before AVR and broad-spectrum antibiotic strict prophylaxis before any surgical, endoscopic, dental, or other procedure associated with the chance of bacteremia.
2. All centers performing AVR should report their results to a national database such as the STS ACSD.
3. To evaluate meaningfully the choice of appropriate prosthesis it is imperative to have standardized guidelines for reporting mortality and morbidity after valve interventions [159]. Much of the confusion and conflicting evidence comparing different valve types derives from the heterogeneity of the patient samples studied and the different definitions used in reporting complications and structural valve deterioration (SVD) rates. Freedom from reoperation for SVD underestimates the true incidence of SVD. Structural valve deterioration should represent dysfunction determined by reoperation, autopsy, or clinical investigation, including periodic echocardiograms. It is also important to distinguish between patient outcome versus valve outcome to counsel individual patients on valve choice. Performance of the prosthesis (valve-related events), when looking at nonfatal complications, is usually reported using the Kaplan-Meier actuarial method with the number at risk at each interval indicated. The Kaplan-Meier method, however, is designed for population studies and overestimates the actual event probability for an individual patient; therefore to predict valve outcome for an individual patient, the cumulative incidence (or observed cumulative frequency) actual statistical method should be used. These actual (cumulative incidence) estimates are best suited for individual patient counseling and patient management decisions [160].
4. ACE inhibitor therapy should be considered in patients with low EF postoperatively.

There are several options for patients who chose a biologic or tissue valve: Stented xenograft bioprosthesis,

stentless bioprosthesis, homografts (or allografts), and autografts (ie, the Ross procedure). The following discussion is devoted to stented tissue bioprosthesis, as the other biological options are covered elsewhere. There was initial hope that stentless bioprosthesis would more closely mimic the native aortic root, provide better hemodynamics, favor more LV hypertrophy regression, and be associated with longer valve durability, but this has not yet translated into improved clinical outcomes [161]. Unless independent aortic pathology or concern for severe patient-prosthetic mismatch (PPM) necessitates xenograft or homograft aortic root replacement, a stented bioprosthesis should be the biologic valve of choice for routine AVR in the elderly patients who cannot be safely anticoagulated, and patients who select a biological valve for lifestyle considerations.

Several stented bioprosthetic valves are available on the market today for AVR and can be divided into porcine valves, which consist of porcine aortic valve leaflets mounted on stents (some of which are composite construction eliminating the right coronary cusp with its muscular shelf), and pericardial valves (mostly bovine, although an equine pericardial valve is now available), which are fabricated from sheets of pericardium mounted either inside or outside the supporting stent frame. A new category of sutureless and rapidly implantable bioprosthesis now have European CE marks and are undergoing clinical evaluation.

There are several differences between tissue valve types which are purported to confer advantages over their counterparts. These can be divided broadly into stent design and leaflet fixation technique. Stents are made of stainless steel, steel alloy, cobalt chromium alloys, titanium alloys, or plastic polymers. More recent designs have modified the material and flexibility of the annular sewing ring and commissural stent posts, as well as shortening the height of the posts for ease of implant. All biologic valves leaflets undergo collagen cross-linking with glutaraldehyde to block immune response and increase tissue stabilization; however, this creates calcium influx as well as exposes residual phospholipids within the cell membrane, which then serve as calcium binding sites. To mitigate valve calcification most companies have developed proprietary tissue treatments aimed at removing residual glutaraldehyde or phospholipid moieties to reduce calcium binding and hopefully enhance durability. Among these are treatment with alcohol and various antisurfactants but none has proved superior to others.

For standard porcine and pericardial stented bioprosthetic valves, the internal diameter by intraoperative sizing is equal to the selected labeled size of the valve minus 4 mm to 6 mm after insertion; however, comparison data for ex-vivo sizes are typically larger. Hence, a 21-mm labeled bioprosthetic valve may have an internal size of 15 mm to 17 mm. For supraannular valves, the internal size is 2 mm to 4 mm smaller. Hence, for a labeled 21-mm valve the internal diameter may be approximately 17 mm to 19 mm. Although aortic valve sizers reflect the true external diameter of the bioprosthetic ring and struts with some variation in shape, supraannular valves will often fit when an intraannular would not fit; however, care needs to be taken that the coronary ostia do not become obstructed as the supraannular sewing skirt can encroach upon low-lying ostia. When sizing an annulus for a valve, surgeons should initially use a sizer that loosely fits until they become comfortable with the limits of being able to fit a tight-fitting valve.

Pros

Currently available stented bioprosthesis have several advantages, but the main one is the hope to avoid the need for long-term anticoagulation therapy. The thrombotic potential of biologic valves is much lower than their mechanical counterparts. Because the risk of thromboembolic events is higher early postoperatively, current ACCF/AHA guidelines recommend (as IIa) warfarin therapy during the first 3 months after bioprosthetic AVR until the sewing ring is endothelialized, although many major centers just rely on aspirin only [20]. This need for warfarin has been called into question by many major institutions. Currently, more than 30% of centers use only 81 mg aspirin indefinitely for patients in sinus rhythm after bioprosthetic AVR. There are several patient populations in which avoidance of long-term anticoagulation is desirable, including women of childbearing age who wish to start a family and those whose lifestyle or lack of reliable access to health care does not allow frequent anticoagulation monitoring necessary for safe indefinite anticoagulation.

In general, rates of thromboembolic complications (0.6% to 2.3% per year) are similar for carefully anticoagulated patients with mechanical valves and those with bioprosthetic valves not on warfarin. The incidence of high-intensity transient signals from the middle cerebral artery detected by transcranial Doppler is lower with biological valves when compared with mechanical valves, although the clinical importance of this is debated. The main advantage is avoidance of long-term anticoagulation therapy, which should translate to a lower risk of bleeding complications. The risk of major bleeding with long-term anticoagulation is approximately 1% per year; however, this significantly increases with increasing age. The $CHADS_2$ score is a composite score reflecting bleeding risk in which one point is assigned for congestive heath failure, hypertension, age $\geq$75 years, or diabetes mellitus, and two points for prior stroke or transient ischemic attack. Individuals with a $CHADS_2$ score of 3 or greater have significantly higher bleeding rates and may not safely tolerate anticoagulation therapy. As a result, some argue that for elderly patients or those patients at high risk for bleeding who are already receiving warfarin for another reason (eg, atrial fibrillation), a biologic valve still may be the most appropriate choice. Choice of a mechanical valve in these patients exposes them to the risk of anticoagulant-related bleeding as well as the risk of thromboembolism and mechanical valve thrombosis should anticoagulation therapy need to be stopped during a major bleeding episode.

The rates of hemolysis, considered "nonstructural valve deterioration," especially clinically significant hemolysis, are lower with biologic than mechanical valves.

Although the late postoperative rates of SVD are higher with biologic valves compared with mechanical prostheses, the deterioration usually is gradually progressive stenosis for pericardial valves, but occasionally leaflets tears at the commissures may cause acute AR for porcine bioprosthetic valves, allowing detection and monitoring with regular routine echocardiographic follow-up. Echocardiographic evaluation of biologic valves should be performed at discharge, at first follow-up, and then at 3 years in the absence of clinical indication, or whenever there is clinical suspicion of valve dysfunction. Structural valve deterioration of modern mechanical valves is rare if anticoagulation control is good; an exception is late pannus ingrowth.

Biological valves do not have any of the audible metallic clicks that are associated with mechanical valves. Finally, one advantage of a stented bioprosthesis in the aortic position is ease of potential reoperation; it is less complicated to do a redo AVR for SVD of a stented tissue valve than is the case for a stentless tissue valve or xenograft aortic root replacement or for homografts.

Whether the potential for transcatheter valve-in-valve procedures should favor the more frequent use of biological valves, particularly in younger patients, is unknown but debated.

Cons

The main disadvantage of biologic valves compared with mechanical valves is their limited durability, which is most common in younger patients. This exposes the patient to the hemodynamic insult of progressive AS or AR, or both, and eventual need for reoperation. All biologic valves eventually sustain SVD over time at some nonlinear rate. Observational studies show that the SVD rate for current porcine and bovine pericardial bioprosthesis used in the aortic position begins to accelerate after approximately 10 years and continues to increase thereafter in patients aged more than 65 years; the shoulder on the freedom-from-SVD curve occurs much earlier in younger patients, which limits the usefulness of tissue valves in these patients. Other patient-related and valve-related factors also increase the rate of bioprosthetic deterioration [4], for example, female sex, larger valve size, and mitral position.

The age of the patient at the time of implantation is the strongest predictor of accelerated SVD. Younger patients have significantly higher SVD rates. Fifteen years postoperatively, roughly 9% of patients aged more than 65 years of age, 26% of patients aged less than 65 years [7], and nearly 40% of patients aged less than 40 years will have sustained SVD. Certain other medical problems such as end-stage renal disease, hyperparathyroidism, and hypertension can also hasten the development of SVD. In certain patient cohorts such as those on dialysis, life expectancy is so bleak that concern about accelerated SVD is moot and should not prevent them from receiving a biologic valve. It is important not just to take into account the absolute age of the patient, but also their expected biological life expectancy based on the severity of cardiac dysfunction, other cardiac problems, medical comorbidities, and their family history of longevity. There is also no good evidence that statins or antiinflammatory drugs can mitigate this deterioration.

The pathogenesis of SVD in biologic valves is largely thought to be a degenerative process caused by calcium influx. Most companies have developed various proprietary tissue treatments aimed at reducing calcium binding, although some contemporary valves do not offer any specific anticalcification treatment. In general, newer generation tissue valves purport to have lower SVD rates than do older bioprosthesis, but there have been no controlled studies showing a difference in SVD rates between different types of porcine valves. Several reports have claimed lower valve deterioration rates in patients who received bovine pericardial valves, but the definition used in all of these studies is freedom from reoperation for SVD, which underestimates the true SVD incidence. Although there have been many retrospective studies attempting to compare SVD rates among different types of stented bioprosthesis, as of now there are too many confounding variables to make any conclusive statements about relative durability between the porcine aortic and bovine pericardial tissue valves used today in the aortic position.

It should be noted, however, that the mechanisms of deterioration differ between porcine and pericardial tissue valves. Porcine xenograft bioprosthesis tend to develop dysplastic calcification in the leaflets near the commissures (high-stress regions) which leads to leaflet tears and sometimes sudden valvular regurgitation; this can be detected clinically by a new murmur and confirmed by echocardiography. Pericardial xenograft bioprosthesis also calcify, but typically in a diffuse metaplastic manner across the leaflets that can lead to occult severe AS without being detected by a new murmur. The leaflets of both types of bioprosthesis may also develop commissural calcified fusion.

Some have hypothesized that immunologic, arteriosclerotic, and inflammatory processes are also involved in SVD. There was a burst of initial enthusiasm for statin therapy in the hope that their pleiotropic effects would retard SVD, but this has not been proved to date.

Whether stented bioprosthesis used for AVR have inferior hemodynamic performance compared with mechanical valves has been debated. This has led to concern about PPM, especially as biologic valves are more commonly implanted in the elderly with calcified, smaller annuli. Clinical interest in PPM is based on the reports of increased short- and long-term mortality rates as well as less symptomatic improvement if an important degree of PPM exists ($\leq$0.8 or 0.9 cm^2/m^2) [162]. The EOA index, which is obtained by dividing the valve EOA by the patient's body surface area (BSA), should be used for identifying PPM. Many valve companies provide EOA charts plotting valve size against BSA, which can be used as a rough guide for choice of valve size and valve type but should not supersede the clinical judgment of the surgeon and taking into account the severity of the

AS preoperatively and how physically active the patient is likely to be postoperatively. Patient age, sex, LV function and size, and hypertrophy must be considered in choosing an appropriate device.

Stented bioprosthesis should be implanted in the supraannular position to maximize the size of tissue valve that can be implanted. Additionally, two new types of pericardial xenograft valves have the bovine pericardial cusps mounted outside the stent frame for the same reason. Every effort should be made to avoid severe PPM (EOA index <0.65 cm^2/m^2), including selecting a type of bioprosthesis with superior hemodynamic characteristics or resorting to annular enlargement or even complete xenograft or homograft root replacement if necessary in highly selected patients. Moderate PPM (≤ 0.8 or 0.9 cm^2/m^2), however, is generally well tolerated. The patient's activity level, age, sex, ventricular hypertrophy (LV mass), ventricular function, BSA, and severity of AS all should be taken into account. The risk-to-benefit ratio of an annular enlargement procedure to avoid moderate PPM is acceptable in younger patients who can be expected to engage in vigorous physical activities, whereas it would not be prudent in an elderly patient who is sedentary.

The presence of the stents in bioprosthetic tissue valve mounting frame leads to a higher profile substitute valve, more so for porcine tissue valves than pericardial valves, particularly at the nadir of the frame. This hypothetically increases the risk of coronary ostial obstruction. Some tissue valve designs have minimized this with lower profile struts to facilitate implantation. Orienting the struts with the native commissures will generally avoid ostial obstruction in native tricuspid aortic valves. The aortic annulus in patients with bicuspid aortic valves who tend to be younger can be markedly ellipsoidal in shape. Patients with a bicuspid aortic valve frequently also have the left main coronary ostium located more rightward (straight posteriorly) such that the coronaries arise about 180 degrees apart, which must be considered when positioning the struts of the bioprosthesis.

Prosthetic valve endocarditis is a risk for patients with any type of artificial heart valve, and there is no documented difference in this risk between mechanical and tissue valves over the long term. Although the incidence of prosthetic valve endocarditis is low, after the initial 90-day high-hazard phase, aggressive antibiotic prophylaxis for all patients after prosthetic or bioprosthetic AVR is mandatory. Prosthetic valve endocarditis, especially early active prosthetic valve endocarditis, can prove to be a devastating and often fatal complication.

Results

Data harvested from the STS ACSD from 2002 to 2006 show the operative mortality risk in the United States for isolated AVR is 3.2% [84]. In patients undergoing concomitant AVR and CABG, the STS operative mortality risk for the same time period was almost double (5.6%) [163]. Operative risk increases slightly with patient age in the contemporary era, but considerably so if associated comorbidities are present. According to the online STS-PROM risk calculator, the predicted operative mortality risk for a 70 year old without any comorbidities is 0.8% for a male and 1.2% for a female; for an 80-year-old without any comorbidities, it is 1.3% for a male and 2.0% for a female [164].

Nonstructural valve dysfunction, which includes any abnormality not intrinsic to the valve, includes hemolysis (incidence close to 0), significant paravalvular leak (1% to 2% of patients at 1-year follow-up) [165], and PPM (risk of severe PPM 2% to 10% of all patients) [162]. Thromboembolic rates with biologic valves in the aortic position are approximately 0.6% to 2.3% per patient-year. Prosthetic valve endocarditis rates are 0.5% per patient-year [166].

Future of Biological Valves

With the advent of TAVR in very high risk or inoperable patients with AS, there has been much talk about potential "valve-in-valve" implantation as a minimally invasive solution for redo AVR operations when SVD of a bioprosthesis occurs. There have been successful transapical valve-in-valve TAVR cases reported for a failing aortic tissue valve (both stented and stentless) [167, 168], although there is concern for the potential of PPM. Measured postimplantation gradients across the transcatheter heart valve appear to be high after TAVR in surgically implanted valves smaller than 23-mm external diameter. Depending on the specific type of bioprosthesis used initially, valve-in-valve TAVR may not be successful unless the original surgical bioprosthesis was 23 mm or larger given the limited sizes of commercially available transcatheter percutaneous valves available today. The smaller transcatheter heart valve prosthesis being developed will address the size problem but not the PPM problem as internal space is quite limited inside stented bioprosthesis. It remains unknown how many patients will be eligible for this potential treatment of SVD in the future, but valve-in-valve TAVR in the context of a failing AVR bioprosthesis has been shown to be technically feasible.

7. Enlargement of the Aortic Annulus—Recommendations

Class I

1. Patch enlargement of the aortic annulus should be considered when the aortic annulus does not allow implantation of a heart valve with EOA index more than 0.65 cm^2/m^2 [169–171]. (Level of evidence B)

Class IIb

1. Patch enlargement of the aortic annulus may be considered when the aortic annulus does not allow implantation of the heart valve with EOA index of 0.85 cm^2/m^2. (Level of evidence C)

The development of operative techniques to enlarge the aortic annulus and LV outflow tract preceded the knowledge of PPM introduced by Rahimtoola in 1978 [12]. Enlargement of the aortic annulus is performed to allow implantation of larger prosthetic valves to optimize the

effective aortic valve orifice. Surgeons who enlarge the aortic annulus to implant larger prosthetic valves must have a sound knowledge of the anatomy of the aortic root and its relationship with surrounding structures. The Konno procedure, or aortoventriculoplasty, involves incising the aortic root through the right aortic sinus and into the muscular interventricular septum [172]. This incision creates a muscular ventricular septal defect and by closing the defect with a patch, the aortic annulus is enlarged proportionally to depth of the septal incision and width of the patch. A second patch is needed to close the right ventricular outflow tract (RVOT).

Alternative methods to enlarge the aortic annulus involve incisions in the fibrous portion of the LV outflow tract. In the Manouguian procedure, an incision is made through the commissure of the left and noncoronary cusps and extended into the subcommissural triangle and anterior leaflet of the mitral valve [173]. The dome of the left atrium has to be opened when this incision is extended in to the mitral valve. A patch is used to close the incision and increase the diameter of the aortic annulus. A separate patch may be needed to close the dome of the left atrium. The Nicks procedure for enlargement of the aortic root involves an aortotomy in the middle of the noncoronary aortic sinus, through the aortic annulus and into the intervalvular fibrous body, and may be extended into the anterior leaflet of the mitral valve [174]. Annular enlargement is made with a patch as described above. Another method to implant a prosthetic valve one size larger than the size of the annulus is to suture it in a supraannular position [175]. Most currently used bioprosthetic aortic valves are designed to be secured in the supra-annular position. Alternatively, the midsection of the annulus in each sinus can be excised to gain one size larger valve.

The Konno procedure is far more effective in enlarging the diameter of the LV outflow tract and aortic annulus than the other procedures but it is also more complicated. It is frequently used in children and teenagers with congenitally small roots but less so in adults except for reoperations in young patients with PPM. The procedure can be done with either a homograft or mechanical valves. The Manouguian and the Nicks techniques of patch enlargement of the aortic annulus allow to upsize the prosthetic heart valve by one or two sizes. Attempts to further increase the diameter of the aortic annulus by suturing wider patches deforms the LV outflow tract and causes so much disturbance of flow that may not improve the hemodynamic of the prosthetic valve.

Another option that optimizes EOA in patients with small aortic annulus is replacement of the aortic root with a bioprosthetic stentless valve or a homograft. However, such procedures must balance the potential benefit of implanting a larger valve against the possible increase in operative morbidity and mortality.

It has been shown that the diameter of the aortic annulus is closely related to the patient's BSA [176]. Thus, for a man with BSA of 1.71 m^2 to 1.80 m^2 the mean aortic annulus diameter is 21.5 $\pm$ 2.0 mm, and for a BSA of 2.01 m^2 to 2.10 m^2 the annulus is 23.0 $\pm$1.8 mm based on relaxed aortic root size in cadavers. Women have slightly smaller aortic annulus than men. Patients who need AVR may have an aortic annulus of normal or abnormal diameter depending on the valve pathology, for example the diameter may vary markedly in patients with bicuspid valves.

Patient-prosthesis mismatch has been defined based on the EOA index of the prosthetic valve [169, 170]. It has been determined that the ideal EOA index should be more than 0.85 cm^2/m^2. Moderate PPM is defined as EOA index of more than 0.65 cm^2/m^2 to 0.85 cm^2/m^2 or less, and severe PPM as EOA index of 0.65 cm^2/m^2 or less. To prevent PPM, it is important to match the size of the prosthetic aortic valve EOA to the patient's BSA. The patient's BMI is also an important consideration.

The clinical relevance of PPM has been debated in the literature, with some studies unable to demonstrate a relationship between valve size and outcome [177–179] and others suggesting that PPM increases early and late mortality, decreased exercise tolerance, and decreased LV mass regression [169, 171, 179–182]. Patient-prosthesis mismatch may be particularly important in patients with impaired LV function [169]. Surgeons must therefore be familiar with the EOAs of various mechanical and bioprosthetic valves that they use and at the time of AVR, and an attempt should be made to avoid severe PPM.

Surgeons who routinely used patch enlargement of the aortic annulus during AVR believe this procedure can be added with minimal increase operative mortality and morbidity [183, 184].

8. Homograft (Allograft) Replacement of the Aortic Valve—Recommendations

Class I

1. Homograft replacement of the aortic root should be considered for patients with extensive active endocarditic destruction of the aortic annulus [185–189]. (Level of evidence B)
2. For patients undergoing homograft replacement of the aortic valve, a total root replacement technique is recommended [190, 191]. (Level of evidence B)

Class IIa

1. Homograft replacement of the aortic valve can be considered for patients with endocarditis without annular destruction, especially when the potential for reinfection is elevated [14, 192, 193]. (Level of evidence B)
2. Homograft replacement of the aortic valve can be considered for patients undergoing reoperative aortic root surgery in whom anatomic or physiologic constraints mitigate against more conventional composite graft replacement or for whom life

expectancy is less than the projected durability of the homograft [194–196]. (Level of evidence B)

Class III

1. Homografts are not recommended for routine AVR. Currently available xenografts have excellent hemodynamics, durability comparable to homografts and are simpler to replace [197–199]. (Level of evidence B)

Quality Measures

1. All patients undergoing homograft implantation should receive perioperative prophylactic antibiotics with broad spectrum coverage.
2. All patients with a potential for CAD or coronary anomalies should undergo preoperative evaluation of their coronary anatomy by coronary angiography.
3. Annual transthoracic echocardiogram to evaluate for AS and AR.
4. Antibiotic prophylaxis against endocarditis for prosthetic valves.
5. ACE inhibitor therapy should be considered for patients with low EF postoperatively.

The first successful homograft (allograft) replacement of the aortic valve was reported by Ross in 1962. At that time, the allograft held the promise of being the ideal aortic valve substitute. The ensuing 5 decades of experience with this prosthesis has demonstrated key strengths and weaknesses and has helped to define its current role in the surgical management of aortic valve disease. In the United States over the past 20 years, homografts have been used in less than 3% of AVRs annually. That figure has decreased in recent experience, and the homograft is currently used in approximately 0.2% of AVRs, mostly for endocarditis [200].

Pros

The aortic homograft is human tissue with human anatomy. It has a central orifice with virtually normal hemodynamics and is associated with low transvalvular gradients both at rest and at exercise. This characteristic is of value when treating patients who wish to maintain a physically active lifestyle or younger patients with small aortic roots where the potential for PPM is greater. The potential for thromboembolic problems is negligible and they do not require anticoagulation therapy. Because of its natural pliability, when used as a root replacement, it can conform more readily to deformities and asymmetries present in the recipient root. The homograft's most compelling advantage is that it is devoid of any prosthetic material, which confers an apparent resistance to infection. Additionally, the attached anterior mitral leaflet and muscular cuff can be used to correct defects caused by advanced endocarditis as characterized by extensive annular abscess, fistulas, and annular disruption. It is in the management of advanced native and prosthetic valve endocarditis that the homograft has demonstrated its greatest utility [185–189].

Cons

Homograft implantation is technically more demanding than mechanical or bioprosthetic stented AVR. Three techniques have been employed over time: subcoronary or "freehand" implant, root inclusion cylinder, and total root replacement with coronary ostial reimplantation. Although in select hands the subcoronary technique has produced excellent results [201, 202] and also has been shown to simplify the inevitable reoperation, most experience with this technique has been less favorable owing to the development of AR [191, 203]. This is related to the judgment required to replicate proper commissural spacing and alignment and also related to changes in the geometry of the retained native aortic root. The root inclusion cylinder maintains aortic valve geometry but occupies greater space within the native aortic root, but is useful when large abscesses are present in conjunction with reoperations. Valve sizing is important and there is the potential for hematoma formation between the native aortic wall and the homograft cylinder. Today, total root replacement with coronary ostial mobilization is most commonly employed because it has demonstrated more reproducible results over a spectrum of pathology, bears similarity with the technique for composite valve grafts, does not require precise valve sizing, and can accommodate native annular deformities [190]. Hemostasis can be more challenging than with the other two techniques, especially in the setting of extensive endocarditic annular destruction.

Allowing that worldwide homograft experience is adversely skewed by a greater representation of endocarditis cases, it is clear that even in experienced centers early morbidity and mortality are greater than for AVR with conventional prostheses [14, 192, 193, 201]. Furthermore, the homograft root tends to calcify extensively over time [204], and reoperations are technically challenging and associated with greater perioperative risk.

Homografts are not "immunologically privileged" and residual cells and native proteins elicit a low-grade immunologic and inflammatory response that contributes to structural degeneration over time [205]. Indeed, the greatest disappointment with the homograft experience relates to the issue of SVD. Initially hoped for extended durability has not been realized and is comparable to that of pericardial valves (Fig 22).

The two most commonly employed methods of preservation are, one, cryopreservation in a solution of antibiotics and dimethyl sulfoxide and, two, fresh homografts (stored at 4°C in a solution of antibiotics) that are implanted within weeks of harvest. Cryopreserved valves are more readily available and most commonly used. Although fresh storage results initially in more viable cells and potentially a greater immune response, it appears that there is no significant difference in durability between these two methods of preservation. As with xenografts, patient age at implantation is the single greatest predictor of SVD. Importantly, when adjusted for age at implantation, the durability of homografts closely parallels that of second and third generation xenografts

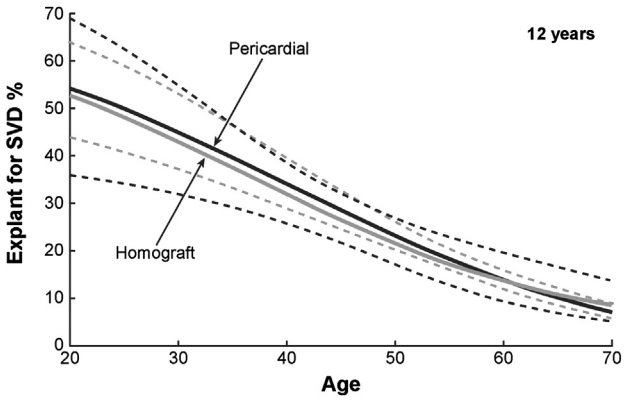

Fig 22. Relationship between age of patient for pericardial or homograft valve and the risk of reoperation within 12 years of surgery. (SVD = structural valve deterioration). This graph is useful for discussing with patients the risk of reoperation for biological aortic valve replacement.

[14, 193, 198, 199]. In a recently reported and rare randomized study comparing homografts to the stentless xenograft, homografts showed greater rates of SVD and need for reoperation at mid-term follow-up [197].

Finally, although the utility of the homograft in treating cases of advanced endocarditis is well established, several centers have reported excellent short and long-term freedom from recurrent infection with the simpler method of mechanical or bioprosthetic valve replacement and annular repair with bovine pericardial patch in the absence of abscesses or extensive tissue destruction or composite graft root replacement [194–196].

Results

Precise comparison and analysis of results is confounded by (1) the variability in methods of homograft preservation and implantation used by and among reporting centers over time; (2) varying prevalence of endocarditis in patient cohorts; (3) study time frames often spanning decades; and (4) the lack of randomized trials. Operative mortality for isolated homograft root replacement is higher even in experienced centers, and ranges from 2% to 8% [14, 191–193, 198, 199, 201, 202]. Overall survival after operation ranges from 50% to 81% and from 35% to 58% at 10 and 20 years, respectively [14, 191–193, 198, 201, 202]. Valve thrombosis is virtually nonexistent and thromboembolic events average 0.5% per patient-year. Ten-year and 20-year freedom from thromboembolism is approximately 93% and 88%, respectively. Homograft durability is primarily dependent on age at implantation, and median time to reoperation for SVD approximates 12, 14, and 16 years for a 30-, 45-, and 60-year-old patient, respectively. In the largest single reported series to date [198], freedom from reoperation at 20 years was 47% for patients aged less than 21 years, 85% for those between 21 and 40 years, 81% for those aged 41 to 60 years, and 94% for patients aged more than 60 years. However, meta-analysis and microsimulation using more contemporaneous data suggest that freedom from reoperation for SVD at 10 years after operation approximates 74%, 82%, 88%, and 92% for ages 35, 45, 55, and 65 years, respectively. At 15 years after operation approximately 35%, 51%, 63%, and 74% of patients aged 35, 45, 55, and 65 years are still free from explant [14, 193, 206]. Freedom from recurrent endocarditis in several larger series of patients undergoing replacement for endocarditis is excellent and ranges from 82% to 92% at 10 years postoperatively [185, 186, 188, 189].

9. Stentless Aortic Valves

Stentless heterograft valves were developed to take advantage of the physiologic nature of homograft valves with a more standardized method of implantation. They are constructed from porcine roots with minimal cloth externally for accepting sutures and tissue ingrowth. There are no rigid components or true sewing ring. Initially stentless valves were used in the subcoronary coronary position for AVR. However, a full root implementation was developed to allow for full root implantation and also mitigate early subcoronary valve failures due to native aortic root dilation. They can be implanted as subcoronary implants, full root replacements, or uncommonly, inclusion roots.

The subcoronary placement of this valve is designed to enable conformation to the patient's own aortic root, reproducing a normal valve/root complex. Clinical studies have shown residual transvalvular gradients similar to native valves and superior to stented valves at early to midterm follow-up [207]. Exercise gradients were also superior with the stentless valves at midterm follow-up indicating the valve may perform better under physiological stresses than stented valves [208]. That may eliminate the theoretical risk of PPM in larger patients with small stented bioprosthesis that have high transprosthetic gradients [209]. Additionally, more physiologic laminar flow patterns the sinuses of Valsalva have been observed in stentless valves and are postulated to decrease the opening and closing stresses on the valve leaflets [210]. Among patients requiring full root replacement, porcine bio roots have excellent hemodynamics and do not require life-long anticoagulation therapy.

The major concerns regarding stentless prostheses relate to risk related to increased technical complexity of implant, particularly versus simple AVR, issues regarding long-term durability, and concern for the safety of valve-in-valve TAVR.

9.1. Subcoronary Stentless Valve Implantation for Aortic Valve Replacement—Recommendations

CLASS I

1. Before subcoronary stentless AVR, all patients who have known CAD, have had a prior myocardial infarction, have angina pectoris as a symptom, or are more than 45 years of age, should have preoperative screening of their coronary arteries, by direct coronary angiography. (Level of evidence C)

2. Intraoperative TEE is recommended to check the valve function. (Level of evidence C)
3. Prophylactic antibiotics for any invasive procedure, including dentistry, are recommended. (Level of evidence C)

CLASS IIB

4. Stentless valves may be a reasonable prosthesis choice in patients aged more than 70 years with nonregurgitant, trileaflet AS who desire a tissue prosthesis and are at risk for PPM. (Level of evidence C)

QUALITY MEASURES

1. Prophylactic gram-positive and gram-negative coverage should be used at the time of surgery.
2. Intraoperative echocardiography should be performed.
3. Postoperative aspirin or clopidogrel should be administered.
4. Patients should be discharged on beta-blockers.
5. ACE inhibitor therapy should be considered in patients with low EF postoperatively.

PROS Stentless valves in the subcoronary position provide excellent hemodynamics with gradients unmatched by traditional stented prostheses and have no requirement for long-term anticoagulation therapy. These excellent hemodynamics are particularly important in small aortic root where a stented prosthesis may have a high residual gradient. They are more readily available than homografts. They do not require obligatory anticoagulation.

CONS Subcoronary stentless valve implantation is substantially more technically demanding and requires significantly longer cardiac ischemic times than traditional stented AVR. Long-term durability of these valves remains unknown and there are concerns of early structural and nonstructural deterioration. Stentless valves have been shown to have higher failure rates due to root dilation splaying out the commissures and causing insufficiency in patients with preoperative AR or bicuspid pathology, although this may be mitigated with preservation of the porcine noncoronary sinus to fixate two of the commissures. There are theoretical concerns that stentless valves may be more prone to coronary coverage during TAVR for prosthetic failure due to their leaflet height and lack of sinuses or a stent. Stentless valve reoperations are reported to have higher mortality than other aortic valve reoperations and frequently require complex root replacement. Nevertheless, the calcification is less than that of a homograft.

RESULTS In a well-designed randomized trial of 99 patients comparing subcoronary stentless valve implantation to a traditional pericardial prosthesis, despite slightly improved gradients in the stentless group, there was no demonstrated benefit in LV mass regression or physical activity status between groups [211]. Recent 10-year follow-up of these patients confirmed better hemodynamics in the stentless group but no difference in LV remodeling or physical activity [161]. These findings have been confirmed in multiple small trials [212, 213]. Durability of stentless valves in the subcoronary position has been reported to be lower than 80% at 8 to 10 years, implying poorer durability than traditional stented prostheses [214]. Freedom from thromboembolism and endocarditis are typically greater than 90% at 7 to 10 years [214].

9.2. Full Aortic Root Replacement With a Stentless Prosthesis—Recommendations

CLASS I

1. Before aortic root replacement, all patients who have known CAD, have had a prior myocardial infarction, have angina pectoris as a symptom, or are aged more than 45 years, should have preoperative screening of their coronary arteries by direct coronary angiography. (Level of evidence C)
2. Intraoperative TEE is required to check the valve function. (Level of evidence C)
3. Prophylactic antibiotics for any invasive procedure including dentistry are recommended. (Level of evidence C)

CLASS IIA

1. Stentless aortic valve full root replacement may be considered in patients aged more than 70 years with aortic root dilation. (Level of evidence C)

CLASS IIB

1. Stentless aortic valve full root replacement may be considered in patients aged more than 70 years at high risk for PPM who desire a tissue prosthesis. (Level of evidence B)

QUALITY MEASURES

1. Prophylactic gram-positive and gram-negative coverage should be used at the time of surgery.
2. Intraoperative echocardiography should be performed.
3. Postoperative aspirin or clopidogrel should be administered.
4. Patients should be discharged on beta-blockers.
5. ACE inhibitor therapy should be considered in patients with low EF postoperatively.

PROS Implantation of a stentless root prosthesis is usually performed as a traditional root implant with interrupted pledgeted sutures and coronary button reimplantation that is intuitive to perform for most cardiac surgeons. A running suture technique may also be used although this is a more technically demanding procedure. Stentless roots provide excellent hemodynamics. In cases of extremely small roots in larger patients, full root implantation may be used for the purposes of aortic root replacement to implant a larger prosthesis size despite lack of intrinsic aneurysmal root pathology. Similarly, a stentless prosthesis may be used in the setting of aortic valve endocarditis with periannular abscess.

CONS Stentless aortic roots are technically more difficult to implant than a stented composite root and lack a robust sewing ring to provide a blood-tight seal in diseased or infected annular tissue. Indeed, the cloth sewing ring may make them more prone to recurrent infection than homografts. They also have a greater potential for distortion as they lack a rigid stent. The long-term durability of stentless valves remains unknown and reoperations are complex. There are theoretical concerns that stentless valves may be more prone to coronary coverage during TAVR for prosthetic failure owing to their leaflet height and lack of stent.

RESULTS Perioperative (30-day) mortality in experienced centers is typically between 2% and 4% for elective operations although in early series it exceeded 10% [215]. In a randomized study of 166 patients, within 8 years of implant, homografts showed significantly poorer freedom from structural failure than the stentless prosthesis for full root replacement [197]. This and several other studies have shown more than 95% freedom from reoperation and more than 85% freedom from echocardiographic valve dysfunction at 7 to 10 years of follow-up with preserved low gradients [197, 216]. Freedom from thromboembolic events and prosthetic endocarditis are generally greater than 90% over the 7 to 10 years [197]. Although reoperation is rare over the medium term, longer term outcomes are still unknown. Reoperations for failed bio roots are purported to have high operative mortality [217].

10. Pulmonary Autograft (Ross Procedure)—Recommendations

Class I

1. The Ross procedure is recommended in infants and small children for whom no satisfactory alternative valve substitute exists. (Level of evidence C)

Class IIb

1. The Ross procedure may be considered in older children and young adults because of low operative risk, but patients and their families must be informed of the possible need for reoperation which increases over time. (Level of evidence C)

Class III

1. The Ross procedure is not recommended for middle-aged or older adults when suitable alternatives to autograft replacement of the aortic valve are available with comparable results and without the need for replacement of the RVOT, as the latter adds the additional risk of pulmonary valve dysfunction and subsequent replacement. (Level of evidence C)
2. The Ross procedure is not recommended for patients with bicuspid valves and AR or aortic dilation if other alternatives are available. (Level of evidence C)

Quality Measures

1. Patients aged 45 years or more or patients who are younger with risk factors for CAD undergoing the Ross procedure should have preoperative coronary artery angiography.
2. Patients undergoing the Ross procedure should be counseled about the risk for reoperation on both the pulmonary autograft and the pulmonary homograft.
3. Annual TTE should be performed to monitor the size of the aortic root and ascending aorta and the function of the autograft and homograft valves.
4. Appropriate prophylaxis against endocarditis should be performed for invasive procedures.
5. ACE inhibitor drug therapy should be considered in patients with low EF postoperatively.

The pulmonary autograft (Ross procedure) for replacement of the aortic valve was introduced by Dr Donald Ross in l967. It involves replacement of the aortic valve or aortic root with the pulmonary valve, which is excised en bloc from the RVOT. A pulmonary homograft is most commonly used to replace the RVOT. Substantial experience with the procedure has been accumulated over the past 25 years.

Pros

At experienced centers, the procedure can be accomplished with extremely low mortality in selected young adults and children [15, 218–226]. Ten-year survival is excellent, more than 90%, and approaches that for age- and sex-matched populations. Hemodynamic performance is excellent, anticoagulation is not required, thromboembolic events are rare, and infection infrequent. It is an important therapeutic option for infants and children where alternative substitutes perform poorly [225, 226].

Cons

Long-term follow-up has demonstrated progressive dilation of the autograft when used as a root replacement, neoaortic valve regurgitation, and need for reoperation on the autograft as well as on the allograft in the RVOT [15, 218–224, 226]. Use of the root inclusion rather than the root replacement technique (the most widely utilized) to prevent autograft dilation has not reduced the rate of reoperation [222, 224]. The risk of dilation appears to be increased in patients with bicuspid valves, particularly if associated with AR or aortic dilation [224].

Results

Operative mortality in the largest reported series has ranged between 0.5% and 3.9% [15, 218–224, 226]. Major postoperative complications were infrequent. Minimal gradients have been observed across the autografts and these remain stable. Mild to moderate gradients exist across the valve substitutes in the RVOT, and some become sufficiently severe to require percutaneous or open surgical procedures for correction [15, 218–224, 226]. Ten-year survival has ranged between 92% and 98% and is remarkably consistent among centers [218–224]. Survival approaches that for

age-and sex-matched populations [219, 220, 224]. Among children requiring AVR, use of the Ross procedure confers a survival advantage over mechanical valves in younger children but not in young adults [225, 226].

The principal limitations of the procedure are progressive dilation of the autograft at the sinus and commissural levels with the root replacement technique, neoaortic valve regurgitation with both the root replacement and inclusion techniques, and the need for reoperation on the autograft and the homograft in the RVOT.

The percentage of patients free from reoperation on the autograft at 10 years varies from 75% to 94% among the large reported series [218–222, 224]. Longer follow-up from the largest reported series of patients (n = 487) reported by Elkins and colleagues [221] indicates a continued decline in the number of patients free of reoperation or valve-related death (86% at 10 years and 74% at 16 years). Freedom from reoperation on the pulmonary allograft in the RVOT is better and more consistent, ranging from 90% to 97% at 10 years [218–224]. Freedom from any reoperation is reported less frequently, and varies from 73% to 90% in four series at 10 years [218, 219, 223, 224].

Endocarditis occurs infrequently (25 of 1,660 patients [1.5%]) with data suitable for analysis in the large series [218–224]. Major thromboembolic episodes (principally stroke) occurred in 11 of the 1,160 patients (0.7%), and in several instances were associated with the development of endocarditis.

The availability of bioprosthetic aortic valve substitutes that have acceptable hemodynamic characteristics, do not require anticoagulant therapy, and have comparable late rates of reoperation on the aortic valve or root, calls into question the role of the Ross procedure for all but infants and small children for whom no suitable alternative valve substitute is available.

11. Balloon Aortic Valvuloplasty—Recommendations

Class IIa

1. BAV can be useful as bridge to AVR in hemodynamically unstable adult patients with severe AS where immediate AVR is not feasible. (Level of evidence C)
2. BAV should be considered for patients with contra indications to AVR who can potentially be bridged to AVR or TAVR in future. (Level of evidence C)
3. BAV should be considered in severely symptomatic patients with multiple comorbidities where contribution of AS to symptomatology such as chronic pulmonary disease or poor LV function, remains unclear. (Level of evidence C)

Class IIb

1. BAV may be reasonable in severely symptomatic patients where AVR is not an option for symptom relief. (Level of evidence C)
2. BAV may be considered in patients with symptomatic severe AS who require urgent major noncardiac surgery. (Level of evidence C)
3. BAV may be considered as a palliative measure in individual cases when surgery is contraindicated because of severe comorbidities. (Level of evidence C)
4. Hemodynamic assessment including cardiac output, aortic, LV and pulmonary pressures may be considered before, during and after the procedure. (Level of evidence C)
5. Rapid ventricular pacing may be performed to stabilize balloon during inflation unless self seating dumbbell shaped or other specifically designed balloons are available that do not require pacing. (Level of evidence C)

Quality Measures

1. Candidacy for AVR should be thoroughly assessed in collaboration with cardiac surgery.
2. Assessment of annular diameter and preprocedural AR should be carefully made with appropriate imaging.
3. Vascular access should be carefully evaluated with angiography before insertion of the closure device and a large sheath.
4. Stepwise dilation of the aortic valve can be used to achieve desired hemodynamic improvement.
5. Hemodynamic monitoring during BAV should include aortic diastolic pressure, LV filling pressures and cardiac output.
6. Procedural outcomes with special attention to groin complications, AR, and procedural mortality should be monitored.
7. Patients should be monitored for the rate at which the patients are bridged to surgical AVR or TAVR.

Balloon aortic valvuloplasty is performed mainly to bridge high-risk patients to surgical AVR or TAVR. Reasons for bridging include temporary contraindications to valve replacement (sepsis, severe debilitation, acute neurological event, coagulopathy, congestive heart failure, ventilator dependence etc.), significant other cardiac lesions (coronary, mitral valve, tricuspid valve, myocardial disease) where relative contribution of AS to heart failure remains questionable, or in patients with severe noncardiac comorbidities where role of AS in presenting symptoms is difficult to determinate (eg, severe lung disease, cirrhosis, severe debilitation, etc) [227]. Infrequently, BAV can be used for patients with symptomatic severe AS who require urgent major noncardiac surgery. Rarely, it can be helpful for palliation in adult patients with AS in whom AVR cannot be performed because of serious comorbid conditions, although short-lived improvement makes such an effort a temporary success. Sometimes BAV is helpful to assess the contribution of AS to respiratory failure when combined with severe chronic obstructive pulmonary disease. A marked improvement suggests that

AS is a major contributor although lack of improvement is not very specific for pulmonary problems.

Balloon aortic valvuloplasty can be performed either with retrograde or antegrade approach [228, 229]. The retrograde approach entails femoral arterial access. In the antegrade approach from the femoral vein, a transseptal puncture is performed and the aortic valve is approached through the mitral valve going antegrade through the left ventricle.

Pros

Balloon aortic valvuloplasty provides the only treatment option for hemodynamically unstable patients who are not candidates for surgical or transcatheter AVR. Hemodynamic improvement is rapid which provides an opportunity to manage comorbidities while more definitive valve replacement is planned.

Retrograde BAV is technically easier but requires reasonable groin access. Antegrade BAV can be performed in patients with poor arterial access but can be more challenging especially in patients with small left ventricles, severe mitral regurgitation or hemodynamic instability.

Cons

Procedural efficacy is only moderate with a typical AVA of less than 1.0 cm^2. Procedural risk is also not trivial and depending on the patient population there can be as high as 10% 30-day mortality with the procedure. Further, the procedural benefits are short lived with most patients restenosing in 6 months.

There are several improvements to the procedure that may help with each of the above issues. With rapid pacing of the ventricle and use of larger balloons, an AVA of more than 1.0 cm^2 is feasible in increasingly larger number of patients although conclusive data are lacking. Mortality can be reduced by better management of the vascular access site. Restenosis risk is still a problem but since the most common indication of this procedure is a bridge to more definitive therapy, it may not be a fundamental limitation. Conversely, use of BAV as a stand-alone procedure has limited value unless combined with bridging to surgical AVR or TAVR. Balloon aortic valvuloplasty combined with radiation has not received much acceptance.

Results

Procedural success is classically defined as more than 25% increase in AVA or more than 50% reduction in mean aortic gradient. Procedural mortality (1% to 5%) is primarily from AR, and 30-day mortality (6% to 10%) results from persistent heart failure along with other comorbidities [227, 230–236]. One-year mortality in patients not bridged to AVR is 40% to 60%, very similar to the estimated mortality of symptomatic AS patients treated with medical management alone. Serious vascular complications rates were reported to be more than 20% in the past, but with recent improvements in closure devices and availability of smaller profile balloons, these rates are in 1% to 2% range [237–239]. Repeat valvuloplasties for recurrent symptoms in inoperable patients have been successfully accomplished with very similar risks and outcomes as the first BAV, but subsequent BAV procedures have less success. The recently reported PARTNER B trial suggested survival to 2 years was improved in medically treated patients who also underwent BAV for AV, although the merits of advocating BAV in patients not eligible for TAVR is debatable [81].

12. Transcatheter Aortic Valve Replacement

Transcatheter aortic valve replacement has been used worldwide in more than 40,000 cases to date at the time of writing, using balloon expandable and self-expanding valves. This extensive experience suggests similar procedural success. Introduction into the United States is relatively recent with the completion of the PARTNER trial using a balloon expandable valve and the FDA approval for nonoperative patients. The US Pivotal trial for a self-expanding valve is under way and was expected to complete enrollment in 2012. Guidelines can only be constructed for approved devices, thus limiting the committee despite extensive data from abroad. The guidelines for TAVR are thus constructed with this in mind and reflect what is currently allowed in the United States and may be incomplete outside this country. With the completion of current and future trials and potential FDA approvals, the committee may issue an addendum to these guidelines as appropriate.

12.1. TAVR With the Balloon-Expandable Valve—Recommendations[1]

CLASS I

1. Evaluation for TAVR should be performed by a multidisciplinary team and panel [81, 240]. (Level of evidence A)
2. TAVR should be performed by a multidisciplinary cardiovascular and cardiac surgery team [81, 240]. (Level of evidence A)
3. If available as part of a research protocol or after FDA approval, transfemoral AVR is recommended in inoperable patients provided they have an expected survival of greater than 1 year [81]. (Level of evidence A)
4. If available as part of a research protocol or after FDA approval, transfemoral, transaortic, transaxillary, or transapical AVR with the balloon expandable valve can be considered in patients who are operative candidates and have a predicted surgical mortality greater than 15% and an STS score greater than 10% by two independent surgical assessments [240]. (Level of evidence A)
5. TAVR should be performed in a hybrid operating or catheterization room dedicated to the procedure and not with mobile c-arms [81, 240]. (Level of evidence B)

[1]The self-expanding nitinol bioprosthesis is currently available in Europe and is under investigation in the US Pivotal trials, but US recommendations are not available.

CLASS III

1. Transfemoral aortic valve implantation with a balloon-expandable valve should not be performed in patients who are not at high risk for conventional surgery. (Level of evidence C)
2. Transfemoral aortic valve implantation with a balloon-expandable valve should not be performed in patients who have other comorbidities that limit 1-year survival or whose extreme frailty limits the likelihood of functional recovery after TAVR. (Level of evidence C)

QUALITY MEASURES

1. Patients being considered for TAVR should have surgical assessment by a multidisciplinary team including two independent surgeons to determine operative risk. Objective measures of risk such as the EuroSCORE and STS risk score should be used to document risk but should not be used independent of a surgical assessment.
2. Patients being considered for TAVR will need a thorough preoperative assessment including TTE, diagnostic catheterization, PFTs, and CT scan.
3. Asymptomatic mild or moderate CAD does not need to be treated before TAVR. Clinically significant CAD that would impact the safety of TAVR procedure should be revascularized before valve implantation.
4. Vascular access should be assessed by iliac and femoral angiography as well as CT angiography. In patients with renal insufficiency, vessel anatomy can be assessed by IVUS and noncontrast CT. All studies should be reviewed by the physicians responsible for potential vascular repair.
5. Intraprocedural TEE should be employed to assist with, TAVR planning, valve positioning, and valve assessment after deployment.
6. TAVR procedures should be performed by a cardiovascular medicine and cardiac surgery multidisciplinary team with extensive experience with high-risk valve surgery and percutaneous coronary interventions and balloon valvuloplasty.
7. Patients should be followed with annual TTE to assess valve function and monitor paravalvular AR.
8. Patients should continue on a regimen of clopidogrel for 3 to 6 months and aspirin indefinitely after TAVR. In patients with atrial fibrillation, aspirin and warfarin should be continued indefinitely if feasible.
9. All centers performing TAVR should report their results to a national database.
10. Procedure time, fluoroscopy time, transfusion requirements, use of cardiopulmonary bypass, number of valves placed, need for sternotomy or conversion to conventional surgery, vascular complications, and amount of contrast used should be measured for all cases.
11. Patients should be given routine antibiotic prophylaxis for all invasive procedures and routine dental work.

The notion of TAVR started gaining momentum in the early 1990s when Andersen and associates [241] demonstrated that a tissue valve mounted within a stent could be delivered into the aorta in a closed-chest animal model. The first successful human case of TAVR in a patient with AS was performed in 2002 by Cribier and colleagues [242]. This initial case was performed with the first version of a balloon expandable transcatheter equine pericardial valve through the antegrade transfemoral vein approach in a patient who was refused for operation. This approach, which required a transseptal catheterization, was technically challenging and associated with frequent complications [243]. Eventually the transseptal antegrade approach was abandoned in favor of the currently accepted retrograde transfemoral arterial approach.

Two major TAVR valves are in clinical trials in the United States, and these have been widely implanted outside the US. Two available versions of the balloon-expandable transcatheter valve are under investigation. The version initially studied in pivotal clinical trials in the United States consists of a trileaflet bovine pericardial valve that is hand sutured into a stainless steel, tubular, slotted, balloon expandable stent. There are 23-mm and 26-mm diameter valve sizes that can accommodate aortic annulus sizes between 18 mm and 25 mm, with a 29-mm valve available in some countries. At the time of the procedure, the sterile stent valve is crimped onto a standard balloon catheter. The device is advanced retrograde through a common femoral artery access site through either a 22F or 24F sheath depending on the valve size selected. Under fluoroscopic guidance, the valve is advanced, positioned, and deployed with balloon inflation within the diseased native aortic valve. Brief rapid right ventricular pacing is utilized during deployment to provide mechanical asystole, which minimizes valve motion and migration. This procedure is usually done under general anesthesia with the assistance of transesophageal echocardiography.

The newest version of the balloon-expandable transcatheter valve has a lower profile delivery system (18F and 19F) that allows the entire system to be used in smaller iliofemoral vessels.

The self-expanding nitinol valve has porcine pericardial leaflets. It is also delivered retrograde in the femoral artery with an 18F introduction system. Experience is also growing with delivering this valve in both a subclavian or transaortic approach. Two sizes are available in the United States for the pivotal trials, namely, a 26-mm labeled valve for annular sizes 20 mm to 23 mm and a 29-mm valve for annular sizes 24 mm to 27 mm. The US trial has an extreme risk arm for severe, symptomatic AS with a predicted risk of death or irreversible morbidity at 30 days exceeding 50%. The primary endpoint is all-cause death or stroke at 1 year. The high-risk arm is enrolling patients with a predicted risk of death of at least 15% with a primary endpoint of death at 1 year. Trial enrollment was expected to be completed in 2012. The version of the self-expanding stent being studied in the US Pivotal trial is a nitinol frame with a trileaflet porcine pericardial valve. This valve comes in sizes of 23 mm, 26 mm, 29 mm,

and 31 mm covering annular sizes from 18 mm to 29 mm. At the time of the procedure, the valve is crimped on the provided sterile delivery system and delivered retrograde by either the femoral, transaxillary, or direct aortic routes for the trial. A BAV is generally done under rapid ventricular pacing. The valve is then positioned under fluoroscopic and echocardiographic control and is deployed in a controlled fashion without the necessity of rapid ventricular pacing. The extreme risk arm of this US pivotal trial has been filled and the high-risk arm was expected to fill during 2012.

PROS At the implanting centers for the randomized trail, transfemoral AVR was performed with acceptable 30-day and midterm mortality in appropriately selected high risk or extreme surgical risk patients [81, 240, 244–247]. Recent studies have shown that more than 30% of patients with symptomatic AS do not undergo surgical AVR [248]. Many of these patients would now be candidates for TAVR. Hemodynamic results after TAVR have been excellent with valve areas comparable to those of surgically implanted aortic valves [81, 240, 246, 247]. To date, there has been no evidence of prosthetic valve restenosis in midterm follow-up. There is no need for long-term anticoagulation therapy with this valve, and valve-related thromboembolic events have been observed rarely. The procedure can often be performed percutaneously, including arterial access and closure. Self-expanding valves are also easy to insert and also have a lower profile and can be used in patients with more severe AR. At this time the balloon implantable valves have not been studied in patients with severe AR.

CONS The procedure remains challenging and should be limited to experienced operators owing to the frequent occurrence of periprocedural complications [81, 240, 246, 247]. The current generation devices require large sheaths, 22F and 24F for the balloon expandable valve and 18F for the self-expanding valve. That limits the ability to perform transfemoral aortic valve implantation in patients with peripheral vascular disease. It also results in vascular complications that are often problematic and may result in increased mortality. In addition, there is a risk of embolic events, especially cerebrovascular, related to traversing the aorta and aortic valve with the delivery catheter. Another concern with TAVR is paravalvular AR, which is generally mild, but in a small percentage of patients (7% to 10%) moderate or severe paravalvular AR has been reported. Other complications such as annular rupture and coronary occlusion or heart block are rare but unpredictable. If complications do occur or the currently available valve is malpositioned, the device is not retrievable or repositionable. The nitinol self-expanding valve has been associated with a higher incidence of heart block and the need for pacemakers in approximately 20% of patients [249].

To establish a universal standard for evaluating TAVR outcomes, the Valve Academic Research Consortium definitions were established (Table 4) to track outcomes.

RESULTS Over the last several years, there have been numerous trials published evaluating transfemoral AVR with both valve types. These studies have all been observational registries in high surgical risk patients deemed either inoperable or operable high-risk candidates for conventional AVR. Operative and 30-day mortality in these series ranged from 7.3% to 12%. Valve function was excellent in all cases, with minimal gradients across the valve and valve areas greater than 1.5 cm^2 [81, 240, 246–248, 250, 251].

Recent studies have reported improved procedural outcomes after TAVR. The European SAPIEN Aortic Bioprosthesis European Outcome (SOURCE) registry was initiated to collect outcomes after TAVR after commercial approval in Europe [252]. Procedural success in this series was reported at 95.1% with a 30-day mortality of 6.3%. Other procedural complications were similar to earlier series with 2.4% strokes and 10.6% major vascular complications. One-year survival after transfemoral AVR in this study was 81.1% [253]. Of the 32 centers in this study, 23 (72%) had never done a transfemoral valve implantation before the study. These data suggest that the device improvements as well as improved patient selection and procedural techniques will continue to result in improved acute results. Similar results have been repeated for the nitinol self-expanding valves.

Long-term results are limited in these early series. One-year mortality has been remarkably consistent between the different studies, varying between 18.9% and 26% [246, 247, 251, 253]. The majority of deaths were nonvalve related. In a series published by Webb and coworkers [247], the 1-year valve-related mortality was less than 5% and the all-cause mortality was 26%. There have been no reports of SVD in these studies at 1 year, and valve areas have remained more than 1.5 cm^2. Initial paravalvular AR has not changed significantly during 1-year follow-up. There have been no reported cases of valve migration or strut fractures of the support frame. Concern that paraaortic valve regurgitation may result in increased hemolysis or endocarditis has not been seen; however, continued heart failure related to regurgitation requires further evaluation.

The PARTNER B trial showed that TAVR reduces mortality in patients with AS who cannot have surgical AVR [81]. At 26 centers, 699 patients who had severe AS who were at high risk for operation were randomly assigned to either AVR or TAVR (transfemoral or transapical approach) using a balloon expandable bovine pericardial valve. The primary endpoint was death from any cause at 1 year and the primary hypothesis was that TAVR is noninferior to AVR.

The PARTNER trials are the only published randomized trial evaluating transcatheter AVR. Entry criteria included severe AS defined as less than 0.8 cm^2 area and mean valve gradient 40 mm Hg or more or peak velocity $\geq$4.0 m/s or greater. High-risk patients were required to have an STS score of 10% or higher and a surgeon assessment of the predicted 30-day mortality of 15% or greater. Inoperable patients had to have a combined risk of death or irreversible risk of serious morbidity more than 50%. Patients were assessed by a multidisciplinary team and panel, and the TAVR

procedure was performed by a multidisciplinary cardiac surgery and cardiovascular team. The primary endpoint was all-cause mortality at 1 year (noninferiority design in the high-risk surgical arm and superiority design in the inoperable study).

In the nonoperative arm of the trial, 30-day mortality after TAVR was 6.4% versus 2.8% in the medically treated patients ($p = 0.41$) [81]. Procedural complications were similar to earlier trials with a 5.0% major stroke, 16.2% major vascular complication, and 16.8% major bleeding event rates. Valve hemodynamics were excellent, with a mean valve area of 1.5 cm^2. Paravalvular leak remained a problem with 13% of patients having more than 2+ regurgitation after the procedure. One-year survival was dramatically improved with a 20% reduction in absolute mortality in patients treated with TAVR versus medical therapy, 30.7% versus 50.7% ($p < 0.0001$). There were also significant improvements in New York Heart Association (NYHA) functional class and 6-minute walk distances. There was a separate quality of life substudy that revealed dramatic improvements after TAVR compared with medical therapy that were sustained out to 1 year. The results from the nonoperative arm of the PARTNER trial demonstrated that TAVR is the standard of care for inoperable patients and should be offered to appropriate candidates [254].

In the high-risk operative arm of the PARTNER trial, 492 patients were randomized between transfemoral TAVR and surgery [240]. Thirty-day and 1-year mortality were not significantly different between transfemoral TAVR and surgery, 3.3% versus 6.2% at 30 days ($p = 0.13$) and 22.2% versus 26.4% at 1 year ($p = 0.29$). That met the prespecified criteria for noninferiority (difference −4.2%, 95% upper confidence limit 2.3%, predefine margin 7.5%; $p = 0.002$ for noninferiority). There was no significant difference in rates of major strokes after transfemoral TAVR compared with surgical AVR at 30 days (2.5% versus 1.4%, $p = 0.37$) or 1 year (3.5% versus 1.4%, $p = 0.15$). Including all strokes and transient ischemic attacks, events were more frequent after transfemoral TAVR than after AVR at 30 days (4.6% versus 1.4%, $p = 0.04$) and at 1 year (6.1% or 1.9% $p = 0.03$). Major vascular complications were more frequent after TAVR (14.2% versus 3.2%, $p < 0.01$), whereas major bleeding (10.9% versus 23.1%, $p < 0.01$) and new-onset atrial fibrillation (7.5% versus 18.6%, $p < 0.01$) were more frequent after AVR. Symptom improvement favored TAVR at 30 days but was similar after 1 year. Paravalvular regurgitation was more frequent after TAVR than AVR ($p < 0.001$). The trial concluded that for patients with severe AS who are at high risk for surgery, TAVR and AVR was associated similar survival after 1 year, although there were important differences in periprocedural hazards [240].

In addition to the above studies for native AS, there has been limited experience with TAVR for failed aortic and mitral bioprosthesis. The largest series includes 24 patients, of whom 10 underwent TAVR for a failed aortic bioprosthesis [168]. There were no deaths at 30 days among these patients. In the future, these procedures may be performed through the transfemoral approach with improvements in the device and procedural technique. However, candidates will be limited by the type and size of aortic bioprosthesis initially implanted, and patients with small surgical valves will not be candidates with the current generation devices.

13. Transarterial Aortic Valves: New Developments in Percutaneous Aortic Valves

13.1. New Valves and Delivery Systems

Currently available valves appear to offer the potential for relatively durable clinical benefit [247, 255]. Nevertheless, current valves have limitations, particularly in terms of deliverability, deployment, and annular sealing [256, 257]. Valves and valve delivery systems function synergistically, and changes in one component necessitate changes in the other.

Perhaps the greatest urgency is to reduce the risk of arterial injury through the development of lower profile delivery systems [256–259]. Approaches to further miniaturization include use of reengineered lower profile delivery catheters, more compressible frame designs constructed of newer alloys, thinner and more compressible leaflet materials, thinner walled sheaths or expandable sheath systems, and systems that remove the need to introduce an expanding balloon inside an expandable frame (self-expanding, non–balloon expandable, or sequential balloon introduction systems).

Newer systems will likely incorporate features to facilitate positioning (recapture, reposition, and redeploy), sealing [260–262], coronary access [263–266] and, if these are not optimal, retrieval. A number of valves are undergoing early clinical evaluation and many more are in development [267–270]. In seeking lower profiles, retrievability, and other enhancements it will be important not to sacrifice ease of insertion, frame strength, hemodynamic function, or durability [271], the latter of which will become increasingly important as the procedure is more widely applied and in younger patients [272, 273].

13.2. Stroke Prevention

The reported incidence of clinically diagnosed stroke in current high-risk registries ranges from 2% to 6.4% [246, 247]. The majority of strokes are likely embolic and are due to mobilization of atheromatous and calcific emboli from the ascending aorta and native valve. Manipulation within the native valves appears to be an important factor. Brain MRI and transcranial Doppler suggest that subclinical brain embolization occurs in the majority of patients, raising concerns about neurocognitive decline [274, 275].

Whether preprocedural echocardiographic or CT screening for arch atheroma is of value is unknown. Future delivery systems are likely to be lower profile and less traumatic. Whether there is a difference in risk of stroke according to valve type or access approached is unknown [252, 276]. A number of embolic control devices are under investigation such as deflection and filtering devices. Whether this will translate into clinical benefit is also unknown.

13.3. Procedural Imaging

High-quality fluoroscopic imaging is a prerequisite for TAVR. Portable fluoroscopic imaging systems are rarely adequate owing to the limitations of these systems in terms of image quality and review as well as flexibility and camera positioning. Prompt access to transthoracic and transesophageal echocardiographic imaging when needed to assess valve positioning and function, ventricular function and filling, and pericardial effusions is a necessity [277–280]. Three-dimensional TEE guidance during valve implantation maybe of value, but the necessity of this is controversial for some devices [279, 281, 282].

A number of advanced imaging systems are under development that utilize computerized real-time fluoroscopic guidance [278], in-laboratory three-dimensional angiographic reconstruction, CT coregistration [283], real-time magnetic resonance [284], or other modalities. Such systems are intended to assist in the evaluation of the aortic valvular complex and accurate positioning of the prosthesis. While promising, the role of these systems remains to be determined.

13.4. Hybrid Suites

Typically, TAVR is performed in either a hybrid cardiac catheterization laboratory or hybrid operating room setting. The requirement for high-quality fluoroscopic imaging and ready access to rarely used catheterization equipment may not be achieved in a standard operating room environment. Conversely, a standard cardiac catheterization laboratory may not offer optimal sterility or options for anesthetic or surgical support. The possibility of unexpected hemodynamic instability in patients with AS argues for ready access to temporary cardiopulmonary support. Consequently, the concept of a "hybrid" suite optimized for both endovascular and open surgical procedures is recommended. It seems likely that optimal outcomes will be achieved in this optimal environment.

13.5. Endovascular Access

Transvenous access to the aortic valve was problematic and has been abandoned in favor of transarterial access from the femoral artery. Early systems required surgical cutdown and open repair of the femoral artery. With increasing experience and a progressive reduction in catheter size, percutaneous closure is becoming increasingly reliable and will likely be routine [285].

The major limitation of arterial access remains the risk of vascular injury [271, 286]. Transapical access avoids the risk of arterial injury and provides ready access to the aortic valve [287]. It has been suggested the risk of aortic atheroembolism may be lower than retrograde approaches, although evidence for this is lacking. Limitations include the risk of apical injury, mitral injury, and thoracotomy. Percutaneous apical closure devices are under investigation but as yet untried.

Other access alternatives have included retroperitoneal access to the iliac artery and direct access to the aorta. The minimal invasive upper sternal J incision [102] and small right anterior thoracotomy with access to the ascending aorta has become popular in many centers [288–290]. Recently open transaxillary or subclavian arteries access has found greater favor [291–294]. Disadvantages include the need for a cutdown, risk to mammary arterial grafts, compression of the delivery catheter, and surgical repair should injury occur.

13.6. Valve-in-Valve

Implantation of transcatheter valves within dysfunctional or malpositioned transcatheter valves has been demonstrated to be feasible and potentially effective [261, 262, 271, 295, 296]. Similarly experience with transcatheter "valve-in-valve" implantation has been favorable in patients with failed surgical bioprostheses [168, 178, 262, 288, 296–301]. Although experience has been favorable it may be difficult if not impossible to evaluate all of the possible combinations of types and sizes of prosthetic valves. The implications for valvular function and durability are unknown.

13.7. TAVR in Lower Risk Patients

The FDA has made it clear that to use TAVR in lower risk patients, randomized trials are required. Two trials are planned and have obtained FDA approval to proceed. The two trials, PARTNER II A and SURTAVI have similar enrollment criteria, including STS score 4 or higher. The PARTNER trial will enroll 2,000 patients and SURTAVI, 1,860 patients.

14. Transapical Aortic Valve—Recommendations

Class I

1. Transapical insertion of a balloon expandable aortic valve is recommended in patients with symptomatic severe AS who are considered to be at excessive risk for conventional AVR and are not candidates for a transfemoral approach due to preexisting peripheral vasculature disease, and who have an expected survival of at least 1 year [240]. (Level of evidence B)
2. Evaluation for TAVR should be performed by a multidisciplinary team and panel [81, 240]. (Level of evidence A)
3. TAVR should be performed by a multidisciplinary cardiovascular and cardiac surgery team with extensive experience with high-risk valve surgery and percutaneous coronary interventions and balloon valvuloplasty [81, 240]. (Level of evidence A)
4. If available as part of a research protocol or after FDA approval, transfemoral, transaortic, transaxillary, or transapical AVR with the balloon expandable valve can be considered in patients who are operative candidates and have a predicted surgical mortality greater than 15% and an STS score greater than 10% by two independent surgical assessments [240]. (Level of evidence A)
5. TAVR should be performed in a hybrid operating or catheterization room dedicated to the procedure and not with mobile c-arms [81, 240]. (Level of evidence B)

Class IIa

1. Transapical insertion of a balloon expandable aortic valve may be a reasonable alternative in patients with critical AS who have an estimated mortality of at least 15% as independently judged by two cardiothoracic surgeons, or who have a predicted risk of mortality using the STS-PROM algorithm of 10% or greater, and do not have access for the transfemoral approach. The PARTNER A trial was not powered to access noninferiority. (Level of evidence C)

Class III

1. Transapical insertion of a balloon expandable aortic valve is not recommended for low-risk patients with critical AS who are considered good candidates for conventional valve replacement. (Level of evidence C)

Quality Measures

1. All patients referred for transapical TAVR, should be evaluated by multidisciplinary team and two cardiothoracic surgeons to determine suitability for conventional valve surgery.
2. All patients being considered for transapical TAVR should have a preoperative left heart catheterization, TTE, PFTs, and a CT scan of the chest, abdomen, and pelvis through the femoral heads.
3. Intraoperative TEE should be used in addition to fluoroscopy to adequately position the valve for deployment.
4. Procedure time, fluoroscopy time, transfusion requirements, use of cardiopulmonary bypass, number of valves placed, need for sternotomy or conversion to conventional surgery, vascular complications, and amount of contrast used should be measured for all cases.
5. Patients should be placed on double antiplatelet agents for at least 3 to 6 months unless contraindicated, and aspirin indefinitely after the procedure.
6. All patients should have a yearly TTE and physical examination.
7. Patients should be given routine antibiotic prophylaxis for all invasive procedures and routine dental work.
8. Patients should be enrolled in a national registry database.

Early investigation into using the LV apex as an access site for catheter based implantation of a balloon expandable aortic valve was initially performed as a collaborative effort between both surgeons and cardiologists [86, 302]. Building upon this preliminary research, the first successful transapical implantation was performed at St Paul's Hospital in Vancouver, British Columbia, Canada, in 2005 [303].

Transapical valve implantation is performed through an anterior thoracotomy, usually entering the fifth or sixth intercostal space or resecting a short piece of rib to reach the LV apex. The optimal insertion site for the delivery sheath is in the muscular portion of the apex, which is slightly cephalad and lateral to the true apex of the heart. Tapping the apex of the left ventricle while watching the TEE helps confirm the correct entry site. Hemostatic control of the insertion site is obtained using either purse-string or opposing U-type sutures, with as many as three sutures. The valve comes in two sizes, 23 mm and 26 mm, both of which are delivered through a 26F sheath. A balloon valvuloplasty is performed to create space for blood to flow around the prosthesis as it is positioned in the annulus. Optimal positioning is achieved using fluoroscopy and TEE such that native annulus hinge points bisect the midposition of the prosthesis. Rapid ventricular pacing is performed to reduce cardiac output during valve deployment to reduce the risk of prosthesis embolization. More recently, many centers deploy the valve slowly so that fine adjustments can be performed during deployment for optimal positioning. Sheath removal and closure of the LV apex is performed on a depressurized heart in many centers by rapidly pacing the heart ventricle to reduce the patient's systolic blood pressure.

Compared with the transfemoral approach, for most centers the transapical technique is generally faster, uses less contrast, and requires shorter fluoroscopy times. Additionally, control of valve placement is enhanced with the transapical approach owing to the stiffness of the delivery catheter and the short working distance between the apical insertion site and the aortic annulus. The PARTNER trial results containing the outcomes of a high-risk group of patients having transapical aortic valve implantation are published [240].

Pros

Transapical valve implantation can be performed closed chest, beating heart, and without the use of cardiopulmonary bypass, even in nonoperable or prohibitive-risk patients. This approach is particularly efficacious for patients who have had previous bypass grafting or cardiac surgery as it obviates the risk of cardiac or inadvertent graft injury due to repeat sternotomy. Compared with transfemoral TAVR, sheath size for valve delivery is not a limiting factor in patient selection for the transapical approach. This flexibility in sheath size also enables modifications to be made to the structure of the valve to reduce the propensity for paravalvular leak, additions that would be challenging with peripherally implanted devices due to an emphasis on profile size. Some data suggest the risk of stroke is lower with the transapical approach.

Transapical valve implantation can be successfully performed in patients with occlusive peripheral vascular disease and in patients with diminutive or tortuous peripheral vessels. Additionally, anatomic factors such as true porcelain aorta, which would be a contraindication to conventional AVR, are amenable to a transapical approach. The hemodynamic performance of the valves has been excellent, with low gradients and impressive orifice areas, even in patients with small aortic annuli [304, 305].

As with the transfemoral approach, the transapical approach has also been utilized as the access site of

choice for the implantation of a transcatheter valve into a degenerated bioprosthetic valve [306]. The ability to avoid a redo valve replacement with its attendant morbidity and mortality is a significant benefit of transcatheter technology. Although feasible through a transfemoral approach, the LV apex is a good access site for catheter based mitral valve replacement as it precludes the need for a transseptal approach, thus simplifying the procedure. Current research is focused on developing technology to enable a port access transapical procedure to be performed.

Cons

There remains a significant learning curve to achieve mastery of the transapical procedure. Procedural steps to be mastered include exposure and control of the LV apex, valve positioning and deployment, and control of the choreography of the procedure. Significant complications, including catastrophic LV apical bleeding, were noted in several early reports. Other complications noted with the transapical procedure as with the transfemoral approach include embolization of the valve, either distally into the aorta or proximally into the left ventricle, coronary obstruction, and aortic root rupture. Appropriate patient selection is critical to ensuring optimal outcomes with the transapical procedure, particularly in regard to the recognition of unfavorable procedural anatomy.

Paravalvular leak remains a consistent finding in the majority of patients undergoing both transapical and transfemoral aortic valve implantation. Although hemolysis and endocarditis have not been significantly associated with this finding, the long-term implications for the energy loss associated with paravalvular leak are unknown [307]. Valve durability also remains unknown, particularly in regard to the effect that crimping of the valve onto the delivery balloon has on leaflet structure and longevity. To date, the failure mode of the valve also remains unknown although root thrombus restricting leaflet motion has been noted.

Contraindications for the transapical procedure include calcification of the pericardium or LV apex, patch repair of the apex secondary to an aneurysmectomy, LV apex thrombus, or severe respiratory insufficiency that would be exacerbated by a thoracotomy. Additionally, certain anatomic abnormalities that preclude accessing the LV apex, such as extreme rotation of the heart or previous pneumonectomy resulting in dislocation of the heart into either the right or left chest, rule out a transapical approach.

Results

The majority of the early results reported on the transapical procedure were observational in nature, describing either feasibility outcomes or early multiple-center experiences. Svensson and colleagues [302] reporting the first 40 transapical aortic valve implantations performed in the United States in an extremely high risk population with patients having an STS-PROM score more than 15% or inoperability described a procedural success rate of 87.5% and a 30-day survival of 82.5%. The European multiple-center feasibility study, the TRAVERCE ((Trans-Apical Surgical Delivery of the Cribier-Edwards Aortic Bioprothesis Clinical Feasibility) trial, reported a larger cohort of 168 patients, showing a procedural success rate of 95.8% and 30-day survival of 85% [308]. These studies were performed early in the investigators TAVR experience using first-generation technology that included a 33F delivery sheath in many patients.

Improved survival was demonstrated as center experience increased. Rodes-Cabau and colleagues [246] reported the results of the Canadian Multicenter experience looking at outcomes in 168 transfemoral patients and 177 transapical patients. Overall procedural success was 93.3%, with a 30-day mortality of 9.5% for the transfemoral patients compared with 11.3% for the transapical group. There were no differences between the transapical or transfemoral patients in regard to 12- and 24-month survival.

Recently transapical outcomes have also been compared with a propensity-matched cohort of patients having conventional AVR surgery. Walther and associates [309] demonstrated 30-day, 6-month, and 1-year survival of 90%, 75%, and 74%, respectively, for the transapical group compared with 85%, 70%, and 69%, respectively ($p = 0.547$), in the conventional surgery patients. Valve function was excellent in the transapical group with low mean gradients and velocities across the prostheses over time.

The largest study reporting outcomes with transapical valve implantation is the European SOURCE registry, a 32-center registry designed to collect data during the first year of commercial activity after approval in Europe [252]; 575 transapical aortic valve implantations were included in the registry. Procedural success in the transapical group was 92.7%, with a 30-day mortality of 10.3%. Other procedural complications such as stroke and vascular access complications were low at 2.6% and 2.4% respectively. Of note, the majority of the centers had no transcatheter experience before beginning the registry.

The transapical technique has also been used to perform valve-in-valve implantations for failed bioprosthetic valves. These valves have been transapically inserted into degenerated bioprosthetic valves in the aortic, tricuspid, pulmonary, and mitral position. A recent large series of 24 patients reported by Webb and associates [168] demonstrated a 30-day mortality of 4.2% and no more than mild regurgitation after implantation.

The PARTNER trial data reported transapical outcomes in a high-risk cohort of patients compared with conventional surgery. The data showed the transapical arm of the PARTNER A patients had more cerebrovascular disease, had more CABG or PCI, more peripheral vascular disease, atrial fibrillation, more severe AS (as risk factor for stroke), more liver disease, and porcelain aorta. In comparing the as-treated data, the transapical TAVR mortality was 8.7% and AVR 7.6% ($p = 0.29$) and stroke/transient ischemic attack for transapical TAVR 7.9% and AVR 5.5% ($p = 0.5$). Of note, as-treated stroke/transient ischemic attack in the transfemoral TAVR was 4.6% versus 1.4% for AVR ($p = 0.04$). The trial was not powered sufficiently to determine if the transapical approach data were noninferior to open AVR [240].

Many centers are using transaortic, transsubclavian, or other alternative approaches for TAVR. These have not been studied in prospective studies but case series show promise.

15. Transaortic Valve Replacement—Recommendations

Class I

1. Evaluation for TAVR should be performed by a multidisciplinary team and panel [81, 240]. (Level of evidence A)
2. TAVR should be performed by a multidisciplinary cardiovascular and cardiac surgery team [81, 240]. (Level of evidence A)
3. If available as part of a research protocol or after FDA approval, transfemoral, transaortic, transaxillary, or transapical AVR with the balloon expandable valve can be considered in patients who are operative candidates and have a predicted surgical mortality greater than 15% and an STS score greater than 10% by two independent surgical assessments [240]. (Level of evidence A)
4. TAVR should be performed in a hybrid operating or catheterization room dedicated to the procedure and not with mobile c-arms [81, 240]. (Level of evidence B)

Class IIa

1. Direct aortic insertion of a self-expanding or balloon expandable aortic valve may be a reasonable alternative in patients with critical aortic stenosis who are contraindicated for conventional aortic valve replacement and are not candidates for a transfemoral approach due to preexisting peripheral vasculature disease, and who have an expected survival of at least 1 year. (Level of evidence B)
2. Direct aortic insertion of a self-expanding or balloon expandable aortic valve may be a reasonable alternative in patients with critical aortic stenosis who have an estimated mortality of at least 15% as independently judged by two cardiothoracic surgeons or who have a predicted risk of mortality using the STS-PROM algorithm of 10% or greater and do not have access for the transfemoral approach. (Level of evidence C)

Class III

1. Direct aortic insertion of a self-expanding or balloon expandable aortic valve is not recommended in low-risk patients with critical aortic stenosis who are considered good candidates for conventional valve replacement. (Level of evidence C)

Quality Measures

1. All patients referred for direct aortic TAVR, should be evaluated by multidisciplinary team and two cardiothoracic surgeons to determine suitability for conventional valve surgery.
2. All patients being considered for direct aortic TAVR should have a preoperative left-side heart catheterization, transthoracic echocardiogram, PFTs, and a CT scan of the chest, abdomen, and pelvis through the femoral heads.
3. Intraoperative TEE should be used in addition to fluoroscopy to adequately position the valve for deployment.
4. Procedure time, fluoroscopy time, transfusion requirements, use of cardiopulmonary bypass, number of valves placed, need for sternotomy or conversion to conventional surgery, vascular complications, and amount of contrast used should be measured for all cases.
5. Patients should be placed on a regimen of double antiplatelet agents for at least 6 months unless contraindicated and aspirin indefinitely after the procedure.
6. All patients should have a yearly transthoracic echocardiogram and physical examination.
7. Patients should be given routine antibiotic prophylaxis for all invasive procedures and routine dental work.

Early investigation into using the ascending thoracic aorta as an access site for catheter-based implantation of a balloon expandable aortic valve was initially performed as a collaborative effort between both surgeons and cardiologists.

Direct aortic valve implantation is performed through a small right anterior thoracotomy or an upper right "J" hemisternotomy through the second or third interspace [102]. Both provide good access to the ascending aorta for sheath insertion and allow ascending aortic cannulation in a fashion familiar to all cardiac surgeons. Both self-expanding and balloon expandable valves may be placed using this approach. Careful planning is important in choosing a direct aortic approach. If a line is drawn on the chest CT from the sternum to the spine and the ascending aorta is to the left of this line, a right thoracotomy approach may be difficult and better exposure obtained through ministernotomy. If there is a patent LIMA graft, a right thoracotomy generally allows aortic access away from the position of the LIMA. Hemostatic control of the insertion site is obtained using two concentric pledgeted pursestrings. This approach is amenable to both the currently widely used valves and allows access to all sheath sizes required. A balloon valvuloplasty is performed to create space for blood to flow around the prosthesis as it is positioned in the annulus. Optimal positioning is achieved using fluoroscopy and TEE so that native annulus hinge points bisect the midposition of the prosthesis. Valve deployment is done in the standard fashion according to the valve type chosen. Sheath removal and closure of the ascending aorta is familiar to cardiac surgeons and done in a standard fashion.

Compared with the transfemoral approach, many centers find the direct aortic access technique is often

faster, uses less contrast, and requires shorter fluoroscopy times. Additionally, control of valve placement is enhanced with the direct aortic approach owing to the short working distance between the aortic insertion site and the aortic annulus allowing more precise control and less stored energy in the delivery system. Direct aortic access is part of the CoreValve US Pivotal trial, which was expected to reach completion in 2012.

Pros

Direct aortic valve implantation can be performed closed chest, beating heart, and without the use of cardiopulmonary bypass, even in nonoperable or prohibitive-risk patients. This approach is particularly efficacious using the right thoracotomy approach for patients who have had previous bypass grafting or cardiac surgery as it obviates the risk of cardiac or inadvertent graft injury due to repeat sternotomy. Compared with transfemoral aortic valve implantation, sheath size for valve delivery is not a limiting factor in patient selection for the direct approach. This flexibility in sheath size also enables modifications to be to future valves and may allow port access with the thoracotomy approach in the future. Unlike transapical, both the current balloon expandable and self-expanding valves can be deployed using this access. Unlike transapical, all cardiac surgeons have extensive experience placing large bore cannulae into the ascending aorta. Valve positioning and deployment have been found, as is the case with transapical also, to be simpler and more precise owing to the closeness to the deployment site and lack of stored energy of the direct route to the aortic valve. Additionally, in the event of a catastrophic local insertion site complication, graft replacement of the ascending aorta in an appropriate patient is a familiar procedure to cardiac surgeons. A filtering umbrella can be inserted at the time of the procedure. The approach can also be used to quickly convert patients to full cardiopulmonary bypass if needed.

Cons

Complications can occur including rare catastrophic ascending aortic bleeding, which mimics the potential seen in any aortic cannulation for standard CPB. Appropriate patient selection is critical to ensuring optimal outcomes with the direct aortic procedure, particularly in regard to the recognition of unfavorable procedural anatomy for reoperations and calcified aortas.

Contraindications for the direct aortic procedure include atheroma or calcification of the ascending aorta that the surgeon believes precludes placement and safe closure of the aorta. Additionally, certain factors may preclude a direct aortic approach such as anatomic displacement of the aorta (pneumonectomy).

Results

The direct aortic approach to TAVR was not included in the PARTNER trial but there is a growing experience.

16. Transaxillary or Subclavian Valve Approach—Recommendations

Class I

1. Evaluation for TAVR should be performed by a multidisciplinary team and panel [81, 240]. (Level of evidence A)
2. TAVR should be performed by a multidisciplinary cardiovascular and cardiac surgery team [81, 240]. (Level of evidence A)
3. If available as part of a research protocol or after FDA approval, transfemoral, transaortic, transaxillary, or transapical AVR with the balloon expandable valve can be considered for patients who are operative candidates and have a predicted surgical mortality greater than 15% and an STS score greater than 10% by two independent surgical assessments [240]. (Level of evidence A)
4. TAVR should be performed in a hybrid operating or catheterization room dedicated to the procedure and not with mobile c-arms [81, 240]. (Level of evidence B)

Class IIa

1. Transaxillary or subclavian insertion of a self-expanding or balloon expandable aortic valve may be a reasonable alternative in patients with critical aortic stenosis who are contraindicated for conventional aortic valve replacement and are not candidates for a transfemoral approach because of preexisting peripheral vasculature disease, and who have an expected survival of at least 1 year. (Level of evidence B)
2. Transaxillary or subclavian insertion of a self-expanding or balloon expandable aortic valve may be a reasonable alternative in patients with critical aortic stenosis who have an estimated mortality of at least 15% as independently judged by two cardiothoracic surgeons, or who have a predicted risk of mortality using the STS-PROM algorithm of 10% or greater and do not have access for the transfemoral approach. (Level of evidence C)

Class III

1. Transaxillary or subclavian insertion of a self-expanding or balloon expandable aortic valve is not recommended for low-risk patients with critical aortic stenosis who are considered good candidates for conventional valve replacement. (Level of evidence C)

Quality Measures

1. All patients referred for transaxillary or subclavian TAVR should be evaluated by multidisciplinary team and two cardiothoracic surgeons to determine suitability for conventional valve surgery.
2. All patients being considered for transaxillary or subclavian TAVR should have a preoperative left-side heart catheterization, transthoracic echocardiogram,

PFTs, and a CT scan of the chest, abdomen, and pelvis through the femoral heads.
3. Intraoperative transesophageal echocardiography should be used in addition to fluoroscopy to adequately position the valve for deployment.
4. Procedure time, fluoroscopy time, transfusion requirements, use of cardiopulmonary bypass, number of valves placed, need for sternotomy or conversion to conventional surgery, vascular complications, and amount of contrast used should be measured for all cases.
5. Patients should be placed on a regimen of double antiplatelet agents for at least 6 months unless contraindicated and aspirin indefinitely after the procedure.
6. All patients should have a yearly TTE and physical examination.
7. Patients should be given routine antibiotic prophylaxis for all invasive procedures and routine dental work.

The axillary artery is exposed in the deltopectoral groove. Many cardiac surgeons are familiar with this approach for axillary cannulation. The sheath may be inserted through a graft sutured to the artery or directly inserted by the Seldinger technique. The subclavian artery can be used in the supraclavicular approach but this is less common. The carotid arteries or innominate artery have also been used for access.

Pros

Transaxillary or subclavian TAVR access, like transfemoral, does not require the opening of a major body cavity and can be done under local anesthesia as necessary. The catheter insertion site is closer to the deployment site than transfemoral, generally leading to easier and more accurate deployment.

Cons

Use of transaxillary or subclavian access on the right side requires an annular angle from horizontal of 30 degrees or less, and the left is similar to transfemoral, requiring an angle from horizontal of 70 degrees or less. Use on the left can be complicated by dependency on a patent left internal thoracic artery bypass.

17. Aortic Valve Leaflet Remodeling, Reimplantation, and Repair

The reason for trying to preserve the aortic valve or repair regurgitant valves in patients with root dilation or bicuspid valves is because these are usually young patients, and mechanical valve insertion means a lifetime of anticoagulation therapy and no possibility of implantation of a percutaneous valve at a later stage. The other alternative of a biological valve is associated with reduced durability at a younger age. The root- and valve-preserving alternatives are remodeling, reimplantation, bicuspid valve repair, or sinotubular junction tailoring [1, 14, 20, 69, 72, 99, 310–335]. More recent data show that late survival and risk of reoperation is lower for both bicuspid and tricuspid valve repairs when compared with biological AVR in younger patents [336] (Figs 23 to 27). Survival is equivalent to age- and gender-matched population.

17.1. Remodeling—Recommendations

CLASS I

1. Aortic valve repairs should be checked by intraoperative TEE after the repairs is completed. (Level of evidence C)
2. Patients should be followed postoperatively by yearly echocardiograms after aortic valve repair. (Level of evidence C)

CLASS IIA

1. Root remodeling may be considered for patients with significantly dilated roots and bicuspid valves or patients with acute aortic dissection, including excision of the non coronary sinus as a remodeling procedure, also known as the Wolfe procedure. (Level of evidence C)

CLASS III

1. Root remodeling should be avoided in patients with connective tissue disorders. (Level of evidence C)

QUALITY MEASURES

1. Perioperative gram-positive and gram-negative antibiotic coverage should be used.
2. Intraoperative transesophageal echocardiography should be performed.
3. Postoperative beta-blockers should be used.

PROS Aortic valve repair is a relatively straightforward procedure when performed by expert aortic valve surgeons with good initial results and a not-excessive cross-clamp time. Most surgeons are comfortable doing coronary artery reattachments, using either free buttons or the inclusion technique. The aortic annulus and commissures are less likely to be distorted. Remodeling works well for patients who have bicuspid valves and root dilation.

CONS The repair of the valve, particularly with leaflet prolapse, is less predictable. Leakage due to a dilated annulus requires an outside banding or subannular

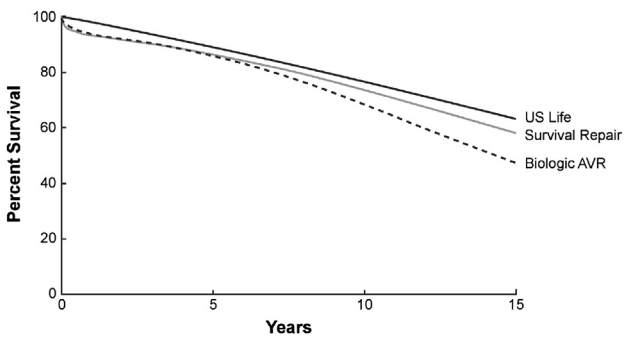

Fig 23. Survival for aortic valve repair, matched age and sex US life population, and matched biological aortic valve replacement (AVR).

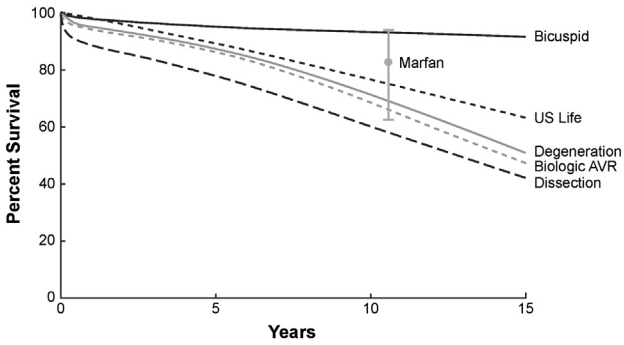

Fig 24. Survival by bicuspid valve or Marfan syndrome aortic valve repair, US matched patients, degenerative root aneurysm/valve repairs of the aorta by tailoring, biological aortic valve replacement (AVR), and aortic dissection with valve repair.

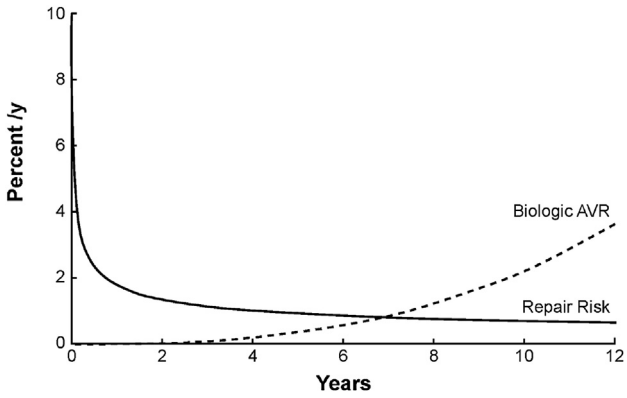

Fig 26. Hazard curves showing increasing risk of biological aortic valve replacement (AVR) failure after approximately 7 years but declining risk with repair.

encircling suture that pleats the annulus down to a normal size. Long-term results show a higher risk of reoperation and valve replacement than the reimplantation operation, particularly for patients with connective tissue disorders such as Marfan syndrome.

RESULTS A less than 1% 30-day mortality rate for elective repairs is to be expected, particularly for prophylactic operations [323, 324, 327]. Long-term durability and freedom from reoperation has varied at 10 years [1, 72, 310, 312–316, 318, 320, 323, 324, 327, 337].

17.2. Reimplantation—Recommendations

CLASS I

1. Root size, particularly at the sinuses of Valsalva should be measured by CT or MRI using the external diameter at its greatest extent. Conventionally TEE is used to measure the internal diameter at its greatest extent, usually from sinus to sinus [1]. (Level of evidence B)
2. Intraoperative TEE is recommended to check the repair. (Level of evidence C)
3. Reimplantation is recommended for young patients, when feasible, who have aortic root dilation, with or without regurgitation, and a tricuspid aortic valve. (Level of evidence C)
4. An aortic root greater than 5.0 cm is recommended as a threshold for prophylactic repair for most patients, including patients with Marfan syndrome. (Level of evidence C)
5. In patient with a family history of aortic dissection and Marfan syndrome, surgery is recommended at a size of 4.5 cm in cross-sectional diameter. (Level of evidence C)
6. Gram-positive and gram-negative prophylactic antibiotics should be administered at the time of surgery. (Level of evidence C)
7. The patient should have yearly echocardiograms. (Level of evidence C)
8. Prophylactic antibiotics for any invasive procedure including dentistry are recommended. (Level of evidence C)

CLASS IIA

1. For patients with Loeys-Dietz syndrome, a threshold of 4.2 cm maybe considered for surgery. (Level of evidence C)
2. The cross-sectional area of the root in square centimeters divided by the patient's height in meters and exceeding 10 may be considered an indication for surgery. (Level of evidence C)

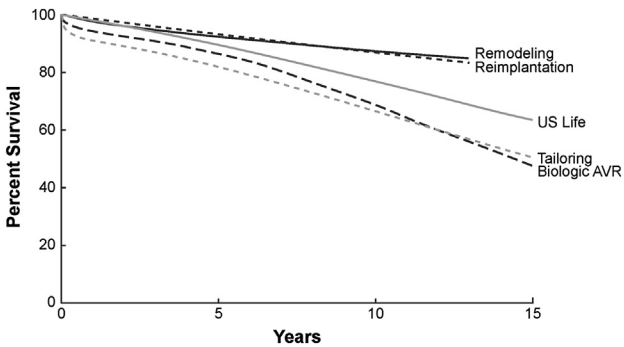

Fig 25. Survival by remodeling, reimplantation, US life, biologic aortic valve replacement (AVR), and tailoring.

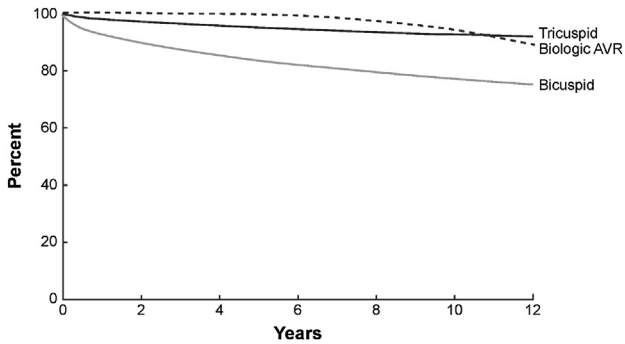

Fig 27. Risk of reoperation by biological aortic valve replacement (AVR), tricuspid valve repair, mostly by modified David reimplantation, and for bicuspid valves.

3. In female patients with a connective tissue disorder who are considering pregnancy, a prophylactic repair may be considered when the aortic root exceeds 4.0 cm. (Level of evidence C)
4. An antiplatelet agent should be considered postoperatively. (Level of evidence C)

NATIONAL QUALITY FORUM MEASURES

1. Prophylactic gram-positive and gram-negative coverage should be used at the time of surgery.
2. Intraoperative echocardiography.
3. Postoperative aspirin or clopidogrel should be administered.
4. Discharge should be on beta-blockers.
5. ACE inhibitor therapy should be considered in patients with low EF postoperatively.

PROS The operation is proven to have good to excellent midterm durability. The late risk of stroke or thromboembolism appears to be low. Correction of AR, either because of malposition of the leaflets or because of annular dilation because of leaflet prolapse, can be corrected without affecting durability. Results have been excellent for tri-leaflet valves, including patients with connective tissue disorders such as Marfan syndrome, Loeys-Dietz syndrome, and Ehlers-Danlos syndrome but less so for patients with bicuspid aortic valves [313, 316, 320, 323, 336].

CONS The operation is technically more demanding and requires judgment based on experience and regularly doing the procedure. The procedure is also associated with the risk of producing fistulas, including perforation of the base of the anterior leaflet of the mitral valve, the right ventricular outflow tract, or ventricular septal defects. Recovery from an intraoperative failure or late failure usually requires an extensive operation and likely insertion of a homograft. Early transient ischemic attacks or amaurosis fugax, probably related to the extensive raw surface area, is a possibility but with the use of clopidogrel this appears to be reduced. Endocarditis can still occur on late follow-up after reimplantation. Several techniques and modifications have been described and which is the ideal one is somewhat uncertain.

RESULTS Less than a 1% mortality rate for elective reimplantation is required to justify the operation as a prophylactic operation. Midterm results better than 95% freedom from reoperation at 10 years have been reported [1, 14, 310, 313, 315-317, 321, 324, 325, 327, 328, 330].

17.3. Bicuspid Valve Repair With or Without Aortic Tube Graft Replacement—Recommendations

CLASS I

1. All patients undergoing bicuspid repair should undergo intraoperative TEE. (Level of evidence C)
2. Prophylactic antibiotics including both gram-positive and gram-negative coverage should be used for patients undergoing bicuspid valve repair. (Level of evidence C)
3. Postoperative beta-blockers should be considered after bicuspid valve repairs. (Level of evidence C)
4. ACE inhibitor therapy should be considered in patients with low EF postoperatively. (Level of evidence C)
5. Patients should be given prophylactic antibiotics at any time that an invasive procedure is done, including dental procedures, after a bicuspid valve repair. (Level of evidence C)

QUALITY MEASURES

1. Prophylactic antibiotics for both gram-negative and gram-positive coverage for the operative procedure.
2. Intraoperative echocardiography.
3. Postoperative beta-blockers and calcium-channel blockers.
4. Patients should be given prophylactic antibiotics any time an invasive procedure is done, including dental procedures.

PROS Repair of a bicuspid valve in young patients may result in good long-term results if in the first 1 or 2 years failure does not occur. The incidences of bleeding, stroke, thromboembolic events, and infection are probably lower than with mechanical valve replacements [312, 336]. Patients do not need to be on warfarin therapy after surgery.

CONS In most patients several steps may be required to successfully repair the leaflets, including Cabrol sutures at the commissures, leaflet plication with a Trussler stitch, and figure-of-eight commissure apical sutures. That requires experience and judgment to result in a successful procedure.

RESULTS An elective surgical mortality rate with or without replacement of the ascending aorta should be less than 1% mortality. Long-term durability is better than 80% out to 10 years, with most failures occurring the first 2 years after repair [1, 14, 69, 72, 310, 312, 315–318, 320, 321, 323–325, 327, 338].

17.4. Tailoring of Sinotubular Junction

In older or high-risk patients with mild to moderate AR due to dilation of the of the sinotubular junction, tailoring down the sinotubular junction to a normal size, approximately 22 mm to 24 mm, depending on the patient's size, may result in good long-term durability [1, 14, 314, 327, 334].

18. Management of Acute Aortic Root and Ascending Aortic Dissection—Recommendations

Class I

1. Timely diagnosis is recommended utilizing cross-sectional imaging techniques or TEE. The latter can be performed in the operating room before sternotomy if needed to confirm the diagnosis [1]. (Level of evidence B)
2. Ascending aortic replacement (including resection of primary aortic tear) should be performed for patients with acute type A aortic dissection [1]. (Level of evidence B)
3. An open distal anastomotic, hemiarch or total arch replacement technique is effective for the distal

reconstruction of an acute type A dissection [1]. (Level of evidence B)
4. Ascending aortic and aortic arch replacement is indicated for patients with acute type A aortic dissection and a primary or secondary tear within the arch that involves or extends beyond the left common carotid arterial ostium with marked dilation of the aortic arch (>50 mm). (Level of evidence C)
5. Aortic root replacement is indicated for patients with acute type A aortic dissection and a primary tear that extends or originates in the left or right coronary sinuses or marked dilation (>45 mm) of the aortic root below the sinotubular junction. (Level of evidence C)
6. Arterial inflow cannulation for cardiopulmonary bypass during type A dissection repair should perfuse the true lumen directly. (Level of evidence C)
7. Long-term radiologic surveillance after aortic dissection with or without surgical reconstruction should be performed at regular intervals of at least every 6 months for the first year and then annually. (Level of evidence C)
8. Long-term annual echocardiographic surveillance is recommended for patients in whom an aortic valve-preserving reconstruction or bioprosthetic valve replacement was performed. (Level of evidence C)

Class IIa

1. It is reasonable to use ABP or RBP with HCA to complete aortic arch reconstructions to reduce neurologic complications [1]. (Level of evidence B)
2. It is reasonable to utilize either an aortic valve-sparing or valve-replacement strategy when managing acute type A dissection if an acceptably low mortality rate can be achieved [1]. (Level of evidence B)
3. It is reasonable to treat acute type A IMH with urgent surgical intervention [1]. (Level of evidence B)
4. Use of intraoperative TEE is encouraged [1]. (Level of evidence B)
5. Postoperative, lifelong cross-sectional radiologic surveillance is reasonable in patients with residual aortic dissecting beyond the replaced aortic segment. (Level of evidence C)

Class IIb

1. Medical management and longitudinal surveillance may be considered to treat high-risk patients with asymptomatic, radiologically stable type A IMH. (Level of evidence C)
2. Medical management and longitudinal surveillance may be considered in patients with type B dissections involving the aortic arch. (Level of evidence C)
3. Annual echocardiography may be considered in type A aortic dissection patients in whom the aortic valve was resuspended, preserved or replaced with a bioprosthesis. (Level of evidence C)

Quality Measures

1. Prophylactic perioperative antibiotics should be given for 24 to 48 hours at the surgeons discretion.
2. Patients should be discharged on beta-blocker therapy.
3. Patients with concomitant CAD should be discharged on oral antiplatelet therapy.
4. Patients with concomitant CAD should be discharged on drug therapy for lowering low-density lipoprotein cholesterol.
5. ACE inhibitor therapy should be considered in patients with low EF postoperatively.

The diagnosis and initial management of aortic dissection patients was extensively reviewed in the 2010 guideline for the management of patients with thoracic aortic disease produced by ACCF/AHA, AATS, and STS [1]. The surgical treatment and guidelines from that document are referred to in this manuscript.

The dismal prognosis (60% 1-year mortality) of medically managed acute type A aortic dissection was demonstrated in 1991 [339]. Even before that time it was apparent that acute surgical intervention through replacement of the ascending aorta dramatically reduced the acute mortality of type A dissection so that centers of excellence now have hospital and 1-year mortality rates of 5% to 26% (Table 5) [340–351]. Consequently, patients who present with acute type A aortic dissection should undergo immediate ascending aortic replacement except perhaps in cases of markedly advanced age or comorbid status or those presenting with devastating neurologic injury or bowel gangrene [352]. With respect to age, it is clear that outcomes are considerably worse in the elderly; nevertheless, appropriately selected patients, even into their ninth decade, can have a reasonable survival with surgery [353–357]. Equally, the presentation of acute devastating stroke was in years past a recognized marker of very poor outcome [349, 358]. However, in recent years evidence has been accumulating that suggests that some patients who present with significant stroke, even coma and acute type A aortic dissection, can have a reasonable chance of survival with acute surgical intervention [345, 352, 359–361].

Acute type A IMH, a variant of aortic dissection, can give rise to the same devastating complications as those arising from acute type A aortic dissection [331]. Data from the International Registry of Acute Aortic Dissection database and others demonstrate that IMH, while appearing to carry a better general prognosis than overt dissection, still carries a significantly better chance of long-term survival with ascending aortic replacement compared with medical management [362-368]. However, given the more indolent course of many type A IMH patients, delayed surgical intervention in high-risk patients, and in selected cases medical management, may be reasonable for clinically and radiologically stable patients [362, 369].

The diagnosis of acute type A aortic dissection or IMH is best achieved by CT angiography, magnetic resonance angiography, or TEE. Magnetic resonance angiography may be less practical in the setting of an acute chest or back pain syndrome and should not delay

Table 5. Results of Aortic Dissection Surgery

Study	Years	No. Pts.	Clamped Distal	Open Distal/ Hemiarch	Total Arch	HCA Alone	HCA RCP	HCA ACP	Valve Resusp.	Root Replace.	VSRR	AVR + Supracor	Mortality
Sun et al, 2009	2003–07	107			100%			100%	78.5%	19.6%		1.9%	4.7%
Stevens et al, 2009	1979–03	195	13%	84%	3%	46%	12%	29%	60%	24%		5%	13%
Fattouch et al, 2009	1992–06	189		83%	17%	31%	33%	36%	15.8%	18%	16.4%	14.8%	15.6%
Bakhtiary et al, 2008	2000–06	120		90%	10%			100%	30%	20%	39%	11%	5%
Knipp et al, 2007	1995–03	3,013	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	26%
Zierer et al, 2007	1984–05	175	17%	83%		39%	32%		NA	NA	NA	NA	18%
IRAD, 2006	1996–03	273	15%	76.8%	9.2%	28%	57%	NA	70%	30%	NA	NA	13.9%
IRAD, 2005	1996–01	526	NA	NA	12%	NA	NA	NA	NA	32%	NA	NA	25%
Kallenbach, et al, 2004	1990–03	257		81%	19%	100%	NA	NA	56.4%	24.9%	18.7%		24%
Chiappini, et al, 2004	1976–01	315	27.9%	67.7%	4.4%	39.7%	0.9%	31.7%	75.9%	14.6%	3.8%	5.7%	19.7%
Bavaria, et al, 2002	1992–02	163		95%	5%	0%	100%	0%	83%	17%			9.8%

ACP = antegrade cerebral perfusion; AVR = aortic valve replacement; HCA = hypothermic circulatory arrest; NA = not applicable; Pts. = patients; RCP = retrograde cerebral perfusion; Replace. = replacement; Resusp. = resuspension; VSRR = valve separate root repair.

timely surgical intervention. Consequently, it is appropriate to utilize CT angiography for diagnosis of dissection given its speed, accuracy, and availability. When the diagnosis is suspected or presumed based on other objective data not intended to identify dissection (such as TTE or chest radiography), it is reasonable to forego additional imaging and perform definitive TEE intraoperatively before opening the patient's chest. Serum D-dimer level is a remarkably sensitive but not specific biomarker for acute aortic dissection [370]. Once the diagnosis is made, most centers usually do not perform preoperative coronary angiography as a routine because it may delay operative intervention [371–373]. If, however, coronary angiography can be performed while the operating room is being prepared, this is reasonable. For patients with a high risk for CAD, coronary angiography may be a good option for hemodynamically stable patients [1].

The primary goals of type A aortic dissection repair should be to remove the primary tear site, to restore aortic valvular competency, and to reconstitute true lumen flow while obliterating false lumen blood flow in hopes of collectively preventing rupture, myocardial infarction, stroke, malperfusion, and death. Establishment of adequate arterial pressure monitoring from multiple sites to ensure uniform perfusion throughout the body during and after the reconstruction is important. The route of access to deliver arterial inflow for acute aortic dissection continues to be debated without resolution of superiority of technique (ie, axillary, subclavian, femoral, or central aortic) [139, 341, 349, 374–381]. Regardless of access approach, it is imperative that true lumen cannulation is established and maintained because false lumen cannulation and perfusion can significantly impair the adequacy of regional tissue bed perfusion and increase the risk of aortic disruption or stroke. Myocardial protection is conventional, as with open heart surgery. Directed brain monitoring and protection strategies are advocated by some during aortic dissection repair to reduce the incidence of perioperative stroke [1].

The aortic root should be assessed to establish (1) the candidacy for aortic valve preservation; (2) patency and integrity of the coronary ostia; and (3) the need for aortic root replacement. The same factors that impact aortic valve management in the setting of isolated AS or AR are relevant at the time of aortic dissection repair with the additional factor that patient longevity is significantly impacted by the dissection process itself particularly in patients with residual arch and descending thoracic arch dissection and a patent false lumen [346, 382–384]. With 10-year survival ranging from 40% to 80% among surgically treated patients with type A dissection, bioprosthetic AVR may often be appropriate [351, 369, 385–388].

The distal extent of aortic replacement should be dependent on the presence and extent of an aortic tear (not extent of dissection) in the aortic arch, aortic arch diameter, and the ability to perform a durable distal anastomosis that will adequately restore distal true lumen

flow and exclude false lumen flow. In the majority of cases, with the possible exception of DeBakey type II dissections, the distal reconstruction requires a period of circulatory arrest to allow for open interrogation and reconstruction of the aortic arch. Successful circulatory arrest outcomes are realized with the use of deep HCA and, more recently, with moderate hypothermia used in conjunction with unilateral or bilateral ABP. The addition of either ABP or RBP may allow for safer, longer circulatory arrest periods with lower brain complications. Single-institution comparisons of circulatory arrest and brain perfusion strategies have been inconclusive in demonstrating superiority of HCA with ABP or HCA with RBP compared with HCA alone [337, 389-394]. Reliable comparisons of HCA with ABP to HCA with RBP are scant largely because of institutional biases directing one strategy over the other. There has been a trend worldwide toward evolving from a strategy of deep HCA (14°C to 18°C) HCA with ABP or RBP to moderate HCA (25°C to 30°C) with ABP with the enthusiasm based on apparently equivalent results with the benefit of shorter cardiopulmonary bypass time [374, 380, 395]. However, reported series to date have included predominantly elective aortic arch surgeries, not aortic dissection repairs, which may require longer circulatory arrest periods for complex repairs. Furthermore, the incidence of multiple organ failure, because of poor visceral protection, may be greater.

There is a divergence of expert opinion on the safety of applying a total arch replacement strategy to the majority of acute type A dissections (based largely on the Japanese experience) as opposed to the more limited open distal or hemiarch replacement strategy that is generally favored worldwide. This discrepancy persists because of continued concerns that broadly applied total arch replacement for type A aortic dissection invokes a higher risk of morbidity and mortality. The addition of endovascular stents at the time of the repair is still being investigated.

Optimal aortic wall repair strategies at either the proximal or distal extent of ascending aortic replacement continue to evolve; these have included neomedial reconstruction, intimal and adventitial reinforcement with felt, and biologic glues [349, 396, 397]. Early enthusiasm for the use of "biologic" glues has waned more recently because of reports of tissue necrosis, anastomotic breakdown, pseudoaneurysm formation, and embolization [398–402].

Longitudinal radiologic surveillance (through CT angiography or magnetic resonance angiography) after the diagnosis or repair of aortic dissection should be routinely performed. When renal insufficiency is present, consideration should be given to alter a surveillance strategy to eliminate the incidence of contrast-induced nephropathy by using unenhanced imaging techniques that still offer the minimum of quantifying diameter and aneurysmal growth. Surveillance over the course of the first year after aortic dissection should be every 6 months to allow identification of patients with rapidly expanding aneurysmal dissections who are at greatest risk for a second aortic catastrophe, and thereafter annually.

Results

Hospital mortality after type A aortic dissection repair in the current era ranges between 5% and 26% (Table 1) [341–343, 345–351]. This fairly broad range of reported hospital mortality reflects data accumulated over many years when treatment protocols were evolving and institutional infrastructures, experience, and treatment biases were changing. Neurologic complication rates are even more difficult to compare among the treatment strategies because neurologic outcome reporting has been widely variable. Neurologic complication rates range from 2.8% to 30% depending on the inclusion of permanent stroke, paraplegia, and temporary neurologic dysfunction [337, 341–343, 345–351, 354, 361, 389, 391–393].

19. Ascending Aorta and Aortic Arch—Recommendations

Class I

1. All patients with suspected thoracic aortic disease on the basis of family history, symptoms, or physical examination should have the entire thoracic aorta imaged. (Level of evidence C)
2. All patients with a bicuspid aortic valve should undergo imaging of the thoracic aorta [1]. (Level of evidence B)
3. All patients with Marfan syndrome or Loeys-Dietz syndrome or mutations associated with aortic disease or dissection should have the entire aorta imaged and appropriate blood testing performed for genetic mutations [1]. (Level of evidence B)
4. First-degree relatives of young patients with a bicuspid aortic valve or genetic mutation associated aortic disease of the thoracic aortic disease should be advised to be further investigated. (Level of evidence C)
5. All patients for whom planned elective valvular surgery is planned and who have associated thoracic aortic disease should undergo preoperative cardiac catheterization [1]. (Level of evidence B)
6. Additional testing to quantitate a patient's comorbid status and develop a risk profile is recommended. These tests may include for particularly high-risk patients CT of the chest if not already done, PFTs, 24-hour Holter monitoring, noninvasive carotid screening, brain imaging, echocardiography, neurocognitive testing, and assessment of degree of frailty. (Level of evidence C)
7. Intraoperative TEE is recommended for all patients undergoing surgery for thoracic aortic disease. (Level of evidence C)
8. Surgical repair is recommended when the ascending aorta or aortic root exceeds 5.5 cm if the patient has no genetically based aortic disease and is otherwise a suitable candidate for surgery [1]. (Level of evidence B)

9. Patients with genetically associated aortic diseases, including those with a bicuspid aortic valve, should undergo surgery at diameters exceeding 5.0 cm unless a family history of aortic dissection is present, then it is acceptable to lower the threshold to 4.5 cm. Alternatively, patients with a maximal ascending aortic area (Πr^2, cm^2) to height in meters ratio exceeding 10 should be considered for surgery [1]. (Level of evidence B)
10. Patients with a growth rate exceeding 0.5 cm per year should be recommended to undergo surgery if no other limitations apply [1]. (Level of evidence B)
11. For patients with Loeys-Dietz syndrome or confirmed TGFBR1 or TGFBR2 mutation should be evaluated for repair of the aorta when the diameter exceeds 4.2 cm. (Level of evidence C)
12. For patients undergoing cardiac surgery other than for aortic indications, aortic repair is recommended when diameter exceeds 4.5 cm [1]. (Level of evidence B)
13. Aortic diameters should be measured at right angles to the axis of flow, which requires the use of three-dimensional reconstructive software. The maximal diameters at each segment of the aorta should be reported. Echocardiography measures internal diameters while CT and MRI measures external diameters, and thus some allowance should be made for echocardiographic measurements being smaller. (Level of evidence C)
14. Separate valve and ascending aortic replacement are recommended for patients without significant aortic root dilation, for elderly patients, and for young patients with minimal dilation in whom a biological valve is being inserted or a bicuspid valve is being repaired [1]. (Level of evidence B)
15. Patients with Marfan, Loeys-Dietz, and Ehlers-Danlos syndromes and root dilation should undergo excision of the sinuses in combination with a modified David valve reimplantation procedure if technically feasible or insertion of a valve graft conduit [1]. (Level of evidence B)
16. For more complicated arch reconstructions requiring extended periods of circulatory arrest, use of adjunctive brain perfusion techniques is recommended [1]. (Level of evidence B)

Class IIa

1. Regular echocardiography and MRI or CT evaluation after repair of thoracic aortic disease is reasonable. (Level of evidence C)

Quality Measures

1. Prophylactic antibiotics for both gram-negative and gram-positive coverage should be administered for the operative procedure.
2. Intraoperative TEE is recommended in all patients.
3. All patients with a bicuspid aortic valve, Marfan, Loeys-Dietz, and Ehlers-Danlos syndromes, and a history consistent with familial thoracic aortic disease the first-degree relatives should undergo imaging of the thoracic aorta.
4. MRI or CT evaluation should be considered after surgical repair.
5. ACE inhibitor therapy should be considered in patients with low EF postoperatively.

Repair of the ascending aorta and/or the arch entails resection of the diseased aortic segment and replacement with an interposition conduit. Currently, the procedure is performed with cardiopulmonary bypass and cardiac arrest with or without HCA. Patients with ascending aneurysms often have concomitant aortic valve or root pathology, which may be addressed simultaneously. Patients with arch disease often have multisegment involvement, and so arch repair is usually combined with ascending repair to address proximal pathology and the elephant trunk procedure is used to prepare for later treatment of distal aortic pathology.

Pros

Ascending and arch aortic aneurysms predictably lead to dissection, rupture, and death depending on size, morphology, and etiology of the disease [328, 403, 404]. Occasionally a very large aneurysm or those associated with anomalous vasculature can cause focal compressive symptoms. Otherwise, most aneurysms are found incidentally or by screening those known to be at elevated risk for aneurysm formation such as those with Marfan syndrome, Loeys-Dietz syndrome, familial thoracic aortic disease, a bicuspid aortic valve, or other mutations associated with aortic disease [405–407]. Indications for operative repair of the proximal aorta in asymptomatic patients are based on the predictability of death from aortic complications. Surgery is indicated when the risk of aortic complications outweighs the risk of repair. Elective prophylactic repair can be performed safely and durably with experience and proper patient selection for all variations of proximal aortic repair, even the most extensive disease [338, 408–419]. Timely repair of aortic aneurysms prolongs survival and approaches that of age-matched controls in select populations [72, 407, 413] (Figs 24–27). Clearly, the institutional outcomes and experience must be taken into account when recommending prophylactic surgery since the operative death risk must be lower than that of the risk of dissection or rupture.

Cons

Emergency repair of dissection or rupture can be life-saving, but these patients are clearly at higher operative risk than patients undergoing elective prophylactic repair [411, 412, 415]. The challenge is to balance the risks of aortic complications against the risk of aortic repair. Serious acute complications of proximal aortic repair include death, stroke, and respiratory failure [338, 411, 415, 419]. Elderly patients and patients with emergency indications may be at higher risk for perioperative bleeding. Patients with atherosclerotic and atheromatous disease involving the arch are at increased risk of embolic stroke [338, 411, 414, 415]. Although the use of circulatory

arrest theoretically reduces the risk of embolization by minimizing the need for aortic manipulation, longer periods of circulatory arrest and cardiopulmonary bypass are associated with neurologic deficit [338]. It is important to note that patients successfully operated on for aortic dissection have a markedly reduced late survival rate.

Results

Mortality associated with ascending or arch aortic repair ranges from less than 1% to 15% depending on the urgency, operative center, and indications [338, 408–419]. Emergency indications, older age, and more extensive repair in the arch requiring longer pump times are predictive of worse outcome. At experienced centers, mortality for primary elective repair of the ascending aorta is consistently less than 5% and is reported by some centers to be 1%. Rates of perioperative stroke range from 0% to 7% depending on the atheroma burden in the aortic arch, cardiopulmonary bypass time, and the duration of circulatory arrest [338, 411, 414, 419]. The risk of stroke increases significantly during circulatory arrest lasting more than 40 minutes [338]. Reoperation for bleeding occurs in less than 5% [413] but may be as high as 17% of patients with the most extensive disease. Long-term survival ranges from 50% to 93% at 10 years [410–413].

Further Research Needed

Endovascular therapies have quickly made a major impact in the treatment of disease involving the descending aorta. Several reports describe the use of this technology in the ascending aorta and aortic arch either as purely endovascular repair or as a hybrid approach in combination with open surgery [420]. Feasibility has been documented with these approaches but further device development and understanding of the disease processes is necessary. There is a need for additional studies focused on outcomes for various subsets of proximal aortic repair based on morphology and etiology. There is a need for improved genetic and biologic understanding of the mechanisms of aneurysm formation and directed medical prophylaxis to slow the process [421].

20. Statistical Analysis of Procedure Success, Safety, and Long-Term Effectiveness

Over the last 5 decades, a number of events and longitudinal processes have been observed and documented after aortic valve and ascending aorta repair and replacement that relate to procedure success (whether the intended procedure was accomplished as intended [ease of insertion]), safety (whether the device inserted, the repair, or the procedure to accomplish these has caused patient morbidity directly or indirectly), and effectiveness (whether the device or repair accomplished its intended purpose of providing clinical benefit versus nonintervention). Typical examples of procedure success include secure fixation and deployment of a prosthetic heart valve, secure replacement of the ascending aorta, and repair of a purely regurgitant aortic valve without introducing stenosis or leaving residual regurgitation. Typical examples of safety include the risk of systemic emboli necessitating anticoagulation of a thrombogenic heart valve replacement device with its attendant risks of hemorrhage, catastrophic prosthesis failure, prosthetic valve endocarditis, hemolysis from periprosthetic regurgitation, stroke, paraplegia, and death early after a procedure. Typical examples of effectiveness are elimination or substantial reduction of gradient across the LV outflow tract by valve replacement (giving rise to terms of reduced benefit such as PPM [12]), durability of repair, decreased hospitalizations for valve-related heart failure, and finally long-term patient survival.

A number of quantitative and qualitative measures for success, safety, and effectiveness and their definitions have served the surgical community for decades, are well understood by readers of the surgical literature, and are embodied in regulations such as those of the FDA. With advent of percutaneous and endovascular techniques to address these heretofore surgical diseases, a new group of interventionalists coming from different backgrounds, training, and experience is just now becoming familiar with these measures. This is resulting in refinement of definitions and development of joint documents by surgeons and interventional cardiologists (Table 4) [422].

In addition, because of 50 years of experience, standards have been set for many long-term safety and durability measures in terms of objective performance criteria with which new heart valve prostheses must comply [423, 424]. These standards of comparison are not well suited to new types of devices applied to patient populations not formerly considered for open cardiac surgery.

In 2008 the AATS, the STS, and the European Association for Cardio-Thoracic Surgery revised guidelines, first issued in 1988, for reporting mortality and morbidity after heart valve interventions [159, 425, 426]. These guidelines do not clearly differentiate procedure success, safety, and effectiveness measures. Rather, they establish definitions of morbidity that are applicable to at least AVR, including TAVR, although not explicitly addressing those specific to either TAVR or ascending aorta procedures.

In the preceding text, a number of measures, including observations, complications and morbidity, time-related events, and longitudinal data have been described. In many trials, including those with FDA encouragement, composite endpoints have been used to measure device success. The challenge of composite endpoints, however, is that they combine different types of data, for example, death (binary data), stroke (time-dependent event), and NYHA functional class or aortic valve regurgitation (longitudinal time-dependent data).

In the following text, some of these will be categorized into measures of procedure success, safety, and effectiveness, with remarks about some that contain elements arguably related to two or all categories. In a final section we will highlight appropriate data analysis methods that amplify those of Section 5 of the 2008 valve reporting guidelines [159].

20.1. Procedure Success

Although procedural success—whether the intended procedure was accomplished as intended—has been implicit in surgical thinking from the beginning of heart valve replacement and treatment of the diseased ascending aorta, the advent of TAVR has made it important to be explicit. Questions today such as whether or not the valve was deployed, has been deployed to its intended location, been expanded properly or has required open AVR or transcatheter valve-in-valve, and patients left with minimal periprosthetic leakage mirror questions in previous decades, such as whether the minor and major orifices of a mechanical prosthesis have been properly directed, whether there is periprosthetic leakage, or whether both leaflets of a bileaflet prosthetic valve are opening and closing.

In general, definitions of procedural success are dependent on the particular procedure performed. For TAVR, Valve Academic Research Consortium (VARC) participants have proposed a technical composite endpoint that includes successful vascular access, delivery and deployment of the device, and successful retrieval of the delivery system; correct positioning of the device; achieving intended performance of the prosthesis; and only the first valve deployed implanted in the intended location [422].

Some aspects of procedure success become measures of safety when success has not been achieved. A prosthesis may be properly seated but obstruct a coronary artery orifice; an ascending aortic posterior suture line may leak and require reoperation to stop bleeding and prevent pseudoaneurysm formation; a percutaneous valve may migrate; simple AVR in an elderly woman with a thick septum may lead to LV cavity obliteration and outflow gradient [427].

20.2. Safety

Traditionally, safety—whether the procedure has caused patient morbidity directly or indirectly—has been assessed in terms of events that occur either in-hospital, within 30 days of the procedure, or a composite of hospital death and deaths within 30 days for patients discharged alive before 30 days [422, 423]. However, for aortic valve repair and replacement, and surgery on the ascending aorta, it has long been recognized that there are also long-term safety measures that must be evaluated [159, 177].

20.2.1. SHORT-TERM SAFETY MEASURES Nearly all the morbidities identified in surgical society guidelines, by the FDA, and by watchdog groups have now also been included in the VARC definitions [159, 422, 425, 426]. The choice of in-hospital or 30 days is arbitrary, and scientifically should include the entire early hazard phase, which may be considerably prolonged beyond 30 days. In the United States, a period of 90 days is considered the extent of recovery from major procedures such as valve replacement or ascending aorta surgery. This period was adopted by the surgical community in their guidelines but not by the VARC [159, 422]. From a practical perspective, ascertaining 30- or 90-day morbidity events requires active follow-up of all patients, and that may not be economically feasible.

20.2.2. LONG-TERM SAFETY MEASURES Long-term safety measures include nonstructural dysfunction of many types, ranging from periprosthetic leakage to hemolysis to panus ingrowth, valve thrombosis, stroke from thromboembolism, anticoagulant-related bleeding, prosthetic valve endocarditis, higher risk of stroke, and complications of reintervention. Long-term safety measures also include catastrophic structural prosthesis failure, such as outlet strut fracture and occluder escape observed with the Bjork-Shiley mechanical valve [159, 428, 429]. For surgical AVR, the FDA has focused on developing objective performance criteria for safety events and determining the necessary amount of long-term active follow-up (length and number of patients) to adequately assess risks with meaningfully narrow confidence limits.

There are patient-related risk factors associated with some of these safety endpoints. For example, a person experiencing a preimplant stroke is at increased risk of a postimplant stroke. Similarly, once a person has had a thromboembolism, he or she is at increased risk of another event [430]. Thus, we consider the interaction of patients with thrombogenicity of their implanted prosthesis to constitute a potential danger of these devices, and therefore that is a safety issue.

20.3. Long-Term Effectiveness

Effectiveness—whether the device or repair is accomplishing its intended purpose of providing clinical benefit—of AVR can be assessed by (1) prosthetic valve performance, (2) patient longevity, and (3) patient well-being.

20.3.1. PROSTHETIC VALVE PERFORMANCE The intended purpose of AVR or repair is to produce a competent valve with minimal stenosis or valvular leakage, including perivalvular. All prosthetic devices incur transprosthesis energy loss, usually estimated as a pressure gradient that increases in vivo with exercise [431–433]. In some patients, stenosis produced by the prosthesis is of sufficient severity to cause symptoms, called PPM [12]. There is currently considerable controversy as to how serious a problem this is. Surprisingly, echocardiographic longitudinal valve gradient data (often expressed as EOA) by prosthesis type, model, and size (in itself a controversial issue) are sparse.

In addition to effectiveness of valve replacement on relieving native AS or AR, performance of prosthetic heart valves includes intrinsic properties, such as static and dynamic in vitro performance. In vivo indirect estimates of performance include reversal of heart chamber and myocardial remodeling. A prosthetic valve should reverse morphologic and functional changes brought about by aortic valve disease to the extent that permanent damage remits. These, too, are longitudinal data. Generally, changes occur most rapidly in the first few months after valve replacement, then plateau. As noted,

some remodeling cannot be reversed, such as myocardial fibrosis in AS leading to long-standing diastolic dysfunction or the continuing inflammatory processes of rheumatic heart disease.

Bioprostheses in particular exhibit longitudinal reduction in performance from intrinsic prosthesis deterioration, or SVD. Over time, this may lead to regurgitation or stenosis that may eventuate in device replacement. The rate of deterioration accelerates across time, well characterized by a Weibull function [434]. A universally found risk factor for accelerating this rate is younger age at implant [14]. Periodic, routine echocardiographic surveillance is required to detect SVD and to determine timing of reintervention.

Structural valve deterioration of certain bioprosthesis is a slow process occurring over 10 to 20 years. This slow process is characterized as intrinsic durability. Other bioprosthesis may exhibit more rapid, but usually not catastrophic, failure that requires reoperation. For practical reasons, SVD classically has been assessed as time to reoperation to replace the prosthesis rather than as the longitudinal process it is. Reoperation for SVD has the advantage of being a hard endpoint that can be portrayed actuarially, but the disadvantage is inherent bias (generally underestimation) introduced by variation in indication and timing of reintervention by primary physicians, cardiologists, surgeons, and patients themselves.

Durability of aortic valve repair is generally assessed by echocardiographic estimates of developing stenosis or regurgitation. These are longitudinal data representing "snapshots in time" of the state of the repair and not time-to-event data. Accuracy of evaluating durability of valve repair depends on intensity of echocardiographic assessment.

20.3.2. LONGEVITY A primary clinical benefit of aortic valve repair or replacement and of repair of the ascending aorta versus nonintervention (medical) therapy is prolonging life. This endpoint can be estimated by assessing time-related, long-term all-cause mortality and comparing it with natural history without intervention (or to non-interventional therapy) [435]. It may be argued that this hard endpoint is diluted by non–valve-related causes of death and by deaths associated with valve-related morbidity (safety). Attempts to define valve-related or cardiac-related death as a more specific endpoint are thwarted by subjectivity, poor family reporting, ever diminishing autopsy investigation, inaccurate mode of death reported on death certificates, and increasing use of national death registries that poorly differentiate mode of death, if at all.

Compounding estimation of effectiveness of preventing premature death is the lack of contemporary data on natural history of aortic valve and ascending aorta disease. Even the report of PARTNER data involves a highly select group of "natural history" patients [81, 240]. Thus, inferences about clinical benefit rely on data from an era of not only no valve replacement, but also less sophisticated medical therapy [435].

A controversial way that mortality after valve replacement has been assessed has been to informally compare it with that of an age-race-sex–matched reference population. Use of such a reference standard began in the field of oncology when it was suggested that "cure" in a population sense was when survival of the treated population was commensurate with that of the matched population life table [436]. It is argued on the one hand that the "noise" of nonrelated causes of death is reflected in this general population reference; it has been argued on the other hand that such a reference assumes incorrectly that patients undergoing heart valve procedures are representative of the general population. Indeed, for elderly patients, a subset is selected that is likely to have good long-term survival and indeed after AVR, patients after the age of 80 years have better survival than the general population. Nevertheless, the general finding that the younger the patient at AVR, the worse is his or her survival with respect to the general population is valuable information for stimulating research directed toward increasing the benefits of valve replacement [435].

20.3.3. PATIENT WELL-BEING Patient well-being classically has been assessed by the nonamended original definition of the NYHA functional classes. This graded variable (statistically known as an ordinal variable) is subjective, but can be made less so by assessing the individual data elements stipulated for each classification and deriving NYHA class algorithmically. Going a step further, the 6-minute walk test or 5-meter walk test in trial patients make more objective those less specific data elements related to ability to walk certain distances; the 5-meter walk test is easier to administer [93, 437].

Two important analytic issues arise with self-reported well-being assessment instruments: (1) interruption of the longitudinal sequence of assessments by death, and (2) recognition that these instruments capture a snapshot in time and require a longitudinal sequence of reassessments to identify a pattern of change in a particular patient set [438]. Some have addressed death by coding it as NYHA class V; others have imputed the lowest scores on quality-of-life instruments. An assumption is that there is steady deterioration of well-being to death from valve-related disease, but that does not account for other unrelated and competing modes of death.

Despite many years of AVR experience, there is a paucity of reports on longitudinal well-being assessment by instruments other than NYHA functional class. A common error in reports that have been published has been the assumption that assessment results are events (eg, status at last follow-up) rather than as a sequence of snapshots in time, for which longitudinal data analysis methods must be applied. There are also limited data on functional health status assessed objectively, such as by serial formal exercise testing.

20.4. Statistical Analysis

The measurements, events, and longitudinal data described for procedure success, short- and long-term safety, and effectiveness can be grouped into three general types of analysis: analysis of static (non–time-related) data, analysis of time-to-event data, and analysis of longitudinal data.

20.4.1. ANALYSIS OF STATIC MEASUREMENTS Observation of procedure success and short-term morbidity can be expressed in a non–time-related fashion by descriptive summary statistics. These include means and standard deviations for continuous variables unless the distribution of values is skewed, in which case typically nonparametric median and percentiles are appropriate. Events are summarized by simple proportions accompanied by confidence limits (intervals). These may be compared with external standards such as risk-adjusted estimates of observed versus predicted proportions based on the STS ACSD [84].

Analysis of these data to generate risk-adjusted assessment has generally used parametric models such as linear regression for continuous variables and logistic regression for binary variables. Limitations of this approach include the additive assumption of these models (each factor considered is weighted by a coefficient that accounts for all other variables in the models and these weighted factors are added together). Another assumption is that the scale of measurement for continuous variables is linear with respect to model assumptions, which may not be true. These limitations can be circumvented by considering multiplicative factors and by transformation of measurement scale, respectively. Alternatively, machine-learning non–model-based equivalents of linear and logistic regression may be used; this includes random forest methodology [439, 440] that automatically accounts for complex interactions among variables and nonlinearities with respect to the outcomes assessed.

20.4.2. ANALYSIS OF TIME-RELATED EVENTS For so-called terminating events (death, removal of a prosthesis, and other one-time events), the most common non–model-based estimator is the Kaplan-Meier product-limit actuarial method. This method is defined in the probability domain. An alternative is the Nelson estimator, which is defined in the cumulative hazard domain [441]. Both yield comparable results. The advantage of the Nelson method is that it can also accommodate repeating (nonterminating) events, such as thromboembolism and bleeding episodes. A new Kaplan-Meier or Nelson estimate is made at the time of occurrence of each event. Generally, these estimates are portrayed graphically across time. These estimates should be accompanied at least periodically by confidence limits and a depiction of number of patients traced beyond a given set of points in time.

The temporal pattern of risk of time-related events is expressed by the hazard function (instantaneous risk of an event). Nonparametric estimates of the hazard function are usually noisy, so parametric methods may be used to estimate the temporal pattern of risk [442]. A flaw in statistical analysis of some long-term safety events is that it has often been assumed that risk remains the same across time (constant hazard at a so-called linearized rate) [443]. This assumption makes computations of hazard rates simple, namely, the number of events observed divided by the patient-years of follow-up. However, the assumption may not be true. For example, prosthetic valve endocarditis generally has an early peaking hazard phase followed by a lower constant hazard phase; that means that in short follow-up the linearized rate will be high, and in longer-term follow-up lower. Structural valve deterioration has an accelerated late hazard; the linearized rate is small for short follow-up and large for longer follow-up. Characterizing the actual hazard function is not difficult and is recommended; a constant hazard may be confirmed [444].

If a device is itself being characterized, it can be argued that patient death is merely a censoring mechanism, just like end of follow-up or removal of the device, and that Kaplan-Meier or Nelson estimates are appropriate [445]. The estimates accurately assess the probability or risk of events related to an aortic valve prosthesis. When estimating the probability of an individual patient experiencing a valve-related event, the patient is the unit of interest, and other competing risks such as death must be considered. These estimates will be highly patient-specific, because there are many patient factors that relate to long-term mortality. A limitation of competing risk estimates is that it is assumed that the valve events and the patient's demise are unrelated (noninformative censoring). That may not be true, and methods to estimate the magnitude of informative censoring are an active topic of statistical research [446].

Not addressed by surgical or VARC guidelines is an estimate of the adverse effect of safety events on longevity. One way to assess the effect is to estimate survival after occurrence of the safety event. In a population, these events should result in an acute decrease in survival. A second way is to analyze safety events as time-varying covariables in one of two ways: as abrupt changes in level of the hazard function (the most common approach) or as a modulation of hazard (modulated renewal analysis, commonly performed in industrial settings) [447]. Time-varying covariable analysis has two advantages. First, it permits one to assess quantitatively the effect of the events. Second, it permits calculation of potential survival were these events not to have occurred.

Risk factors may be associated with shorter time to events. The two most common approaches for identifying risk factors have been (1) semiparametric Cox proportional hazard regression [448] and (2) parametric multiphase hazard function regression [442]. For some events, particularly mortality, the proportionality assumption of Cox regression is not reasonable; generally, factors related to early mortality have to do with the status of the patient at operation, whereas factors related to late mortality have more to do with chronic comorbidities (including age). Multiphase hazard regression accounts for nonproportional hazards and permits identification of variables that relate to different temporal phases of risk. An alternative to both of these methods is machine learning nonparametric methods such as the random forest survival method [440].

20.4.3. ANALYSIS OF LONGITUDINAL DATA Longitudinal data may be continuous (transprosthesis gradient), ordinal (NYHA functional class), or binary (episodes of atrial fibrillation).

Values for these outcomes are generally assessed at infrequent intervals that vary from patient to patient. As for competing risks, any series of measurements is truncated by demise of the patient. A universal characteristic of longitudinal repeated measures data is that variability within the sequence of measurements for a given patient is less than variability among different patients. Thus statistical analysis must take into account these two sources of variability [449, 450].

Unfortunately, current standard statistical packages tend not to have procedures that model first the underlying ensemble average temporal pattern and then identify factors associated with modulation of that longitudinal pattern. However, progress is being made in developing such methods.

There are important limitations in analysis of longitudinal data. Patients experiencing symptoms or suspected of having developing problems may be assessed more often than those not having these. The result is an estimated ensemble average weighted (biased) unfavorably. A second limitation is wide variation in assessment frequency. A third limitation is that device removal and death compete with continued longitudinal assessment. It is assumed that these events are unrelated to longitudinal evolution of data. This is certainly not true, for example, of SVD. Methods to assess the effect of evolving longitudinal status data on events such as death are an active area of statistical research.

20.5. Future Needs

Over the last 5 decades, terminology for describing, and methods for assessing, success, safety, and long-term effectiveness of aortic valve and thoracic aorta replacement developed within the framework of single disciplines. With advent of percutaneous and endovascular techniques, more attention must be focused on accurate and harmonized definitions, cross-disciplinary data, robust long-term surveillance, and more meaningful analysis using new analytic methods.

20.5.1. DEFINITIONS Definitions of postprocedural events that evolved within single disciplines now require shared understanding of their meaning and standardized definitions. Cardiologists may not understand the term "structural valve deterioration" even after reading its surgical definition; surgeons may not understand cardiologists' focus on major adverse cardiac events, which grew out of reporting adverse events related to ischemic heart disease interventions; cardiovascular surgeons may not know the definitions of types I to V endovascular leak nor appreciate their importance; none of the disciplines may understand current nomenclature and diagnostic criteria for strokes that continue to evolve in neurology. Thus, there is increasing need for, and value in, a shared nomenclature with clear definitions harmonized across disciplines.

20.5.2. DATA With procedures for the same diagnosis increasingly carried out in different departments by physicians with differing background and training, and with differing local, regional, national, and international reporting mechanisms, it has become increasingly difficult to monitor comprehensively the success, safety, and effectiveness of treating aortic valve and thoracic aorta disease. Cardiac surgeons report to the STS ACSD and interventional cardiologists to the ACC national cardiovascular data registry. Vascular surgeons performing endovascular procedures have limited national reporting. Yet all these databases, assembled along traditional discipline lines for assessing and improving quality, need to be consolidated across these lines and barriers. The efforts of both STS and ACC to address these issues, particularly for TAVR, are a step forward. In the USA, for CMS payment, reporting to the ACC/STS TVT registry is required and further studies on outcomes and appropriateness use are expected.

20.5.3. RANDOMIZED TRIALS Objective performance criteria have been the mainstay of past assessment of new cardiac valves [424]. Increasingly, randomized trials will be required until new objective performance criteria can be established. Likely, randomized trials will compare existing devices and procedures against new or modified devices and not new devices against untreated natural history or medical therapy alone.

20.5.4. SURVEILLANCE Long-term surveillance for safety and effectiveness is resource intensive and may not be economically sustainable. Increasingly active patient follow-up is being hampered by confidentiality and privacy regulations and idiosyncratic interpretation of these by local institutional review boards. Three alternatives to traditional follow-up are emerging. The first is reliance on national registries for vital status [451, 452]. These registries do not, however, help in detecting adverse nonfatal events. The second is linkage of data to either private or national insurers and payors to assemble a longitudinal patient record that may document these morbid events. The third is perhaps the most interesting: social networks. Already, patients can report side effects of neurologic drugs on Web sites such a patientslikeme.com. Although the data are not risk adjusted, nor do they track individual patients longitudinally, nor is it known how representative the participants may be, as a general surveillance method for adverse events, these networks may be the most cost-effective follow-up mechanism.

20.5.5. ANALYTIC METHODS Both new and seldom-used analytic methods are worth exploring in the future. Many years ago, Wayne Nelson of General Electric augmented time-to-event methods with cost of each event: the cumulative cost function [441]. The cost can be monetary; it can also be a scale of morbidity [442].

Earlier, machine learning methods were discussed. These encompass a growing set of procedures that may supplant parametric logistic regression and survival models. They have superior predictive power compared with traditional statistical models [453].

Longitudinal data analysis is still in its infancy. However, the pervasiveness of those kind of data are stimulating statistical development of the field, although translation into useful software is lagging. Just as machine learning techniques have developed robust survival analysis methods, no doubt robust machine-learning

techniques for longitudinal data analysis will soon emerge.

Finally, a particularly daunting statistical challenge is assessing the interplay among evolving outcomes. What is the influence of evolving bioprosthesis deterioration on death or quality of life? What is the influence of residual myocardial diastolic dysfunction on survival? How do risk factors simultaneously influence the degree of coupling between or among outcomes? Important questions such as these are hard to answer at the present time, but statistical scientists are developing theory and methods to address this.

These and other new methods may at first appear as daunting to those caring for patients as were logistic regression, actuarial analysis, and competing risks analysis over the last 5 decades. To the extent, however, that they help us generate important new knowledge to better perform the right procedure for the right patient at the right time, we should welcome them and try to understand their place in the armamentarium of methods to assess procedure success, safety, and long-term effectiveness of aortic valve and thoracic aorta procedures.

21. Proposed National Quality Forum-Based Quality Measures

1. Patients with valvular heart disease are evaluated by multidisciplinary specialists including a cardiologist and cardiac surgeon.
2. Preoperative echocardiography.
3. Preoperative CT for reoperation and TAVR.
4. Aortic stenosis indication less than 0.8 cm^2 or 0.5 cm^2/m^2, plus gradient more than 40 mm Hg mean or 64 mm Hg peak (>4 m/s) for isolated stenotic valve.
5. Cardiac catheterization for patients aged more than 45 years.
6. Pulmonary function tests.
7. Prophylactic antibiotics with both gram-positive and gram-negative coverage.
8. Antibiotics given within 30 minutes of incision.
9. Intraoperative transesophageal echocardiogram.
10. Multidisciplinary evaluation and insertion team for percutaneous AVR/TAVR.
11. Warfarin therapy for mechanical valves.
12. Aspirin or warfarin for biological valves.
13. ACE inhibitor therapy should be considered in patients with low EF postoperatively.
14. Postoperative echocardiogram less than 30 days after surgery.

22. Summary

These guidelines have summarized the current knowledge in the treatment of aortic valve and aortic disease. Clearly there are many questions and these can only partially be answered from incomplete data sets. Undoubtedly, newer iterations will update these guidelines. The choice of the best procedure or valve for patients is dependent on many factors as discussed above and no procedure or device is ideal. Ultimately it is up to the patient, the cardiologist, and surgeon to reach a decision on appropriate treatment. Table 6 summarizes the benefits of current devices relative to other options for the relative target population.

Table 6. Summary of Valve Characteristics

Valve	Ease	Safety	EOA	Durability	EF Survival
BAVR		X			X
Reimplantation		X	X	X	X
Mechanical AVR	X	X	X	X	
Ross			X		
Stentless			X		
Homograft			X		
Hancock/Mosaic	X	X		X	X
Magna		X	X	X	?
Perimount	X	X		X	X
Trifecta		X	X	?	?
Perceval			X	?	?
Intuity			X	?	?
TAVR: PARTNER B	X	X	X	X	X
TAVR: PARTNER A	X		X		
CoreValve	X		X		

AVR = aortic valve replacement; BAVR = bicuspid aortic valve repair; EF = event-free; EOA = effective orifice area; PARTNER = Placement of Aortic Transcatheter trial; TAVR = transcatheter aortic valve replacement.

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Appendix 1: STS Data Collection Form for Valves, Version 2.73

For STS data collection form for valves, version 2.73, see: http://www.sts.org/sites/default/files/documents/STSAdultCVDataCollectionForm2_73.pdf and related information at: http://www.sts.org/sts-national-database/database-managers/adult-cardiac-surgery-database/data-collection.

Appendix 2: Potential Author Conflicts of Interest Due to Relationships With Industry and Other Entities — Svensson LG, et al. Aortic Valve and Ascending Aorta Guidelines for Management and Quality Measures. Ann Thorac Surg 2013;95:S1–S66.

Author	Disclosure (yes/no)	If yes, name of entity with which relationship exists or existed within past 12 months
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David H. Adams	Yes	Medtronic
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Aortic Valve and Ascending Aorta Guidelines for Management and Quality Measures

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