

AHA/ACC Guideline

2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: Executive Summary A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Developed in Collaboration With the American Association for Thoracic Surgery, American Society of Echocardiography, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthesiologists, and Society of Thoracic Surgeons

WRITING COMMITTEE MEMBERS*

Rick A. Nishimura, MD, MACC, FAHA, Co-Chair†; Catherine M. Otto, MD, FACC, FAHA, Co-Chair†; Robert O. Bonow, MD, MACC, FAHA†; Blase A. Carabello, MD, FACC*†; John P. Erwin III, MD, FACC, FAHA‡; Robert A. Guyton, MD, FACC*§; Patrick T. O'Gara, MD, FACC, FAHA†; Carlos E. Ruiz, MD, PhD, FACC†; Nikolaos J. Skubas, MD, FASE¶; Paul Sorajja, MD, FACC, FAHA#; Thoralf M. Sundt III, MD***††; James D. Thomas, MD, FASE, FACC, FAHA‡‡

ACC/AHA TASK FORCE MEMBERS

Jeffrey L. Anderson, MD, FACC, FAHA, Chair; Jonathan L. Halperin, MD, FACC, FAHA, Chair-Elect; Nancy M. Albert, PhD, CCNS, CCRN, FAHA; Biykem Bozkurt, MD, PhD, FACC, FAHA; Ralph G. Brindis, MD, MPH, MACC; Mark A. Creager, MD, FACC, FAHA§§; Lesley H. Curtis, PhD, FAHA; David DeMets, PhD; Robert A. Guyton, MD, FACC§§; Judith S. Hochman, MD, FACC, FAHA; Richard J. Kovacs, MD, FACC, FAHA; E. Magnus Ohman, MD, FACC; Susan J. Pressler, PhD, RN, FAHA; Frank W. Sellke, MD, FACC, FAHA; Win-Kuang Shen, MD, FACC, FAHA; William G. Stevenson, MD, FACC, FAHA§§; Clyde W. Yancy, MD, FACC, FAHA§§

*Writing committee members are required to recuse themselves from voting on sections to which their specific relationships with industry and other entities may apply; see Appendix 1 for recusal information.

†ACC/AHA representative.

‡ACC/AHA Task Force on Performance Measures liaison.

§ACC/AHA Task Force on Practice Guidelines liaison.

¶Society of Cardiovascular Anesthesiologists representative.

#Society for Cardiovascular Angiography and Interventions representative.

**American Association for Thoracic Surgery representative.

††Society of Thoracic Surgeons representative.

‡‡American Society of Echocardiography representative.

§§Former Task Force member during the writing effort.

Full-text guideline available at: *Circulation*. 2014;129:e521–e643.

This document was approved by the American College of Cardiology Board of Trustees and the American Heart Association Science Advisory and Coordinating Committee in January 2014.

The online-only Data Supplement is available with this article at <http://circ.ahajournals.org/lookup/suppl/doi:10.1161/CIR.000000000000029/-/DC1>.

The online-only Comprehensive Relationships With Industry table is available with this article at <http://circ.ahajournals.org/lookup/suppl/doi:10.1161/CIR.000000000000029/-/DC2>.

The American Heart Association requests that this document be cited as follows: Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP III, Guyton RA, O'Gara PT, Ruiz CE, Skubas NJ, Sorajja P, Sundt TM III, Thomas JD. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;129:2440–2492.

This article has been copublished in the *Journal of the American College of Cardiology*.

Copies: This document is available on the World Wide Web sites of the American Heart Association (my.americanheart.org) and the American College of Cardiology (www.cardiosource.org). A copy of the document is available at <http://my.americanheart.org/statements> by selecting either the "By Topic" link or the "By Publication Date" link. To purchase additional reprints, call 843-216-2533 or e-mail kelle.ramsay@wolterskluwer.com.

Expert peer review of AHA Scientific Statements is conducted by the AHA Office of Science Operations. For more on AHA statements and guidelines development, visit <http://my.americanheart.org/statements> and select the "Policies and Development" link.

Permissions: Multiple copies, modification, alteration, enhancement, and/or distribution of this document are not permitted without the express permission of the American Heart Association. Instructions for obtaining permission are located at http://www.heart.org/HEARTORG/General/Copyright-Permission-Guidelines_UCM_300404_Article.jsp. A link to the "Copyright Permissions Request Form" appears on the right side of the page.

(*Circulation*. 2014;129:2440–2492.)

© 2014 by the American Heart Association, Inc. and the American College of Cardiology Foundation.

Circulation is available at <http://circ.ahajournals.org>

DOI: 10.1161/CIR.000000000000029

Table of Contents

Preamble	2441	10.1.1. Diagnosis and Follow-Up	2463
1. Introduction	2444	10.1.2. Intervention	2463
1.1. Methodology and Evidence Review	2444	10.2. Antithrombotic Therapy for Prosthetic Valves	2464
1.2. Organization of the Writing Committee	2444	10.3. Bridging Therapy for Prosthetic Valves	2466
1.3. Document Review and Approval	2444	10.4. Excessive Anticoagulation and Serious Bleeding With Prosthetic Valves	2466
1.4. Scope of the Guideline	2444	10.5. Prosthetic Valve Thrombosis	2466
2. General Principles	2444	10.5.1. Diagnosis and Follow-Up	2466
2.1. Evaluation of the Patient With Suspected VHD	2444	10.5.2. Medical Therapy	2467
2.2. Definitions of Severity of Valve Disease	2445	10.5.3. Intervention	2467
2.3. Diagnostic Testing—Diagnosis and Follow-Up: Recommendations	2445	10.6. Prosthetic Valve Stenosis	2467
2.4. Basic Principles of Medical Therapy: Recommendations	2446	10.7. Prosthetic Valve Regurgitation	2467
2.5. Evaluation of Surgical and Interventional Risk	2446	11. Infective Endocarditis: Recommendations	2467
2.6. The Heart Valve Team and Heart Valve Centers of Excellence: Recommendations	2446	11.1. Diagnosis and Follow-Up	2467
3. Aortic Stenosis: Recommendations	2447	11.2. Medical Therapy	2469
3.1. Stages of Valvular AS	2448	11.3. Intervention	2469
3.2. Diagnosis and Follow-Up	2449	12. Pregnancy and VHD: Recommendations	2471
3.3. Medical Therapy	2450	12.1. Native Valve Stenosis	2471
3.4. Timing of Intervention	2450	12.1.1. Diagnosis and Follow-Up	2471
3.5. Choice of Intervention	2451	12.1.2. Medical Therapy	2471
4. Aortic Regurgitation: Recommendations	2452	12.1.3. Intervention	2472
4.1. Stages of Chronic Aortic Regurgitation	2452	12.2. Native Valve Regurgitation	2473
4.2. Diagnosis and Follow-Up	2452	12.2.1. Diagnosis and Follow-Up	2473
4.3. Medical Therapy	2452	12.2.2. Medical Therapy	2473
4.4. Timing of Intervention	2452	12.2.3. Intervention	2473
5. Bicuspid Aortic Valve and Aortopathy: Recommendations	2454	12.3. Prosthetic Valves in Pregnancy	2474
5.1. Diagnosis and Follow-Up	2454	12.3.1. Diagnosis and Follow-Up	2474
5.2. Intervention	2454	12.3.2. Medical Therapy	2475
6. Mitral Stenosis: Recommendations	2455	13. Surgical Considerations: Recommendations	2475
6.1. Stages of MS	2455	13.1. Evaluation of Coronary Anatomy	2475
6.2. Diagnosis and Follow-Up	2455	13.2. Concomitant Procedures	2475
6.3. Medical Therapy	2455	13.2.1. Intervention for CAD	2475
6.4. Intervention	2456	13.2.2. Intervention for AF	2475
7. Mitral Regurgitation: Recommendations	2457	14. Noncardiac Surgery in Patients With VHD: Recommendations	2476
7.1. Stages of Chronic MR	2457	References	2476
7.2. Chronic Primary MR	2458	Appendix 1. Author Relationships With Industry and Other Entities (Relevant)	2486
7.2.1. Diagnosis and Follow-Up	2458	Appendix 2. Reviewer Relationships With Industry and Other Entities (Relevant)	2488
7.2.2. Medical Therapy	2458		
7.2.3. Intervention	2459		
7.3. Chronic Secondary MR	2461		
7.3.1. Diagnosis and Follow-Up	2461		
7.3.2. Medical Therapy	2461		
7.3.3. Intervention	2461		
8. Tricuspid Valve Disease: Recommendations	2461		
8.1. Stages of TR	2461		
8.2. Tricuspid Regurgitation	2461		
8.2.1. Diagnosis and Follow-Up	2461		
8.2.2. Medical Therapy	2462		
8.2.3. Intervention	2462		
8.3. Stages of Tricuspid Stenosis	2463		
8.4. Tricuspid Stenosis	2463		
8.4.1. Diagnosis and Follow-Up	2463		
8.4.2. Intervention	2463		
9. Stages of Pulmonic Valve Disease	2463		
10. Prosthetic Valves: Recommendations	2463		
10.1. Evaluation and Selection of Prosthetic Valves	2463		

Preamble

The medical profession should play a central role in evaluating evidence related to drugs, devices, and procedures for detection, management, and prevention of disease. When properly applied, expert analysis of available data on the benefits and risks of these therapies and procedures can improve the quality of care, optimize patient outcomes, and favorably affect costs by focusing resources on the most effective strategies. An organized and directed approach to a thorough review of evidence has resulted in the production of clinical practice guidelines that assist clinicians in selecting the best management strategy for an individual patient. Moreover, clinical practice guidelines can provide a foundation for other applications, such as performance measures, appropriate use criteria, and both quality improvement and clinical decision support tools.

The American College of Cardiology (ACC) and the American Heart Association (AHA) have jointly engaged in the production of guidelines in the area of cardiovascular disease since 1980. The ACC/AHA Task Force on Practice

Guidelines (Task Force) directs this effort by developing, updating, and revising practice guidelines for cardiovascular diseases and procedures.

Experts in the subject under consideration are selected from both ACC and AHA to examine subject-specific data and write guidelines. Writing committees are specifically charged with performing a literature review; weighing the strength of evidence for or against particular tests, treatments, or procedures; and including estimates of expected health outcomes where such data exist. Patient-specific modifiers, comorbidities, and issues of patient preference that may influence the choice of tests or therapies are considered, as well as frequency of follow-up and cost effectiveness. When available, information from studies on cost is considered; however, a review of data on efficacy and outcomes constitutes the primary basis for preparing recommendations in this guideline.

In analyzing the data and developing recommendations and supporting text, the writing committee uses evidence-based methodologies developed by the Task Force.¹ The Class of Recommendation (COR) is an estimate of the size of the treatment effect, with consideration given to risks versus benefits, as well as evidence and/or agreement that a given treatment or procedure is or is not useful/effective or in some situations may cause harm. The Level of Evidence (LOE) is an estimate of the certainty or precision of the treatment effect. The writing committee reviews and ranks evidence supporting each recommendation, with the weight of evidence ranked as LOE A, B, or C, according to specific definitions. The schema for the COR and LOE is summarized in Table 1, which also provides suggested phrases for writing recommendations within each COR. Studies are identified as observational, retrospective, prospective, or randomized, as appropriate. For certain conditions for which inadequate data are available, recommendations are based on expert consensus and clinical experience and are ranked as LOE C. When recommendations at LOE C are supported by historical clinical data, appropriate references (including clinical reviews) are cited if available. For issues with sparse available data, a survey of current practice among the clinician members of the writing committee is the basis for LOE C recommendations and no references are cited.

A new addition to this methodology is separation of the Class III recommendations to delineate whether the recommendation is determined to be of “no benefit” or is associated with “harm” to the patient. In addition, in view of the increasing number of comparative effectiveness studies, comparator verbs and suggested phrases for writing recommendations for the comparative effectiveness of one treatment or strategy versus another are included for COR I and IIa, LOE A or B only.

In view of the advances in medical therapy across the spectrum of cardiovascular diseases, the Task Force has designated the term guideline-directed medical therapy (GDMT) to represent optimal medical therapy as defined by ACC/AHA guideline (primarily Class I)-recommended therapies. This new term, GDMT, is used herein and throughout subsequent guidelines.

Because the ACC/AHA practice guidelines address patient populations (and clinicians) residing in North America, drugs that are not currently available in North America are discussed in the text without a specific COR. For studies performed in large numbers of subjects outside North America, each writing

committee reviews the potential impact of different practice patterns and patient populations on the treatment effect and relevance to the ACC/AHA target population to determine whether the findings should inform a specific recommendation.

The ACC/AHA practice guidelines are intended to assist clinicians in clinical decision making by describing a range of generally acceptable approaches to the diagnosis, management, and prevention of specific diseases or conditions. The guidelines attempt to define practices that meet the needs of most patients in most circumstances. The ultimate judgment about care of a particular patient must be made by the clinician and patient in light of all the circumstances presented by that patient. As a result, situations may arise in which deviations from these guidelines may be appropriate. Clinical decision making should involve consideration of the quality and availability of expertise in the area where care is provided. When these guidelines are used as the basis for regulatory or payer decisions, the goal should be improvement in quality of care. The Task Force recognizes that situations arise in which additional data are needed to inform patient care more effectively; these areas are identified within each respective guideline when appropriate.

Prescribed courses of treatment in accordance with these recommendations are effective only if followed. Because lack of patient understanding and adherence may adversely affect outcomes, clinicians should make every effort to engage the patient's active participation in prescribed medical regimens and lifestyles. In addition, patients should be informed of the risks, benefits, and alternatives to a particular treatment and should be involved in shared decision making whenever feasible, particularly for COR IIa and IIb, for which the benefit-to-risk ratio may be lower.

The Task Force makes every effort to avoid actual, potential, or perceived conflicts of interest that may arise as a result of relationships with industry and other entities (RWI) among the members of the writing committee. All writing committee members and peer reviewers of the guideline are required to disclose all current healthcare-related relationships, including those existing 12 months before initiation of the writing effort.

In December 2009, the ACC and AHA implemented a new RWI policy that requires the writing committee chair plus a minimum of 50% of the writing committee to have no relevant RWI (Appendix 1 includes the ACC/AHA definition of relevance). The Task Force and all writing committee members review their respective RWI disclosures during each conference call and/or meeting of the writing committee, and members provide updates to their RWI as changes occur. All guideline recommendations require a confidential vote by the writing committee and require approval by a consensus of the voting members. Authors' and peer reviewers' RWI pertinent to this guideline are disclosed in Appendixes 1 and 2. Members may not draft or vote on any recommendations pertaining to their RWI. Members who recused themselves from voting are indicated in the list of writing committee members with specific section recusals noted in Appendix 1. In addition, to ensure complete transparency, writing committee members' comprehensive disclosure information—including RWI not pertinent to this document—is available as an [online supplement](#).

Table 1. Applying Classification of Recommendations and Level of Evidence

		SIZE OF TREATMENT EFFECT											
		CLASS I <i>Benefit >>> Risk</i> Procedure/Treatment SHOULD be performed/administered	CLASS IIa <i>Benefit >> Risk</i> Additional studies with <i>focused objectives needed</i> IT IS REASONABLE to perform procedure/administer treatment	CLASS IIb <i>Benefit ≥ Risk</i> Additional studies with <i>broad objectives needed; additional registry data would be helpful</i> Procedure/Treatment MAY BE CONSIDERED	CLASS III <i>No Benefit or CLASS III Harm</i>								
				<table border="1"> <thead> <tr> <th></th> <th>Procedure/ Test</th> <th>Treatment</th> </tr> </thead> <tbody> <tr> <td>COR III: No benefit</td> <td>Not Helpful</td> <td>No Proven Benefit</td> </tr> <tr> <td>COR III: Harm</td> <td>Excess Cost w/o Benefit or Harmful</td> <td>Harmful to Patients</td> </tr> </tbody> </table>		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
	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											
ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT	LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	<ul style="list-style-type: none"> Recommendation that procedure or treatment is useful/effective Sufficient evidence from multiple randomized trials or meta-analyses 	<ul style="list-style-type: none"> Recommendation in favor of treatment or procedure being useful/effective Some conflicting evidence from multiple randomized trials or meta-analyses 	<ul style="list-style-type: none"> Recommendation's usefulness/efficacy less well established Greater conflicting evidence from multiple randomized trials or meta-analyses 	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> Recommendation that procedure or treatment is useful/effective Evidence from single randomized trial or nonrandomized studies 	<ul style="list-style-type: none"> Recommendation in favor of treatment or procedure being useful/effective Some conflicting evidence from single randomized trial or nonrandomized studies 	<ul style="list-style-type: none"> Recommendation's usefulness/efficacy less well established Greater conflicting evidence from single randomized trial or nonrandomized studies 	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> Recommendation that procedure or treatment is useful/effective Only expert opinion, case studies, or standard of care 	<ul style="list-style-type: none"> Recommendation in favor of treatment or procedure being useful/effective Only diverging expert opinion, case studies, or standard of care 	<ul style="list-style-type: none"> Recommendation's usefulness/efficacy less well established Only diverging expert opinion, case studies, or standard of care 	<ul style="list-style-type: none"> 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 performed/administered/other is not useful/beneficial/effective	COR III: Harm potentially harmful causes harm associated with excess morbidity/mortality should not be performed/administered/other							
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										

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. Although randomized trials are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

*Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as sex, age, history of diabetes mellitus, history of prior myocardial infarction, history of heart failure, and prior aspirin use.

†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.

Comprehensive disclosure information for the Task Force is also available online at <http://www.cardiosource.org/en/ACC/About-ACC/Who-We-Are/Leadership/Guidelines-and-Documents-Task-Forces.aspx>. The ACC and AHA exclusively sponsor the work of the writing committee without commercial support. Writing committee members volunteered their time for this activity. Guidelines are official policy of both the ACC and AHA.

In an effort to maintain relevance at the point of care for clinicians, the Task Force continues to oversee an ongoing process improvement initiative. As a result, several changes to these guidelines will be apparent, including limited narrative text, a focus on summary and evidence tables (with references linked to abstracts in PubMed), and more liberal use of summary recommendation tables (with references that support LOE) to serve as a quick reference.

In April 2011, the Institute of Medicine released 2 reports: *Finding What Works in Health Care: Standards for Systematic Reviews* and *Clinical Practice Guidelines We Can Trust*.^{2,3} It is noteworthy that the Institute of Medicine cited ACC/AHA practice guidelines as being compliant with many of the proposed standards. A thorough review of these reports and of our current methodology is under way, with further enhancements anticipated.

The recommendations in this guideline are considered current until they are superseded by a focused update, the full-text guideline is revised, or until a published addendum declares it out of date and no longer official ACC/AHA policy. The reader is encouraged to consult the full-text guideline⁴ for additional guidance and details about valvular heart disease (VHD), since the executive summary contains only the recommendations.

Jeffrey L. Anderson, MD, FACC, FAHA
Chair, ACC/AHA Task Force on Practice Guidelines

1. Introduction

1.1. Methodology and Evidence Review

The recommendations listed in this document are, whenever possible, evidence based. An extensive review was conducted on literature published through November 2012, and other selected references through October 2013 were reviewed by the guideline writing committee. The relevant data are included in evidence tables in the [Data Supplement](#). Searches were extended to studies, reviews, and other evidence conducted on human subjects and that were published in English from PubMed, EMBASE, Cochrane, Agency for Healthcare Research and Quality Reports, and other selected databases relevant to this guideline. Key search words included but were not limited to the following: *valvular heart disease, aortic stenosis, aortic regurgitation, bicuspid aortic valve, mitral stenosis, mitral regurgitation, tricuspid stenosis, tricuspid regurgitation, pulmonic stenosis, pulmonic regurgitation, prosthetic valves, anticoagulation therapy, infective endocarditis, cardiac surgery, and transcatheter aortic valve replacement*. Additionally, the committee reviewed documents related to the subject matter previously published by the ACC and AHA. The references selected and published in this document are representative and not all-inclusive.

1.2. Organization of the Writing Committee

The committee was composed of clinicians, who included cardiologists, interventionalists, surgeons, and anesthesiologists. The committee included representatives from the American Association for Thoracic Surgery, American Society of Echocardiography (ASE), Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthesiologists, and Society of Thoracic Surgeons (STS).

1.3. Document Review and Approval

This document was reviewed by 2 official reviewers each nominated by both the ACC and the AHA, as well as 1 reviewer each from the American Association for Thoracic Surgery, ASE, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthesiologists, and STS and 39 individual content reviewers (which included representatives from the following ACC committees and councils: Adult Congenital and Pediatric Cardiology Section, Association of International Governors, Council on Clinical Practice, Cardiovascular Section Leadership Council, Geriatric Cardiology Section Leadership Council, Heart Failure and Transplant Council, Interventional Council, Lifelong Learning Oversight Committee, Prevention of Cardiovascular Disease Committee, and Surgeon Council). Reviewers' RWI information was distributed to the writing committee and is published in this document (Appendix 2).

This document was approved for publication by the governing bodies of the ACC and the AHA and endorsed by the American Association for Thoracic Surgery, ASE, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthesiologists, and STS.

1.4. Scope of the Guideline

The focus of this guideline is the diagnosis and management of adult patients with valvular heart disease (VHD). A full revision of the original 1998 VHD guideline was made in 2006, and an update was made in 2008.⁵ Some recommendations from the earlier VHD guidelines have been updated as warranted by new evidence or a better understanding of earlier evidence, whereas others that were inaccurate, irrelevant, or overlapping were deleted or modified. Throughout, our goal was to provide the clinician with concise, evidence-based, contemporary recommendations and the supporting documentation to encourage their use.

The full-text version of this guideline⁴ was created in a different format from prior VHD guidelines to facilitate access to concise, relevant bytes of information at the point of care when clinical knowledge is needed the most. Thus, each COR is followed by a brief paragraph of supporting text and references. Where applicable, sections were divided into subsections of 1) diagnosis and follow-up, 2) medical therapy, and 3) intervention. The purpose of these subsections was to categorize the COR according to the clinical decision-making pathways that caregivers use in the management of patients with VHD. New recommendations for assessment of the severity of valve lesions have been proposed, based on current natural history studies of patients with VHD. The relevant data are included in evidence tables in the Data Supplement of the full-text guideline.⁴

The present document applies to adult patients with VHD. Management of patients with congenital heart disease (CHD) and infants and children with valve disease are not addressed here. The document recommends a combination of lifestyle modifications and medications that constitute GDMT. Both for GDMT and other recommended drug treatment regimens, the reader is advised to confirm dosages with product insert material and to carefully evaluate for contraindications and drug–drug interactions. Table 2 is a list of associated guidelines that may be of interest to the reader. The table is intended for use as a resource and obviates the need to repeat extant guideline recommendations.

2. General Principles

2.1. Evaluation of the Patient With Suspected VHD

Patients with VHD may present with a heart murmur, symptoms, or incidental findings of valvular abnormalities on chest imaging or noninvasive testing. Irrespective of the presentation, all patients with known or suspected VHD should undergo an initial meticulous history and physical examination, as well as a chest x-ray and electrocardiogram. A comprehensive transthoracic echocardiogram (TTE) with 2-dimensional imaging and Doppler interrogation should then be performed to correlate findings with initial impressions based on the initial clinical evaluation. The TTE will also be able to provide additional information, such as the effect of the valve lesion on the cardiac chambers and great vessels, and to assess for other concomitant valve lesions. Other ancillary testing such as transesophageal echocardiography (TEE), computed tomography (CT) or cardiac magnetic resonance (CMR) imaging, stress

Table 2. Associated Guidelines and Statements

Title	Organization	Publication Year/Reference
Recommendations for Evaluation of the Severity of Native Valvular Regurgitation With Two-Dimensional and Doppler Echocardiography	ASE	2003 ⁶
Guidelines for the Management of Adults With Congenital Heart Disease	ACC/AHA	2008 ⁸
Echocardiographic Assessment of Valve Stenosis: EAE/ASE Recommendations for Clinical Practice	EAE/ASE	2009 ⁹
Recommendations for Evaluation of Prosthetic Valves With Echocardiography and Doppler Ultrasound	ASE	2009 ¹⁰
Guideline for the Diagnosis and Treatment of Hypertrophic Cardiomyopathy	ACCF/AHA	2011 ¹¹
Guidelines on the Management of Cardiovascular Diseases During Pregnancy	ESC	2011 ¹²
Antithrombotic and Thrombolytic Therapy for Valvular Disease: Antithrombotic Therapy and Prevention of Thrombosis	ACCP	2012 ¹³
Guidelines on the Management of Valvular Heart Disease	ESC/EACTS	2012 ¹⁴
Guideline for the Management of Heart Failure	ACCF/AHA	2013 ¹⁵
Guideline for the Management of Patients With Atrial Fibrillation	AHA/ACC/HRS	2014 ¹⁶

ACC indicates American College of Cardiology; ACCF, American College of Cardiology Foundation; ACCP, American College of Chest Physicians; AF, atrial fibrillation; AHA, American Heart Association; ASE, American Society of Echocardiography; EACTS, European Association for Cardio-Thoracic Surgery; EAE, European Association of Echocardiography; ESC, European Society of Cardiology; and VHD, valvular heart disease.

testing, and diagnostic hemodynamic cardiac catheterization may be required to determine the optimal treatment for a patient with VHD. An evaluation of the possible surgical risk for each individual patient should be performed if intervention is contemplated, as well as other contributing factors such as the presence and extent of comorbidities and frailty. Follow-up of these patients is important and should consist of an annual history and physical examination in most stable patients. An evaluation of the patient may be necessary sooner than annually if there is a change in the patient's symptoms. In some valve lesions there may be unpredictable adverse consequences on the left ventricle in the absence of symptoms necessitating more frequent follow-up. The frequency of repeat testing, such as echocardiography, will be dependent on the severity of the valve lesion and its effect on the left or right ventricle, coupled with the known natural history of the valve lesion.

2.2. Definitions of Severity of Valve Disease

Classification of the severity of valve lesions should be based on multiple criteria, including the initial findings on the physical examination, which should then be correlated with data from a comprehensive TTE. Intervention should primarily be performed on patients with severe VHD in addition to other criteria outlined in this document.

This document provides a classification of the progression of VHD with 4 stages (A to D) similar to that proposed by the “2013 ACCF/AHA Guideline for the Management of Heart Failure.”¹⁸ Indication for intervention in patients with VHD is dependent on 1) the presence or absence of symptoms; 2) the severity of VHD; 3) the response of the left and/or right ventricle to the volume or pressure overload caused by VHD; 4) the effect on the pulmonary or systemic circulation; and 5) a change in heart rhythm. The stages take into consideration all of these important factors (Table 3). The criteria for the stages of each individual valve lesion are listed in Section 3.1, Section 4.1, Section 6.1, Section 7.1, Section 8.1, Section 8.3, and Section 9.

The purpose of valvular intervention is to improve symptoms and/or prolong survival, as well as to minimize the risk of VHD-related complications such as asymptomatic irreversible ventricular dysfunction, pulmonary hypertension, stroke, and atrial fibrillation (AF). Thus, the criteria for “severe” VHD are based on studies describing the natural history of patients with unoperated VHD, as well as observational studies relating the onset of symptoms to measurements of severity. In patients with stenotic lesions, there is an additional category of “very severe” stenosis based on studies of the natural history showing that prognosis becomes poorer as the severity of stenosis increases.

2.3. Diagnostic Testing—Diagnosis and Follow-Up: Recommendations

See Table 4 for the frequency of echocardiograms in asymptomatic patients with VHD and normal left ventricular (LV) function.

Table 3. Stages of Progression of VHD

Stage	Definition	Description
A	At risk	Patients with risk factors for development of VHD
B	Progressive	Patients with progressive VHD (mild-to-moderate severity and asymptomatic)
C	Asymptomatic severe	Asymptomatic patients who have the criteria for severe VHD: C1: Asymptomatic patients with severe VHD in whom the left or right ventricle remains compensated C2: Asymptomatic patients with severe VHD, with decompensation of the left or right ventricle
D	Symptomatic severe	Patients who have developed symptoms as a result of VHD

VHD indicates valvular heart disease.

Class I

1. TTE is recommended in the initial evaluation of patients with known or suspected VHD to confirm the diagnosis, establish etiology, determine severity, assess hemodynamic consequences, determine prognosis, and evaluate for timing of intervention.¹⁹⁻³⁴ (*Level of Evidence: B*)
2. TTE is recommended in patients with known VHD with any change in symptoms or physical examination findings. (*Level of Evidence: C*)
3. Periodic monitoring with TTE is recommended in asymptomatic patients with known VHD at intervals depending on valve lesion, severity, ventricular size, and ventricular function. (*Level of Evidence: C*)
4. Cardiac catheterization for hemodynamic assessment is recommended in symptomatic patients when noninvasive tests are inconclusive or when there is a discrepancy between the findings on noninvasive testing and physical examination regarding severity of the valve lesion. (*Level of Evidence: C*)

Class IIa

1. Exercise testing is reasonable in selected patients with asymptomatic severe VHD to 1) confirm the absence of symptoms, or 2) assess the hemodynamic response to exercise, or 3) determine prognosis.³⁵⁻³⁹ (*Level of Evidence: B*)

2.4. Basic Principles of Medical Therapy: Recommendations

Class I

1. Secondary prevention of rheumatic fever is indicated in patients with rheumatic heart disease, specifically mitral stenosis (MS).⁴⁰ (*Level of Evidence: C*)

Class IIa

1. Prophylaxis against infective endocarditis (IE) is reasonable for the following patients at highest

risk for adverse outcomes from IE before dental procedures that involve manipulation of gingival tissue, manipulation of the periapical region of teeth, or perforation of the oral mucosa⁴¹⁻⁴³ (*Level of Evidence: B*):

- Patients with prosthetic cardiac valves;
- Patients with previous IE;
- Cardiac transplant recipients with valve regurgitation due to a structurally abnormal valve; or
- Patients with CHD with:
 - Unrepaired cyanotic CHD, including palliative shunts and conduits;
 - Completely repaired congenital heart defect repaired with prosthetic material or device, whether placed by surgery or catheter intervention, during the first 6 months after the procedure; or
 - Repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device.

Class III: No Benefit

1. Prophylaxis against IE is not recommended in patients with VHD who are at risk of IE for nondental procedures (eg, TEE, esophagogastroduodenoscopy, colonoscopy, or cystoscopy) in the absence of active infection.⁴⁴ (*Level of Evidence: B*)

2.5. Evaluation of Surgical and Interventional Risk

See Table 5 for risk assessment combining STS risk estimate, frailty, major organ system dysfunction, and procedure-specific impediments.

2.6. The Heart Valve Team and Heart Valve Centers of Excellence: Recommendations

Class I

1. Patients with severe VHD should be evaluated by a multidisciplinary Heart Valve Team when intervention is considered. (*Level of Evidence: C*)

Table 4. Frequency of Echocardiograms in Asymptomatic Patients With VHD and Normal Left Ventricular Function

Stage	Valve Lesion			
	Aortic Stenosis*	Aortic Regurgitation	Mitral Stenosis	Mitral Regurgitation
Progressive (stage B)	Every 3–5 y (mild severity V_{max} 2.0–2.9 m/s)	Every 3–5 y (mild severity) Every 1–2 y (moderate severity)	Every 3–5 y (MVA >1.5 cm ²)	Every 3–5 y (mild severity) Every 1–2 y (moderate severity)
	Every 1–2 y (moderate severity V_{max} 3.0–3.9 m/s)			
Severe (stage C)	Every 6–12 mo (V_{max} ≥4 m/s)	Every 6–12 mo Dilating LV: more frequently	Every 1–2 y (MVA 1.0–1.5 cm ²) Once every year (MVA <1.0 cm ²)	Every 6–12 mo Dilating LV: more frequently

Patients with mixed valve disease may require serial evaluations at intervals earlier than recommended for single valve lesions.

*With normal stroke volume.

LV indicates left ventricle; MVA, mitral valve area; VHD, valvular heart disease; and V_{max} , maximum velocity.

Table 5. Risk Assessment Combining STS Risk Estimate, Frailty, Major Organ System Dysfunction, and Procedure-Specific Impediments

	Low Risk (Must Meet ALL Criteria in This Column)	Intermediate Risk (Any 1 Criterion in This Column)	High Risk (Any 1 Criterion in This Column)	Prohibitive Risk (Any 1 Criterion in This Column)
STS PROM*	<4% AND	4%–8% OR	>8% OR	Predicted risk with surgery of death or major morbidity (all-cause) >50% at 1 y
Frailty†	None AND	1 Index (mild) OR	≥2 Indices (moderate to severe) OR	
Major organ system compromise not to be improved postoperatively‡	None AND	1 Organ system OR	No more than 2 organ systems OR	≥3 Organ systems OR
Procedure-specific impediment§	None	Possible procedure-specific impediment	Possible procedure-specific impediment	Severe procedure-specific impediment

*Use of the STS PROM to predict risk in a given institution with reasonable reliability is appropriate only if institutional outcomes are within 1 standard deviation of STS average observed/expected ratio for the procedure in question.

†Seven frailty indices: Katz Activities of Daily Living (independence in feeding, bathing, dressing, transferring, toileting, and urinary continence) and independence in ambulation (no walking aid or assist required or 5-meter walk in <6 s). Other scoring systems can be applied to calculate no, mild-, or moderate-to-severe frailty.

‡Examples of major organ system compromise: Cardiac—severe LV systolic or diastolic dysfunction or RV dysfunction, fixed pulmonary hypertension; CKD stage 3 or worse; pulmonary dysfunction with FEV1 <50% or DLCO₂ <50% of predicted; CNS dysfunction (dementia, Alzheimer’s disease, Parkinson’s disease, CVA with persistent physical limitation); GI dysfunction—Crohn’s disease, ulcerative colitis, nutritional impairment, or serum albumin <3.0; cancer—active malignancy; and liver—any history of cirrhosis, variceal bleeding, or elevated INR in the absence of VKA therapy.

§Examples: tracheostomy present, heavily calcified ascending aorta, chest malformation, arterial coronary graft adherent to posterior chest wall, or radiation damage.

CKD indicates chronic kidney disease; CNS, central nervous system; CVA, stroke; DLCO₂, diffusion capacity for carbon dioxide; FEV1, forced expiratory volume in 1 s; GI, gastrointestinal; INR, international normalized ratio; LV, left ventricular; PROM, predicted risk of mortality; RV, right ventricular; STS, Society of Thoracic Surgeons; and VKA, vitamin K antagonist.

Class IIa

- 1. Consultation with or referral to a Heart Valve Center of Excellence is reasonable when discussing treatment options for 1) asymptomatic patients with severe VHD, 2) patients who may benefit from valve repair versus valve replacement, or 3) patients with multiple comorbidities for whom valve intervention is considered. (Level of Evidence: C)**

A competent, practicing cardiologist should have the ability to diagnose and direct the treatment of most patients with VHD. For instance, otherwise healthy patients with severe VHD who become symptomatic should nearly always be considered for intervention. However, more complex decision-making processes may be required in select patient populations, such as those who have asymptomatic severe VHD, those who are at high risk for intervention, or those who could benefit from specialized therapies such as valve repair or transcatheter valve intervention.

The management of patients with complex severe VHD is best achieved by a Heart Valve Team composed primarily of a cardiologist and surgeon (including a structural valve interventionist if a catheter-based therapy is being considered). In selected cases, there may be a multidisciplinary, collaborative group of caregivers, including cardiologists, structural valve interventionists, cardiovascular imaging specialists, cardiovascular surgeons, anesthesiologists, and nurses, all of whom have expertise in the management and outcomes of patients with complex VHD. The Heart Valve Team should optimize patient selection for available procedures through a comprehensive understanding of the risk–benefit ratio of different treatment strategies. This is particularly beneficial in patients in whom there are several

options for treatment, such as the elderly high-risk patient with severe symptomatic aortic stenosis (AS) being considered for transcatheter aortic valve replacement (TAVR) or surgical aortic valve replacement (AVR). The patient and family should be sufficiently educated by the Heart Valve Team about all alternatives for treatment so that their expectations can be met as fully as possible using a shared decision-making approach.

The optimal care of the patient with complex heart disease is best performed in centers that can provide all available options for diagnosis and management, including the expertise for complex aortic or mitral valve repair, aortic surgery, and transcatheter therapies. This has led to the development of Heart Valve Centers of Excellence. Heart Valve Centers of Excellence 1) are composed of experienced healthcare providers with expertise from multiple disciplines; 2) offer all available options for diagnosis and management, including complex valve repair, aortic surgery, and transcatheter therapies; 3) participate in regional or national outcome registries; 4) demonstrate adherence to national guidelines; 5) participate in continued evaluation and quality improvement processes to enhance patient outcomes; and 6) publicly report their available mortality and success rates. Decisions about intervention at the Heart Valve Centers of Excellence should be dependent on the centers’ publicly available mortality rates and operative outcomes. It is recognized that some Heart Valve Centers of Excellence may have expertise in select valve problems.

3. Aortic Stenosis: Recommendations

See Table 6 for the stages of valvular AS; Tables 7 and 8 for a summary of recommendations for choice and timing of intervention; and Figure 1 for indications for AVR in patients with AS.

Table 6. Stages of Valvular AS

Stage	Definition	Valve Anatomy	Valve Hemodynamics	Hemodynamic Consequences	Symptoms
A	At risk of AS	<ul style="list-style-type: none"> Bicuspid aortic valve (or other congenital valve anomaly) Aortic valve sclerosis 	<ul style="list-style-type: none"> Aortic $V_{max} < 2$ m/s 	<ul style="list-style-type: none"> None 	<ul style="list-style-type: none"> None
B	Progressive AS	<ul style="list-style-type: none"> Mild-to-moderate leaflet calcification of a bicuspid or trileaflet valve with some reduction in systolic motion or Rheumatic valve changes with commissural fusion 	<ul style="list-style-type: none"> Mild AS: Aortic $V_{max} < 2.0$–2.9 m/s or mean $\Delta P < 20$ mm Hg Moderate AS: Aortic $V_{max} < 3.0$–3.9 m/s or mean ΔP 20–39 mm Hg 	<ul style="list-style-type: none"> Early LV diastolic dysfunction may be present Normal LVEF 	<ul style="list-style-type: none"> None
C: Asymptomatic severe AS					
C1	Asymptomatic severe AS	<ul style="list-style-type: none"> Severe leaflet calcification or congenital stenosis with severely reduced leaflet opening 	<ul style="list-style-type: none"> Aortic $V_{max} \geq 4$ m/s or mean $\Delta P \geq 40$ mm Hg AVA typically is ≤ 1.0 cm² (or AVAi ≤ 0.6 cm²/m²) Very severe AS is an aortic $V_{max} \geq 5$ m/s or mean $\Delta P \geq 60$ mm Hg 	<ul style="list-style-type: none"> LV diastolic dysfunction Mild LV hypertrophy Normal LVEF 	<ul style="list-style-type: none"> None: Exercise testing is reasonable to confirm symptom status
C2	Asymptomatic severe AS with LV dysfunction	<ul style="list-style-type: none"> Severe leaflet calcification or congenital stenosis with severely reduced leaflet opening 	<ul style="list-style-type: none"> Aortic $V_{max} \geq 4$ m/s or mean $\Delta P \geq 40$ mm Hg AVA typically ≤ 1.0 cm² (or AVAi ≤ 0.6 cm²/m²) 	<ul style="list-style-type: none"> LVEF $< 50\%$ 	<ul style="list-style-type: none"> None
D: Symptomatic severe AS					
D1	Symptomatic severe high-gradient AS	<ul style="list-style-type: none"> Severe leaflet calcification or congenital stenosis with severely reduced leaflet opening 	<ul style="list-style-type: none"> Aortic $V_{max} \geq 4$ m/s or mean $\Delta P \geq 40$ mm Hg AVA typically ≤ 1.0 cm² (or AVAi ≤ 0.6 cm²/m²) but may be larger with mixed AS/AR 	<ul style="list-style-type: none"> LV diastolic dysfunction LV hypertrophy Pulmonary hypertension may be present 	<ul style="list-style-type: none"> Exertional dyspnea or decreased exercise tolerance Exertional angina Exertional syncope or presyncope
D2	Symptomatic severe low-flow/low-gradient AS with reduced LVEF	<ul style="list-style-type: none"> Severe leaflet calcification with severely reduced leaflet motion 	<ul style="list-style-type: none"> AVA ≤ 1.0 cm² with resting aortic $V_{max} < 4$ m/s or mean $\Delta P < 40$ mm Hg Dobutamine stress echocardiography shows AVA ≤ 1.0 cm² with $V_{max} \geq 4$ m/s at any flow rate 	<ul style="list-style-type: none"> LV diastolic dysfunction LV hypertrophy LVEF $< 50\%$ 	<ul style="list-style-type: none"> HF Angina Syncope or presyncope
D3	Symptomatic severe low-gradient AS with normal LVEF or paradoxical low-flow severe AS	<ul style="list-style-type: none"> Severe leaflet calcification with severely reduced leaflet motion 	<ul style="list-style-type: none"> AVA ≤ 1.0 cm² with aortic $V_{max} < 4$ m/s or mean $\Delta P < 40$ mm Hg Indexed AVA ≤ 0.6 cm²/m² and Stroke volume index < 35 mL/m² Measured when patient is normotensive (systolic BP < 140 mm Hg) 	<ul style="list-style-type: none"> Increased LV relative wall thickness Small LV chamber with low stroke volume Restrictive diastolic filling LVEF $\geq 50\%$ 	<ul style="list-style-type: none"> HF Angina Syncope or presyncope

AR indicates aortic regurgitation; AS, aortic stenosis; AVA, aortic valve area; AVAi, aortic valve area indexed to body surface area; BP, blood pressure; HF, heart failure; LV, left ventricular; LVEF, left ventricular ejection fraction; ΔP , pressure gradient; and V_{max} , maximum aortic velocity.

3.1. Stages of Valvular AS

Medical and interventional approaches to the management of patients with valvular AS depend on accurate diagnosis of the cause and stage of the disease process. Table 6 shows the stages of AS ranging from patients at risk of AS (stage A) or with progressive hemodynamic obstruction

(stage B) to severe asymptomatic (stage C) and symptomatic AS (stage D). Each of these stages is defined by valve anatomy, valve hemodynamics, the consequences of valve obstruction on the left ventricle and vasculature, as well as by patient symptoms. Hemodynamic severity is best characterized by the transaortic maximum velocity (or mean

Table 7. Summary of Recommendations for AS: Timing of Intervention

Recommendations	COR	LOE	References
AVR is recommended for symptomatic patients with severe high-gradient AS who have symptoms by history or on exercise testing (stage D1)	I	B	10,57–59
AVR is recommended for asymptomatic patients with severe AS (stage C2) and LVEF <50%	I	B	60,61
AVR is indicated for patients with severe AS (stage C or D) when undergoing other cardiac surgery	I	B	62,63
AVR is reasonable for asymptomatic patients with very severe AS (stage C1, aortic velocity ≥5.0 m/s) and low surgical risk	Ila	B	64,65
AVR is reasonable in asymptomatic patients (stage C1) with severe AS and decreased exercise tolerance or an exercise fall in BP	Ila	B	27,38
AVR is reasonable in symptomatic patients with low-flow/low-gradient severe AS with reduced LVEF (stage D2) with a low-dose dobutamine stress study that shows an aortic velocity ≥4.0 m/s (or mean pressure gradient ≥40 mm Hg) with a valve area ≤1.0 cm ² at any dobutamine dose	Ila	B	66–68
AVR is reasonable in symptomatic patients who have low-flow/low-gradient severe AS (stage D3) who are normotensive and have an LVEF ≥50% if clinical, hemodynamic, and anatomic data support valve obstruction as the most likely cause of symptoms	Ila	C	N/A
AVR is reasonable for patients with moderate AS (stage B) (aortic velocity 3.0–3.9 m/s) who are undergoing other cardiac surgery	Ila	C	N/A
AVR may be considered for asymptomatic patients with severe AS (stage C1) and rapid disease progression and low surgical risk	Ilb	C	N/A

AS indicates aortic stenosis; AVR, aortic valve replacement by either surgical or transcatheter approach; BP, blood pressure; COR, Class of Recommendation; LOE, Level of Evidence; LVEF, left ventricular ejection fraction; and N/A, not applicable.

pressure gradient) when the transaortic volume flow rate is normal. However, some patients with AS have a low trans-aortic volume flow rate due to either LV systolic dysfunction with a low left ventricular ejection fraction (LVEF) or due to a small hypertrophied left ventricle with a low stroke volume. These categories of severe AS pose a diagnostic and management challenge distinctly different from the challenges faced by the majority of patients with AS, who have a high gradient and velocity when AS is severe. These special subgroups with low-flow AS are designated D2 (with a low LVEF) and D3 (with a normal LVEF).

The definition of severe AS is based on natural history studies of patients with unoperated AS, which show that the prognosis is poor once there is a peak aortic valve velocity of >4.0 m per second, corresponding to a mean aortic valve gradient >40 mm Hg. In patients with low forward flow, severe AS can be present with lower aortic valve velocities and lower aortic valve gradients. Thus, an aortic valve area should be calculated in these patients. The prognosis of patients with AS is poorer when the aortic valve area is <1.0 cm². At normal flow rates, an aortic valve area of <0.8 cm² correlates with a mean aortic valve gradient >40 mm Hg. However, symptomatic patients with a calcified aortic valve with reduced opening and an aortic valve area between 0.8 cm² and 1.0 cm² should be closely evaluated to determine whether they would benefit from valve intervention. Meticulous attention to detail is required when assessing aortic valve hemodynamics, either with Doppler echocardiography or cardiac catheterization, and the inherent variability of the measurements and calculations should always be considered in clinical-decision making.

3.2. Diagnosis and Follow-Up

The overall approach to the initial diagnosis of VHD is discussed in Section 2.3, and additional considerations specific to patients with AS are addressed here.

Class I

1. TTE is indicated in patients with signs or symptoms of AS or a bicuspid aortic valve for accurate diagnosis of the cause of AS, hemodynamic severity, LV size, and systolic function, and for determining prognosis and timing of valve intervention.^{26,27,45} (Level of Evidence: B)

Class IIa

1. Low-dose dobutamine stress testing using echocardiographic or invasive hemodynamic measurements is reasonable in patients with stage D2 AS with all of the following^{46–48} (Level of Evidence: B):
 - a. Calcified aortic valve with reduced systolic opening;
 - b. LVEF less than 50%;
 - c. Calculated valve area 1.0 cm² or less; and
 - d. Aortic velocity less than 4.0 m per second or mean pressure gradient less than 40 mm Hg.
2. Exercise testing is reasonable to assess physiological changes with exercise and to confirm the absence of symptoms in asymptomatic patients with a calcified aortic valve and an aortic velocity 4.0 m per second or greater or mean pressure gradient 40 mm Hg or higher (stage C).^{27,37,38,49} (Level of Evidence: B)

Class III: Harm

1. Exercise testing should not be performed in symptomatic patients with AS when the aortic velocity is 4.0 m per second or greater or mean pressure gradient is 40 mmHg or higher (stage D) 50. (Level of Evidence: B)

Table 8. Summary of Recommendations for AS: Choice of Surgical or Transcatheter Intervention

Recommendations	COR	LOE	References
Surgical AVR is recommended in patients who meet an indication for AVR (Section 3.4) with low or intermediate surgical risk (Section 2.5 in the full-text guideline)	I	A	69,70
For patients in whom TAVR or high-risk surgical AVR is being considered, members of a Heart Valve Team should collaborate to provide optimal patient care	I	C	N/A
TAVR is recommended in patients who meet an indication for AVR for AS who have a prohibitive surgical risk and a predicted post-TAVR survival >12 mo	I	B	71,72
TAVR is a reasonable alternative to surgical AVR in patients who meet an indication for AVR (Section 3.4) and who have high surgical risk (Section 2.5 in the full-text guideline)	IIa	B	73,74
Percutaneous aortic balloon dilation may be considered as a bridge to surgical or transcatheter AVR in severely symptomatic patients with severe AS	IIb	C	N/A
TAVR is not recommended in patients in whom existing comorbidities would preclude the expected benefit from correction of AS	III: No Benefit	B	71

AS indicates aortic stenosis; AVR, aortic valve replacement; COR, Class of Recommendation; LOE, Level of Evidence; N/A, not applicable; and TAVR, transcatheter aortic valve replacement.

3.3. Medical Therapy

Class I

1. Hypertension in patients at risk for developing AS (stage A) and in patients with asymptomatic AS (stages B and C) should be treated according to standard GDMT, started at a low dose, and gradually titrated upward as needed with frequent clinical monitoring.^{51–53} (*Level of Evidence: B*)

Class IIb

1. Vasodilator therapy may be reasonable if used with invasive hemodynamic monitoring in the acute management of patients with severe decompensated AS (stage D) with New York Heart Association (NYHA) class IV heart failure (HF) symptoms. (*Level of Evidence: C*)

Class III: No Benefit

1. Statin therapy is not indicated for prevention of hemodynamic progression of AS in patients with mild-to-moderate calcific valve disease (stages B to D).^{54–56} (*Level of Evidence: A*)

3.4. Timing of Intervention

See Table 7 for a summary of recommendations from this section.

Class I

1. AVR is recommended in symptomatic patients with severe AS (stage D1) with^{10,57–59} (*Level of Evidence: B*):
 - a. Decreased systolic opening of a calcified or congenitally stenotic aortic valve; and
 - b. An aortic velocity 4.0 m per second or greater or mean pressure gradient 40 mm Hg or higher; and
 - c. Symptoms of HF, syncope, exertional dyspnea, angina, or presyncope by history or on exercise testing.

2. AVR is recommended for asymptomatic patients with severe AS (stage C2) and an LVEF less than 50% with decreased systolic opening of a calcified aortic valve with an aortic velocity 4.0 m per second or greater or mean pressure gradient 40 mm Hg or higher.^{60,61} (*Level of Evidence: B*)
2. AVR is indicated for patients with severe AS (stage C or D) when undergoing cardiac surgery for other indications when there is decreased systolic opening of a calcified aortic valve and an aortic velocity 4.0 m per second or greater or mean pressure gradient 40 mm Hg or higher.^{62,63} (*Level of Evidence: B*)

Class IIa

1. AVR is reasonable for asymptomatic patients with very severe AS (stage C1) with^{64,65} (*Level of Evidence: B*):
 - a. Decreased systolic opening of a calcified valve;
 - b. An aortic velocity 5.0 m per second or greater or mean pressure gradient 60 mm Hg or higher; and
 - c. A low surgical risk.
2. AVR is reasonable in apparently asymptomatic patients with severe AS (stage C1) with^{27,38} (*Level of Evidence: B*):
 - a. A calcified aortic valve;
 - b. An aortic velocity of 4.0 m per second to 4.9 m per second or mean pressure gradient of 40 mm Hg to 59 mm Hg; and
 - c. An exercise test demonstrating decreased exercise tolerance or a fall in systolic blood pressure (BP).
3. AVR is reasonable in symptomatic patients with low-flow/low-gradient severe AS with reduced LVEF (stage D2) with a^{66–68} (*Level of Evidence: B*):
 - a. Calcified aortic valve with reduced systolic opening;
 - b. Resting valve area.10 cm² or less;
 - c. Aortic velocity less than 4.0 m per second or mean pressure gradient less than 40 mm Hg;
 - d. LVEF less than 50%; and

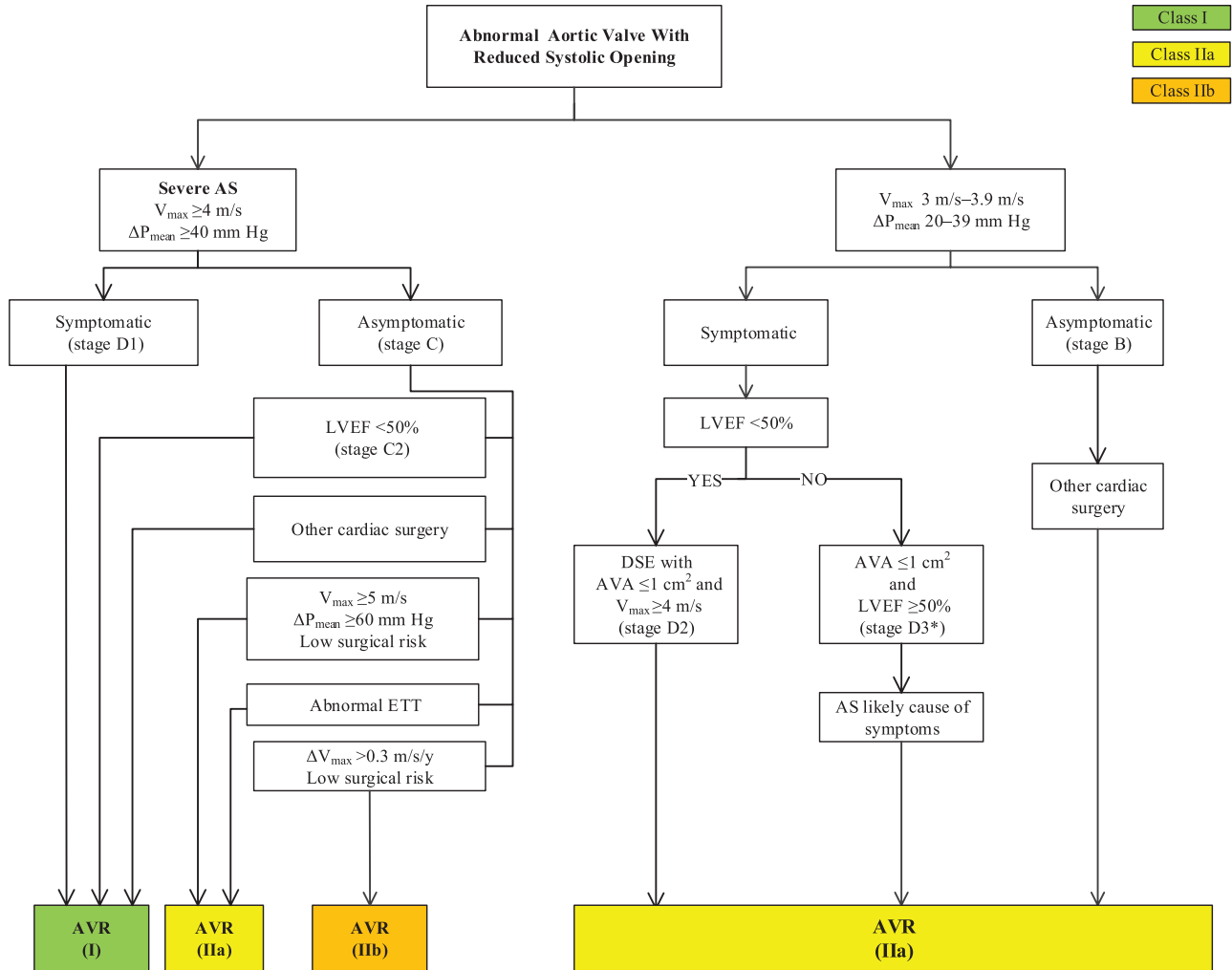


Figure 1. Indications for AVR in Patients With AS. Arrows show the decision pathways that result in a recommendation for AVR. Periodic monitoring is indicated for all patients in whom AVR is not yet indicated, including those with asymptomatic AS (stage D or C) and those with low-gradient AS (stage D2 or D3) who do not meet the criteria for intervention. *AVR should be considered with stage D3 AS only if valve obstruction is the most likely cause of symptoms, stroke volume index is <35 mL/m², indexed AVA is ≤0.6 cm²/m², and data are recorded when the patient is normotensive (systolic BP <140 mm Hg). AS indicates aortic stenosis; AVA, aortic valve area; AVR, aortic valve replacement by either surgical or transcatheter approach; BP, blood pressure; DSE, dobutamine stress echocardiography; ETT, exercise treadmill test; LVEF, left ventricular ejection fraction; ΔP_{mean}, mean pressure gradient; and V_{max}, maximum velocity.

e. A low-dose dobutamine stress study that shows an aortic velocity 4.0 m per second or greater or mean pressure gradient 40 mm Hg or higher with a valve area 1.0 cm² or less at any dobutamine dose.

4. AVR is reasonable in symptomatic patients with low-flow/low-gradient severe AS (stage D3) with an LVEF 50% or greater, a calcified aortic valve with significantly reduced leaflet motion, and a valve area 1.0 cm² or less only if clinical, hemodynamic, and anatomic data support valve obstruction as the most likely cause of symptoms and data recorded when the patient is normotensive (systolic BP <140 mm Hg) indicate (Level of Evidence: C):

- a. An aortic velocity less than 4.0 m per second or mean pressure gradient less than 40 mm Hg; and
- b. A stroke volume index less than 35 mL/m²; and
- c. An indexed valve area 0.6 cm²/m² or less.

5. AVR is reasonable for patients with moderate AS (stage B) with an aortic velocity between 3.0 m per

second and 3.9 m per second or mean pressure gradient between 20 mm Hg and 39 mm Hg who are undergoing cardiac surgery for other indications. (Level of Evidence: C)

Class IIb

- 1. AVR may be considered for asymptomatic patients with severe AS (stage C1) with an aortic velocity 4.0 m per second or greater or mean pressure gradient 40 mm Hg or higher if the patient is at low surgical risk and serial testing shows an increase in aortic velocity 0.3 m/s or greater per year. (Level of Evidence: C)

3.5. Choice of Intervention

See Table 8 for a summary of recommendations from this section.

Class I

1. **Surgical AVR is recommended in patients who meet an indication for AVR (Section 3.4) with low or intermediate surgical risk (Section 2.5 in the full-text guideline).^{69,70} (Level of Evidence: A)**
2. **For patients in whom TAVR or high-risk surgical AVR is being considered, a Heart Valve Team consisting of an integrated, multidisciplinary group of healthcare professionals with expertise in VHD, cardiac imaging, interventional cardiology, cardiac anesthesia, and cardiac surgery should collaborate to provide optimal patient care. (Level of Evidence: C)**
3. **TAVR is recommended in patients who meet an indication for AVR (Section 3.4) who have a prohibitive risk for surgical AVR (Section 2.5 in the full-text guideline) and a predicted post-TAVR survival greater than 12 months.^{71,72} (Level of Evidence: B)**

Class IIa

1. **TAVR is a reasonable alternative to surgical AVR in patients who meet an indication for AVR (Section 3.4) and who have high surgical risk for surgical AVR (Section 2.5 in the full-text guideline).^{73,74} (Level of Evidence: B)**

Class IIb

1. **Percutaneous aortic balloon dilation may be considered as a bridge to surgical AVR or TAVR in patients with severe symptomatic AS. (Level of Evidence: C)**

Class III: No Benefit

1. **TAVR is not recommended in patients in whom existing comorbidities would preclude the expected benefit from correction of AS.⁷¹ (Level of Evidence: B)**

4. Aortic Regurgitation: Recommendations**4.1. Stages of Chronic Aortic Regurgitation**

The most common causes of chronic aortic regurgitation (AR) in the United States and other developed countries are bicuspid aortic valve and calcific valve disease. In addition, AR frequently arises from primary diseases causing dilation of the ascending aorta or the sinuses of Valsalva. Another cause of AR is rheumatic heart disease (the leading cause in many developing countries). In the majority of patients with AR, the disease course is chronic and slowly progressive with increasing LV volume overload and LV adaptation via chamber dilation and hypertrophy. Management of patients with AR depends on accurate diagnosis of the cause and stage of the disease process. Table 9 shows the stages of AR ranging from patients at risk of AR (stage A) or with progressive mild-to-moderate AR (stage B) to severe asymptomatic (stage C) and

symptomatic AR (stage D). Each of these stages is defined by valve anatomy, valve hemodynamics, severity of LV dilation, and LV systolic function, as well as by patient symptoms.

See Figure 2 for indications for AVR for chronic AR.

4.2. Diagnosis and Follow-Up**Class I**

1. **TTE is indicated in patients with signs or symptoms of AR (stages A to D) for accurate diagnosis of the cause of regurgitation, regurgitant severity, and LV size and systolic function, and for determining clinical outcome and timing of valve intervention.^{34,75–84} (Level of Evidence: B)**
2. **TTE is indicated in patients with dilated aortic sinuses or ascending aorta or with a bicuspid aortic valve (stages A and B) to evaluate the presence and severity of AR.⁸⁵ (Level of Evidence: B)**
3. **CMR is indicated in patients with moderate or severe AR (stages B, C, and D) and suboptimal echocardiographic images for the assessment of LV systolic function, systolic and diastolic volumes, and measurement of AR severity.^{86,87} (Level of Evidence: B)**

4.3. Medical Therapy**Class I**

1. **Treatment of hypertension (systolic BP >140 mmHg) is recommended in patients with chronic AR (stages B and C), preferably with dihydropyridine calcium channel blockers or angiotensin-converting enzyme (ACE) inhibitors/angiotensin-receptor blockers (ARBs).^{83,88} (Level of Evidence: B)**

Class IIa

1. **Medical therapy with ACE inhibitors/ARBs and beta blockers is reasonable in patients with severe AR who have symptoms and/or LV dysfunction (stages C2 and D) when surgery is not performed because of comorbidities.^{89,90} (Level of Evidence: B)**

4.4. Timing of Intervention

See Table 10 for a summary of recommendations from this section.

Class I

1. **AVR is indicated for symptomatic patients with severe AR regardless of LV systolic function (stage D).^{33,91,92} (Level of Evidence: B)**
2. **AVR is indicated for asymptomatic patients with chronic severe AR and LV systolic dysfunction (LVEF <50%) at rest (stage C2) if no other cause for systolic dysfunction is identified.^{91,93–95} (Level of Evidence: B)**
3. **AVR is indicated for patients with severe AR (stage C or D) while undergoing cardiac surgery for other indications. (Level of Evidence: C)**

Table 9. Stages of Chronic AR

Stage	Definition	Valve Anatomy	Valve Hemodynamics	Hemodynamic Consequences	Symptoms
A	At risk of AR	<ul style="list-style-type: none"> Bicuspid aortic valve (or other congenital valve anomaly) Aortic valve sclerosis Diseases of the aortic sinuses or ascending aorta History of rheumatic fever or known rheumatic heart disease IE 	<ul style="list-style-type: none"> AR severity: none or trace 	<ul style="list-style-type: none"> None 	<ul style="list-style-type: none"> None
B	Progressive AR	<ul style="list-style-type: none"> Mild-to-moderate calcification of a trileaflet valve bicuspid aortic valve (or other congenital valve anomaly) Dilated aortic sinuses Rheumatic valve changes Previous IE 	<ul style="list-style-type: none"> Mild AR: <ul style="list-style-type: none"> Jet width <25% of LVOT; Vena contracta <0.3 cm; RVol <30 mL/beat; RF <30%; ERO <0.10 cm²; Angiography grade 1+ Moderate AR: <ul style="list-style-type: none"> Jet width 25%–64% of LVOT; Vena contracta .03–0.6 cm; RVol 30–59 mL/beat; RF 30%–49%; ERO .010–0.29 cm²; Angiography grade 2+ 	<ul style="list-style-type: none"> Normal LV systolic function Normal LV volume or mild LV dilation 	<ul style="list-style-type: none"> None
C	Asymptomatic severe AR	<ul style="list-style-type: none"> Calcific aortic valve disease Bicuspid valve (or other congenital abnormality) Dilated aortic sinuses or ascending aorta Rheumatic valve changes IE with abnormal leaflet closure or perforation 	<ul style="list-style-type: none"> Severe AR: <ul style="list-style-type: none"> Jet width ≥65% of LVOT; Vena contracta >0.6 cm; Holodiastolic flow reversal in the proximal abdominal aorta RVol ≥60 mL/beat; RF ≥50%; ERO ≥0.3 cm²; Angiography grade 3+ to 4+; In addition, diagnosis of chronic severe AR requires evidence of LV dilation 	<p>C1: Normal LVEF (≥50%) and mild-to-moderate LV dilation (LVESD ≤50 mm)</p> <p>C2: Abnormal LV systolic function with depressed LVEF (<50%) or severe LV dilatation (LVESD >50 mm or indexed LVESD >25 mm/m²)</p>	<ul style="list-style-type: none"> None; exercise testing is reasonable to confirm symptom status
D	Symptomatic severe AR	<ul style="list-style-type: none"> Calcific valve disease Bicuspid valve (or other congenital abnormality) Dilated aortic sinuses or ascending aorta Rheumatic valve changes Previous IE with abnormal leaflet closure or perforation 	<ul style="list-style-type: none"> Severe AR: <ul style="list-style-type: none"> Doppler jet width ≥65% of LVOT; Vena contracta >0.6 cm; Holodiastolic flow reversal in the proximal abdominal aorta; RVol ≥60 mL/beat; RF ≥50%; ERO ≥0.3 cm²; Angiography grade 3+ to 4+; In addition, diagnosis of chronic severe AR requires evidence of LV dilation 	<ul style="list-style-type: none"> Symptomatic severe AR may occur with normal systolic function (LVEF ≥50%), mild-to-moderate LV dysfunction (LVEF 40%–50%), or severe LV dysfunction (LVEF <40%); Moderate-to-severe LV dilation is present 	<ul style="list-style-type: none"> Exertional dyspnea or angina or more severe HF symptoms

AR indicates aortic regurgitation; ERO, effective regurgitant orifice; HF, heart failure; IE, infective endocarditis; LV, left ventricular; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic dimension; LVOT, left ventricular outflow tract; RF, regurgitant fraction; and RVol, regurgitant volume.

Class IIa

- AVR is reasonable for asymptomatic patients with severe AR with normal LV systolic function (LVEF ≥50%) but with severe LV dilation (LV end-systolic dimension [LVESD] >50 mm or indexed LVESD >25 mm/m²) (stage C2).^{96–98} (Level of Evidence: B)**
- AVR is reasonable in patients with moderate AR (stage B) while undergoing surgery on the ascending aorta, coronary artery bypass graft (CABG), or mitral valve surgery. (Level of Evidence: C)**

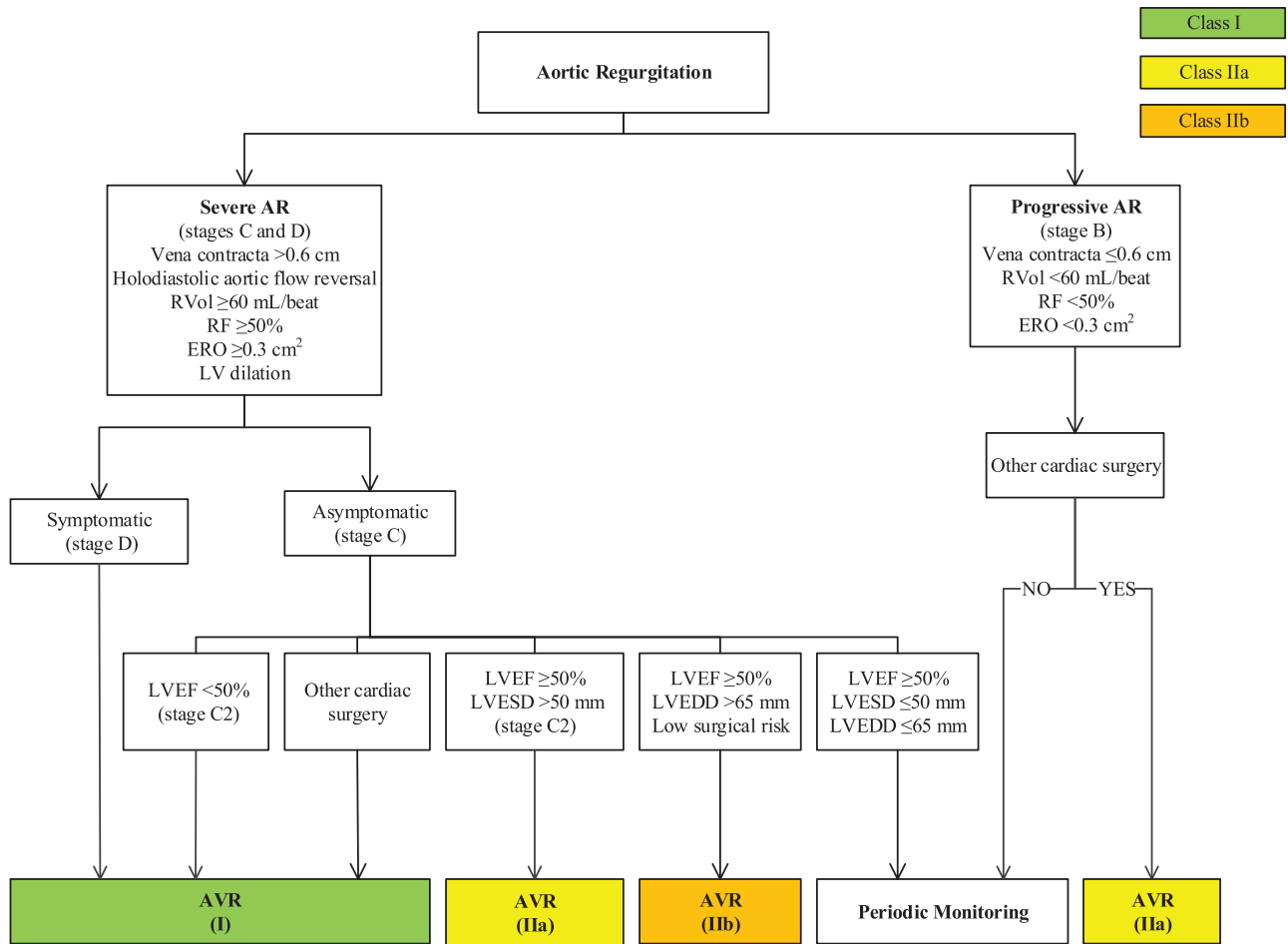


Figure 2. Indications for AVR for Chronic AR. AR indicates aortic regurgitation; AVR, aortic valve replacement (valve repair may be appropriate in selected patients); ERO, effective regurgitant orifice; LV, left ventricular; LVESD, left ventricular end-systolic dimension; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic dimension; RF, regurgitant fraction; and RVol, regurgitant volume.

Class IIb

1. AVR may be considered for asymptomatic patients with severe AR and normal LV systolic function at rest (LVEF ≥50%, stage C1) but with progressive severe LV dilatation (LV end-diastolic dimension >65 mm) if surgical risk is low. (Level of Evidence: C)

5. Bicuspid Aortic Valve and Aortopathy: Recommendations

5.1. Diagnosis and Follow-Up

Class I

1. An initial TTE is indicated in patients with a known bicuspid aortic valve to evaluate valve morphology, to measure the severity of AS and AR, and to assess the shape and diameter of the aortic sinuses and ascending aorta for prediction of clinical outcome and to determine timing of intervention.⁹⁹⁻¹⁰⁴ (Level of Evidence: B)
2. Aortic magnetic resonance angiography or CT angiography is indicated in patients with a bicuspid aortic valve when morphology of the aortic sinuses, sinotubular junction, or ascending aorta cannot be assessed accurately or fully by echocardiography. (Level of Evidence: C)

3. Serial evaluation of the size and morphology of the aortic sinuses and ascending aorta by echocardiography, CMR, or CT angiography is recommended in patients with a bicuspid aortic valve and an aortic diameter greater than 4.0 cm, with the examination interval determined by the degree and rate of progression of aortic dilation and by family history. In patients with an aortic diameter greater than 4.5 cm, this evaluation should be performed annually. (Level of Evidence: C)

5.2. Intervention

Class I

1. Operative intervention to repair the aortic sinuses or replace the ascending aorta is indicated in patients with a bicuspid aortic valve if the diameter of the aortic sinuses or ascending aorta is greater than 5.5 cm.¹⁰⁵⁻¹⁰⁷ (Level of Evidence: B)

Class IIa

1. Operative intervention to repair the aortic sinuses or replace the ascending aorta is reasonable in patients with bicuspid aortic valves if the diameter of the

Table 10. Summary of Recommendations for AR Intervention

Recommendations	COR	LOE	References
AVR is indicated for symptomatic patients with severe AR regardless of LV systolic function (stage D)	I	B	33,91,92
AVR is indicated for asymptomatic patients with chronic severe AR and LV systolic dysfunction (LVEF <50% (stage C2)	I	B	91,93–95
AVR is indicated for patients with severe AR (stage C or D) while undergoing cardiac surgery for other indications	I	C	N/A
AVR is reasonable for asymptomatic patients with severe AR with normal LV systolic function (LVEF ≥50%) but with severe LV dilation (LVESD >50 mm, stage C2)	Ila	B	96–98
AVR is reasonable in patients with moderate AR (stage B) who are undergoing other cardiac surgery	Ila	C	N/A
AVR may be considered for asymptomatic patients with severe AR and normal LV systolic function (LVEF ≥50%, stage C1) but with progressive severe LV dilation (LVEDD >65 mm) if surgical risk is low*	Ilb	C	N/A

*Particularly in the setting of progressive LV enlargement.

AR indicates aortic regurgitation; AVR, aortic valve replacement; COR, Class of Recommendation; LOE, Level of Evidence; LV, left ventricular; LVEDD, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic dimension; and N/A, not applicable.

aortic sinuses or ascending aorta is greater than 5.0 cm and a risk factor for dissection is present (family history of aortic dissection or if the rate of increase in diameter is ≥0.5 cm per year). (Level of Evidence: C)

- 2. Replacement of the ascending aorta is reasonable in patients with a bicuspid aortic valve who are undergoing aortic valve surgery because of severe AS or AR (Sections 3.4 and 4.4) if the diameter of the ascending aorta is greater than 4.5 cm. (Level of Evidence: C)**

6. Mitral Stenosis: Recommendations

6.1. Stages of MS

Medical and interventional approaches to the management of patients with valvular MS depend on accurate diagnosis of the cause and stage of the disease process. Table 11 shows the stages of mitral valve disease ranging from patients at risk of MS (stage A) or with progressive hemodynamic obstruction (stage B) to severe asymptomatic (stage C) and symptomatic MS (stage D). Each of these stages is defined by valve anatomy, valve hemodynamics, the consequences of valve obstruction on the left atrium (LA) and pulmonary circulation, and patient symptoms. The anatomic features of the stages of MS are based on a rheumatic etiology for the disease. There are patients who have a nonrheumatic etiology of MS due to senile calcific disease (Section 6.3 in the full text) in whom there is a heavily calcified mitral annulus with extension of the calcium into the leaflets. Hemodynamic severity is best characterized by the planimetered mitral valve area and the calculated mitral valve area from the diastolic pressure half-time. The definition of “severe” MS is based on the severity at which symptoms occur as well as the severity at which intervention will improve symptoms. Thus, a mitral valve area ≤1.5 cm² is considered severe. This usually corresponds to a transmitral mean gradient of >5 mmHg to 10 mmHg at a normal heart rate. However, the mean pressure gradient is highly dependent on the transvalvular flow and diastolic filling period and will vary greatly with changes in heart rate. The diastolic pressure half-time is dependent not only on the degree of mitral obstruction but also the compliance of the left ventricle and LA and other measures of mitral valve area, such as the continuity

equation or the proximal isovelocity surface area, may be used if discrepancies exist.

Supporting References: 108–114

See Figure 3 for indications for intervention for rheumatic MS.

6.2. Diagnosis and Follow-Up

Class I

- 1. TTE is indicated in patients with signs or symptoms of MS to establish the diagnosis, quantify hemodynamic severity (mean pressure gradient, mitral valve area, and pulmonary artery pressure), assess concomitant valvular lesions, and demonstrate valve morphology (to determine suitability for mitral commissurotomy).^{9,115–123} (Level of Evidence: B)**
- 2. TEE should be performed in patients considered for percutaneous mitral balloon commissurotomy to assess the presence or absence of left atrial thrombus and to further evaluate the severity of mitral regurgitation (MR).^{116,124–126} (Level of Evidence: B)**
- 3. Exercise testing with Doppler or invasive hemodynamic assessment is recommended to evaluate the response of the mean mitral gradient and pulmonary artery pressure in patients with MS when there is a discrepancy between resting Doppler echocardiographic findings and clinical symptoms or signs. (Level of Evidence: C)**

6.3. Medical Therapy

Class I

- 1. Anticoagulation (vitamin K antagonist [VKA] or heparin) is indicated in patients with 1) MS and AF (paroxysmal, persistent, or permanent), 2) MS and a prior embolic event, or 3) MS and a left atrial thrombus.^{127–133} (Level of Evidence: B)**

Class IIa

- 1. Heart rate control can be beneficial in patients with MS and AF and fast ventricular response. (Level of Evidence: C)**

Table 11. Stages of MS

Stage	Definition	Valve Anatomy	Valve Hemodynamics	Hemodynamic Consequences	Symptoms
A	At risk of MS	<ul style="list-style-type: none"> Mild valve doming during diastole 	<ul style="list-style-type: none"> Normal transmitral flow velocity 	<ul style="list-style-type: none"> None 	<ul style="list-style-type: none"> None
B	Progressive MS	<ul style="list-style-type: none"> Rheumatic valve changes with commissural fusion and diastolic doming of the mitral valve leaflets Planimetered MVA >1.5 cm² 	<ul style="list-style-type: none"> Increased transmitral flow velocities MVA >1.5 cm² Diastolic pressure half-time <150 ms 	<ul style="list-style-type: none"> Mild-to-moderate LA enlargement Normal pulmonary pressure at rest 	<ul style="list-style-type: none"> None
C	Asymptomatic severe MS	<ul style="list-style-type: none"> Rheumatic valve changes with commissural fusion and diastolic doming of the mitral valve leaflets Planimetered MVA ≤1.5 cm² (MVA ≤1.0 cm² with very severe MS) 	<ul style="list-style-type: none"> MVA ≤1.5 cm² (MVA ≤1.0 cm² with very severe MS) Diastolic pressure half-time ≥150 ms (Diastolic pressure half-time ≥220 ms with very severe MS) 	<ul style="list-style-type: none"> Severe LA enlargement Elevated PASP >30 mm Hg 	<ul style="list-style-type: none"> None
D	Symptomatic severe MS	<ul style="list-style-type: none"> Rheumatic valve changes with commissural fusion and diastolic doming of the mitral valve leaflets Planimetered MVA ≤1.5 cm² 	<ul style="list-style-type: none"> MVA ≤1.5 cm² (MVA ≤1.0 cm² with very severe MS) Diastolic pressure half-time ≥150 ms (Diastolic pressure half-time ≥220 ms with very severe MS) 	<ul style="list-style-type: none"> Severe LA enlargement Elevated PASP >30 mm Hg 	<ul style="list-style-type: none"> Decreased exercise tolerance Exertional dyspnea

The transmitral mean pressure gradient should be obtained to further determine the hemodynamic effect of the MS and is usually >5 mm Hg to 10 mm Hg in severe MS; however, due to the variability of the mean pressure gradient with heart rate and forward flow, it has not been included in the criteria for severity.

LA indicates left atrial; LV, left ventricular; MS, mitral stenosis; MVA, mitral valve area; and PASP, pulmonary artery systolic pressure.

Class IIb

- Heart rate control may be considered for patients with MS in normal sinus rhythm and symptoms associated with exercise.^{134,135} (*Level of Evidence: B*)

6.4. Intervention

See Table 12 for a summary of recommendations from this section.

Class I

- Percutaneous mitral balloon commissurotomy is recommended for symptomatic patients with severe MS (mitral valve area ≤1.5 cm², stage D) and favorable valve morphology in the absence of left atrial thrombus or moderate-to-severe MR.^{108–112,114,136} (*Level of Evidence: A*)
- Mitral valve surgery (repair, commissurotomy, or valve replacement) is indicated in severely symptomatic patients (NYHA class III to IV) with severe MS (mitral valve area ≤1.5 cm², stage D) who are not high risk for surgery and who are not candidates for or who have failed previous percutaneous mitral balloon commissurotomy.^{137–142} (*Level of Evidence: B*)
- Concomitant mitral valve surgery is indicated for patients with severe MS (mitral valve area ≤1.5 cm², stage C or D) undergoing cardiac surgery for other indications. (*Level of Evidence: C*)

Class IIa

- Percutaneous mitral balloon commissurotomy is reasonable for asymptomatic patients with very severe

MS (mitral valve area ≤1.0 cm², stage C) and favorable valve morphology in the absence of left atrial thrombus or moderate-to-severe MR.^{121,143–145} (*Level of Evidence: C*)

- Mitral valve surgery is reasonable for severely symptomatic patients (NYHA class III to IV) with severe MS (mitral valve area ≤1.5 cm², stage D), provided there are other operative indications (eg, aortic valve disease, coronary artery disease (CAD), tricuspid regurgitation (TR), aortic aneurysm). (*Level of Evidence: C*)

Class IIb

- Percutaneous mitral balloon commissurotomy may be considered for asymptomatic patients with severe MS (mitral valve area ≤1.5 cm², stage C) and valve morphology favorable for percutaneous mitral balloon commissurotomy in the absence of left atrial thrombus or moderate-to-severe MR who have new onset of AF. (*Level of Evidence: C*)
- Percutaneous mitral balloon commissurotomy may be considered for symptomatic patients with mitral valve area greater than 1.5 cm² if there is evidence of hemodynamically significant MS based on pulmonary artery wedge pressure greater than 25 mm Hg or mean mitral valve gradient greater than 15 mm Hg during exercise. (*Level of Evidence: C*)
- Percutaneous mitral balloon commissurotomy may be considered for severely symptomatic patients (NYHA class III to IV) with severe MS (mitral valve area ≤1.5 cm², stage D) who have a suboptimal valve anatomy and who are not candidates for surgery or at high risk for surgery. (*Level of Evidence: C*)

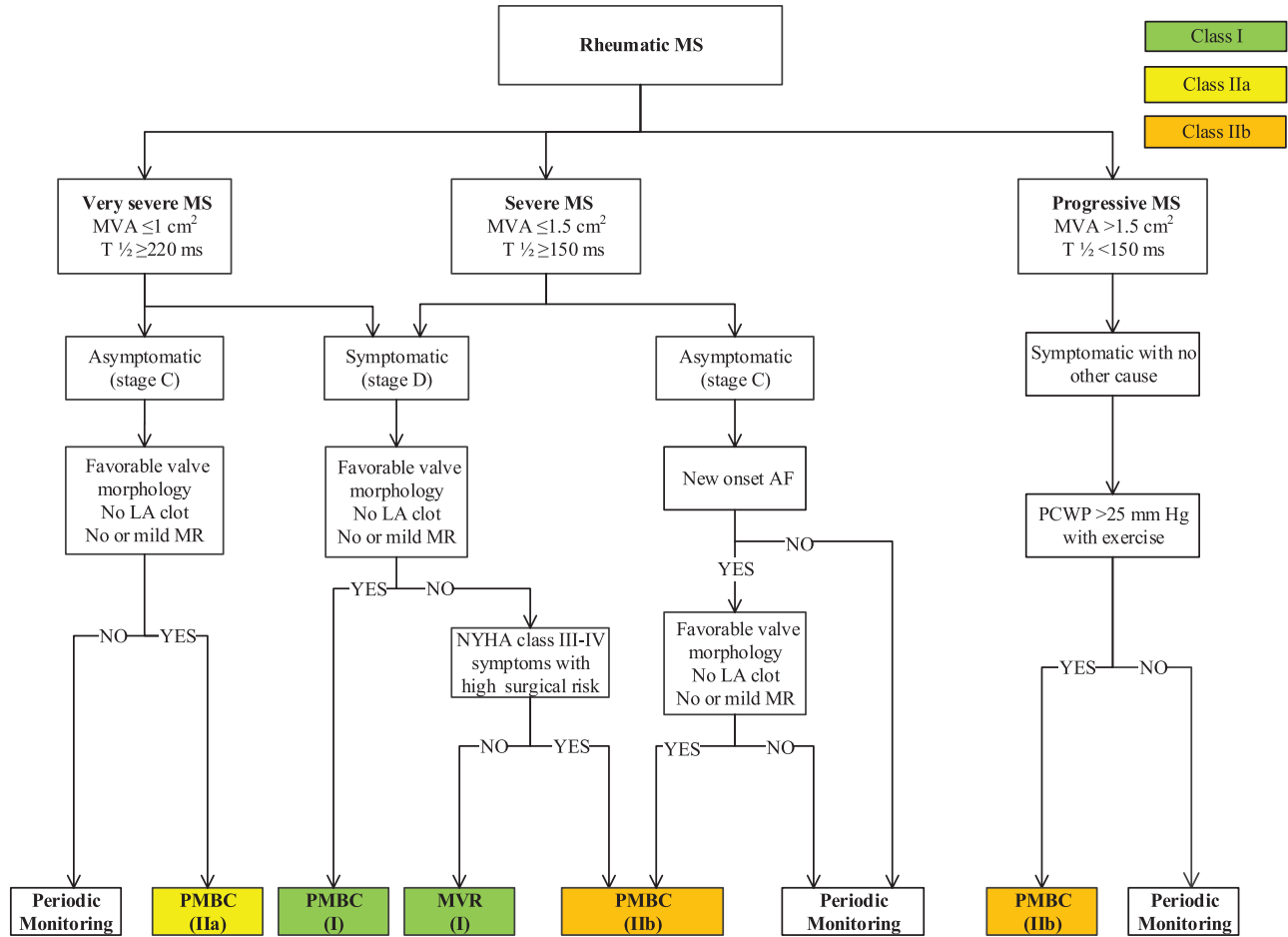


Figure 3. Indications for Intervention for Rheumatic MS. AF indicates atrial fibrillation; LA, left atrial; MR, mitral regurgitation; MS, mitral stenosis; MVA, mitral valve area; MVR, mitral valve surgery (repair or replacement); NYHA, New York Heart Association; PCWP, pulmonary capillary wedge pressure; PMBC, percutaneous mitral balloon commissurotomy; and T ½, pressure half-time.

- 4. Concomitant mitral valve surgery may be considered for patients with moderate MS (mitral valve area 1.6 cm² to 2.0 cm²) undergoing cardiac surgery for other indications. (Level of Evidence: C)
- 5. Mitral valve surgery and excision of the left atrial appendage may be considered for patients with severe MS (mitral valve area ≤1.5 cm², stages C and D) who have had recurrent embolic events while receiving adequate anticoagulation. (Level of Evidence: C)

7. Mitral Regurgitation: Recommendations

7.1. Stages of Chronic MR

In assessing the patient with chronic MR, it is critical to distinguish between chronic *primary* (degenerative) MR and chronic *secondary* (functional) MR, as these 2 conditions have more differences than similarities.

In chronic *primary* MR, the pathology of ≥1 of the components of the valve (leaflets, chordae tendineae, papillary muscles, annulus) causes valve incompetence with systolic regurgitation of blood from the left ventricle to the LA (Table 13). The most common cause of chronic *primary* MR in developed countries is mitral valve prolapse, which

has a wide spectrum of etiology and presentation. Younger populations present with severe myxomatous degeneration with gross redundancy of both anterior and posterior leaflets and the chordal apparatus (Barlow’s valve). Alternatively, older populations present with fibroelastic deficiency disease, in which lack of connective tissue leads to chordal rupture. The differentiation between these 2 etiologies has important implications for operative intervention. Other less common causes of chronic *primary* MR include IE, connective tissue disorders, rheumatic heart disease, cleft mitral valve, and radiation heart disease. If the subsequent volume overload of chronic *primary* MR is prolonged and severe, it causes myocardial damage, HF, and eventual death. Correction of the MR is curative. Thus, MR is “the disease.”

In chronic *secondary* MR, the mitral valve is usually normal (Table 14). Instead, severe LV dysfunction is caused either by CAD, related myocardial infarction (ischemic chronic *secondary* MR), or idiopathic myocardial disease (nonischemic chronic *secondary* MR). The abnormal and dilated left ventricle causes papillary muscle displacement, which in turn results in leaflet tethering with associated annular dilation that prevents coaptation. Because MR is only 1 component of the disease (severe LV dysfunction,

Table 12. Summary of Recommendations for MS Intervention

Recommendations	COR	LOE	References
PMBC is recommended for symptomatic patients with severe MS (MVA ≤ 1.5 cm ² , stage D) and favorable valve morphology in the absence of contraindications	I	A	108–112,114
Mitral valve surgery is indicated in severely symptomatic patients (NYHA class III/IV) with severe MS (MVA ≤ 1.5 cm ² , stage D) who are not high risk for surgery and who are not candidates for or failed previous PMBC	I	B	137–142
Concomitant mitral valve surgery is indicated for patients with severe MS (MVA ≤ 1.5 cm ² , stage C or D) undergoing other cardiac surgery	I	C	N/A
PMBC is reasonable for asymptomatic patients with very severe MS (MVA ≤ 1.0 cm ² , stage C) and favorable valve morphology in the absence of contraindications	IIa	C	121,143–145
Mitral valve surgery is reasonable for severely symptomatic patients (NYHA class III/IV) with severe MS (MVA ≤ 1.5 cm ² , stage D), provided there are other operative indications	IIa	C	N/A
PMBC may be considered for asymptomatic patients with severe MS (MVA ≤ 1.5 cm ² , stage C) and favorable valve morphology who have new onset of AF in the absence of contraindications	IIb	C	N/A
PMBC may be considered for symptomatic patients with MVA > 1.5 cm ² if there is evidence of hemodynamically significant MS during exercise	IIb	C	N/A
PMBC may be considered for severely symptomatic patients (NYHA class III/IV) with severe MS (MVA ≤ 1.5 cm ² , stage D) who have suboptimal valve anatomy and are not candidates for surgery or at high risk for surgery	IIb	C	N/A
Concomitant mitral valve surgery may be considered for patients with moderate MS (MVA 1.6–2.0 cm ²) undergoing other cardiac surgery	IIb	C	N/A
Mitral valve surgery and excision of the left atrial appendage may be considered for patients with severe MS (MVA ≤ 1.5 cm ² , stages C and D) who have had recurrent embolic events while receiving adequate anticoagulation	IIb	C	N/A

AF indicates atrial fibrillation; COR, Class of Recommendation; LOE, Level of Evidence; MS, mitral stenosis; MVA, mitral valve area; NYHA, New York Heart Association; and PMBC, percutaneous mitral balloon commissurotomy.

coronary disease, or idiopathic myocardial disease are the others), restoration of mitral valve competence is not by itself curative; thus, the best therapy for chronic *secondary* MR is much less clear than it is for chronic *primary* MR. The data are limited, and there is greater difficulty in defining the severity of MR in patients with *secondary* MR than in those with *primary* MR. In patients with *secondary* MR, adverse outcomes are associated with a smaller calculated effective regurgitant orifice compared to *primary* MR due to multiple reasons. The MR will likely progress due to the associated progressive LV systolic dysfunction and adverse remodeling. In addition, there is an underestimation of effective regurgitant orifice area by the 2-dimensional echocardiography–derived flow convergence method due to the crescentic shape of the regurgitant orifice. There are the additional clinical effects of a smaller amount of regurgitation in the presence of compromised LV systolic function and baseline elevated filling pressures.

7.2. Chronic Primary MR

7.2.1. Diagnosis and Follow-Up

Class I

1. TTE is indicated for baseline evaluation of LV size and function, right ventricular (RV) function and left atrial size, pulmonary artery pressure, and mechanism and severity of primary MR (stages A to D) in any patient suspected of having chronic primary MR.^{6,23,146–162} (Level of Evidence: B)
2. CMR is indicated in patients with chronic primary MR to assess LV and RV volumes, function, or MR

severity and when these issues are not satisfactorily addressed by TTE.^{157,163,164} (Level of Evidence: B)

3. Intraoperative TEE is indicated to establish the anatomic basis for chronic primary MR (stages C and D) and to guide repair.^{165,166} (Level of Evidence: B)
4. EE is indicated for evaluation of patients with chronic primary MR (stages B to D) in whom noninvasive imaging provides nondiagnostic information about severity of MR, mechanism of MR, and/or status of LV function. (Level of Evidence: C)

Class IIa

1. Exercise hemodynamics with either Doppler echocardiography or cardiac catheterization is reasonable in symptomatic patients with chronic primary MR where there is a discrepancy between symptoms and the severity of MR at rest (stages B and C).^{167,168} (Level of Evidence: B)
2. Exercise treadmill testing can be useful in patients with chronic primary MR to establish symptom status and exercise tolerance (stages B and C). (Level of Evidence: C)

7.2.2. Medical Therapy

Class IIa

1. Medical therapy for systolic dysfunction is reasonable in symptomatic patients with chronic primary MR (stage D) and LVEF less than 60% in whom surgery is not contemplated.^{169–173} (Level of Evidence: B)

Table 13. Stages of Primary MR

Grade	Definition	Valve Anatomy	Valve Hemodynamics*	Hemodynamic Consequences	Symptoms
A	At risk of MR	<ul style="list-style-type: none"> Mild mitral valve prolapse with normal coaptation Mild valve thickening and leaflet restriction 	<ul style="list-style-type: none"> No MR jet or small central jet area <20% LA on Doppler Small vena contracta <0.3 cm 	<ul style="list-style-type: none"> None 	<ul style="list-style-type: none"> None
B	Progressive MR	<ul style="list-style-type: none"> Severe mitral valve prolapse with normal coaptation Rheumatic valve changes with leaflet restriction and loss of central coaptation Prior IE 	<ul style="list-style-type: none"> Central jet MR 20%–40% LA or late systolic eccentric jet MR Vena contracta <0.7 cm Regurgitant volume <60 mL Regurgitant fraction <50% ERO <0.40 cm² Angiographic grade 1–2+ 	<ul style="list-style-type: none"> Mild LA enlargement No LV enlargement Normal pulmonary pressure 	<ul style="list-style-type: none"> None
C	Asymptomatic severe MR	<ul style="list-style-type: none"> Severe mitral valve prolapse with loss of coaptation or flail leaflet Rheumatic valve changes with leaflet restriction and loss of central coaptation Prior IE Thickening of leaflets with radiation heart disease 	<ul style="list-style-type: none"> Central jet MR >40% LA or holosystolic eccentric jet MR Vena contracta ≥0.7 cm Regurgitant volume ≥60 mL Regurgitant fraction ≥50% ERO ≥0.40 cm² Angiographic grade 3–4+ 	<ul style="list-style-type: none"> Moderate or severe LA enlargement LV enlargement Pulmonary hypertension may be present at rest or with exercise C1: LVEF >60% and LVESD <40 mm C2: LVEF ≤60% and LVESD ≥40 mm 	<ul style="list-style-type: none"> None
D	Symptomatic severe MR	<ul style="list-style-type: none"> Severe mitral valve prolapse with loss of coaptation or flail leaflet Rheumatic valve changes with leaflet restriction and loss of central coaptation Prior IE Thickening of leaflets with radiation heart disease 	<ul style="list-style-type: none"> Central jet MR >40% LA or holosystolic eccentric jet MR Vena contracta ≥0.7 cm Regurgitant volume ≥60 mL Regurgitant fraction ≥50% ERO ≥0.40 cm² Angiographic grade 3–4+ 	<ul style="list-style-type: none"> Moderate or severe LA enlargement LV enlargement Pulmonary hypertension present 	<ul style="list-style-type: none"> Decreased exercise tolerance Exertional dyspnea

*Several valve hemodynamic criteria are provided for assessment of MR severity, but not all criteria for each category will be present in each patient. Categorization of MR severity as mild, moderate, or severe depends on data quality and integration of these parameters in conjunction with other clinical evidence.

ERO indicates effective regurgitant orifice; IE, infective endocarditis; LA, left atrium/atrial; LV, left ventricular; LVEF, left ventricular ejection fraction; LVESD; left ventricular end-systolic dimension; and MR, mitral regurgitation.

Class III: No Benefit

- 1. Vasodilator therapy is not indicated for normotensive asymptomatic patients with chronic primary MR (stages B and C1) and normal systolic LV function.**^{173–178} (Level of Evidence: B)

7.2.3. Intervention

See Table 15 for a summary of recommendations from this section.

Class I

- 1. Mitral valve surgery is recommended for symptomatic patients with chronic severe primary MR**

(stage D) and LVEF greater than 30%.^{156,179} (Level of Evidence: B)

- 2. Mitral valve surgery is recommended for asymptomatic patients with chronic severe primary MR and LV dysfunction (LVEF 30% to 60% and/or LVESD ≥40 mm, stage C2).**^{150–153,180–182} (Level of Evidence: B)
- 3. Mitral valve repair is recommended in preference to mitral valve replacement (MVR) when surgical treatment is indicated for patients with chronic severe primary MR limited to the posterior leaflet.**^{155,183–198} (Level of Evidence: B)
- 4. Mitral valve repair is recommended in preference to MVR when surgical treatment is indicated for patients with chronic severe primary MR involving**

Table 14. Stages of Secondary MR

Grade	Definition	Valve Anatomy	Valve Hemodynamics*	Associated Cardiac Findings	Symptoms
A	At risk of MR	<ul style="list-style-type: none"> Normal valve leaflets, chords, and annulus in a patient with coronary disease or cardiomyopathy 	<ul style="list-style-type: none"> No MR jet or small central jet area <20% LA on Doppler Small vena contracta <0.30 cm 	<ul style="list-style-type: none"> Normal or mildly dilated LV size with fixed (infarction) or inducible (ischemia) regional wall motion abnormalities Primary myocardial disease with LV dilation and systolic dysfunction 	<ul style="list-style-type: none"> Symptoms due to coronary ischemia or HF may be present that respond to revascularization and appropriate medical therapy
B	Progressive MR	<ul style="list-style-type: none"> Regional wall motion abnormalities with mild tethering of mitral leaflet Annular dilation with mild loss of central coaptation of the mitral leaflets 	<ul style="list-style-type: none"> ERO <0.20 cm²† Regurgitant volume <30 mL Regurgitant fraction <50% 	<ul style="list-style-type: none"> Regional wall motion abnormalities with reduced LV systolic function LV dilation and systolic dysfunction due to primary myocardial disease 	<ul style="list-style-type: none"> Symptoms due to coronary ischemia or HF may be present that respond to revascularization and appropriate medical therapy
C	Asymptomatic severe MR	<ul style="list-style-type: none"> Regional wall motion abnormalities and/or LV dilation with severe tethering of mitral leaflet Annular dilation with severe loss of central coaptation of the mitral leaflets 	<ul style="list-style-type: none"> ERO ≥0.20 cm²† Regurgitant volume ≥30 mL Regurgitant fraction ≥50% 	<ul style="list-style-type: none"> Regional wall motion abnormalities with reduced LV systolic function LV dilation and systolic dysfunction due to primary myocardial disease 	<ul style="list-style-type: none"> Symptoms due to coronary ischemia or HF may be present that respond to revascularization and appropriate medical therapy
D	Symptomatic severe MR	<ul style="list-style-type: none"> Regional wall motion abnormalities and/or LV dilation with severe tethering of mitral leaflet Annular dilation with severe loss of central coaptation of the mitral leaflets 	<ul style="list-style-type: none"> ERO ≥0.20 cm²† Regurgitant volume ≥30 mL Regurgitant fraction ≥50% 	<ul style="list-style-type: none"> Regional wall motion abnormalities with reduced LV systolic function LV dilation and systolic dysfunction due to primary myocardial disease 	<ul style="list-style-type: none"> HF symptoms due to MR persist even after revascularization and optimization of medical therapy Decreased exercise tolerance Exertional dyspnea

*Several valve hemodynamic criteria are provided for assessment of MR severity, but not all criteria for each category will be present in each patient. Categorization of MR severity as mild, moderate, or severe depends on data quality and integration of these parameters in conjunction with other clinical evidence.

†The measurement of the proximal isovelocity surface area by 2D TTE in patients with secondary MR underestimates the true ERO due to the crescentic shape of the proximal convergence.

2D indicates 2-dimensional; ERO, effective regurgitant orifice; HF, heart failure; LA, left atrium; LV, left ventricular; MR, mitral regurgitation; and TTE, transthoracic echocardiogram.

the anterior leaflet or both leaflets when a successful and durable repair can be accomplished.^{195–197,199–203}
(Level of Evidence: B)

- Concomitant mitral valve repair or MVR is indicated in patients with chronic severe primary MR undergoing cardiac surgery for other indications.²⁰⁴
(Level of Evidence: B)

Class IIa

- Mitral valve repair is reasonable in asymptomatic patients with chronic severe primary MR (stage C1) with preserved LV function (LVEF >60% and LVESD <40 mm) in whom the likelihood of a successful and durable repair without residual MR is greater than 95% with an expected mortality rate of less than 1% when performed at a Heart Valve Center of Excellence.^{149,203,205–209} (Level of Evidence: B)
- Mitral valve repair is reasonable for asymptomatic patients with chronic severe nonrheumatic primary MR (stage C1) and preserved LV function (LVEF >60% and LVESD <40 mm) in whom there is a high likelihood of a successful and durable repair with 1)

new onset of AF or 2) resting pulmonary hypertension (pulmonary artery systolic arterial pressure >50 mm Hg).^{154,205,210–215} (Level of Evidence: B)

- Concomitant mitral valve repair is reasonable in patients with chronic moderate primary MR (stage B) when undergoing cardiac surgery for other indications. (Level of Evidence: C)

Class IIb

- Mitral valve surgery may be considered in symptomatic patients with chronic severe primary MR and LVEF less than or equal to 30% (stage D). (Level of Evidence: C)
- Mitral valve repair may be considered in patients with rheumatic mitral valve disease when surgical treatment is indicated if a durable and successful repair is likely or when the reliability of long-term anticoagulation management is questionable.^{194,202,203} (Level of Evidence: B)
- Transcatheter mitral valve repair may be considered for severely symptomatic patients (NYHA class III to IV) with chronic severe primary MR (stage D) who have favorable anatomy for the repair procedure and

a reasonable life expectancy but who have a prohibitive surgical risk because of severe comorbidities and remain severely symptomatic despite optimal GDMT for HF.²¹⁶ (*Level of Evidence: B*)

Class III: Harm

1. MVR should not be performed for the treatment of isolated severe primary MR limited to less than one half of the posterior leaflet unless mitral valve repair has been attempted and was unsuccessful.^{195–198} (*Level of Evidence: B*)

7.3. Chronic Secondary MR

7.3.1. Diagnosis and Follow-Up

Class I

1. TTE is useful to establish the etiology of chronic secondary MR (stages B to D) and the extent and location of wall motion abnormalities and to assess global LV function, severity of MR, and magnitude of pulmonary hypertension. (*Level of Evidence: C*)
2. Noninvasive imaging (stress nuclear/positron emission tomography, CMR, or stress echocardiography), cardiac CT angiography, or cardiac catheterization, including coronary arteriography, is useful to establish etiology of chronic secondary MR (stages B to D) and/or to assess myocardial viability, which in turn may influence management of functional MR. (*Level of Evidence: C*)

7.3.2. Medical Therapy

Class I

1. Patients with chronic secondary MR (stages B to D) and HF with reduced LVEF should receive standard GDMT therapy for HF, including ACE inhibitors, ARBs, beta blockers, and/or aldosterone antagonists as indicated.^{128,217–221} (*Level of Evidence: A*)
2. Cardiac resynchronization therapy with biventricular pacing is recommended for symptomatic patients with chronic severe secondary MR (stages B to D) who meet the indications for device therapy.^{222,223} (*Level of Evidence: A*)

7.3.3. Intervention

See Table 16 for a summary of recommendations for this section and Figure 4 for indications for surgery for MR.

Class IIa

1. Mitral valve surgery is reasonable for patients with chronic severe secondary MR (stages C and D) who are undergoing CABG or AVR. (*Level of Evidence: C*)

Class IIb

1. Mitral valve repair or replacement may be considered for severely symptomatic patients (NYHA class III to IV) with chronic severe secondary MR (stage

D) who have persistent symptoms despite optimal GDMT for HF.^{224–235} (*Level of Evidence: B*)

2. Mitral valve repair may be considered for patients with chronic moderate secondary MR (stage B) who are undergoing other cardiac surgery. (*Level of Evidence: C*)

8. Tricuspid Valve Disease: Recommendations

8.1. Stages of TR

Trace-to-mild degrees of TR of no physiological consequence are commonly detected on TTE in subjects with anatomically normal valves. *Primary* disorders of the tricuspid apparatus that can lead to more significant degrees of TR include rheumatic disease, prolapse, congenital disease (Ebstein's), IE, radiation, carcinoid, blunt chest wall trauma, RV endomyocardial biopsy-related trauma, and intra-annular RV pacemaker or implantable cardioverter-defibrillator leads. Approximately 80% of cases of significant TR are *functional* in nature and related to tricuspid annular dilation and leaflet tethering in the setting of RV remodeling due to pressure and/or volume overload. The tricuspid annulus is a saddle-shaped ellipsoid that becomes planar and circular as it dilates in an anterior-posterior direction and will often not return to its normal size and configuration after relief of RV overload. Table 17 shows the stages (A through D) of *primary* and *functional* TR as defined for other valve lesions. Severe TR (stages C and D) is associated with poor prognosis independent of age, LV and RV function, and RV size. Patients with signs or symptoms of right HF would fit into the stage D category even if they do not meet other hemodynamic or morphological criteria.

Supporting Reference: 236

8.2. Tricuspid Regurgitation

See Figure 5 for indications for surgery.

8.2.1. Diagnosis and Follow-Up

Class I

1. TTE is indicated to evaluate severity of TR, determine etiology, measure sizes of right-sided chambers and inferior vena cava, assess RV systolic function, estimate pulmonary artery systolic pressure, and characterize any associated left-sided heart disease. (*Level of Evidence: C*)

Class IIa

1. Invasive measurement of pulmonary artery pressures and pulmonary vascular resistance can be useful in patients with TR when clinical and noninvasive data regarding their values are discordant. (*Level of Evidence: C*)

Class IIb

1. CMR or real-time 3-dimensional echocardiography may be considered for assessment of RV systolic function and systolic and diastolic volumes in patients with severe TR (stages C and D) and suboptimal 2-dimensional echocardiograms. (*Level of Evidence: C*)

Table 15. Summary of Recommendations for Chronic Primary MR

Recommendations	COR	LOE	References
MV surgery is recommended for symptomatic patients with chronic severe primary MR (stage D) and LVEF >30%	I	B	156,179
MV surgery is recommended for asymptomatic patients with chronic severe primary MR and LV dysfunction (LVEF 30%–60% and/or LVESD ≥40 mm, stage C2)	I	B	150–153,180–182
MV repair is recommended in preference to MVR when surgical treatment is indicated for patients with chronic severe primary MR limited to the posterior leaflet	I	B	155,183–198
MV repair is recommended in preference to MVR when surgical treatment is indicated for patients with chronic severe primary MR involving the anterior leaflet or both leaflets when a successful and durable repair can be accomplished	I	B	195–197,199–203
Concomitant MV repair or replacement is indicated in patients with chronic severe primary MR undergoing cardiac surgery for other indications	I	B	204
MV repair is reasonable in asymptomatic patients with chronic severe primary MR (stage C1) with preserved LV function (LVEF >60% and LVESD <40 mm) in whom the likelihood of a successful and durable repair without residual MR is >95% with an expected mortality rate of <1% when performed at a Heart Valve Center of Excellence	IIa	B	149,203,205–209
MV repair is reasonable for asymptomatic patients with chronic severe nonrheumatic primary MR (stage C1) and preserved LV function in whom there is a high likelihood of a successful and durable repair with 1) new onset of AF or 2) resting pulmonary hypertension (PA systolic arterial pressure >50 mm Hg)	IIa	B	154,205,210–215
Concomitant MV repair is reasonable in patients with chronic moderate primary MR (stage B) undergoing cardiac surgery for other indications	IIa	C	N/A
MV surgery may be considered in symptomatic patients with chronic severe primary MR and LVEF ≤30% (stage D)	IIb	C	N/A
MV repair may be considered in patients with rheumatic mitral valve disease when surgical treatment is indicated if a durable and successful repair is likely or if the reliability of long-term anticoagulation management is questionable	IIb	B	194,202,203
Transcatheter MV repair may be considered for severely symptomatic patients (NYHA class III/IV) with chronic severe primary MR (stage D) who have a reasonable life expectancy but a prohibitive surgical risk because of severe comorbidities	IIb	B	216
MVR should not be performed for treatment of isolated severe primary MR limited to less than one half of the posterior leaflet unless MV repair has been attempted and was unsuccessful	III: Harm	B	195–198

AF indicates atrial fibrillation; COR, Class of Recommendation; LOE, Level of Evidence; LV, left ventricular; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic dimension; MR, mitral regurgitation; MV, mitral valve; MVR, mitral valve replacement; N/A, not applicable; NYHA, New York Heart Association; and PA, pulmonary artery.

2. Exercise testing may be considered for the assessment of exercise capacity in patients with severe TR with no or minimal symptoms (stage C). (Level of Evidence: C)

8.2.2. Medical Therapy

Class IIa

1. Diuretics can be useful for patients with severe TR and signs of right-sided HF (stage D). (Level of Evidence: C)

Class IIb

1. Medical therapies to reduce elevated pulmonary artery pressures and/or pulmonary vascular resistance might be considered in patients with severe functional TR (stages C and D). (Level of Evidence: C)

8.2.3. Intervention

Class I

1. Tricuspid valve surgery is recommended for patients with severe TR (stages C and D) undergoing left-sided valve surgery. (Level of Evidence: C)

Class IIa

1. Tricuspid valve repair can be beneficial for patients with mild, moderate, or greater functional TR (stage B) at the time of left-sided valve surgery with either 1) tricuspid annular dilation or 2) prior evidence of right HF.^{237–246} (Level of Evidence: B)
2. Tricuspid valve surgery can be beneficial for patients with symptoms due to severe primary TR that are unresponsive to medical therapy (stage D). (Level of Evidence: C)

Class IIb

1. Tricuspid valve repair may be considered for patients with moderate functional TR (stage B) and pulmonary artery hypertension at the time of left-sided valve surgery. (Level of Evidence: C)
2. Tricuspid valve surgery may be considered for asymptomatic or minimally symptomatic patients with severe primary TR (stage C) and progressive degrees of moderate or greater RV dilation and/or systolic dysfunction. (Level of Evidence: C)
3. Reoperation for isolated tricuspid valve repair or replacement may be considered for persistent

Table 16. Summary of Recommendations for Chronic Severe Secondary MR

Recommendations	COR	LOE	References
MV surgery is reasonable for patients with chronic severe secondary MR (stages C and D) who are undergoing CABG or AVR	Ia	C	N/A
MV surgery may be considered for severely symptomatic patients (NYHA class III/IV) with chronic severe secondary MR (stage D)	Iib	B	224–235
MV repair may be considered for patients with chronic moderate secondary MR (stage B) who are undergoing other cardiac surgery	Iib	C	N/A

AVR indicates aortic valve replacement; CABG, coronary artery bypass graft; COR, Class of Recommendation; LOE, Level of Evidence; MR, mitral regurgitation; MV, mitral valve; N/A, not applicable; and NYHA, New York Heart Association.

symptoms due to severe TR (stage D) in patients who have undergone previous left-sided valve surgery and who do not have severe pulmonary hypertension or significant RV systolic dysfunction. (Level of Evidence: C)

8.3. Stages of Tricuspid Stenosis

See Table 18 for the stages of severe tricuspid stenosis (TS).

8.4. Tricuspid Stenosis

8.4.1. Diagnosis and Follow-Up

Class I

1. TTE is indicated in patients with TS to assess the anatomy of the valve complex, evaluate severity of stenosis, and characterize any associated regurgitation and/or left-sided valve disease. (Level of Evidence: C)

Class Iib

1. Invasive hemodynamic assessment of severity of TS may be considered in symptomatic patients when clinical and noninvasive data are discordant. (Level of Evidence: C)

8.4.2. Intervention

Class I

1. Tricuspid valve surgery is recommended for patients with severe TS at the time of operation for left-sided valve disease. (Level of Evidence: C)
2. Tricuspid valve surgery is recommended for patients with isolated, symptomatic severe TS. (Level of Evidence: C)

Class Iib

1. Percutaneous balloon tricuspid commissurotomy might be considered in patients with isolated, symptomatic severe TS without accompanying TR. (Level of Evidence: C)

9. Stages of Pulmonic Valve Disease

See Table 19 for the stages of severe pulmonic regurgitation and Table 20 for the stages of severe pulmonic stenosis.

10. Prosthetic Valves: Recommendations

10.1. Evaluation and Selection of Prosthetic Valves

10.1.1. Diagnosis and Follow-Up

Class I

1. An initial TTE study is recommended in patients after prosthetic valve implantation for evaluation of valve hemodynamics.^{248–251} (Level of Evidence: B)
2. Repeat TTE is recommended in patients with prosthetic heart valves if there is a change in clinical symptoms or signs suggesting valve dysfunction. (Level of Evidence: C)
3. TEE is recommended when clinical symptoms or signs suggest prosthetic valve dysfunction. (Level of Evidence: C)

Class Iia

1. Annual TTE is reasonable in patients with a bioprosthetic valve after the first 10 years, even in the absence of a change in clinical status. (Level of Evidence: C)

10.1.2. Intervention

See Table 21 for a summary of recommendations for prosthetic valve choice.

Class I

1. The choice of valve intervention, that is, repair or replacement, as well as type of prosthetic heart valve, should be a shared decision-making process that accounts for the patient's values and preferences, with full disclosure of the indications for and risks of anticoagulant therapy and the potential need for and risk of reoperation. (Level of Evidence: C)
2. A bioprosthesis is recommended in patients of any age for whom anticoagulant therapy is contraindicated, cannot be managed appropriately, or is not desired. (Level of Evidence: C)

Class Iia

1. A mechanical prosthesis is reasonable for AVR or MVR in patients less than 60 years of age who do not have a contraindication to anticoagulation.^{252–254} (Level of Evidence: B)

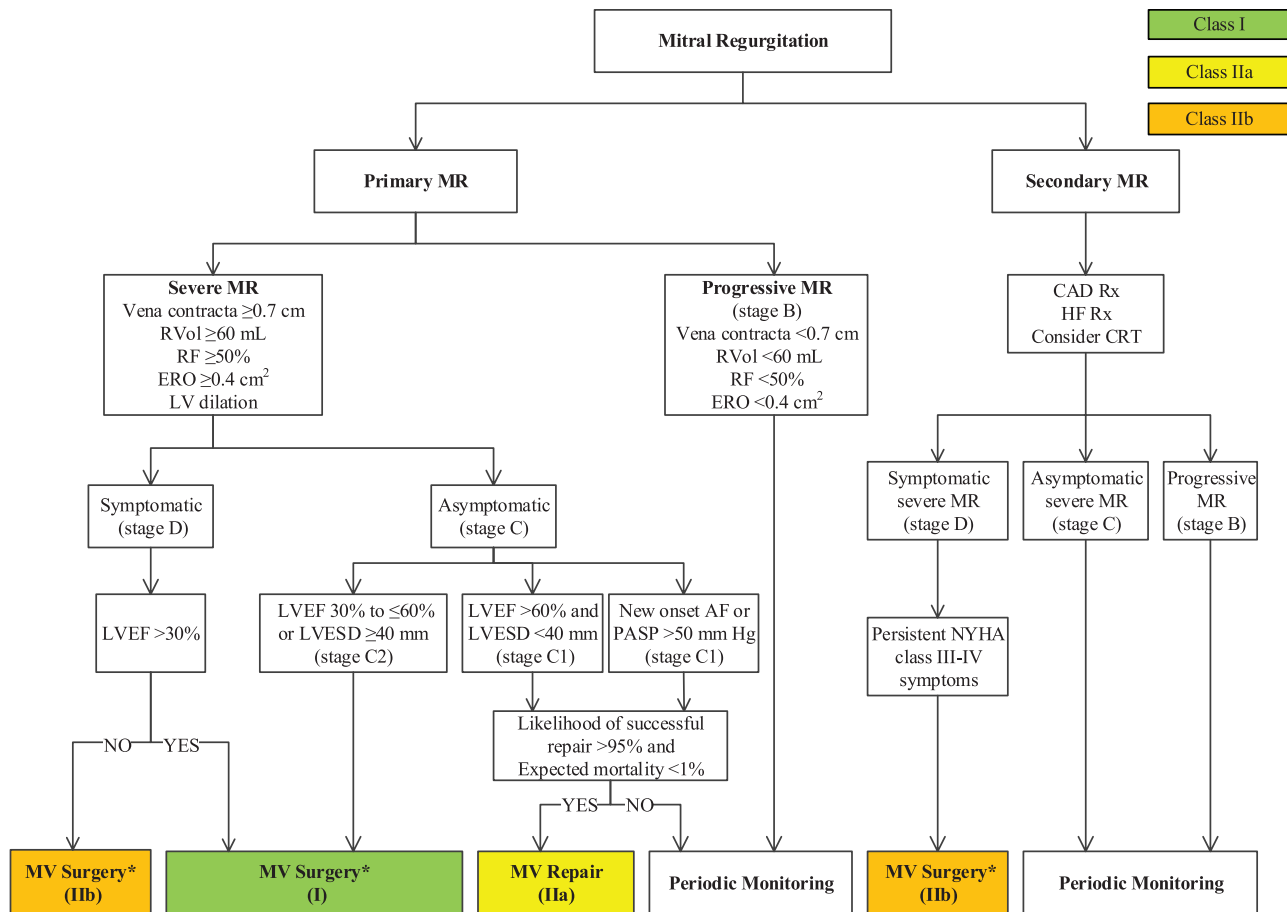


Figure 4. Indications for Surgery for MR. *Mitral valve repair is preferred over MVR when possible. AF indicates atrial fibrillation; CAD, coronary artery disease; CRT, cardiac resynchronization therapy; ERO, effective regurgitant orifice; HF, heart failure; LV, left ventricular; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic dimension; MR, mitral regurgitation, MV, mitral valve; MVR, mitral valve replacement; NYHA, New York Heart Association; PASP, pulmonary artery systolic pressure; RF, regurgitant fraction; RVol, regurgitant volume; and Rx, therapy.

2. A bioprosthesis is reasonable in patients more than 70 years of age.²⁵⁵⁻²⁵⁸ (Level of Evidence: B)
3. Either a bioprosthetic or mechanical valve is reasonable in patients between 60 and 70 years of age.^{259,260} (Level of Evidence: B)

Class IIb

1. Replacement of the aortic valve by a pulmonary autograft (the Ross procedure), when performed by an experienced surgeon, may be considered in young patients when VKA anticoagulation is contraindicated or undesirable. (Level of Evidence: C)

10.2. Antithrombotic Therapy for Prosthetic Valves

Class I

1. Anticoagulation with a VKA and international normalized ratio (INR) monitoring is recommended in patients with a mechanical prosthetic valve.²⁶¹⁻²⁶³ (Level of Evidence: A)

2. Anticoagulation with a VKA to achieve an INR of 2.5 is recommended in patients with a mechanical AVR (bileaflet or current-generation single tilting disc) and no risk factors for thromboembolism.²⁶⁴⁻²⁶⁶ (Level of Evidence: B)
3. Anticoagulation with a VKA is indicated to achieve an INR of 3.0 in patients with a mechanical AVR and additional risk factors for thromboembolic events (AF, previous thromboembolism, LV dysfunction, or hypercoagulable conditions) or an older-generation mechanical AVR (such as ball-in-cage).²⁶⁷ (Level of Evidence: B)
4. Anticoagulation with a VKA is indicated to achieve an INR of 3.0 in patients with a mechanical MVR.^{267,268} (Level of Evidence: B)
5. Aspirin 75 mg to 100 mg daily is recommended in addition to anticoagulation with a VKA in patients with a mechanical valve prosthesis.^{269,270} (Level of Evidence: A)

Class IIa

1. Aspirin 75 mg to 100 mg per day is reasonable in all patients with a bioprosthetic aortic or mitral valve.²⁷¹⁻²⁷⁴ (Level of Evidence: B)

Table 17. Stages of TR

Stage	Definition	Valve Anatomy	Valve Hemodynamics*	Hemodynamic Consequences	Symptoms
A	At risk of TR	Primary <ul style="list-style-type: none"> Mild rheumatic change Mild prolapse Other (eg, IE with vegetation, early carcinoid deposition, radiation) Intra-annular RV pacemaker or ICD lead Postcardiac transplant (biopsy related) Functional <ul style="list-style-type: none"> Normal Early annular dilation 	<ul style="list-style-type: none"> No or trace TR 	<ul style="list-style-type: none"> None 	<ul style="list-style-type: none"> None or in relation to other left heart or pulmonary/pulmonary vascular disease
B	Progressive TR	Primary <ul style="list-style-type: none"> Progressive leaflet deterioration/destruction Moderate-to-severe prolapse, limited chordal rupture Functional <ul style="list-style-type: none"> Early annular dilation Moderate leaflet tethering 	Mild TR <ul style="list-style-type: none"> Central jet area <5.0 cm² Vena contracta width not defined CW jet density and contour: soft and parabolic Hepatic vein flow: systolic dominance Moderate TR <ul style="list-style-type: none"> Central jet area 5–10 cm² Vena contracta width not defined but <0.70 cm CW jet density and contour: dense, variable contour Hepatic vein flow: systolic blunting 	Mild TR <ul style="list-style-type: none"> RV/RA/IVC size normal Moderate TR <ul style="list-style-type: none"> No RV enlargement No or mild RA enlargement No or mild IVC enlargement with normal respirophasic variation Normal RA pressure 	<ul style="list-style-type: none"> None or in relation to other left heart or pulmonary/pulmonary vascular disease
C	Asymptomatic severe TR	Primary <ul style="list-style-type: none"> Flail or grossly distorted leaflets Functional <ul style="list-style-type: none"> Severe annular dilation (>40 mm or 21 mm/m²) Marked leaflet tethering 	<ul style="list-style-type: none"> Central jet area >10.0 cm² Vena contracta width >0.7 cm CW jet density and contour: dense, triangular with early peak Hepatic vein flow: systolic reversal 	<ul style="list-style-type: none"> RV/RA/IVC dilated with decreased IVC respirophasic variation Elevated RA pressure with “c-V” wave Diastolic interventricular septal flattening may be present 	<ul style="list-style-type: none"> None, or in relation to other left heart or pulmonary/pulmonary vascular disease
D	Symptomatic severe TR	Primary <ul style="list-style-type: none"> Flail or grossly distorted leaflets Functional <ul style="list-style-type: none"> Severe annular dilation (>40 mm or >21 mm/m²) Marked leaflet tethering 	<ul style="list-style-type: none"> Central jet area >10.0 cm² Vena contracta width >0.70 cm CW jet density and contour: dense, triangular with early peak Hepatic vein flow: systolic reversal 	<ul style="list-style-type: none"> RV/RA/IVC dilated with decreased IVC respirophasic variation Elevated RA pressure with “c-V” wave Diastolic interventricular septal flattening Reduced RV systolic function in late phase 	<ul style="list-style-type: none"> Fatigue, palpitations, dyspnea, abdominal bloating, anorexia, edema

CW indicates continuous wave; ICD, implantable cardioverter-defibrillator; IE, infective endocarditis; IVC, inferior vena cava; RA, right atrium; RV, right ventricle; and TR, tricuspid regurgitation.

*Several valve hemodynamic criteria are provided for assessment of severity of TR, but not all criteria for each category will necessarily be present in every patient. Categorization of severity of TR as mild, moderate, or severe also depends on image quality and integration of these parameters with clinical findings.

2. Anticoagulation with a VKA is reasonable for the first 3 months after bioprosthetic MVR or repair to achieve an INR of 2.5.²⁷⁵ (Level of Evidence: C)

2. Clopidogrel 75 mg daily may be reasonable for the first 6 months after TAVR in addition to life-long aspirin 75 mg to 100 mg daily. (Level of Evidence: C)

Class IIb

1. Anticoagulation, with a VKA, to achieve an INR of 2.5 may be reasonable for the first 3 months after bioprosthetic AVR.²⁷⁶ (Level of Evidence: B)

Class III: Harm

1. Anticoagulant therapy with oral direct thrombin inhibitors or anti-Xa agents should not be used in patients with mechanical valve prostheses.^{277–279} (Level of Evidence: B)

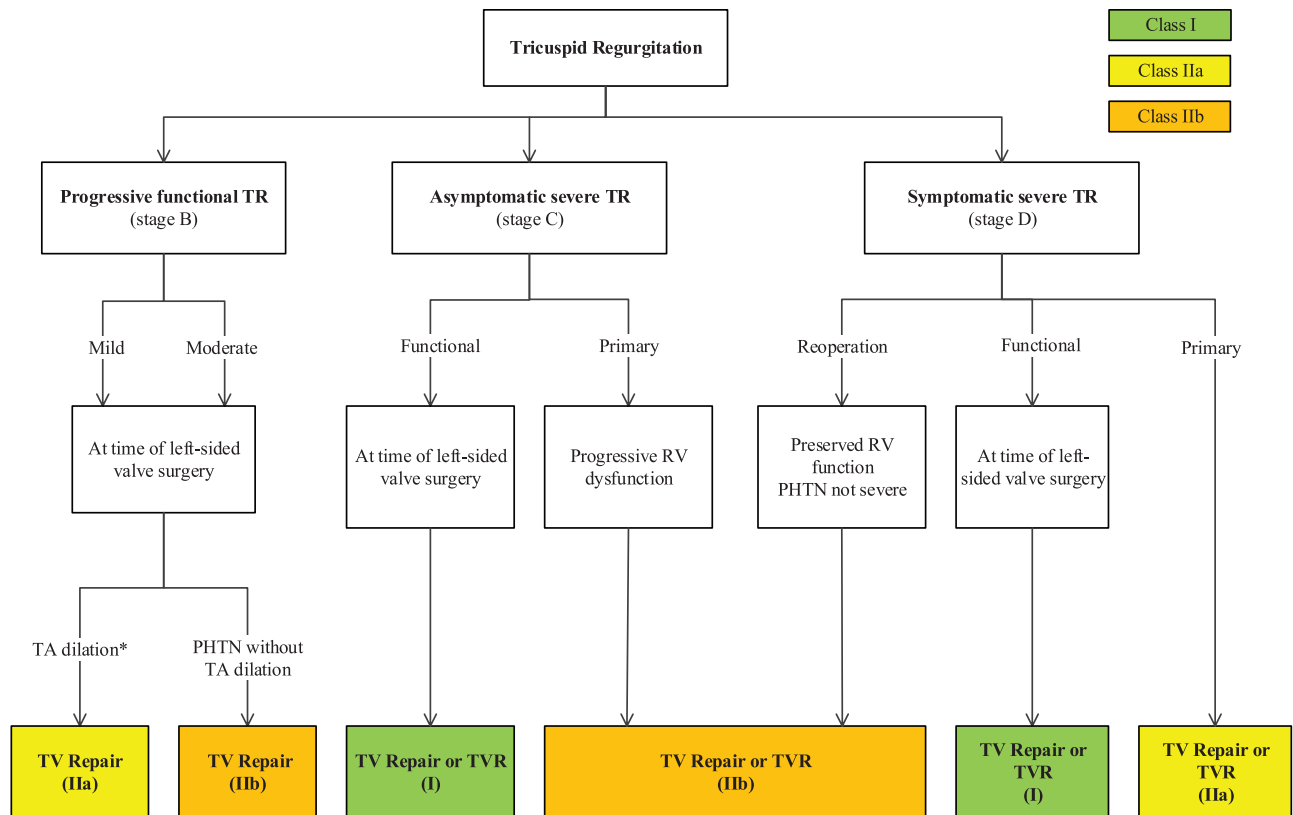


Figure 5. Indications for Surgery. *See Table 17 for definition of stages. TA dilation is defined by >40 mm on TTE (>21 mm/m²) or >70 mm on direct intraoperative measurement. LV indicates left ventricular; PHTN, pulmonary hypertension; RV, right ventricular; TA, tricuspid annular; TR, tricuspid regurgitation; TTE, transthoracic echocardiogram; TV, tricuspid valve; and TVR, tricuspid valve replacement.

10.3. Bridging Therapy for Prosthetic Valves

Class I

- Continuation of VKA anticoagulation with a therapeutic INR is recommended in patients with mechanical heart valves undergoing minor procedures (such as dental extractions or cataract removal) where bleeding is easily controlled. (*Level of Evidence: C*)
- Temporary interruption of VKA anticoagulation, without bridging agents while the INR is subtherapeutic, is recommended in patients with a bileaflet mechanical AVR and no other risk factors for thrombosis who are undergoing invasive or surgical procedures. (*Level of Evidence: C*)
- Bridging anticoagulation with either intravenous unfractionated heparin (UFH) or subcutaneous low-molecular-weight heparin (LMWH) is recommended during the time interval when the INR is subtherapeutic preoperatively in patients who are undergoing invasive or surgical procedures with a 1) mechanical AVR and any thromboembolic risk factor, 2) older-generation mechanical AVR, or 3) mechanical MVR. (*Level of Evidence: C*)

Class IIa

- Administration of fresh frozen plasma or prothrombin complex concentrate is reasonable in patients

with mechanical valves receiving VKA therapy who require emergency noncardiac surgery or invasive procedures. (*Level of Evidence: C*)

10.4. Excessive Anticoagulation and Serious Bleeding With Prosthetic Valves

See Figure 6 for anticoagulation for prosthetic valves.

Class IIa

- Administration of fresh frozen plasma or prothrombin complex concentrate is reasonable in patients with mechanical valves and uncontrollable bleeding who require reversal of anticoagulation.^{280,281} (*Level of Evidence: B*)

10.5. Prosthetic Valve Thrombosis

See Figure 7 for evaluation and management of suspected valve thrombosis.

10.5.1. Diagnosis and Follow-Up

Class I

- TTE is indicated in patients with suspected prosthetic valve thrombosis to assess hemodynamic severity and follow resolution of valve dysfunction.^{282,283} (*Level of Evidence: B*)

Table 18. Stages of Severe TS

Stage	Definition	Valve Anatomy	Valve Hemodynamics	Hemodynamic Consequences	Symptoms
C, D	Severe TS	<ul style="list-style-type: none"> Thickened, distorted, calcified leaflets 	<ul style="list-style-type: none"> T ½ ≥190 ms Valve area ≤1.0 cm² 	<ul style="list-style-type: none"> RA/IVC enlargement 	<ul style="list-style-type: none"> None or variable and dependent on severity of associated valve disease and degree of obstruction

The transtricuspid diastolic gradient is highly variable and is affected by heart rate, forward flow, and phases of the respiratory cycle. However, severe TS usually has mean pressure gradients >5 to 10 mm Hg at heart rate 70 bpm.

bpm indicates beats per minute; IVC, inferior vena cava; RA, right atrium; T ½, pressure half-time; and TS, tricuspid stenosis.⁹

2. TEE is indicated in patients with suspected prosthetic valve thrombosis to assess thrombus size and valve motion.^{283–285} (*Level of Evidence: B*)

Class IIa

1. Fluoroscopy or CT is reasonable in patients with suspected valve thrombosis to assess valve motion. (*Level of Evidence: C*)

10.5.2. Medical Therapy

Class IIa

- 1. Fibrinolytic therapy is reasonable for patients with a thrombosed left-sided prosthetic heart valve, recent onset (<14 days) of NYHA class I to II symptoms, and a small thrombus (<0.8 cm²).**^{283,286} (*Level of Evidence: B*)
- 2. Fibrinolytic therapy is reasonable for thrombosed right-sided prosthetic heart valves.**^{287,288} (*Level of Evidence: B*)

10.5.3. Intervention

Class I

1. Emergency surgery is recommended for patients with a thrombosed left-sided prosthetic heart valve with NYHA class III to IV symptoms.^{287,289,290} (*Level of Evidence: B*)

Class IIa

1. Emergency surgery is reasonable for patients with a thrombosed left-sided prosthetic heart valve with a mobile or large thrombus (>0.8 cm²).^{283,285,290} (*Level of Evidence: C*)

10.6. Prosthetic Valve Stenosis

Class I

1. Repeat valve replacement is indicated for severe symptomatic prosthetic valve stenosis. (*Level of Evidence: C*)

10.7. Prosthetic Valve Regurgitation

Class I

1. Surgery is recommended for operable patients with mechanical heart valves with intractable hemolysis or HF due to severe prosthetic or paraprosthetic regurgitation.^{291,292} (*Level of Evidence: B*)

Class IIa

- 1. Surgery is reasonable for operable patients with severe symptomatic or asymptomatic bioprosthetic regurgitation.** (*Level of Evidence C*)
- 2. Percutaneous repair of paravalvular regurgitation is reasonable in patients with prosthetic heart valves and intractable hemolysis or NYHA class III/IV HF who are at high risk for surgery and have anatomic features suitable for catheter-based therapy when performed in centers with expertise in the procedure.**^{293–295} (*Level of Evidence B*)

11. Infective Endocarditis: Recommendations

11.1. Diagnosis and Follow-Up

See Figure 8 for recommendations for imaging studies in native valve endocarditis and prosthetic valve endocarditis.

Table 19. Stages of Severe Pulmonic Regurgitation

Stage	Definition	Valve Anatomy	Valve Hemodynamics	Hemodynamic Consequences	Symptoms
C, D	Severe PR	<ul style="list-style-type: none"> Distorted or absent leaflets, annular dilation 	<ul style="list-style-type: none"> Color jet fills RVOT CW jet density and contour: dense laminar flow with steep deceleration slope; may terminate abruptly 	<ul style="list-style-type: none"> Paradoxical septal motion (volume overload pattern) RV enlargement 	<ul style="list-style-type: none"> None or variable and dependent on cause of PR and RV function

CW indicates continuous wave; PR, pulmonic regurgitation; RV, right ventricular; and RVOT, right ventricular outflow tract.²⁴⁷

Table 20. Stages of Severe Pulmonic Stenosis

Stage	Definition	Valve Anatomy	Valve Hemodynamics	Hemodynamic Consequences	Symptoms
C, D	Severe PS	<ul style="list-style-type: none"> Thickened, distorted, possibly calcified leaflets with systolic doming and/or reduced excursion Other anatomic abnormalities may be present, such as narrowed RVOT 	<ul style="list-style-type: none"> $V_{max} > 4$ m/s; peak instantaneous gradient > 64 mm Hg 	<ul style="list-style-type: none"> RVH Possible RV, RA enlargement Poststenotic enlargement of main PA 	<ul style="list-style-type: none"> None or variable and dependent on severity of obstruction

PA indicates pulmonary artery; PS, pulmonic stenosis; RA, right atrium; RV, right ventricle; RVH, right ventricular hypertrophy; RVOT, right ventricular outflow; and V_{max} maximal pulmonic valve jet velocity.⁹

Class I

- At least 2 sets of blood cultures should be obtained in patients at risk for IE (eg, those with congenital or acquired VHD, previous IE, prosthetic heart valves, certain congenital or heritable heart malformations, immunodeficiency states, injection drug users) who have unexplained fever for more than 48 hours²⁹⁶ (*Level of Evidence: B*) or patients with newly diagnosed left-sided valve regurgitation. (*Level of Evidence: C*)
- The Modified Duke Criteria should be used in evaluating a patient with suspected IE (Tables 24 and 25 in the full-text guideline).^{297–300} (*Level of Evidence: B*)
- Patients with IE should be evaluated and managed with consultation of a multispecialty Heart Valve Team including an infectious disease specialist, cardiologist, and cardiac surgeon. In surgically managed patients, this team should also include a cardiac anesthesiologist.³⁰¹ (*Level of Evidence: B*)
- TTE is recommended in patients with suspected IE to identify vegetations, characterize the hemodynamic severity of valvular lesions, assess ventricular function and pulmonary pressures, and detect complications.^{302–306} (*Level of Evidence: B*)
- TEE is recommended in all patients with known or suspected IE when TTE is nondiagnostic, when complications have developed or are clinically suspected, or when intracardiac device leads are present.^{307–315} (*Level of Evidence: B*)

- TTE and/or TEE are recommended for re-evaluation of patients with IE who have a change in clinical signs or symptoms (eg, new murmur, embolism, persistent fever, HF, abscess, or atrioventricular heart block) and in patients at high risk of complications (eg, extensive infected tissue/large vegetation on initial echocardiogram or staphylococcal, enterococcal, fungal infections).^{316,317} (*Level of Evidence: B*)
- Intraoperative TEE is recommended for patients undergoing valve surgery for IE.^{318,319} (*Level of Evidence: B*)

Class IIa

- TEE is reasonable to diagnose possible IE in patients with *Staphylococcal aureus* bacteremia without a known source.^{320–322} (*Level of Evidence: B*)
- TEE is reasonable to diagnose IE of a prosthetic valve in the presence of persistent fever without bacteremia or a new murmur.^{323,324} (*Level of Evidence: B*)
- Cardiac CT is reasonable to evaluate morphology/anatomy in the setting of suspected paravalvular infections when the anatomy cannot be clearly delineated by echocardiography.^{325–328} (*Level of Evidence: B*)

Class IIb

- TEE might be considered to detect concomitant staphylococcal IE in nosocomial *Staphylococcal aureus* bacteremia with a known portal of entry from an extracardiac source.^{329–331} (*Level of Evidence: B*)

Table 21. Summary of Recommendations for Prosthetic Valve Choice

Recommendations	COR	LOE	References
Choice of valve intervention and prosthetic valve type should be a shared decision process	I	C	N/A
A bioprosthesis is recommended in patients of any age for whom anticoagulant therapy is contraindicated, cannot be managed appropriately, or is not desired	I	C	N/A
A mechanical prosthesis is reasonable for AVR or MVR in patients <60 y of age who do not have a contraindication to anticoagulation	IIa	B	252–254
A bioprosthesis is reasonable in patients >70 y of age	IIa	B	255–258
Either a bioprosthetic or mechanical valve is reasonable in patients between 60 y and 70 y of age	IIa	B	259,260
Replacement of the aortic valve by a pulmonary autograft (the Ross procedure), when performed by an experienced surgeon, may be considered in young patients when VKA anticoagulation is contraindicated or undesirable	IIb	C	N/A

AVR indicates aortic valve replacement; COR, Class of Recommendation; LOE, Level of Evidence; MVR, mitral valve replacement; N/A, not applicable; and VKA, vitamin K antagonist.

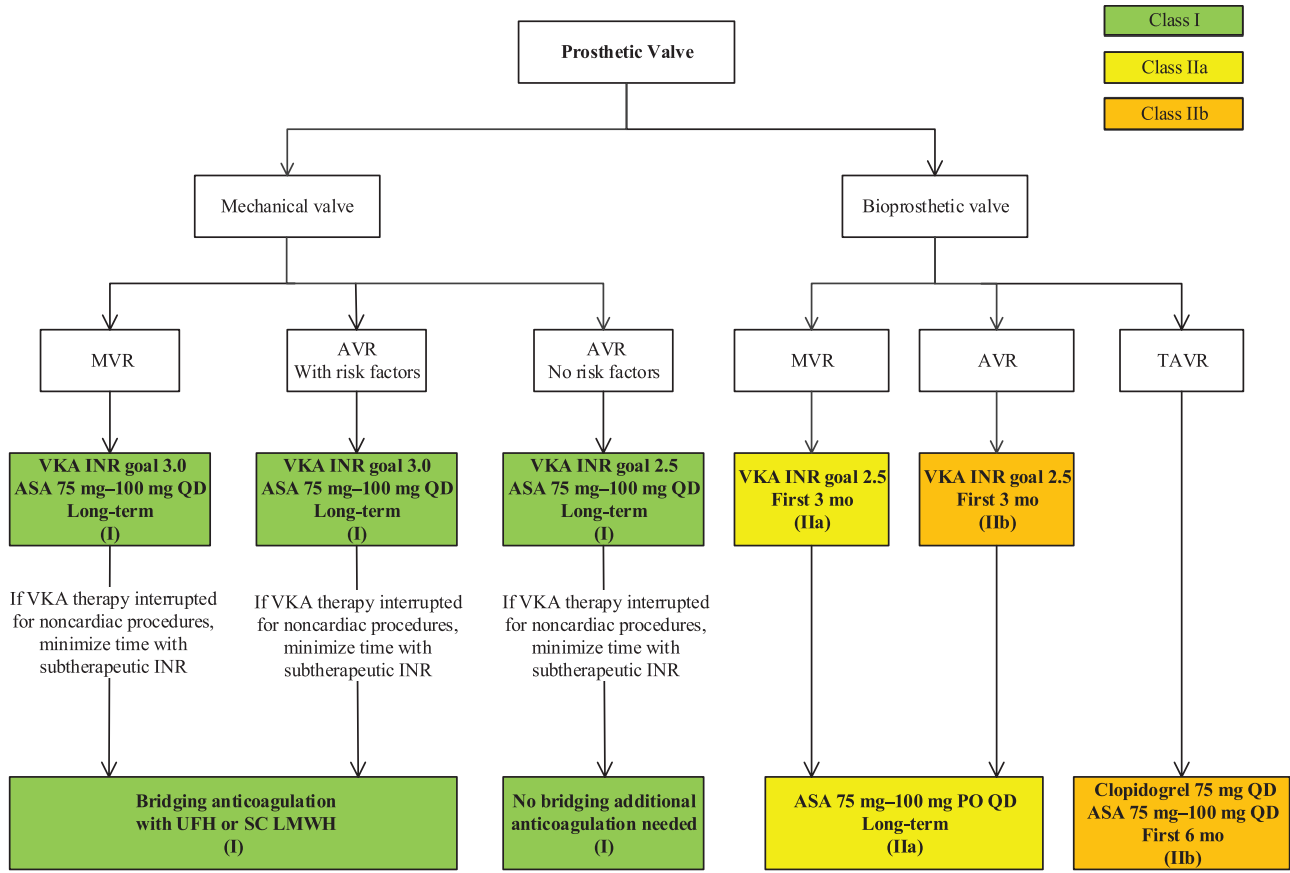


Figure 6. Anticoagulation for Prosthetic Valves. Risk factors include AF, previous thromboembolism, LV dysfunction, hypercoagulable condition, and older-generation mechanical AVR. AF indicates atrial fibrillation; ASA, aspirin; AVR, aortic valve replacement; INR, international normalized ratio; LMWH, low-molecular-weight heparin; MVR, mitral valve replacement; PO, by mouth; QD, every day; SC, subcutaneous; TAVR, transcatheter aortic valve replacement; UFH, unfractionated heparin; and VKA, vitamin K antagonist.

11.2. Medical Therapy

Class I

1. Appropriate antibiotic therapy should be initiated and continued after blood cultures are obtained with guidance from antibiotic sensitivity data and infectious disease consultants.²⁹⁶ (Level of Evidence: B)

Class IIa

1. It is reasonable to temporarily discontinue anticoagulation in patients with IE who develop central nervous system symptoms compatible with embolism or stroke regardless of the other indications for anticoagulation.³³²⁻³³⁷ (Level of Evidence: B)

Class IIb

1. Temporary discontinuation of VKA anticoagulation might be considered in patients receiving VKA anticoagulation at the time of IE diagnosis.^{333,338-341} (Level of Evidence: B)

Class III: Harm

1. Patients with known VHD should not receive antibiotics before blood cultures are obtained for unexplained fever. (Level of Evidence: C)

11.3. Intervention

See Figure 9 for diagnosis and treatment of IE.

Class I

1. Decisions about timing of surgical intervention should be made by a multispecialty Heart Valve Team of cardiology, cardiothoracic surgery, and infectious disease specialists.³⁰¹ (Level of Evidence: B)
2. Early surgery (during initial hospitalization before completion of a full therapeutic course of antibiotics) is indicated in patients with IE who present with valve dysfunction resulting in symptoms of HF.³⁴²⁻³⁴⁷ (Level of Evidence: B)
3. Early surgery (during initial hospitalization before completion of a full therapeutic course of antibiotics) is indicated in patients with left-sided IE caused by *Staphylococcal aureus*, fungal, or other highly resistant organisms.³⁴⁷⁻³⁵⁴ (Level of Evidence: B)

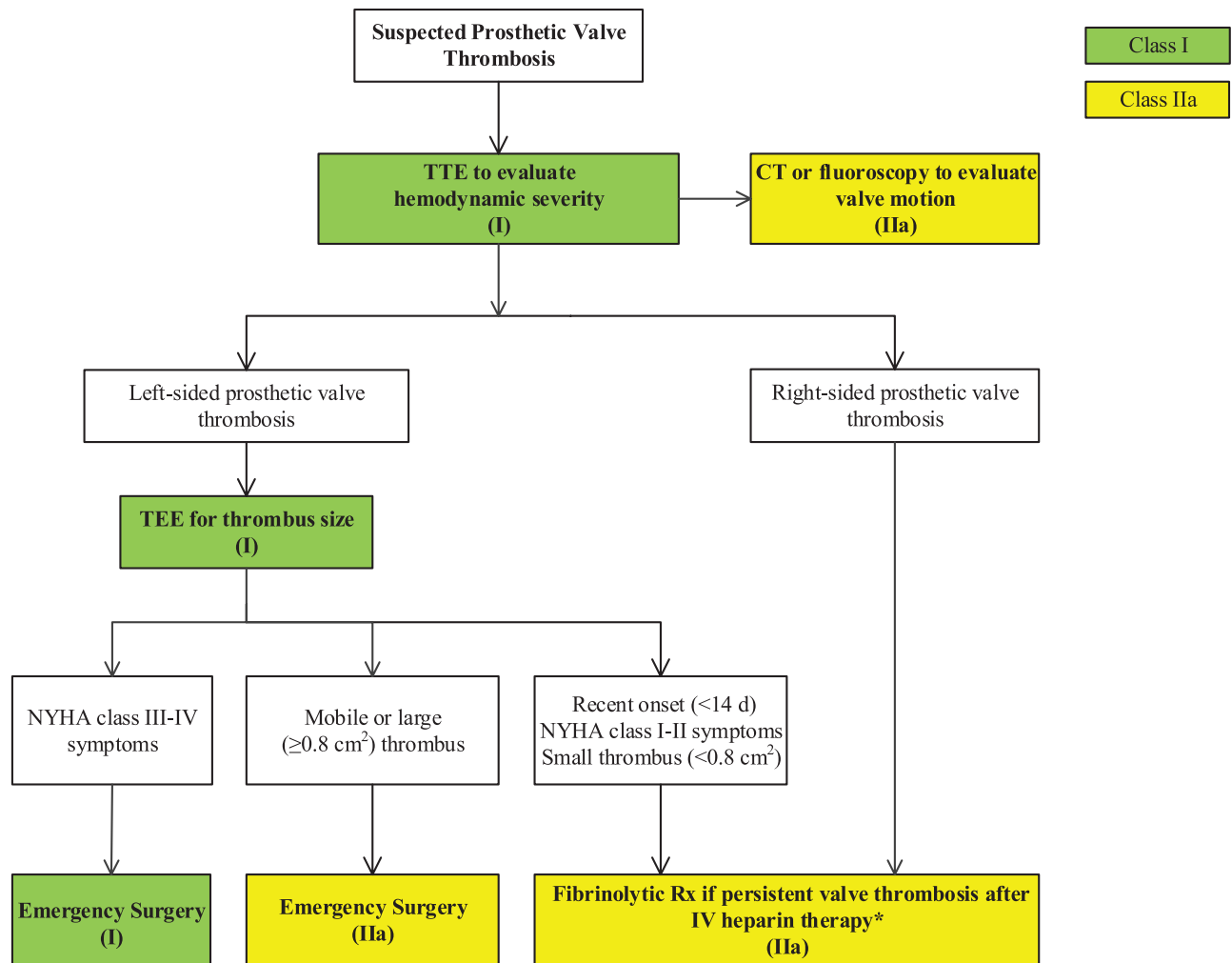


Figure 7. Evaluation and Management of Suspected Prosthetic Valve Thrombosis. *See full-text guideline for dosage recommendations. CT indicates computed tomography; IV, intravenous; NYHA, New York Heart Association; Rx, therapy; TEE, transesophageal echocardiography; and TTE, transthoracic echocardiography.

4. Early surgery (during initial hospitalization before completion of a full therapeutic course of antibiotics) is indicated in patients with IE complicated by heart block, annular or aortic abscess, or destructive penetrating lesions.^{347,355–359} (Level of Evidence: B)
5. Early surgery (during initial hospitalization before completion of a full therapeutic course of antibiotics) for IE is indicated in patients with evidence of persistent infection as manifested by persistent bacteremia or fevers lasting longer than 5 to 7 days after onset of appropriate antimicrobial therapy.^{347,352,353,360–362} (Level of Evidence: B)
6. Surgery is recommended for patients with prosthetic valve endocarditis and relapsing infection (defined as recurrence of bacteremia after a complete course of appropriate antibiotics and subsequently negative blood cultures) without other identifiable source for portal of infection. (Level of Evidence: C)
7. Complete removal of pacemaker or defibrillator systems, including all leads and the generator, is indicated as part of the early management plan in patients with IE with documented infection of the device or leads.^{363–366} (Level of Evidence: B)

Class IIa

1. Complete removal of pacemaker or defibrillator systems, including all leads and the generator, is reasonable in patients with valvular IE caused by *Staphylococcal aureus* or fungi, even without evidence of device or lead infection.^{363–366} (Level of Evidence: B)
2. Complete removal of pacemaker or defibrillator systems, including all leads and the generator, is reasonable in patients undergoing valve surgery for valvular IE. (Level of Evidence: C)
3. Early surgery (during initial hospitalization before completion of a full therapeutic course of antibiotics) is reasonable in patients with IE who present with recurrent emboli and persistent vegetations despite appropriate antibiotic therapy.^{302,367,368} (Level of Evidence: B)

Class IIb

1. Early surgery (during initial hospitalization before completion of a full therapeutic course of antibiotics)

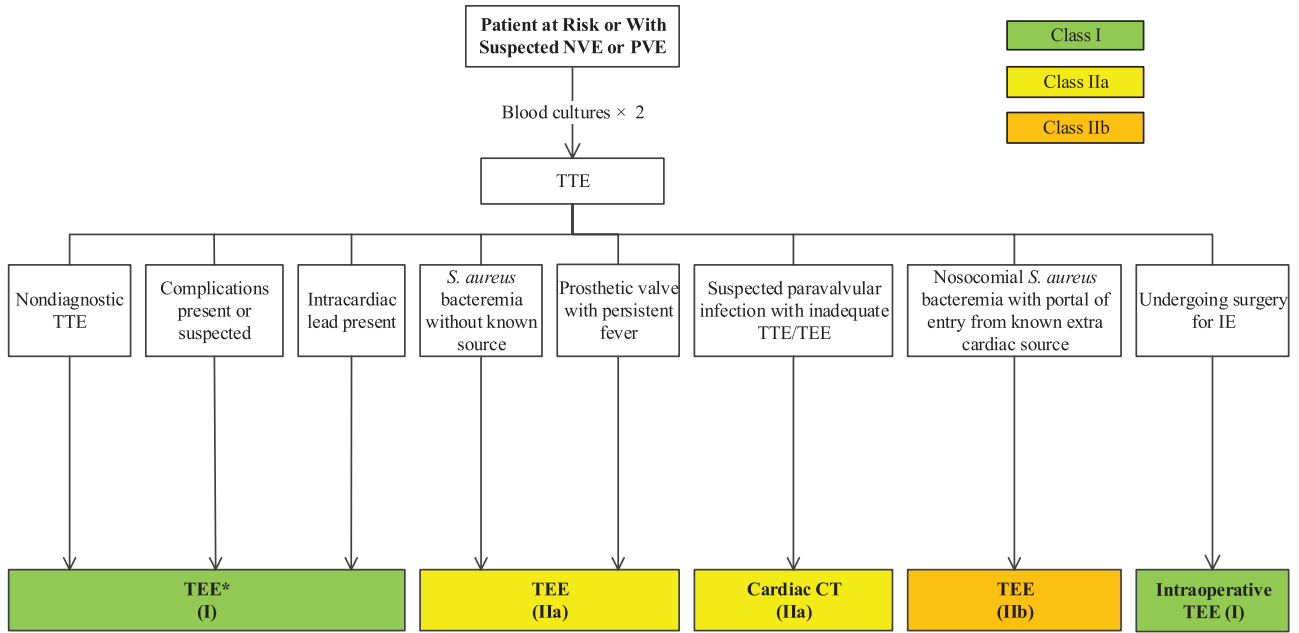


Figure 8. Recommendations for Imaging Studies in NVE and PVE. *Repeat TEE and/or TTE recommended for reevaluation of patients with IE and a change in clinical signs or symptoms and in patients at high risk of complications. CT indicates computed tomography; IE, infective endocarditis; NVE, native valve endocarditis; PVE, prosthetic valve endocarditis; *S. aureus*, *Staphylococcus aureus*; TEE, transesophageal echocardiography; and TTE, transthoracic echocardiography.

may be considered in patients with native valve endocarditis who exhibit mobile vegetations greater than 10 mm in length (with or without clinical evidence of embolic phenomenon).^{302,367,368} (Level of Evidence: B)

12. Pregnancy and VHD: Recommendations

12.1. Native Valve Stenosis

Class I

1. All patients with suspected valve stenosis should undergo a clinical evaluation and TTE before pregnancy. (Level of Evidence: C)
2. All patients with severe valve stenosis (stages C and D) should undergo prepregnancy counseling by a cardiologist with expertise in managing patients with VHD during pregnancy. (Level of Evidence: C)
3. All patients referred for a valve operation before pregnancy should receive prepregnancy counseling by a cardiologist with expertise in managing patients with VHD during pregnancy about the risks and benefits of all options for operative interventions, including mechanical prosthesis, bioprosthesis, and valve repair. (Level of Evidence: C)
4. Pregnant patients with severe valve stenosis (stages C and D) should be monitored in a tertiary care center with a dedicated Heart Valve Team of cardiologists, surgeons, anesthesiologists, and obstetricians with expertise in the management of high-risk cardiac patients during pregnancy. (Level of Evidence: C)

12.1.1. Diagnosis and Follow-Up

Class IIa

1. Exercise testing is reasonable in asymptomatic patients with severe AS (aortic velocity ≥ 4.0 m per second or mean pressure gradient ≥ 40 mm Hg, stage C) before pregnancy. (Level of Evidence: C)

12.1.2. Medical Therapy

Class I

1. Anticoagulation should be given to pregnant patients with MS and AF unless contraindicated. (Level of Evidence: C)

Class IIa

1. Use of beta blockers as required for rate control is reasonable for pregnant patients with MS in the absence of contraindication if tolerated. (Level of Evidence: C)

Class IIb

1. Use of diuretics may be reasonable for pregnant patients with MS and HF symptoms (stage D). (Level of Evidence: C)

Class III: Harm

1. ACE inhibitors and ARBs should not be given to pregnant patients with valve stenosis.³⁶⁹⁻³⁷¹ (Level of Evidence: B)

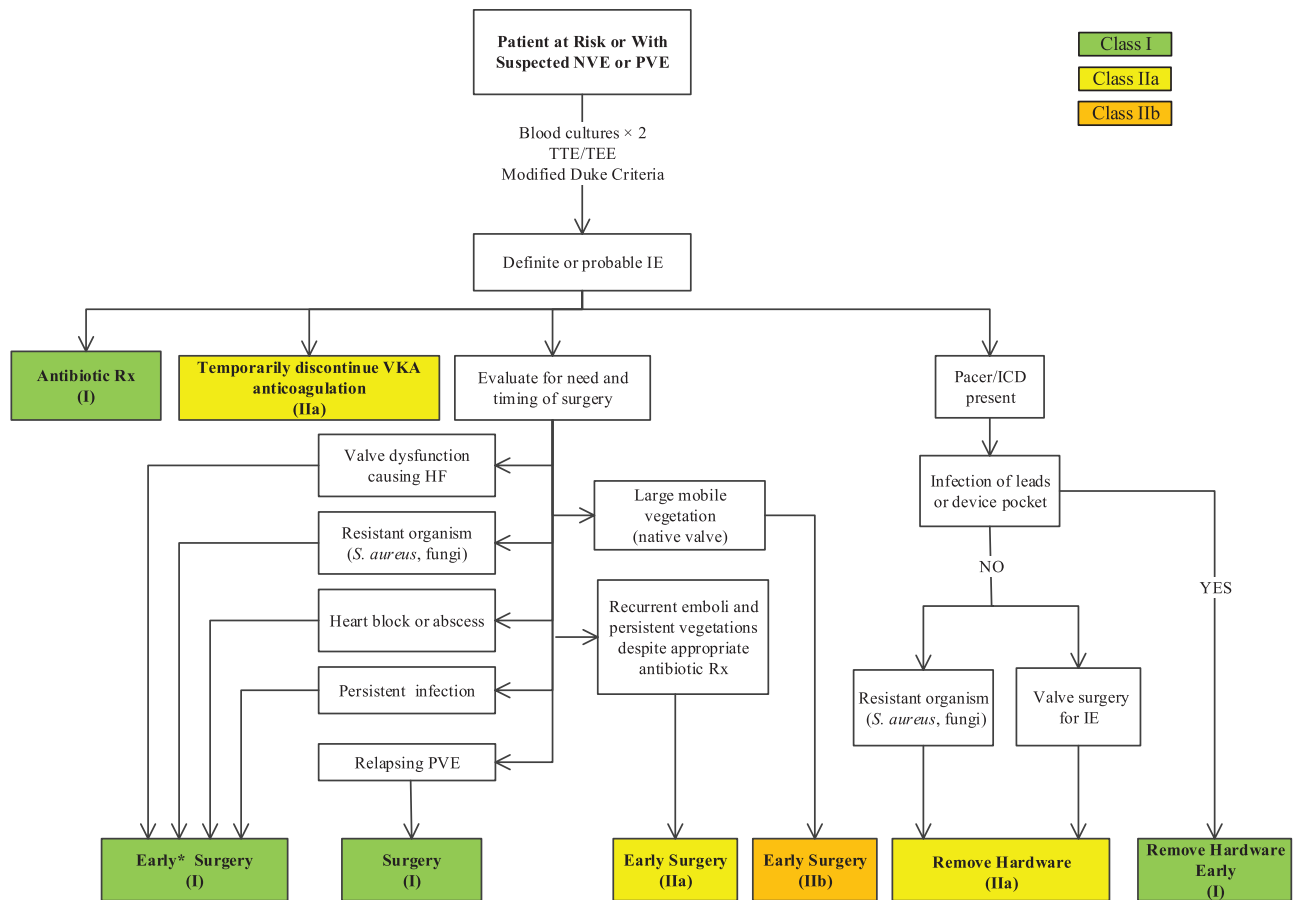


Figure 9. Diagnosis and Treatment of IE. *Early surgery defined as during initial hospitalization before completion of a full therapeutic course of antibiotics. HF indicates heart failure; ICD, implantable cardioverter-defibrillator; IE, infective endocarditis; NVE, native valve endocarditis; PVE, prosthetic valve endocarditis; Rx, therapy; *S. aureus*, *Staphylococcus aureus*; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography; and VKA, vitamin K antagonist.

12.1.3. Intervention

Class I

1. Valve intervention is recommended before pregnancy for symptomatic patients with severe AS (aortic velocity ≥ 4.0 m per second or mean pressure gradient ≥ 40 mmHg, stage D). (Level of Evidence: C)
2. Valve intervention is recommended before pregnancy for symptomatic patients with severe MS (mitral valve area ≤ 1.5 cm², stage D). (Level of Evidence: C)
3. Percutaneous mitral balloon commissurotomy is recommended before pregnancy for asymptomatic patients with severe MS (mitral valve area ≤ 1.5 cm², stage C) who have valve morphology favorable for percutaneous mitral balloon commissurotomy. (Level of Evidence: C)

Class IIa

1. Valve intervention is reasonable before pregnancy for asymptomatic patients with severe AS (aortic velocity ≥ 4.0 m per second or mean pressure gradient ≥ 40 mmHg, stage C). (Level of Evidence: C)

2. Percutaneous mitral balloon commissurotomy is reasonable for pregnant patients with severe MS (mitral valve area ≤ 1.5 cm², stage D) with valve morphology favorable for percutaneous mitral balloon commissurotomy who remain symptomatic with NYHA class III to IV HF symptoms despite medical therapy.^{372–376} (Level of Evidence: B)
3. Valve intervention is reasonable for pregnant patients with severe MS (mitral valve area ≤ 1.5 cm², stage D) and valve morphology not favorable for percutaneous mitral balloon commissurotomy only if there are refractory NYHA class IV HF symptoms. (Level of Evidence: C)
4. Valve intervention is reasonable for pregnant patients with severe AS (mean pressure gradient ≥ 40 mmHg, stage D) only if there is hemodynamic deterioration or NYHA class III to IV HF symptoms.^{377–383} (Level of Evidence: B)

Class III: Harm

1. Valve operation should not be performed in pregnant patients with valve stenosis in the absence of severe HF symptoms. (Level of Evidence: C)

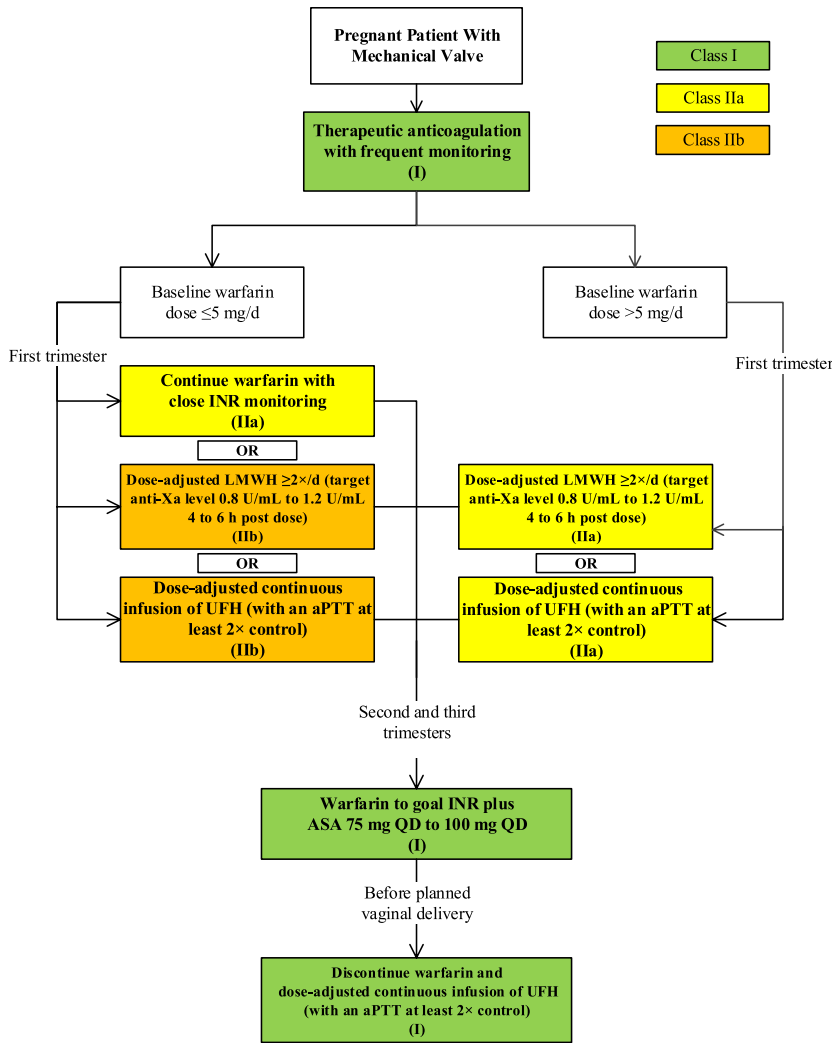


Figure 10. Anticoagulation of Pregnant Patients With Mechanical Valves. aPTT indicates activated partial thromboplastin time; ASA, aspirin; INR, international normalized ratio; LMWH, low-molecular-weight heparin; QD, once daily; and UFH, unfractionated heparin.

12.2. Native Valve Regurgitation

12.2.1. Diagnosis and Follow-Up

Class I

1. All patients with suspected valve regurgitation should undergo a clinical evaluation and TTE before pregnancy. (Level of Evidence: C)
2. All patients with severe valve regurgitation (stages C and D) should undergo pre-pregnancy counseling by a cardiologist with expertise in managing patients with VHD during pregnancy. (Level of Evidence: C)
3. All patients referred for a valve operation before pregnancy should receive pre-pregnancy counseling by a cardiologist with expertise in managing patients with VHD during pregnancy regarding the risks and benefits of all options for operative interventions, including mechanical prosthesis, bioprosthesis, and valve repair. (Level of Evidence: C)
4. Pregnant patients with severe regurgitation (stages C and D) should be monitored in a tertiary care center with a dedicated Heart Valve Team of cardiologists, surgeons, anesthesiologists, and obstetricians with

expertise in managing high-risk cardiac patients. (Level of Evidence: C)

Class IIa

1. Exercise testing is reasonable in asymptomatic patients with severe valve regurgitation (stage C) before pregnancy. (Level of Evidence: C)

12.2.2. Medical Therapy

Class III: Harm

1. ACE inhibitors and ARBs should not be given to pregnant patients with valve regurgitation.³⁶⁹⁻³⁷¹ (Level of Evidence: B)

12.2.3. Intervention

Class I

1. Valve repair or replacement is recommended before pregnancy for symptomatic women with severe valve regurgitation (stage D). (Level of Evidence: C)

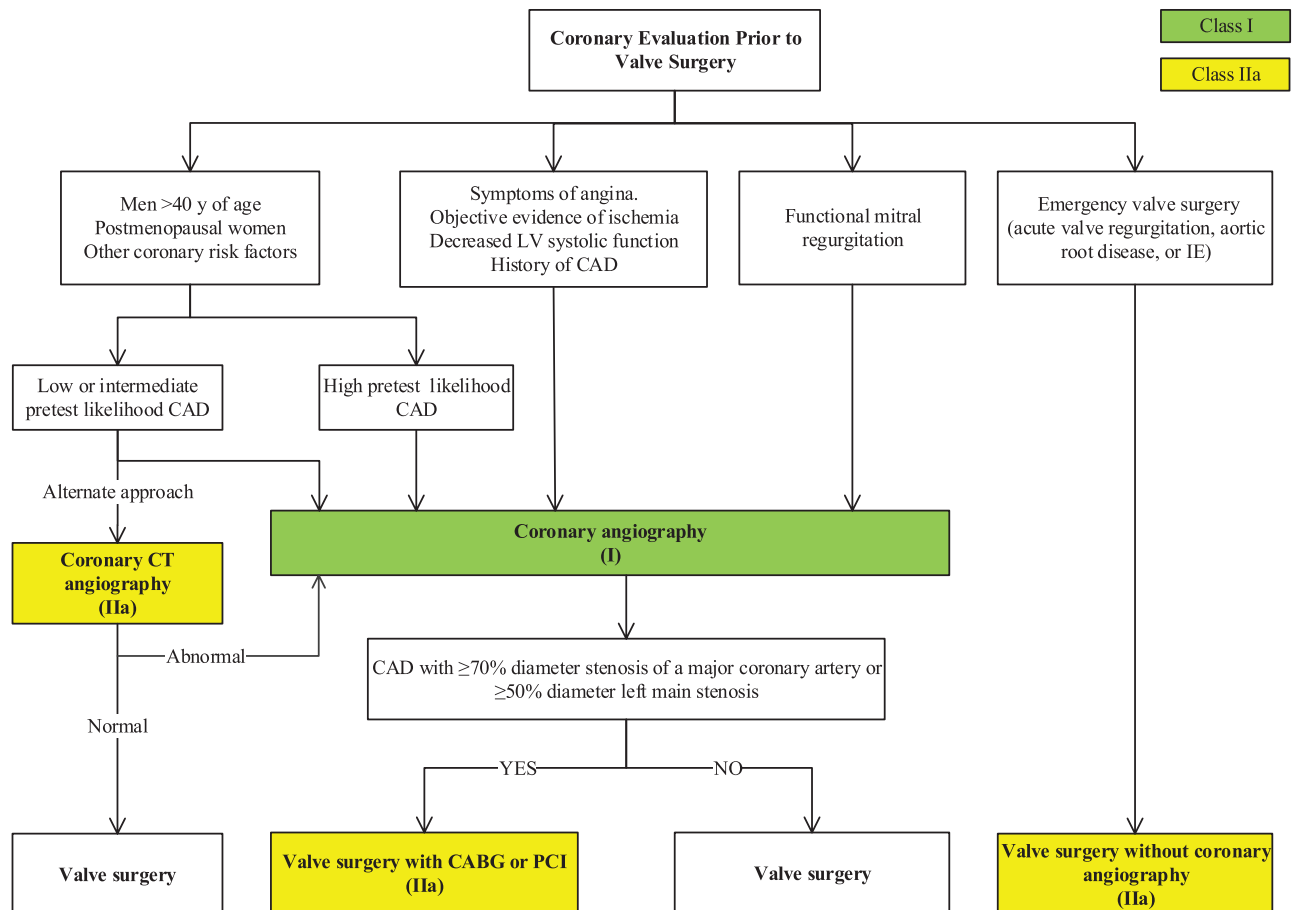


Figure 11. Evaluation and Management of CAD in Patients Undergoing Valve Surgery. CABG indicates coronary artery bypass graft; CAD, coronary artery disease; CT, computed tomography; IE, infective endocarditis; LV, left ventricular; and PCI, percutaneous coronary intervention.

Class IIa

1. Valve operation for pregnant patients with severe valve regurgitation is reasonable only if there are refractory NYHA class IV HF symptoms (stage D). (*Level of Evidence: C*)

Class IIb

1. Valve repair before pregnancy may be considered in the asymptomatic patient with severe MR (stage C) and a valve suitable for valve repair, but only after detailed discussion with the patient about the risks and benefits of the operation and its outcome on future pregnancies. (*Level of Evidence: C*)

Class III: Harm

1. Valve operations should not be performed in pregnant patients with valve regurgitation in the absence of severe intractable HF symptoms. (*Level of Evidence: C*)

12.3. Prosthetic Valves in Pregnancy

12.3.1. Diagnosis and Follow-Up

Class I

1. All patients with a prosthetic valve should undergo a clinical evaluation and baseline TTE before pregnancy. (*Level of Evidence: C*)
2. All patients with a prosthetic valve should undergo prepregnancy counseling by a cardiologist with expertise in managing patients with VHD during pregnancy. (*Level of Evidence: C*)
3. TTE should be performed in all pregnant patients with a prosthetic valve if not done before pregnancy. (*Level of Evidence: C*)
4. Repeat TTE should be performed in all pregnant patients with a prosthetic valve who develop symptoms. (*Level of Evidence: C*)
5. TEE should be performed in all pregnant patients with a mechanical prosthetic valve who have prosthetic valve obstruction or experience an embolic event. (*Level of Evidence: C*)
6. Pregnant patients with a mechanical prosthesis should be monitored in a tertiary care center with a dedicated Heart Valve Team of cardiologists,

surgeons, anesthesiologists, and obstetricians with expertise in the management of high-risk cardiac patients. (*Level of Evidence: C*)

12.3.2. Medical Therapy

See Figure 10 for anticoagulation of pregnant patients with mechanical valves.

Class I

1. Therapeutic anticoagulation with frequent monitoring is recommended for all pregnant patients with a mechanical prosthesis.^{384,385} (*Level of Evidence: B*)
2. Warfarin is recommended in pregnant patients with a mechanical prosthesis to achieve a therapeutic INR in the second and third trimesters.^{386–391} (*Level of Evidence: B*)
3. Discontinuation of warfarin with initiation of intravenous UFH (with an activated partial thromboplastin time [aPTT] >2 times control) is recommended before planned vaginal delivery in pregnant patients with a mechanical prosthesis. (*Level of Evidence: C*)
4. Low-dose aspirin (75 mg to 100 mg) once per day is recommended for pregnant patients in the second and third trimesters with either a mechanical prosthesis or bioprosthesis. (*Level of Evidence: C*)

Class IIa

1. Continuation of warfarin during the first trimester is reasonable for pregnant patients with a mechanical prosthesis if the dose of warfarin to achieve a therapeutic INR is 5 mg per day or less after full discussion with the patient about risks and benefits.^{384,385,390–393} (*Level of Evidence: B*)
2. Dose-adjusted LMWH at least 2 times per day (with a target anti-Xa level of 0.8 U/mL to 1.2 U/mL, 4 to 6 hours postdose) during the first trimester is reasonable for pregnant patients with a mechanical prosthesis if the dose of warfarin is greater than 5 mg per day to achieve a therapeutic INR.^{386–389,394,395} (*Level of Evidence: B*)
3. Dose-adjusted continuous intravenous UFH (with an aPTT at least 2 times control) during the first trimester is reasonable for pregnant patients with a mechanical prosthesis if the dose of warfarin is greater than 5 mg per day to achieve a therapeutic INR.^{384,385,392} (*Level of Evidence: B*)

Class IIb

1. Dose-adjusted LMWH at least 2 times per day (with a target anti-Xa level of 0.8 U/mL to 1.2 U/mL, 4 to 6 hours postdose) during the first trimester may be reasonable for pregnant patients with a mechanical prosthesis if the dose of warfarin is 5 mg per day or less to achieve a therapeutic INR.^{386–389,394–396} (*Level of Evidence: B*)
2. Dose-adjusted continuous infusion of UFH (with aPTT at least 2 times control) during the first trimester may

be reasonable for pregnant patients with a mechanical prosthesis if the dose of warfarin is 5 mg per day or less to achieve a therapeutic INR.^{384,385,392} (*Level of Evidence: B*)

Class III: Harm

1. LMWH should not be administered to pregnant patients with mechanical prostheses unless anti-Xa levels are monitored 4 to 6 hours after administration.^{387,388,394,395,397} (*Level of Evidence: B*)

13. Surgical Considerations: Recommendations

13.1. Evaluation of Coronary Anatomy

See Figure 11 for evaluation and management of CAD in patients undergoing valve surgery.

Class I

1. Coronary angiography is indicated before valve intervention in patients with symptoms of angina, objective evidence of ischemia, decreased LV systolic function, history of CAD, or coronary risk factors (including men age >40 years and postmenopausal women). (*Level of Evidence: C*)
2. Coronary angiography should be performed as part of the evaluation of patients with chronic severe secondary MR. (*Level of Evidence: C*)

Class IIa

1. Surgery without coronary angiography is reasonable for patients having emergency valve surgery for acute valve regurgitation, disease of the aortic sinuses or ascending aorta, or IE. (*Level of Evidence: C*)
2. CT coronary angiography is reasonable to exclude the presence of significant obstructive CAD in selected patients with a low/intermediate pretest probability of CAD. A positive coronary CT angiogram (the presence of any epicardial CAD) can be confirmed with invasive coronary angiography.^{398–404} (*Level of Evidence: B*)

13.2. Concomitant Procedures

13.2.1. Intervention for CAD

Class IIa

1. CABG or percutaneous coronary intervention is reasonable in patients undergoing valve repair or replacement with significant CAD ($\geq 70\%$ reduction in luminal diameter in major coronary arteries or $\geq 50\%$ reduction in luminal diameter in the left main coronary artery). (*Level of Evidence: C*)

13.2.2. Intervention for AF

Class IIa

1. A concomitant maze procedure is reasonable at the time of mitral valve repair or replacement

for treatment of chronic, persistent AF. (*Level of Evidence: C*)

2. A full biatrial maze procedure, when technically feasible, is reasonable at the time of mitral valve surgery, compared with a lesser ablation procedure, in patients with chronic, persistent AF.^{405,406} (*Level of Evidence: B*)

Class IIb

1. A concomitant maze procedure or pulmonary vein isolation may be considered at the time of mitral valve repair or replacement in patients with paroxysmal AF that is symptomatic or associated with a history of embolism on anticoagulation. (*Level of Evidence: C*)
2. Concomitant maze procedure or pulmonary vein isolation may be considered at the time of cardiac surgical procedures other than mitral valve surgery in patients with paroxysmal or persistent AF that is symptomatic or associated with a history of emboli on anticoagulation. (*Level of Evidence: C*)

Class III: No Benefit

1. Catheter ablation for AF should not be performed in patients with severe MR when mitral repair or replacement is anticipated, with preference for the combined maze procedure plus mitral valve repair.⁴⁰⁷ (*Level of Evidence: B*)

14. Noncardiac Surgery in Patients With VHD: Recommendations

Class IIa

1. Moderate-risk elective noncardiac surgery with appropriate intraoperative and postoperative hemodynamic monitoring is reasonable to perform in patients with asymptomatic severe AS.^{408–411} (*Level of Evidence: B*)
2. Moderate-risk elective noncardiac surgery with appropriate intraoperative and postoperative hemodynamic monitoring is reasonable to perform in patients with asymptomatic severe MR. (*Level of Evidence: C*)
3. Moderate-risk elective noncardiac surgery with appropriate intraoperative and postoperative hemodynamic monitoring is reasonable to perform in patients with asymptomatic severe AR and a normal LVEF. (*Level of Evidence: C*)

Class IIb

1. Moderate-risk elective noncardiac surgery in patients with appropriate intraoperative and postoperative hemodynamic monitoring may be reasonable to perform in asymptomatic patients with severe MS if valve morphology is not favorable for percutaneous balloon mitral commissurotomy. (*Level of Evidence: C*)

Presidents and Staff

American College of Cardiology

John Gordon Harold, MD, MACC, President
Shalom Jacobovitz, Chief Executive Officer
William J. Oetgen, MD, MBA, FACC, Executive Vice President, Science, Education, and Quality
Charlene L. May, Senior Director, Science and Clinical Policy

American College of Cardiology/American Heart Association

Lisa Bradfield, CAE, Director, Science and Clinical Policy
Emily Cottrell, MA, Specialist, Science and Clinical Policy

American Heart Association

Mariell Jessup, MD, FACC, FAHA, President
Nancy Brown, Chief Executive Officer
Rose Marie Robertson, MD, FAHA, Chief Science Officer
Gayle R. Whitman, PhD, RN, FAHA, FAAN, Senior Vice President, Office of Science Operations
Marco Di Buono, PhD, Vice President of Science and Research
Jody Hundley, Production Manager, Scientific Publications, Office of Science Operations

References

1. ACCF/AHA Task Force on Practice Guidelines. Methodology Manual and Policies From the ACCF/AHA Task Force on Practice Guidelines. American College of Cardiology Foundation and American Heart Association, Inc. [cardiosource.org](http://assets.cardiosource.com/Methodology_Manual_for_ACC_AHA_Writing_Committees.pdf). 2010. Available at: http://assets.cardiosource.com/Methodology_Manual_for_ACC_AHA_Writing_Committees.pdf and http://my.americanheart.org/idc/groups/ahamah-public/@wcm/@sop/documents/downloadable/ucm_319826.pdf. Accessed February 24, 2014.
2. Committee on Standards for Developing Trustworthy Clinical Practice Guidelines; Institute of Medicine; Clinical Practice Guidelines We Can Trust. Washington, D.C.: The National Academies Press; 2013.
3. Committee on Standards for Systematic Reviews of Comparative Effectiveness Research, Institute of Medicine; Finding What Works in Health Care: Standards for Systematic Reviews. Washington, DC: The National Academies Press; 2011.
4. Nishimura R, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;129:e521–e643.
5. Bonow RO, Carabello BA, Chatterjee K, et al. 2008 focused update incorporated into the ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to revise the 1998 guidelines for the management of patients with valvular heart disease). *Circulation*. 2008;118:e523–661.
6. Zoghbi WA, Enriquez-Sarano M, Foster E, et al. Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography. *J Am Soc Echocardiogr*. 2003;16:777–802.
7. Deleted in press.
8. Warnes CA, Williams RG, Bashore TM, et al. ACC/AHA 2008 guidelines for the management of adults with congenital heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Develop Guidelines on the Management of Adults With Congenital Heart Disease). *Circulation*. 2008;118:e714–833.
9. Baumgartner H, Hung J, Bermejo J, et al. Echocardiographic assessment of valve stenosis: EAE/ASE recommendations for clinical practice. *Eur J Echocardiogr*. 2009;10:1–25.
10. Zoghbi WA, Chambers JB, Dumesnil JG, et al. Recommendations for evaluation of prosthetic valves with echocardiography and Doppler ultrasound: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Task Force on Prosthetic Valves, developed in conjunction with the American College of Cardiology Cardiovascular

- Imaging Committee, Cardiac Imaging Committee of the American Heart Association, the European Association of Echocardiography, a registered branch of the European Society of Cardiology, the Japanese Society of Echocardiography and the Canadian Society of Echocardiography. *J Am Soc Echocardiogr*. 2009;22:975–1014.
11. Gersh BJ, Maron BJ, Bonow RO, et al. 2011 ACCF/AHA guideline for the diagnosis and treatment of hypertrophic cardiomyopathy: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Developed in collaboration with the American Association for Thoracic Surgery, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *Circulation*. 2011;124:e783–831.
 12. Regitz-Zagrosek V, Blomstrom LC, Borghi C, et al. ESC guidelines on the management of cardiovascular diseases during pregnancy: the Task Force on the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC). *Eur Heart J*. 2011;32:3147–97.
 13. Whitlock RP, Sun JC, Fremes SE, et al. Antithrombotic and thrombolytic therapy for valvular disease: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012;141:e576S–e600S.
 14. Vahanian A, Alfieri O, Andreotti F, et al. Guidelines on the management of valvular heart disease (version 2012). *Eur Heart J*. 2012;33:2451–96.
 15. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2013;128:e240–327.
 16. January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Developed in Collaboration With the Society of Thoracic Surgeons. *Circulation*. 2014; first published on March 28, 2014, as doi:10.1161/CIR.0000000000000041.
 17. Deleted in press.
 18. Deleted in press.
 19. Carabello BA, Williams H, Gash AK, et al. Hemodynamic predictors of outcome in patients undergoing valve replacement. *Circulation*. 1986;74:1309–16.
 20. Currie PJ, Seward JB, Chan KL, et al. Continuous wave Doppler determination of right ventricular pressure: a simultaneous Doppler-catheterization study in 127 patients. *J Am Coll Cardiol*. 1985;6:750–6.
 21. Currie PJ, Seward JB, Reeder GS, et al. Continuous-wave Doppler echocardiographic assessment of severity of calcific aortic stenosis: a simultaneous Doppler-catheter correlative study in 100 adult patients. *Circulation*. 1985;71:1162–9.
 22. Dujardin KS, Seward JB, Orszulak TA, et al. Outcome after surgery for mitral regurgitation. Determinants of postoperative morbidity and mortality. *J Heart Valve Dis*. 1997;6:17–21.
 23. Enriquez-Sarano M, Avierinos JF, Messika-Zeitoun D, et al. Quantitative determinants of the outcome of asymptomatic mitral regurgitation. *N Engl J Med*. 2005;352:875–83.
 24. Enriquez-Sarano M, Tajik AJ, Schaff HV, et al. Echocardiographic prediction of left ventricular function after correction of mitral regurgitation: results and clinical implications. *J Am Coll Cardiol*. 1994;24:1536–43.
 25. Nishimura RA, Rihal CS, Tajik AJ, et al. Accurate measurement of the transmitral gradient in patients with mitral stenosis: a simultaneous catheterization and Doppler echocardiographic study. *J Am Coll Cardiol*. 1994;24:152–8.
 26. Oh JK, Taliencio CP, Holmes DRJ, et al. Prediction of the severity of aortic stenosis by Doppler aortic valve area determination: prospective Doppler-catheterization correlation in 100 patients. *J Am Coll Cardiol*. 1988;11:1227–34.
 27. Otto CM, Burwash IG, Legget ME, et al. Prospective study of asymptomatic valvular aortic stenosis. Clinical, echocardiographic, and exercise predictors of outcome. *Circulation*. 1997;95:2262–70.
 28. Otto CM, Nishimura RA, Davis KB, et al. Doppler echocardiographic findings in adults with severe symptomatic valvular aortic stenosis. Balloon Valvuloplasty Registry Echocardiographers. *Am J Cardiol*. 1991;68:1477–84.
 29. Otto CM, Pearlman AS, Comess KA, et al. Determination of the stenotic aortic valve area in adults using Doppler echocardiography. *J Am Coll Cardiol*. 1986;7:509–17.
 30. Otto CM, Pearlman AS, Gardner CL. Hemodynamic progression of aortic stenosis in adults assessed by Doppler echocardiography. *J Am Coll Cardiol*. 1989;13:545–50.
 31. Pellikka PA, Sarano ME, Nishimura RA, et al. Outcome of 622 adults with asymptomatic, hemodynamically significant aortic stenosis during prolonged follow-up. *Circulation*. 2005;111:3290–5.
 32. Zile MR, Gaasch WH, Carroll JD, et al. Chronic mitral regurgitation: predictive value of preoperative echocardiographic indexes of left ventricular function and wall stress. *J Am Coll Cardiol*. 1984;3:235–42.
 33. Dujardin KS, Enriquez-Sarano M, Schaff HV, et al. Mortality and morbidity of aortic regurgitation in clinical practice. A long-term follow-up study. *Circulation*. 1999;99:1851–7.
 34. Bonow RO, Lakatos E, Maron BJ, et al. Serial long-term assessment of the natural history of asymptomatic patients with chronic aortic regurgitation and normal left ventricular systolic function. *Circulation*. 1991;84:1625–35.
 35. Aviles RJ, Nishimura RA, Pellikka PA, et al. Utility of stress Doppler echocardiography in patients undergoing percutaneous mitral balloon valvotomy. *J Am Soc Echocardiogr*. 2001;14:676–81.
 36. Otto CM, Pearlman AS, Kraft CD, et al. Physiologic changes with maximal exercise in asymptomatic valvular aortic stenosis assessed by Doppler echocardiography. *J Am Coll Cardiol*. 1992;20:1160–7.
 37. Lancellotti P, Lebois F, Simon M, et al. Prognostic importance of quantitative exercise Doppler echocardiography in asymptomatic valvular aortic stenosis. *Circulation*. 2005;112:1377–82.
 38. Marechaux S, Hachicha Z, Bellouin A, et al. Usefulness of exercise-stress echocardiography for risk stratification of true asymptomatic patients with aortic valve stenosis. *Eur Heart J*. 2010;31:1390–7.
 39. Messika-Zeitoun D, Johnson BD, Nkomo V, et al. Cardiopulmonary exercise testing determination of functional capacity in mitral regurgitation: physiologic and outcome implications. *J Am Coll Cardiol*. 2006;47:2521–7.
 40. Gerber MA, Baltimore RS, Eaton CB, et al. Prevention of rheumatic fever and diagnosis and treatment of acute Streptococcal pharyngitis: a scientific statement from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young, the Interdisciplinary Council on Functional Genomics and Translational Biology, and the Interdisciplinary Council on Quality of Care and Outcomes Research. *Circulation*. 2009;119:1541–51.
 41. Horstkotte D. Contribution for choosing the optimal prophylaxis of bacterial endocarditis. *Eur Heart J*. 1987;8:739–81.
 42. Strom BL, Abrutyn E, Berlin JA, et al. Dental and cardiac risk factors for infective endocarditis. A population-based, case-control study. *Ann Intern Med*. 1998;129:761–9.
 43. Duval X, Alla F, Hoen B, et al. Estimated risk of endocarditis in adults with predisposing cardiac conditions undergoing dental procedures with or without antibiotic prophylaxis. *Clin Infect Dis*. 2006;42:e102–7.
 44. Guarner-Argente C, Shah P, Buchner A, et al. Use of antimicrobials for EUS-guided FNA of pancreatic cysts: a retrospective, comparative analysis. *Gastrointest Endosc*. 2011;74:81–6.
 45. Galan A, Zoghbi WA, Quinones MA. Determination of severity of valvular aortic stenosis by Doppler echocardiography and relation of findings to clinical outcome and agreement with hemodynamic measurements determined at cardiac catheterization. *Am J Cardiol*. 1991;67:1007–12.
 46. Lin SS, Roger VL, Pascoe R, et al. Dobutamine stress Doppler hemodynamics in patients with aortic stenosis: feasibility, safety, and surgical correlations. *Am Heart J*. 1998;136:1010–16.
 47. Monin JL, Monchi M, Gest V, et al. Aortic stenosis with severe left ventricular dysfunction and low transvalvular pressure gradients: risk stratification by low-dose dobutamine echocardiography. *J Am Coll Cardiol*. 2001;37:2101–7.
 48. Clavel MA, Fuchs C, Burwash IG, et al. Predictors of outcomes in low-flow, low-gradient aortic stenosis: results of the multicenter TOPAS Study. *Circulation*. 2008;118:S234–42.
 49. Das P, Rimington H, Chambers J. Exercise testing to stratify risk in aortic stenosis. *Eur Heart J*. 2005;26:1309–13.
 50. Atterhog JH, Jonsson B, Samuelsson R. Exercise testing: a prospective study of complication rates. *Am Heart J*. 1979;98:572–79.
 51. O'Brien KD, Zhao XQ, Shavelle DM, et al. Hemodynamic effects of the angiotensin-converting enzyme inhibitor, ramipril, in patients with mild to moderate aortic stenosis and preserved left ventricular function. *J Investig Med*. 2004;52:185–91.
 52. Chockalingam A, Venkatesan S, Subramaniam T, et al. Safety and efficacy of angiotensin-converting enzyme inhibitors in symptomatic severe aortic stenosis: Symptomatic Cardiac Obstruction-Pilot Study of Enalapril in Aortic Stenosis (SCOPE-AS). *Am Heart J*. 2004;147:E19.
 53. Nadir MA, Wei L, Elder DH, et al. Impact of renin-angiotensin system blockade therapy on outcome in aortic stenosis. *J Am Coll Cardiol*. 2011;58:570–6.

54. Rossebø AB, Pedersen TR, Boman K, et al. Intensive lipid lowering with simvastatin and ezetimibe in aortic stenosis. *N Engl J Med*. 2008;359:1343–56.
55. Cowell SJ, Newby DE, Prescott RJ, et al. A randomized trial of intensive lipid-lowering therapy in calcific aortic stenosis. *N Engl J Med*. 2005;352:2389–97.
56. Chan KL, Teo K, Dumesnil JG, et al. Effect of lipid lowering with rosuvastatin on progression of aortic stenosis: results of the aortic stenosis progression observation: measuring effects of rosuvastatin (ASTRONOMER) trial. *Circulation*. 2010;121:306–14.
57. Otto CM, Pearlman AS. Doppler echocardiography in adults with symptomatic aortic stenosis. Diagnostic utility and cost-effectiveness. *Arch Intern Med*. 1988;148:2553–60.
58. Turina J, Hess O, Sepulcri F, et al. Spontaneous course of aortic valve disease. *Eur Heart J*. 1987;8:471–83.
59. Kelly TA, Rothbart RM, Cooper CM, et al. Comparison of outcome of asymptomatic to symptomatic patients older than 20 years of age with valvular aortic stenosis. *Am J Cardiol*. 1988;61:123–30.
60. Connolly HM, Oh JK, Orszulak TA, et al. Aortic valve replacement for aortic stenosis with severe left ventricular dysfunction. Prognostic indicators. *Circulation*. 1997;95:2395–400.
61. Tribouilloy C, Levy F, Rusinaru D, et al. Outcome after aortic valve replacement for low-flow/low-gradient aortic stenosis without contractile reserve on dobutamine stress echocardiography. *J Am Coll Cardiol*. 2009;53:1865–73.
62. Rosenhek R, Binder T, Porenta G, et al. Predictors of outcome in severe, asymptomatic aortic stenosis. *N Engl J Med*. 2000;343:611–7.
63. Smith WT, Ferguson TB Jr, Ryan T, et al. Should coronary artery bypass graft surgery patients with mild or moderate aortic stenosis undergo concomitant aortic valve replacement? A decision analysis approach to the surgical dilemma. *J Am Coll Cardiol*. 2004;44:1241–7.
64. Lancellotti P, Donal E, Magne J, et al. Risk stratification in asymptomatic moderate to severe aortic stenosis: the importance of the valvular, arterial and ventricular interplay. *Heart*. 2010;96:1364–71.
65. Rosenhek R, Zilberszac R, Schemper M, et al. Natural history of very severe aortic stenosis. *Circulation*. 2010;121:151–6.
66. Nishimura RA, Grantham JA, Connolly HM, et al. Low-output, low-gradient aortic stenosis in patients with depressed left ventricular systolic function: the clinical utility of the dobutamine challenge in the catheterization laboratory. *Circulation*. 2002;106:809–13.
67. Monin JL, Quere JP, Monchi M, et al. Low-gradient aortic stenosis: operative risk stratification and predictors for long-term outcome: a multicenter study using dobutamine stress hemodynamics. *Circulation*. 2003;108:319–24.
68. Fougeres E, Tribouilloy C, Monchi M, et al. Outcomes of pseudo-severe aortic stenosis under conservative treatment. *Eur Heart J*. 2012;33:2426–33.
69. Horstkotte D, Loogen F. The natural history of aortic valve stenosis. *Eur Heart J*. 1988;9 (Suppl E): 57–64.
70. O'Brien SM, Shahian DM, Filardo G, et al. The Society of Thoracic Surgeons 2008 cardiac surgery risk models: part 2—isolated valve surgery. *Ann Thorac Surg*. 2009;88:S23–S42.
71. Kodali SK, Williams MR, Smith CR, et al. Two-year outcomes after transcatheter or surgical aortic-valve replacement. *N Engl J Med*. 2012;366:1686–95.
72. Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med*. 2010;363:1597–607.
73. Makkar RR, Fontana GP, Jilaihawi H, et al. Transcatheter aortic-valve replacement for inoperable severe aortic stenosis. *N Engl J Med*. 2012;366:1696–704.
74. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med*. 2011;364:2187–98.
75. Detaint D, Messika-Zeitoun D, Maalouf J, et al. Quantitative echocardiographic determinants of clinical outcome in asymptomatic patients with aortic regurgitation: a prospective study. *J Am Coll Cardiol*. 2008;51:1–11.
76. Pizarro R, Bazzino OO, Oberti PF, et al. Prospective validation of the prognostic usefulness of B-type natriuretic peptide in asymptomatic patients with chronic severe aortic regurgitation. *J Am Coll Cardiol*. 2011;58:1705–14.
77. Teague SM, Heinsimer JA, Anderson JL, et al. Quantification of aortic regurgitation utilizing continuous wave Doppler ultrasound. *J Am Coll Cardiol*. 1986;8:592–99.
78. Bonow RO, Rosing DR, McIntosh CL, et al. The natural history of asymptomatic patients with aortic regurgitation and normal left ventricular function. *Circulation*. 1983;68:509–17.
79. Scognamiglio R, Fasoli G, Dalla VS. Progression of myocardial dysfunction in asymptomatic patients with severe aortic insufficiency. *Clin Cardiol*. 1986;9:151–6.
80. Siemenczuk D, Greenberg B, Morris C, et al. Chronic aortic insufficiency: factors associated with progression to aortic valve replacement. *Ann Intern Med*. 1989;110:587–92.
81. Tornos MP, Olona M, Permanyer-Miranda G, et al. Clinical outcome of severe asymptomatic chronic aortic regurgitation: a long-term prospective follow-up study. *Am Heart J*. 1995;130:333–9.
82. Ishii K, Hirota Y, Suwa M, et al. Natural history and left ventricular response in chronic aortic regurgitation. *Am J Cardiol*. 1996;78:357–61.
83. Scognamiglio R, Rahimtoola SH, Fasoli G, et al. Nifedipine in asymptomatic patients with severe aortic regurgitation and normal left ventricular function. *N Engl J Med*. 1994;331:689–94.
84. Borer JS, Hochreiter C, Herrold EM, et al. Prediction of indications for valve replacement among asymptomatic or minimally symptomatic patients with chronic aortic regurgitation and normal left ventricular performance. *Circulation*. 1998;97:525–34.
85. Attenhofer JCH, Turina J, Mayer K, et al. Echocardiography in the evaluation of systolic murmurs of unknown cause. *Am J Med*. 2000;108:14–20.
86. Gelfand EV, Hughes S, Hauser TH, et al. Severity of mitral and aortic regurgitation as assessed by cardiovascular magnetic resonance: optimizing correlation with Doppler echocardiography. *J Cardiovasc Magn Reson*. 2006;8:503–7.
87. Cawley PJ, Hamilton-Craig C, Owens DS, et al. Prospective comparison of valve regurgitation quantitation by cardiac magnetic resonance imaging and transthoracic echocardiography. *Circ Cardiovasc Imaging*. 2013;6:48–57.
88. Evangelista A, Tornos P, Sambola A, et al. Long-term vasodilator therapy in patients with severe aortic regurgitation. *N Engl J Med*. 2005;353:1342–9.
89. Sondergaard L, Aldershvile J, Hildebrandt P, et al. Vasodilatation with felodipine in chronic asymptomatic aortic regurgitation. *Am Heart J*. 2000;139:667–74.
90. Elder DH, Wei L, Szwejkowski BR, et al. The impact of renin-angiotensin-aldosterone system blockade on heart failure outcomes and mortality in patients identified to have aortic regurgitation: a large population cohort study. *J Am Coll Cardiol*. 2011;58:2084–91.
91. Greves J, Rahimtoola SH, McAnulty JH, et al. Preoperative criteria predictive of late survival following valve replacement for severe aortic regurgitation. *Am Heart J*. 1981;101:300–8.
92. Klodas E, Enriquez-Sarano M, Tajik AJ, et al. Optimizing timing of surgical correction in patients with severe aortic regurgitation: role of symptoms. *J Am Coll Cardiol*. 1997;30:746–52.
93. Forman R, Firth BG, Barnard MS. Prognostic significance of preoperative left ventricular ejection fraction and valve lesion in patients with aortic valve replacement. *Am J Cardiol*. 1980;45:1120–25.
94. Chaliki HP, Mohty D, Avierinos JF, et al. Outcomes after aortic valve replacement in patients with severe aortic regurgitation and markedly reduced left ventricular function. *Circulation*. 2002;106:2687–93.
95. Bhudia SK, McCarthy PM, Kumpati GS, et al. Improved outcomes after aortic valve surgery for chronic aortic regurgitation with severe left ventricular dysfunction. *J Am Coll Cardiol*. 2007;49:1465–71.
96. Bonow RO, Dodd JT, Maron BJ, et al. Long-term serial changes in left ventricular function and reversal of ventricular dilatation after valve replacement for chronic aortic regurgitation. *Circulation*. 1988;78:1108–20.
97. Van Rossum AC, Visser FC, Sprenger M, et al. Evaluation of magnetic resonance imaging for determination of left ventricular ejection fraction and comparison with angiography. *Am J Cardiol*. 1988;62:628–33.
98. Gaasch WH, Carroll JD, Levine HJ, et al. Chronic aortic regurgitation: prognostic value of left ventricular end-systolic dimension and end-diastolic radius/thickness ratio. *J Am Coll Cardiol*. 1983;1:775–82.
99. Pachulski RT, Weinberg AL, Chan KL. Aortic aneurysm in patients with functionally normal or minimally stenotic bicuspid aortic valve. *Am J Cardiol*. 1991;67:781–82.
100. Hahn RT, Roman MJ, Mogtader AH, et al. Association of aortic dilation with regurgitant, stenotic and functionally normal bicuspid aortic valves. *J Am Coll Cardiol*. 1992;19:283–88.
101. Nistri S, Sorbo MD, Marin M, et al. Aortic root dilatation in young men with normally functioning bicuspid aortic valves. *Heart*. 1999;82:19–22.
102. Keane MG, Wiegers SE, Plappert T, et al. Bicuspid aortic valves are associated with aortic dilatation out of proportion to coexistent valvular lesions. *Circulation*. 2000;102:III35–9.

103. Novaro GM, Tiong IY, Pearce GL, et al. Features and predictors of ascending aortic dilatation in association with a congenital bicuspid aortic valve. *Am J Cardiol.* 2003;92:99–101.
104. Schaefer BM, Lewin MB, Stout KK, et al. The bicuspid aortic valve: an integrated phenotypic classification of leaflet morphology and aortic root shape. *Heart.* 2008;94:1634–8.
105. Tzemos N, Therrien J, Yip J, et al. Outcomes in adults with bicuspid aortic valves. *JAMA.* 2008;300:1317–25.
106. Michelena HI, Khanna AD, Mahoney D, et al. Incidence of aortic complications in patients with bicuspid aortic valves. *JAMA.* 2011;306:1104–12.
107. Davies RR, Goldstein LJ, Coady MA, et al. Yearly rupture or dissection rates for thoracic aortic aneurysms: simple prediction based on size. *Ann Thorac Surg.* 2002;73:17–27.
108. Arora R, Nair M, Kalra GS, et al. Immediate and long-term results of balloon and surgical closed mitral valvotomy: a randomized comparative study. *Am Heart J.* 1993;125:1091–4.
109. Turi ZG, Reyes VP, Raju BS, et al. Percutaneous balloon versus surgical closed commissurotomy for mitral stenosis. A prospective, randomized trial. *Circulation.* 1991;83:1179–85.
110. Patel JJ, Shama D, Mitha AS, et al. Balloon valvuloplasty versus closed commissurotomy for pliable mitral stenosis: a prospective hemodynamic study. *J Am Coll Cardiol.* 1991;18:1318–22.
111. Ben FM, Ayari M, Maatouk F, et al. Percutaneous balloon versus surgical closed and open mitral commissurotomy: seven-year follow-up results of a randomized trial. *Circulation.* 1998;97:245–50.
112. Cotrufo M, Renzulli A, Ismeno G, et al. Percutaneous mitral commissurotomy versus open mitral commissurotomy: a comparative study. *Eur J Cardiothorac Surg.* 1999;15:646–51.
113. Hugenholtz PG, Ryan TJ, Stein SW, et al. The spectrum of pure mitral stenosis. Hemodynamic studies in relation to clinical disability. *Am J Cardiol.* 1962;10:773–84.
114. Reyes VP, Raju BS, Wynne J, et al. Percutaneous balloon valvuloplasty compared with open surgical commissurotomy for mitral stenosis. *N Engl J Med.* 1994;331:961–7.
115. Sugeng L, Weinert L, Lammertin G, et al. Accuracy of mitral valve area measurements using transthoracic rapid freehand 3-dimensional scanning: comparison with noninvasive and invasive methods. *J Am Soc Echocardiogr.* 2003;16:1292–300.
116. Schlosshan D, Aggarwal G, Mathur G, et al. Real-time 3D transesophageal echocardiography for the evaluation of rheumatic mitral stenosis. *J Am Coll Cardiol Img.* 2011;4:580–8.
117. Leavitt JI, Coats MH, Falk RH. Effects of exercise on transmitral gradient and pulmonary artery pressure in patients with mitral stenosis or a prosthetic mitral valve: a Doppler echocardiographic study. *J Am Coll Cardiol.* 1991;17:1520–6.
118. Chung CS, Karamanoglu M, Kovacs SJ. Duration of diastole and its phases as a function of heart rate during supine bicycle exercise. *Am J Physiol Heart Circ Physiol.* 2004;287:H2003–8.
119. Zoghbi WA, Chambers JB, Dumesnil JG, et al. Recommendations for evaluation of prosthetic valves with echocardiography and doppler ultrasound: a report From the American Society of Echocardiography's Guidelines and Standards Committee and the Task Force on Prosthetic Valves, developed in conjunction with the American College of Cardiology Cardiovascular Imaging Committee, Cardiac Imaging Committee of the American Heart Association, the European Association of Echocardiography, a registered branch of the European Society of Cardiology, the Japanese Society of Echocardiography and the Canadian Society of Echocardiography. *J Am Soc Echocardiogr.* 2009;22:975–1014.
120. Wilkins GT, Weyman AE, Abascal VM, et al. Percutaneous balloon dilatation of the mitral valve: an analysis of echocardiographic variables related to outcome and the mechanism of dilatation. *Br Heart J.* 1988;60:299–308.
121. Abascal VM, Wilkins GT, O'Shea JP, et al. Prediction of successful outcome in 130 patients undergoing percutaneous balloon mitral valvotomy. *Circulation.* 1990;82:448–56.
122. Cannan CR, Nishimura RA, Reeder GS, et al. Echocardiographic assessment of commissural calcium: a simple predictor of outcome after percutaneous mitral balloon valvotomy. *J Am Coll Cardiol.* 1997;29:175–80.
123. Thomas JD, Wilkins GT, Choong CY, et al. Inaccuracy of mitral pressure half-time immediately after percutaneous mitral valvotomy. Dependence on transmitral gradient and left atrial and ventricular compliance. *Circulation.* 1988;78:980–93.
124. Ellis K, Ziada KM, Vivekananthan D, et al. Transthoracic echocardiographic predictors of left atrial appendage thrombus. *Am J Cardiol.* 2006;97:421–5.
125. Kronzon I, Tunick PA, Glassman E, et al. Transesophageal echocardiography to detect atrial clots in candidates for percutaneous transseptal mitral balloon valvuloplasty. *J Am Coll Cardiol.* 1990;16:1320–2.
126. Tessier P, Mercier LA, Burelle D, et al. Results of percutaneous mitral commissurotomy in patients with a left atrial appendage thrombus detected by transesophageal echocardiography. *J Am Soc Echocardiogr.* 1994;7:394–9.
127. Wilson JK, Greenwood WF. The natural history of mitral stenosis. *Can Med Assoc J.* 1954;71:323–31.
128. Rowe JC, Bland EF, Sprague HB, et al. The course of mitral stenosis without surgery: ten- and twenty-year perspectives. *Ann Intern Med.* 1960;52:741–9.
129. Olesen KH. The natural history of 271 patients with mitral stenosis under medical treatment. *Br Heart J.* 1962;24:349–57.
130. Szekely P. Systemic embolism and anticoagulant prophylaxis in rheumatic heart disease. *Br Med J.* 1964;1:1209–12.
131. Perez-Gomez F, Alegria E, Berjon J, et al. Comparative effects of antiplatelet, anticoagulant, or combined therapy in patients with valvular and nonvalvular atrial fibrillation: a randomized multicenter study. *J Am Coll Cardiol.* 2004;44:1557–66.
132. Omran H, Rang B, Schmidt H, et al. Incidence of left atrial thrombi in patients in sinus rhythm and with a recent neurologic deficit. *Am Heart J.* 2000;140:658–62.
133. Singer DE, Albers GW, Dalen JE, et al. Antithrombotic therapy in atrial fibrillation: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest.* 2008;133:546S–92S.
134. Stoll BC, Ashcom TL, Johns JP, et al. Effects of atenolol on rest and exercise hemodynamics in patients with mitral stenosis. *Am J Cardiol.* 1995;75:482–4.
135. Monmeneu Menadas JV, Marin OF, Reyes GF, et al. Beta-blockade and exercise capacity in patients with mitral stenosis in sinus rhythm. *J Heart Valve Dis.* 2002;11:199–203.
136. Bouleti C, Iung B, Laouenan C, et al. Late results of percutaneous mitral commissurotomy up to 20 years: development and validation of a risk score predicting late functional results from a series of 912 patients. *Circulation.* 2012;125:2119–27.
137. Ellis LB, Singh JB, Morales DD, et al. Fifteen- to twenty-year study of one thousand patients undergoing closed mitral valvuloplasty. *Circulation.* 1973;48:357–64.
138. John S, Bashi VV, Jairaj PS, et al. Closed mitral valvotomy: early results and long-term follow-up of 3724 consecutive patients. *Circulation.* 1983;68:891–6.
139. Finnegan JO, Gray DC, MacVaugh H 3rd, et al. The open approach to mitral commissurotomy. *J Thorac Cardiovasc Surg.* 1974;67:75–82.
140. Mullin MJ, Engelman RM, Isom OW, et al. Experience with open mitral commissurotomy in 100 consecutive patients. *Surgery.* 1974;76:974–82.
141. Halseth WL, Elliott DP, Walker EL, et al. Open mitral commissurotomy. A modern re-evaluation. *J Thorac Cardiovasc Surg.* 1980;80:842–8.
142. Gross RI, Cunningham JN Jr, Snively SL, et al. Long-term results of open radical mitral commissurotomy: ten year follow-up study of 202 patients. *Am J Cardiol.* 1981;47:821–5.
143. Iung B, Cormier B, Ducimetiere P, et al. Functional results 5 years after successful percutaneous mitral commissurotomy in a series of 528 patients and analysis of predictive factors. *J Am Coll Cardiol.* 1996;27:407–14.
144. Arat N, Altay H, Korkmaz S, et al. The effect of baseline pulmonary artery pressure on right ventricular functions after mitral balloon valvuloplasty for rheumatic mitral stenosis: a tissue Doppler imaging study. *Turk Kardiyol Dern Ars.* 2008;36:223–30.
145. Vincens JJ, Temizer D, Post JR, et al. Long-term outcome of cardiac surgery in patients with mitral stenosis and severe pulmonary hypertension. *Circulation.* 1995;92:III137–42.
146. Recusani F, Bargiggia GS, Yoganathan AP, et al. A new method for quantification of regurgitant flow rate using color Doppler flow imaging of the flow convergence region proximal to a discrete orifice. An in vitro study. *Circulation.* 1991;83:594–604.
147. Bargiggia GS, Tronconi L, Sahn DJ, et al. A new method for quantitation of mitral regurgitation based on color flow Doppler imaging of flow convergence proximal to regurgitant orifice. *Circulation.* 1991;84:1481–9.
148. Rivera JM, Vandervoort PM, Thoreau DH, et al. Quantification of mitral regurgitation with the proximal flow convergence method: a clinical study. *Am Heart J.* 1992;124:1289–96.

149. Rosenhek R, Rader F, Klaar U, et al. Outcome of watchful waiting in asymptomatic severe mitral regurgitation. *Circulation*. 2006;113:2238–44.
150. Crawford MH, Soucek J, Oprian CA, et al. Determinants of survival and left ventricular performance after mitral valve replacement. Department of Veterans Affairs Cooperative Study on Valvular Heart Disease. *Circulation*. 1990;81:1173–81.
151. Enriquez-Sarano M, Tajik AJ, Schaff HV, et al. Echocardiographic prediction of survival after surgical correction of organic mitral regurgitation. *Circulation*. 1994;90:830–7.
152. Tribouilloy C, Grigioni F, Avierinos JF, et al. Survival implication of left ventricular end-systolic diameter in mitral regurgitation due to flail leaflets a long-term follow-up multicenter study. *J Am Coll Cardiol*. 2009;54:1961–8.
153. Grigioni F, Tribouilloy C, Avierinos JF, et al. Outcomes in mitral regurgitation due to flail leaflets a multicenter European study. *J Am Coll Cardiol*. 2008;1:133–41.
154. Ghoreishi M, Evans CF, deFilippi CR, et al. Pulmonary hypertension adversely affects short- and long-term survival after mitral valve operation for mitral regurgitation: implications for timing of surgery. *J Thorac Cardiovasc Surg*. 2011;142:1439–52.
155. Rozich JD, Carabello BA, Usher BW, et al. Mitral valve replacement with and without chordal preservation in patients with chronic mitral regurgitation. Mechanisms for differences in postoperative ejection performance. *Circulation*. 1992;86:1718–26.
156. Tribouilloy CM, Enriquez-Sarano M, Schaff HV, et al. Impact of preoperative symptoms on survival after surgical correction of organic mitral regurgitation: rationale for optimizing surgical indications. *Circulation*. 1999;99:400–5.
157. Pflugfelder PW, Sechtem UP, White RD, et al. Noninvasive evaluation of mitral regurgitation by analysis of left atrial signal loss in cine magnetic resonance. *Am Heart J*. 1989;117:1113–9.
158. Pu M, Prior DL, Fan X, et al. Calculation of mitral regurgitant orifice area with use of a simplified proximal convergence method: initial clinical application. *J Am Soc Echocardiogr*. 2001;14:180–5.
159. Pu M, Vandervoort PM, Greenberg NL, et al. Impact of wall constraint on velocity distribution in proximal flow convergence zone. Implications for color Doppler quantification of mitral regurgitation. *J Am Coll Cardiol*. 1996;27:706–13.
160. Lang RM, Badano LP, Tsang W, et al. EAE/ASE recommendations for image acquisition and display using three-dimensional echocardiography. *J Am Soc Echocardiogr*. 2012;25:3–46.
161. Witkowski TG, Thomas JD, Debonnaire PJ, et al. Global longitudinal strain predicts left ventricular dysfunction after mitral valve repair. *Eur Heart J Cardiovasc Imaging*. 2013;14:69–76.
162. Magne J, Mahjoub H, Pierard LA, et al. Prognostic importance of brain natriuretic peptide and left ventricular longitudinal function in asymptomatic degenerative mitral regurgitation. *Heart*. 2012;98:584–91.
163. Ozdogan O, Yuksel A, Gurgun C, et al. Evaluation of the severity of mitral regurgitation by the use of signal void in magnetic resonance imaging. *Echocardiography*. 2009;26:1127–35.
164. Myerson SG, Francis JM, Neubauer S. Direct and indirect quantification of mitral regurgitation with cardiovascular magnetic resonance, and the effect of heart rate variability. *MAGMA*. 2010;23:243–9.
165. Dahm M, Iversen S, Schmid FX, et al. Intraoperative evaluation of reconstruction of the atrioventricular valves by transesophageal echocardiography. *Thorac Cardiovasc Surg*. 1987;35 Spec No 2:140–2.
166. Saiki Y, Kasegawa H, Kawase M, et al. Intraoperative TEE during mitral valve repair: does it predict early and late postoperative mitral valve dysfunction? *Ann Thorac Surg*. 1998;66:1277–81.
167. Tischler MD, Cooper KA, Rowen M, et al. Mitral valve replacement versus mitral valve repair. A Doppler and quantitative stress echocardiographic study. *Circulation*. 1994;89:132–7.
168. Magne J, Lancellotti P, Pierard LA. Exercise-induced changes in degenerative mitral regurgitation. *J Am Coll Cardiol*. 2010;56:300–9.
169. Tsutsui H, Spinale FG, Nagatsu M, et al. Effects of chronic beta-adrenergic blockade on the left ventricular and cardiocyte abnormalities of chronic canine mitral regurgitation. *J Clin Invest*. 1994;93:2639–48.
170. Varadarajan P, Joshi N, Appel D, et al. Effect of Beta-blocker therapy on survival in patients with severe mitral regurgitation and normal left ventricular ejection fraction. *Am J Cardiol*. 2008;102:611–5.
171. Ahmed MI, Aban I, Lloyd SG, et al. A randomized controlled phase IIb trial of beta(1)-receptor blockade for chronic degenerative mitral regurgitation. *J Am Coll Cardiol*. 2012;60:833–8.
172. Nemoto S, Hamawaki M, De Freitas G, et al. Differential effects of the angiotensin-converting enzyme inhibitor lisinopril versus the beta-adrenergic receptor blocker atenolol on hemodynamics and left ventricular contractile function in experimental mitral regurgitation. *J Am Coll Cardiol*. 2002;40:149–54.
173. Schon HR. Hemodynamic and morphologic changes after long-term angiotensin converting enzyme inhibition in patients with chronic valvular regurgitation. *J Hypertens Suppl*. 1994;12:S95–S104.
174. Tischler MD, Rowan M, LeWinter MM. Effect of enalapril therapy on left ventricular mass and volumes in asymptomatic chronic, severe mitral regurgitation secondary to mitral valve prolapse. *Am J Cardiol*. 1998;82:242–5.
175. Wisenbaugh T, Sinovich V, Dullabh A, et al. Six month pilot study of captopril for mildly symptomatic, severe isolated mitral and isolated aortic regurgitation. *J Heart Valve Dis*. 1994;3:197–204.
176. Dujardin KS, Enriquez-Sarano M, Bailey KR, et al. Effect of losartan on degree of mitral regurgitation quantified by echocardiography. *Am J Cardiol*. 2001;87:570–6.
177. Harris KM, Aeppli DM, Carey CF. Effects of angiotensin-converting enzyme inhibition on mitral regurgitation severity, left ventricular size, and functional capacity. *Am Heart J*. 2005;150:1106.
178. Kizilbash AM, Willett DL, Brickner ME, et al. Effects of afterload reduction on vena contracta width in mitral regurgitation. *J Am Coll Cardiol*. 1998;32:427–31.
179. Gillinov AM, Mihaljevic T, Blackstone EH, et al. Should patients with severe degenerative mitral regurgitation delay surgery until symptoms develop? *Ann Thorac Surg*. 2010;90:481–8.
180. Grigioni F, Enriquez-Sarano M, Ling LH, et al. Sudden death in mitral regurgitation due to flail leaflet. *J Am Coll Cardiol*. 1999;34:2078–85.
181. Schuler G, Peterson KL, Johnson A, et al. Temporal response of left ventricular performance to mitral valve surgery. *Circulation*. 1979;59:1218–31.
182. Starling MR. Effects of valve surgery on left ventricular contractile function in patients with long-term mitral regurgitation. *Circulation*. 1995;92:811–8.
183. Rushmer RF. Initial phase of ventricular systole: asynchronous contraction. *Am J Physiol*. 1956;184:188–94.
184. Hansen DE, Sarris GE, Niczyporuk MA, et al. Physiologic role of the mitral apparatus in left ventricular regional mechanics, contraction synergy, and global systolic performance. *J Thorac Cardiovasc Surg*. 1989;97:521–33.
185. Sarris GE, Cahill PD, Hansen DE, et al. Restoration of left ventricular systolic performance after reattachment of the mitral chordae tendineae. The importance of valvular-ventricular interaction. *J Thorac Cardiovasc Surg*. 1988;95:969–79.
186. Goldman ME, Mora F, Guarino T, et al. Mitral valvuloplasty is superior to valve replacement for preservation of left ventricular function: an intraoperative two-dimensional echocardiographic study. *J Am Coll Cardiol*. 1987;10:568–75.
187. David TE, Burns RJ, Bacchus CM, et al. Mitral valve replacement for mitral regurgitation with and without preservation of chordae tendineae. *J Thorac Cardiovasc Surg*. 1984;88:718–25.
188. Hennein HA, Swain JA, McIntosh CL, et al. Comparative assessment of chordal preservation versus chordal resection during mitral valve replacement. *J Thorac Cardiovasc Surg*. 1990;99:828–36.
189. Cohn LH. Surgery for mitral regurgitation. *JAMA*. 1988;260:2883–7.
190. Cosgrove DM, Chavez AM, Lytle BW, et al. Results of mitral valve reconstruction. *Circulation*. 1986;74:182–7.
191. STS online risk calculator. Available at: <http://riskcalc.sts.org/STSWebRiskCalc273/de.aspx>. 2013 Accessed February 24, 2014.
192. David TE, Uden DE, Strauss HD. The importance of the mitral apparatus in left ventricular function after correction of mitral regurgitation. *Circulation*. 1983;68:II76–82.
193. Horskotte D, Schulte HD, Bircks W, et al. The effect of chordal preservation on late outcome after mitral valve replacement: a randomized study. *J Heart Valve Dis*. 1993;2:150–8.
194. Vassileva CM, Mishkel G, McNeely C, et al. Long-Term survival of patients undergoing mitral valve repair and replacement: a longitudinal analysis of Medicare fee-for-service beneficiaries. *Circulation*. 2013;127:1870–6.
195. Braunberger E, Deloche A, Berrebi A, et al. Very long-term results (more than 20 years) of valve repair with carpentier's techniques in non-rheumatic mitral valve insufficiency. *Circulation*. 2001;104:18–11.

196. David TE, Ivanov J, Armstrong S, et al. A comparison of outcomes of mitral valve repair for degenerative disease with posterior, anterior, and bileaflet prolapse. *J Thorac Cardiovasc Surg.* 2005;130:1242–9.
197. McClure RS, Athanopoulos LV, McGurk S, et al. One thousand minimally invasive mitral valve operations: early outcomes, late outcomes, and echocardiographic follow-up. *J Thorac Cardiovasc Surg.* 2013;145:1199–206.
198. Gammie JS, Sheng S, Griffith BP, et al. Trends in mitral valve surgery in the United States: results from the Society of Thoracic Surgeons Adult Cardiac Surgery Database. *Ann Thorac Surg.* 2009;87:1431–7.
199. Chikwe J, Goldstone AB, Passage J, et al. A propensity score-adjusted retrospective comparison of early and mid-term results of mitral valve repair versus replacement in octogenarians. *Eur Heart J.* 2011;32:618–26.
200. Badhwar V, Peterson ED, Jacobs JP, et al. Longitudinal outcome of isolated mitral repair in older patients: results from 14,604 procedures performed from 1991 to 2007. *Ann Thorac Surg.* 2012;94:1870–7.
201. Grossi EA, Galloway AC, Miller JS, et al. Valve repair versus replacement for mitral insufficiency: when is a mechanical valve still indicated? *J Thorac Cardiovasc Surg.* 1998;115:389–94.
202. Chauvaud S, Fuzellier JF, Berrebi A, et al. Long-term (29 years) results of reconstructive surgery in rheumatic mitral valve insufficiency. *Circulation.* 2001;104:112–5.
203. Bolling SF, Li S, O'Brien SM, et al. Predictors of mitral valve repair: clinical and surgeon factors. *Ann Thorac Surg.* 2010;90:1904–11.
204. Gillinov AM, Blackstone EH, DM Cosgrove, III et al. Mitral valve repair with aortic valve replacement is superior to double valve replacement. *J Thorac Cardiovasc Surg.* 2003;125:1372–87.
205. Kang DH, Kim JH, Rim JH, et al. Comparison of early surgery versus conventional treatment in asymptomatic severe mitral regurgitation. *Circulation.* 2009;119:797–804.
206. Gillinov AM, Blackstone EH, Nowicki ER, et al. Valve repair versus valve replacement for degenerative mitral valve disease. *J Thorac Cardiovasc Surg.* 2008;135:885–93.
207. Duran CM, Gometza B, Saad E. Valve repair in rheumatic mitral disease: an unsolved problem. *J Card Surg.* 1994;9:282–5.
208. Suri RM, Vanoverschelde JL, Grigioni F, et al. Association between early surgical intervention vs watchful waiting and outcomes for mitral regurgitation due to flail mitral valve leaflets. *JAMA.* 2013;310:609–16.
209. Suri RM, Schaff HV, Dearani JA, et al. Recovery of left ventricular function after surgical correction of mitral regurgitation caused by leaflet prolapse. *J Thorac Cardiovasc Surg.* 2009;137:1071–6.
210. Ngaage DL, Schaff HV, Mullany CJ, et al. Influence of preoperative atrial fibrillation on late results of mitral repair: is concomitant ablation justified? *Ann Thorac Surg.* 2007;84:434–42.
211. Raine D, Dark J, Bourke JP. Effect of mitral valve repair/replacement surgery on atrial arrhythmia behavior. *J Heart Valve Dis.* 2004;13:615–21.
212. Cox JL. The surgical treatment of atrial fibrillation. IV. Surgical technique. *J Thorac Cardiovasc Surg.* 1991;101:584–92.
213. Kobayashi J, Kosakai Y, Isobe F, et al. Rationale of the Cox maze procedure for atrial fibrillation during redo mitral valve operations. *J Thorac Cardiovasc Surg.* 1996;112:1216–21.
214. Kawaguchi AT, Kosakai Y, Sasako Y, et al. Risks and benefits of combined maze procedure for atrial fibrillation associated with organic heart disease. *J Am Coll Cardiol.* 1996;28:985–90.
215. Olasinska-Wisniewska A, Mularek-Kubzdela T, Grajek S, et al. Impact of atrial remodeling on heart rhythm after radiofrequency ablation and mitral valve operations. *Ann Thorac Surg.* 2012;93:1449–55.
216. Feldman T, Foster E, Glower DD, et al. Percutaneous repair or surgery for mitral regurgitation. *N Engl J Med.* 2011;364:1395–406.
217. Effect of enalapril on mortality and the development of heart failure in asymptomatic patients with reduced left ventricular ejection fractions. The SOLVD Investigators. *N Engl J Med.* 1992;327:685–91.
218. Granger CB, McMurray JJ, Yusuf S, et al. Effects of candesartan in patients with chronic heart failure and reduced left-ventricular systolic function intolerant to angiotensin-converting-enzyme inhibitors: the CHARM-Alternative trial. *Lancet.* 2003;362:772–6.
219. Eriksson SV, Eneroth P, Kjekshus J, et al. Neuroendocrine activation in relation to left ventricular function in chronic severe congestive heart failure: a subgroup analysis from the Cooperative North Scandinavian Enalapril Survival Study (CONSENSUS). *Clin Cardiol.* 1994;17:603–6.
220. Pitt B, Zannad F, Remme WJ, et al. The effect of spironolactone on morbidity and mortality in patients with severe heart failure. Randomized Aldactone Evaluation Study Investigators. *N Engl J Med.* 1999;341:709–17.
221. Krum H, Roecker EB, Mohacsi P, et al. Effects of initiating carvedilol in patients with severe chronic heart failure: results from the COPERNICUS Study. *JAMA.* 2003;289:712–18.
222. St John Sutton MG, Plappert T, Abraham WT, et al. Effect of cardiac resynchronization therapy on left ventricular size and function in chronic heart failure. *Circulation.* 2003;107:1985–90.
223. van Bommel RJ, Marsan NA, Delgado V, et al. Cardiac resynchronization therapy as a therapeutic option in patients with moderate-severe functional mitral regurgitation and high operative risk. *Circulation.* 2011;124:912–9.
224. Grigioni F, Enriquez-Sarano M, Zehr KJ, et al. Ischemic mitral regurgitation: long-term outcome and prognostic implications with quantitative Doppler assessment. *Circulation.* 2001;103:1759–64.
225. Lancellotti P, Gerard PL, Pierard LA. Long-term outcome of patients with heart failure and dynamic functional mitral regurgitation. *Eur Heart J.* 2005;26:1528–32.
226. Trichon BH, Felker GM, Shaw LK, et al. Relation of frequency and severity of mitral regurgitation to survival among patients with left ventricular systolic dysfunction and heart failure. *Am J Cardiol.* 2003;91:538–43.
227. Rossi A, Dini FL, Faggiano P, et al. Independent prognostic value of functional mitral regurgitation in patients with heart failure. A quantitative analysis of 1256 patients with ischaemic and non-ischaemic dilated cardiomyopathy. *Heart.* 2011;97:1675–80.
228. Fattouch K, Guccione F, Sampognaro R, et al. POINT: Efficacy of adding mitral valve restrictive annuloplasty to coronary artery bypass grafting in patients with moderate ischemic mitral valve regurgitation: a randomized trial. *J Thorac Cardiovasc Surg.* 2009;138:278–85.
229. Mihaljevic T, Lam BK, Rajeswaran J, et al. Impact of mitral valve annuloplasty combined with revascularization in patients with functional ischemic mitral regurgitation. *J Am Coll Cardiol.* 2007;49:2191–201.
230. Wu AH, Aaronson KD, Bolling SF, et al. Impact of mitral valve annuloplasty on mortality risk in patients with mitral regurgitation and left ventricular systolic dysfunction. *J Am Coll Cardiol.* 2005;45:381–7.
231. Harris KM, TM Sundt, III et al. Can late survival of patients with moderate ischemic mitral regurgitation be impacted by intervention on the valve? *Ann Thorac Surg.* 2002;74:1468–75.
232. Benedetto U, Melina G, Roscitano A, et al. Does combined mitral valve surgery improve survival when compared to revascularization alone in patients with ischemic mitral regurgitation? A meta-analysis on 2479 patients. *J Cardiovasc Med (Hagerstown).* 2009;10:109–14.
233. Deja MA, Grayburn PA, Sun B, et al. Influence of mitral regurgitation repair on survival in the surgical treatment for ischemic heart failure trial. *Circulation.* 2012;125:2639–48.
234. Cohn LH, Rizzo RJ, Adams DH, et al. The effect of pathophysiology on the surgical treatment of ischemic mitral regurgitation: operative and late risks of repair versus replacement. *Eur J Cardiothorac Surg.* 1995;9:568–74.
235. Chan KM, Punjabi PP, Flather M, et al. Coronary artery bypass surgery with or without mitral valve annuloplasty in moderate functional ischemic mitral regurgitation: final results of the Randomized Ischemic Mitral Evaluation (RIME) trial. *Circulation.* 2012;126:2502–10.
236. Nath J, Foster E, Heidenreich PA. Impact of tricuspid regurgitation on long-term survival. *J Am Coll Cardiol.* 2004;43:405–9.
237. Dreyfus GD, Corbi PJ, Chan KM, et al. Secondary tricuspid regurgitation or dilatation: which should be the criteria for surgical repair? *Ann Thorac Surg.* 2005;79:127–32.
238. Chan V, Burwash IG, Lam BK, et al. Clinical and echocardiographic impact of functional tricuspid regurgitation repair at the time of mitral valve replacement. *Ann Thorac Surg.* 2009;88:1209–15.
239. Calafiore AM, Gallina S, Iaco AL, et al. Mitral valve surgery for functional mitral regurgitation: should moderate-or-more tricuspid regurgitation be treated? a propensity score analysis. *Ann Thorac Surg.* 2009;87:698–703.
240. Di Mauro M, Bivona A, Iaco AL, et al. Mitral valve surgery for functional mitral regurgitation: prognostic role of tricuspid regurgitation. *Eur J Cardiothorac Surg.* 2009;35:635–9.
241. Van de Veire NR, Braun J, Delgado V, et al. Tricuspid annuloplasty prevents right ventricular dilatation and progression of tricuspid regurgitation in patients with tricuspid annular dilatation undergoing mitral valve repair. *J Thorac Cardiovasc Surg.* 2011;141:1431–9.
242. Yilmaz O, Suri RM, Dearani JA, et al. Functional tricuspid regurgitation at the time of mitral valve repair for degenerative leaflet prolapse: the case for a selective approach. *J Thorac Cardiovasc Surg.* 2011;142:608–13.

243. Calafiore AM, Iaco AL, Romeo A, et al. Echocardiographic-based treatment of functional tricuspid regurgitation. *J Thorac Cardiovasc Surg*. 2011;142:308–13.
244. Navia JL, Brozzi NA, Klein AL, et al. Moderate tricuspid regurgitation with left-sided degenerative heart valve disease: to repair or not to repair? *Ann Thorac Surg*. 2012;93:59–67.
245. Kim JB, Yoo DG, Kim GS, et al. Mild-to-moderate functional tricuspid regurgitation in patients undergoing valve replacement for rheumatic mitral disease: the influence of tricuspid valve repair on clinical and echocardiographic outcomes. *Heart*. 2012;98:24–30.
246. Benedetto U, Melina G, Angeloni E, et al. Prophylactic tricuspid annuloplasty in patients with dilated tricuspid annulus undergoing mitral valve surgery. *J Thorac Cardiovasc Surg*. 2012;143:632–8.
247. Lancellotti P, Tribouilloy C, Hagendorff A, et al. European Association of Echocardiography recommendations for the assessment of valvular regurgitation. Part 1: aortic and pulmonary regurgitation (native valve disease). *Eur J Echocardiogr*. 2010;11:223–44.
248. Burstow DJ, Nishimura RA, Bailey KR, et al. Continuous wave Doppler echocardiographic measurement of prosthetic valve gradients. A simultaneous Doppler-catheter correlative study. *Circulation*. 1989;80:504–14.
249. Baumgartner H, Khan S, DeRobertis M, et al. Effect of prosthetic aortic valve design on the Doppler-catheter gradient correlation: an in vitro study of normal St. Jude, Medtronic-Hall, Starr-Edwards and Hancock valves. *J Am Coll Cardiol*. 1992;19:324–32.
250. Vandervoort PM, Greenberg NL, Powell KA, et al. Pressure recovery in bileaflet heart valve prostheses. Localized high velocities and gradients in central and side orifices with implications for Doppler-catheter gradient relation in aortic and mitral position. *Circulation*. 1995;92:3464–72.
251. Dumesnil JG, Honos GN, Lemieux M, et al. Validation and applications of indexed aortic prosthetic valve areas calculated by Doppler echocardiography. *J Am Coll Cardiol*. 1990;16:637–43.
252. Hammermeister K, Sethi GK, Henderson WG, et al. Outcomes 15 years after valve replacement with a mechanical versus a bioprosthetic valve: final report of the Veterans Affairs randomized trial. *J Am Coll Cardiol*. 2000;36:1152–8.
253. Badhwar V, Ofenloch JC, Rovin JD, et al. Noninferiority of closely monitored mechanical valves to bioprostheses overshadowed by early mortality benefit in younger patients. *Ann Thorac Surg*. 2012;93:748–53.
254. Weber A, Noureddine H, Englberger L, et al. Ten-year comparison of pericardial tissue valves versus mechanical prostheses for aortic valve replacement in patients younger than 60 years of age. *J Thorac Cardiovasc Surg*. 2012;144:1075–83.
255. Banbury MK, DM Cosgrove, III, Thomas JD, et al. Hemodynamic stability during 17 years of the Carpentier-Edwards aortic pericardial bioprosthesis. *Ann Thorac Surg*. 2002;73:1460–5.
256. Dellgren G, David TE, Raanani E, et al. Late hemodynamic and clinical outcomes of aortic valve replacement with the Carpentier-Edwards Perimount pericardial bioprosthesis. *J Thorac Cardiovasc Surg*. 2002;124:146–54.
257. Borger MA, Ivanov J, Armstrong S, et al. Twenty-year results of the Hancock II bioprosthesis. *J Heart Valve Dis*. 2006;15:49–55.
258. Myken PS, Bech-Hansen O. A 20-year experience of 1712 patients with the Biocor porcine bioprosthesis. *J Thorac Cardiovasc Surg*. 2009;137:76–81.
259. Oxenham H, Bloomfield P, Wheatley DJ, et al. Twenty year comparison of a Bjork-Shiley mechanical heart valve with porcine bioprostheses. *Heart*. 2003;89:715–21.
260. Stassano P, Di Tommaso L, Monaco M, et al. Aortic valve replacement: a prospective randomized evaluation of mechanical versus biological valves in patients ages 55 to 70 years. *J Am Coll Cardiol*. 2009;54:1862–8.
261. Cannegieter SC, Rosendaal FR, Briet E. Thromboembolic and bleeding complications in patients with mechanical heart valve prostheses. *Circulation*. 1994;89:635–41.
262. Stein PD, Alpert JS, Bussey HI, et al. Antithrombotic therapy in patients with mechanical and biological prosthetic heart valves. *Chest*. 2001;119:220S–7S.
263. Schlitt A, von Bardeleben RS, Ehrlich A, et al. Clopidogrel and aspirin in the prevention of thromboembolic complications after mechanical aortic valve replacement (CAPTA). *Thromb Res*. 2003;109:131–5.
264. Torella M, Torella D, Chiodini P, et al. LOWERing the INTensity of oral anticoGulant Therapy in patients with bileaflet mechanical aortic valve replacement: results from the “LOWERING-IT” Trial. *Am Heart J*. 2010;160:171–8.
265. Hering D, Piper C, Bergemann R, et al. Thromboembolic and bleeding complications following St. Jude Medical valve replacement: results of the German Experience With Low-Intensity Anticoagulation Study. *Chest*. 2005;127:53–9.
266. Acar J, Iung B, Boissel JP, et al. AREVA: multicenter randomized comparison of low-dose versus standard-dose anticoagulation in patients with mechanical prosthetic heart valves. *Circulation*. 1996;94:2107–12.
267. Horstkotte D, Scharf RE, Schultheiss HP. Intracardiac thrombosis: patient-related and device-related factors. *J Heart Valve Dis*. 1995;4:114–20.
268. Pruefer D, Dahm M, Dohmen G. Intensity of oral anticoagulation after implantation of St. Jude Medical mitral or multiple valve replacement: lessons learned from GELIA (GELIA 5). *Eur Heart J*. 2001;3:Q43.
269. Meschengieser SS, Fondevila CG, Frontrath J, et al. Low-intensity oral anticoagulation plus low-dose aspirin versus high-intensity oral anticoagulation alone: a randomized trial in patients with mechanical prosthetic heart valves. *J Thorac Cardiovasc Surg*. 1997;113:910–6.
270. Turpie AG, Gent M, Laupacis A, et al. A comparison of aspirin with placebo in patients treated with warfarin after heart-valve replacement. *N Engl J Med*. 1993;329:524–9.
271. Heras M, Chesebro JH, Fuster V, et al. High risk of thromboemboli early after bioprosthetic cardiac valve replacement. *J Am Coll Cardiol*. 1995;25:1111–9.
272. Colli A, Mestres CA, Castella M, et al. Comparing warfarin to aspirin (WoA) after aortic valve replacement with the St. Jude Medical Epic heart valve bioprosthesis: results of the WoA Epic pilot trial. *J Heart Valve Dis*. 2007;16:667–71.
273. Aramendi JJ, Mestres CA, Martinez-Leon J, et al. Triflusal versus oral anticoagulation for primary prevention of thromboembolism after bioprosthetic valve replacement (trac): prospective, randomized, co-operative trial. *Eur J Cardiothorac Surg*. 2005;27:854–60.
274. Nunez L, Gil AM, Larrea JL, et al. Prevention of thromboembolism using aspirin after mitral valve replacement with porcine bioprosthesis. *Ann Thorac Surg*. 1984;37:84–7.
275. Russo A, Grigioni F, Avierinos JF, et al. Thromboembolic complications after surgical correction of mitral regurgitation incidence, predictors, and clinical implications. *J Am Coll Cardiol*. 2008;51:1203–11.
276. Merie C, Kober L, Skov OP, et al. Association of warfarin therapy duration after bioprosthetic aortic valve replacement with risk of mortality, thromboembolic complications, and bleeding. *JAMA*. 2012;308:2118–25.
277. FDA Drug Safety Communication: Pradaxa (dabigatran etexilate mesylate) should not be used in patients with mechanical prosthetic heart valves. FDA. 2012. Available at: <http://www.fda.gov/Drugs/DrugSafety/ucm332912.htm>. Accessed February 20, 2014.
278. Van de Werf F, Brueckmann M, Connolly SJ, et al. A comparison of dabigatran etexilate with warfarin in patients with mechanical heart valves: THE Randomized, phase II study to evaluate the safety and pharmacokinetics of oral dabigatran etexilate in patients after heart valve replacement (RE-ALIGN). *Am Heart J*. 2012;163:931–7.
279. Eikelboom JW, Connolly SJ, Brueckmann M, et al. Dabigatran versus warfarin in patients with mechanical heart valves. *N Engl J Med*. 2013;369:1206–14.
280. Weibert RT, Le DT, Kayser SR, et al. Correction of excessive anticoagulation with low-dose oral vitamin K1. *Ann Intern Med*. 1997;126:959–62.
281. Yiu KH, Siu CW, Jim MH, et al. Comparison of the efficacy and safety profiles of intravenous vitamin K and fresh frozen plasma as treatment of warfarin-related over-anticoagulation in patients with mechanical heart valves. *Am J Cardiol*. 2006;97:409–11.
282. Barbetseas J, Nagueh SF, Pitsavos C, et al. Differentiating thrombus from pannus formation in obstructed mechanical prosthetic valves: an evaluation of clinical, transthoracic and transesophageal echocardiographic parameters. *J Am Coll Cardiol*. 1998;32:1410–7.
283. Tong AT, Roudaut R, Ozkan M, et al. Transesophageal echocardiography improves risk assessment of thrombolysis of prosthetic valve thrombosis: results of the international PRO-TEE registry. *J Am Coll Cardiol*. 2004;43:77–84.
284. Roudaut R, Serri K, Lafitte S. Thrombosis of prosthetic heart valves: diagnosis and therapeutic considerations. *Heart*. 2007;93:137–42.
285. Deviri E, Sareli P, Wisenbaugh T, et al. Obstruction of mechanical heart valve prostheses: clinical aspects and surgical management. *J Am Coll Cardiol*. 1991;17:646–50.
286. Roudaut R, Lafitte S, Roudaut MF, et al. Fibrinolysis of mechanical prosthetic valve thrombosis: a single-center study of 127 cases. *J Am Coll Cardiol*. 2003;41:653–8.

287. Keuleers S, Herijgers P, Herregods MC, et al. Comparison of thrombolysis versus surgery as a first line therapy for prosthetic heart valve thrombosis. *Am J Cardiol*. 2011;107:275–9.
288. Caceres-Loriga FM, Perez-Lopez H, Morlans-Hernandez K, et al. Thrombolysis as first choice therapy in prosthetic heart valve thrombosis. A study of 68 patients. *J Thromb Thrombolysis*. 2006;21:185–90.
289. Karthikeyan G, Senguttuvan NB, Joseph J, et al. Urgent surgery compared with fibrinolytic therapy for the treatment of left-sided prosthetic heart valve thrombosis: a systematic review and meta-analysis of observational studies. *Eur Heart J*. 2013;34:1557–66.
290. Roudaut R, Lafitte S, Roudaut MF, et al. Management of prosthetic heart valve obstruction: fibrinolysis versus surgery. Early results and long-term follow-up in a single-centre study of 263 cases. *Arch Cardiovasc Dis*. 2009;102:269–77.
291. Miller DL, Morris JJ, Schaff HV, et al. Reoperation for aortic valve periprosthetic leakage: identification of patients at risk and results of operation. *J Heart Valve Dis*. 1995;4:160–5.
292. Akins CW, Bitondo JM, Hilgenberg AD, et al. Early and late results of the surgical correction of cardiac prosthetic paravalvular leaks. *J Heart Valve Dis*. 2005;14:792–9.
293. Sorajja P, Cabalka AK, Hagler DJ, et al. Percutaneous repair of paravalvular prosthetic regurgitation: acute and 30-day outcomes in 115 patients. *Circ Cardiovasc Interv*. 2011;4:314–21.
294. Ruiz CE, Jelmin V, Kronzon I, et al. Clinical outcomes in patients undergoing percutaneous closure of periprosthetic paravalvular leaks. *J Am Coll Cardiol*. 2011;58:2210–7.
295. Sorajja P, Cabalka AK, Hagler DJ, et al. Long-term follow-up of percutaneous repair of paravalvular prosthetic regurgitation. *J Am Coll Cardiol*. 2011;58:2218–24.
296. Lopez J, Sevilla T, Vilacosta I, et al. Prognostic role of persistent positive blood cultures after initiation of antibiotic therapy in left-sided infective endocarditis. *Eur Heart J*. 2012.
297. Durack DT, Lukes AS, Bright DK. New criteria for diagnosis of infective endocarditis: utilization of specific echocardiographic findings. Duke Endocarditis Service. *Am J Med*. 1994;96:200–9.
298. Kupferwasser LI, Darius H, Muller AM, et al. Diagnosis of culture-negative endocarditis: the role of the Duke criteria and the impact of transesophageal echocardiography. *Am Heart J*. 2001;142:146–52.
299. Li JS, Sexton DJ, Mick N, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. *Clin Infect Dis*. 2000;30:633–8.
300. Perez-Vazquez A, Farinas MC, Garcia-Palomo JD, et al. Evaluation of the Duke criteria in 93 episodes of prosthetic valve endocarditis: could sensitivity be improved? *Arch Intern Med*. 2000;160:1185–91.
301. Botelho-Nevers E, Thuny F, Casalta JP, et al. Dramatic reduction in infective endocarditis-related mortality with a management-based approach. *Arch Intern Med*. 2009;169:1290–8.
302. Mugge A, Daniel WG, Frank G, et al. Echocardiography in infective endocarditis: reassessment of prognostic implications of vegetation size determined by the transthoracic and the transesophageal approach. *J Am Coll Cardiol*. 1989;14:631–8.
303. Burger AJ, Peart B, Jabi H, et al. The role of two-dimensional echocardiography in the diagnosis of infective endocarditis [corrected]. *Angiology*. 1991;42:552–60.
304. Irani WN, Grayburn PA, Afridi I. A negative transthoracic echocardiogram obviates the need for transesophageal echocardiography in patients with suspected native valve active infective endocarditis. *Am J Cardiol*. 1996;78:101–3.
305. Liu YW, Tsai WC, Hsu CH, et al. Judicious use of transthoracic echocardiography in infective endocarditis screening. *Can J Cardiol*. 2009;25:703–5.
306. Kemp WE Jr, Citrin B, Byrd BF 3rd. Echocardiography in infective endocarditis. *South Med J*. 1999;92:744–54.
307. Erbel R, Rohmann S, Drexler M, et al. Improved diagnostic value of echocardiography in patients with infective endocarditis by transesophageal approach. A prospective study. *Eur Heart J*. 1988;9:43–53.
308. Daniel WG, Mugge A, Martin RP, et al. Improvement in the diagnosis of abscesses associated with endocarditis by transesophageal echocardiography. *N Engl J Med*. 1991;324:795–800.
309. Sochowski RA, Chan KL. Implication of negative results on a mono-plane transesophageal echocardiographic study in patients with suspected infective endocarditis. *J Am Coll Cardiol*. 1993;21:216–21.
310. Shively BK, Gurule FT, Roldan CA, et al. Diagnostic value of transesophageal compared with transthoracic echocardiography in infective endocarditis. *J Am Coll Cardiol*. 1991;18:391–7.
311. Pedersen WR, Walker M, Olson JD, et al. Value of transesophageal echocardiography as an adjunct to transthoracic echocardiography in evaluation of native and prosthetic valve endocarditis. *Chest*. 1991;100:351–6.
312. Ronderos RE, Portis M, Stoermann W, et al. Are all echocardiographic findings equally predictive for diagnosis in prosthetic endocarditis? *J Am Soc Echocardiogr*. 2004;17:664–9.
313. Roe MT, Abramson MA, Li J, et al. Clinical information determines the impact of transesophageal echocardiography on the diagnosis of infective endocarditis by the duke criteria. *Am Heart J*. 2000;139:945–51.
314. Karalis DG, Bansal RC, Hauck AJ, et al. Transesophageal echocardiographic recognition of subaortic complications in aortic valve endocarditis. Clinical and surgical implications. *Circulation*. 1992;86:353–62.
315. El-Ahdab F, Benjamin DK Jr, Wang A, et al. Risk of endocarditis among patients with prosthetic valves and *Staphylococcus aureus* bacteremia. *Am J Med*. 2005;118:225–9.
316. Mylonakis E, Calderwood SB. Infective endocarditis in adults. *N Engl J Med*. 2001;345:1318–30.
317. Rohmann S, Erbel R, Darius H, et al. Prediction of rapid versus prolonged healing of infective endocarditis by monitoring vegetation size. *J Am Soc Echocardiogr*. 1991;4:465–74.
318. Shapira Y, Weisenberg DE, Vaturi M, et al. The impact of intraoperative transesophageal echocardiography in infective endocarditis. *Isr Med Assoc J*. 2007;9:299–302.
319. Yao F, Han L, Xu ZY, et al. Surgical treatment of multivalvular endocarditis: twenty-one-year single center experience. *J Thorac Cardiovasc Surg*. 2009;137:1475–80.
320. Watanakunakorn C. *Staphylococcus aureus* endocarditis at a community teaching hospital, 1980 to 1991. An analysis of 106 cases. *Arch Intern Med*. 1994;154:2330–5.
321. Abraham J, Mansour C, Veledar E, et al. *Staphylococcus aureus* bacteremia and endocarditis: the Grady Memorial Hospital experience with methicillin-sensitive *S aureus* and methicillin-resistant *S aureus* bacteremia. *Am Heart J*. 2004;147:536–9.
322. Kaasch AJ, Fowler VG Jr, Rieg S, et al. Use of a simple criteria set for guiding echocardiography in nosocomial *Staphylococcus aureus* bacteremia. *Clin Infect Dis*. 2011;53:1–9.
323. San Martin J, Sarria C, de las Cuevas C, et al. Relevance of clinical presentation and period of diagnosis in prosthetic valve endocarditis. *J Heart Valve Dis*. 2010;19:131–8.
324. Knudsen JB, Fuursted K, Petersen E, et al. Failure of clinical features of low probability endocarditis. The early echo remains essential. *Scand Cardiovasc J*. 2011;45:133–8.
325. Feuchtnr GM, Stolzmann P, Dichtl W, et al. Multislice computed tomography in infective endocarditis: comparison with transesophageal echocardiography and intraoperative findings. *J Am Coll Cardiol*. 2009;53:436–44.
326. Gahide G, Bommart S, Demaria R, et al. Preoperative evaluation in aortic endocarditis: findings on cardiac CT. *AJR Am J Roentgenol*. 2010;194:574–8.
327. Lentini S, Monaco F, Tancredi F, et al. Aortic valve infective endocarditis: could multi-detector CT scan be proposed for routine screening of concomitant coronary artery disease before surgery? *Ann Thorac Surg*. 2009;87:1585–7.
328. Fagman E, Perrotta S, Bech-Hanssen O, et al. ECG-gated computed tomography: a new role for patients with suspected aortic prosthetic valve endocarditis. *Eur Radiol*. 2012;22:2407–14.
329. Fowler VG Jr, Li J, Corey GR, et al. Role of echocardiography in evaluation of patients with *Staphylococcus aureus* bacteremia: experience in 103 patients. *J Am Coll Cardiol*. 1997;30:1072–8.
330. Rasmussen RV, Host U, Arpi M, et al. Prevalence of infective endocarditis in patients with *Staphylococcus aureus* bacteraemia: the value of screening with echocardiography. *Eur J Echocardiogr*. 2011;12:414–20.
331. Sullenberger AL, Avedissian LS, Kent SM. Importance of transesophageal echocardiography in the evaluation of *Staphylococcus aureus* bacteremia. *J Heart Valve Dis*. 2005;14:23–8.
332. Masuda J, Yutani C, Waki R, et al. Histopathological analysis of the mechanisms of intracranial hemorrhage complicating infective endocarditis. *Stroke*. 1992;23:843–50.
333. Tornos P, Almirante B, Mirabet S, et al. Infective endocarditis due to *Staphylococcus aureus*: deleterious effect of anticoagulant therapy. *Arch Intern Med*. 1999;159:473–5.
334. Carpenter JL, McAllister CK. Anticoagulation in prosthetic valve endocarditis. *South Med J*. 1983;76:1372–5.

335. Lieberman A, Hass WK, Pinto R, et al. Intracranial hemorrhage and infarction in anticoagulated patients with prosthetic heart valves. *Stroke*. 1978;9:18–24.
336. Wilson WR, Geraci JE, Danielson GK, et al. Anticoagulant therapy and central nervous system complications in patients with prosthetic valve endocarditis. *Circulation*. 1978;57:1004–7.
337. Ananthasubramaniam K, Beattie JN, Rosman HS, et al. How safely and for how long can warfarin therapy be withheld in prosthetic heart valve patients hospitalized with a major hemorrhage? *Chest*. 2001;119:478–84.
338. Pruitt AA, Rubin RH, Karchmer AW, et al. Neurologic complications of bacterial endocarditis. *Medicine (Baltimore)*. 1978;57:329–43.
339. Chan KL, Tam J, Dumesnil JG, et al. Effect of long-term aspirin use on embolic events in infective endocarditis. *Clin Infect Dis*. 2008;46:37–41.
340. Fang MC, Go AS, Chang Y, et al. Death and disability from warfarin-associated intracranial and extracranial hemorrhages. *Am J Med*. 2007;120:700–5.
341. Rasmussen RV, Snygg-Martin U, Olaison L, et al. Major cerebral events in *Staphylococcus aureus* infective endocarditis: is anticoagulant therapy safe? *Cardiology*. 2009;114:284–91.
342. Jault F, Gandjbakhch I, Rama A, et al. Active native valve endocarditis: determinants of operative death and late mortality. *Ann Thorac Surg*. 1997;63:1737–41.
343. Hasbun R, Vikram HR, Barakat LA, et al. Complicated left-sided native valve endocarditis in adults: risk classification for mortality. *JAMA*. 2003;289:1933–40.
344. Kiefer T, Park L, Tribouilloy C, et al. Association between valvular surgery and mortality among patients with infective endocarditis complicated by heart failure. *JAMA*. 2011;306:2239–47.
345. Tornos P, Sanz E, Permanyer-Miralda G, et al. Late prosthetic valve endocarditis. Immediate and long-term prognosis. *Chest*. 1992;101:37–41.
346. Gordon SM, Serkey JM, Longworth DL, et al. Early onset prosthetic valve endocarditis: the Cleveland Clinic experience 1992–1997. *Ann Thorac Surg*. 2000;69:1388–92.
347. Wang A, Athan E, Pappas PA, et al. Contemporary clinical profile and outcome of prosthetic valve endocarditis. *JAMA*. 2007;297:1354–61.
348. Remadi JP, Habib G, Nadjji G, et al. Predictors of death and impact of surgery in *Staphylococcus aureus* infective endocarditis. *Ann Thorac Surg*. 2007;83:1295–302.
349. Hill EE, Herijgers P, Claus P, et al. Infective endocarditis: changing epidemiology and predictors of 6-month mortality: a prospective cohort study. *Eur Heart J*. 2007;28:196–203.
350. Aksoy O, Sexton DJ, Wang A, et al. Early surgery in patients with infective endocarditis: a propensity score analysis. *Clin Infect Dis*. 2007;44:364–72.
351. Ellis ME, Al-Abdely H, Sandridge A, et al. Fungal endocarditis: evidence in the world literature, 1965–1995. *Clin Infect Dis*. 2001;32:50–62.
352. Wolff M, Witchitz S, Chastang C, et al. Prosthetic valve endocarditis in the ICU. Prognostic factors of overall survival in a series of 122 cases and consequences for treatment decision. *Chest*. 1995;108:688–94.
353. Chirouze C, Cabell CH, Fowler VG Jr, et al. Prognostic factors in 61 cases of *Staphylococcus aureus* prosthetic valve infective endocarditis from the International Collaboration on Endocarditis merged database. *Clin Infect Dis*. 2004;38:1323–7.
354. Melgar GR, Nasser RM, Gordon SM, et al. Fungal prosthetic valve endocarditis in 16 patients. An 11-year experience in a tertiary care hospital. *Medicine (Baltimore)*. 1997;76:94–103.
355. Wang K, Gobel F, Gleason DF, et al. Complete heart block complicating bacterial endocarditis. *Circulation*. 1972;46:939–47.
356. Middlemost S, Wisenbaugh T, Meyerowitz C, et al. A case for early surgery in native left-sided endocarditis complicated by heart failure: results in 203 patients. *J Am Coll Cardiol*. 1991;18:663–7.
357. Chan KL. Early clinical course and long-term outcome of patients with infective endocarditis complicated by perivalvular abscess. *CMAJ*. 2002;167:19–24.
358. Jault F, Gandjbakhch I, Chastre JC, et al. Prosthetic valve endocarditis with ring abscesses. Surgical management and long-term results. *J Thorac Cardiovasc Surg*. 1993;105:1106–13.
359. Anguera I, Miro JM, Vilacosta I, et al. Aorto-cavitary fistulous tract formation in infective endocarditis: clinical and echocardiographic features of 76 cases and risk factors for mortality. *Eur Heart J*. 2005;26:288–97.
360. Klieverik LM, Yacoub MH, Edwards S, et al. Surgical treatment of active native aortic valve endocarditis with allografts and mechanical prostheses. *Ann Thorac Surg*. 2009;88:1814–21.
361. Hill EE, Herijgers P, Claus P, et al. Abscess in infective endocarditis: the value of transesophageal echocardiography and outcome: a 5-year study. *Am Heart J*. 2007;154:923–8.
362. Manne MB, Shrestha NK, Lytle BW, et al. Outcomes after surgical treatment of native and prosthetic valve infective endocarditis. *Ann Thorac Surg*. 2012;93:489–93.
363. Sohail MR, Uslan DZ, Khan AH, et al. Infective endocarditis complicating permanent pacemaker and implantable cardioverter-defibrillator infection. *Mayo Clin Proc*. 2008;83:46–53.
364. Athan E, Chu VH, Tattevin P, et al. Clinical characteristics and outcome of infective endocarditis involving implantable cardiac devices. *JAMA*. 2012;307:1727–35.
365. Rundstrom H, Kennergren C, Andersson R, et al. Pacemaker endocarditis during 18 years in Goteborg. *Scand J Infect Dis*. 2004;36:674–9.
366. Ho HH, Siu CW, Yiu KH, et al. Prosthetic valve endocarditis in a multicenter registry of Chinese patients. *Asian Cardiovasc Thorac Ann*. 2010;18:430–4.
367. Thuny F, Di Salvo G, Belliard O, et al. Risk of embolism and death in infective endocarditis: prognostic value of echocardiography: a prospective multicenter study. *Circulation*. 2005;112:69–75.
368. Kang DH, Kim YJ, Kim SH, et al. Early surgery versus conventional treatment for infective endocarditis. *N Engl J Med*. 2012;366:2466–73.
369. Schaefer C. Angiotensin II-receptor-antagonists: further evidence of fetotoxicity but not teratogenicity. *Birth Defects Res A Clin Mol Teratol*. 2003;67:591–4.
370. Cooper WO, Hernandez-Diaz S, Arbogast PG, et al. Major congenital malformations after first-trimester exposure to ACE inhibitors. *N Engl J Med*. 2006;354:2443–51.
371. Shotan A, Widerhorn J, Hurst A, et al. Risks of angiotensin-converting enzyme inhibition during pregnancy: experimental and clinical evidence, potential mechanisms, and recommendations for use. *Am J Med*. 1994;96:451–6.
372. Abouzied AM, Al Abbady M, Al Gendy MF, et al. Percutaneous balloon mitral commissurotomy during pregnancy. *Angiology*. 2001;52:205–9.
373. Ben FM, Gamra H, Betbout F, et al. Percutaneous balloon mitral commissurotomy during pregnancy. *Heart*. 1997;77:564–7.
374. de Souza JA, Martinez EE Jr, Ambrose JA, et al. Percutaneous balloon mitral valvuloplasty in comparison with open mitral valve commissurotomy for mitral stenosis during pregnancy. *J Am Coll Cardiol*. 2001;37:900–3.
375. Glantz JC, Pomerantz RM, Cunningham MJ, et al. Percutaneous balloon valvuloplasty for severe mitral stenosis during pregnancy: a review of therapeutic options. *Obstet Gynecol Surv*. 1993;48:503–8.
376. Iung B, Cormier B, Elias J, et al. Usefulness of percutaneous balloon commissurotomy for mitral stenosis during pregnancy. *Am J Cardiol*. 1994;73:398–400.
377. Tzemos N, Silversides CK, Colman JM, et al. Late cardiac outcomes after pregnancy in women with congenital aortic stenosis. *Am Heart J*. 2009;157:474–80.
378. Banning AP, Pearson JF, Hall RJ. Role of balloon dilatation of the aortic valve in pregnant patients with severe aortic stenosis. *Br Heart J*. 1993;70:544–5.
379. Easterling TR, Chadwick HS, Otto CM, et al. Aortic stenosis in pregnancy. *Obstet Gynecol*. 1988;72:113–8.
380. Lao TT, Adelman AG, Sermer M, et al. Balloon valvuloplasty for congenital aortic stenosis in pregnancy. *Br J Obstet Gynaecol*. 1993;100:1141–2.
381. McIvor RA. Percutaneous balloon aortic valvuloplasty during pregnancy. *Int J Cardiol*. 1991;32:1–3.
382. Myerson SG, Mitchell AR, Ormerod OJ, et al. What is the role of balloon dilatation for severe aortic stenosis during pregnancy? *J Heart Valve Dis*. 2005;14:147–50.
383. Tumelero RT, Duda NT, Tognon AP, et al. Percutaneous balloon aortic valvuloplasty in a pregnant adolescent. *Arq Bras Cardiol*. 2004;82:98–7.
384. Chan WS, Anand S, Ginsberg JS. Anticoagulation of pregnant women with mechanical heart valves: a systematic review of the literature. *Arch Intern Med*. 2000;160:191–196.
385. Meschengieser SS, Fondevila CG, Santarelli MT, et al. Anticoagulation in pregnant women with mechanical heart valve prostheses. *Heart*. 1999;82:23–6.
386. Abildgaard U, Sandset PM, Hammerstrom J, et al. Management of pregnant women with mechanical heart valve prosthesis: thromboprophylaxis with low molecular weight heparin. *Thromb Res*. 2009;124:262–7.

387. McLintock C, McCowan LM, North RA. Maternal complications and pregnancy outcome in women with mechanical prosthetic heart valves treated with enoxaparin. *BJOG*. 2009;116:1585–92.
388. Oran B, Lee-Parritz A, Ansell J. Low molecular weight heparin for the prophylaxis of thromboembolism in women with prosthetic mechanical heart valves during pregnancy. *Thromb Haemost*. 2004;92:747–51.
389. Quinn J, Von Klemperer K, Brooks R, et al. Use of high intensity adjusted dose low molecular weight heparin in women with mechanical heart valves during pregnancy: a single-center experience. *Haematologica*. 2009;94:1608–12.
390. Sillesen M, Hjortdal V, Vejstrup N, et al. Pregnancy with prosthetic heart valves - 30 years' nationwide experience in Denmark. *Eur J Cardiothorac Surg*. 2011;40:448–54.
391. De Santo LS, Romano G, Della Corte A, et al. Mechanical aortic valve replacement in young women planning on pregnancy: maternal and fetal outcomes under low oral anticoagulation, a pilot observational study on a comprehensive pre-operative counseling protocol. *J Am Coll Cardiol*. 2012;59:1110–5.
392. Salazar E, Izaguirre R, Verdejo J, et al. Failure of adjusted doses of subcutaneous heparin to prevent thromboembolic phenomena in pregnant patients with mechanical cardiac valve prostheses. *J Am Coll Cardiol*. 1996;27:1698–703.
393. Vitale N, De Feo M, Cotrufo M. Anticoagulation for prosthetic heart valves during pregnancy: the importance of warfarin daily dose. *Eur J Cardiothorac Surg*. 2002;22:656.
394. Rowan JA, McCowan LM, Raudkivi PJ, et al. Enoxaparin treatment in women with mechanical heart valves during pregnancy. *Am J Obstet Gynecol*. 2001;185:633–7.
395. James AH, Brancazio LR, Gehrig TR, et al. Low-molecular-weight heparin for thromboprophylaxis in pregnant women with mechanical heart valves. *J Matern Fetal Neonatal Med*. 2006;19:543–9.
396. Yinon Y, Siu SC, Warshafsky C, et al. Use of low molecular weight heparin in pregnant women with mechanical heart valves. *Am J Cardiol*. 2009;104:1259–63.
397. Ginsberg JS, Chan WS, Bates SM, et al. Anticoagulation of pregnant women with mechanical heart valves. *Arch Intern Med*. 2003;163:694–8.
398. Mark DB, Berman DS, Budoff MJ, et al. ACCF/ACR/AHA/NASCI/SAIP/SCAI/SCCT 2010 expert consensus document on coronary computed tomographic angiography: a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents. *Circulation*. 2010;121:2509–43.
399. Gilard M, Cornily JC, Penneç PY, et al. Accuracy of multislice computed tomography in the preoperative assessment of coronary disease in patients with aortic valve stenosis. *J Am Coll Cardiol*. 2006;47:2020–4.
400. Manghat NE, Morgan-Hughes GJ, Broadley AJ, et al. 16-detector row computed tomographic coronary angiography in patients undergoing evaluation for aortic valve replacement: comparison with catheter angiography. *Clin Radiol*. 2006;61:749–57.
401. Meijboom WB, Mollet NR, Van Mieghem CA, et al. Pre-operative computed tomography coronary angiography to detect significant coronary artery disease in patients referred for cardiac valve surgery. *J Am Coll Cardiol*. 2006;48:1658–65.
402. Reant P, Brunot S, Lafitte S, et al. Predictive value of noninvasive coronary angiography with multidetector computed tomography to detect significant coronary stenosis before valve surgery. *Am J Cardiol*. 2006;97:1506–10.
403. Scheffel H, Leschka S, Plass A, et al. Accuracy of 64-slice computed tomography for the preoperative detection of coronary artery disease in patients with chronic aortic regurgitation. *Am J Cardiol*. 2007;100:701–6.
404. Galas A, Hryniewiecki T, Kepka C, et al. May dual-source computed tomography angiography replace invasive coronary angiography in the evaluation of patients referred for valvular disease surgery? *Kardiol Pol*. 2012;70:877–82.
405. Doukas G, Samani NJ, Alexiou C, et al. Left atrial radiofrequency ablation during mitral valve surgery for continuous atrial fibrillation: a randomized controlled trial. *JAMA*. 2005;294:2323–9.
406. Blomstrom-Lundqvist C, Johansson B, Berglin E, et al. A randomized double-blind study of epicardial left atrial cryoablation for permanent atrial fibrillation in patients undergoing mitral valve surgery: the SWEDish Multicentre Atrial Fibrillation study (SWEDMAF). *Eur Heart J*. 2007;28:2902–8.
407. Liu X, Tan HW, Wang XH, et al. Efficacy of catheter ablation and surgical CryoMaze procedure in patients with long-lasting persistent atrial fibrillation and rheumatic heart disease: a randomized trial. *Eur Heart J*. 2010;31:2633–41.
408. Calleja AM, Dommaraju S, Gaddam R, et al. Cardiac risk in patients aged >75 years with asymptomatic, severe aortic stenosis undergoing noncardiac surgery. *Am J Cardiol*. 2010;105:1159–63.
409. Zahid M, Sonel AF, Saba S, et al. Perioperative risk of noncardiac surgery associated with aortic stenosis. *Am J Cardiol*. 2005;96:436–8.
410. Torsher LC, Shub C, Rettke SR, et al. Risk of patients with severe aortic stenosis undergoing noncardiac surgery. *Am J Cardiol*. 1998;81:448–52.
411. Agarwal S, Rajamanickam A, Bajaj NS, et al. Impact of aortic stenosis on postoperative outcomes after noncardiac surgeries. *Circ Cardiovasc Qual Outcomes*. 2013;6:193–200.

KEY WORDS: AHA Scientific Statements ■ anticoagulation therapy ■ aortic stenosis ■ aortic regurgitation ■ bicuspid aortic valve ■ cardiac surgery ■ heart valves ■ infective endocarditis ■ mitral stenosis ■ mitral regurgitation ■ prosthetic valves ■ pulmonic regurgitation ■ pulmonic stenosis ■ transcatheter aortic valve replacement ■ tricuspid stenosis ■ tricuspid regurgitation ■ valvular heart disease

Appendix 1. Author Relationships With Industry and Other Entities (Relevant)—2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease

Committee Member	Employment	Consultant	Speaker's Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness	Voting Recusals by Section*
Rick A. Nishimura, <i>Co-Chair</i>	Mayo Clinic, Division of Cardiovascular Disease—Judd and Mary Morris Leighton Professor of Medicine	None	None	None	None	None	None	None
Catherine M. Otto, <i>Co-Chair</i>	University of Washington, Division of Cardiology—Professor of Medicine	None	None	None	None	None	None	None
Robert O. Bonow	Northwestern University Medical School—Goldberg Distinguished Professor	None	None	None	None	None	None	None
Blase A. Carabello	VA Medical Center—Professor of Medicine, Baylor College of Medicine	None	None	None	None	<ul style="list-style-type: none"> • Edwards Lifesciences (DSMB)† • Medtronic† 	None	2.4.2, 3.2.3, 3.2.4, 4.3.3, 5.1.3, 6.2.3, 7.3.1.1, 7.3.3, 7.4.3, 8.2.3, 11.1.1, 11.1.2, 11.2.2, 11.3.2, 11.4, 11.6.1, 11.6.2, 11.6.3, 11.7.3, 11.8.3, 12.2.1, 12.2.3, 13.1, 13.1.2, 13.1.3, 13.2.1, 13.2.3, 13.3.1, 13.3.2, 14.1, and 14.2.2.
John P. Erwin, III	Scott and White Hospital and Clinic—Senior Staff Cardiologist, Associate Professor of Medicine	None	None	None	None	None	None	None
Robert A. Guyton	Emory Clinic, Inc.—Professor and Chief, Division of Cardiothoracic Surgery	<ul style="list-style-type: none"> • Medtronic 	None	None	None	None	<ul style="list-style-type: none"> • Defendant, cardiac surgery, 2013 	2.4.2, 3.2.3, 3.2.4, 4.3.3, 5.1.3, 6.2.3, 7.3.1.1, 7.3.3, 7.4.3, 8.2.3, 11.1.1, 11.1.2, 11.2.2, 11.3.2, 11.4, 11.6.1, 11.6.2, 11.6.3, 11.7.3, 11.8.3, 12.2.1, 12.2.3, 13.1, 13.1.2, 13.1.3, 13.2.1, 13.2.3, 13.3.1, 13.3.2, 14.1, and 14.2.2.
Patrick T. O'Gara	Brigham and Women's Hospital—Professor of Medicine; Harvard Medical School—Director of Clinical Cardiology	None	None	None	None	None	None	None

(Continued)

Appendix 1. Continued

Committee Member	Employment	Consultant	Speaker's Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness	Voting Recusals by Section*
Carlos E. Ruiz	Lenox Hill Heart and Vascular Institute of New York—Professor and Chief, Division of Pediatric Cardiology	None	None	None	None	None	None	None
Nikolaos J. Skubas	Weill Cornell Medical College—Associate Professor of Anesthesiology and Director of Cardiac Anesthesia	None	None	None	None	None	None	None
Paul Sorajja	Mayo Clinic—Associate Professor of Medicine	None	None	• Intellectual property in patent on percutaneous closure of paravalvular prosthetic regurgitation	None	None	None	None
Thoralf M. Sundt, III	Massachusetts General Hospital—Chief, Division Cardiac Surgery	• St. Jude Medical	None	None	None	None	• AATS, Secretary-Elect	2.4.2, 3.2.3, 3.2.4, 4.3.3, 5.1.3, 6.2.3, 7.3.1.1, 7.3.3, 7.4.3, 8.2.3, 11.1.1, 11.1.2, 11.2.2, 11.3.2, 11.4, 11.6.1, 11.6.2, 11.6.3, 11.7.3, 11.8.3, 12.2.1, 12.2.3, 13.1, 13.1.2, 13.1.3, 13.2.1, 13.2.3, 13.3.1, 13.3.2, 14.1, and 14.2.2.
James D. Thomas	Cleveland Clinic—Professor of Medicine and Biomedical Engineering	None	None	None	None	None	None	None

This table represents the relationships of committee members with industry and other entities that were determined to be relevant to this document. These relationships were reviewed and updated in conjunction with all meetings and/or conference calls of the writing committee during the document development process. The table does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of ≥5% of the voting stock or share of the business entity, or ownership of ≥\$10 000 of the fair market value of the business entity; or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. Relationships that exist with no financial benefit are also included for the purpose of transparency. Relationships in this table are modest unless otherwise noted. According to the ACC/AHA, a person has a *relevant* relationship IF: a) The *relationship or interest* relates to the same or similar subject matter, intellectual property or asset, topic, or issue addressed in the *document*; or b) The *company/entity* (with whom the relationship exists) makes a drug, drug class, or device addressed in the *document*, or makes a competing drug or device addressed in the *document*; or c) The *person or a member of the person's household*, has a reasonable potential for financial, professional or other personal gain or loss as a result of the issues/content addressed in the *document*.

*Writing committee members are required to recuse themselves from voting on sections to which their specific relationships with industry and other entities may apply. Section numbers pertain to those in the full-text guideline.

†No financial benefit.

AATS indicates American Association of Thoracic Surgery; DSMB, data safety monitoring board; and VA, Veterans Affairs.

Appendix 2. Reviewer Relationships With Industry and Other Entities (Relevant)—2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease

Reviewer	Representation	Employment	Consultant	Speaker's Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Blair D. Erb	Official Reviewer—ACC Board of Trustees	Bozeman Deaconess Cardiology Consultants—Physician	None	None	None	None	• Medtronic	None
Mario J. Garcia	Official Reviewer—AHA	Montefiore Medical Center-Albert Einstein College of Medicine—Chief, Division of Cardiology	None	None	None	None	• Medtronic† • Pfizer	None
Smadar Kort	Official Reviewer—ACC Board of Governors	Stony Brook University Medical Center—Clinical Professor of Medicine; Director, Echocardiography Laboratory; Director, Cardiovascular Imaging	None	None	None	None	• Pfizer	None
Richard J. Kovacs	Official Reviewer—ACC/AHA Task Force on Practice Guidelines	Indiana University—Clinical Director and Professor of Clinical Medicine, Krannert Institute of Cardiology; Associate Dean for Clinical Research	• Biomedical Systems • Insight Pharmaceuticals • Theravance*	None	None	None	• Cook Incorporated-Med Institute* • Eli Lilly* (DSMB)	None
David H. Adams	Organizational Reviewer—AATS	The Mount Sinai Medical Center—Marie-Josée and Henry R. Kravis Professor; Chairman, Department of Cardiothoracic Surgery	None	None	None	None	• Edward Lifesciences* Medtronic	None
Howard Herrmann	Organizational Reviewer—SCAI	University of Pennsylvania Perelman School of Medicine—Professor of Medicine; Director, Interventional Cardiology Program	• Paieon • Siemens Medical • St. Jude Medical	None	• Micro-Interventional Devices* • Abbott Vascular* • Edward Lifesciences* • Medtronic† • Siemens Medical* • St. Jude Medical • WL Gore and Associates	None	None	None
Sunil V. Mankad	Organizational Reviewer—ASE	Mayo Clinic—Associate Professor of Medicine	None	None	None	None	None	None
Patrick McCarthy	Organizational Reviewer—STS	Northwestern University, Feinberg School of Medicine—Surgical Director, Bluhm Cardiovascular Institute	• Abbott Vascular* • Baxter • Edward Lifesciences*	None	• Cardious • Edward Lifesciences* • MiCardia	None	• Direct Flow	None
Stanton K. Shernan	Organizational Reviewer—SCA	Brigham and Women's Hospital	None	• Philips Healthcare	None	None	• National Board of Echocardiography Officer†	• Defendant, Echocardiography, 2012
Mouaz H. Al-Mallah	Content Reviewer—Prevention of Cardiovascular Disease Committee	King Abdul-Aziz Cardiac Center—Associate Professor of Medicine	• Bracco	None	None	None	None	None

(Continued)

Appendix 2. Continued

Reviewer	Representation	Employment	Consultant	Speaker's Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Nancy M. Albert	Content Reviewer—ACC/AHA Task Force on Practice Guidelines	Cleveland Clinic Foundation—Senior Director of Nursing Research and Clinical Nursing Specialists, Kaufman Center for Heart Failure	• Medtronic	None	None	None	None	None
Jeffrey L. Anderson	Content Reviewer—ACC/AHA Task Force on Practice Guidelines	Intermountain Medical Center—Associate Chief of Cardiology	• Sanofi-aventis	None	None	• GlaxoSmithKline	None	None
Robert H. Beekman	Content Reviewer—Adult Congenital and Pediatric Cardiology Section	Cincinnati Children's Hospital Medical Center—Division of Cardiology	• St. Jude Medical	None	None	None	None	None
Vera A. Bittner	Content Reviewer—Prevention of Cardiovascular Disease Committee	University of Alabama at Birmingham—Professor of Medicine; Director, Cardiac Rehabilitation	Novartis	None	None	• Amgen • AstraZeneca† • Eli Lilly† • GlaxoSmithKline* • NIH/Joint Abbott* • Sanofi-aventis† • Schering Plough†	• Pfizer	None
Biykem Bozkurt	Content Reviewer—ACC/AHA Task Force on Practice Guidelines	Michael E. DeBakey VA Medical Center—Mary and Gordon Cain Chair and Professor of Medicine	None	None	None	• Forest Pharmaceuticals—PI*	• Amgen • Corthera • Novartis	None
Joseph Cleveland	Content Reviewer—Heart Failure and Transplant Council	University of Colorado Anschutz Medical Center—Professor of Surgery; Surgical Director, Cardiac Transplantation and Mechanical Circulatory Support	Sorin	None	None	Heartware	None	None
Salvatore P. Costa	Content Reviewer	Geisel School of Medicine at Dartmouth—Associate Professor of Medicine; Dartmouth-Hitchcock Medical Center Section of Cardiology—Medical Director, Echocardiography Lab	None	None	None	• Edwards Lifesciences (PARTNERS2 Trial)—Co-PI†	None	None
Lesley Curtis	Content Reviewer—ACC/AHA Task Force on Practice Guidelines	Duke University School of Medicine—Associate Professor in Medicine	None	None	None	• GE Healthcare** • GlaxoSmithKline* • Johnson and Johnson*	None	None
Lxarry S. Dean	Content Reviewer—Intervention Council	University of Washington School of Medicine—Professor of Medicine and Surgery; Director, UW Medicine Regional Heart Center	• Philips Medical	• Daiichi-Sankyo • Eli Lilly	Emageon	• Edwards Lifesciences*	None	None
Jeanne M. DeCara	Content Reviewer—Council on Clinical Practice	University of Chicago Medicine—Associate Professor of Medicine, Section of Cardiology	None	None	None	None	None	None

(Continued)

Appendix 2. Continued

Reviewer	Representation	Employment	Consultant	Speaker's Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Susan Farkas	Content Reviewer—ACC Board of Governors	Sanford Medical Center Fargo—Cardiologist	None	None	None	None	None	None
Frederico Gentile	Content Reviewer	Centro Medico Diagnostico	None	None	None	None	None	None
Linda Gillam	Content Reviewer	Morristown Medical Center—Professor of Cardiology; Vice Chair, Cardiovascular Medicine	None	None	None	• Edwards Lifesciences†	• Edwards Lifesciences†	None
Charles Hogue, Jr	Content Reviewer	Johns Hopkins University School of Medicine—Professor of Anesthesiology & Critical Care Medicine; Chief, Division of Adult Anesthesia	None	None	None	None	• Merck (DSMB)	• Defendant, Operative Mortality, 2012
Pei-Hsiu Huang	Content Reviewer—Content Lifelong Learning Oversight Committee (Educational)	Sutter Medical Center—Interventional Cardiologist	None	None	None	• St. Jude Medical • Boston Scientific • Abbott Vascular	None	None
Judy W. Hung	Content Reviewer	Harvard Medical School—Associate Professor of Medicine; Massachusetts General Hospital—Associate Director, Echocardiography	None	None	None	None	None	None
Bernard Iung	Content Reviewer	Bichat Hospital—Professor of Cardiology	• Abbott • Boehringer Ingelheim • Edwards Lifesciences • Valtech	None	None	None	• Archives of Cardiovascular Disease (Associate Editor)† • Boehringer Ingelheim†	None
Amar Krishnaswamy	Content Reviewer—Content Lifelong Learning Oversight Committee (Educational)	Cleveland Clinic—Associate Staff, Robert and Suzanne Tomsich Department of Cardiovascular Medicine	None	None	None	None	None	None
David Lanfear	Content Reviewer—Heart Failure and Transplant Council	Henry Ford Hospital—Assistant Professor, Heart and Vascular Institute in the Center for Health Services Research	• Thoratec	None	None	• Amgen* • Biocontrol* • CardioRentis	None	None
Richard Lange	Content Reviewer	University of Texas Health Science Center at San Antonio—Professor of Medicine	None	None	None	None	None	None
M. Regina Lantin-Hermoso	Content Reviewer—Adult Congenital and Pediatric Cardiology Section	Texas Children's Hospital Heart Center—Associate Professor of Pediatrics, Section of Cardiology; Medical Director, Cardiology Clinics	None	None	None	None	None	None

(Continued)

Appendix 2. Continued

Reviewer	Representation	Employment	Consultant	Speaker's Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
D. Craig Miller	Content Reviewer	Stanford University Medical Center, Cardiothoracic Surgery Clinic—Professor of Cardiovascular Surgery	<ul style="list-style-type: none"> • Abbott Vascular • Medtronic[†] • Medtronic Heart Valve Division • MitraClip • Edwards Lifesciences[†] • St. Jude Medical 	None	None	• Edwards Lifesciences [†]	None	None
Tom C. Nguyen	Content Reviewer—Content Lifelong Learning Oversight Committee (Educational)	University of Texas Health Science Center at Houston—Assistant Professor of Cardiovascular Surgery	None	None	None	None	None	None
Philippe Pibarot	Content Reviewer	Laval University—Professor, Department of Medicine; University of Cardiology and Pneumology of Québec—Chair, Canada Research Chair in Valvular Heart Diseases	None	None	None	• Edwards Lifesciences [†]	None	None
Geetha Raghuvver	Content Reviewer—ACC Board of Governors	University of Missouri-Kansas City School of Medicine—Associate Professor of Pediatrics; Pediatric Cardiologist	None	None	None	None	None	None
Michael J. Reardon	Content Reviewer	Methodist DeBakey Heart & Vascular Center—Professor of Cardiothoracic Surgery	Medtronic	None	None	• Medtronic	None	None
Raphael Rosenhek	Content Reviewer	Medical University of Vienna—Associate Professor, Department of Cardiology	None	<ul style="list-style-type: none"> • Abbott • Edwards Lifesciences 	None	None	None	None
Hartzell V. Schaff	Content Reviewer	Mayo Clinic—Stuart W. Harrington Professor of Surgery	None	None	None	None	None	None
Allan Schwartz	Content Reviewer	Columbia University—Chief, Division of Cardiology	None	None	None	None	None	None
Frank W. Sellke	Content Reviewer—ACC/AHA Task Force on Practice Guidelines	Rhode Island Hospital—Chief, Division of Cardiothoracic Surgery and Lifespan Heart Center	None	None	None	<ul style="list-style-type: none"> • CLS Behring • The Medicines Company 	<ul style="list-style-type: none"> • CLS Behring • The Medicines Company 	None
Dipan Shah	Content Reviewer—Cardiovascular Section Leadership Council	Houston Methodist DeBakey Heart & Vascular Center—Director, Cardiovascular MRI Laboratory; Weill Cornell Medical College—Assistant Professor of Medicine	None	<ul style="list-style-type: none"> • AstraZeneca[*] • Lantheus Medical Imaging 	None	<ul style="list-style-type: none"> • Astellas[*] • Siemens Medical Solutions[*] 	None	None
Win-Kuang Shen	Content Reviewer—ACC/AHA Task Force on Practice Guidelines	Mayo Clinic Arizona, Phoenix Campus—Professor of Medicine; Consultant	None	None	None	None	None	None

(Continued)

Appendix 2. Continued

Reviewer	Representation	Employment	Consultant	Speaker's Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Adam Skolnick	Content Reviewer—Geriatric Cardiology Section Leadership Council	NYU School of Medicine—Assistant Professor of Medicine, Leon H. Charney Division of Cardiology; Associate Director, Health Care Center	None	None	None	None	None	None
Craig R. Smith	Content Reviewer	Columbia University College of Physicians and Surgeons—Professor of Surgery; Chair, Department of Surgery; New York-Presbyterian Hospital/ Columbia University Medical Center—Surgeon-in-Chief	None	None	None	• Edwards Lifesciences—PI	None	None
Ruth H. Strasser	Content Reviewer—AIG	Heart Centre, University Hospital, University of Technology, Dresden—Professor, Director, and Chair, Internal Medicine and Cardiology Clinic; Medical Director, Heart Centre	None	None	None	None	• Abbott† • AstraZeneca† • Bayer† • Biosensors† • Pfizer†	None
Rakesh Suri	Content Reviewer	Mayo Clinic—Associate Professor of Surgery	None	None	None	None	• Edwards Lifesciences† • Sorin† • St. Jude Medical†	None
Vinod Thourani	Content Reviewer—Surgeon Council	Emory University	• Edward Lifesciences • Sorin • St. Jude Medical	None	• Apica Cardiovascular†	Maquet	None	None
Alec Vahanian	Content Reviewer	Hospital Bichat—Department de Cardiologie	• Abbott Vascular • Edwards Lifesciences • Medtronic • St. Jude Medical • Valtech	None	None	None	None	None
Andrew Wang	Content Reviewer	Duke University Medical Center—Professor of Medicine	None	None	None	• Abbott Vascular† • Edwards Lifesciences†	None	• Defendant, Sudden death, 2012

This table represents the relationships of reviewers with industry and other entities that were disclosed at the time of peer review and determined to be relevant to this document. It does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of ≥5% of the voting stock or share of the business entity, or ownership of ≥\$10 000 of the fair market value of the business entity; or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. A relationship is considered to be modest if it is less than significant under the preceding definition. Relationships that exist with no financial benefit are also included for the purpose of transparency. Relationships in this table are modest unless otherwise noted. Names are listed in alphabetical order within each category of review. According to the ACC/AHA, a person has a *relevant* relationship IF: a) The *relationship or interest* relates to the same or similar subject matter, intellectual property or asset, topic, or issue addressed in the *document*; or b) The *company/entity* (with whom the relationship exists) makes a drug, drug class, or device addressed in the *document*, or makes a competing drug or device addressed in the *document*; or c) The *person or a member of the person's household*, has a reasonable potential for financial, professional or other personal gain or loss as a result of the issues/content addressed in the *document*.

*No financial benefit.

†Significant relationship.

AATS indicates American Association for Thoracic Surgery; ACC, American College of Cardiology; AHA, American Heart Association; AIG, Association of International Governors; ASE, American Society of Echocardiography; DSMB, Data and Safety Monitoring Board; MRI, magnetic resonance imaging; NIH, National Institutes of Health; NYU, New York University; PARTNERS, Placement of Aortic Transcatheter Valves; PI, Principal Investigator; SCA, Society of Cardiovascular Anesthesiologists; SCAI, Society for Cardiovascular Angiography and Interventions; STS, Society of Thoracic Surgeons; and VA, Veterans Affairs.