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ACC/AHA GUIDELINES CLARIFICATION

Surgery for Aortic Dilatation in Patients With Bicuspid Aortic Valves

A Statement of Clarification From the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

Endorsed by the American College of Radiology, American Association for Thoracic Surgery, American Society of Echocardiography, American Stroke Association, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine, Society of Cardiovascular Anesthesiologists, Society of Interventional Radiology, and the Society of Thoracic Surgeons

2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM Guidelines for the Diagnosis and Management of Patients With Thoracic Aortic Disease Representative Members*

Loren F. Hiratzka, MD, FACC, FAHA, *Chair*

Mark A. Creager, MD, FACC, FAHA†
Eric M. Isselbacher, MD, FACC
Lars G. Svensson, MD, PhD, FACC

2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease Representative Members*

Rick A. Nishimura, MD, MACC, FAHA, *Chair*

Robert O. Bonow, MD, MACC, FAHA
Robert A. Guyton, MD, FACC†
Thoralf M. Sundt III, 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 Task Force on Clinical Practice Guidelines Liaison.

This document was approved by the American College of Cardiology Board of Trustees and Executive Committee, the American Heart Association Science Advisory and Coordinating Committee, and the American Heart Association and Executive Committee in August 2015, and by the TAD partner organizations (AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM).

The online-only comprehensive table of author relationships with industry and other entities is available at http://jaccjacc.acc.org/Clinical_Document/TAD_VHD_Guideline_Clarification_Author_Comprehensive_RWI_Table.doc.

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ACC/AHA Task Force Members

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E. Magnus Ohman, MD, FACC‡
Susan J. Pressler, PhD, RN, FAHA
Frank W. Sellke, MD, FACC, FAHA‡
Win-Kuang Shen, MD, FACC, FAHA‡
Duminda N. Wijeysundera, MD, PhD

‡Former Task Force member; current member during this writing effort.

ABSTRACT

Two guidelines from the American College of Cardiology (ACC), the American Heart Association (AHA), and collaborating societies address the risk of aortic dissection in patients with bicuspid aortic valves and severe aortic enlargement: the "2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM Guidelines for the Diagnosis and Management of Patients With Thoracic Aortic Disease" (J Am Coll Cardiol 2010;55:e27–130) and the "2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease" (J Am Coll Cardiol 2014;63:e57–185). However, the 2 guidelines differ with regard to the recommended threshold of aortic root or ascending aortic dilatation that would justify surgical intervention in patients with bicuspid aortic valves. The ACC and AHA therefore convened a subcommittee representing members of the 2 guideline writing committees to review the evidence, reach consensus, and draft a statement of clarification for both guidelines. This statement of clarification uses the ACC/AHA revised structure for delineating the Class of Recommendation and Level of Evidence to provide recommendations that replace those contained in Section 9.2.2.1 of the thoracic aortic disease guideline and Section 5.1.3 of the valvular heart disease guideline.

The association between bicuspid aortic valve (BAV) and dilatation of the aortic root and ascending aorta is well established, as is the risk of aortic dissection in patients with BAV and severe aortic enlargement. However, data are limited with regard to the aortic diameter at which the risk of dissection is high enough to warrant operative intervention in patients who do not otherwise fulfill criteria for aortic valve replacement (AVR) on the basis of severe aortic stenosis or aortic regurgitation. Two guidelines from the American College of Cardiology/American Heart Association (ACC/AHA) and collaborating societies differed with regard to the recommended threshold of aortic root or ascending aortic dilatation that would justify surgical intervention in such patients (1,2). A subcommittee representing members of the 2 writing committees, which met current organizational policies for disclosure of relationships with industry (Appendix 1), was convened to review the evidence, reach consensus, and draft the present statement as an addendum to both guidelines. The evidence table to support this addendum is available as an Online Data Supplement. This statement was approved by the 2 guideline writing committees, underwent peer review (Appendix 2), and received formal approval by the ACC and AHA and endorsements by partner/collaborating organizations. The following recommendations replace those contained in Sections 9.2.2.1 and 5.1.3, respectively, of the original guidelines (1,2) and use the revised structure for delineating the Class of Recommendation and Level of Evidence adopted by the ACC/AHA Task Force on Clinical Practice Guidelines (3) (**Table 1**, Recommendations Table, **Table 2**).

TABLE 1 **Applying Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care* (Updated August 2015)**

CLASS (STRENGTH) OF RECOMMENDATION

CLASS I (STRONG) — **Benefit >>> Risk**

Suggested phrases for writing recommendations:
- Is recommended
- Is indicated/useful/effective/beneficial
- Should 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

CLASS IIa (MODERATE) — **Benefit >> Risk**

Suggested phrases for writing recommendations:
- Is reasonable
- Can be useful/effective/beneficial
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is probably recommended/indicated in preference to treatment B
  - It is reasonable to choose treatment A over treatment B

CLASS IIb (WEAK) — **Benefit ≥ Risk**

Suggested phrases for writing recommendations:
- May/might be reasonable
- May/might be considered
- Usefulness/effectiveness is unknown/unclear/uncertain or not well established

CLASS III: No Benefit (MODERATE) — **Benefit = Risk**
(Generally, LOE A or B use only)

Suggested phrases for writing recommendations:
- Is not recommended
- Is not indicated/useful/effective/beneficial
- Should not be performed/administered/other

CLASS III: Harm (STRONG) — **Risk > Benefit**

Suggested phrases for writing recommendations:
- Potentially harmful
- Causes harm
- Associated with excess morbidity/mortality
- Should not be performed/administered/other

LEVEL (QUALITY) OF EVIDENCE‡

LEVEL A
- High-quality evidence‡ from more than 1 RCT
- Meta-analyses of high-quality RCTs
- One or more RCTs corroborated by high-quality registry studies

LEVEL B-R (Randomized)
- Moderate-quality evidence‡ from 1 or more RCTs
- Meta-analyses of moderate-quality RCTs

LEVEL B-NR (Nonrandomized)
- Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies
- Meta-analyses of such studies

LEVEL C-LD (Limited Data)
- Randomized or nonrandomized observational or registry studies with limitations of design or execution
- Meta-analyses of such studies
- Physiological or mechanistic studies in human subjects

LEVEL C-EO (Expert Opinion)

Consensus of expert opinion based on clinical experience

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR I and IIa; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

Intervention in Patients With BAV and Dilatation of the Aortic Root (Sinuses) or Ascending Aorta: Recommendations

COR	LOE	RECOMMENDATIONS
I	B-NR	**1. Operative intervention to repair or replace the aortic root (sinuses) or replace the ascending aorta is indicated in asymptomatic patients with BAV if the diameter of the aortic root or ascending aorta is 5.5 cm or greater (4–8).** See Online Data Supplement. There is uncertainty about whether patients with BAV should undergo aortic repair at diameters smaller than those recommended for patients with ascending aortic aneurysms in the setting of a tricuspid aortic valve. Both the histology and mechanical properties of the ascending aorta differ between those with BAV and those with tricuspid aortic valves, raising the possibility that the aortic wall may be more vulnerable to dissection in those with BAV (4–6). Conversely, among patients presenting with acute type A aortic dissection, the mean diameter of the aortic root or ascending aorta may actually be greater in those with BAV than in those with tricuspid valves (7,8). Such conflicting evidence and the lack of sufficient prospective observational or randomized trial data create uncertainty about the diameter at which aortic root or ascending aortic repair should be performed in those with BAV. There is broad agreement, however, that those with aortic root or ascending aortic aneurysms, regardless of etiology, merit surgical repair when the aortic diameter is ≥5.5 cm, and this threshold should apply to those with BAV as well.
IIa	B-NR	**1. Operative intervention to repair or replace the aortic root (sinuses) or replace the ascending aorta is reasonable in asymptomatic patients with BAV if the diameter of the aortic root or ascending aorta is 5.0 cm or greater and an additional risk factor for dissection is present (e.g., family history of aortic dissection or aortic growth rate ≥0.5 cm per year) or if the patient is at low surgical risk and the surgery is performed by an experienced aortic surgical team in a center with established expertise in these procedures (2,7–9).** See Online Data Supplement. In patients determined to have higher risk of dissection on the basis of family history or rapid aortic expansion (≥0.5 cm per year), surgical intervention is reasonable when the aortic diameter reaches ≥5.0 cm. Patients with BAV tend to present with aortic dissection at younger ages than patients with tricuspid aortic valves (7–9), and those with large asymptomatic aneurysms may benefit from prophylactic aortic repair at younger ages than patients with tricuspid aortic valves who have similarsized aneurysms. Observational data support operation for patients with aortic root diameter ≥5.0 cm (10). Therefore, repair or replacement of the aortic root or replacement of the ascending aorta is reasonable when the aortic diameter is ≥5.0 cm in patients with BAV who are at low surgical risk according to the "2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease" (**Table 2**) (2) when the operation is performed by experienced surgeons in centers with established expertise in these procedures to ensure low risk of morbidity and mortality. Whether the diameter threshold for surgery differs according to the level of maximum dilatation (aortic sinuses versus ascending aorta) requires further investigation. In shortstatured patients with Turner syndrome and BAV, absolute measurement of aortic root or ascending aortic diameter may not predict the risk of aortic dissection as well as aortic diameter index ≥2.5 cm/m^2 (11,12). In addition, in 1 study of patients with BAV, a maximum aortic root cross-sectional area-to-height ratio ≥10 cm^2/m was also a predictor of aortic dissection (10).
IIa	C-EO	**2. Replacement of the ascending aorta is reasonable in patients with BAV undergoing AVR because of severe aortic stenosis or aortic regurgitation when the diameter of the ascending aorta is greater than 4.5 cm (13–17).** … For patients with BAV, data are limited with regard to the aortic diameter at which the risk of dissection is high enough to warrant replacement of the ascending aorta at the time of AVR. The risk of progressive aortic dilatation and dissection after AVR in patients with BAV has been the subject of several studies, but definitive data are lacking (13–17).

TABLE 2 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**	
Frailty†	None **AND**	1 Index (mild) **OR**	≥2 Indices (moderate to severe) **OR**	Predicted risk with surgery of death or major morbidity (all-cause) >50% at 1 y **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-m 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 FEV_1 <50% or DL co_2 <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, cerebrovascular accident (stroke); DL co_2, diffusion capacity for carbon dioxide; FEV_1, 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.

Reproduced from Nishimura et al. (2).

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KEY WORDS ACC/AHA Clinical Practice Guidelines, anticoagulation therapy, heart valves, thoracic aortic aneurysm, thoracic aortic disease, thoracic aortic dissection, valvular heart disease

APPENDIX 1. AUTHOR RELATIONSHIPS WITH INDUSTRY AND OTHER ENTITIES (RELEVANT)—SURGERY FOR AORTIC DILATATION IN PATIENTS WITH BICUSPID AORTIC VALVES: A STATEMENT OF CLARIFICATION FROM THE ACC/AHA TASK FORCE ON CLINICAL PRACTICE GUIDELINES (DECEMBER 2014)

Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness	Voting Recusals*
Loren F. Hiratzka, TAD, Chair	TriHealth Heart Institute—Medical Director, Cardiac Surgery	None	None	None	None	None	None	None
Rick A. Nishimura, VHD, Chair	Mayo Clinic, Division of Cardiovascular Disease—Judd and Mary Morris Leighton Professor of Medicine	None	None	None	None	None	None	None
Mark A. Creager, TAD Liaison	Dartmouth-Hitchcock Medical Center—Director, Heart and Vascular Center and Geisel School of Medicine at Dartmouth—Professor of Medicine	None	None	None	None	None	None	None
Robert A. Guyton, VHD Liaison	Emory Healthcare—Professor and Chief, Division of Cardiothoracic Surgery	• Medtronic†	None	None	None	None	None	Recused
Eric M. Isselbacher, TAD	Massachusetts General Hospital—Co-Director Thoracic Aortic Center; Harvard Medical School—Associate Professor of Medicine	None	None	None	None	None	None	None
Lars G. Svensson, TAD	Cleveland Clinic, Heart and Vascular Institute—Chairman; Cleveland Clinic Lerner College of Medicine of Case Western Reserve University—Professor of Surgery	None	None	None	None	• Posthorax	None	Recused
Robert O. Bonow, VHD	Northwestern University Feinberg School of Medicine—Goldberg Distinguished Professor of Cardiology	None	None	None	None	None	None	None
Thoralf M. Sundt III, VHD	Massachusetts General Hospital—Chief, Division of Cardiac Surgery; Harvard Medical School—Professor of Surgery	None	None	None	• Edwards Life-Science—Partner trial (PI) • Medtronic—Perigon trial (PI)	None	None	Recused

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†Significant relationship.

ACC indicates American College of Cardiology; AHA, American Heart Association; PI, principal investigator; TAD, thoracic aortic disease; and VHD, valvular heart disease.

APPENDIX 2. REVIEWER RELATIONSHIPS WITH INDUSTRY AND OTHER ENTITIES (RELEVANT)—SURGERY FOR AORTIC DILATATION IN PATIENTS WITH BICUSPID AORTIC VALVES: A STATEMENT OF CLARIFICATION FROM THE ACC/AHA TASK FORCE ON CLINICAL PRACTICE GUIDELINES (JUNE 2015)

Reviewer	Representation	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
David H. Adams	Official Reviewer—AATS	The Mount Sinai Medical Center—Marie-Josee and Henry R. Kravis Professor; Chairman, Department of Cardiothoracic Surgery	• Edward Lifesciences* • Medtronic*	None	None	None	None	None
Albert T. Cheung	Official Reviewer—SCA	Stanford University School of Medicine—Professor, Department of Anesthesiology; Division Chief, Cardiothoracic Anesthesiology; Program Director, Adult Cardiothoracic Anesthesiology	• Covidien	None	None	None	None	None
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Antionette S. Gomes	Official Reviewer—AHA	UCLA School of Medicine—Professor, Radiology and Medicine	None	None	None	None	None	None
Anuj Gupta	Official Reviewer—ACC Board of Governors	University of Maryland School of Medicine—Assistant Professor of Medicine and Director, Cardiac Catheterization Laboratory	None	None	None	• Direct Flow Medical (Co-PI)† • Edwards (Co-PI)† • Medtronic (Co-PI)†	None	None
Jonathan L. Halperin	Official Reviewer—ACC/AHA Task Force on Clinical Practice Guidelines	Mt. Sinai Medical Center—Professor of Medicine	• Medtronic	None	None	None	None	None
Clifford J. Kavinsky	Official Reviewer—SCAI	Rush-Presbyterian-St. Luke's Medical Center—Training Director	None	None	None	None	None	None

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Reviewer	Representation	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
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*Significant relationship.

†No financial benefit.

AATS indicates American Association for Thoracic Surgery; ACC, American College of Cardiology; ACR, American College of Radiology; AHA, American Heart Association; ASE, American Society of Echocardiography; ASA, American Stroke Association; PI, principal investigator; SCA, Society of Cardiovascular Anesthesiologists; SCAI, Society for Cardiovascular Angiography and Interventions; SIR, Society of Interventional Radiology; STS, Society of Thoracic Surgeons; and SVM, Society of Vascular Medicine.