2018 AHA/ACC Guideline for the Management of Adults With Congenital Heart Disease

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2018 AHA/ACC Guideline for the Management of Adults With Congenital Heart Disease

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

Developed in Collaboration With the American Association for Thoracic Surgery, American Society of Echocardiography, Heart Rhythm Society, International Society for Adult Congenital Heart Disease, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons

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Preamble

Since 1980, the American College of Cardiology (ACC) and American Heart Association (AHA) have translated scientific evidence into clinical practice guidelines (guidelines) with recommendations to improve cardiovascular health. These guidelines, which are based on systematic methods to evaluate and classify evidence, provide a cornerstone for quality cardiovascular care. The ACC and AHA sponsor the development and publication of guidelines without commercial support, and members of each organization volunteer their time to the writing and review efforts. Guidelines are official policy of the ACC and AHA.

Intended Use

Practice guidelines provide recommendations applicable to patients with or at risk of developing cardiovascular disease. The focus is on medical practice in the United States, but guidelines developed in collaboration with other organizations can have a global impact. Although guidelines may be used to inform regulatory or payer decisions, they are intended to improve patients' quality of care and align with patients' interests. Guidelines are intended to define practices meeting the needs of patients in most, but not all, circumstances and should not replace clinical judgment.

Clinical Implementation

Management in accordance with guideline recommendations is effective only when followed by both practitioners and patients. Adherence to recommendations can be enhanced by shared decision-making between clinicians and patients, with patient engagement in selecting interventions on the basis of individual values, preferences, and associated conditions and comorbidities.

Methodology and Modernization

The ACC/AHA Task Force on Clinical Practice Guidelines (Task Force) continuously reviews, updates, and modifies guideline methodology on the basis of published standards from organizations, including the Institute of Medicine (P-1, P-2), and on the basis of internal reevaluation. Similarly, the presentation and delivery of guidelines are reevaluated and modified on the basis of evolving technologies and other factors to facilitate optimal dissemination of information to healthcare professionals at the point of care.

Toward this goal, this guideline continues the introduction of an evolved format of presenting guideline recommendations and associated text called the "modular knowledge chunk format." Each modular "chunk" includes a table of related recommendations, a brief synopsis, recommendation-specific supportive text, and when appropriate, flow diagrams or additional tables. References are provided at the end of the document in their respective sections. Additionally, this format will facilitate seamless updating of guidelines with focused updates as new evidence is published, as well as content tagging for rapid electronic retrieval of related recommendations on a topic of interest. This evolved approach format was instituted when this guideline was near completion; therefore, the present document represents a transitional format that best suits the text as written. Future guidelines will fully implement this format, including provisions for limiting the amount of text in a guideline.

Recognizing the importance of cost–value considerations in certain guidelines, when appropriate and feasible, an analysis of the value of a drug, device, or intervention may be performed in accordance with the ACC/AHA methodology (P-3).

To ensure that guideline recommendations remain current, new data are reviewed on an ongoing basis, with full guideline revisions commissioned in approximately 6-year cycles. Publication of new, potentially practice-changing study results that are relevant to an existing or new drug, device, or management strategy will prompt evaluation by the Task Force, in consultation with the relevant guideline writing committee, to determine whether a focused update should be commissioned. For

additional information and policies regarding guideline development, we encourage readers to consult the ACC/AHA guideline methodology manual (P-4) and other methodology articles (P-5–P-8).

Selection of Writing Committee Members

The Task Force strives to avoid bias by selecting experts from a broad array of backgrounds. Writing committee members represent different geographic regions, sexes, ethnicities, races, intellectual perspectives/biases, and scopes of clinical practice. The Task Force may also invite organizations and professional societies with related interests and expertise to participate as partners, collaborators, or endorsers.

Relationships With Industry and Other Entities

The ACC and AHA have rigorous policies and methods to ensure that guidelines are developed without bias or improper influence. The complete relationships with industry and other entities (RWI) policy can be found at http://www.acc.org/guidelines/about-guidelines-and-clinical-documents/relationships-with-industry-policy. Appendix 1 of the present document lists writing committee members' relevant RWI. For the purposes of full transparency, writing committee members' comprehensive disclosure information is available online (http://jaccjacc.acc.org/Clinical_Document/ACHD_Exec_Summ_and_Full_Text__Comp_RWI_Table_08-02-18.pdf). Comprehensive disclosure information for the Task Force is available at http://www.acc.org/guidelines/about-guidelines-and-clinical-documents/guidelines-and-documents-task-forces.

Evidence Review and Evidence Review Committees

In developing recommendations, the writing committee uses evidence-based methodologies that are based on all available data (P-4–P-7). Literature searches focus on randomized controlled trials (RCTs) but also include registries, nonrandomized comparative and descriptive studies, case series, cohort studies, systematic reviews, and expert opinion. Only key references are cited.

An independent evidence review committee (ERC) is commissioned when there are 1 or more questions deemed of utmost clinical importance that merit formal systematic review. The systematic review will determine which patients are most likely to benefit from a drug, device, or treatment strategy and to what degree. Criteria for commissioning an ERC and formal systematic review include: a) the absence of a current authoritative systematic review, b) the feasibility of defining the benefit and risk in a time frame consistent with the writing of a guideline, c) the relevance to a substantial number of patients, and d) the likelihood that the findings can be translated into actionable recommendations. ERC members may include methodologists, epidemiologists, healthcare providers, and biostatisticians. The recommendations developed by the writing committee on the basis of the systematic review are marked with "SR".

Guideline-Directed Management and Therapy

The term guideline-directed management and therapy (GDMT) encompasses clinical evaluation, diagnostic testing, and pharmacological and procedural treatments. For these and all recommended drug treatment regimens, the reader should confirm the dosage by reviewing product insert material and evaluate the treatment regimen for contraindications and interactions. The recommendations are limited to drugs, devices, and treatments approved for clinical use in the United States.

Class of Recommendation and Level of Evidence

The Class of Recommendation (COR) indicates the strength of the recommendation, encompassing the estimated magnitude and certainty of benefit in proportion to risk. The Level of Evidence (LOE) rates the quality of scientific evidence that supports the intervention on the basis of the type, quantity, and consistency of data from clinical trials and other sources (Table 1) (P-4–P-6).

Glenn N. Levine, MD, FACC, FAHA
Chair, ACC/AHA Task Force on Clinical Practice Guidelines

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) *(Generally, LOE A or B use only)*	**Benefit = Risk**
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.

1. Introduction

1.1. Methodology and Evidence Review

The recommendations listed in this guideline are, whenever possible, evidence-based. An initial extensive evidence review, which included literature derived from research involving human subjects, published in English, and indexed in MEDLINE (through PubMed), EMBASE, the Cochrane Library, the Agency for Healthcare Research and Quality, and other selected databases relevant to this guideline, was conducted from April 2014 to November 2014. Key search words included but were not limited to the following: *adult congenital heart disease, anesthesia, aortic aneurysm, aortic stenosis, atrial septal defect, arterial switch operation, bradycardia, bicuspid aortic valve, cardiac catheterization, cardiac imaging, cardiovascular magnetic resonance, cardiac reoperation, cardiovascular surgery, chest x-ray, cirrhosis, coarctation of the aorta, congenital heart defects, congenitally corrected transposition of the great arteries, contraception, coronary artery abnormalities, cyanotic congenital heart disease, dextro-transposition of the great arteries, double inlet left ventricle, Ebstein anomaly, echocardiography, Eisenmenger syndrome, electrocardiogram, endocarditis, exercise test, Fontan, heart catheterization, heart defect, heart failure, infertility, l-transposition of the great arteries, medical therapy, myocardial infarction, noncardiac surgery, patent ductus arteriosus, perioperative care, physical activity, postoperative complications, pregnancy, preoperative assessment, psychosocial, pulmonary arterial hypertension, hypoplastic left heart syndrome, pulmonary regurgitation, pulmonary stenosis, pulmonary valve replacement, right heart obstruction, right ventricle to pulmonary artery conduit, single ventricle, supravalvular pulmonary stenosis, surgical therapy, tachyarrhythmia, tachycardia, tetralogy of Fallot, transplantation, tricuspid atresia, Turner syndrome,* and *ventricular septal defect.* Additional relevant studies published through January 2018, during the guideline writing process, were also considered by the writing committee, and added to the evidence tables when appropriate. The final evidence tables, included in the Online Data Supplement, summarize the evidence used by the writing committee to formulate recommendations. References selected and published in this document are representative and not all-inclusive.

As noted in the preamble, an independent ERC was commissioned to perform a formal systematic review of critical clinical questions related to adult congenital heart disease (ACHD), the results of which were considered by the writing committee for incorporation into this guideline. Concurrent with this process, writing committee members evaluated study data relevant to the rest of the guideline. The findings of the ERC and the writing committee members were formally presented and discussed, and then recommendations were developed. The systematic review reports on “Medical Therapy for Systemic Right Ventricles: A Systematic Review (Part 1) for the 2018 AHA/ACC Guideline for the Management of Adults With Congenital Heart Disease” (S1.1-1) and “Interventional Therapy Versus Medical Therapy for Secundum Atrial Septal Defect: A Systematic Review (Part 2) for the 2018 AHA/ACC Guideline for the Management of Adults With Congenital Heart Disease” (S1.1-2) are published in conjunction with this guideline.

1.2. Organization of the Writing Committee

The writing committee consisted of pediatric and adult congenital cardiologists, interventional cardiologists, electrophysiologists, surgeons, and an advance practice nurse. The writing committee included representatives from the ACC, AHA, and American Association for Thoracic Surgery (AATS), American Society of Echocardiography (ASE), Heart Rhythm Society (HRS), International Society for Adult Congenital Heart Disease (ISACHD), Society for Cardiovascular Angiography and Interventions (SCAI), and the Society of Thoracic Surgeons (STS).

1.3. Document Review and Approval

This document was reviewed by 3 official reviewers each nominated by the ACC and AHA, and 1 to 2 reviewers each from the AATS, ASE, HRS, ISACHD, SCAI, STS; and 32 individual content reviewers. 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 AATS, ASE, HRS, ISACHD, SCAI, and STS.

1.4. Scope of the Guideline

The 2018 ACHD guideline is a full revision of the "2008 ACC/AHA Guidelines for the Management of Adults with Congenital Heart Disease" (S1.4-1), which was the first U.S. guideline to be published on the topic. This revision uses the 2008 ACHD guideline as a framework and incorporates new data and growing ACHD expertise to develop recommendations. Congenital heart disease (CHD) encompasses a range of structural cardiac abnormalities present before birth attributable to abnormal fetal cardiac development but does not include inherited disorders that may have cardiac manifestations such as Marfan syndrome or hypertrophic cardiomyopathy. Also not included are anatomic variants such as patent foramen ovale. Valvular heart disease (VHD) may be congenital, so management overlaps with the "2014 AHA/ACC Guidelines for the Management of Patients With Valvular Heart Disease" (S1.4-2), particularly for bicuspid aortic valve (BAV) disease. Where overlap exists, this document focuses on the diagnosis and treatment of congenital valve disease when it differs from acquired valve disease, whether because of anatomic differences, presence of concomitant lesions, or differences to consider given the relatively young age of patients with ACHD. This guideline is not intended to apply to children (<18 years of age) with CHD or adults with acquired VHD, heart failure (HF), or other cardiovascular diseases.

The prevalence of ACHD is growing because of the success of pediatric cardiology and congenital cardiac surgery in diagnosing and treating congenital heart defects in children. Improved survival to adulthood is most striking for those with the most severe disease, with survival to age 18 years now expected for 90% of children diagnosed with severe CHD (S1.4-3–S1.4-5). Patients with ACHD are a heterogeneous population, both in underlying anatomy and physiology, as well as surgical repair or palliation. Consequently, although the prevalence of ACHD is increasing, the population of patients with a given congenital abnormality or specific repair may be relatively small (S1.4-3, S1.4-6–S1.4-8).

Patients with CHD are not cured of their disease after successful treatment in childhood. Almost all patients with ACHD will have sequelae of either their native CHD or its surgical repair or palliation, although these sequelae can take decades to manifest. The heterogeneity of the population and the long, symptom-free intervals constrain the ability to generate data applicable across the population of ACHD or to adults with specific lesions or repairs. Despite the difficulty in studying ACHD populations, there is a growing body of high-quality data in these patients to guide the care of this relatively "new" population and, whenever feasible, these data were used to develop recommendations. Recommendations are made based on the available data; however, when important clinical issues lacked data, first principles, extrapolation from data in other populations, and expert consensus are used to guide care. Patients with ACHD may have concomitant disease to which other existing guidelines apply, such as coronary artery disease, HF, and arrhythmias. The data from acquired heart disease populations may apply to some patients with ACHD, and those circumstances are acknowledged in these recommendations and referenced accordingly.

Patients with ACHD who are cared for in ACHD centers have better outcomes than those cared for in centers without ACHD expertise (S1.4-9), and this need for specialized care is noted throughout

the guideline. These recommendations are intended to provide guidance to a wide variety of providers caring for patients with ACHD, including general, pediatric, and ACHD cardiologists, as well as surgeons, primary care providers, and other healthcare providers.

In developing the 2018 ACHD guideline, the writing committee reviewed previously published guidelines and related scientific statements. Table 2 contains a list of publications and scientific statements deemed pertinent to this writing effort; it is intended for use as a resource and does not repeat existing guideline recommendations.

Table 2. Associated Guidelines and Statements

Title	Organization	Publication Year (Reference)
Guidelines		
Syncope	ACC/AHA/HRS	2017 (S1.4-10)
Supraventricular tachycardia	ACC/AHA/HRS	2015 (S1.4-11)
Cardiopulmonary resuscitation and emergency cardiovascular care—Part 8: postcardiac arrest care	AHA	2015 (S1.4.12)
Non-ST-elevation acute coronary syndromes	AHA/ACC	2014 (S1.4-13)
Perioperative cardiovascular evaluation and noncardiac surgery	ACC/AHA	2014 (S1.4-14)
Atrial fibrillation	AHA/ACC/HRS	2014 (S1.4-15)
Stable ischemic heart disease	ACC/AHA/ACP/AATS/PCNA/SCAI/STS	2014 (S1.4-16), 2012 (S1.4-17)
Assessment of cardiovascular risk	ACC/AHA	2014 (S1.4-18)
Blood cholesterol to reduce atherosclerotic cardiovascular risk in adults	ACC/AHA	2014 (S1.4-19)
Overweight and obesity in adults	AHA/ACC/TOS	2014 (S1.4-20)
Lifestyle management to reduce cardiovascular risk	AHA/ACC	2014 (S1.4-21)
Valvular heart disease	AHA/ACC	2017 (S1.4-22)
High blood pressure in adults	ACC/AHA/AAPA/ABC/ACPM/AGS/ APhA/ASH/ASPC/NMA/PCNA	2017 (S1.4-23)
Aortic valve and ascending aorta	STS	2013 (S1.4-24)
ST-elevation myocardial infarction	ACC/AHA	2013 (S1.4-25)
Heart failure	ACC/AHA/HFSA	2017 (S1.4-26)
Device-based therapy for cardiac rhythm abnormalities	ACC/AHA/HRS	2012 (S1.4-27)
Coronary artery bypass graft surgery	ACC/AHA	2011 (S1.4-28)
Percutaneous coronary intervention	ACC/AHA/SCAI	2011 (S1.4-29)
Secondary prevention and risk reduction therapy	AHA/ACC	2011 (S1.4-30)
Cardiovascular disease in women	AHA/ACC	2011 (S1.4-31)
Grown-up congenital heart disease	ESC	2010 (S1.4-32)
Thoracic aortic disease	ACC/AHA/AATS/ACR/ASA/SCA/ SCAI/SIR/STS/SVM	2010 (S1.4-33)
Adult congenital heart disease	CCS	2010 (S1.4-34)
Infective endocarditis	ESC	2009 (S1.4-35)

Scientific statements		
Imaging for patients with transposition of the great arteries	ASE	2016 (S1.4-36)
Cardiac chamber quantification by echocardiography	ASE	2015 (S1.4-37)
Consensus on arrhythmia management in ACHD	PACES/HRS	2014 (S1.4-38)
Imaging for patients with repaired tetralogy of Fallot	ASE	2014 (S1.4-39)
Thoracic aortic disease	CCS	2014 (S1.4-40)
Promotion of physical activity for children and adults with CHD	AHA	2013 (S1.4-41)
Neurodevelopmental outcomes in children with CHD	AHA	2012 (S1.4-42)
Pregnancy in women with heart disease	ESC	2011 (S1.4-43)
Transition to adulthood for adolescents with CHD	AHA	2011 (S1.4-44)
Pulmonary hypertension	ACC/AHA	2009 (S1.4-45)
Prevention of infective endocarditis	AHA	2007 (S1.4-46)

AATS indicates American Association for Thoracic Surgery; ABC, Association of Black Cardiologists; ACC, American College of Cardiology; ACHD, adult congenital heart disease; ACP, American College of Physicians; ACPM, American College of Preventive Medicine; ACR, American College of Radiology; AGS, American Geriatrics Society; AHA, American Heart Association; APhA, American Pharmacists Association; ASA, American Stroke Association; ASE, American Society of Echocardiography; ASH, American Society of Hypertension; ASPC, American Society of Preventive Cardiology; CCS, Canadian Cardiovascular Society; CHD, congenital heart disease; ESC, European Society of Cardiology; HFSA, Heart Failure Society of America; HRS, Heart Rhythm Society; NMA, National Medical Association; PACES, Pediatric and Congenital Electrophysiology Society; PCNA, Preventive Cardiovascular Nurses Association; SCA, Society of Cardiovascular Anesthesiologists; SCAI, Society for Cardiovascular Angiography and Interventions; SIR, Society of Interventional Radiology; STS, Society of Thoracic Surgeons; SVM, Society for Vascular Medicine; and TOS, The Obesity Society.

1.5. Abbreviations

Abbreviation	Meaning/Phrase
3D	3-dimensional
AAOCA	anomalous aortic origin of the coronary artery
ACHD	adult congenital heart disease
AP	anatomic and physiological
AR	aortic regurgitation
ASD	atrial septal defect
AVSD	atrioventricular septal defect
BAV	bicuspid aortic valve
CCT	cardiac computed tomography
CCTGA	congenitally corrected transposition of the great arteries
CHD	congenital heart disease
CMR	cardiovascular magnetic resonance
CoA	coarctation of the aorta
CPET	cardiopulmonary exercise test
CT	computed tomography
CTA	computed tomography angiography
d-TGA	dextro-transposition of the great arteries
ECG	electrocardiogram
ERC	evidence review committee
GDMT	guideline-directed management and therapy
HF	heart failure
ICD	implantable cardioverter-defibrillator
IE	infective endocarditis
LV	left ventricular
LVOT	left ventricular outflow tract
PA	pulmonary artery
PAH	pulmonary arterial hypertension
PDA	patent ductus arteriosus
PR	pulmonary regurgitation
PS	pulmonary stenosis
QoL	quality of life
Qp:Qs	pulmonary–systemic blood flow ratio
RCT	randomized controlled trial
RV	right ventricular
RVOT	right ventricular outflow tract
SCD	sudden cardiac death
SubAS	subaortic stenosis
TEE	transesophageal echocardiography
TGA	transposition of the great arteries
TOF	tetralogy of Fallot
TR	tricuspid regurgitation
TTE	transthoracic echocardiography
VHD	valvular heart disease
VSD	ventricular septal defect
VT	ventricular tachycardia

2. Background and Pathophysiology

2.1. Anatomic and Physiological Terms

The International Society for Nomenclature of Pediatric and Congenital Heart Disease (also known as the Nomenclature Working Group) defined, codified, mapped, and archived examples of nomenclatures and developed standards for terminology (S2.1-1– S2.1-5). The International Paediatric and Congenital Cardiac Code (IPCCC) nomenclature for anatomic lesions and repairs is used in this guideline (http://ipccc.net) (S2.1-6).

2.2. Severity of ACHD

In a patient with CHD, severity of disease is determined by native anatomy, surgical repair, and current physiology. Prior documents, including the 2008 ACHD guideline (S2.2-1), relied primarily on anatomic classifications to rank severity of disease. However, patients with the same underlying anatomy may have very different repairs and experienced variable physiological consequences of those repairs. For example, a patient with tetralogy of Fallot (TOF) after a valve-sparing primary repair may have excellent biventricular function with normal exercise capacity and no arrhythmias, whereas another patient of the same age with TOF may have had palliative shunting followed by a transannular patch repair resulting in severe pulmonary regurgitation (PR) with right ventricular (RV) enlargement, biventricular dysfunction, and ventricular tachycardia (VT). To categorize disease severity in CHD in a more comprehensive way, the writing committee developed an ACHD Anatomic and Physiological (AP) classification system (Tables 3 and 4) that incorporates the previously described CHD anatomic variables as well as physiological variables, many of which have prognostic value in patients with ACHD.

Table 3. Physiological Variables as Used in ACHD AP Classification

Variable	Description
Aortopathy	Aortic enlargement is common in some types of CHD and after some repairs. Aortic enlargement may be progressive over a lifetime. There is no universally accepted threshold for repair, nor is the role of indexing to body size clearly defined in adults, as is done in pediatric populations. For purposes of categorization and timing of follow-up imaging (S2.2-2–S2.2-4): • Mild aortic enlargement is defined as maximum diameter 3.5–3.9 cm • Moderate aortic enlargement is defined as maximum diameter 4.0–4.9 cm • Severe aortic enlargement is defined as maximum diameter ≥5.0 cm
Arrhythmia	Arrhythmias are very common in patients with ACHD and may be both the cause and consequence of deteriorating hemodynamics, valvular dysfunction, or ventricular dysfunction. Arrhythmias are associated with symptoms, outcomes, and prognosis (S2.2-5–S2.2-8), thus are categorized based on presence and response to treatment. • No arrhythmia: No documented clinically relevant atrial or ventricular tachyarrhythmias • Arrhythmia not requiring treatment: Bradyarrhythmia, atrial or ventricular tachyarrhythmia not requiring antiarrhythmic therapy, cardioversion, or ablation • Arrhythmia controlled with therapy:

	○ Bradyarrhythmia requiring pacemaker implantation ○ Atrial or ventricular tachyarrhythmia requiring antiarrhythmic therapy, cardioversion, or ablation ○ AF and controlled ventricular response ○ Patients with an ICD • Refractory arrhythmias: ○ Atrial or ventricular tachyarrhythmia currently unresponsive to or refractory to antiarrhythmic therapy or ablation
Concomitant VHD	Severity defined according to the 2014 VHD guideline (S2.2-2). • Mild VHD • Moderate VHD • Severe VHD
End-organ dysfunction	Clinical and/or laboratory evidence of end-organ dysfunction (S2.2-9–S2.2-11) including: • Renal (kidney) • Hepatic (liver) • Pulmonary (lung)
Exercise capacity	Patients with ACHD are often asymptomatic notwithstanding exercise limitations demonstrated as diminished exercise capacity when evaluated objectively (S2.2-12–S2.2-14). Thus, assessment of both subjective and objective exercise capacity is important (see NYHA classification system below). Exercise capacity is associated with prognosis (S2.2-15–S2.2-17). • Abnormal objective cardiac limitation to exercise is defined as an exercise maximum ventilatory equivalent of oxygen below the range expected for the specific CHD anatomic diagnosis (S2.2-18). • Expected norms for CPET values should take into account age, sex, and underlying congenital diagnosis. Published studies with institution-specific norms can be used as guides, bearing in mind variability among institutional norms and ranges.
Hypoxemia/hypoxia/cyanosis	See Section 3.16. for detailed definition of cyanosis. • Hypoxemia is defined as oxygen saturation measured by pulse oximetry at rest ≤90%. • Severe hypoxemia is defined as oxygen saturation at rest <85%. • In patients with normal or high hemoglobin concentrations, severe hypoxemia will be associated with visible cyanosis (which requires ≥5 g/L desaturated hemoglobin to be appreciated). • The terms cyanosis and hypoxemia (or hypoxia) are sometimes used interchangeably. Such interchangeability would not apply; however, in the presence of anemia, severe hypoxemia can be present without visible cyanosis.
NYHA functional classification system (S2.2-19)	**Class** **Functional Capacity** **I** Patients with cardiac disease but resulting in no limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain. **II** Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain. **III** Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain. **IV** Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of HF or the anginal

	syndrome may be present even at rest. If any physical activity is undertaken, discomfort increases.
Pulmonary hypertension	Pulmonary hypertension is a broad term that encompasses pulmonary arterial hypertension, which is pulmonary hypertension with increased pulmonary vascular resistance. This document defines PH and PAH as they are used in the field of pulmonary hypertension. Pulmonary hypertension is defined as: • Mean PA pressure by right heart catheterization ≥25 mm Hg. PAH is defined as: • Mean PA pressure by right heart catheterization ≥25 mm Hg and a pulmonary capillary wedge pressure ≤15 mm Hg and pulmonary vascular resistance ≥3 Wood units (S2.2-20)
Shunt (hemodynamically significant shunt)	An intracardiac shunt is hemodynamically significant if: • There is evidence of chamber enlargement distal to the shunt • And/or evidence of sustained Qp:Qs ≥1.5:1 • An intracardiac shunt not meeting these criteria would be described as small or trivial
Venous and arterial stenosis	• Aortic recoarctation after CoA repair • Supravalvular aortic obstruction • Venous baffle obstruction • Supravalvular pulmonary stenosis • Branch PA stenosis • Stenosis of cavopulmonary connection • Pulmonary vein stenosis

ACHD indicates adult congenital heart disease; AF, atrial fibrillation; AP, anatomic and physiological; CHD, congenital heart disease; CoA, coarctation of the aorta; CPET, cardiopulmonary exercise test; HF, heart failure; ICD, implantable cardioverter-defibrillator; NYHA, New York Heart Association; PA, pulmonary artery; PAH, pulmonary arterial hypertension; Qp:Qs, pulmonary–systemic blood flow ratio; and VHD, valvular heart disease.

Table 4. ACHD AP Classification
(CHD Anatomy + Physiological Stage = ACHD AP Classification)

CHD Anatomy*
I: Simple
Native disease • Isolated small ASD • Isolated small VSD • Mild isolated pulmonic stenosis **Repaired conditions** • Previously ligated or occluded ductus arteriosus • Repaired secundum ASD or sinus venosus defect without significant residual shunt or chamber enlargement • Repaired VSD without significant residual shunt or chamber enlargement
II: Moderate Complexity
Repaired or unrepaired conditions • Aorto-left ventricular fistula • Anomalous pulmonary venous connection, partial or total • Anomalous coronary artery arising from the pulmonary artery • Anomalous aortic origin of a coronary artery from the opposite sinus

• AVSD (partial or complete, including primum ASD) • Congenital aortic valve disease • Congenital mitral valve disease • Coarctation of the aorta • Ebstein anomaly (disease spectrum includes mild, moderate, and severe variations) • Infundibular right ventricular outflow obstruction • Ostium primum ASD • Moderate and large unrepaired secundum ASD • Moderate and large persistently patent ductus arteriosus • Pulmonary valve regurgitation (moderate or greater) • Pulmonary valve stenosis (moderate or greater) • Peripheral pulmonary stenosis • Sinus of Valsalva fistula/aneurysm • Sinus venosus defect • Subvalvar aortic stenosis (excluding HCM; HCM not addressed in these guidelines) • Supravalvar aortic stenosis • Straddling atrioventricular valve • Repaired tetralogy of Fallot • VSD with associated abnormality and/or moderate or greater shunt
III: Great Complexity (or Complex)
• Cyanotic congenital heart defect (unrepaired or palliated, all forms) • Double-outlet ventricle • Fontan procedure • Interrupted aortic arch • Mitral atresia • Single ventricle (including double inlet left ventricle, tricuspid atresia, hypoplastic left heart, any other anatomic abnormality with a functionally single ventricle) • Pulmonary atresia (all forms) • TGA (classic or d-TGA; CCTGA or l-TGA) • Truncus arteriosus • Other abnormalities of atrioventricular and ventriculoarterial connection (i.e., crisscross heart, isomerism, heterotaxy syndromes, ventricular inversion)
Physiological Stage
A
• NYHA FC I symptoms • No hemodynamic or anatomic sequelae • No arrhythmias • Normal exercise capacity • Normal renal/hepatic/pulmonary function
B
• NYHA FC II symptoms • Mild hemodynamic sequelae (mild aortic enlargement, mild ventricular enlargement, mild ventricular dysfunction) • Mild valvular disease

• Trivial or small shunt (not hemodynamically significant) • Arrhythmia not requiring treatment • Abnormal objective cardiac limitation to exercise
C
• NYHA FC III symptoms • Significant (moderate or greater) valvular disease; moderate or greater ventricular dysfunction (systemic, pulmonic, or both) • Moderate aortic enlargement • Venous or arterial stenosis • Mild or moderate hypoxemia/cyanosis • Hemodynamically significant shunt • Arrhythmias controlled with treatment • Pulmonary hypertension (less than severe) • End-organ dysfunction responsive to therapy
D
• NYHA FC IV symptoms • Severe aortic enlargement • Arrhythmias refractory to treatment • Severe hypoxemia (almost always associated with cyanosis) • Severe pulmonary hypertension • Eisenmenger syndrome • Refractory end-organ dysfunction

*This list is not meant to be comprehensive; other conditions may be important in individual patients.
ACHD indicates adult congenital heart disease; AP, anatomic and physiological; ASD, atrial septal defect; AVSD, atrioventricular septal defect; CCTGA, congenitally corrected transposition of the great arteries; CHD, congenital heart disease; d-TGA, dextro-transposition of the great arteries; FC, functional class; HCM, hypertrophic cardiomyopathy; l-TGA, levo-transposition of the great arteries; NYHA, New York Heart Association; TGA, transposition of the great arteries; and VSD, ventricular septal defect.

2.3. The ACHD AP Classification

The ACHD AP classification (Tables 3 and 4), newly elaborated in this guideline, is intended to capture the complexity of ACHD anatomy and physiology, which are not always correlated. Certain anatomic abnormalities of clinical importance are shared across diagnoses (e.g., aortic enlargement), which may be found in patients with BAV, coarctation of the aorta (CoA), transposition of the great arteries, and TOF, amongst others. In every patient, anatomic and physiological variables should be considered. In using Tables 3 and 4, a patient should be classified based on the "highest" relevant anatomic or physiological feature. For example, a normotensive patient with repaired CoA, normal exercise capacity, and normal end-organ function would be ACHD AP classification IIA, whereas an otherwise similar patient with ascending aortic diameter of 4.0 cm would be ACHD AP classification IIB, and if moderate aortic stenosis were also present, the ACHD AP classification would be IIC.

Patients with ACHD may have baseline exercise limitations, cyanosis, end-organ dysfunction, or other clinically important comorbidities related to their CHD. They are also at risk of HF, arrhythmias, sudden cardiac death (SCD), and development or progression of cardiac symptoms such as dyspnea, chest pain, and exercise intolerance. Concomitant valvular disease or aortic pathology may be present.

There are growing data regarding the prognostic implications of these variables in patients with ACHD, but not the abundance of data available for patients with acquired heart disease (S2.3-1–S2.3-16).

The variables forming part of the ACHD AP classification (Table 3) were selected because data exist suggesting their importance in prognosis, management, or quality of life (QoL). As new data become available, we expect changes in the relative weights attributed to the components of the ACHD AP classification and perhaps new components, resulting in a scheme that ever more precisely tracks overall severity of disease and need for more or less intensive follow-up and management.

Similar to the New York Heart Association (NYHA) classification of functional status, patients may move from one ACHD AP classification to another over time. If clinical status worsens, the classification will change to a higher severity group, but improvement in status, for example after an intervention such as valve replacement or control of arrhythmia, can result in change to a lower severity classification. Such movement among classes is unlike the AHA HF A to D classification (S2.3-17), in which patients move in only one direction. This ACHD AP classification is used throughout this document, particularly when considering follow-up visits and need for testing. As the ACHD AP classification worsens because of changes in physiology (e.g., development of arrhythmias, HF, end-organ disease), the nature and frequency of recommended follow-up visits and testing will also change, adapting to the patient's changing circumstance instead of depending solely on a description of anatomic disease, which may not adequately discriminate physiological changes that alter severity over time.

Some patients with ACHD may have substantial acquired comorbidities unrelated to CHD and, as a consequence, their follow-up strategies might be more appropriately based on other existing guidelines for acquired heart disease. For example, an 80-year-old patient who has a small atrial septal defect (ASD), but whose symptoms are related to diastolic HF, chronic kidney disease caused by hypertension and diabetes mellitus, and moderate aortic stenosis is well-suited to be followed according to existing guidelines for those diseases, rather than according to the ACHD AP classification for the ASD. Nevertheless, the added hemodynamic complexity brought by the ASD must be kept in mind.

Throughout this document, the ACHD AP classification is used to help guide resource utilization, including ACHD consultation and routine diagnostic studies.

3. General Principles

See Online Data Supplements 1 and 2 for additional data supporting this section.

3.1. ACHD Program

Patients with complex CHD have generally better outcomes when cared for in an integrated, collaborative, and multidisciplinary program (S3.1-1). Many medical issues in patients with ACHD involve cardiac sequelae, and the diagnosis and management may require cardiac anesthesiologists, electrophysiologists, and interventional cardiologists; imaging services such as cardiovascular magnetic resonance (CMR)/cardiac computed tomography (CCT); and pulmonary hypertension services with expertise in ACHD (Table 5). Appropriate specialty care must be available to address pregnancy, acquired cardiovascular disease, and acute noncardiac illness complicating CHD, management of which is frequently more complicated in patients with ACHD.

Although individual providers may be community-based affiliates, ACHD programs are inpatient, outpatient, and hospital-based with staffing and expertise available on-site or accessible when needed (Table 5).

Table 5. Key Personnel and Services Recommended for ACHD Programs

Personnel
ACHD board-eligible/board-certified cardiologists
Congenital cardiac surgeons
Nurses/physician assistants/nurse practitioners
Cardiac anesthesiologists with CHD training/expertise
Multidisciplinary teams: • High-risk obstetrics • Pulmonary hypertension • HF/transplant • Genetics • Hepatology • Cardiac pathology • Rehabilitation services • Social services • Psychological services • Financial counselors
Services
Echocardiography, including TEE and intraoperative TEE*
CHD diagnostic and interventional catheterization*
CHD electrophysiology/pacing/ICD implantation*: • Exercise testing • Echocardiographic • Radionuclide • Cardiopulmonary
Cardiac imaging/radiology*: • CMR • CCT • Nuclear medicine
Information technology: • Data collection • Database support • Quality assessment review/protocols

*These modalities must be supervised/performed and interpreted by clinicians with expertise and/or training in CHD.
ACHD indicates adult congenital heart disease; CCT, cardiac computed tomography; CHD, congenital heart disease; CMR, cardiovascular magnetic resonance; HF, heart failure; ICD, implantable cardioverter-defibrillator; and TEE, transesophageal echocardiography.

3.2. Access to Care

Recommendation for Access to Care Referenced studies that support the recommendation are summarized in Online Data Supplement 3.		
COR	**LOE**	**Recommendation**
I	**B-NR**	**1. Physicians caring for patients with ACHD should support access to care by a) assuring smooth transitions for adolescents and young adults from pediatric to adult providers (S3.2-1, S3.2-2) (Level of Evidence: B-NR); and b) promoting awareness of the need for lifelong specialized care through outreach and educational programs (Level of Evidence: C-EO).**
	C-EO	

Synopsis

As patients with ACHD grow beyond the pediatric age group, continued access to specialized cardiovascular care presents several challenges:

- Lack of guided transfer from pediatric to adult care;
- Insufficient availability of ACHD programs;
- Inadequate insurance coverage;
- Deficient education of patients and caregivers regarding ACHD;
- Inadequate resources for patients with cognitive or psychosocial impairment;
- Lack of comprehensive case management; and
- Different needs for evaluation and management compared with adults with acquired cardiovascular disease.

Recommendation-Specific Supportive Text

1. Many patients with CHD face gaps in care during and after adolescence (S3.2-2). Common reasons include lack of knowledge regarding need for follow-up, inability to find specialized providers, insurance issues, and feeling well (S3.2-1). Patients with gaps in care are more likely to develop medical problems requiring intervention than those receiving continuous care (S3.2-3, S3.2-4). Canadian patients with CHD in specialized care programs had lower mortality than those in centers without ACHD expertise (S3.2-5). Improving transition programs and recognizing the importance of long-term care will hopefully improve access to specialty care. Insurance barriers and lack of specialty providers for the large number of patients are issues; thus, relationships with regulatory agencies to address these challenges are important.

3.3. Delivery of Care

Recommendations for Delivery of Care Referenced studies that support recommendations are summarized in Online Data Supplements 3, 4, and 5.		
COR	**LOE**	**Recommendations**
I	**B-NR**	**1. Patients with ACHD AP classification IB-D, IIA-D, and IIIA-D* should be managed in collaboration with an ACHD cardiologist (S3.3-1).**
I	**C-LD**	**2. Cardiac surgery, catheter-based interventional cardiac procedures, and electrophysiological procedures involving congenital heart lesions in patients with ACHD should be performed by operators with expertise in CHD procedures and in collaboration with an ACHD cardiologist (S3.3-1, S3.3-2).**

*See Tables 3 and 4 for details on the ACHD Anatomic and Physiological classification system.

Recommendation-Specific Supportive Text

1. Patients with ACHD, particularly those with more severe CHD, cared for in specialized centers have lower mortality than those managed without specialized care (S3.3-1). Although clinical practice guidelines can be helpful, many management decisions for patients with ACHD must be based on insufficient data or care guidelines and require clinical experience often involving multiple members of an ACHD team. Patients with complex anatomic and physiological forms of ACHD may need approaches to evaluation and treatment that differ from those applicable to adults without ACHD who have valve disease, HF, or arrhythmias.

From a practical perspective, it may be difficult to identify clinicians with expertise in ACHD, and expertise in ACHD varies across medical and surgical specialties. Some specialties, such as cardiology and congenital heart surgery, have defined ACHD fellowship training and board certification, whereas for others, ACHD expertise is gained by focused experience during training and practice.

In 2012, the American Board of Medical Specialties approved ACHD as a subspecialty of internal medicine ("adult") cardiology and pediatric cardiology. Therefore, for cardiologists, one marker of ACHD expertise is board eligibility/board certification in ACHD. There are expert ACHD clinicians who are not board-certified, including those whose expertise was acquired before the development of formal certification programs and those trained outside the United States who may also have different pathways to achieve ACHD expertise. Expertise in the surgical management of patients with ACHD may be identified through board eligibility/board certification in congenital heart surgery. There are expert ACHD surgeons who are not board-certified, including those surgeons trained in other countries who are not eligible for certification in the United States.

Specific ACHD training options are not generally available for cardiac anesthesiologists, but many of them develop expertise through training in pediatric anesthesiology, cardiac anesthesiology, mentoring, and practice experience. Other providers involved in the care of patients with ACHD (e.g., obstetricians, pulmonologists, radiologists, nurse practitioners, physician assistants) derive expertise from training and/or practice. Individual providers may gain ACHD expertise in a specific area or discipline, such as intraoperative transesophageal echocardiography (TEE) or interpretation of CMR.

2. Patients with ACHD who are undergoing invasive cardiovascular procedures in specialized ACHD centers generally have better outcomes, including survival, than those managed in other care settings (S3.3-2). Special attention is required to ensure appropriate periprocedural care, including identification of procedure-related risk factors and availability of ancillary imaging (S3.3-3–S3.3-10).

Table 6 addresses delivery of care where circumstances of ACHD expertise may improve patient outcomes.

Table 6. Delivery of Care: Circumstances Where ACHD Expertise May Improve Outcomes

Circumstance	Possible Solution	Rationale	Example
Care of patients in the lowest ACHD AP classification (IA)*	1. Face-to-face consultation with an ACHD cardiologist. 2. Collaborative care planning between an ACHD patient's general cardiologist or primary care provider and an ACHD cardiologist.	1. Patients in ACHD AP classification IA* are likely to be asymptomatic and not require frequent routine congenital cardiac care. 2. The very long-term outcomes of patients with ACHD AP classification IA* lesions have not been well described, although available data suggest that patients with simple CHD have higher cardiac mortality in long-term follow-up than age-matched controls (S3.3-11). 3. Consultation with an ACHD cardiologist should help to accurately assess the patient's ACHD AP class, provide information regarding potential long-term outcomes, and reinforce signs and symptoms that should prompt further evaluation.	Patients with small VSDs are thought to have excellent long-term survival, although complications (double-chamber RV, IE, aortic valve prolapse and aortic regurgitation) may manifest in adulthood; consequently, patients with small VSDs warrant lifelong follow-up (S3.3-12).
Cardiac imaging of patients with ACHD	Imaging studies should be performed and interpreted by individuals with expertise in CHD imaging.	1. The complexity and variability of lesions, repairs, and sequelae in CHD constrain the use of standard protocols and sequences and often require modification of plans during acquisition of images, as well as specialized skills in interpretation. Thus, CHD expertise is helpful for optimal quality and interpretation of cardiac imaging studies. 2. Use of a multimodality cardiac imaging approach can be used for patients with ACHD, accounting for patient-specific considerations, strengths and weaknesses of each modality, institutional resources, and expertise. 3. ACHD programs need a dedicated CMR service, and CMR expertise is integral to an ACHD program, as is expertise in ACHD CCT (S3.3-13, S3.3-14).	Although imaging of a patient with TOF may seem straightforward because many have familiar chamber and great vessel relationships, there are nuances to echocardiographic imaging of RV size and function, PR severity, and/or location of right ventricular outflow tract obstruction that affect clinical care and are thus best carried out by sonographers and echocardiographers with appropriate expertise. Similarly, expertise in congenital CMR is important in evaluating patients with TOF, as RV volumes and function are key components in evaluation for timing of pulmonary valve replacement (S3.3-15, S3.3-16).
Electrophysiological care of patients with ACHD	Perform procedures in electrophysiology laboratories equipped for 3D mapping and ablation and involve specialists experienced in the	Examples of diagnostic questions best answered by electrophysiological study: a) evaluation of the conduction system in cases of suspected postsurgical conduction abnormalities b) evaluation of syncope	Bradyarrhythmia and tachyarrhythmias are common in TGA with atrial switch patients and may seem "straightforward," but the altered anatomy adds complexity to the procedures and emphasizes the need for

	management of arrhythmias in patients with ACHD.	c) diagnosis of the mechanism of supraventricular tachycardia or wide complex tachycardia d) programmed ventricular stimulation particularly in patients following repair of TOF and its variants (Section 4.4.1.) as well as preoperative assessment of arrhythmia substrates that may be amenable to operative intervention, such as an atrial maze procedure for atrial arrhythmias. The latter procedure is commonly used at the time of conversion of atriopulmonary connection Fontan, and may also be useful in other forms of repaired CHD with postoperative atrial arrhythmias such as TOF.	specialized equipment and expertise to ensure the best chance for procedural success. For example: 1) pacemaker placement in a patient with TGA with atrial switch can be challenging because of the altered atrial anatomy and interatrial baffle that will necessitate placement of an atrial lead in the anatomic left atrium, often scarred such that tissue amenable to pacing is difficult to find; and 2) atrial flutter is a common arrhythmia in TGA with atrial switch, but the flutter circuit may be on the systemic side of the interatrial baffle and thus may require baffle puncture or retrograde approach to effectively ablate the circuit.
Diagnostic and interventional cardiac procedures, including electrophysiology procedures	1. Perform procedure in a hospital with cardiologists, anesthesiologists, surgeons, and other providers with expertise in the management of patients with ACHD. 2. Consultation with providers with ACHD expertise may be substituted if the procedure is urgent such that timely transfer is not feasible.	1. Patients with ACHD often have complex underlying cardiac anatomy and physiology. 2. The data obtained and the interventions performed during ACHD cardiac procedures are difficult to sort out without specialized knowledge of the CHD. 3. An ACHD program has additional resources such as cardiac anesthesia, congenital cardiac surgery, and specialty cardiac imaging, should the need for those services arise during or after the procedure.	In patients with CHD, the presence of anatomic and physiological complexity from the specific defect or surgical palliation, may change the overall care plan and procedural decision-making. Procedures that may seem straightforward, such as pacemaker implantation or ASD closure, may be more complex when accounting for the nuances imparted by CHD.
Administration of anesthesia for invasive procedures in patients with ACHD AP classification IB-D, IIA-D, and IIIA-D*	1. Performed by, or in collaboration with, an anesthesiologist with expertise in the management of patients with ACHD. 2. If clinical urgency precludes transfer, consultation with an anesthesiologist with ACHD expertise would be of benefit to on-site providers who do not have ACHD expertise.	1. ACHD-specific issues need to be addressed when considering anesthesia, including underlying cardiac physiology and hemodynamics, and the effects of anesthetic medications and ventilation strategies. 2. Many patients with ACHD have had surgeries in the past, which may have created or identified airway or vascular access concerns. Patients with ACHD can also have underlying restrictive and/or obstructive lung disease that should be considered (S3.3-17, S3.3-18).	The application of anesthesia for laparoscopic procedures can be especially challenging in Fontan patients. Significant cardiovascular and respiratory alterations may occur as a result of increased intra-abdominal pressure and decreased venous return. Abdominal insufflation may lead to lower preload and hypotension, while at the same time elevating systemic vascular resistance and compromising cardiac output. Elevations in pulmonary vascular

			resistance attributable to hypercarbia can be caused by either direct carbon dioxide absorption or hypoventilation (S3.3-19).
Patients with ACHD and pulmonary hypertension	1. Consultation with experts in pulmonary hypertension and ACHD to assist in the interpretation of diagnostic and invasive studies and determine the best course of management.	1. PAH imparts a poor prognosis compared with CHD without PAH. Because of the complexity of PAH in the setting of CHD, patients with ACHD benefit from the expertise of both ACHD providers and pulmonary hypertension providers (S3.3-20–S3.3-28).	Management of PAH in patients with shunts can be difficult. For example, in patients for whom PAH treatment is expected to allow subsequent closure of a shunt, cohort series demonstrate progression of pulmonary vascular resistance or late mortality if defects with associated pulmonary vascular resistance elevation beyond 2.5 Wood units (≥4 Wood units/m^2) or Qp:Qs ≥3 were closed (S3.3-29, S3.3-30). The utility of acute administration of pulmonary vasodilator therapy as a marker of reversibility of pulmonary vascular resistance remains uncertain. “Treat-to-repair” strategies involving use of PAH therapies to bring pulmonary vascular resistance into a range where repair can be considered have been applied, but the utility of such strategies also remains uncertain.

*See Tables 3 and 4 for details on the ACHD AP classification system.

3D indicates 3-dimensional; ACHD, adult congenital heart disease; AP, anatomic and physiological; ASD, atrial septal defect; CCT, cardiac computed tomography; CHD, congenital heart disease; CMR, cardiovascular magnetic resonance; IE, infective endocarditis; PAH, pulmonary arterial hypertension; PR, pulmonary regurgitation; Qp:Qs, pulmonary–systemic blood flow ratio; RV, right ventricle; TGA, transposition of the great arteries; TOF, tetralogy of Fallot; and VSD, ventricular septal defect.

3.4. Evaluation of Suspected and Known CHD

Tools commonly used in the evaluation of adults with suspected or known acquired cardiovascular disease are also valuable in the evaluation of patients with ACHD. Some tools (e.g., echocardiography) are regularly used in the serial evaluation of patients with ACHD, whereas other tools (e.g., CMR and CCT) may have more utility in the evaluation and management of patients with ACHD than in patients with acquired cardiovascular disease (Tables 7 and 8). Cost and risk to patients can be minimized by ensuring studies are acquired and interpreted by centers and providers with CHD expertise.

3.4.1. Electrocardiogram

Recommendations for Electrocardiogram		
COR	**LOE**	**Recommendations**
I	**C-EO**	**1. A standard 12-lead electrocardiogram (ECG) is recommended in adults with CHD with serial assessment depending on the specific ACHD AP classification or when symptoms develop or worsen.**
I	**C-EO**	**2. Ambulatory electrocardiographic monitoring should be performed in patients with CHD who are at risk of tachyarrhythmia, bradyarrhythmia or heart block, or when symptoms possibly of arrhythmic origin develop.**

Recommendation-Specific Supportive Text

1. The ECG is an essential part of a complete cardiovascular evaluation of a patient with ACHD, similar to elements of the physical examination. Regardless of anatomic diagnosis, it is important to obtain an ECG at baseline for comparison to any subsequently obtained ECG, because an abnormal baseline ECG is expected in many forms of CHD, particularly those who have undergone surgical repair. A follow-up ECG is recommended in specific lesions and in the setting of new or worsening congestion or low cardiac output syndrome (Table 7).

2. Asymptomatic arrhythmias seen in patients with ACHD may be associated with development of symptoms and increased risk of death, and are more common in particular lesions or repairs. Bradyarrhythmias or tachyarrhythmias may occur, with some requiring treatment even when asymptomatic. For example, sinus node dysfunction is common in patients with atrial switch repairs of transposition of the great arteries (TGA), whereas complete heart block is seen in patients with congenitally corrected transposition of the great arteries (CCTGA) or late after atrioventricular septal defect (AVSD) repair, especially in those patients with transient postoperative heart block (S3.4.1-1–S3.4.1-3). Some of these events have occurred as late as 15 years after surgery. The atrioventricular node is typically displaced inferiorly in AVSD, which is associated with relative hypoplasia of the left anterior fascicle (S3.4.1-4). Atrial tachyarrhythmias are common in atrial switch repairs of TGA, Fontan repairs, and Ebstein anomaly (S3.4.1-5–S3.4.1-7). Thus, baseline and periodic screening for asymptomatic arrhythmias with ambulatory electrocardiographic monitoring is advised to ensure that asymptomatic arrhythmias that would warrant a change in therapy are not present (S3.4.1-8), acknowledging the limitations of monitoring over short periods of time. Any symptoms of arrhythmia should prompt investigation to establish an accurate diagnosis and direct subsequent therapy.

Table 7. Use of ECGs in ACHD Evaluation

- Identification of sinus bradycardia or junctional rhythm in patients at risk of sinus node dysfunction (especially after the Mustard, Senning, Glenn, or Fontan procedure)
- Identification of clinically inapparent intra-atrial re-entry tachycardia in patients who have had atriotomy
- Identification of atrioventricular block in patients at risk for progression of atrioventricular conduction system disease (especially CCTGA)
- Evaluation of rhythm in patients with pacemakers
- Measurement of QRS duration in patients after repair of TOF and as part of CRT evaluation
- Preoperatively to compare with postoperative ECGs in patients undergoing heart surgery and noncardiac surgery
- Postoperatively to identify arrhythmias (e.g., atrial ectopic tachycardia, atrial flutter, AF, junctional ectopic tachycardia, atrioventricular block)
- Diagnosis of Wolff-Parkinson-White Syndrome in patients with Ebstein anomaly
- Initial evaluation of suspected acute coronary syndromes

ACHD indicates adult congenital heart disease; AF, atrial fibrillation; CCTGA, congenitally corrected transposition of the great arteries; CRT, cardiac resynchronization therapy; ECG, electrocardiogram; and TOF, tetralogy of Fallot.

3.4.2. Ionizing Radiation Principles

Recommendation for Ionizing Radiation Principles Referenced studies that support the recommendation are summarized in Online Data Supplement 6.		
COR	**LOE**	**Recommendation**
I	**B-NR**	**1. Strategies to limit and monitor radiation exposure are recommended during imaging of patients with ACHD, with studies not involving ionizing radiation chosen whenever appropriate (S3.4.2-1–S3.4.2-4).**

Recommendation-Specific Supportive Text

1. Low-dose ionizing radiation is a known carcinogen, and certain levels of exposure similar to medical exposure have been associated with later malignancy (S3.4.2-5, S3.4.2-6). Patients with ACHD have multiple potential exposures to low-dose ionizing radiation throughout their lifetimes from cardiac catheterizations, computed tomographic (CT) scans, nuclear perfusion scans, stress tests, and chest x-rays. It remains unclear whether there is an increased risk of malignancy among patients with ACHD, but the exposure levels from multiple procedures are in the range of concern. Every effort should be made to use tests without radiation whenever possible or to select protocols with the lowest possible doses of radiation compatible with securing the needed clinical information.

3.4.3. Echocardiography

Recommendations for Echocardiography Referenced studies that support recommendations are summarized in Online Data Supplement 7.		
COR	**LOE**	**Recommendations**
I	**B-NR**	**1. Intraoperative TEE is recommended to guide surgical repair of CHD in adults (S3.4.3-1).**

I	**C-EO**	**2. Patients with ACHD should undergo transthoracic echocardiography (TTE) for initial assessment, with timing of serial assessment based on anatomic and physiological severity and clinical status.**

Recommendation-Specific Supportive Text

1. A large retrospective study has shown that the routine use of intraoperative TEE has a substantial impact on patient care, leading to alteration of planned procedure or revision of the initial repair in 14% of cases and was also determined to be cost-effective (S3.4.3-1).

2. For patients with ACHD in whom abnormalities and changes that may be identified on echocardiography (e.g., valvular or ventricular function or pulmonary pressures) commonly influence management decisions; echocardiography is an indispensable tool in the initial and serial follow-up evaluation. TTE is also valuable in the initial and serial evaluation of patients without symptoms or changes in examination (Table 8).

3.4.4. CMR Imaging

Recommendations for CMR Imaging Referenced studies that support recommendations are summarized in Online Data Supplement 8.		
COR	**LOE**	**Recommendations**
I	**B-NR**	**1. In patients with ACHD who have or who are at risk of developing RV enlargement and dysfunction, serial CMR is recommended for quantitative assessment of RV size and function (S3.4.4-1–S3.4.4-3).**
IIa	**C-LD**	**2. CMR can be useful in the initial evaluation and serial assessment of selected patients with CHD based on anatomic complexity and clinical status (S3.4.4-1, S3.4.4-2, S3.4.4-4–S3.4.4-10).**

Recommendation-Specific Supportive Text

1. CMR plays a valuable role in assessment of RV size and function, because it provides data that are reproducible and more reliable than data obtained with alternative imaging techniques (S3.4.4-1–S3.4.4-4). Real-time 3-dimensional (3D) echocardiography is an emerging technique that shows some promise for replacing CCT and even CMR for serial studies, especially when focusing on ventricular volumes and intracardiac structures only, and if reasonably complete data sets can be obtained (S3.4.4-11).

2. CMR has unique value in the assessment and serial follow-up of patients with ACHD, because it offers unrestricted access to the heart and great vessels noninvasively and without ionizing radiation. The complexity and variability of lesions, repairs, and sequelae in CHD constrain the use of standard protocols and sequences, and often require modification of plans during acquisition of images, as well as specialized skills in interpretation (S3.4.4-12, S3.4.4-13). Thus, a dedicated CMR service is integral to an ACHD program (S3.4.4-4, S3.4.4-5). CMR can provide exquisite anatomic detail and unique physiological information in many forms of CHD. It has a particularly important role in the assessment of extracardiac cardiovascular defects (e.g., CoA, aortic aneurysm, and abnormalities of the thoracic arterial and venous anatomy and connections) (S3.4.4-6, S3.4.4-7). The elucidation of uncommon, complex forms and variations of CHD is routinely facilitated by a CMR study (S3.4.4-5). Contraindications to CMR are common in patients with ACHD, so they should be sought and confirmed. However, the high value of serial CMR has encouraged modification of newer pacemakers, leads, and other devices and imaging protocols to facilitate imaging in an expanding subset of patients with ACHD who have had previous instrumentation. If a contraindication is confirmed, alternative forms of imaging, especially CCT, can obtain much of the information otherwise obtained from CMR and some unique information not

provided by CMR (S3.4.4-14). However, CCT has the disadvantage of substantial patient exposure to ionizing radiation, especially when serial studies are contemplated over a lifetime (S3.4.4-9). Real-time 3D echocardiography shows promise for replacing CCT and even CMR for serial studies, especially when focusing on ventricular volumes and intracardiac structures only, and if reasonably complete data sets can be obtained (Tables 8 and 9) (S3.4.4-11, S3.4.4-15).

Table 8. Circumstances Where CMR, CCT, TEE, and/or Cardiac Catheterization May be Superior to TTE

- Assessment of RV size and function in repaired TOF, systemic right ventricles, and other conditions associated with RV volume and pressure overload (S3.4.4-1, S3.4.4-3)
- Identification of anomalous pulmonary venous connections (S3.4.4-16)
  - Serial assessment of thoracic aortic aneurysms, especially when the dilation might extend beyond the echocardiographic windows (S3.4.4-7)
- Accurate assessment of PA pressure and pulmonary vascular resistance
- Assessment for recoarctation of the aorta
- Sinus venosus defects
- Vascular rings
- Evaluation of coronary anomalies
- Quantification of valvular regurgitation

CCT indicates cardiac computed tomography; CMR, cardiovascular magnetic resonance; PA, pulmonary artery; RV, right ventricular; TEE, transesophageal echocardiography; and TOF, tetralogy of Fallot.

Table 9. Comparison of Imaging Modalities Useful in ACHD Evaluation

	Radiation Exposure	Relative Cost	Ventricular Volumes/Function	Valvular Structure/ Function	Coronary Anatomy and Course	Extracardiac Vascular Anatomy
Echocardiography	No	$	++	+++	+/-	+/-
CMR	No	$$	+++	++	++*	+++
CCT	Yes	$$	+*	+	+++	+++
Cardiac catheterization	Yes	$$	+	++	+++	++

*In specific gated imaging protocols.
$ indicates less expensive; $$, more expensive; +/-, possible value; +, good; ++, very good; and +++, excellent.
ACHD indicates adult congenital heart disease; CCT, cardiac computed tomography; and CMR, cardiovascular magnetic resonance.

3.4.5. Cardiac Computed Tomography

Recommendation for Cardiac Computed Tomography Referenced studies that support the recommendation are summarized in Online Data Supplement 9.		
COR	**LOE**	**Recommendation**
IIa	**C-LD**	**1. CCT imaging can be useful in patients with ACHD when information that cannot be obtained by other diagnostic modalities is important enough to justify the exposure to ionizing radiation (S3.4.5-1, S3.4.5-2).**

Recommendation-Specific Supportive Text

1. The most important disadvantage of CCT (including CT angiography) as an imaging technique is the associated exposure to ionizing radiation. This is especially problematic in patients with ACHD in whom serial assessments are contemplated over a lifetime (S3.4.5-1). Gating CCT to the ECG allows image

acquisition during multiple phases of the cardiac cycle, thereby providing cine imaging and the ability to select phases of the cycle of specific interest (usually end-systole and end-diastole), at the cost of increased radiation dose. Electrocardiographic gating is generally unnecessary when the focus is assessment of extracardiac vascular structures, which can consequently be imaged using substantially lower doses of ionizing radiation. Ongoing development of protocols and equipment that reduce radiation exposure are welcome advances (S3.4.5-2).

3.4.6. Cardiac Catheterization

Recommendations for Cardiac Catheterization Referenced studies that support recommendations are summarized in Online Data Supplement 10.		
COR	**LOE**	**Recommendations**
I	**C-LD**	**2. Cardiac catheterization (hemodynamic and/or angiographic) in patients with ACHD AP classification II and III, or interventional cardiac catheterization in patients with ACHD AP classification I to III should be performed by, or in collaboration with, cardiologists with expertise in ACHD (S3.4.6-1–S3.4.6-4).**
IIa	**B-NR**	**3. In patients with a low or intermediate pretest probability of coronary artery disease (CAD), use of CT coronary angiography is reasonable to exclude significant obstructive CAD when cardiac catheterization has significant risk or because of patient preference (S3.4.6-5–S3.4.6-9).**

Recommendation-Specific Supportive Text

1. Cardiac catheterization remains a standard tool when diagnosis, prognosis, or management require a) more precise definition of anatomy than is achievable via advanced noninvasive imaging (e.g., structures with low flow or those shielded from other techniques), b) calculation of pressures and resistances, or c) physiological or anatomic simulation to allow additional calculation or anatomic visualization. Cardiac catheterization can provide unique information not reliably available from other diagnostic modalities (e.g., direct pressure measurement in a vessel or chamber, determination of pulmonary artery (PA) pressures and resistance, and optimal imaging of vessels in which flow is compromised). Procedures should be planned with appreciation of the anatomy and physiology likely to be encountered, including sequelae and residua of prior surgery and interventions.

The expansion of interventional catheter techniques has dramatically expanded possibilities for interventional treatment for an increasing number of conditions. Operators require specialized training and expertise in ACHD. In addition, catheterization laboratories specially equipped with devices and tools used in ACHD intervention are needed and personnel trained in their use. Such equipment and expertise differ from those found in catheterization laboratories devoted primarily to diagnostic catheterization and coronary interventions.

2. For patients at low or intermediate risk of obstructive coronary disease, CT coronary angiography can be an alternative to cardiac catheterization for assessing coronary artery course and patency.

3.4.7. Exercise Testing

Recommendations for Exercise Testing Referenced studies that support recommendations are summarized in Online Data Supplement 11.		
COR	**LOE**	**Recommendations**
IIa	**B-NR**	**1. In patients with ACHD, cardiopulmonary exercise testing (CPET) can be useful for baseline functional assessment and serial testing (S3.4.7-1, S3.4.7-2).**
IIa	**C-LD**	**2. In symptomatic patients with ACHD, a 6-minute walk test can be useful to objectively assess symptom severity, functional capacity, and response to therapy (S3.4.7-3, S3.4.7-4).**

Recommendation-Specific Supportive Text

1. Patients with ACHD often overestimate their physical capabilities and underreport limitations. In contrast to patients with acquired heart disease, patients with ACHD may never have experienced ”normal” function. Decline in physical capacity may occur imperceptibly over many years (S3.4.7-1, S3.4.7-2). Consequently, tools more precise than patient history are necessary for evaluation and serial follow-up of functional capacity. CPET provides objective, reproducible, and repeatable assessment of the cardiovascular, respiratory, and muscular systems and has been shown to have prognostic value in patients with a wide variety of ACHD conditions (S3.4.7-1).

2. In severely impaired patients with ACHD, or those who cannot complete CPET for other reasons, the 6-minute walk test provides a more limited set of data, which nevertheless has prognostic value beyond history alone (S3.4.7-3, S3.4.7-4).

3.5. Transition Education

Recommendation for Transition Education Referenced studies that support the recommendation are summarized in Online Data Supplement 12.		
COR	**LOE**	**Recommendation**
I	**B-NR**	**1. Clinicians caring for patients with CHD should deliver developmentally appropriate transition education to adolescent and young patients with CHD, and to their families/support network (S3.5-1, S3.5-2).**

Recommendation-Specific Supportive Text

1. Preparing a patient for independent cardiac care is an ongoing process that should start in early adolescence if not sooner (S3.5-3) and may extend beyond 18 years of age in many patients. The recommendation and goals for transition and transition education have been described and include verbal, written, and experiential efforts to teach patients and families about their specific heart disease, expectations, and concerns regarding CHD, as well as skills to navigate the healthcare system as an adult (S3.5-4). Lack of education about the need for transition and lifelong cardiac care leads to gaps in care that can result in increased hospitalizations, need for urgent intervention, and increased morbidity (S3.5-5, S3.5-6). A structured approach to transition education improves health related knowledge and self-management (S3.5-1, S3.5-2). This education is a continual process that includes after transfer to an ACHD care provider (S3.5-4).

3.6. Exercise and Sports

Recommendations for Exercise and Sports Referenced studies that support recommendations are summarized in Online Data Supplement 13.		
COR	**LOE**	**Recommendations**
I	**C-LD**	**1. Clinicians should assess activity levels at regular intervals and counsel patients with ACHD about the types and intensity of exercise appropriate to their clinical status (S3.6-1–S3.6-9).**
IIa	**C-LD**	**2. CPET can be useful to guide activity recommendations for patients with ACHD (S3.6-10, S3.6-11).**
IIa	**B-NR**	**3. Cardiac rehabilitation can be useful to increase exercise capacity in patients with ACHD (S3.6-12, S3.6-13).**

Synopsis

Historically, guidelines for physical activity among patients with CHD have focused on restriction, rather than promotion of activity (S3.6-14, S3.6-15). Because of fears of adverse events such as SCD or aortic dissection, recommendations derived from those that apply to competitive sports (S3.6-16) have been applied to recreational activities despite the absence of evidence on the risk or safety of moderate activity. The 2015 "Eligibility and Disqualification Recommendations for Competitive Athletes With Cardiovascular Abnormalities: Task Force 4: Congenital Heart Disease" (S3.6-14) does work toward encouraging participation and shared decision-making with patients regarding competitive sports participation. Most patients with ACHD can safely engage in regular, moderate physical activity. A few conditions, such as systemic ventricular systolic dysfunction, systemic ventricular outflow tract obstruction, hemodynamically significant arrhythmias, or aortic dilation, warrant more cautious recommendations (S3.6-17).

Recommendation-Specific Supportive Text

1. Physical activity is widely recognized as being beneficial to the physical and mental health of those who participate (S3.6-2–S3.6-4). There is conflicting evidence regarding physical activity levels in patients with CHD, with some suggesting the tendency for less activity (S3.6-5, S3.6-9) and a greater prevalence of obesity (S3.6-1) than in the general population. Studies describe the beneficial effects and safety of exercise programs for patients across the spectrum of CHD (S3.6-18, S3.6-19). Activity recommendations should be individualized based on the patient's clinical status and their interests (S3.6-20).

2. There is evidence that exercise capacity varies among congenital heart defects, with declining capacity (generally) as complexity increases (S3.6-10, S3.6-11). Knowledge of the typical exercise capacity for patients with a specific lesion is important when making appropriate activity recommendations (S3.6-10). Self-directed activity is usually at 40% to 60% of maximal exercise capacity, whereas fitness training occurs at 60% to 80% of maximal capacity (S3.6-20). Exercise capacity is defined in relation to maximal oxygen consumption. The writing committee recognizes that not all ACHD centers will have the resources to conduct CPET, which is the preferred method of evaluation. If CPET cannot be performed, other exercise tests using an established treadmill or bicycle ergometer protocol are an acceptable alternative for assessing exercise capacity, recognizing that valuable information may be unavailable compared with CPET.

3. As with other populations of cardiac patients, inactivity leads to reduced exercise performance. Regular exercise and cardiac rehabilitation may improve exercise capacity and HF symptoms, and ought to be encouraged (S3.6-6, S3.6-7, S3.6-21, S3.6-22).

3.7. Mental Health and Neurodevelopmental Issues

Recommendations for Mental Health and Neurodevelopmental Issues Referenced studies that support recommendations are summarized in Online Data Supplement 14.		
COR	**LOE**	**Recommendations**
I	**B-NR**	**1. Patients with ACHD should be evaluated for depression and anxiety (S3.7-1–S3.7-3).**
IIa	**B-NR**	**2. Referral for mental health evaluation and treatment is reasonable in patients with ACHD (S3.7-1–S3.7-4).**
IIb	**B-NR**	**3. Neurodevelopmental or neuropsychological testing may be considered in some patients with ACHD to guide therapies that enhance academic, behavioral, psychosocial, and adaptive functioning (S3.7-5–S3.7-9).**

Synopsis

Mental health and neurodevelopmental issues are common in patients with ACHD and may significantly affect QoL. Neurodevelopmental abnormalities are more frequently seen in children who have complex disease, complex surgical repairs, and other characteristics (S3.7-10–S3.7-12). There is extensive literature in the pediatric population on the frequency and importance of neurodevelopmental abnormalities, However, many adults may not have been evaluated as children in accordance with current diagnostic and treatment strategies (S3.7-13, S3.7-14). Neurodevelopmental disorders, such as impairment of cognition, social skills and communication, and attention disorders, are often underrecognized even though appropriate diagnosis, treatment, and rehabilitation may be beneficial in optimizing function and QoL. An AHA scientific statement describes the common neurodevelopmental disorders affecting children with CHD and may inform neurodevelopmental issues related to adults with CHD (S3.7-13).

Recommendation-Specific Supportive Text

1. Anxiety and depression are underrecognized in the ACHD population. Point-of-care assessment with simple questions about anxiety and depression should be included in the symptom review.

2. Anxiety and depression are prevalent among patients with ACHD. Self-reported symptoms are incomplete to identify the existence of mood disorders. Structured professional psychological evaluation can identify up to 50% more patients with mood disorders (S3.7-1).

3. Although there is limited evidence on neurodevelopmental and neuropsychological issues in patients with ACHD, there is increasing evidence of the neurodevelopmental impact of CHD and surgery in childhood (S3.7-6, S3.7-8, S3.7-9). It is likely that this impact will persist into adulthood and may manifest in lower educational and occupational achievement. This is particularly evident in patients with genetic conditions such as 22q11 deletion and trisomy 21.

3.8. Endocarditis Prevention

Patients with ACHD have an increased risk of developing infective endocarditis (IE) (S3.8-1, S3.8-2). The most common pathogens responsible for IE include *Streptococcus viridans, Staphylococcus* species, and *Enterococcus* species. Despite advances in antimicrobial therapy and surgical techniques, IE remains a condition associated with significant morbidity and mortality. Numerous guidelines are available with recommendations on the prevention and diagnosis of IE (S3.8-3–S3.8-5). These guidelines include consistent descriptions of the patients at highest risk of adverse effects from endocarditis. Antibiotic

prophylaxis continues to be recommended for patients with high-risk characteristics, which are often found in patients with ACHD (S3.8-2). These patients include:

- Those with previous IE;
- Patients with prosthetic valves (biological and mechanical, surgical and transcatheter);
- Patients within 6 months of placement of prosthetic material;
- Patients with residual intracardiac shunts at the site of or adjacent to previous repair with prosthetic material or devices; or
- Patients with uncorrected cyanotic heart disease.

See Online Data Supplement 15 for referenced studies.

3.9. Concomitant Syndromes

Recommendation for Concomitant Syndromes Referenced studies that support the recommendation are summarized in Online Data Supplement 16.		
COR	**LOE**	**Recommendation**
IIa	**B-NR**	**1. Genetic testing for 22q11 deletions is reasonable for patients with conotruncal cardiac defects (S3.9-1, S3.9-2).**

Synopsis

Patients with genetic syndromes may have phenotypic manifestations and associated CHD as clinical features of the genetic abnormality. An underlying chromosomal abnormality exists in at least 10% of infants with CHD and may not have been previously tested in patients with ACHD (S3.9-3). Clinicians caring for patients with ACHD should recognize the potential for undiagnosed genetic abnormalities that may affect overall health (Table 10) and pursue appropriate evaluation.

Recommendation-Specific Supportive Text

1. Several forms of CHD may be associated with underlying genetic syndromes (Table 10). Some genetic syndromes may not be phenotypically apparent in adults, and prior childhood genetic workup may not be readily available; therefore, genetic syndromes may be missed in patients with ACHD. Many of these syndromes may have important clinical comorbidities, including but not limited to learning disabilities, psychiatric conditions, and reproductive disorders. Up to 5% of children born with CHD have DiGeorge syndrome (22q11.2 deletion), the congenital heart defects most commonly associated being those of conotruncal origin. DiGeorge syndrome is an autosomal dominant condition. Therefore, genetic testing is reasonable for patients with ACHD with conotruncal defects for recognition and management of comorbidities and for counseling on the potential risk of recurrence in offspring (S3.9-4, S3.9-5).

Table 10. Underlying Genetic Syndromes Commonly Associated With CHD (S3.9-4, S3.9-6)

Syndrome	Genetic Abnormality	Clinical Features	Common Cardiac Findings
DiGeorge syndrome (velocardiofacial syndrome)	22q11.2 deletion	Thymic and parathyroid hypoplasia, immunodeficiency, low-set ears, hypocalcemia, speech and learning disorders, renal anomalies, psychiatric disease 25%–75% have CHD, depending on age studied (S3.9-7, S3.9-8)	IAA type B, aortic arch anomalies, truncus arteriosus, TOF
Down syndrome	Trisomy 21	Developmental disability,	ASD, VSD, AVSD, TOF

		characteristic facial features, hypotonia, palmar crease 40%–50% have CHD	
Holt–Oram syndrome (S3.9-9)	TBX5	Upper limb skeletal abnormalities 75% have CHD	ASD, VSD, MV disease
Klinefelter syndrome	47 XXY	Tall stature, hypoplastic testes, delayed puberty, developmental disability 50% have CHD	PDA, ASD, MV prolapse
Noonan syndrome (S3.9-10)	PTPN11, KRAS, SOS1 RAF1, NRAS, BRAF, MAP2K1	Facial anomalies, webbed neck, chest deformity, short stature, lymphatic abnormalities, bleeding abnormalities 80% have CHD	PS, ASD, HCM
Turner syndrome	45X	Short stature, webbed neck, lymphedema, primary amenorrhea 30% have CHD Risk of aortic dissection	Coarctation, BAV, aortic stenosis, hypoplastic left heart, ascending aortopathy
Williams syndrome	7q11.23 deletion	Elfin face, social personality, hearing loss, developmental delay, infantile hypercalcemia 50%–80% have CHD	Supravalvar aortic stenosis, peripheral PS

ASD indicates atrial septal defect; AVSD, atrioventricular septal defect; BAV, bicuspid aortic valve; CHD, congenital heart disease; HCM, hypertrophic cardiomyopathy; IAA, interrupted aortic arch; MV, mitral valve; PDA, patent ductus arteriosus; PS, pulmonary stenosis; TOF, tetralogy of Fallot; and VSD, ventricular septal defect.

3.10. Acquired Cardiovascular Disease

Patients with ACHD can acquire other cardiovascular diseases such as hypertension, atherosclerotic coronary artery disease, vascular disease, stroke, and HF (S3.10-1–S3.10-3). The impact of acquired heart disease is increasing as the lifespan of patients with ACHD extends. Myocardial infarction is one of the leading contributing causes of death for late surviving adults with acyanotic CHD (S3.10-4). Major adverse cardiac events, such as HF, percutaneous coronary intervention, coronary artery bypass graft surgery, malignant arrhythmia, cardiac shock, and placement of an implantable cardioverter-defibrillator (ICD), are also quite prevalent (S3.10-5, S3.10-6). Overall, cardiovascular reasons account for approximately 77% of all deaths in patients with ACHD, with approximately half attributable to chronic HF (S3.10-7). Evaluation for acquired cardiac conditions is warranted in patients with risk factors, although results of testing (e.g., stress perfusion studies) should account for preexisting abnormalities caused by CHD, recognizing prior interventions can mimic abnormalities otherwise suggestive of acquired heart disease (S3.10-8).

In patients with ACHD, prevention and treatment of conditions predisposing to acquired cardiovascular disease such as diabetes mellitus, obesity, hypertension, dyslipidemia, and/or similar comorbidities are important. Given the increased risk of acquired cardiovascular disease with age, promoting a healthy lifestyle is important in all patients with ACHD, although there are not data demonstrating the effects of risk reduction on clinical outcomes specific to the ACHD population. Emphasizing the importance of daily physical activity according to functional capacity, and decreasing sedentary behavior as appropriate for the patient's clinical status is essential when counseling patients with congenital heart defects (S3.10-9). Interestingly, most patients with ACHD lead healthier lifestyles compared with control patients (S3.10-10), suggesting that this patient population may be receptive to advice and may continue to benefit from recommendations about diet, activity, and modifiable risk factors.

See Online Data Supplement 17 for referenced studies.

3.11. Noncardiac Medical Issues

Recommendation for Noncardiac Medical Issues Referenced studies that support the recommendation are summarized in Online Data Supplement 18.		
COR	**LOE**	**Recommendation**
I	**C-LD**	**1. Patients with ACHD at risk for hepatitis C should be screened and vaccinated for viral hepatitis and treated as appropriate (S3.11-1).**

Recommendation-Specific Supportive Text

1. Patients with ACHD are at risk of hepatitis C because of blood exposure during cardiac surgery. Hepatitis screening is warranted especially in those with exposure to blood products before universal screening for hepatitis C, which began in 1992. Hepatitis vaccination and/or consultation with a hepatologist should also be offered where appropriate, particularly in patients with ACHD with concomitant liver disease (e.g., Fontan patients).

3.12. Noncardiac Surgery

Recommendations for Noncardiac Surgery Referenced studies that support recommendations are summarized in Online Data Supplement 18.		
COR	**LOE**	**Recommendations**
I	**C-LD**	**1. Optimization before and close surveillance after invasive procedures, regardless of the complexity of the anatomic defect or type of procedure is beneficial for patients with ACHD (S3.12-1–S3.12-4).**
I	**B-NR**	**2. In patients with ACHD AP classification IB-D, IIA-D, and IIIA-D* noncardiac surgical and interventional procedures should be performed in a hospital with or in consultation with experts in ACHD when possible (S3.12-1, S3.12-3, S3.12-5–S3.12-9).**

*See Tables 3 and 4 for details on the ACHD AP classification system.

Synopsis

Patients with ACHD may have greater operative risk than patients without ACHD. The ”2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery” (S3.12-10) may be applied; however, those guidelines may not apply directly. One must remain cognizant that there are differences in cardiac issues commonly present in patients with ACHD, such as mechanisms for ventricular dysfunction, type and mechanisms of arrhythmia, and the probability of coronary artery disease. The 2014 guideline (S3.12-10) was developed primarily with evidence and experience derived from, and related to, patients with acquired heart disease. Thus, the evidence supporting recommendations regarding risk indices and management strategies may not apply to many patients with ACHD.

Recommendation-Specific Supportive Text

1. A checklist of issues to consider in the assessment and management of patients with ACHD undergoing noncardiac surgery is presented in Table 11. Patients with ACHD may present with nonroutine and unusual physiological challenges (e.g., those related to fluid balance in the setting of single ventricle or the impact of vascular resistances on shunts in cyanotic patients) (S3.12-2–S3.12-4).

Heightened surveillance may mandate extended postoperative intensive or other high-acuity care (S3.12-2).

2. Case series and analysis of administrative databases confirm that surgical procedures in patients with ACHD carry greater risk than in patients without ACHD (S3.12-1–S3.12-3, S3.12-6, S3.12-8, S3.12-11–S3.12-13). Risk relates to the specific type of ACHD, surgical procedure, urgency of intervention, and availability of specialized resources (S3.12-1, S3.12-3–S3.12-6, S3.12-8, S3.12-14). Noncardiac surgery is usually accomplished without substantial morbidity or mortality, but even minor surgery can be complicated in patients with ACHD. Surgery that is low risk in the general population may be associated with higher risk in the ACHD population (S3.12-1, S3.12-6). Patients with ACHD may present with nonroutine and unusual physiological challenges (e.g., those related to fluid balance in the setting of single ventricle or the impact of vascular resistances on shunts in cyanotic patients) (S3.12-2, S3.12-4).

When possible, patients with ACHD, especially those with complex disease (ACHD AP classification II and III) and/or whose disease has progressed (stages B, C, D) (Tables 3 and 4), should receive preoperative evaluation and surgery or other nonsurgical intervention within an ACHD program. Because the inability to access resources or urgent conditions may preclude transfer or timely consultation, collaboration with members of the multidisciplinary ACHD team may be helpful. Clear processes for timely consultation and support are needed to manage the physiological challenges presented by patients with ACHD related to fluid balance, vascular resistance, and shunts (S3.12-3, S3.12-4). A checklist of issues to consider in assessment and management of patients with ACHD undergoing noncardiac surgery is presented in Table 11.

Table 11. ACHD Management Issues for Noncardiac Surgery

Clarify CHD diagnosis
➢ Clarify prior procedures, residua, sequelae, and current status, including ACHD AP classification
➢ Be aware that history obtained from only the patient and family may be faulty or incomplete
➢ Obtain and review old records to ensure accurate understanding of past procedures and clinical course
➢ Complete additional investigations required to define ACHD AP classification
➢ Develop management strategies to minimize risk and optimize outcome
Factors associated with increased risk of perioperative morbidity and mortality (S3.12-12): • Cyanosis • Congestive HF • Poor general health • Younger age • Pulmonary hypertension • Operations on the respiratory and nervous systems • Complex CHD • Urgent/emergency procedures
Issues to consider: • Endocarditis prophylaxis • Complications related to underlying hemodynamics • Abnormal venous and/or arterial anatomy affecting venous and arterial access • Persistent shunts

- Valvular disease
- Arrhythmias, including bradyarrhythmias
- Erythrocytosis
- Pulmonary vascular disease
- Meticulous line care (also consider air filters for intravenous lines) to reduce risk of paradoxic embolus in patients who are cyanotic because of right-to-left shunts
- Adjustment of anticoagulant volume in tubes for some blood work in cyanotic patients
- Prevention of venous thrombosis
- Monitoring of renal and liver function
- Periprocedure anticoagulation
- Possible need for nonconventional drug dosing
- Increased prevalence of hepatitis C infection because of prior procedures and remote blood transfusions
- Developmental disability

ACHD indicates adult congenital heart disease; AP, anatomic and physiological; CHD, congenital heart disease; and HF, heart failure.

3.13. Pregnancy, Reproduction, and Sexual Health

3.13.1. Pregnancy

Recommendations for Pregnancy Referenced studies that support recommendations are summarized in Online Data Supplement 19.		
COR	**LOE**	**Recommendations**
I	**C-LD**	**1. Women with CHD should receive prepregnancy counseling with input from an ACHD cardiologist to determine maternal cardiac, obstetrical and fetal risks, and potential long-term risks to the mother (S3.13.1-1–S3.13.1-4).**
I	**C-LD**	**2. An individualized plan of care that addresses expectations and contingencies should be developed for and with women with CHD who are pregnant or who may become pregnant and shared with the patient and all caregivers (S3.13.1-2, S3.13.1-3).**
I	**B-NR**	**3. Women with CHD receiving chronic anticoagulation should be counseled, ideally before conception, on the risks and benefits of specific anticoagulants during pregnancy (S3.13.1-5, S3.13.1-6).**
I	**B-NR**	**4. Women with ACHD AP classification IB-D, IIA-D, and IIIA-D* should be managed collaboratively during pregnancy by ACHD cardiologists, obstetricians, and anesthesiologists experienced in ACHD (S3.13.1-2, S3.13.1-7, S3.13.1-8).**
I	**C-EO**	**5. In collaboration with an ACHD cardiologist to ensure accurate assessment of pregnancy risk, patients at high risk of maternal morbidity or mortality, including women with pulmonary arterial hypertension (PAH), Eisenmenger syndrome, severe systemic ventricular dysfunction, severe left-sided obstructive lesions, and/or ACHD AP classification ID, IID, IIID* should be counseled against becoming pregnant or be given the option of terminating pregnancy.**
I	**B-NR**	**6. Men and women of childbearing age with CHD should be counseled on**

		the risk of CHD recurrence in offspring (S3.13.1-9).
IIa	**B-NR**	**7. Exercise testing can be useful for risk assessment in women with ACHD AP classification IC-D, IIA-D, and IIIA-D* who are considering pregnancy (S3.13.1-10, S3.13.1-11).**
IIa	**B-NR**	**8. When either parent has CHD, it is reasonable to perform fetal echocardiography (S3.13.1-12, S3.13.1-13).**

*See Tables 3 and 4 for the ACHD AP classification system.

Synopsis

Most data regarding cardiac and obstetric risk to women with CHD during pregnancy derive from retrospective case series (S3.13.1-2–S3.13.1-5, S3.13.1-8, S3.13.1-10, S3.13.1-12, S3.13.1-14–S3.13.1-20). Many women with CHD considering pregnancy may have received inconsistent guidance regarding pregnancy risks (S3.13.1-21). Several risk scores have been developed to risk-stratify women with heart disease desiring pregnancy (S3.13.1-2, S3.13.1-7), and a prospective validation study suggests that the World Health Organization classification is the most accurate prediction model (S3.13.1-11). Although many women with CHD tolerate the hemodynamic changes of pregnancy, others may face significant immediate or late risks of pregnancy including volume overload, arrhythmias, progressive cardiac dysfunction, and death. Cardiac medications may need to be adjusted during pregnancy and counseling provided to discuss the options for and potential impact of those changes. Some specific complications may be more common in women with certain types of CHD, such as hypertension, which is more common in women with coarctation (S3.13.1-22, S3.13.1-23). The offspring of patients with ACHD have an increased risk of CHD and other events such as prematurity (S3.13.1-24). All women with CHD should receive appropriate counseling regarding contraception choices. A multidisciplinary team that includes ACHD specialists and maternal-fetal medicine obstetricians with expertise in caring for women with heart disease is appropriate for achieving optimal outcomes.

Recommendation-Specific Supportive Text

1. Prepregnancy counseling allows for an individualized risk assessment. This will include discussing maternal risks for pregnancy, delivery, and postpartum period, and medications that may be teratogenic and require alternative therapies (e.g., angiotensin-converting enzyme inhibitors/angiotensin-receptor blockers). Additionally, counseling should include a discussion related to fetal risk in regard to CHD transmission and overall risk to the health of the fetus. ACHD cardiologists are valuable in accurately assessing pregnancy risks. Risk may be overestimated or underestimated by providers without expertise in CHD and pregnancy, leading to patients' receiving inaccurate recommendations on risks of pregnancy, risks of delivery, and the type of delivery (e.g., the incorrect notion that most women with CHD require cesarean delivery for cardiac reasons).

2. This care plan should address maternal cardiac risks on the basis of the individual patient's anatomy and physiology. Clear documentation is important so that all providers are well aware of the risks and expected outcomes, including risk of maternal volume shifts, arrhythmias, labor and delivery plan, and need for maternal cardiac monitoring when indicated. Contingency plans for anticipated complications related to the presence of CHD should also be developed.

3. Chronic anticoagulation during pregnancy is associated with increased risk of maternal bleeding and thrombotic events as well as a higher risk of fetal loss, and in the case of warfarin, the risk of teratogenicity (S3.13.1-5, S3.13.1-14). The choice of specific anticoagulant must balance maternal well-being and risks for mother and fetus, and should be individualized. Patients with mechanical valves should be treated according to GDMT (S3.13.1-25).

4. The hemodynamic changes of pregnancy, labor, and delivery can result in hemodynamic decompensation for some women with CHD (S3.13.1-1, S3.13.1-7, S3.13.1-15, S3.13.1-24). Management involving the expertise of ACHD, maternal-fetal medicine, and anesthesiology should help anticipate and mitigate some of the potentially detrimental maternal or fetal outcomes.

5. Women at high risk include, but are not limited to, those diagnosed with cardiac conditions that meet World Health Organization maternal cardiac risk classification IV (S3.13.1-26).

a. PAH of any cause
b. Severe systemic ventricular dysfunction: LV ejection fraction <30% and/or NYHA III–IV symptoms
c. Severe left heart obstruction
d. Severe native coarctation (S3.13.1-16, S3.13.1-27, S3.13.1-28)

These patients have an extremely high risk of maternal mortality or severe morbidity, and if pregnant, the option of pregnancy termination should be discussed

6. Prepregnancy counseling regarding the risk of CHD recurrence in offspring provides helpful information to parents to inform decision-making regarding family planning and delivery options, and should allow adequate time dedicated to answering important questions from the parents.

7. CPET performed before conception can predict maternal and neonatal outcomes in pregnant women with CHD. A blunted heart rate response to exercise in women with CHD is associated with a higher risk of maternal cardiac and neonatal adverse events (S3.13.1-11).

8. If the patient with CHD or their partner is pregnant, there is an increased risk of CHD in the offspring and fetal echocardiography can be useful in defining whether CHD is present, and if so, help to determine the course of action at the time of delivery. There are data to suggest a prenatal diagnosis improves neonatal survival, although selection bias (e.g., preoperative deaths, family preference) is a limitation for many studies, so benefit has been more difficult than expected to prove (S3.13.1-13, S3.13.1-29, S3.13.1-30).

3.13.2. Contraception

Recommendations for Contraception Referenced studies that support recommendations are summarized in Online Data Supplement 20.		
COR	**LOE**	**Recommendations**
I	**C-LD**	**1. Women of childbearing potential with CHD should be counseled about the risks associated with pregnancy and appropriate contraceptive options (S3.13.2-1–S3.13.2-3).**
III: Harm	**B-NR**	**2. Estrogen-containing contraceptives are potentially harmful for women with CHD who are at high risk of thromboembolic events (e.g., cyanosis, Fontan physiology, mechanical valves, prior thrombotic events, PAH) (S3.13.2-4, S3.13.2-5).**

Synopsis

The use of contraceptive agents should be balanced against the risks of pregnancy in every woman with CHD after menarche (S3.13.2-6). There are no data on the safety of various contraceptive techniques in patients with ACHD.

Recommendation-Specific Supportive Text

1. The individualized benefits and risks of each contraceptive therapy must be determined based on the patient's anatomy and physiology in consultation with a gynecologist. This counseling should include the expected failure rates of contraceptive options and the anticipated maternal and fetal risks of unplanned pregnancy, with these issues revisited on a regular basis.

Contraceptive choices include combined hormonal (estrogen/progesterone) contraception, progesterone-only agents, intrauterine devices, barrier methods, and permanent sterilization. Low-dose combination oral contraceptive (≤20 mcg of ethinyl estradiol) is an option except in women who are at increased risk of thrombosis (S3.13.2-4). Medroxyprogesterone acetate is a less effective method of contraception, and the potential for fluid retention must be considered (S3.13.2-5). Intrauterine devices are highly effective methods of contraception; however, women may experience vasovagal reactions at the time of implant. Tubal ligation is generally safe with recognized risks associated with anesthesia and abdominal insufflation. An efficacious option is a vasectomy for the male partner; however, the long-term prognosis of the female patient with CHD must be considered and discussed openly. In the case of unplanned pregnancy with desire for termination, the morning-after pill (levonorgestrel) is safe for women, but acute fluid retention is a risk to be considered.

2. Women with CHD who are at high risk of thrombosis include those with cyanosis, Fontan physiology, mechanical valves, prior thrombotic events, and PAH. In women who are at high risk of thrombosis and who receive warfarin, there are no data on which to base a recommendation or counseling as to whether it is safe to use estrogen-containing contraception. It is unclear whether the use of warfarin offsets adequately the additional risk of thrombosis related to pregnancy in high-risk patients.

3.13.3. Infertility Treatment

Menstrual cycle disorders are not uncommon in women with CHD. In small case series of women with CHD, various causes for infertility were documented including primary and secondary amenorrhea, oligomenorrhea, and uterine anomalies (S3.13.3-1, S3.13.3-2). In more complex forms of CHD (e.g., the population with Fontan palliation), the prevalence of primary amenorrhea may be as high as 40% (S3.13.3-2). Menarche occurs at an older age in these women than in the general population (S3.13.3-2). Women with CHD also have higher rates of spontaneous abortion and miscarriage (S3.13.3-3–S3.13.3-5). The prevalence of infertility in men with CHD is unknown. Each patient with ACHD should be counseled regarding the potential for infertility and referral to a specialized reproductive endocrinologist when appropriate, although there is little specific guidance for women based on types of CHD. Alternative options for family planning including assisted reproductive technologies and adoption is appropriate, and risks versus benefits of all options are addressed during counseling.

3.13.4. Sexual Function

Sexuality is an important element of QoL. Although there are data that sexual function is a concern in both women and men, there is minimal evidence on the prevalence of sexual concerns among adults with CHD and far less to guide interventions (S3.13.4-1).

Concerns with sexual health are present in 20% to 40% of men with CHD (S3.13.4-2–S3.13.4-4). Erectile dysfunction is reported by up to 42% of men with CHD (S3.13.4-1, S3.13.4-3). Men with CHD report being in sexual relationships significantly less often than the general population (S3.13.4-1, S3.13.4-4). Among men with CHD who report sexual health concerns, there is a high level of psychological distress and diminished QoL (S3.13.4-1, S3.13.4-2, S3.13.4-4, S3.13.4-5). The ACHD provider should be mindful of this often-unspoken concern and create an environment in which the patient feels comfortable addressing concerns about their sexuality.

See Online Data Supplement 21 for referenced studies.

3.14. Heart Failure and Transplant

3.14.1. Heart Failure

Recommendation for Heart Failure Referenced studies that support the recommendation are summarized in Online Data Supplement 22.		
COR	**LOE**	**Recommendation**
I	**C-LD**	**1. Consultation with ACHD and HF specialists is recommended for patients with ACHD and HF or severe ventricular dysfunction (S3.14.1-1–S3.14.1-4).**

Synopsis

HF is a significant issue in patients with ACHD. It is common, associated with morbidity and mortality, and is anticipated to increase in prevalence. However, despite the clinical importance of HF in patients with ACHD and efforts to study the effects of medication and device therapy in these patients, there are no data to support treatment recommendations. For patients with biventricular physiology, systemic left ventricular (LV) dysfunction, no repairable residual hemodynamic abnormalities, and persistent HF symptoms, standard GDMT is ostensibly preferable to no treatment. However, expectations of its benefit should be tempered, and risk may be different in patients with acquired CVD, because CHD patients have not been included in the trials by which those guidelines were developed.

Recommendation-Specific Supportive Text

1. HF is common in patients with ACHD and is associated with increased morbidity and mortality (S3.14.1-1–S3.14.1-4). There are many causes of HF symptoms that may be reversible, including valve dysfunction, shunts, arrhythmias, venous obstruction, and systolic and/or diastolic ventricular dysfunction, which require evaluation and treatment when possible. Unlike acquired HF, and despite the clinical importance of HF in ACHD, data to support a treatment recommendations including typical HF medical therapy (e.g., angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, beta blockers, and aldosterone antagonists) (S3.14.1-5) are limited in patients with ACHD (S3.14.1-6–S3.14.1-22). HF in patients with ACHD is multifactorial and may manifest as variable response to pharmacotherapy. Advanced HF therapies may be technically difficult or considered too late in the course. Thus, timely evaluation by ACHD and HF specialists is crucial to optimal care of such patients.

3.14.2. Heart Transplant

Because of the prevalence of HF among patients with CHD, heart transplantation is increasingly being considered as a therapeutic option. Data on proper timing of transplantation are limited, particularly for individual lesions. Larger studies based on transplant databases do not allow for analysis based on the type of CHD (S3.14.2-1–S3.14.2-4). Currently, patients with ACHD may have fewer mechanical circulatory devices (e.g., ventricular-assist devices), which may lower their listing status and hence potential for organ receipt (S3.14.2-1, S3.14.2-2, S3.14.2-4–S3.14.2-7).

Although specific criteria for timing of referral for transplantation are desirable, universal recommendations cannot be made based on current data. Generally, published data show that immediate and early posttransplantation risk is higher in ACHD than in acquired heart disease because of increased perioperative mortality (S3.14.2-2). However, once beyond the perioperative period, patients with ACHD do as well as or better than those with acquired heart disease, with expected 10-year survival equivalent to or better than that of patients without ACHD (S3.14.2-2–S3.14.2-4, S3.14.2-6, S3.14.2-7). Risks for poor outcomes include single ventricle anatomy, anatomic complexity, protein-

losing enteropathy, or high titers of panel reactive antibodies (S3.14.2-8, S3.14.2-9). The current allocation system puts patients with ACHD at a disadvantage. Rather than priority dictated by the usual accepted risk markers, patients with ACHD are often listed by "exception," a process that requires the clinician to argue that the patient warrants higher priority than would be evident by applying the used risk markers. There is also significant mortality for patients with ACHD while on the waitlist (S3.14.2-10, S3.14.2-11). Surgical alternatives to transplantation exist for some patients with CHD (e.g., valve replacement, shunt closure), but these patients are at high risk of perioperative mortality (S3.14.2-12). Ideally, providers will consider early referral to a transplant center with expertise in ACHD transplantation when transplantation becomes a relevant clinical consideration. Additionally, it is advisable to consider options for transplantation or ventricular assist device as a backup before other high-risk surgery is pursued.

See Online Data Supplement 23 for referenced studies.

3.14.3. Multiorgan Transplant

Recognizing the vulnerability of many organ systems in patients with CHD, multiorgan transplantation is often considered, although infrequently performed. Multiorgan transplantation requires a multidisciplinary and comprehensive approach with thoughtful planning and communication among practitioners.

Multiorgan transplantation may be performed as sequential operations or as a single operation. Typically, simultaneous multiorgan procedure in patients with CHD will be heart-lung transplantation for conditions that result in irreversible pulmonary hypertension such as Eisenmenger syndrome. (S3.14.3-1, S3.14.3-2). Fewer than 100 heart-lung transplants are performed internationally each year, with a median survival of 3.3 years and 10-year survival of 32% (S3.14.3-3). Survival is worse for heart-lung recipients than single-organ heart or lung recipients possibly, in part, because of longer wait times (S3.14.3-4).

The occurrence of simultaneous heart-liver transplantation is an option in patients with severe right-sided HF and in single ventricle patients after Fontan palliation. Given the recognized vulnerability of the liver to injury in Fontan patients and the fact that heart alone transplantation outcomes have been poor in patients with concomitant liver dysfunction, transplant centers may favor heart-liver transplantation in those with cirrhosis, but this policy is not universal. Fewer than 15 such procedures are performed annually in the United States, and approximately 20% of patients are referred because of underlying CHD (S3.14.3-5, S3.14.3-6). Consequently, experience with these procedures is limited (S3.14.3-5, S3.14.3-7), and heterogeneity makes generalizability difficult. Data are insufficient to support recommendations. For all patients, survival mimics that for liver transplantation alone with 1-, 2-, and 5-year survival at 84%, 74%, and 72%, respectively (S3.14.3-6). Outcomes in Fontan patients with or without cirrhosis are not necessarily different in those who receive heart transplantation alone (S3.14.3-5, S3.14.3-8). Multicenter data gathering on patients considered for multiorgan transplantation are needed to inform future recommendations for these therapies.

3.15. Palliative Care

Recommendation for Palliative Care Referenced studies that support the recommendation are summarized in Online Data Supplement 24.		
COR	**LOE**	**Recommendation**
IIa	**B-NR**	**1. Discussion of end-of-life issues and advance directives can be beneficial for patients with ACHD or their surrogates (S3.15-1–S3.15-3).**

Recommendation-Specific Supportive Text

1. Patients with ACHD sometimes have significant morbidities not amenable to effective medical or surgical treatment and may be best managed using the consultative expertise of palliative care specialists. Accurate predictions of prognosis in ACHD are difficult, and patients commonly receive aggressive treatments during their terminal admission (S3.15-4). There is a discrepancy between patient-reported interest in discussing advanced directives and physician-reported discussions, with more patients interested in such discussions than recognized by providers (S3.15-1, S3.15-2). Early discussion of advance planning is favored by nearly twice as many patients as physicians (S3.15-3). Early discussion of end-of-life issues is consistent with patient-centered care and patient satisfaction and can facilitate palliative care. Although discussing end-of-life options would seem appropriate for all patients, there are circumstances (e.g., cultural or cognitive) when those conversations may not be appropriate. Similarly, although the goal is not to wait to discuss end-of-life until death is imminent, such discussion may not have the same benefit for young patients who are clinically well with low-risk disease. Thus, it is important to always have and encourage the option to discuss end-of-life issues, but timing of conversation is individualized.

3.16. Cyanosis

The definition of cyanosis is “blueish discoloration of the skin and/or mucous membranes resulting from inadequate oxygenation of the blood.” Generally, for cyanosis to be visible, at least 5 g/L of unsaturated hemoglobin in tissue is needed (S3.16-1). Anemia may result in hypoxemia that is not manifest as cyanosis. In this guideline, “cyanosis” is used as a generic term to identify hypoxemia caused by right-to-left shunting of blood, but not all hypoxemic patients will be visibly cyanotic at all times.

Cyanotic heart disease encompasses a widely heterogeneous group; therefore, an individualized approach is needed for each patient according to the clinical details.

Secondary erythrocytosis (a physiological increase in red blood cell mass in response to hypoxemia) and polycythemia (a neoplastic proliferation of hematopoietic cells including the red blood cell line) are fundamentally different conditions that require different treatments. In secondary erythrocytosis, the patient’s own homeostatic processes generally direct achievement of an optimal level of red cell mass, estimated by hemoglobin and hematocrit (S3.16-2).

Iron deficiency is frequently encountered in cyanotic individuals (S3.16-3). In addition to contributing to symptoms, iron deficiency causes a reduction of hemoglobin without a proportional change in hematocrit and thus compromises systemic oxygen transport without lowering viscosity (S3.16-3). Symptoms mimic those of hyperviscosity. Consequences of iron deficiency may include stroke and myocardial ischemia (S3.16-4–S3.16-6), although published findings are inconsistent. Iron deficiency requires assessment of serum iron, ferritin, and transferrin levels, because mean corpuscular volume is not a reliable screening test (S3.16-7). Limited data suggest that treatment of transferrin saturation <20% with iron supplementation until iron stores are replete can be done safely (S3.16-8).

Although there is an exponential relationship between viscosity and hematocrit, available data do not justify a cut point for a ”safe” hematocrit (S3.16-3). There is no clear correlation between viscosity, iron deficiency, and a patient’s symptoms or clinical condition (S3.16-3). The nature and cause of hyperviscosity symptoms are not well understood. The severity and frequency of symptoms of hyperviscosity do not correlate with measured hematocrit. Phlebotomy is, therefore, rarely necessary in patients with secondary erythrocytosis, and routine phlebotomy is not supported by data. Patients with suspected hyperviscosity need to be rehydrated either with oral fluids or intravenous normal saline solution as a first-line therapy, evaluated for iron deficiency, and treated if appropriate. Phlebotomy

(with equal volume fluid replacement) is sometimes performed in special cases wherein, after adequate hydration, hematocrit remains higher than the patient's baseline and symptoms persist, or there is evidence of end-organ damage attributable to hyperviscosity (e.g., myocardial ischemia, transient ischemic attack/stroke) (S3.16-9, S3.16-10).

Observational studies in cyanotic individuals have shown evidence of altered synthesis and function of clotting factors that may contribute to both hypo- and hypercoagulability (S3.16-11, S3.16-12), and thrombosis and bleeding (particularly epistaxis or hemoptysis) have been described in patients with Eisenmenger syndrome, which may be life-threatening (S3.16-13–S3.16-15). These disparate trends preclude developing universally applicable recommendations, including use of antiplatelet or anticoagulant therapy in these patients (S3.16-16). Similarly, there is not a clear role for preoperative phlebotomy to improve coagulation properties.

Cyanotic heart disease is a multisystem disorder. Manifestations, in addition to those already discussed, include renal dysfunction, gout, infections, and osteoarthropathy. Alterations can be found of myocardial (S3.16-17, S3.16-18), cerebral (S3.16-19), and retinal blood flow (S3.16-20), and kidney function (S3.16-21). Providers should recognize multiorgan susceptibility and avoid treatments that may have adverse noncardiac effects. Additional practices that may contribute to effective management of cyanotic patients are listed in Table 12.

Table 12. Specific Management Practices for Cyanotic CHD

- Recording clinical oxygen saturation at rest (>5 min) rather than immediately after effort (e.g., walking into a clinic examination room).
- Meticulous intravenous care to avoid air or particulate matter, which may include use of air/particulate filters on all intravenous access lines, when feasible, and careful de-airing of all lines.
- Cerebral imaging for any new headache or neurologic sign to assess for possible cerebral abscess, hemorrhage, or stroke.
- Measurement of serum uric acid and treatment with allopurinol in a patient with a history of gout.
- Supplemental oxygen as needed for symptom relief but not to a target oxygen saturation level and not if there is no demonstrable symptomatic benefit.
- Avoidance of or cautious use of therapies that may reduce the patient's hypoxia-mediated drive to ventilation, such as narcotics or, in rare circumstances, excess supplemental oxygen (S3.16-22).
- Anesthesia by providers with expertise in anesthesia for patients with ACHD for any noncardiac surgery.
- Non-estrogen–containing birth control for women of child-bearing potential (intrauterine device may be a preferred option). Avoidance of birth control entirely is not a safe, acceptable option.
- Patients can travel safely on commercial airlines without undue risk (S3.16-23). Preflight simulation testing or mandated supplemental oxygen are not usually indicated, although adequate hydration and movement during the flight are appropriate.
- Measurement of coagulation parameters (e.g., activated partial thromboplastin time, international normalized ratio, thrombin time) in a patient with an elevated hematocrit >55% requires adjustment of anticoagulant volume in the blood collection vials to account for reduced plasma volume in the draw (S3.16-24).

ACHD indicates adult congenital heart disease and CHD, congenital heart disease.

See Online Data Supplement 25 for referenced studies.

3.17. Pharmacological Therapy for ACHD

Patients with ACHD are commonly excluded from clinical trials, and there are few data to guide pharmacological therapies. Although it may be tempting to extrapolate from management guidelines developed for patients without CHD (e.g., HF guidelines) (S3.17-1), treatments may not have the same benefit in the heterogeneous population of patients with ACHD and in some cases may cause harm. The evaluation of new symptoms in a patient with ACHD must be tailored to the patient's anatomy, surgical repair, and physiology. Before considering pharmacological therapies, evaluation for residual shunts, baffle stenosis, valvular or conduit dysfunction, and collateral vessels, any of which may be amenable to interventions, is an important consideration.

The literature documenting pharmacological therapies for patients with ACHD is limited to small studies with limited duration of drug administration and follow-up. Additionally, the endpoints used are often surrogate markers that have not been validated for clinical decision-making, and studies are also often underpowered. However, studies in patients with ACHD do exist and evaluate conventional pharmacological therapy, especially for HF and for arrhythmia, including beta blockers, angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, and aldosterone antagonists, although results vary (S3.17-2–S3.17-9).

Pharmacological therapies in patients with ACHD are often directed to specific conditions (i.e., beta blockers for arrhythmia treatment). However, there are limited data examining the benefits of beta blockers in specific ACHD populations. Results from a small study indicate that beta-blocker therapy may have potential to improve functional class in patients with a systemic right ventricle and a pacemaker (S3.17-2). Angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers have also been assessed in small studies in specific ACHD populations in which no significant benefit on ventricular function or exercise capacity has been proven (S3.17-6–S3.17-8). Data from 1 small trial with a short follow-up interval in patients with a systemic right ventricle suggest that eplerenone may be associated with reduced myocardial fibrosis, as assessed by imaging (S3.17-3).

Some pharmacological therapies affecting the pulmonary vasculature (e.g., endothelin-receptor antagonists and phosphodiesterase type-5 [PDE-5] inhibitors) have a beneficial effect on long-term outcomes in patients with Eisenmenger syndrome (S3.17-10). Similarly, there are limited data on the use of pulmonary vasodilator therapy in Fontan patients, in whom the pulmonary vascular resistance may be abnormal (S3.17-11–S3.17-13). Because of the lack of data, clinical recommendations regarding pharmacological therapy for patients with ACHD are unsupported. Individualized care is needed, recognizing the potential benefits and risks of the therapy relative to patient-specific anatomic and physiological issues.

See Online Data Supplement 22 for referenced studies.

4. Specific Lesions

4.1. Shunt Lesions

4.1.1. Atrial Septal Defect

Recommendations for Atrial Septal Defect Referenced studies that support recommendations are summarized in Online Data Supplement 26 and the systematic review report (S4.1.1-1).		
COR	**LOE**	**Recommendations**
		Diagnostic
I	C-EO	1. Pulse oximetry at rest and during exercise is recommended for evaluation of adults with unrepaired or repaired ASD with residual shunt to determine the direction and magnitude of the shunt.
I	B-NR	2. CMR, CCT, and/or TEE are useful to evaluate pulmonary venous connections in adults with ASD (S4.1.1-2–S4.1.1-4).
I	B-NR	3. Echocardiographic imaging is recommended to guide percutaneous ASD closure (S4.1.1-5, S4.1.1-6).
		Therapeutic
I	B-NR^{SR}	4. In adults with isolated secundum ASD causing impaired functional capacity, right atrial and/or RV enlargement, and net left-to-right shunt sufficiently large to cause physiological sequelae (e.g., pulmonary–systemic blood flow ratio [Qp:Qs] ≥1.5:1) without cyanosis at rest or during exercise, transcatheter or surgical closure to reduce RV volume and improve exercise tolerance is recommended, provided that systolic PA pressure is less than 50% of systolic systemic pressure and pulmonary vascular resistance is less than one third of the systemic vascular resistance (S4.1.1-7–S4.1.1-12).
I	B-NR	5. Adults with primum ASD, sinus venosus defect or coronary sinus defect causing impaired functional capacity, right atrial and/or RV enlargement and net left-to-right shunt sufficiently large to cause physiological sequelae (e.g., Qp:Qs ≥1.5:1) without cyanosis at rest or during exercise, should be surgically repaired unless precluded by comorbidities, provided that systolic PA pressure is less than 50% of systemic pressure and pulmonary vascular resistance is less than one third of the systemic vascular resistance (S4.1.1-13, S4.1.1-14).
IIa	C-LD^{SR}	6. In asymptomatic adults with isolated secundum ASD, right atrial and RV enlargement, and net left-to-right shunt sufficiently large to cause physiological sequelae (e.g., Qp:Qs 1.5:1 or greater), without cyanosis at rest or during exercise, transcatheter or surgical closure is reasonable to reduce RV volume and/or improve functional capacity, provided that systolic PA pressure is less than 50% of systemic pressure and pulmonary vascular resistance is less than one third systemic resistance (S4.1.1-7–S4.1.1-10, S4.1.1-12).
IIa	C-LD	7. Surgical closure of a secundum ASD in adults is reasonable when a concomitant surgical procedure is being performed and there is a net left-to-right shunt sufficiently large to cause physiological sequelae (e.g., Qp:Qs 1.5:1 or greater) and right atrial and RV enlargement without cyanosis at rest or during exercise (S4.1.1-15–S4.1.1-18).
IIb	B-NR	8. Percutaneous or surgical closure may be considered for adults with ASD when net left-to-right shunt (Qp:Qs) is 1.5:1 or greater, PA systolic

		pressure is 50% or more of systemic arterial systolic pressure, and/or pulmonary vascular resistance is greater than one third of the systemic resistance (S4.1.1-19, S4.1.1-20).
III: Harm	**C-LD**	**9. ASD closure should not be performed in adults with PA systolic pressure greater than two thirds systemic, pulmonary vascular resistance greater than two thirds systemic, and/or a net right-to-left shunt (S4.1.1-21, S4.1.1-22).**

Synopsis

ASDs are common and may occur as a consequence of different anatomic defects, including secundum ASD, primum ASD, sinus venosus defect (not properly a defect in the atrial septum but considered in this section), and coronary sinus septal defect. Left-to-right shunting may result in right heart enlargement and RV dysfunction and, in a minority of patients, PAH. Some patients may have right-to-left shunting or paradoxical embolism, and some may develop arrhythmias. Percutaneous device or surgical closure are the mainstays of therapy in those with hemodynamic or clinical consequences of the defect. Severe PAH is a contraindication to closure, and its presence must be accurately excluded before closure (S4.1.1-21–S4.1.1-23).

ASD may occur with other congenital cardiac abnormalities. In some circumstances, such as in patients with Ebstein anomaly and pulmonary stenosis (PS) or right HF, the physiology related to the ASD is substantially more complex, and ASD closure could result in clinical deterioration. Therefore, these recommendations regarding ASD address only isolated ASDs and not ASD associated with complex CHD.

The "Interventional Therapy Versus Medical Therapy for Secundum Atrial Septal Defect: A Systematic Review (Part 2) for the 2018 AHA/ACC Guideline for the Management of Adults With Congenital Heart Disease" (S4.1.1-1) has additional data and analyses. The results from the question "are outcomes in asymptomatic patients with unoperated secundum ASD and RV dilatation improved after percutaneous or surgical closure?" and the writing committee's review of the totality of the literature were used to frame decision-making. Recommendations that are based on a body of evidence that includes the systematic review conducted by the ERC are denoted by the superscript SR (e.g., LOE B-R^{SR}).

See Section 3.3 for recommendations on who should perform surgeries, cardiac catheterization, and other procedures in these patients; Section 3.4 for recommendations on diagnostic evaluation; Section 4.4.6 for evaluation and management of severe PAH and Eisenmenger syndrome; and Figure 1 for a diagnostic and treatment algorithm for secundum ASD. See Table 13 for routine follow-up and testing intervals.

Recommendation-Specific Supportive Text

1. Pulse oximetry is useful in defining shunt direction at rest and with exercise, which will help guide decisions regarding therapeutic options. Pulse oximetry at rest and with exercise may identify patients with increased pulmonary arterial resistance and shunt reversal. In a subset of patients with resting systemic oxygen saturation >90%, a decrease in oxygen saturation with activity to <90% may occur, emphasizing the importance of performing resting and ambulatory pulse oximetry assessment.

2. TTE has limited use in assessment of anomalous pulmonary venous connections in adults with ASD. Moreover, the poor visualization of the superior and posterior atrial septum by TTE in adults may require testing with other imaging modalities to clearly define septal anatomy. TEE is excellent for visualization of the entire atrial septum as well as pulmonary venous connections. Anomalous right

upper and middle lobe pulmonary venous connections often occur in combination with superior sinus venosus defect; TEE is excellent for visualization of this combination but may not visualize other anomalous pulmonary venous connections. Cross-sectional imaging with CMR or CCT is ideal for delineating pulmonary venous connections, particularly those that are associated with veins that may be difficult or impossible to image by echocardiography (e.g., innominate vein or vertical vein). CMR has the advantages of not involving ionizing radiation and ability to quantify degree of shunting.

3. It is considered standard of care to use echocardiographic imaging to guide closure of interatrial communications. TEE and intracardiac echocardiography are the most widely studied and used modalities for guidance of ASD closure. Defect size, defect morphology, atrial rim adequacy, pulmonary venous anomalies, and left atrial appendage thrombus can all be evaluated using TEE. Echocardiography is also used to determine sizing either by balloon diameter producing complete occlusion of the defect ("stop flow" diameter) or by direct visualization and measurement using intracardiac echocardiography. Echocardiography can assess for pericardial effusion and for thrombi on wires or devices. TTE has also been studied for guiding percutaneous ASD closure but is not widely used for this purpose.

4. Cardiac catheterization is performed at the time of transcatheter ASD closure. Provided noninvasive imaging is of sufficiently high quality to estimate pulmonary artery pressures and shunt magnitude, not every patient with an ASD requires a diagnostic catheterization before surgical closure. However, a diagnostic catheterization may be necessary to determine detailed hemodynamics for decision-making or to clarify discrepant or inconclusive noninvasive imaging data. Patients with reduced functional capacity presumed caused by hemodynamically important secundum ASD (moderate or large left-to-right shunt and evidence of right heart volume overload in the absence of significant PAH) benefit from surgical or transcatheter closure of the secundum ASD (S4.1.1-8, S4.1.1-10). Patients who do not undergo ASD closure have worse long-term outcomes, including more atrial arrhythmias, reduced functional capacity, and eventually greater degrees of PAH. Older adults should be evaluated for left atrial hypertension resulting from diastolic dysfunction, which may cause similar symptoms but could result in clinical worsening after ASD closure because of further increase in left atrial pressures when blood from the relatively restrictive and higher pressure left atrium can no longer decompress into the lower pressure right atrium. Cyanosis with exercise typically occurs in association with poor RV diastolic compliance and hemodynamics with exercise, and the ASD acts as a "pop-off" to maintain cardiac output. However, exercise-induced cyanosis is not an absolute contraindication to ASD closure, because there are rare cases of either streaming or directed tricuspid regurgitation (TR) leading to right-to-left shunting with exercise not related to abnormal RV diastolic pressures that may allow for closure after expert evaluation. Data are most compelling that closure improves functional status, although some descriptive studies support improved long-term outcomes after closure as well (S4.1.1-7–S4.1.1-12).

5. Available percutaneously deployed ASD closure devices are approved for closure of secundum-type defects. Primum, sinus venosus, and coronary sinus ASDs should be closed surgically because of the absence of appropriate rims for percutaneous device placement and the proximity of the atrioventricular valves and conduction system to the closure device. Congenital heart surgeons are trained in the nuances of repair of such defects, including common association with anomalous pulmonary venous connection and abnormalities of the atrioventricular valves (S4.1.1-24, S4.1.1-25).

6. Patients who do not undergo ASD closure have worse long-term outcomes, including more atrial arrhythmias, reduced functional capacity, and eventually greater degrees of PAH (S4.1.1-7–S4.1.1-10, S4.1.1-12). However, concomitant diseases may influence the anticipated benefit of ASD closure in ameliorating symptoms and improving functional capacity, and it has not been clearly demonstrated that ASD closure in asymptomatic adults prevents long-term complications. Data suggest that ASD closure improves functional capacity but, in patients with normal functional capacity, the long-term

benefit of ASD closure is less clear (S4.1.1-1, S4.1.1-9). Pending further study, it is reasonable to close an ASD that is hemodynamically important in the absence of significant PAH. Older adults should be evaluated for left atrial hypertension resulting from diastolic dysfunction that may cause symptoms simulating those from an ASD alone, in whom ASD closure could result in clinical worsening because of further increase in left atrial pressure because the relatively restrictive and higher pressure left atrium can no longer decompress into the lower pressure right atrium. Concomitant tricuspid annuloplasty can be of benefit in patients with moderate or more TR, as the additional volume load may adversely affect RV remodeling.

7. If surgical treatment is necessary for other congenital or acquired cardiac conditions and the patient has a secundum ASD, it is reasonable to perform ASD closure at the time of surgery. When there is moderate or greater TR, tricuspid valve repair may improve RV remodeling.

8. To evaluate the patient with PAH and ASD, ensure the shunt remains left to right despite elevated pulmonary vascular resistance and/or pulmonary pressure and that pulmonary pressure and PVR are accurately measured. In this circumstance, data derived from invasive hemodynamic assessment are important in clarifying the appropriate course of action. The exclusion of patients with severe PAH from ASD closure may eventually be obviated by PA vasodilator and remodeling therapy with prostaglandins, endothelin blockers, and PDE-5 inhibitors. Because of the complexity of the hemodynamics in such patients, collaboration between ACHD and pulmonary hypertension providers is important. Pretreatment with PAH therapies and pulmonary arterial remodeling agents, with a demonstrated reduction in pulmonary arterial resistance of >20%, portends a favorable prognosis after ASD closure (S4.1.1-26).

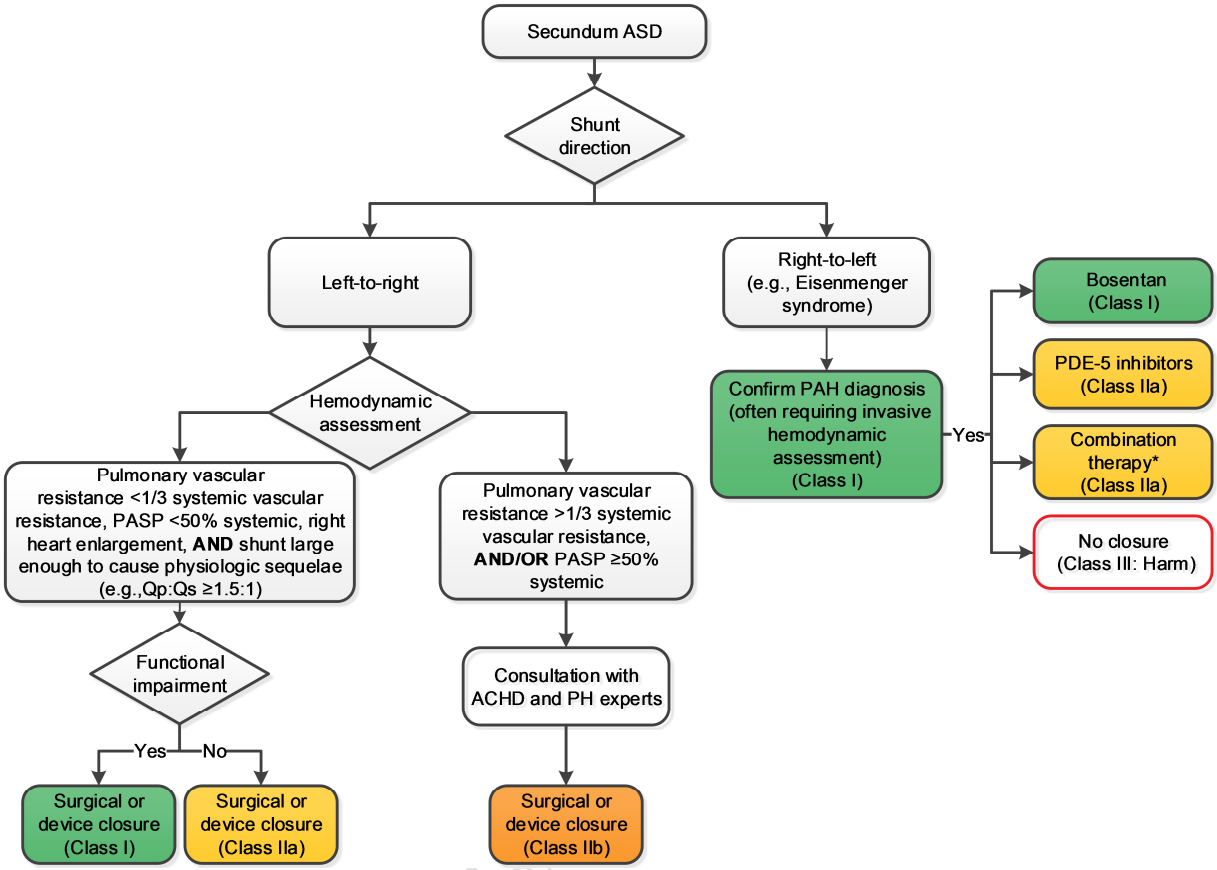
9. Morbidity and mortality are prohibitively high when surgical repair is attempted in patients with open shunts, such as ASD when Eisenmenger syndrome is present (S4.1.1-21, S4.1.1-22).

Table 13. ASD: Routine Follow-Up and Testing Intervals

Frequency of Routine Follow-Up and Testing	Physiological Stage A* (mo)	Physiological Stage B* (mo)	Physiological Stage C* (mo)	Physiological Stage D* (mo)
Outpatient ACHD cardiologist	36–60	24	6–12	3–6
ECG	36–60	24	12	12
TTE	36–60	24	12	12
Pulse oximetry	As needed	As needed	Each visit	Each visit
Exercise test†	As needed	As needed	12–24	6–12

*See Tables 3 and 4 for details on the ACHD AP classification system.
†6-minute walk test or CPET, depending on the clinical indication.
ACHD indicates adult congenital heart disease; CPET, cardiopulmonary exercise test; ECG, electrocardiogram; and TTE, transthoracic echocardiogram.

Figure 1. Secundum ASD



*Combination therapy with bosentan and PDE-5 inhibitor if symptomatic improvement does not occur with either alone.
ACHD indicates adult congenital heart disease; ASD, atrial septal defect; PAH, pulmonary artery hypertension; PASP, pulmonary artery systolic pressure; PDE-5, phosphodiesterase type-5 inhibitors; PH, pulmonary hypertension; and Qp:Qs, pulmonary–systemic blood flow ratio.

4.1.2. Anomalous Pulmonary Venous Connections

Recommendations for Anomalous Pulmonary Venous Connections Referenced studies that support recommendations are summarized in Online Data Supplement 27.		
COR	**LOE**	**Recommendations**
		Diagnostic
I	**B-NR**	**1. CMR or CTA is recommended for evaluation of partial anomalous pulmonary venous connection (S4.1.2-1–S4.1.2-4).**
IIa	**B-NR**	**2. Cardiac catheterization can be useful in adults with partial anomalous pulmonary venous connection to further define hemodynamics (S4.1.2-5, S4.1.2-6).**
		Therapeutic
I	**B-NR**	**3. Surgical repair is recommended for patients with partial anomalous pulmonary venous connection when functional capacity is impaired and**

		RV enlargement is present, there is a net left-to-right shunt sufficiently large to cause physiological sequelae (e.g., Qp:Qs ≥1.5:1), PA systolic pressure is less than 50% systemic pressure, and pulmonary vascular resistance is less than one third of systemic resistance (S4.1.2-5).
I	**B-NR**	**4. Repair of partial anomalous pulmonary venous connection is recommended at the time of closure of a sinus venosus defect or ASD (S4.1.2-7).**
I	**B-NR**	**5. Repair of a scimitar vein is recommended in adults when functional capacity is impaired, evidence of RV volume overload is present, there is a net left-to-right shunt sufficiently large to cause physiological sequelae (e.g., Qp:Qs ≥1.5:1), PA systolic pressure is less than 50% systemic pressure and pulmonary vascular resistance is less than one third systemic (S4.1.2-5, S4.1.2-8, S4.1.2-9).**
IIa	**B-NR**	**6. Surgery can be useful for right- or left-sided partial anomalous pulmonary venous connection in asymptomatic adults with RV volume overload, net left-to-right shunt sufficiently large to cause physiological sequelae (e.g., Qp:Qs ≥1.5:1), pulmonary pressures less than 50% systemic and pulmonary vascular resistance less than one third systemic (S4.1.2-5).**
IIa	**B-NR**	**7. Surgery can be useful for repair of a scimitar vein in adults with evidence of RV volume overload, with Qp:Qs 1.5:1 or greater (S4.1.2-5, S4.1.2-9).**

Synopsis

Abnormal connection between a pulmonary vein and systemic vein will result in volume overload of the right heart, with a physiological effect similar to that of an ASD. However, in the absence of an associated ASD, anomalous pulmonary venous connection differs in that there is no potential for right-to-left shunting, and the magnitude of the left-to-right shunt is not exacerbated by the development of acquired left heart disease. The most common anomalous pulmonary venous connection is of the right upper pulmonary vein to the superior vena cava (S4.1.2-10), which may be associated with a sinus venosus defect. Other abnormal connections include right pulmonary vein(s) to the inferior vena cava (often via a so-called ”scimitar vein” and associated with sequestration of the right lower lobe), left upper pulmonary vein(s) to the left innominate vein, and right upper pulmonary vein(s) connecting high on the superior vena cava. Long-term sequelae of anomalous pulmonary venous connections reflect the impact of right heart volume overload and are similar to the sequelae of ASDs. Surgical repair can be challenging as low-velocity venous flow imparts risk of thrombosis of the surgically operated vein.

See Section 3.3 for recommendations on who should perform surgeries, cardiac catheterization, and other procedures in these patients; Section 3.4 for recommendations on diagnostic evaluation; and Section 4.4.6 for evaluation and management of severe PAH and Eisenmenger syndrome.

Recommendation-Specific Supportive Text

1. Cross-sectional imaging with CMR or CTA is ideal for delineating pulmonary venous connections. CMR has the advantage of not using ionizing radiation and may also quantify the degree of shunting. Echocardiography is an important part of the evaluation and may identify the anomalous veins (S4.1.2-11), particularly in patients with excellent acoustic windows; however, CMR and CTA are superior for evaluating extracardiac vascular anatomy.

2. In higher-risk patients, invasive hemodynamic assessment can be useful for direct measurement of pressures, quantification of shunt magnitude, and measurement of pulmonary arterial resistance and

responsiveness to pulmonary vasodilator therapy. Invasive hemodynamic assessment is especially important in adult patients who are being considered for surgical correction.

3. It is unusual for a single anomalous pulmonary venous connection of only 1 pulmonary lobe to result in a sufficient volume load to justify surgical repair. However, if a patient has symptoms referable to the shunt, there is >1 anomalous vein, and a moderate or large left-to-right shunt, then surgical repair is associated with a reduction in RV size and PA pressure (S4.1.2-5). Pulmonary hypertension is a risk for adverse outcomes with surgery.

4. Surgery usually involves intracaval baffling into the left atrium, Warden procedure (S4.1.2-12), or direct reimplantation of the anomalous pulmonary vein directly into the left atrium.

5. Surgical repair of a scimitar vein includes direct reimplantation of the scimitar vein into the left atrium, conduit placement to the left atrium, or intracaval baffling. This surgery can be technically challenging with a greater risk of postoperative vein thrombosis than is associated with more common and simpler anomalous pulmonary vein abnormalities (S4.1.2-10). Pulmonary hypertension is associated with poor outcomes.

6. It is unusual for a single anomalous pulmonary venous connection from only one pulmonary lobe to result in a sufficient volume load to justify surgical repair. However, if there is >1 anomalous vein and a moderate or large left-to-right shunt, then surgical repair is associated with a reduction in RV size and PA pressure and can be useful (S4.1.2-5).

7. Surgical repair of a scimitar vein includes direct reimplantation of the scimitar vein into the left atrium, side-to-side anastomosis of the scimitar vein to the left atrium and closure of its connection to the inferior vena cava or intracaval baffling. This surgery can be technically challenging with a greater risk of postoperative vein thrombosis than is associated with simpler anomalous pulmonary vein abnormalities (S4.1.2-10).

4.1.3. Ventricular Septal Defect

Recommendations for Ventricular Septal Defect Referenced studies that support recommendations are summarized in Online Data Supplement 28.		
COR	**LOE**	**Recommendations**
Therapeutic		
I	**B-NR**	**1) Adults with a VSD and evidence of left ventricular volume overload and hemodynamically significant shunts (Qp:Qs ≥1.5:1) should undergo VSD closure, if PA systolic pressure is less than 50% systemic and pulmonary vascular resistance is less than one third systemic (S4.1.3-1).**
IIa	**C-LD**	**2) Surgical closure of perimembranous or supracristal VSD is reasonable in adults when there is worsening aortic regurgitation (AR) caused by VSD (S4.1.3-1, S4.1.3-2).**
IIb	**C-LD**	**3) Surgical closure of a VSD may be reasonable in adults with a history of IE caused by VSD if not otherwise contraindicated (S4.1.3-3).**
IIb	**C-LD**	**4) Closure of a VSD may be considered in the presence of a net left-to-right shunt (Qp:Qs ≥1.5:1) when PA systolic pressure is 50% or more than systemic and/or pulmonary vascular resistance is greater than one third systemic (S4.1.3-4–S4.1.3-6).**
III: Harm	**C-LD**	**5) VSD closure should not be performed in adults with severe PAH with PA systolic pressure greater than two thirds systemic, pulmonary vascular**

		resistance greater than two thirds systemic and/or a net right-to-left shunt (S4.1.3-7–S4.1.3-9).

Synopsis

Ventricular septal defects (VSDs) initially create a volume load to the left heart, and the magnitude of hemodynamic impact is directly related to the size of the shunt and afterload to the ventricles. Isolated VSDs are the most commonly encountered form of CHD in the pediatric population (S4.1.3-10– S4.1.3-14). Most isolated muscular and perimembranous VSDs are small and close spontaneously. The spectrum of isolated residual VSDs encountered in the adult patient includes:

1. Small restrictive defects. The pulmonary vascular resistance is not significantly elevated and the left-to-right shunt is small (Qp:Qs <1.5:1).
2. Large nonrestrictive defects in cyanotic patients who have developed Eisenmenger syndrome, with pulmonary vascular resistance at systemic levels and shunt reversal (right-to-left).
3. Patients with moderately restrictive defects (Qp:Qs ≥1.5:1 and <2:1) who have not undergone closure for some reason. These patients often have mild-to-moderate PAH.
4. Patients who have had their defects closed in childhood. These patients may have VSD patch leaks.

See Section 3.3 for recommendations on who should perform surgeries, cardiac catheterization, and other procedures in these patients; Section 3.4 for recommendations on diagnostic evaluation; Section 4.4.6 for evaluation and management of severe PAH and Eisenmenger syndrome; Figure 2 for a diagnostic and treatment algorithm for ventricular level shunt; and Table 14 for routine testing and follow-up intervals.

Recommendation-Specific Supportive Text

1. In the absence of aortic valve prolapse and regurgitation or IE, small restrictive defects of the muscular or membranous septum may be watched conservatively without need for operative intervention. In a long-term follow-up registry, the overall survival rate was 87% for all patients with unoperated VSD at 25 years (S4.1.3-1). For patients with small defects (Qp:Qs <1.5:1 and low PA pressure), the survival rate was 96%. Patients with moderate and large defects fared worse with 25-year survival of 86% and 61%, respectively. Those with Eisenmenger syndrome (cyanosis/hypoxemia caused by reversal of shunt to right-to-left) had a much lower 25-year survival (42%). Larger defects may be repaired but only in the absence of severe PAH and severely elevated pulmonary vascular resistance, the presence of which incurs a high perioperative risk S4.1.3-15).

Life expectancy after VSD closure in an adult is not normal but has improved over the past 50 years. Transcatheter device occlusion of muscular and perimembranous VSD is feasible, and trials have demonstrated a good safety and efficacy profile (S4.1.3-16, S4.1.3-17). VSD in adults is most commonly either small, or large and associated with Eisenmenger syndrome; therefore, data regarding optimal management of moderate VSD in adults are lacking because of relative infrequency of a hemodynamically significant VSD for which closure is an option.

2. Small restrictive defects of the muscular or membranous septum may be managed by observation without need for operative intervention. However, 6% of patients with small supracristal (subaortic) or perimembranous defects may develop aortic valve prolapse and resultant AR that may be progressive (S4.1.3-1, S4.1.3-2, S4.1.3-18). There is a paucity of data supporting the timing of VSD closure in patients with AR. Ideally, the VSD is closed if AR is progressive to avoid the continued worsening of AR and the need for aortic valve replacement. In the presence of a VSD, an aortic valve cusp (usually the right coronary cusp) may prolapse and partially or completely close the VSD, often with associated AR. At the

time of VSD closure, aortic valve repair may be performed in an effort to stabilize or improve AR. For patients who meet GDMT criteria for aortic valve replacement, this may be performed concomitant with VSD closure (S4.1.3-19).

3. In patients with unrepaired VSD, there is an increased risk of IE, typically involving the tricuspid and pulmonic valves.

4. Early attempts at surgical closure of nonrestrictive VSD in patients with Eisenmenger syndrome were associated with an unacceptably high risk of mortality, and the practice was quickly abandoned. However, there are adult patients with large VSD and PAH who may benefit from closure of the VSD if the net shunt is left-to-right either at baseline or with PAH therapies. The use of fenestrated devices and fenestrated surgical patches in these patients leaves a small residual shunt to allow decompression of the right heart (S4.1.3-5, S4.1.3-6). In theory, treatment of these patients with PAH therapies before closure could improve outcomes.

5. Closure of nonrestrictive VSD in adults with Eisenmenger syndrome who do not demonstrate left-to-right shunting and a decline in pulmonary vascular resistance with PAH therapies carries a high risk of mortality and should not be performed (S4.1.3-7- S4.1.3-9).

Table 14. VSD: Routine Follow-Up and Testing Intervals

Frequency of Routine Follow-Up and Testing	Physiological Stage A* (mo)	Physiological Stage B* (mo)	Physiological Stage C* (mo)	Physiological Stage D* (mo)
Outpatient ACHD cardiologist	36	24	6–12	3–6
ECG	36	24	12	12
TTE	36	24	12	12
Pulse oximetry	As needed	As needed	Each visit	Each visit
Exercise test†	As needed	As needed	12–24	6–12

*See Tables 3 and 4 for details on the ACHD AP classification system.
†6-minute walk test or CPET, depending on the clinical circumstance.
ACHD indicates adult congenital heart disease; CPET, cardiopulmonary exercise test; ECG, electrocardiogram; TTE, transthoracic echocardiogram; and VSD, ventricular septal defect.

Figure 2. Hemodynamically Significant Ventricular Level Shunt

*Combination therapy with bosentan and PDE-5 inhibitor, if symptomatic improvement does not occur with either alone.
ACHD indicates adult congenital heart disease; AR, aortic regurgitation; IE, infective endocarditis; LV, left ventricular; PAH, pulmonary artery hypertension; PASP, pulmonary artery systolic pressure; PDE-5, phosphodiesterase type-5 inhibitors; PH, pulmonary hypertension; Qp:Qs, pulmonary–systemic blood flow ratio; and VSD, ventricular septal defect.

4.1.4. Atrioventricular Septal Defect

Recommendations for Atrioventricular Septal Defect Referenced studies that support recommendations are summarized in Online Data Supplement 29.		
COR	**LOE**	**Recommendations**
Diagnostic		
IIa	**C-EO**	**1. Cardiac catheterization can be useful in adults with atrioventricular septal defect when pulmonary hypertension is suspected.**
Therapeutic		

I	**C-LD**	**2. Surgery for severe left atrioventricular valve regurgitation is recommended per GDMT indications for mitral regurgitation (S4.1.4-1–S4.1.4-4).**
I	**C-EO**	**3. Surgery for primary repair of atrioventricular septal defect or closure of residual shunts in adults with repaired atrioventricular septal defect is recommended when there is a net left-to-right shunt (Qp:Qs ≥1.5:1), PA systolic pressure less than 50% systemic and pulmonary vascular resistance less than one third systemic.**
IIa	**C-EO**	**4. Operation for discrete LVOT obstruction in adults with atrioventricular septal defect is reasonable with a maximum gradient of 50 mm Hg or greater, a lesser gradient if HF symptoms are present, or if concomitant moderate-to-severe mitral or AR are present.**
IIb	**C-EO**	**5. Surgery for primary repair of atrioventricular septal defect or closure of residual shunts in adults with repaired atrioventricular septal defect may be considered in the presence of a net left-to-right shunt (Qp:Qs ≥1.5:1), if PA systolic pressure is 50% or more systemic, and/or pulmonary vascular resistance is greater than one third systemic.**
III: Harm	**C-LD**	**6. Surgery for primary repair of atrioventricular septal defect or closure of residual shunts in adults with repaired atrioventricular septal defect should not be performed with PA systolic pressure greater than two thirds systemic, pulmonary vascular resistance greater than two thirds systemic, or a net right-to-left shunt (S4.1.4-5, S4.1.4-6).**

Synopsis

AVSDs represent about 4% to 5% of congenital heart defects and include a primum ASD, inlet VSD, and common atrioventricular valve. They can occur in several anatomic variations including partial AVSD with only a primum ASD component and typically a cleft left atrioventricular valve, complete AVSD with both ASD and VSD and a common atrioventricular valve, and transitional and intermediate AVSD with incomplete atrial and VSDs and/or incomplete abnormalities of the common atrioventricular valve. AVSD anatomy is also commonly described by the Rastelli classification (S4.1.4-7, S4.1.4-8). The Rastelli classification describes anatomic variations of the superior bridging leaflet of the atrioventricular valve. In addition to the Rastelli classification or other similar descriptors, the relative sizes of the ventricles as balanced or unbalanced guide the type of repair (e.g., biventricular or single ventricle repair). This section refers to patients with balanced AVSD and biventricular repair. AVSD also occurs in association with other congenital lesions including TOF, CoA, and heterotaxy. There is also a strong association with syndromes, most commonly trisomy 21 (Down syndrome).

From a management perspective, most adults with AVSD will have had surgical repair as children. If those with complete AVSD (with large ASD and VSD) are not repaired early in life (typically <6 months of age), irreversible pulmonary vascular disease usually develops resulting in Eisenmenger physiology, precluding complete repair. For those who underwent a surgical repair, long-term follow-up is required to monitor for left atrioventricular valve regurgitation and stenosis, left ventricular outflow tract (LVOT) obstruction attributable to the abnormal shape of the LVOT, and tachyarrhythmias and bradyarrhythmias. Left atrioventricular valve regurgitation is the most common reason for later surgical reintervention. There are few long-term follow-up studies of patients after AVSD repair in childhood, so the most effective and efficient timing and type of surveillance are still being evaluated.

The atrioventricular node is typically displaced inferiorly in AVSD and is associated with relative hypoplasia of the left anterior fascicle (S4.1.4-9). Late-onset complete heart block (as late as 15 years

after surgery) has been noted after surgery in patients operated on for AVSD who were discharged from the hospital with normal conduction, although more commonly seen in those patients with transient postoperative heart block. Regular monitoring for symptoms and screening with an ECG are important to evaluate for conduction abnormalities (S4.1.4-10).

See Section 3.3 for recommendations on who should perform surgeries, cardiac catheterization, and other procedures in these patients; Section 3.4 for recommendations on diagnostic evaluation; Section 4.1.1 for recommendations on primum ASD; Section 4.4.6 for evaluation and management of severe PAH and Eisenmenger syndrome associated with AVSD; and Table 15 for routine testing and follow-up intervals.

Recommendation-Specific Supportive Text

1. Invasive hemodynamic assessment still has an important role as a confirmatory tool and for the evaluation of pulmonary vasoreactivity, which does carry prognostic significance for adults with shunts.

2. Although the left atrioventricular valve in an AVSD malformation is not anatomically the same as a mitral valve, one can extrapolate the criteria for consideration of left atrioventricular valve surgery from the VHD guideline for mitral regurgitation and mitral stenosis (S4.1.4-1). In extrapolating these criteria, there are important potential differences in this patient population compared with those with acquired mitral valve disease. There are anatomic differences in position of the annulus, papillary muscles and the morphology of the LVOT, which is an anterior, narrow, and potentially obstructed structure, such that congenital surgical expertise is needed. Patients with an AVSD have typically had at least 1 prior attempt to repair the AVSD, have different risks of arrhythmia, and may have other anatomic lesions (e.g., subaortic stenosis [subAS]). In 1 meta-analysis of studies of adult left atrioventricular valve surgery in patients with AVSD, the risk of needing a pacemaker was higher in those who underwent valve replacement than in those who underwent repair (S4.1.4-2). In another single-center study, one third of repaired patients required an additional reoperation (S4.1.4-3). When replacement is required, the choice to use mechanical versus bioprosthetic valve is individualized, but a mechanical valve is usually necessary because of the potential for LVOT obstruction from the struts of the bioprosthetic valve. Nevertheless, valve repair is preferred to valve replacement when it is technically feasible.

3. There are no large studies on residual shunts in patients with AVSD, but extrapolating from information on residual isolated ASD or isolated VSD, a moderate or large residual shunt is likely to result in worsening clinical status over time and thus merits consideration of repair (S4.1.4-11–S4.1.4-13). See Sections 4.1.1 and 4.1.3 for related considerations regarding ASD and/or VSD. Pulse oximetry at rest and with ambulation may identify patients with increased pulmonary resistance and shunt reversal. There is a subset of patients with resting systemic oxygen saturation >90% who will have a decrease in oxygen saturation with activity to <90%, emphasizing the importance of performing resting and ambulatory pulse oximetry assessment.

4. Patients with AVSD are at risk of LVOT obstruction because of the abnormal anatomy of the LVOT. Surgical resection of LVOT obstruction in association with AVSD is reasonable when there is moderate-to-severe obstruction or less obstruction but associated HF or mitral regurgitation or AR. In isolated subAS studies, worse outcomes were revealed in patients with maximum gradients ≥50 mm Hg or with gradients <50 mm Hg in association with symptoms of HF (S4.1.4-14–S4.1.4-17). Importantly the LVOT obstruction in AVSD may not be discrete and, therefore, surgical repair may be more complex. When evaluating patients with tunnel-like or complex LVOT obstruction, the peak Doppler gradients and Bernoulli equation may inaccurately reflect the severity of obstruction, and cardiac catheterization may be needed.

5. Patients with AVSD, particularly those with Down syndrome, are at high risk of developing pulmonary vascular disease resulting in Eisenmenger syndrome (S4.1.4-18, S4.1.4-19). For those who continue to have a net left-to-right shunt despite elevated PA pressures, closure of the defect may prevent exacerbation of PAH. This is an unusual circumstance and decision-making requires collaboration with ACHD and pulmonary hypertension providers.

6. Morbidity and mortality are prohibitively high when surgical repair is attempted in patients with open shunts such as AVSD when Eisenmenger syndrome is present (S4.1.4-5, S4.1.4-6).

Table 15. AVSD: Routine Follow-Up and Testing Intervals

Frequency of Routine Follow-Up and Testing	Physiological Stage A* (mo)	Physiological Stage B* (mo)	Physiological Stage C* (mo)	Physiological Stage D* (mo)
Outpatient ACHD cardiologist	24–36	24	6–12	3–6
ECG	24–36	24	12	12
TTE	24–36	24	12	12
Pulse oximetry	As needed	As needed	Each visit	Each visit
Exercise test†	As needed	As needed	12–24	6–12

*See Tables 3 and 4 for details on the ACHD AP classification system.
†6-minute walk test or CPET, depending on the clinical indication.
ACHD indicates adult congenital heart disease; AVSD, atrioventricular septal defect; CPET, cardiopulmonary exercise testing; ECG, electrocardiogram; and TTE, transthoracic echocardiogram.

4.1.5. Patent Ductus Arteriosus

Recommendations for Patent Ductus Arteriosus Referenced studies that support recommendations are summarized in Online Data Supplement 30.		
COR	**LOE**	**Recommendations**
		Diagnostic
I	**C-EO**	**1. Measurement of oxygen saturation should be performed in feet and both hands in adults with a PDA to assess for the presence of right-to-left shunting.**
IIa	**C-EO**	**2. In addition to the standard diagnostic tools, cardiac catheterization can be useful in patients with PDA and suspected pulmonary hypertension (Section 3.5).**
		Therapeutic
I	**C-LD**	**3. PDA closure in adults is recommended if left atrial or LV enlargement is present and attributable to PDA with net left-to-right shunt, PA systolic pressure less than 50% systemic and pulmonary vascular resistance less than one third systemic (S4.1.5-1–S4.1.5-3).**
IIb	**B-NR**	**4. PDA closure in adults may be considered in the presence of a net left-to-right shunt if PA systolic pressure is 50% or greater systemic, and/or pulmonary vascular resistance is greater than one third systemic (S4.1.5-3, S4.1.5-4).**
III: Harm	**C-LD**	**5. PDA closure should not be performed in adults with a net right-to-left shunt and PA systolic pressure greater than two thirds systemic or pulmonary vascular resistance greater than two thirds systemic (S4.1.5-5).**

Synopsis

The ductus arteriosus is a vascular connection between the aorta and PA that is present in fetal life. It typically closes shortly after birth but, in some people, it will remain patent. Patent ductus arteriosus (PDA) is found in about 0.3% to 0.8% of term infants and is twice as common in females as males (S4.1.5-6–S4.1.5-8). The clinical and physiological manifestations of the PDA are dependent on the size of the vessel and the relative systemic and pulmonary vascular resistances. The PDA can range from a small hemodynamically insignificant lesion that is not heard on auscultation to one that without intervention is large enough to cause congestive HF and pulmonary hypertension. Many PDAs are now closed in infancy or childhood with catheter-based or surgical approaches. For those whose ductus remains patent in adulthood, catheter-based or surgical intervention consideration depends on the symptoms and physiological expression of the lesion. Follow-up of these patients as adults is important for all, although timing and testing will vary among individuals.

See Section 3.3 for recommendations on who should perform surgeries, cardiac catheterization, and other procedures in these patients; Section 3.4 for recommendations on diagnostic evaluation; Section 4.4.6 for recommendations on severe PAH (4.4.6.1) and Eisenmenger syndrome (4.4.6.2) associated with PDA; and Table 16 for routine testing and follow-up intervals.

Recommendation-Specific Supportive Text

1. Because cyanosis caused by right-to-left shunting in PDA may manifest predominantly downstream from the ductal insertion into the aorta, accurate assessment of oxygen saturation by oximetry and assessment of cyanosis should be done in the feet and both hands. As with other types of shunts, pulse oximetry with ambulation as well as at rest may identify patients with increased pulmonary arterial resistance and dynamic shunt reversal induced by exercise. A subset of patients with resting systemic oxygen saturation >90% will have a decrease in oxygen saturation with activity to <90%, emphasizing the importance of performing resting and ambulatory pulse oximetry assessment.

2. Invasive hemodynamic assessment still has an important role as a confirmatory tool and for the evaluation of pulmonary vasoreactivity, which carries prognostic significance (S4.1.5-1, S4.1.5-4).

3. When signs of volume overload are indicative of significant left-to-right shunt, closing the PDA is likely to prevent further left atrial or LV enlargement, progression or development of PAH, and pulmonary hypertension secondary to left HF and will possibly provide symptom relief if symptoms are present. Closure is typically performed percutaneously with good success and minimal complications (S4.1.5-2). Pulmonary blood flow and thus Qp:Qs can be difficult to calculate accurately because of differences in right/left PA blood flow caused by the flow from the PDA. Invasive hemodynamics including pulmonary vascular resistance are generally relied on for decision-making. Surgical closure can be performed but is potentially hazardous in adults because of calcification and tissue fragility.

4. Even with elevated pulmonary pressure and elevated pulmonary vascular resistance, closure of a PDA may improve clinical status in some patients with persistent left-to-right shunting and prevent further progression of PAH (S4.1.5-3, S4.1.5-4). Consultation with ACHD and pulmonary hypertension providers is important given the low frequency of this circumstance and the complexity of decision-making.

5. Morbidity and mortality are high when closure of a shunt is attempted in patients with Eisenmenger physiology with elevated pulmonary pressure and net right-to-left shunting (S4.1.5-5).

Table 16. PDA: Routine Follow-Up and Testing Intervals

Frequency of Routine Follow-Up	Physiological	Physiological	Physiological	Physiological

and Testing	Stage A* (mo)	Stage B* (mo)	Stage C* (mo)	Stage D* (mo)
Outpatient ACHD cardiologist	36–60	24	6–12	3–6
ECG	36–60	24	12	12
TTE	36–60	24	12	12
Pulse oximetry†	As needed	As needed	Each visit	Each visit
Exercise test‡	As needed	As needed	12–24	6–12

*See Tables 3 and 4 for details on the ACHD AP classification system.
†Upper and lower extremity.
‡6-minute walk test or CPET, depending on the clinical indication.
ACHD indicates adult congenital heart disease; ECG, electrocardiogram; CPET, cardiopulmonary exercise test; PDA, patent ductus arteriosus; and TTE, transthoracic echocardiogram.

4.2. Left-Sided Obstructive Lesions

4.2.1. Cor Triatriatum

Recommendations for Cor Triatriatum Referenced studies that support recommendations are summarized in Online Data Supplement 31.		
COR	**LOE**	**Recommendations**
		Diagnostic
I	**B-NR**	**1. Adults presenting with cor triatriatum sinister should be evaluated for other congenital abnormalities, particularly ASD, VSD, and anomalous pulmonary venous connection (S4.2.1-1).**
IIa	**B-NR**	**2. In adults with prior repair of cor triatriatum sinister and recurrent symptoms, it is reasonable to evaluate for pulmonary vein stenosis (S4.2.1-2).**
		Therapeutic
I	**B-NR**	**3. Surgical repair is indicated for adults with cor triatriatum sinister for symptoms attributable to the obstruction or a substantial gradient across the membrane (S4.2.1-3)**

Synopsis

Cor triatriatum occurs when a membrane divides either the left atrium (sinister), or right atrium (dexter). Cor triatriatum sinister is usually associated with other congenital malformations, specifically ASD, VSD, or anomalous pulmonary venous connection (partial or total) (S4.2.1-1–S4.2.1-4). The left atrial appendage is invariably in the same chamber as the mitral valve, separated from the pulmonary veins by the membrane. Supravalvular mitral stenosis is typically caused by a fibrous ring on the atrial side of the mitral valve, separating the mitral valve from both the left atrial appendage and the pulmonary veins. The finding will have similar physiology to cor triatriatum and similar indications for intervention. It can be associated with an abnormal mitral valve that may also require intervention. Supravalvular mitral stenosis often comprises one part of a more complex sequence of serial left-sided inflow and outflow obstructions (i.e., Shone complex).

See Section 3.3 for recommendations on who should perform surgeries, cardiac catheterization, and other procedures in these patients; and Section 3.4 for recommendations on diagnostic evaluation.

Recommendation-Specific Supportive Text

1. Cor triatriatum sinister is a membrane spanning the left atrium. Surgery has been largely successful with relatively few early or late deaths, which are usually attributable to associated congenital

abnormalities (S4.2.1-4). The gradient across the defect at the time of surgery was at least 8 mm Hg (mean 17 mm Hg; range 8 to 40 mm Hg) (S4.2.1-3). After repair, recurrence of stenosis is not expected. Although pulmonary vein stenosis has been demonstrated before and after surgery (S4.2.1-2), it is not usually progressive over time and has not been associated with PAH.

2. Pulmonary venous stenosis has been demonstrated before and after surgery, but it is not usually progressive over time and has not been associated with PAH.

3. Although risks of isolated cor triatriatum sinister surgery is low, it should be performed when there is evidence of a substantial gradient. In 1 series, the mean gradient at the time of surgical repair was at least 8 mm Hg (S4.2.1-3). It is conceivable that on occasion, clinical circumstances (i.e., symptoms, arrhythmia) would warrant intervention in patients with lower gradients.

4.2.2. Congenital Mitral Stenosis

Recommendation for Congenital Mitral Stenosis Referenced studies that support the recommendation are summarized in Online Data Supplement 32.		
COR	**LOE**	**Recommendation**
I	**B-NR**	**1. Adults with congenital mitral stenosis or a parachute mitral valve should be evaluated for other left-sided obstructive lesions (S4.2.2-1, S4.2.2-2).**

Synopsis

Congenital mitral valve disease may be anatomically complex and is often accompanied by other lesions. Indications for intervention in mitral stenosis are described in the 2014 VHD guideline (S4.2.2-3) and apply to those patients with congenital mitral stenosis. Balloon mitral valvuloplasty is rarely, if ever, indicated or effective in congenital mitral stenosis.

See Section 3.3 for recommendations on who should perform surgeries, cardiac catheterization, and other procedures in these patients; Section 3.4 for recommendations on diagnostic evaluation; and Table 17 for routine testing and follow-up intervals.

Recommendation-Specific Supportive Text

1. Parachute mitral valve is most commonly found in the presence of other congenital abnormalities such as the components of Shone complex. Recurrence and progression of the various associated lesions are expected, subsequent surgeries are common, and mortality may be associated with other defects (S4.2.2-2). Therefore, these patients require follow-up at a center where such abnormalities can be followed and future interventions considered. Choices and techniques for valve repair or replacement are based on consideration of coexisting abnormalities including the likelihood of future surgery.

Table 17. Congenital Mitral Stenosis: Routine Follow-Up and Testing Intervals

Frequency of Routine Follow-Up and Testing	Physiological Stage A* (mo)	Physiological Stage B* (mo)	Physiological Stage C* (mo)	Physiological Stage D* (mo)
Outpatient ACHD cardiologist	24	24	6–12	3–6
ECG	24	24	12	12
TTE	24	24	12	12
Exercise test†	As needed	24	24	12

*See Tables 3 and 4 for details on the ACHD AP classification system.
†6-minute walk test or CPET, depending on the clinical indication.
ACHD indicates adult congenital heart disease; CPET, cardiopulmonary exercise test; ECG, electrocardiogram; and TTE, transthoracic echocardiogram.

4.2.3. Subaortic Stenosis

Recommendations for Subaortic Stenosis Referenced studies that support recommendations are summarized in Online Data Supplement 33.		
COR	**LOE**	**Recommendations**
Diagnostic		
IIb	**C-LD**	**1. Stress testing for adults with LVOT obstruction to determine exercise capacity, symptoms, electrocardiographic changes, or arrhythmias may be reasonable in the presence of otherwise equivocal indications for intervention (S4.2.3-1, S4.2.3-2).**
Therapeutic		
I	**C-EO**	**2. Surgical intervention is recommended for adults with subAS, a maximum gradient 50 mm Hg or more and symptoms attributable to the subAS.**
I	**C-LD**	**3. Surgical intervention is recommended for adults with subAS and less than 50 mm Hg maximum gradient and HF or ischemic symptoms, and/or LV systolic dysfunction attributable to subAS (S4.2.3-3).**
IIb	**C-LD**	**4. To prevent the progression of AR, surgical intervention may be considered for asymptomatic adults with subAS and at least mild AR and a maximum gradient of 50 mm Hg or more (S4.2.3-4–S4.2.3-6).**

Synopsis

SubAS may occur as a discrete membrane below the aortic valve in the LVOT, as a longer tunnel-like obstruction, as a consequence of chordal attachments in patients with abnormalities such as AVSD, or because of surgical repairs involving VSD baffled to a transposed aorta, such as seen in the Rastelli operation. SubAS may occur in isolation or as part of a suite of abnormalities. In adults with Shone complex or its variants, subAS may be one of several LV obstructive lesions, including variants of congenital mitral stenosis, supravalvular mitral stenosis, valvular aortic stenosis, supravalvular aortic stenosis, and CoA (S4.2.3-7).

SubAS tends to recur, particularly when initial resection is needed in childhood. Surgical repair for subAS carries a 10% to 15% risk of complete heart block (S4.2.3-6). SubAS may be first diagnosed in adulthood and may be confused with hypertrophic obstructive cardiomyopathy when LV hypertrophy of sufficient severity has developed such that the subaortic membrane is less evident on imaging.

The recommendations in this guideline apply to subAS caused by a discrete membrane or tunnel-like obstruction. Similar principles may apply to more complex causes of subAS, but insufficient data exist to support recommendations for more complex lesions, and extrapolation needs to take the additional anatomic complexity into account.

Turbulent flow created distal to the subaortic obstruction may cause barotrauma to the adjacent aortic valve leaflets and result in progressive AR, which may itself become clinically significant. Resection of the subaortic obstruction ideally delays or prevents the eventual need for aortic valve replacement, and concomitant aortic valve repair could also help delay the need for aortic valve replacement in these cases.

See Section 3.3 for recommendations on who should perform surgeries, cardiac catheterization, and other procedures in these patients; Section 3.4 for recommendations on diagnostic evaluation; and Table 18 for routine testing and follow-up intervals.

Recommendation-Specific Supportive Text

1. Exercise stress testing may be reasonable in the assessment of exercise capacity, stress-induced arrhythmias, and ischemia in patients with subAS and may be considered as an adjunct to echocardiographic imaging.

2. Patients with symptomatic subAS should attain symptomatic improvement from surgical relief of the obstruction. In some cases, concomitant AVR may be needed, if indicated according to GDMT.

3. Patients with depressed LV systolic function and severe subAS may not manifest a resting gradient of ≥50 mm Hg. In this population, evaluation and decisions regarding surgical relief of LVOT obstruction can be extrapolated from the existing aortic stenosis data and should be considered as per the 2014 VHD guideline (S4.2.3-8). Additionally, patients with preserved LV systolic function but poor LV compliance may present with signs or symptoms of HF and a resting maximum gradient <50 mm Hg. These patients may benefit from surgical relief of LVOT obstruction. Patients with evidence of resting or stress-induced ischemia in the absence of obstructive coronary artery disease and in the presence of moderate subAS (maximum gradient >30 mm Hg and <50 mm Hg) may benefit from surgical relief of subAS (S4.2.3-9).

4. Discrete subAS tends to be progressive with age, and patients with a resting maximum gradient ≥50 mm Hg are more likely to have progressive subAS and concomitant moderate or severe aortic valve regurgitation (S4.2.3-4). Therefore, surgical intervention may be considered in the asymptomatic patient with severe subAS. Tunnel-type subAS, which is often associated with a small aortic valve annulus, is associated with worse long-term outcomes and a higher risk of recurrence after surgical resection compared with subAS caused by a discrete membrane (S4.2.3-5). Surgical intervention on patients with asymptomatic subAS (maximum gradient ≥50 mm Hg) with preserved LV ejection fraction may delay progression of, or improve the degree of, aortic valve regurgitation. SubAS in adults may progress more slowly than in children, and although mild AR is common, it may not be progressive in medium-term follow-up (S4.2.3-10).

Table 18. Subaortic Stenosis: Routine Follow-Up and Testing Intervals

Frequency of Routine Follow-Up and Testing	Physiological Stage A* (mo)	Physiological Stage B* (mo)	Physiological Stage C* (mo)	Physiological Stage D* (mo)
Outpatient ACHD cardiologist	24	24	6–12	3–6
ECG	24	24	12	12
TTE	24	24	12	12
Exercise test†	As needed	24	24	12

*See Tables 3 and 4 for details on the ACHD AP classification system.
†6-minute walk test or CPET, depending on the clinical indication.
ACHD indicates adult congenital heart disease; CPET, cardiopulmonary exercise test; ECG, electrocardiogram; SubAS, subaortic stenosis; and TTE, transthoracic echocardiogram.

4.2.4. Congenital Valvular Aortic Stenosis

Recommendations for Congenital Valvular Aortic Stenosis Referenced studies that support recommendations are summarized in Online Data Supplement 34.		
COR	**LOE**	**Recommendations**
Diagnostic		
I	**B-NR**	**1. Adults with bicuspid aortic valve should be evaluated for coarctation of the aorta by clinical examination and imaging studies (S4.2.4-1).**
IIa	**B-NR**	**2. It is reasonable to screen first-degree relatives of patients with bicuspid**

		aortic valve or unicuspid aortic valve with echocardiography for valve disease and aortopathy (S4.2.4-2–S4.2.4-4).
Therapeutic		
IIb	**B-NR**	**3. In adults with bicuspid aortic valve stenosis and a noncalcified valve with no more than mild AR meeting indications for intervention per GDMT (S4.2.4-5), it may be reasonable to treat with balloon valvuloplasty (S4.2.4-6).**

Synopsis

Indications for aortic valve replacement according to the 2014 VHD guideline (S4.2.4-5) generally apply. Recommendations above deal with issues specific to congenital aortic valve disease, which includes BAV, as well as unicuspid aortic valve and aortic stenosis caused by hypoplastic aortic annulus. The underlying anatomy must be taken into account in patients with congenital aortic stenosis, as intervention may need to include annular enlarging procedures and other surgical techniques not commonly used in valvular aortic stenosis. These patients are often young adults, for whom lifestyle considerations such as athletic endeavors, employment, and childbearing may influence the type of intervention.

See Section 3.4 for recommendations on diagnostic evaluation; and Table 19 for routine testing and follow-up intervals.

Recommendation-Specific Supportive Text

1. CoA has a male-to-female ratio of 1.5:1 (S4.2.4-7–S4.2.4-13). A BAV is present in 50% to 70% of cases of CoA. Given the association of these abnormalities, evaluation of patients with BAV for CoA is warranted.

2. BAV is the most prevalent congenital cardiac abnormality with an estimated prevalence of 4.6 per 1,000 live births, and is 1.5 times more prevalent in males than females (S4.2.4-7–S4.2.4-13). Most cases are spontaneous; however, familial inheritance may occur in an autosomal dominant pattern with variable penetrance. On echocardiographic screening, 1 study reports the prevalence of asymptomatic BAV in first-degree relatives of patients is 9%, and 32% of first-degree relatives without a BAV will have an abnormal aorta (S4.2.4-4).

3. Calcification of the aortic valve in adults necessitates that most patients who require therapy for aortic stenosis will require aortic valve replacement per GDMT (S4.2.4-5). However, young patients with congenitally abnormal valves and relatively little calcification may be candidates for balloon valvuloplasty. Balloon valvuloplasty may improve the degree of stenosis and symptoms in patients with mobile noncalcified BAV stenosis. In general, the valves that would be amenable to successful balloon valvuloplasty are found in young patients, who are often <25 years of age. Restenosis will occur over time and in a relatively short time in some patients. Balloon valvuloplasty of calcified BAV is associated with decreased efficacy and an increased risk of AR (S4.2.4-14, S4.2.4-15). Although transcatheter interventions for aortic stenosis are increasingly commonly performed in older adults and, thus, there are increasing numbers of interventional cardiologists technically skilled at balloon aortic valvuloplasty and transcatheter aortic valve replacement, the differences in anatomy and patient population necessitate collaboration with an ACHD cardiologist for younger patients.

Table 19. Congenital Aortic Stenosis: Routine Follow-Up and Testing Intervals*

Stage	Frequency of Echocardiogram
Progressive (Stage B)	Every 3–5 y (mild severity, Vmax 2.0–2.9 m/s) Every 1–2 y (moderate severity, Vmax 3.0–3.9 m/s)
Severe (Stage C)	Every 6–12 mo (Vmax ≥4.0 m/s)
Aortic dilation >4.5 cm	Every 12 mo (echocardiogram, MRI or CT)

*Modified from existing GDMT for valvular heart disease (S4.2.4-5).
CT indicates computed tomography; GDMT, guideline-directed management and therapy; MRI, magnetic resonance imaging; and Vmax, maximum velocity.

4.2.4.1. Turner Syndrome

Recommendations for Turner Syndrome Referenced studies that support recommendations are summarized in Online Data Supplement 35.		
COR	**LOE**	**Recommendations**
Diagnostic		
I	**B-NR**	**1. Women with Turner syndrome should be evaluated for bicuspid aortic valve, coarctation of the aorta, and enlargement of the ascending aorta (S4.2.4.1-1).**
Therapeutic		
IIa	**B-NR**	**2. Prophylactic replacement of the aortic root or ascending aorta in adults with Turner syndrome is reasonable when the aortic diameter is 2.5 cm/m^2 or greater (S4.2.4.1-2).**

Synopsis

The management of valve dysfunction is generally as directed by the 2014 VHD guideline (S4.2.4.1-3). Aortopathy is a commonly associated condition, and frequently involves the mid-ascending aorta, which may not be reliably seen on TTE. Measurement of aortic dimensions with magnetic resonance angiography and CCT has not been standardized, and clinicians should be wary of comparisons of reported diameters between modalities. Side-by-side comparisons are more reliable for detecting changes over time. Baseline and routine serial measurements of the aortic size are useful, with imaging interval determined by the indexed size and rate of progression. Pregnancy in Turner syndrome, which often requires assisted reproductive technology, is associated with an increased risk of aortic dissection, especially if there is a preexisting abnormality of the aortic valve or aorta (S4.2.4.1-4).

Recommendation-Specific Supportive Text

1. Women with Turner syndrome are at substantial risk of BAV, CoA, and aortic enlargement, which can result in morbidity and mortality if left untreated. Therefore, evaluation is necessary to help decide what interventions may be necessary and provide accurate risk assessment for exercise, pregnancy, or other considerations that could be influenced by aortic pathology.

2. Because of case series reporting dissection at smaller aortic diameters than in non-Turner aortopathy, prophylactic surgery is reasonable at lower diameters, particularly if rapid dilation is present. Measurements must take into account the patient's stature either by indexing to body surface area utilizing Turner-specific normative data or by using ratio of aortic area to body height (S4.2.4.1-5–S4.2.4.1-7).

4.2.4.2. Aortopathies

Several CHD subtypes and/or repairs are associated with enlargement of the aorta. The management of these varies by condition, as some are perceived to have a stronger association with aortic dissection or rupture than others, although the true natural history of most is unknown. There is wide heterogeneity of timing of surgical referral, which makes interpretation of longitudinal studies problematic.

BAV is the most common CHD, is associated with aortopathy, and is of high concern for aortic complications, as discussed in other guideline statements (S4.2.4.2-1–S4.2.4.2-3). Although in many published series of aortic dissection, BAV patients account for a higher proportion of dissections than expected from prevalence of BAV in the general population alone, the risk of dissection or rupture amongst all BAV patients is less clear. The largest population study reported a 0.5% risk of aortic rupture or dissection after a mean of 16 years of follow-up (S4.2.4.2-4), although 11% underwent elective aortic surgery. Risk factors for aortic complications were age and an enlarged aorta at baseline. Frequency of dissection in BAV disease is higher in adults with Turner syndrome.

A dilated neoaortic root after a Ross procedure is not uncommon, although only a single dissection has been reported (S4.2.4.2-5). Because of this, it is generally believed that prophylactic root replacement strategies based on sinus of Valsalva diameters can be less aggressive after a Ross procedure than in a native BAV patient, but practice patterns vary. Most patients with a Ross repair had underlying congenitally abnormal aortic valves (BAV or unicuspid aortic valve) and, therefore, are at risk of the ascending aortic dilation typical of those abnormalities. Thus, in addition to the dilation at the sinuses of Valsalva associated with the Ross repair, dilation of the native ascending aorta above the sinotubular junction can also occur.

Although patients with conotruncal abnormalities (TOF, dextrotransposition of the great arteries [d-TGA] after arterial switch (S4.2.4.2-6–S4.2.4.2-8), pulmonary atresia with VSD, truncus arteriosus) commonly have aortic diameters of 40 mm to 50 mm, aortic complications are extremely rare (only 6 published case reports) (S4.2.4.2-9–S4.2.4.2-14). Therefore, there is no strong justification for empiric prophylactic surgery in such patients based solely on aortic diameter. Watchful observation has often been recommended unless surgery is being undertaken for other indications (S4.2.4.2-15). However, there are rare patients who develop substantially greater aortic enlargement and for whom prophylactic surgery may have more of a role. Risk factor management such as control of hypertension is important. There are no RCTs evaluating the efficacy of medical therapy to reduce the rate of progression of aortic dilation or incidence of aortic dissection in this population.

See Online Data Supplement 36 for referenced studies.

4.2.5. Supravalvular Aortic Stenosis

Recommendations for Supravalvular Aortic Stenosis Referenced studies that support recommendations are summarized in Online Data Supplement 37.		
COR	**LOE**	**Recommendations**
Diagnostic		
I	**C-LD**	**1. Aortic imaging using TTE, TEE, CMR, or CTA is recommended in adults with Williams syndrome or patients suspected of having supravalvular aortic stenosis (S4.2.5-1).**
I	**C-LD**	**2. Coronary imaging is recommended in patients with Williams syndrome and supravalvular aortic stenosis presenting with symptoms of coronary ischemia (S4.2.5-2–S4.2.5-4).**

Therapeutic		
I	B-NR	**3. Surgical repair is recommended for adults with supravalvular aortic stenosis (discrete or diffuse) and symptoms or decreased LV systolic function deemed secondary to aortic obstruction (S4.2.5-5–S4.2.5-8).**
I	C-LD	**4. Coronary artery revascularization is recommended in symptomatic adults with supravalvular aortic stenosis and coronary ostial stenosis (S4.2.5-4, S4.2.5-9).**

Synopsis

Supravalvular aortic stenosis is a relatively rare condition overall but is seen commonly in patients with Williams syndrome or homozygous familial hypercholesterolemia. The stenotic ridge tends to occur distal to the coronary artery orifices at the sinotubular junction. In addition to pressure load physiology similar to other causes of LVOT obstruction, coronary abnormalities can occur, including significant coronary ostial stenosis resulting in risk of SCD and anesthesia risk (S4.2.5-10–S4.2.5-14). Unlike subAS or valvular aortic stenosis, the coronary arteries are exposed to the higher pressure generated by the supravalvular obstruction.

See Section 3.3 for recommendations on who should perform surgeries, cardiac catheterization, and other procedures in these patients; Section 3.4 for recommendations on diagnostic evaluation; and Table 20 for routine testing and follow-up intervals.

Recommendation-Specific Supportive Text

1. TTE with Doppler imaging is useful in deriving peak and mean pressure gradients across the area of supravalvular aortic stenosis from apical, suprasternal, and right parasternal views; however, visualization of the full extent of supravalvular aortic stenosis with TTE is limited. TEE is superior in this regard, and 3D TEE allows excellent visualization of the narrowed ascending aorta. CMR and CTA provide comprehensive and detailed images of supravalvular aortic stenosis and are used with echocardiography in the assessment of patients before and after repair (S4.2.5-15).

2. Impaired coronary perfusion may occur because of varying degrees of aortic valve leaflet adhesion to the narrowed sinotubular junction or because of fibrotic thickening in the area immediately surrounding the coronary ostia. This causes ostial stenosis with restriction in diastolic filling of the coronary arteries; the left coronary is most frequently involved. TEE with Doppler can be used in the assessment of proximal coronary patency and to search for flow turbulence. CMR can also be used in assessing the coronary ostia. Electrocardiographic-gated CT coronary angiography or invasive selective coronary angiography provides excellent visualization of the coronary arterial anatomy.

3. Supravalvular aortic stenosis is usually a progressive problem with a progressive increase in LV systolic pressure resulting in exertional symptoms and, if the stenosis is severe, eventual decreases in LV systolic function.

4. Impaired coronary perfusion may occur because of varying degrees of aortic valve leaflet adhesion to the narrowed sinotubular junction with restriction in diastolic filling of the coronary arteries; the left coronary is most frequently involved. Surgical coronary revascularization is recommended for patients with symptoms of coronary ischemia.

Table 20. Supravalvular Aortic Stenosis: Routine Follow-Up and Testing Intervals

Frequency of Routine Follow-Up and Testing	Physiological Stage A* (mo)	Physiological Stage B* (mo)	Physiological Stage C* (mo)	Physiological Stage D* (mo)
Outpatient ACHD cardiologist	24	24	6–12	3–6
ECG	24	24	12	12
TTE†	24	24	12	12
CMR‡/CCT§	36–60	36–60	36–60	36–60
Exercise test‖	As needed	24	24	12

*See Tables 3 and 4 for details on the ACHD AP classification system.
†Routine TTE may be unnecessary in a year when CMR imaging is performed unless clinical indications warrant otherwise.
‡CMR may be indicated for assessment of aortic anatomy. Baseline study is recommended with periodic follow-up CMR, with frequency of repeat imaging determined by anatomic and physiological findings.
§If CCT is used instead of CMR imaging, the frequency should be weighed against radiation exposure.
‖6-minute walk test or CPET, depending on the clinical indication.
ACHD indicates adult congenital heart disease; CCT, cardiac computed tomography; CMR, cardiovascular magnetic resonance; CPET, cardiopulmonary exercise test; ECG, electrocardiogram; and TTE, transthoracic echocardiogram.

4.2.6. Coarctation of the Aorta

Recommendations for Coarctation of the Aorta Referenced studies that support recommendations are summarized in Online Data Supplement 38.		
COR	**LOE**	**Recommendations**
		Diagnostic
I	B-NR	**1. Initial and follow-up aortic imaging using CMR or CTA is recommended in adults with coarctation of the aorta, including those who have had surgical or catheter intervention (S4.2.6-1–S4.2.6-3).**
I	C-EO	**2. Resting blood pressure should be measured in upper and lower extremities in all adults with coarctation of the aorta.**
IIa	C-LD	**3. Ambulatory blood pressure monitoring in adults with coarctation of the aorta can be useful for diagnosis and management of hypertension (S4.2.6-4).**
IIb	B-NR	**4. Screening for intracranial aneurysms by magnetic resonance angiography or CTA may be reasonable in adults with coarctation of the aorta (S4.2.6-5, S4.2.6-6).**
IIb	C-LD	**5. Exercise testing to evaluate for exercise-induced hypertension may be reasonable in adults with coarctation of the aorta who exercise (S4.2.6-4, S4.2.6-7).**
		Therapeutic
I	B-NR	**6. Surgical repair or catheter-based stenting is recommended for adults with hypertension and significant native or recurrent coarctation of the aorta (S4.2.6-1, S4.2.6-2, S4.2.6-8–S4.2.6-12).**
I	C-EO	**7. GDMT is recommended for treatment of hypertension in patients with coarctation of the aorta (S4.2.6-13).**
IIb	B-NR	**8. Balloon angioplasty for adults with native and recurrent coarctation of the aorta may be considered if stent placement is not feasible and surgical intervention is not an option (S4.2.6-14).**

Synopsis

CoA typically occurs near the ductal remnant and left subclavian artery. Hypertension is the most common sequela of CoA, whether repaired or unrepaired. BAV is commonly associated with CoA and is present in more than half of CoA patients (S4.2.6-15–S4.2.6-21). Intracranial aneurysms may occur. Ascending aortic aneurysms are often found in those with BAV, and aneurysms are seen at the site of coarctation repair in the descending thoracic aorta or arch. Dissection can occur, presumably more likely in the setting of poorly controlled hypertension. Even with excellent repair, hypertension remains common and predisposes to later myocardial infarction, stroke, and HF.

See Section 3.3 for recommendations on who should perform surgeries, cardiac catheterization, and other procedures in these patients; Section 3.4 for recommendations on diagnostic evaluation; and Table 21 for routine testing and follow-up intervals.

Recommendation-Specific Supportive Text

1. Complications of CoA repair include recoarctation, aneurysm, pseudoaneurysm, and dissection. Long-term follow-up after successful surgical intervention for CoA reveals that 11% of patients may require reintervention for restenosis, visualized by CMR or CTA (if CMR is contraindicated or there is a history of stent therapy) and supported by physical examination findings (S4.2.6-1). Although evidence of recoarctation can be found on clinical examination and echocardiography, aneurysms near the site of repair may not be well seen by echocardiography. Patients who have undergone surgical patch repair are at an increased risk of developing aneurysms that can be evaluated by CMR or CTA. After successful transcatheter intervention with stenting or balloon angioplasty, follow-up CMR or CTA imaging is recommended to evaluate for long-term complications (e.g., aneurysm formation, stent fracture, or stent migration) (S4.2.6-1). The same CMR or CTA study will also evaluate the ascending aorta, which may become aneurysmal over the years of follow-up.

2. Unoperated adults with CoA almost invariably present with systemic arterial hypertension measured in the upper extremities. Brachial and femoral pulse timing and amplitude evaluation on physical examination reveals a delay or decrease in amplitude of the femoral pulse. Upper and lower extremity noninvasive blood pressure measurement is recommended in all patients with unoperated or operated/intervened CoA.

3. Upper body systemic hypertension is prevalent in patients with unoperated coarctation and may be present in up to one third of patients who have undergone operative or transcatheter intervention (S4.2.6-2). Systemic hypertension may not consistently be identifiable at rest; therefore, ambulatory blood pressure monitoring can be useful in identifying and appropriately managing patients with ambulatory hypertension.

4. Multiple studies have demonstrated an increased frequency of intracranial aneurysm in adults with CoA. Approximately 10% of patients with CoA have intracranial aneurysms identified on magnetic resonance angiography or CTA. Increasing age has been identified as a risk factor. Many such identified aneurysms are small; however, the expected outcome and ideal management of such aneurysms are not clear. Providers and patients should be aware of management uncertainties when considering routine screening for aneurysms (S4.2.6-22). Additionally, there are some data suggesting that intracranial aneurysms are not commonly found in children and teenagers with CoA (S4.2.6-23), reinforcing the possibility that coarctation alone may not be sufficient for development of intracranial aneurysm, and other factors, such as hypertension and/or age, play a role in development and progression of aneurysms.

5. Despite successful surgical repair or transcatheter intervention, hypertension can persist and may not be identified during resting blood pressure measurement. Up to 80% of patients with prior CoA intervention manifest an abnormally elevated upper extremity exercise blood pressure response, and peak blood pressure is correlated with increased LV mass (S4.2.6-24). Moreover, restenosis of the previously repaired or stented region may be identified by increased peak blood pressure response, increased upper to lower extremity blood pressure gradient with exercise, and increased Doppler velocity across the coarctation site during exercise TTE.

6. Significant native or recurrent aortic coarctation has been defined as follows: upper extremity/lower extremity resting peak-to-peak gradient >20 mm Hg or mean Doppler systolic gradient >20 mm Hg; upper extremity/lower extremity gradient >10 mm Hg or mean Doppler gradient >10 mm Hg plus either decreased LV systolic function or AR; upper extremity/lower extremity gradient >10 mm Hg or mean Doppler gradient >10 mm Hg with collateral flow (S4.2.6-2, S4.2.6-8, S4.2.6-12). This should be coupled with anatomic evidence for CoA, typically defined by advanced imaging (CMR, CTA). The best evidence to proceed with intervention for CoA includes systemic hypertension, upper extremity/lower extremity blood pressure gradient and echocardiography Doppler gradient as defined above, and anatomic evidence of CoA. Multiple factors help determine whether surgery or stenting is optimal, including anatomic features such as proximity of native coarctation to head and neck vessels or concomitant aneurysm, and, if stenting, whether a covered stent is needed.

7. The long-term complications of CoA are generally related to chronic upper body systemic hypertension, therefore, systemic hypertension should be identified by resting, ambulatory, or exercise blood pressure assessment and medical treatment should follow GDMT (S4.2.6-13, S4.2.6-25)

8. Balloon angioplasty alone is associated with a higher rate of intimal tears and aneurysm formation compared with stent placement.

Table 21. CoA: Routine Follow-Up and Testing Intervals

Frequency of Routine Follow-Up and Testing	Physiological Stage A*(mo)	Physiological Stage B*(mo)	Physiological Stage C*(mo)	Physiological Stage D*(mo)
Outpatient ACHD cardiologist	24	24	6–12	3–6
ECG	24	24	12	12
TTE†	24	24	12	12
CMR‡/CCT§	36–60	36–60	12–24	12–24
Exercise test ‖	36	24	24	12

*See Tables 3 and 4 for details on the ACHD AP classification system.
†Routine TTE may be unnecessary in a year when CMR imaging is performed unless clinical indications warrant otherwise.
‡CMR may be indicated for assessment of aortic size and aortic arch/coarctation repair site anatomy. Baseline study is recommended with periodic follow-up CMR, with frequency of repeat imaging determined by anatomic and physiological findings.
§CCT may be used if CMR is not feasible and to evaluate cross-sectional imaging status–post-stent therapy for coarctation of the aorta; the frequency should be weighed against radiation exposure.
‖6-minute walk test or CPET, depending on the clinical indication.
ACHD indicates adult congenital heart disease; CCT, cardiac computed tomography; CMR, cardiovascular magnetic resonance imaging; CoA, coarctation of the aorta; CPET, cardiopulmonary exercise; ECG, electrocardiogram; and TTE, transthoracic echocardiogram.

4.3. Right-Sided Lesions

4.3.1. Valvular Pulmonary Stenosis

Recommendations for Valvular Pulmonary Stenosis Referenced studies that support recommendations are summarized in Online Data Supplement 39.		
COR	**LOE**	**Recommendations**
I	**B-NR**	**1. In adults with moderate or severe valvular pulmonary stenosis and otherwise unexplained symptoms of HF, cyanosis from interatrial right-to-left communication, and/or exercise intolerance, balloon valvuloplasty is recommended (S4.3.1-1–S4.3.1-4).**
I	**B-NR**	**2. In adults with moderate or severe valvular pulmonary stenosis and otherwise unexplained symptoms of HF, cyanosis, and/or exercise intolerance who are ineligible for or who failed balloon valvuloplasty, surgical repair is recommended (S4.3.1-1, S4.3.1-5–S4.3.1-8)**
IIa	**C-EO**	**3. In asymptomatic adults with severe valvular pulmonary stenosis, intervention is reasonable.**

Synopsis

Valvular PS is one of the most common congenital heart defects, estimated to occur in up to 7% of children born with CHD (S4.3.1-9–S4.3.1-11). Some common findings associated with isolated valvular PS include a dilated main PA and dysplastic valve cusps. Surgical or catheter-based intervention depends on degree of obstruction, RV pressure and function, and associated symptoms. Patients with isolated pulmonary valve stenosis (native or recurrent after an intervention) require ongoing cardiac follow-up and monitoring for evidence of progressive valve stenosis or regurgitation, RV hypertrophy, HF, and arrhythmias (S4.3.1-12). Patients with mild native pulmonary valve stenosis (Table 22) have a reassuring natural history, and intervention is not usually necessary. Patients with severe PS (Table 22) usually require intervention in childhood with a good prognosis into adulthood (S4.3.1-6). Patients with moderate stenosis (Table 22) have more variable histories, with some having received surgical or catheter intervention in childhood or adulthood and some not. Patients with moderate PS, whether native or postintervention, have a good long-term outcome, although some will go on to require an intervention in adulthood because of progressive PS or, commonly, significant PR as a sequela of earlier intervention.

Pulmonary atresia with intact ventricular septum is a rare congenital heart lesion that is associated with varying degrees of RV hypoplasia and tricuspid valve hypoplasia in addition to pulmonary valve atresia. Adults with pulmonary atresia with intact ventricular septum followed various surgical pathways in childhood, either biventricular repair, 1 1/2 ventricular repair, Fontan procedure, transplant, or shunt palliation (S4.3.1-13). Adults with history of pulmonary atresia with intact ventricular septum have a high incidence of need for reintervention and management of atrial arrhythmias (S4.3.1-14, S4.3.1-15). Restrictive RV physiology is common in adults with history of pulmonary atresia with intact ventricular septum and may be associated with substantial ventricular fibrosis (S4.3.1-16) and RV-dependent coronary circulation.

See Section 3.3 for recommendations on who should perform surgeries, cardiac catheterization, and other procedures in these patients; Section 3.4 for recommendations on diagnostic evaluation; Table 23 for routine testing and follow-up intervals; and Figure 3 for a diagnostic and treatment algorithm for isolated PR after repair of PS.

Recommendation-Specific Supportive Text

1. In patients with moderate or severe isolated pulmonary valve stenosis, pulmonary balloon valvuloplasty is safe and effective in reducing the pulmonary valve gradient and improving symptoms in most patients

2. Surgical valvotomy is usually sufficient, particularly when the pulmonary annulus is not hypoplastic. Pulmonary valve replacement may be necessary when there is marked dysplasia of the pulmonary valve or significant hypoplasia of the annulus.

3. Relief of a severely stenotic pulmonary valve in an asymptomatic patient will reduce the RV pressure and the possibility of potential sequelae. As in symptomatic patients, the procedure can be performed by surgery or interventional catheterization with low morbidity and mortality. If intervention is deferred, careful follow-up to evaluate for symptoms, decline in exercise capacity, worsening RV function, or development of cyanosis is important and may prompt reconsideration of intervention.

Table 22. Severity of RVOT Obstruction

Mild	Peak gradient <36 mm Hg (peak velocity <3 m/s)
Moderate	Peak gradient 36–64 mm Hg (peak velocity 3–4 m/s)
Severe	Peak gradient 64 mm Hg (peak velocity >4 m/s); mean gradient >35 mm Hg

Estimations of RV systolic pressure by TR velocity is part of the echocardiographic assessment of RV obstruction, as Doppler measurements across the RV obstruction itself may be unreliable.
RV indicates right ventricular; RVOT, right ventricular outflow tract; and TR, tricuspid regurgitation.

Table 23. Valvular PS: Routine Follow-Up and Testing Intervals

Frequency of Routine Follow-Up and Testing	Physiological Stage A* (mo)	Physiological Stage B* (mo)	Physiological Stage C* (mo)	Physiological Stage D* (mo)
Outpatient ACHD cardiologist	36–60	24	6–12	3–6
ECG	36–60	24	12	12
TTE	36–60	24	12	12
Exercise test†	As needed	24	24	12

*See Tables 3 and 4 for details on the ACHD AP classification system.
†6-minute walk test or CPET, depending on clinical indication.
ACHD indicates adult congenital heart disease; CPET, cardiopulmonary exercise test; ECG, electrocardiogram; PS, pulmonary stenosis; and TTE, transthoracic echocardiogram.

4.3.1.1. Isolated PR After Repair of PS

Recommendations for Isolated PR After Repair of Pulmonary Stenosis		
COR	**LOE**	**Recommendations**
I	**C-EO**	**1. In symptomatic patients with moderate or greater PR resulting from treated isolated pulmonary stenosis, with RV dilation or RV dysfunction, pulmonary valve replacement is recommended.**
I	**C-EO**	**2. For asymptomatic patients with residual PR resulting from treatment of isolated pulmonary stenosis with a dilated right ventricle, serial follow-up is recommended.**
IIb	**C-EO**	**3. In asymptomatic patients with moderate or greater PR resulting from**

		treatment of isolated pulmonary stenosis with progressive RV dilation and/or RV dysfunction, pulmonary valve replacement may be reasonable.

Synopsis

Although many patients with valvular PS do not require intervention, some have PS that is severe enough to warrant intervention, often in infancy or childhood. PS can be alleviated either by surgical valvotomy or with balloon valvuloplasty. Either surgical or catheter intervention may result in hemodynamically important PR that can result in symptoms, RV enlargement, and/or dysfunction requiring pulmonary valve replacement.

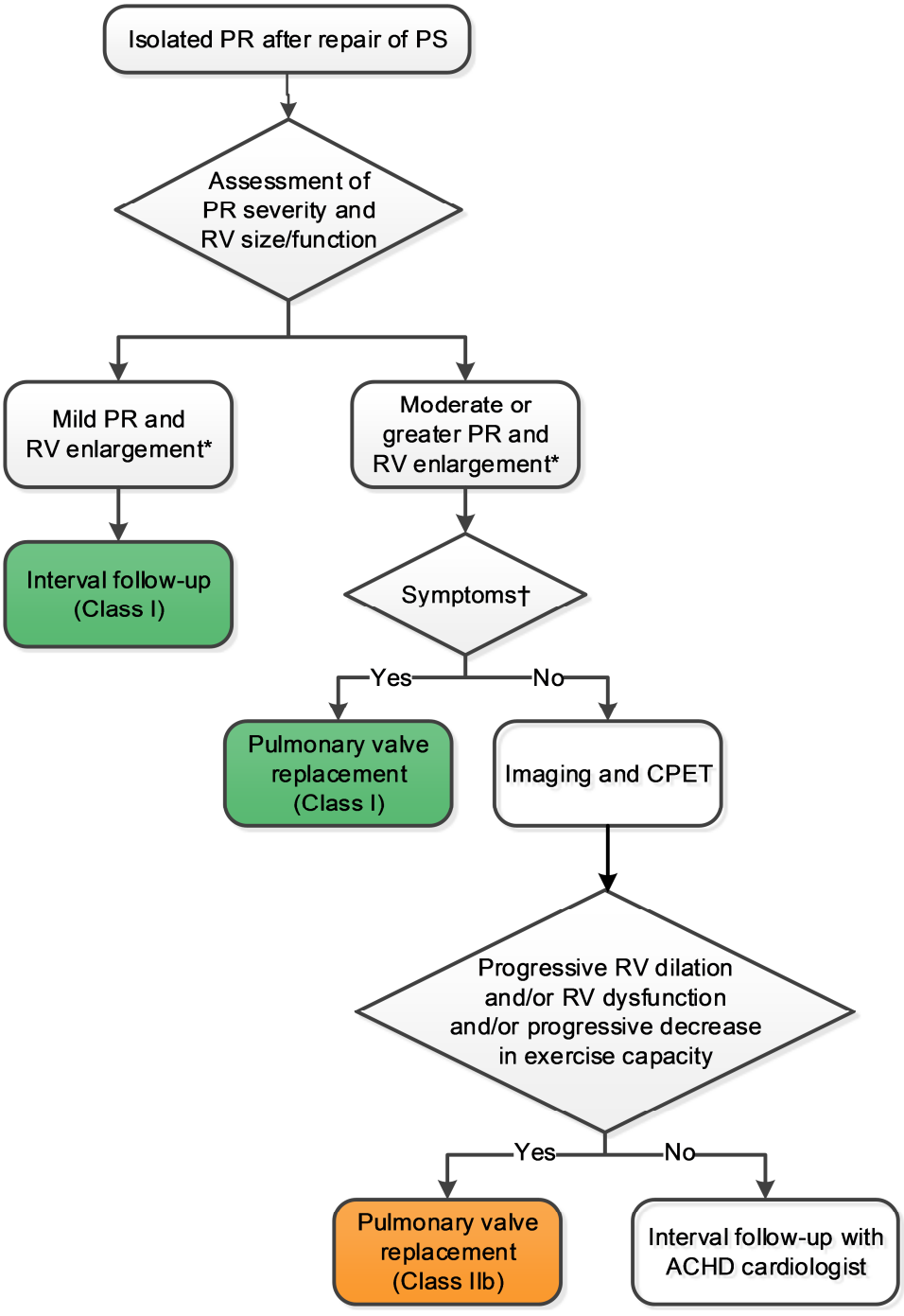
Recommendation-Specific Supportive Text

1. Patients with isolated PS who have previously undergone an intervention on the pulmonary valve require ongoing clinical follow-up and monitoring of PR, RV size and function, and functional capacity. This may include echocardiography, CPET, and advanced imaging. The right ventricle in patients with PR after intervention for PS may be smaller than in patients with TOF; however, patients with PR may have evidence of decreased RV ejection fraction or decreased exercise capacity. Pulmonary valve replacement can improve symptoms for patients with symptoms that are attributable to moderate or greater PR, and can improve RV size and/or RV function if there is RV dilation or decreased RV ejection fraction.

2. PR resulting from treatment of isolated PS may have progressive impact on RV size and function, and may result in symptoms, such that pulmonary valve replacement would be considered. Serial follow-up for clinical evaluation, CPET, and imaging to evaluate for symptoms, exercise intolerance attributable to PR, and/or RV dilation or RV dysfunction will allow appropriate timing of intervention if needed.

3. There are no data to suggest appropriate timing for pulmonary valve replacement in the presence of RV dilation, but it is likely inappropriate to directly extrapolate the data applicable to patients with TOF (S4.3.1.1-1). However, RV dilation or dysfunction should improve, or at least not progress further, if the volume overload from PR is alleviated by pulmonary valve replacement. Thus, although specific RV size criteria are not available for these patients to determine timing of pulmonary valve replacement, patients with progressively worsening RV size or function presumably represent a subset of patients for whom valve replacement could be beneficial.

Figure 3. Isolated PR After Repair of PS



*Significant PR causes RV dilation. If a patient has moderate or greater PR and normal RV size, most likely the estimation of PR severity is inaccurate or there may be restrictive RV physiology, which would warrant further investigation.
†Symptoms may include dyspnea, chest pain, and/or exercise intolerance referable to PR or otherwise unexplained.
ACHD indicates adult congenital heart disease; CPET, cardiopulmonary exercise test; PR, pulmonary regurgitation; PS, pulmonary stenosis; and RV, right ventricular.

4.3.2. Branch and Peripheral Pulmonary Stenosis

Recommendations for Branch and Peripheral PS Referenced studies that support recommendations are summarized in Online Data Supplement 40.		
COR	**LOE**	**Recommendations**
		Diagnostic
I	**B-NR**	**1. For adults with peripheral or branch PS, ongoing surveillance is recommended (S4.3.2-1, S4.3.2-2).**
		Therapeutic
IIa	**B-NR**	**2. In adults with peripheral or branch PA stenosis, PA dilation and stenting can be useful (S4.3.2-2, S4.3.2-3).**

Synopsis

Pulmonary branch and peripheral PS can be isolated, occur as part of a constellation of right ventricular outflow tract (RVOT) obstruction, or be found in association with a syndrome (e.g., Noonan, Alagille, Williams, maternal rubella exposure). Intervention decisions are typically based on symptoms, distribution of pulmonary blood flow, RV function, and RV systolic pressure. TTE is a good modality to obtain RV pressure and function but does not adequately image the peripheral pulmonary arteries. Alternative imaging (e.g., CMR, CCT) can visualize anatomic obstructions and branch PA anatomy. In addition, CMR and pulmonary perfusion testing can quantify relative pulmonary blood flow.

See Section 3.3 for recommendations on who should perform surgeries, cardiac catheterization, and other procedures in these patients; Section 3.4 for recommendations on diagnostic evaluation; and Table 24 for routine testing and follow-up intervals.

Recommendation-Specific Supportive Text

1. Cardiac follow-up and imaging may include evaluation of RV pressure; quantifying relative pulmonary blood flow and imaging for evidence of residual lesions or PA obstruction or aneurysm at sites of prior intervention; and in-stent stenosis and/or stent fracture (the latter often best seen by fluoroscopy). Stenting of branch PA stenosis is effective in reducing the pressure gradients, but patients often require further intervention (S4.3.2-2). In-stent stenosis with a reduction in the ipsilateral pulmonary blood flow is seen in approximately 25% of patients after percutaneous PA angioplasty and stent placement, more common in patients with abnormal pulmonary arteries, such as those with TOF or Williams syndrome (S4.3.2-1). Regular surveillance and imaging, with intervention as required, may prevent the development of RV hypertension and its sequelae (S4.3.2-1).

2. Balloon angioplasty or stenting of a peripheral PA is effective in reducing pressure gradients and improving pulmonary blood flow. Indications for pulmonary angioplasty or stenting include symptoms attributed to the decreased pulmonary blood flow, focal narrowing, abnormal differential perfusion, and/or elevated RV pressure. The decision for intervention with PA angioplasty or stenting includes assessment of clinical symptoms, imaging, and discussion with an ACHD interventional cardiologist.

Table 24. Branch and Peripheral PS: Routine Follow-Up and Testing Intervals

Frequency of Routine Follow-Up and Testing	Physiological Stage A* (mo)	Physiological Stage B* (mo)	Physiological Stage C* (mo)	Physiological Stage D* (mo)
Outpatient ACHD cardiologist	24–36	24	6–12	3–6
ECG	24–36	24	12	12
TTE†	24–36	24	12	12

CMR‡/CCT§	36–60	36–60	24–36	24–36
Exercise test ‖	36	24	24	12

*See Tables 3 and 4 for details on the ACHD AP classification system.
†Routine TTE may be unnecessary in a year when CMR imaging is performed unless clinical indications warrant otherwise.
‡CMR may be indicated for assessment of branch PS. Baseline study is recommended with periodic follow-up CMR, with frequency of repeat imaging determined by anatomic and physiological findings.
§CCT may be used if CMR is not feasible and to evaluate cross-sectional imaging status and post-stent therapy for peripheral PS; the frequency should be weighed against radiation exposure.
‖6-minute walk test or CPET, depending on clinical indication.
ACHD indicates adult congenital heart disease; CCT, cardiac computed tomography; CMR, cardiovascular magnetic resonance imaging; CPET, cardiopulmonary exercise test; ECG, electrocardiogram; PS, pulmonary stenosis; and TTE, transthoracic echocardiogram.

4.3.3. Double-Chambered Right Ventricle

Recommendations for Double-Chambered Right Ventricle Referenced studies that support recommendations are summarized in Online Data Supplement 41.		
COR	**LOE**	**Recommendations**
I	**C-LD**	**1. Surgical repair for adults with double-chambered right ventricle and moderate or greater outflow obstruction is recommended in patients with otherwise unexplained symptoms of HF, cyanosis, or exercise limitation (S4.3.3-1–S4.3.3-3) (Table 22).**
IIb	**C-LD**	**2. Surgical repair for adults with double-chambered right ventricle with a severe gradient may be considered in asymptomatic patients (S4.3.3-3, S4.3.3-4) (Table 22).**

Synopsis

Double-chambered right ventricle is uncommon in adults. Hypertrophied muscle bundles develop in the RV cavity, creating RVOT obstruction (S4.3.3-5, S4.3.3-6). It is commonly associated with a VSD. Double-chambered right ventricle can be missed on TTE if not sought specifically, and alternative imaging or cardiac catheterization is often required to confirm the diagnosis and establish the hemodynamic impact.

See Section 3.3 for recommendations on who should perform surgeries, cardiac catheterization, and other procedures in these patients; Section 3.4 for recommendations on diagnostic evaluation; and Table 25 for routine testing and follow-up intervals.

Recommendation-Specific Supportive Text

1. Surgery typically involves transatrial or transventricular resection of obstructing muscle bundles and VSD closure if present. Occasionally, patch enlargement of RVOT may be necessary to adequately relieve obstruction.

2. VSD is often present and may communicate with the higher or lower pressure chamber in the right ventricle, with resulting differences in shunt direction and flow characteristics. In patients with a severe gradient through the right ventricle, the VSD may be associated with right-to-left shunting if proximal to the obstruction, or associated with left-to-right shunting if distal. Exercise testing performed in a subjectively asymptomatic patient will often be abnormal. Patients may benefit from repair of both the VSD and outflow obstruction, especially if exercise capacity is decreased.

Table 25. Double-Chambered Right Ventricle: Routine Follow-Up and Testing Intervals

Frequency of Routine Follow-Up and Testing	Physiological Stage A* (mo)	Physiological Stage B* (mo)	Physiological Stage C* (mo)	Physiological Stage D* (mo)
Outpatient ACHD cardiologist	24–36	24	6–12	3–6
ECG	24–36	24	12	12
TTE	24–36	24	12	12
Exercise test†	As needed	24	24	12

*See Tables 3 and 4 for details on the ACHD AP classification system.
†6-minute walk test or CPET, depending on clinical indication.
ACHD indicates adult congenital heart disease; CPET, cardiopulmonary exercise test; ECG, electrocardiogram; and TTE, transthoracic echocardiogram.

4.3.4. Ebstein Anomaly

Recommendations for Ebstein Anomaly Referenced studies that support recommendations are summarized in Online Data Supplement 42.		
COR	**LOE**	**Recommendations**
		Diagnostic
IIa	B-NR	1. In adults with Ebstein anomaly, CMR can be useful to determine anatomy, RV dimensions, and systolic function (S4.3.4-1, S4.3.4-2).
IIa	B-NR	2. In adults with Ebstein anomaly, TEE can be useful for surgical planning if TTE images are inadequate to evaluate tricuspid valve morphology and function (S4.3.4-1).
IIa	B-NR	3. Electrophysiological study with or without catheter ablation can be useful in the diagnostic evaluation of adults with Ebstein anomaly and ventricular preexcitation but without supraventricular tachycardia (S4.3.4-3, S4.3.4-4).
IIa	B-NR	4. In adults with Ebstein anomaly, electrophysiological study (and catheter ablation, if needed) is reasonable before surgical intervention on the tricuspid valve even in the absence of preexcitation or supraventricular tachycardia (S4.3.4-5).
		Therapeutic
I	B-NR	5. Surgical repair or reoperation for adults with Ebstein anomaly and significant TR is recommended when one or more of the following are present: HF symptoms, objective evidence of worsening exercise capacity, progressive RV systolic dysfunction by echocardiography or CMR (S4.3.4-6–S4.3.4-10).
I	C-LD	6. Catheter ablation is recommended for adults with Ebstein anomaly and high-risk pathway conduction or multiple accessory pathways (S4.3.4-3, S4.3.4-11, S4.3.4-12).
IIa	B-NR	7. Surgical repair or reoperation for adults with Ebstein anomaly and significant TR can be beneficial in the presence of progressive RV enlargement, systemic desaturation from right-to-left atrial shunt, paradoxical embolism, and/or atrial tachyarrhythmias (S4.3.4-11, S4.3.4-13, S4.3.4-14).
IIb	B-NR	8. Bidirectional superior cavopulmonary (Glenn) anastomosis at time of Ebstein anomaly repair may be considered for adults when severe RV dilation or severe RV systolic dysfunction is present, LV function is

		preserved, and left atrial pressure and LV end diastolic pressure are not elevated (S4.3.4-6, S4.3.4-15).

Synopsis

Ebstein anomaly is an uncommon congenital heart defect occurring in about 0.005% of live births (S4.3.4-16–S4.3.4-18). It is a malformation of the tricuspid valve and the right ventricle and varies in severity, including babies who do not survive infancy, asymptomatic adults diagnosed incidentally in the sixth and seventh decades of life, and many variations in severity between those extremes. Ebstein anomaly can occur with other defects including ASD, VSD, and PS. A patent foramen ovale, otherwise usually considered normal, may have significant impact in Ebstein anomaly. Accessory pathways and arrhythmias are relatively common. Patient surveillance and management varies depending on age, severity of the lesion, and associated abnormalities including HF, cyanosis, and arrhythmias. Surveillance includes echocardiographic and other advanced imaging to assess RV size and function, rhythm assessment, pulse oximetry, and stress testing. Treatments include medical and surgical therapy for patients with manifest symptoms as well as catheter-based structural and electrophysiological interventions when indicated.

See Section 3.3 for recommendations on who should perform surgeries, cardiac catheterization, and other procedures in these patients; Section 3.4 for recommendations on diagnostic evaluation; and Table 26 for routine testing and follow-up intervals.

Recommendation-Specific Supportive Text

1. Deciphering the anatomy and size of the right atrium and right ventricle in Ebstein anomaly is often difficult using echocardiography alone, particularly in adults. Data obtained from CMR can inform clinical care and surgical planning or decision-making, because CMR data correlate well with intraoperative findings.

2. Two-dimensional and 3D TEE can better define the anatomy and function of the tricuspid valve before surgery and provide valuable information in planning surgical repair.

3. Approximately one third of adults with Ebstein anomaly and ventricular preexcitation have multiple accessory pathways, associated with a high risk of SCD. Adults with Ebstein anomaly also have a high prevalence of atrial tachyarrhythmia (S4.3.4-3, S4.3.4-4). In the setting of ventricular preexcitation, atrial tachyarrhythmia may expose the patient to a higher risk of lethal ventricular arrhythmia. In patients with clinical supraventricular tachycardia, management is according to existing GDMT (S4.3.4-19). A Pediatric & Congenital Electrophysiology Society (PACES)/HRS expert consensus document provides additional information on the management of arrhythmias (S4.3.4-20).

4. Concealed accessory pathways are common in Ebstein anomaly and may coexist with manifest accessory pathways. In addition, preexcitation may be present but difficult to appreciate on the surface ECG. Tricuspid valve surgery can hinder transcatheter access to right-sided accessory pathways and the slow pathway in AV node reentry, such that it may be reasonable to assess for arrhythmia substrates and proceed with catheter ablation if identified, before surgery.

5. Data demonstrate that delay of surgery until HF or RV systolic dysfunction ensues is associated with poorer outcomes; surgery before either of those develops is recommended (S4.3.4-6, S4.3.4-7, S4.3.4-10). Ebstein anomaly is understood as not just valve disease but also a myopathic process. Consequently, threshold for operation may be different than in other RV volume-loading lesions, because there is more concern regarding the capacity of the myopathic Ebstein right ventricle to tolerate a volume load. Also, there are cohort series of Ebstein patients to inform decisions (S4.3.4-6, S4.3.4-7, S4.3.4-10). Surgical repair generally consists of tricuspid valve repair (preferred when feasible)

or replacement, selective plication of atrialized right ventricle, reduction atrioplasty, arrhythmia surgery, and/or closure of atrial level shunt. Surgery may result in improvement of symptoms and functional ability, and prevent or delay worsening symptoms.

6. Adults with Ebstein anomaly and ventricular preexcitation often have multiple accessory pathways, which are associated with a higher risk of SCD. Surgical interruption of accessory pathways is largely reserved for patients who have failed attempts at catheter ablation. High-risk pathways are those with an increased risk of SCD, largely related to VF resulting from rapidly conducting AF. Definition and discussion of high-risk pathways is beyond the scope of these guidelines but can be found elsewhere, such as the "PACES/HRS Expert Consensus Statement on the Recognition and Management of Arrhythmias in ACHD" (S4.3.4-21).

7. Systemic desaturation and arrhythmias are frequently signs of worsening hemodynamics, progressive TR, or worsening RV function. Surgery for the tricuspid valve as well as closure of the ASD or stretched patent foramen ovale and arrhythmia surgery can be beneficial. When arrhythmia surgery is required, it typically involves a modified right atrial maze procedure. In the presence of AF, the addition of a left atrial Cox Maze III procedure can be beneficial to reduce the risk of recurrent AF.

8. The use of the bidirectional cavopulmonary shunt is much more common in children than in adults. When it is applied in the adult, it is usually reserved for patients with severe RV dysfunction with concern that the right ventricle will not tolerate supporting the entirety of stroke volume (S4.3.4-6, S4.3.4-15). Preoperative catheterization to determine hemodynamics and feasibility of applying the bidirectional cavopulmonary shunt becomes progressively more important in older patients, particularly those with longstanding hypertension with LV hypertrophy, which can lead to diastolic dysfunction and elevated pulmonary pressures.

Table 26. Ebstein Anomaly: Routine and Follow-Up and Testing Intervals

Frequency of Routine Follow-Up and Testing	Physiological Stage A* (mo)	Physiological Stage B* (mo)	Physiological Stage C* (mo)	Physiological Stage D* (mo)
Outpatient ACHD cardiologist	12–24	12	6–12	3–6
ECG	12–24	12	12	12
CXR	As needed	As needed	12–24	12–24
TTE†	12–24	12–24	12	12
Pulse oximetry	24	12	Each visit	Each visit
Holter monitor	As needed	As needed	24	12–24
CMR‡/CCT§	60	36	24–36	12–24
Exercise test‖	36	24–36	24	12

*See Tables 3 and 4 for details on the ACHD AP classification system.
†Routine TTE may be unnecessary in a year when CMR imaging is performed unless clinical indications warrant otherwise.
‡CMR may be indicated for assessment of right ventricular size and function. Baseline study is recommended with periodic follow-up CMR, with frequency of repeat imaging determined by anatomic and physiological findings.
§CCT may be used if CMR is not feasible; the frequency should be weighed against radiation exposure.
‖6-minute walk test or CPET, depending on clinical indication.
ACHD indicates adult congenital heart disease; CCT, cardiac computed tomography; CMR, cardiovascular magnetic resonance imaging; CPET, cardiopulmonary exercise test; CXR, chest x-ray; ECG, electrocardiogram; and TTE, transthoracic echocardiogram.

4.3.5. Tetralogy of Fallot

Recommendations for TOF Referenced studies that support recommendations are summarized in Online Data Supplement 43. (See Section 4.3.6. for recommendations regarding evaluation and management of right ventricle–to-PA conduits.)		
COR	**LOE**	**Recommendations**
		Diagnostic
I	B-NR	**1. CMR is useful to quantify ventricular size and function, pulmonary valve function, pulmonary artery anatomy, and left heart abnormalities in patients with repaired TOF (S4.3.5-1).**
I	B-NR	**2. Coronary artery compression testing is indicated before right ventricle–to-PA conduit stenting or transcatheter valve placement in repaired TOF (S4.3.5-2).**
IIa	B-NR	**3. Programmed ventricular stimulation can be useful to risk-stratify adults with TOF and additional risk factors for SCD (S4.3.5-3–S4.3.5-8).**
IIa	C-EO	**4. In patients with repaired TOF, cardiac catheterization with angiography, if indicated, is reasonable to assess hemodynamics when adequate data cannot be obtained noninvasively in the setting of an arrhythmia, HF, unexplained ventricular dysfunction, suspected pulmonary hypertension or cyanosis.**
		Therapeutic
I	B-NR	**5. Pulmonary valve replacement (surgical or percutaneous) for relief of symptoms is recommended for patients with repaired TOF and moderate or greater PR with cardiovascular symptoms not otherwise explained (S4.3.5-9–S4.3.5-11).**
IIa	B-NR	**7. Pulmonary valve replacement (surgical or percutaneous) is reasonable for preservation of ventricular size and function in asymptomatic patients with repaired TOF and ventricular enlargement or dysfunction and moderate or greater PR (S4.3.5-1, S4.3.5-9, S4.3.5-12–S4.3.5-14).**
IIa	B-NR	**8. Primary prevention ICD therapy is reasonable in adults with TOF and multiple risk factors for SCD (S4.3.5-15–S4.3.5-17).**
IIb	C-EO	**9. Surgical pulmonary valve replacement may be reasonable for adults with repaired TOF and moderate or greater PR with other lesions requiring surgical interventions.**
IIb	C-EO	**10. Pulmonary valve replacement, in addition to arrhythmia management, may be considered for adults with repaired TOF and moderate or greater PR and ventricular tachyarrhythmia.**

Synopsis

Long-term survival after surgery for TOF continues to improve. However, residual hemodynamic and electrophysiological abnormalities are common in adulthood. Adults with repaired TOF face an increased risk of arrhythmias, exercise intolerance, HF, and death beginning in early adulthood (S4.3.5-1, S4.3.5-18–S4.3.5-20). Surgical repair of TOF has evolved over time, with relief of the RVOT obstruction usually involving infundibulotomy, resection of obstructive muscle bundles, and the use of a patch to enlarge the pathway from the right ventricle to the pulmonary arteries. These procedures result in scar tissue and create a dyskinetic and often aneurysmal area in the RVOT. Residual RVOT stenosis, branch PA stenosis, residual ASD or VSD, TR, RV dilation and dysfunction, aortic dilation, AR, and LV dysfunction

are some of the anatomic and functional abnormalities encountered in patients with repaired TOF. The most common hemodynamic sequela of TOF repair is PR. Current evidence confirms that adults with repaired TOF are at risk of severe PR, RV dilation and dysfunction, LV dysfunction and electromechanical dyssynchrony, all of which contribute to adverse clinical outcomes late after TOF repair (S4.3.5-1, S4.3.5-20–S4.3.5-24). Despite intense interest and numerous publications on pulmonary valve replacement in adults with repaired TOF, optimal timing for this intervention remains uncertain, and most studies have focused on preoperative RV volumes that would result in normalization of postoperative RV volumes (S4.3.5-9, S4.3.5-14, S4.3.5-25–S4.3.5-27). In adults with repaired TOF, prevalence rates for atrial and ventricular arrhythmias have been estimated to be 20% and 15%, respectively, with steep increases after 45 years of age (S4.3.5-28). The incidence of SCD after surgical repair of TOF is approximately 2% per decade (S4.3.5-18, S4.3.5-21, S4.3.5-24, S4.3.5-29, S4.3.5-30). Currently, factors associated with SCD in patients with TOF have largely been identified from observational, predominantly retrospective studies. Despite numerous studies that identified factors associated with malignant ventricular arrhythmias and SCD, risk stratification remains imperfect.

Primary prevention ICDs should generally be considered in patients who otherwise meet standard qualifying criteria (i.e., LV ejection fraction ≤35% with NYHA class II or III symptoms) (S4.3.5-31–S4.3.5-33). There may be a role for primary prevention ICDs in selected adults with TOF who have additional risk factors for SCD but would not meet standard criteria otherwise.

See Section 3.3 for recommendations on who should perform surgeries, cardiac catheterization, and other procedures in these patients; Section 3.4 for recommendations on diagnostic evaluation; Figure 4 for a diagnostic and treatment algorithm for repaired TOF with residual PR; and Table 27 for routine testing and follow-up intervals.

Recommendation-Specific Supportive Text

1. Cardiac magnetic resonance imaging is the gold standard imaging modality for quantification of right ventricular size and function in patients with repaired TOF. It also allows for quantification of valve regurgitation and pulmonary and systemic flows as well as delineating pulmonary artery anatomy and detection of scar tissue in the ventricular myocardium. Serial cardiac magnetic resonance imaging examinations allows for longitudinal follow-up of patients with repaired TOF and provides useful information that aids in the timing of pulmonary valve replacement (S4.3.5-1, S4.3.5-34–S4.3.5-37).

2. Before any surgical or percutaneous intervention in patients with TOF, the origins and proximal courses of the coronary arteries should be delineated. Patients with repaired TOF and abnormal coronary artery anatomy have a substantial risk of coronary artery compression during percutaneous pulmonary valve replacement or direct injury to the coronary during surgical pulmonary valve replacement. During cardiac catheterization, the coronary pattern may be demonstrated by performing simultaneous RVOT angiography and coronary angiography (S4.3.5-2). Coronary compression testing generally involves simultaneous coronary angiography or aortography and balloon dilation of the RVOT to ascertain whether a balloon expanded stent will compress the coronary artery.

3. Additional risk factors for SCD include (S4.3.5-24, S4.3.5-38, S4.3.5-39):

a. LV systolic or diastolic dysfunction
b. Nonsustained VT, QRS duration ≥180 ms
c. Extensive RV fibrosis by CMR

In adults with TOF, inducible sustained VT has been associated with an increased risk of clinical VT or SCD, beyond standard ECG, hemodynamic, and clinical factors (S4.3.5-5). Programmed ventricular

stimulation is most useful in risk stratifying patients at moderate risk of SCD rather than as a routine surveillance tool in low-risk populations (S4.3.5-7).

4. Cardiac catheterization is the only method that can accurately and reliably determine PA pressure and pulmonary vascular resistance.

5. Symptomatic patients (with dyspnea, chest pain, and/or exercise intolerance otherwise unexplained) with repaired TOF and severe PR who undergo pulmonary valve replacement often report improved functional class after intervention. Improvement in symptoms often correlates with a reduction in RV size and relief of PR (S4.3.5-9–S4.3.5-11). Symptom improvement is more likely in patients with underlying PS and PR than in patients with PR alone. For patients with significant LV or RV dysfunction, pulmonary valve replacement may not be tolerated or sufficient; therefore, evaluation by ACHD cardiologists and HF cardiologists is appropriate to decide appropriate course of action, particularly in deciding if a patient may be appropriate for mechanical circulatory support or heart transplant.

6. Pulmonary valve replacement is reasonable in patients with at least 2 of the following (S4.3.5-1, S4.3.5-9, S4.3.5-12–S4.3.5-14):

a. Mild or greater RV or LV dysfunction
b. Severe RV dilation (RV end-diastolic volume index ≥160 mL/m^2, RV end-systolic volume index ≥80 mL/m^2)
c. RV end-diastolic volume ≥2 times the LV end-diastolic volume
d. RV systolic pressure two thirds or higher systemic pressure
e. Progressive objective reduction in exercise capacity

The increasing use of CMR in the long-term follow-up for patients with repaired TOF has provided quantification of ventricular size, function, and PR. However, there is lack of consensus regarding optimal indications and timing of pulmonary valve replacement in this population. Pulmonary valve replacement results in reduction of RV volume and relief of PR; however, these are only surrogates for outcomes. Many patients with repaired TOF may deny symptoms yet demonstrate reduced exercise tolerance. Pulmonary valve replacement in such patients has been associated with improved functional status (S4.3.5-9, S4.3.5-10).

7. Risk factors for SCD include:

a. LV systolic or diastolic dysfunction
b. Nonsustained VT
c. QRS duration ≥180 ms
d. Extensive RV scarring
e. Inducible sustained VT at electrophysiological study

The largest study of patients with repaired TOF and ICDs included 121 patients from 11 North American and European sites followed for a median of 3.7 years after ICD implantation. Overall, 30% of patients received at least 1 appropriate ICD discharge, corresponding to annual appropriate shock rates of 7.7% and 9.8% for primary and secondary prevention indications, respectively (S4.3.5-16). Unlike patients with acquired HF, evidence suggests that patients with TOF who have inducible sustained polymorphic VT (hazard ratio: 12.9) fare as poorly as or worse than those with inducible sustained monomorphic VT (S4.3.5-5). Negative consequences associated with ICDs in adults with TOF must be carefully considered in selecting appropriate candidates. These include high rates of inappropriate shocks (5% to 6% per year), lead-related complications, and unfavorable patient-reported outcomes, including impaired QoL, anxiety, depression, and psychosexual complications (S4.3.5-15, S4.3.5-17, S4.3.5-40).

8. In patients with repaired TOF and moderate or greater PR who are undergoing cardiac surgery for a separate lesion (e.g., RVOT aneurysm, TR, branch PA stenosis, residual VS D, arrhythmia ablation, coronary artery revascularization, aortic root replacement), it may be reasonable to concurrently perform pulmonary valve replacement (S4.3.5-41).

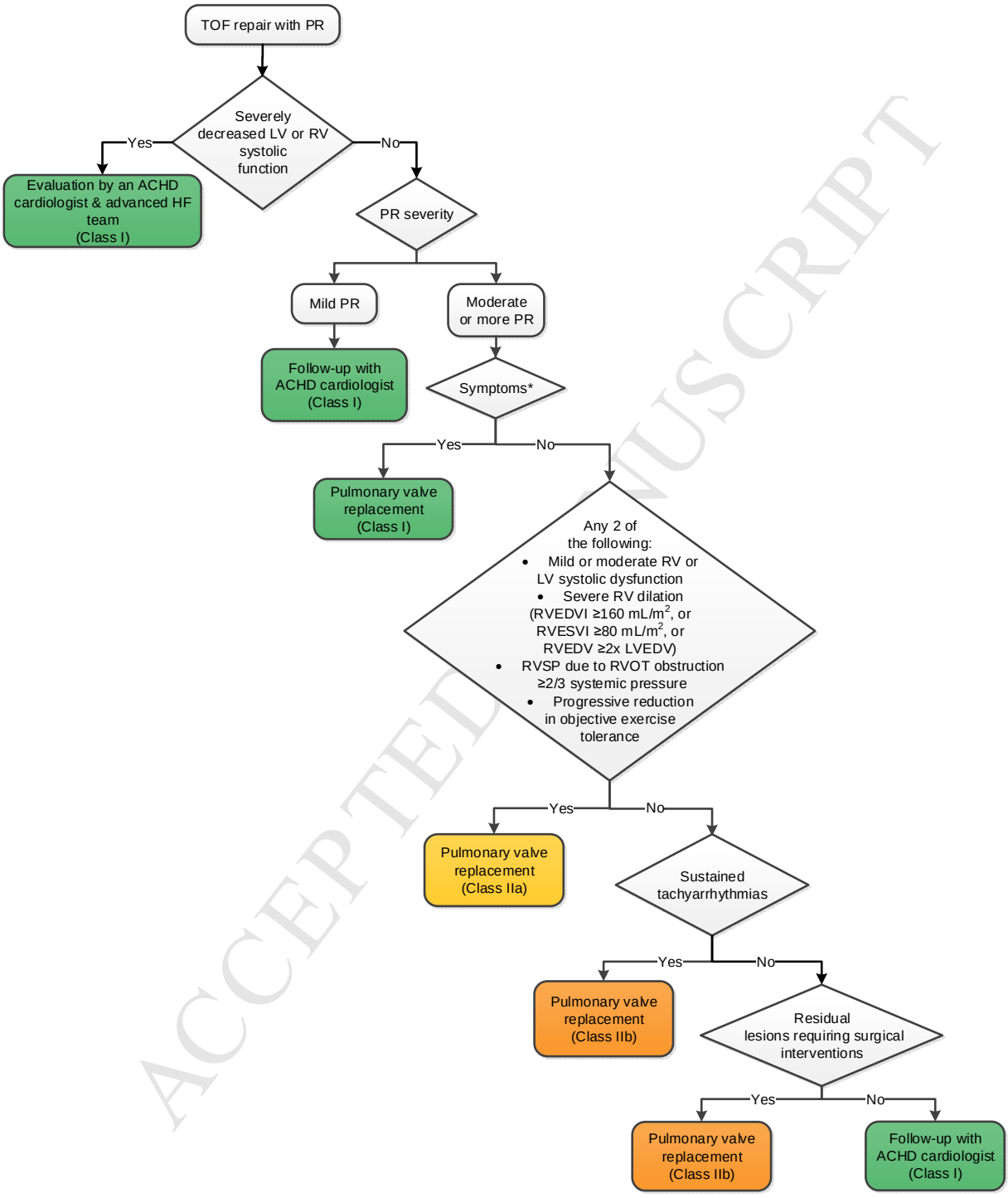
9. Although correction of the hemodynamic lesion (i.e., PR), may be clinically beneficial, pulmonary valve replacement alone has not consistently been demonstrated to reduce risk of subsequent VT or SCD (S4.3.5-42). Thus, in addition to pulmonary valve replacement, VT surgery and/or ICD implantation may be considered (S4.3.5-43).

Table 27. TOF: Routine Follow-Up and Testing Intervals

Frequency of Routine Follow-Up and Testing	Physiological Stage A* (mo)	Physiological Stage B* (mo)	Physiological Stage C* (mo)	Physiological Stage D* (mo)
Outpatient ACHD cardiologist	12–24	12	6–12	3–6
ECG	24	12	12	12
TTE†	24	12–24	12	6–12
Pulse oximetry	As needed	As needed	Each visit	Each visit
Holter monitor	As needed	As needed	12–24	12–24
CMR‡/CCT§	36	24–36	12–24	12–24
Exercise test‖	36–60	24–60	12–24	12–24

*See Tables 3 and 4 for details on the ACHD AP classification system.
†Routine TTE may be unnecessary in a year when CMR imaging is performed unless clinical indications warrant otherwise.
‡CMR may be indicated for assessment of right ventricular size and function, pulmonary valve function, pulmonary artery anatomy and left heart abnormalities. Baseline study is recommended with periodic follow-up CMR, with frequency of repeat imaging determined by anatomic and physiological findings.
§CCT may be used if CMR is not feasible and to evaluate origin and course of the coronary arteries, and cross-sectional imaging status–post-stent therapy. If cardiac CCT is used instead of CMR imaging, the frequency should be weighed against radiation exposure.
‖6-minute walk test or CPET, depending on clinical indication.
ACHD indicates adult congenital heart disease; CCT, cardiac computed tomography; CMR, cardiovascular magnetic resonance imaging; CPET, cardiopulmonary exercise test; ECG, electrocardiogram; TOF, tetralogy of Fallot; and TTE, transthoracic echocardiogram.

Figure 4. Pulmonary Valve Replacement in Patients With TOF Repair and PR



*Symptoms may include dyspnea, chest pain, and/or exercise intolerance referable to PR or otherwise unexplained.
ACHD indicates adult congenital heart disease; HF, heart failure; LV, left ventricular; LVEDV, left ventricular end diastolic volume; PR, pulmonary regurgitation; RV, right ventricular; RVEDV, right ventricular end diastolic volume; RVEDVI, right ventricular end diastolic volume index; RVESVI, right ventricular end systolic volume index; RVOT, right ventricular outflow tract; RVSP, right ventricular systolic pressure; and TOF, tetralogy of Fallot.

4.3.6. Right Ventricle–to-Pulmonary Artery Conduit

Recommendations for Right Ventricle–to-PA Conduit Referenced studies that support recommendations are summarized in Online Data Supplement 44.		
COR	**LOE**	**Recommendations**
		Diagnostic
I	**B-NR**	**1. Coronary artery compression testing with simultaneous coronary angiography and high-pressure balloon dilation in the conduit is indicated before right ventricle–to-PA conduit stenting or transcatheter valve placement (S4.3.6-1, S4.3.6-2).**
I	**B-NR**	**2. In patients with stented right ventricle–to-PA conduits and worsening PS or PR, evaluation for conduit complications should be performed, including fluoroscopy to evaluate for stent fracture and blood cultures to assess for IE (S4.3.6-3, S4.3.6-4).**
IIa	**C-LD**	**3. In adults with right ventricle–to-PA conduit and arrhythmia, congestive HF, unexplained ventricular dysfunction or cyanosis cardiac catheterization is reasonable to assess the hemodynamics (S4.3.6-5, S4.3.6-6).**
		Therapeutic
IIa	**B-NR**	**4. Right ventricle–to-PA conduit intervention is reasonable for adults with right ventricle–to-PA conduit and moderate or greater PR or moderate or greater stenosis (Table 22) with reduced functional capacity or arrhythmia (S4.3.6-7–S4.3.6-11).**
IIb	**B-NR**	**5. Right ventricle–to-PA conduit intervention may be reasonable for asymptomatic adults with right ventricle–to-PA conduit and severe stenosis or severe regurgitation with reduced RV ejection fraction or RV dilation (S4.3.6-12–S4.3.6-14).**

Synopsis

Right ventricle–to-PA conduits are widely used in the treatment of severe RVOT obstructive lesions including pulmonary atresia. These conduits may be homografts or prosthetic conduits with bioprosthetic valves used within the conduit. A minority of conduits may show early dysfunction because of kinking or aneurysmal dilation. The remainder will become dysfunctional over time and usually require replacement or intervention because of progressive stenosis within the conduit or at the valve, and/or valvular regurgitation, at a mean interval of 10 to 15 years from placement, although some conduits may last much longer than that (S4.3.6-15, S4.3.6-16).

See Section 3.3 for recommendations on who should perform surgeries, cardiac catheterization, and other procedures in these patients; Section 3.4 for recommendations on diagnostic evaluation; and Table 28 for routine testing and follow-up intervals.

Recommendation-Specific Supportive Text

1. Coronary compression testing generally involves simultaneous selective coronary angiography or aortography and balloon dilation in the RVOT, to ascertain whether a balloon expanded stent will compress the coronary artery. Coronary artery compression with conduit balloon angioplasty or stenting occurs in approximately 5% to 6% of patients with right ventricle–to-PA conduits and usually involves the left main/left anterior descending in those with conventional coronary anatomy. Patients with

anomalous right or left coronary arteries are at risk of coronary compression as are those with reimplanted coronary arteries.

2. Right ventricle–to-PA conduit stent fracture is common and occurred in approximately 26% of patients in the Melody Valve Investigational Device Exemption trial (S4.3.6-7), especially in patients who did not undergo conduit prestenting. Stent fracture typically presents with progressive stenosis and in those with transcatheter valves may also present with worsening PR. Patients with an increase in PR or PS should have fluoroscopic or x-ray assessment to rule out stent fracture.

Annualized rate of IE is up to 2.4% of patients treated with Melody valve implantation, but infection in most cases involves valves other than the Melody valve, including left-sided valves (S4.3.6-3, S4.3.6-17–S4.3.6-20). Patients typically present with fever and malaise as well as worsening PS or PR. Cases may respond well to medical management with intravenous antibiotics if IE is identified and treatment initiated early in the disease course, although sometimes surgical removal of the valve may be necessary.

3. Although noninvasive imaging with echocardiography, CMR, or CTA provides a reasonably comprehensive assessment of ventricular function, conduit function, and patency as well as pulmonary arterial anatomy, cardiac catheterization is reasonable to directly assess hemodynamics in the setting of clinical decompensation. Direct assessment of intracardiac and pulmonary arterial pressures and cardiac output provides useful information regarding volume status, pulmonary arterial resistance, and degree of conduit stenosis or regurgitation. Because of anatomic and technical factors, noninvasive imaging may provide equivocal information and may underestimate the degree of conduit stenosis or regurgitation; invasive assessment is especially important in such cases.

4. Right ventricle–to-PA conduit intervention includes surgical replacement or percutaneous stenting and/or transcatheter valve placement. Patients with moderate or greater conduit stenosis (Table 22) and/or regurgitation who have reduced exercise capacity or arrhythmias can benefit from surgical or transcatheter conduit intervention to relieve stenosis and/or regurgitation. Transcatheter stenting and pulmonary valve replacement may be performed with high procedural success and low mortality rates, and result in improved hemodynamics and improved exercise capacity. Surgical conduit replacement carries a higher risk of periprocedural complications with good long-term outcomes. Predictors of conduit dysfunction and reoperation include placement of small diameter conduits; therefore, insertion of conduits with the largest possible diameter should be attempted (S4.3.6-8), anticipating that subsequent valve replacement may be via a transcatheter approach.

5. Right ventricle–to-PA conduit intervention, which includes surgical replacement or percutaneous stenting and/or transcatheter valve placement, may be reasonable in asymptomatic patients with severe right ventricle–to-PA conduit stenosis or regurgitation in the presence of reduced RV systolic function or dilation in the expectation of improvement in hemodynamics, decreased RV size, improved RV stroke volume, and improved RV ejection fraction. Moreover, peak oxygen consumption and anaerobic threshold may also improve with conduit intervention.

Table 28. Right Ventricle–to-PA Conduit: Routine Follow-Up and Testing Intervals

Frequency of Routine Follow-Up and Testing	Physiological Stage A* (mo)	Physiological Stage B* (mo)	Physiological Stage C* (mo)	Physiological Stage D* (mo)
Outpatient ACHD cardiologist	12–24	12	6–12	3–6
ECG	12–24	12	12	12
TTE†	12–24	12	12	12
CMR‡/CCT§	36–60	36–60	12–24	12–24

Exercise test‖		As needed	As needed	12–24	12–24

*See Tables 3 and 4 for details on the ACHD AP classification system.
†Routine TTE may be unnecessary in a year when CMR imaging is performed unless clinical indications warrant otherwise.
‡CMR may be indicated for assessment of right ventricular size and function and valvular function, conduit anatomy and pulmonary artery anatomy. Baseline study is recommended with periodic follow-up CMR, with frequency of repeat imaging determined by anatomic and physiological findings.
§CCT may be used if CMR is not feasible and to evaluate cross-sectional imaging status–post-stent therapy. If CCT is used instead of CMR imaging, the frequency should be weighed against radiation exposure.
‖6-minute walk test or CPET, depending on clinical indication.
ACHD indicates adult congenital heart disease; CCT, cardiac computed tomography; CMR, cardiovascular magnetic resonance; CPET, cardiopulmonary exercise test; ECG, electrocardiogram; PA, pulmonary artery; and TTE, transthoracic echocardiogram.

4.4. Complex Lesions

4.4.1. Transposition of the Great Arteries

4.4.1.1. Transposition of the Great Arteries With Atrial Switch

Recommendations for d-TGA With Atrial Switch Referenced studies that support recommendations are summarized in Online Data Supplement 45.		
COR	**LOE**	**Recommendations**
		Diagnostic
I	**C-EO**	**1. Ambulatory monitoring for bradycardia or sinus node dysfunction is recommended for adults with d-TGA with atrial switch, especially if treated with beta blockers or other rate-slowing agents.**
I	**C-EO**	**2. Adults with d-TGA with atrial switch repair should undergo annual imaging with either echocardiography or CMR to evaluate for common long-term complications of the atrial switch.**
IIa	**C-LD**	**3. Assessment for a communication through the interatrial baffle or venous stenosis is reasonable for adults with d-TGA with atrial switch, particularly if transvenous pacemaker/ICD implantation is considered or leads are already present (S4.4.1.1-1).**
		Therapeutic
I	**B-NR**	**4. GDMT with appropriate attention to the need for anticoagulation is recommended to promptly restore sinus rhythm for adults with d-TGA with atrial switch repair presenting with atrial arrhythmia (S4.4.1.1-2).**

Synopsis

Common problems for patients with d-TGA with atrial switch (Mustard or Senning procedure) include leak across or obstruction of the venous pathways, arrhythmias, need for pacemakers/defibrillators, and systolic dysfunction of the systemic ventricle. Although reports describing these sequelae abound, data that inform management decisions are sparse, and many of the most common clinical issues cannot be addressed by data-supported recommendations. Two such issues are medical therapy for RV dysfunction and prevention of SCD.

The systematic review report, “Medical Therapy for Systemic Right Ventricles: A Systematic Review (Part 1) for the 2018 AHA/ACC Guideline for the Management of Adults With Congenital Heart Disease,” has the complete systematic evidence review (S4.4.1.1-3) for additional data and analyses. The results from the question “Are outcomes improved with angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, beta blockers, or aldosterone antagonists alone or in combination in patients with a systemic right ventricle?” and the writing committee’s review of the totality of the

literature demonstrated that medical therapy for systolic ventricular dysfunction remains largely uncertain. Consequently, no recommendations regarding specific medical therapy for systolic dysfunction of the systemic right ventricle can be made.

In addition to the report provided by the ERC regarding angiotensin-converting enzyme inhibitor, angiotensin-receptor blocker, and aldosterone antagonist use for patients with systemic right ventricles, beta blockers and other commonly used HF medications lack data to support recommendations in the treatment of atrial switch patients (S4.4.1.1-4–S4.4.1.1-7). Concerns regarding routine use of beta blockers for asymptomatic RV dysfunction include potentially greater predisposition to bradycardia and limited distensibility of the interatrial baffle, which creates a preload limited physiology (S4.4.1.1-8). Although no clear benefit has been demonstrated for HF medical therapy overall, there is speculation of benefit in more symptomatic patients or those with larger and/or more dysfunctional right ventricles.

Patients with dysfunction of the systemic right ventricle are at risk of developing ventricular arrhythmias. The role of ICD implantation for primary prevention of arrhythmia in patients with a low systemic ventricular ejection fraction is uncertain. This practice is unsupported by any research and cannot be universally recommended. Many such patients do not progress to receive therapies from their device (S4.4.1.1-2). Decisions regarding primary prevention ICD implantation is based on the patients' full clinical presentation and in consultation with cardiac electrophysiologists with ACHD expertise.

See Section 3.3 for recommendations on who should perform surgeries, cardiac catheterization, and other procedures in these patients; Section 3.4 for recommendations on diagnostic evaluation; Table 29 for routine testing and follow-up intervals; and Online Data Supplement 25 for referenced studies.

Recommendation-Specific Supportive Text

1. There is a progressive loss of sinus rhythm in patients who have undergone the Senning or Mustard procedure for d-TGA, and the development of significant sinus bradycardia, while often asymptomatic, is important to identify, because it will influence and limit treatment with antiarrhythmic medications.

2. Patients with d-TGA with atrial switch have abnormal cardiac anatomy, with common long-term complications including systemic RV dysfunction, TR, subpulmonic obstruction, obstruction of systemic or pulmonary venous return, and baffle leaks. Imaging should be goal-directed with an understanding of potential long-term sequelae, and nuanced for the patient’s particular circumstances (S4.4.1.1-9). CMR offers quantification of systemic RV function and should be used routinely unless there are contraindications. Late gadolinium enhancement is an important tool that can identify areas of myocardial scar that are associated with adverse clinical markers including atrial arrhythmia (S4.4.1.1-10). The importance of change in late gadolinium enhancement over time in directing care is less clear, so repetitive use of gadolinium contrast for this purpose is of less value.

3. Recognizing both the abnormal venous pathways after atrial switch palliation and the risk of thromboembolic complications from transvenous pacing leads in those with intracardiac shunts, thorough assessment of the venous pathways for either obstruction or baffle leak is a prudent step before lead placement or revision. Baffle leaks should be sought because they are common and may alter treatment considerations such as thromboembolic concerns or options for closure.

Echocardiography using agitated saline contrast is a sensitive method for this assessment. It is unnecessary on every study, but interval assessment of baffle leak is appropriate, especially in circumstances where therapy may be altered by the result. In some patients, injection in upper and lower extremities may be necessary to evaluate superior and/or inferior systemic venous baffle leak,

respectively, because a negative study from an injection in upper extremity may not exclude an inferior systemic venous baffle leak. Assessment for baffle leak may involve use of TTE with agitated saline contrast, TEE, intracardiac echocardiography, or angiography (S4.4.1.1-1).

4. Sustained intra-atrial reentrant tachycardia is a potential cause of SCD in adults who have undergone atrial switch and puts patients at risk for thromboembolism. Treatment to maintain sinus rhythm may involve antiarrhythmic medication or catheter ablation. Although there are not data demonstrating that maintenance of sinus rhythm prevents SCD, there is evidence that atrial arrhythmias preceded or coexisted with VT in 50% of cases, suggesting that atrial arrhythmias are a common trigger for ventricular arrhythmias (S4.4.1.1-2, S4.4.1.1-11).

There is a biologically plausible explanation that may include longer atrial tachycardia cycle lengths in the context of extensive atrial sutures/scar that could favor rapid (e.g., 1:1) ventricular conduction, a reduction in stroke volume with faster heart rates attributable to poor atrial transport, and myocardial ischemia despite the absence of CAD attributable to an inefficient coronary circulation supplying the systemic ventricle (S4.4.1.1-12). Efforts to maintain sinus rhythm or atrial pacing (and not simply rate control) should be the initial strategy of management, acknowledging that patients may rarely tolerate permanent atrial tachycardia when attempts to maintain sinus rhythm have failed.

Atrial arrhythmias predominantly involve tissue of right atrial origin which, because of the surgical anatomy, is found primarily in the pulmonary venous atrium, making access for catheter ablation challenging.

Table 29. d-TGA With Atrial Switch: Routine Follow-Up and Testing Intervals

Frequency of Routine Follow-Up and Testing	Physiological Stage A* (mo)	Physiological Stage B* (mo)	Physiological Stage C* (mo)	Physiological Stage D* (mo)
Outpatient ACHD cardiologist	12	12	6–12	3–6
ECG	12	12	6–12	6–12
TTE†	12–24	12–24	12	12
Pulse oximetry	12	12	Each visit	Each visit
Holter monitor	24	24	12	12
CMR‡/CCT§	24–36	24	12–24	12–24
Exercise test‖	36	36	24	12

*See Tables 3 and 4 for details on the ACHD AP classification system.
†Routine TTE may be unnecessary in a year when CMR imaging is performed unless clinical indications warrant otherwise.
‡CMR may be indicated for assessment of ventricular size and function, systemic and venous baffle obstruction and leaks, and valvular function. Baseline study is recommended with periodic follow-up CMR, with frequency of repeat imaging determined anatomic and physiological findings.
§CCT may be used if CMR is not feasible and to evaluate cross-sectional imaging status–post-stent therapy. If CCT is used instead of CMR imaging, the frequency should be weighed against radiation exposure.
‖6-minute exercise test or CPET, depending on clinical indication.
ACHD indicates adult congenital heart disease; CCT cardiac computed tomography; CMR, cardiovascular magnetic resonance imaging; CPET, cardiopulmonary exercise test; d-TGA, dextro-transposition of the great arteries; ECG, electrocardiogram; and TTE, transthoracic echocardiogram.

4.4.1.2. Transposition of the Great Arteries With Arterial Switch

Recommendations for d-TGA With Arterial Switch Referenced studies that support recommendations are summarized in Online Data Supplement 46.		
COR	**LOE**	**Recommendations**
Diagnostic		
I	**C-LD**	**1) Baseline and serial imaging with either echocardiography or CMR should be performed in adults with d-TGA with arterial switch who have neoaortic dilation, valve dysfunction or PA or branch PA stenosis or ventricular dysfunction (S4.4.1.2-1–S4.4.1.2-3).**
I	**C-EO**	**2) Coronary revascularization for adults with d-TGA with arterial switch should be planned by surgeons or interventional cardiologists with expertise in revascularization in collaboration with ACHD providers to ensure coronary and pulmonary artery anatomy are understood**
IIa	**B-NR**	**3) It is reasonable to perform anatomic evaluation of coronary artery patency (catheter angiography, or CT or MR angiography) in asymptomatic adults with d-TGA with arterial switch (S4.4.1.2-4, S4.4.1.2-5).**
IIa	**C-EO**	**4) Physiological tests of myocardial perfusion for adults with d-TGA after arterial switch can be beneficial for assessing symptoms suggestive of myocardial ischemia.**
IIa	**C-EO**	**5) GDMT is reasonable to determine the need for coronary revascularization for adults with d-TGA after arterial switch (S4.4.1.2-6–S4.4.1.2-8).**
Therapeutic		
IIa	**C-EO**	**6) GDMT is reasonable to determine indications for aortic valve replacement in adults with d-TGA after arterial switch with severe neoaortic valve regurgitation (S4.4.1.2-6).**
IIa	**C-EO**	**7) Catheter or surgical intervention for PS is reasonable in adults with d-TGA after arterial switch with symptoms of HF or decreased exercise capacity attributable to PS.**

Synopsis

Complications after the arterial switch include: 1) stenosis at the arterial anastomotic sites, most commonly supravalvular PS; 2) neoaortic root dilation; 3) neoaortic valve regurgitation (native pulmonary valve); and 4) coronary obstruction. Evaluation for the first 3 complications listed is accomplished by usual imaging, including echocardiography, CCT, and/or CMR. Coronary complications are inadequately evaluated by resting echocardiography, and stress imaging in asymptomatic patients is not sensitive. It is unclear that coronary abnormalities will present de novo or that those present in childhood will progress. However, because patients did not receive an arterial switch before the late 1980s, the long-term natural history of the coronary arteries after arterial switch is still unknown. This is particularly true regarding the impact of risks for concomitant acquired coronary artery disease in patients whose coronary substrate is not normal. At this time, investigation and management of suspected coronary abnormalities in adults with the arterial switch for TGA should largely be symptom-driven and in accordance with existing guidelines for acquired coronary artery diseases.

Several residua and sequelae in adults after arterial switch merit consideration of reoperation. Severe RVOT obstruction (Table 22) not amenable or responsive to percutaneous treatment is an

indication for reoperation; lesser degrees of obstruction can be considered an indication for intervention if greater degrees of exercise are desired. Pulmonary valve replacement or repair is often considered when severe PR is present and there is significant RV dilation or RV dysfunction. Coronary ostial stenosis late after arterial switch may be repaired by coronary artery bypass graft surgery or ostial arterioplasty techniques. The threshold aortic diameter at which dissection/rupture risk exceeds the risk of operation is not known, and consequently the threshold for prophylactic operation for neoaortic root dilation is undefined.

See Section 3.3 for recommendations on who should perform surgeries, cardiac catheterization, and other procedures in these patients; Section 3.4 for recommendations on diagnostic evaluation; and Table 30 for routine testing and follow-up intervals.

Recommendation-Specific Supportive Text

1. Imaging in patients after arterial switch should be performed with specific sequelae in mind, including PS (recognizing the Lecompte maneuver has been used during surgery in most), and neoaortic root and valve problems. Some patients with early arterial switch repairs had right ventricle–to-PA conduits placed and may have related complications.

2. Because of nuances of the arterial switch, decisions regarding coronary intervention should be considered jointly by ACHD providers and those with expertise in coronary revascularization techniques. Abnormalities commonly occur proximally and close to the anteriorly positioned coronary buttons. Coronary buttons are usually located posterior to the main PA after the Lecompte maneuver. Revascularization techniques may include revision of the coronary buttons, ostioplasty, interposition grafts, or coronary bypass grafting.

3. There is evidence that coronary abnormalities are common after arterial switch (6% to 10%), especially in the setting of coronary anomalies at birth, or extensive manipulation of the coronaries at the time of the operation. However, most coronary problems and events described so far tend to occur in childhood in the first few years after surgery, with limited experience in adults (S4.4.1.2-1, S4.4.1.2-2, S4.4.1.2-4, S4.4.1.2-5), although the prevalence of coronary issues may increase as the population ages. Physiological testing lacks sensitivity. Therefore, a benchmark assessment of the anatomic course and patency of the coronary arteries (i.e., catheter angiography or CT angiography) is prudent in adults in whom this information has not already been obtained. MR coronary angiography may also be an option for evaluating coronary patency (S4.4.1.2-9). Thereafter, coronary investigations will be prompted largely by symptoms.

4. Once the coronary anatomy in an arterial switch recipient is documented, there is little justification for serial anatomic imaging in an asymptomatic individual. Symptomatic patients should be offered stress physiological imaging and repeat anatomic imaging considered if symptoms are suggestive of coronary ischemia (S4.4.1.2-8).

5. Decisions about the indications and approach for coronary intervention after an arterial switch can be guided according to management recommendations for care of atherosclerotic coronary disease, emphasizing prudent medical therapy and a symptom-guided approach to intervention (S4.4.1.2-6, S4.4.1.2-8). The unique aspects of the anatomic abnormalities and unusual course of the proximal coronary arteries must be kept in mind, mandating collaboration between ACHD providers and those with the necessary surgical or interventional expertise.

6. Although some degree of neoaortic valve regurgitation is common, surgery to replace the neoaortic valve has only rarely been reported. Indications for valve replacement should be based on LV size and/or symptoms according to the 2014 VHD guideline (S4.4.1.2-6). The more common concern is dilation of

the neoaortic root with preserved aortic valve competence. Valve-sparing root replacement is often considered in such cases, but surgical options should be individualized based upon anatomy and changes over time. There are not data to support a specific aortic diameter beyond which the risk of dissection or rupture increases sufficiently to warrant prophylactic aortic replacement.

7. PS affects 5% to 15% of patients after arterial switch (S4.4.1.2-1–S4.4.1.2-3, S4.4.1.2-10, S4.4.1.2-11) and may occur anywhere in the pulmonary tree including the pulmonary valve, main PA, and branch pulmonary arteries. Interventional decisions should be guided by a combination of symptoms and severity of stenosis.

Table 30. d-TGA With Arterial Switch: Routine Follow-Up and Testing Intervals

Frequency of Routine Follow-Up and Testing	Physiological Stage A* (mo)	Physiological Stage B* (mo)	Physiological Stage C* (mo)	Physiological Stage D* (mo)
Outpatient ACHD cardiologist	12–24	12	6–12	3–6
ECG	12–24	12–24	12	6
TTE†	12–24	12–24	12	12
CMR‡/CCT§	36–60	24–36	12–24	12–24
Exercise test‖	36–60	36–60	24–36	12–24

*See ACHD AP classification Table 4.
†Routine TTE may be unnecessary in a year when CMR imaging is performed unless clinical indications warrant otherwise.
‡CMR may be indicated for assessment of neoaortic size, the origin and proximal course of the coronary arteries, branch pulmonary arteries, ventricular function and valvular function. Baseline study is recommended with periodic follow-up CMR, with frequency of repeat imaging determined by anatomic and physiological findings.
§CCT or catheterization once to establish knowledge of coronary artery anatomy and then as warranted by clinical condition. CCT may be used if CMR is not feasible and to evaluate coronary artery anatomy and cross-sectional imaging status-post stent therapy. If CCT is used instead of CMR imaging, the frequency should be weighed against radiation exposure.
‖6-minute exercise test or CPET, depending on clinical indication.
ACHD indicates adult congenital heart disease; CCT, cardiac computed tomography; CMR, cardiovascular magnetic resonance imaging; CPET, cardiopulmonary exercise test; d-TGA, dextro-transposition of the great arteries; ECG, electrocardiogram; and TTE, transthoracic echocardiogram.

4.4.1.3. Transposition of the Great Arteries With Rastelli Type Repair

See Section 3.3 for recommendations on who should perform surgeries, cardiac catheterization, and other procedures in these patients; and Section 3.4 for recommendations on diagnostic evaluation.

The Rastelli operation is performed in patients with d-TGA with VSD and PS and for variations of double outlet right ventricle with PS. The operation consists of 2 main components:

1. An intracardiac baffle that directs oxygenated blood from the left ventricle via a nonrestrictive VSD to the aorta.
2. A right ventricle–to-PA conduit, which is usually valved.

The operation is designed to use the morphologic left ventricle as the systemic ventricle and the morphologic right ventricle as the subpulmonic ventricle. Long-term considerations after the Rastelli operation include:

1. Right ventricle–to-PA conduit dysfunction (Section 4.3.6)
2. VSD patch leaks/dehiscence (Section 4.1.3)
3. LV-to-aorta internal baffle stenosis (Section 4.2.3)

4. Scar-based VT

Medical treatment, catheter interventions, and surgical interventions for each of these conditions, which may occur in isolation or in combination, may be considered in accordance with the recommended treatments for each of the individual conditions as outlined in this guideline document.

4.4.1.4. Congenitally Corrected Transposition of the Great Arteries

Recommendations for Congenitally Corrected Transposition of the Great Arteries Referenced studies that support recommendations are summarized in Online Data Supplement 47.		
COR	**LOE**	**Recommendations**
		Diagnostic
IIa	**C-LD**	**1. CMR is reasonable in adults with CCTGA to determine systemic RV dimensions and systolic function (S4.4.1.4-1, S4.4.1.4-2).**
		Therapeutic
I	**B-NR**	**2. Tricuspid valve replacement is recommended for symptomatic adults with CCTGA and severe TR, and preserved or mildly depressed systemic ventricular function (S4.4.1.4-3, S4.4.1.4-4).**
IIa	**C-LD**	**3. Tricuspid valve replacement is reasonable for asymptomatic adults with CCTGA and severe TR with dilation or mild dysfunction of the systemic ventricle (S4.4.1.4-3).**
IIb	**B-NR**	**4. Conduit intervention/replacement may be considered for adults with CCTGA and symptomatic subpulmonary left ventricle–to-PA conduit dysfunction, recognizing that unloading the subpulmonary ventricle may have a detrimental impact on systemic atrioventricular valve function (S4.4.1.4-5).**

Synopsis

The clinical course of adults with CCTGA often depends on the presence and severity of associated cardiac anomalies (S4.4.1.4-6), which will often have required pediatric intervention. Rarely, CCTGA may be first diagnosed in adulthood, particularly if patients do not have associated cardiac lesions. Conduction abnormalities are common, and the prevalence of spontaneous complete heart block increases with age (S4.4.1.4-7, S4.4.1.4-8). PS, ASD, and VSD are common. Seventy percent to 90% of patients with CCTGA have a dysplastic or Ebstein-like malformation of the tricuspid valve. This anatomically abnormal systemic atrioventricular valve is at risk of progressive TR, which is an independent predictor of death in CCTGA (S4.4.1.4-4, S4.4.1.4-9).

The systematic review report, "Medical Therapy for Systemic Right Ventricles: A Systematic Review (Part 1) for the 2018 AHA/ACC Guideline for the Management of Adults With Congenital Heart Disease." (S4.4.1.4-10) addressed the role of medical therapies for management of functional deterioration in systemic RVs (S4.4.1.4-11–S4.4.1.4-13) (see additional details in Section 3.17).

See Section 3.3 for recommendations on who should perform surgeries, cardiac catheterization, and other procedures in these patients; Section 3.4 for recommendations on diagnostic evaluation; and Table 31 for routine testing and follow-up intervals.

Recommendation-Specific Supportive Text

1. CMR is useful for quantification of systemic RV size and function (S4.4.1.4-1, S4.4.1.4-2). Administration of gadolinium contrast is useful in identifying fibrotic myocardium demonstrated by late gadolinium enhancement (S4.4.1.4-14).

2. Symptomatic adults with CCTGA and severe TR with no more than mildly depressed systemic ventricular function should be evaluated for tricuspid valve replacement. In general, tricuspid valve replacement is preferred to tricuspid repair in the adult CCTGA population. TR is often because of a dysplastic tricuspid valve and has been shown to be an independent predictor of death in CCTGA patients (S4.4.1.4-4). Systemic RV dysfunction is often attributable to longstanding TR, and efforts should be made to relieve the TR before worsening dysfunction (S4.4.1.4-3, S4.4.1.4-9). Tricuspid valve repair has been attempted; however, recurrent clinically significant TR is observed frequently after tricuspid valve repair in patients with CCTGA; hence, valve replacement is preferred (S4.4.1.4-15).

3. Many adult CCTGA patients are referred for tricuspid valve replacement late, when symptomatic and already suffering from moderate-to-severe TR and ventricular dysfunction (S4.4.1.4-16). In CCTGA patients referred for TVR, 10-year postoperative survival is <20% when the preoperative systemic ventricular ejection fraction is <40% (S4.4.1.4-9) or 44% (S4.4.1.4-3). In a retrospective review of 46 CCTGA patients referred for TR surgery, preoperative systemic ventricular ejection fraction was the only independent predictor of postoperative systemic ventricular ejection fraction at 1 year (S4.4.1.4-3).

4. Adults with CCTGA and pulmonary atresia or stenosis were often managed in childhood by placing a conduit from the morphologic LV to the PA, and progressive conduit dysfunction is common. Conduit intervention or replacement will diminish the pressure in the subpulmonic ventricle and may result in ventricular septal shift toward the subpulmonic left ventricle, including the septal leaflet of the systemic tricuspid valve and thus can result in worsening of TR and a detrimental impact on systemic RV function (S4.4.1.4-5).

Table 31. CCTGA: Routine Follow-Up and Testing Intervals

Frequency of Routine Follow-Up and Testing	Physiological Stage A* (mo)	Physiological Stage B* (mo)	Physiological Stage C* (mo)	Physiological Stage D* (mo)
Outpatient ACHD cardiologist	12	12	6–12	3–6
ECG	12	12	12	12
TTE†	12–24	12	12	12
Pulse oximetry	As needed	As needed	Each visit	Each visit
Holter monitor	12–60	12–60	12–36	12
CMR‡/CCT§	36–60	36–60	12–24	12
Exercise test ‖	36–60	36–60	12–24	12

*See Tables 3 and 4 for details on the ACHD AP classification system.
†Routine TTE may be unnecessary in a year when CMR imaging is performed unless clinical indications warrant otherwise.
‡CMR may be indicated for assessment of ventricular size and function and valvular function. Baseline study is recommended with periodic follow-up CMR, with frequency of repeat imaging determined by anatomic and physiological findings.
§CCT may be used if CMR is not feasible. If CCT is used instead of CMR imaging, the frequency should be weighed against radiation exposure.
‖6-minute walk test or CPET, depending on clinical indication.
ACHD indicates adult congenital heart disease; CCT, cardiac computed tomography; CCTGA, congenitally corrected transposition of the great arteries; CMR, cardiovascular magnetic resonance imaging; CPET, cardiopulmonary exercise test; ECG, electrocardiogram; and TTE, transthoracic echocardiogram.

4.4.2. Fontan Palliation of Single Ventricle Physiology (Including Tricuspid Atresia and Double Inlet Left Ventricle)

Recommendations for Fontan Palliation of Single Ventricle Physiology Referenced studies that support recommendations are summarized in Online Data Supplement 48.		
COR	**LOE**	**Recommendations**
		Diagnostic
I	C-LD	1. New presentation of an atrial tachyarrhythmia in adults with Fontan palliation should be managed promptly and include prevention of thromboembolic events and consultation with an electrophysiologist with CHD expertise (S4.4.2-1, S4.4.2-2).
I	C-EO	2. Adults after Fontan palliation should be evaluated annually with either echocardiography or CMR.
I	C-EO	3. Cardiac catheterization should be performed in adults before initial Fontan surgery or revision of a prior Fontan connection to assess suitability of preintervention hemodynamics for Fontan physiology or revision of a prior Fontan connection.
I	C-EO	4. New onset or worsening atrial tachyarrhythmias in adults with single ventricle after Fontan palliation should prompt a search for potential hemodynamic abnormalities, which may necessitate imaging and/or cardiac catheterization.
IIa	B-R	5. In adults with Fontan palliation, it is reasonable to encourage a regular exercise program appropriate to their abilities (S4.4.2-3–S4.4.2-5).
IIa	C-LD	6. Imaging of the liver (ultrasonography, CMR, CT) and laboratory evaluation of liver function for fibrosis, cirrhosis, and/or hepatocellular carcinoma are reasonable in adults after Fontan palliation (S4.4.2-6).
IIa	C-EO	7. In adults after Fontan palliation, it is reasonable to perform biochemical and hematological testing on an annual basis especially for liver and renal function.
IIa	C-LD	8. Cardiac catheterization can be useful to evaluate a symptomatic adult after Fontan palliation when noninvasive testing is insufficient to guide therapy (S4.4.2-7, S4.4.2-8).
IIa	C-LD	9. Evaluation for cardiac transplantation is reasonable in adults with Fontan palliation and signs and symptoms of protein-losing enteropathy (S4.4.2-9–S4.4.2-12).
IIb	C-EO	10. It may be reasonable to perform catheterization in asymptomatic adults after Fontan palliation to evaluate hemodynamics, oxygenation and cardiac function to guide optimal medical, interventional and/or surgical therapy.
		Therapeutic
I	C-EO	11. Anticoagulation with a vitamin K antagonist is recommended for adults with Fontan palliation with known or suspected thrombus, thromboembolic events, or prior atrial arrhythmia, and no contraindications to anticoagulation.
IIa	C-LD	12. Catheter ablation can be useful in adults after Fontan palliation with intra-atrial reentrant tachycardia or focal atrial tachycardia (S4.4.2-13–S4.4.2-15).

IIa	**C-LD**	**13. Fontan revision surgery, including arrhythmia surgery as indicated, is reasonable for adults with atriopulmonary Fontan connections with recurrent atrial tachyarrhythmias refractory to pharmacological therapy and catheter ablation who have preserved systolic ventricular function and severe atrial dilation (S4.4.2-16–S4.4.2-18).**
IIa	**B-R**	**14. Pulmonary vasoactive medications can be beneficial to improve exercise capacity in adults with Fontan repair (S4.4.2-19–S4.4.2-25).**
IIb	**B-NR**	**15. Antiplatelet therapy or anticoagulation with a vitamin K antagonist may be considered in adults after Fontan palliation without known or suspected thrombus, thromboembolic events, or prior arrhythmia (S4.4.2-26).**
IIb	**C-LD**	**16. Reoperation or intervention for structural/anatomic abnormalities in a Fontan palliated patient with symptoms or with failure of the Fontan circulation may be considered (S4.4.2-27).**

Synopsis

Fontan repairs are the most common palliation of single ventricle physiology seen in adults. The physiology is complex, with long-term consequences related to the obligatory elevation in central venous pressure and reduced cardiac output. Proposed medical therapy for the "failing Fontan," which may manifest as protein-losing enteropathy, hepatic dysfunction, lower extremity venous congestion, and/or exercise limitation, has included many different modalities, although there is limited proven benefit in published research. Options for medical therapy include aldosterone antagonists or subcutaneous unfractionated heparin, which may stabilize the proteoglycan layer of the gut. PAH therapies are of increasing interest. Endothelin antagonists have been studied in a single RCT, which showed improved exercise capacity in 75 subjects randomized to bosentan compared with placebo (S4.4.2-19). Two other small nonrandomized studies demonstrated minimal response to therapy (S4.4.2-22, S4.4.2-23).

Corticosteroids, specifically budesonide, may be helpful for Fontan patients with hypoalbuminemia in the setting of protein-losing enteropathy poorly responsive to other therapies. Budesonide seems to have fewer systemic effects than other oral steroids; however, close monitoring for signs of hypercortisolism remains necessary (S4.4.2-28, S4.4.2-29). Octreotide may be considered; it is a therapy with favorable but very limited anecdotal experience reported, with further research needed (S4.4.2-28, S4.4.2-30). A combination of these therapies may be applied in an affected patient, as such strategies collectively appear to have produced improved outcome compared with historic controls (S4.4.2-31).

Fontan surgery has been associated with prolongation of atrial refractory periods, extensive atrial scarring, and intra-atrial conduction delay (S4.4.2-32–S4.4.2-38). Sinus node dysfunction occurs in up to 45% of adults during long-term follow-up after Fontan surgery and has been associated with a reduction in preload to the single ventricle, increased pulmonary venous pressure, reduced cardiac output, plastic bronchitis, and protein-losing enteropathy (S4.4.2-39–S4.4.2-43). Transvenous atrial pacing may be feasible in most adults with atriopulmonary Fontan connections and in some with intracardiac lateral tunnels (S4.4.2-44), although the potential for thrombotic complications must be addressed. Ventricular pacing may be performed via the coronary sinus in selected patients, but most require an epicardial approach (S4.4.2-45, S4.4.2-46). Management of atrial arrhythmias is discussed in the associated recommendations.

See Section 3.3 for recommendations on who should perform surgeries, cardiac catheterization and other procedures in these patients; Section 3.4 for recommendations on diagnostic evaluation; and Table 32 for routine testing and follow-up intervals.

Recommendation-Specific Supportive Text

1. Atrial tachyarrhythmias occur in up to 60% of adults with Fontan palliation and are associated with substantial morbidity and mortality (S4.4.2-2). These arrhythmias may be difficult to manage, are usually poorly tolerated, and cause serious hemodynamic compromise often with dire consequences (S4.4.2-1). Therefore, they should be addressed promptly, including urgent consultation with ACHD providers who can help guide immediate management strategies, even if remotely. Consideration for antithrombotic therapy in Fontan patients should take into account the high prevalence of thrombus formation and potentially catastrophic impact of pulmonary or systemic thromboembolus. Standard decision-making strategies about rhythm versus rate control or thromboembolic prophylaxis derived from and recommended for patients with acquired heart disease and AF do not apply to patients with Fontan physiology, for whom rhythm control and anticoagulation are of greater importance than would be concluded from application of the standard algorithms.

Sinus node dysfunction may predispose Fontan patients to atrial tachyarrhythmias, the most common being macro-reentrant circuits or intra-atrial reentrant tachycardia (S4.4.2-13, S4.4.2-47). Nearly 90% of Fontan patients who die from HF have coexisting atrial tachyarrhythmias (S4.4.2-48). Fontan patients are at increased risk of complications from antiarrhythmic therapy, such as torsades de pointes with dofetilide (S4.4.2-49) and amiodarone-induced thyrotoxicosis (S4.4.2-50). Such agents should be used cautiously and in consultation with ACHD cardiologists and electrophysiology specialists with expertise in ACHD.

2. Serial imaging can be valuable for assessing many of the long-term sequelae of Fontan palliation such as thrombosis, right-to-left shunts (e.g., fenestration, intrapulmonary AV malformation), obstructive lesions, systemic AV valve dysfunction, diastolic or systolic ventricular function, collateral burden, and branch PA obstruction. Imaging can be challenging and requires informed understanding about the patient's particular situation. Although CCT is possible in patients with Fontan physiology, it is challenging to ensure contrast dispersal through the pulmonary vasculature because of streaming of venous return to the PA from multiple separate sources (e.g., superior vena cava, inferior vena cava right atrium collaterals) (S4.4.2-51, S4.4.2-52).

3. Hemodynamic assessment, particularly of the pulmonary circulation, is crucial to making informed decisions about the type and timing of surgical intervention.

4. Hemodynamic problems may first manifest through arrhythmia. Thus, first presentation of arrhythmia should warrant thorough review of the patient’s Fontan circulation and ventricular function.

5. Aerobic exercise may help maintain respiratory mechanics, which can improve transpulmonary flow in the Fontan circulation. Stroke volume during exercise and exercise capacity are directly related to skeletal muscle function. Consequently, strength training may improve exercise capacity in patients with Fontan palliation.

6. There is increasing recognition of hepatic vulnerability after Fontan palliation, including cirrhosis (S4.4.2-6, S4.4.2-53) but uncertainty about which patients are at highest risk, or how to address problems when identified. Routine assessment of liver function and structure may help inform broader decisions such as timing and risk of surgery or transplantation, as well as provide insights into the emerging natural history of this unique condition. Consultation with a hepatologist may be of value in interpreting and following the liver abnormalities encountered in patients with Fontan physiology.

7. Recognizing the multiorgan vulnerability of the Fontan circulation, annual routine blood tests may have a role in identifying and addressing problems early.

8. Because of both the anatomic and physiological complexities of these patients, and the potential for concurrent intervention, hemodynamic and interventional cardiac catheterization of the adult with single ventricle/Fontan palliation should be performed only by persons with expertise in CHD in coordination with an ACHD cardiologist. Recognizing that it is difficult to accurately assess Fontan hemodynamics by clinical examination or noninvasive imaging, cardiac catheterization may be needed in these scenarios and others:

a. Interval hemodynamic assessment, as filling pressures, mean PA pressure, and pulmonary vascular resistance may change over time (S4.4.2-8)
b. Creation or closure of a fenestration or veno-veno collaterals, although with uncertain benefit of either intervention (S4.4.2-54–S4.4.2-56)
c. Treatment of baffle obstruction, even in the setting of low or no pressure gradient (S4.4.2-57)
d. Assessment of protein-losing enteropathy or ascites, because elevated Fontan pressure correlates with such complications, and lowering pressures may offer the potential for clinical improvement (S4.4.2-58)
e. Facilitation of transvenous liver biopsy for monitoring liver function including as part of a pretransplantation assessment
f. Preoperative assessment before Fontan revision (S4.4.2-18, S4.4.2-59).

9. Protein-losing enteropathy and plastic bronchitis contribute substantially to perioperative mortality, yet transplantation may be curative (S4.4.2-9, S4.4.2-11). Medical therapy options are often ineffective. Therefore, consideration of transplantation early in the course of PLE may be warranted. Evaluation of additional organs is necessary, particularly the liver, as these patients are susceptible to cirrhosis as a consequence of the Fontan circulation. Although symptoms may improve, there are no published data regarding impact on survival for transplanted Fontan patients with PLE compared with those who do not undergo transplantation.

10. Although catheterization plays an important role in management of single ventricle/Fontan patients, it is often driven by symptoms. The role of routine hemodynamic assessment is less certain.

11. Fontan circulation imparts risk of thrombosis, and anticoagulation with vitamin K antagonists should be offered as preventive therapy in clinical situations including prior arrhythmia (S4.4.2-60). Patients may also benefit from anticoagulation if they have significant residual intracardiac right- to -left shunt or veno-veno collaterals.

12. Catheter ablation has been associated with improved clinical status despite the frequent coexistence of multiple arrhythmia substrates (S4.4.2-61). Given the progressive nature of the atrial myopathy, successful ablation is less frequent than in acquired heart disease or other congenital heart diseases, and recurrence is common. The development of new arrhythmias over time remains problematic, but multiple ablation procedures may be justified in selected patients (S4.4.2-13, S4.4.2-14).

13. Conversion to a total cavopulmonary connection Fontan combined with a modified right atrial Maze procedure may be considered in patients with symptomatic refractory recurrent intra-atrial reentrant tachycardia (S4.4.2-16, S4.4.2-17). In the presence of documented AF, a left atrial Cox Maze procedure may also be indicated (S4.4.2-16, S4.4.2-62). Some patients may not be appropriate surgical candidates for reasons of elevated PA or Fontan pressures, elevated ventricular end-diastolic pressures, or renal or hepatic dysfunction, and the decision to perform Fontan revision surgery is rarely straightforward.

14. Pulmonary vasoactive medications, specifically endothelin receptor antagonists and PDE-5 inhibitors, are of increasing interest as a means of reducing pulmonary vascular resistance and improving cardiac output. In limited studies, use of PDE-5 inhibitors appears favorable for Fontan patients with improvement noted in pulmonary blood flow and exercise capacity (S4.4.2-21, S4.4.2-63). Use of endothelin antagonists has been investigated in a randomized trial (S4.4.2-19). After 14 weeks of randomization in 69 subjects successfully completing the study, there was a modest but significant increase in peak oxygen consumption and exercise duration in those taking bosentan compared with those on placebo.

15. Although anticoagulation is prudent in those with prior arrhythmia or known thromboembolic events, routine use of anticoagulation with vitamin K antagonist cannot as yet be strongly recommended. An RCT in Fontan children/adolescents did not show benefit (S4.4.2-64), although adults later after Fontan may be more at risk. However, a secondary analysis of that RCT as an observational study (S4.4.2-65) found the risk of thromboembolism was lower in those patients on warfarin who consistently achieved minimum target international normalized ratio levels, as well as in those on acetylsalicylic acid compared with patients who often failed to meet target international normalized ratio level. Rates of thrombosis were considerably higher in patients on warfarin who did not consistently achieve target international normalized ratio. A study of modes of death in atriopulmonary Fontan patients demonstrated lower rates of death in patients on "some" antiplatelet agent or anticoagulation compared with those on none (S4.4.2-1). Direct oral anticoagulants are unstudied and thus cannot be recommended at the present time. There are concerns about liver function vulnerability in Fontan patients, which theoretically may increase the risk of complications with some of those agents.

16. There are occasions where surgery or catheter intervention may be alternatives to transplantation for a "failing Fontan" after weighing risks and benefits of the intended procedure (i.e., alleviation of atrioventricular valve regurgitation, systemic or pulmonary venous pathway obstruction). Reoperation for atrioventricular valve regurgitation may be high-risk, particularly when systemic ventricular function is impaired. Although valve repair is preferred and operative risk is usually lower, it is not always possible. Risk of valve replacement in this setting is high.

Table 32. Fontan Palliation: Routine Follow-Up and Testing Intervals

Frequency of Routine Follow-Up and Testing	Physiological Stage A* (mo)	Physiologic al Stage B* (mo)	Physiological Stage C* (mo)	Physiological Stage D* (mo)
Outpatient ACHD cardiologist	12	12	6	3–6
ECG	12	12	6–12	6
TTE†	12	12	12	12
Pulse oximetry	12	12	Each visit	Each visit
Holter monitor	12	12	12	12
CMR‡/CCT§	36	24	24	24
Exercise test‖	36	24	12	12

*See Tables 3 and 4 for details on the ACHD AP classification system.
†Routine TTE may be unnecessary in a year when CMR imaging is performed unless clinical indications warrant otherwise.
‡CMR may be indicated for assessment of the long-term sequelae of Fontan palliation: thrombosis, right-to-left shunts (e.g., fenestration. intrapulmonary atrioventricular malformation), obstructive lesion, systemic atrioventricular valve dysfunction, ventricular size and function, collateral burden, and branch pulmonary artery obstruction. Baseline study is recommended with periodic follow-up CMR, with frequency of repeat imaging determined by anatomic and physiological findings.
§CCT may be used if CMR is not feasible and to evaluate cross-sectional imaging status-post stent therapy. CCT with contrast injection in Fontan patients can be misleading; therefore, it should be done only when clinically indicated and when it can be

appropriately protocoled and interpreted. If CCT is used instead of CMR imaging, the frequency should be weighed against radiation exposure.
‖6-minute walk test or CPET, depending on clinical indication.
ACHD indicates adult congenital heart disease; CCT, cardiac computed tomography; CMR, cardiovascular magnetic resonance imaging; CPET, cardiopulmonary exercise test; ECG, electrocardiogram; and TTE, transthoracic echocardiogram.

4.4.3. Hypoplastic Left Heart Syndrome/Norwood Repair

The Norwood repair is the first of 3 steps in palliation for hypoplastic left heart syndrome and consists of atrial septectomy, transection, and ligation of the distal main PA with construction of a systemic-to-PA shunt, and anastomosis of the proximal stump of the main PA to the hypoplastic ascending aorta with augmentation of the entire aortic arch from the sinotubular junction to beyond the ductus arteriosus. Hypoplastic left heart syndrome is fatal unless surgical palliation is performed in the neonatal period. Subsequent surgeries include a bidirectional cavopulmonary anastomosis (often performed around 6 months of age), followed finally by a Fontan procedure (often at approximately 2 to 4 years of age). Sequelae of hypoplastic left heart syndrome are largely those of the Fontan palliation, but additional concerns related to the underlying anatomy and the Norwood repair is important in patients with hypoplastic left heart syndrome. These include aortic obstruction related to anastomosis of the PA and aorta, and neoaortic dilation. Additionally, native anatomy wherein coronary arteries arise from a small aortic root make coronary ischemia a greater concern than in other underlying disorders managed with Fontan repair. The frequency and spectrum of long-term sequelae specific to the Norwood repair are not yet known.

4.4.4. Truncus Arteriosus

Truncus arteriosus in the adult has almost invariably been repaired in childhood, and in the rare circumstances when an adult has unrepaired truncus arteriosus, Eisenmenger physiology is typical. Pulmonary hypertension may be present in repaired patients. The types of operative repairs may involve VSD closure, right ventricle–to-PA conduit placement, reconstruction of the pulmonary arteries, and replacement of the truncal (neoaortic) valve. Unifocalization of the pulmonary arteries may be necessary in very complex cases. The aorta may be dilated. Recommendations regarding assessment and management of truncus arteriosus can generally be inferred in the recommendations for the specific components, including right ventricle–to-PA conduit, VSD, aortic valve disease, and aortopathies.

4.4.5. Double Outlet Right Ventricle

Double outlet right ventricle is an anatomic descriptor that includes abnormalities similar to TOF in some patients (when the aorta is closely related to the VSD) and similar to d-TGA with a VSD in others (when the PA is more closely related to the VSD than the aorta). Repairs are predicated on the underlying anatomy and may involve VSD closure with relief of PS, right ventricle–to-PA conduit, or Rastelli-type repair. In severe cases, single-ventricle physiology may be present. Consequently, recommendations for the management of a patient with double outlet right ventricle can generally be inferred in the recommendations for the lesion with the most similar anatomy and physiology (e.g., TOF can reasonably be based on the recommendations in Section 4.4.1, recognizing that a patient with double outlet right ventricle is more likely to have residual LVOT obstruction).

4.4.6. Severe PAH and Eisenmenger Syndrome

4.4.6.1. Severe PAH

Recommendations for Severe PAH Referenced studies that support recommendations are summarized in Online Data Supplement 49.		
COR	**LOE**	**Recommendations**
		Diagnostic
I	**B-NR**	**1. Patients with ACHD with pulmonary vascular resistance 2.5 Wood units or greater (≥4 Wood units/m^2) should be assessed collaboratively by an ACHD cardiologist and an expert in pulmonary hypertension to develop a management plan (S4.4.6.1-1–S4.4.6.1-17).**
I	**B-NR**	**2. Adults with septal or great artery shunts should undergo periodic screening for pulmonary hypertension with TTE (S4.4.6.1-1–S4.4.6.1-18).**
I	**B-NR**	**3. Cardiac catheterization to assess pulmonary vascular hemodynamics is recommended for adults with septal or great artery shunts and clinical symptoms, signs, or echocardiographic findings suggestive of pulmonary hypertension (S4.4.6.1-1, S4.4.6.1-2, S4.4.6.1-4, S4.4.6.1-6, S4.4.6.1-7, S4.4.6.1-11, S4.4.6.1-12, S4.4.6.1-15–S4.4.6.1-18).**
I	**B-NR**	**4. In adults with septal or great artery shunts, cardiac catheterization with hemodynamics (performed before or at time of closure) is beneficial to assess suitability for closure (S4.4.6.1-1–S4.4.6.1-17).**
I	**C-EO**	**5. BNP, chest x-ray, 6-minute walk test, and cardiac catheterization are useful for initial and follow-up evaluation of patients with ACHD with PAH.**

Synopsis

Pulmonary hypertension is defined as elevation of mean pulmonary arterial pressure to ≥25 mm Hg at rest and does not imply a specific underlying pathophysiology. Pulmonary hypertension is further classified on the basis of the presumed mechanism (including elevation of pulmonary venous pressure [denoted as "postcapillary pulmonary hypertension"], parenchymal or restrictive lung disease, rheumatologic disease, portal hypertension, toxin exposure, and thromboembolism). It is also classified by developmental or acquired anatomic abnormalities of decreased pulmonary arterial capacitance, impedance, or stenosis throughout the pulmonary arterial vascular bed. PAH as initially described required pulmonary venous pressure ≤15 mm Hg with concomitant elevation of pulmonary vascular resistance. Although left-to-right shunting was the initial research model of triggered PAH, pulmonary hypertension in patients with ACHD can be caused by, or associated with, any of the factors described above. Effective therapies may be specific to the primary mechanism of pulmonary hypertension in a given patient, so patients with CHD should have thorough investigation for all potential contributing etiologies to pulmonary hypertension that may require specific therapy if best clinical outcomes are to be achieved. Adverse effects of pulmonary hypertension therapies in patients with ACHD with pulmonary hypertension may differ from those noted in other patients, because of concomitant multiorgan and vascular effects from longstanding congenital heart and vascular disease.

Shunt-related PAH in patients with ACHD can develop in the pre- or perioperative period but also may develop years to decades after closure of defects. Mechanisms for development of PAH may include genetic factors and environmental exposures. Severity of PAH may range from incidentally noted mild pressure and resistance elevation to profound systemic or suprasystemic levels of PA pressure and pulmonary vascular resistance. If an anatomic defect that allows shunting is present, shunt reversal and

cyanosis may develop as pulmonary resistance rises above systemic resistance (i.e., Eisenmenger syndrome).

See Section 3.3 for recommendations on who should perform surgeries, cardiac catheterization, and other procedures in these patients; Section 3.4 for recommendations on diagnostic evaluation; and Table 33 for routine testing and follow-up intervals.

Recommendation-Specific Supportive Text

1. Patients with ACHD with pulmonary hypertension, particularly PAH, have a poorer prognosis than do patients with ACHD with similar histories and anatomic abnormalities who do not have pulmonary hypertension. The fields of ACHD and pulmonary vascular disease care have increasingly disparate but complementary bodies of knowledge, and both are necessary to achieve optimal outcomes for patients with PAH. Clinicians cross-trained in both subspecialties or partnering experts from each subspecialty appear necessary to fully counsel patients with ACHD with PAH regarding: diagnostic evaluation, prognosis, lifestyle choices, suitability for operative or catheter-based repair of existing shunts or vascular obstructions contributing to PAH, nature and effectiveness of additional medical therapies, mechanical circulatory and pulmonary vascular support, and goals of care.

2. PAH may develop years after shunt closure in patients with ACHD. Predictors for the development or presence of PAH include:

a. Anatomic defects: complete AVSD, sinus venosus defect, large nonrestrictive defect (ASD >2 cm, VSD >1 cm, PDA >0.6 cm), and concomitant ACHD AP classification II or III abnormalities.
b. Preintervention Qp:Qs ≥3 and/or PASP >40 mm Hg.
c. Presence of associated syndrome (e.g., Down syndrome).
d. Older age at repair.
e. Female sex.
f. Otherwise unexplained symptoms potentially attributable to PAH (decreased exercise capacity, syncope, chest pain, hemoptysis).
g. Findings on clinical examination: systemic arterial desaturation, elevated systemic venous pressures, other evidence of fluid retention, loud P2, new TR or PR, new arrhythmia, decreased exercise capacity, electrocardiographic findings consistent with subpulmonary ventricular hypertrophy or dilation. Echocardiography may demonstrate subpulmonic ventricular dysfunction and/or enlargement and estimate central venous and PA pressures. However, echocardiography alone is insufficient to accurately determine PA pressure or pulmonary vascular resistance, so echocardiography is best used in conjunction with data obtained at cardiac catheterization when making decisions about instituting or changing therapy for PAH (S4.4.6.1-19–S4.4.6.1-21).

3. Cardiac catheterization remains the standard for accurate diagnosis of pulmonary hypertension syndromes and for selection of optimal therapies for patients with ACHD with pulmonary hypertension.

4. Mechanical interventions targeting relief of anatomic contributors to PAH (e.g., closure of septal or great arterial defects to eliminate shunting) may be considered as part of short-term plans of care for patients with ACHD with PAH. However, even modest residual levels of PAH substantially determine intermediate and longer-term outcomes. Patients should be followed for pulmonary hypertension.

5. Although history, noninvasive testing, and laboratory analysis (biochemistry and hematology) are all part of the workup of pulmonary hypertension associated with CHD, cardiac catheterization with careful hemodynamic measurements, with or without provocative maneuvers and/or angiography, remains fundamental to accurate diagnosis and design of therapeutic plans.

Table 33. Pulmonary Hypertension and Eisenmenger Syndrome: Routine Follow-Up and Testing Intervals

Frequency of Routine Follow-Up and Testing	Physiological Stage C* (mo)	Physiological Stage D* (mo)
Outpatient ACHD cardiologist	6–12	3–6
ECG	12	12
TTE†	12	12
Pulse oximetry	Each visit	Each visit
CMR‡	As needed	As needed
Exercise test§	6–12	6–12
Cardiac catheterization‖	As needed	As needed

*See Tables 3 and 4 for details on the ACHD AP classification system.
†Routine TTE may be unnecessary in a year when CMR imaging is performed unless clinical indications warrant otherwise.
‡CMR may be indicated for assessment of right ventricular function and CHD anatomy not clarified with TTE. Baseline study is recommended with periodic follow-up CMR, with frequency of repeat imaging determined by anatomic and physiological findings.
§6-minute walk test or CPET, depending on clinical indication.
‖Cardiac catheterization should be performed at baseline and as needed.
ACHD indicates adult congenital heart disease; CMR, cardiovascular magnetic resonance; CPET, cardiopulmonary exercise test; ECG, electrocardiogram; and TTE, transthoracic echocardiogram.

4.4.6.2. Eisenmenger Syndrome

Recommendations for Eisenmenger Syndrome Referenced studies that support recommendations are summarized in Online Data Supplement 50.		
COR	**LOE**	**Recommendations**
		Diagnostic
I	**C-EO**	**1. When evaluating adults with presumed Eisenmenger syndrome, clinicians should confirm diagnostic imaging and cardiac catheterization data accuracy and exclude other potential contributors to right-to-left shunting or pulmonary hypertension.**
		Therapeutic
I	**A**	**2. Bosentan is beneficial in symptomatic adults with Eisenmenger syndrome with ASD or VSD (S4.4.6.2-1–S4.4.6.2-3).**
IIa	**B-R**	**3. In symptomatic adults with Eisenmenger syndrome, bosentan and PDE-5 inhibitors are reasonable in combination if symptomatic improvement does not occur with either medication alone (S4.4.6.2-1, S4.4.6.2-4–S4.4.6.2-6).**
IIa	**C-EO** **B-NR**	**4. Bosentan is a reasonable therapy to treat symptomatic adults with Eisenmenger syndrome with 1 of the following: shunts other than ASD/VSD (e.g., PDA, aortopulmonary window) (Level of Evidence C-EO), or complex congenital heart lesions (S4.4.6.2-1, S4.4.6.2-7) or Down syndrome (S4.4.6.2-4, S4.4.6.2-5, S4.4.6.2-8–S4.4.6.2-10) (Level of Evidence B-NR).**
IIa	**B-NR**	**5. It is reasonable to use PDE-5 inhibitors (e.g., sildenafil, tadalafil) to treat symptomatic adults with Eisenmenger syndrome with ASD, VSD, or great artery shunt (S4.4.6.2-1, S4.4.6.2-11–S4.4.6.2-16).**

Synopsis

Historically Eisenmenger syndrome has been understood as the most advanced form of PAH associated with congenital intracardiac and great arterial shunting. The natural course and outcomes of PAH in patients with ACHD with Eisenmenger syndrome, as contrasted to other adults with PAH, remain incompletely defined. However, it is believed that better survival and functional ability of untreated adults with Eisenmenger syndrome might be explained by sharing of loading conditions between right- and left-sided cardiac chambers, as well as multiorgan system adaptations that develop over time.

The fundamental cause of Eisenmenger syndrome is elevated pulmonary vascular resistance driving right-to-left intracardiac or great arterial shunting leading to systemic arterial desaturation. The risk of development of Eisenmenger syndrome is influenced by concomitant congenital syndromes, anatomic location of congenital defects, size of anatomic defects, genetic factors, and environmental exposures.

Pathophysiological mechanisms contributing to development of Eisenmenger syndrome are not fully understood. Suggested triggers and pathways include blood flow-induced shear and circumferential stress, vasoconstriction, and vascular cell proliferation associated with fibrosis and thrombosis.

Cyanosis, erythrocytosis, abnormalities of loading conditions, and abnormalities of systemic and pulmonary perfusion all contribute to functional incapacity and potential for multiorgan system dysfunction and other sequelae, including stroke, brain abscess, osteoarthropathy, iron deficiency, reduced glomerular clearance and susceptibility to acute renal insufficiency, nephrosis, pulmonary arterial thrombosis and dissection, hemoptysis, pulmonary parenchymal infections, diastolic and systolic cardiac dysfunction, arrhythmia, HF, and SCD.

Palliative therapies that may be helpful include supplemental oxygen if systemic arterial oxygen saturation is empirically noted to rise in response, systemic anticoagulation, and avoidance of circumstances recognized to contribute to risk (e.g., high altitude, pregnancy, exposure to high heat or humidity leading to vasodilation, nephrotoxin exposure, extreme exertion, large shifts in intravascular volume). However, supportive data for these strategies are limited or nonexistent. Systemic anticoagulation has the potential for adverse as well as possible helpful effects.

Mechanical circulatory and pulmonary support, lung transplantation with concomitant repair of anatomic cardiovascular defects, and heart–lung transplantation have all been applied in patients with ACHD with Eisenmenger syndrome with deteriorating functional ability. Indications for such therapies for adults with Eisenmenger syndrome are not standardized; comparative outcomes have not been tested, and to date successes have been limited. However, pharmacological treatment of PAH is helpful in the management of certain patients with Eisenmenger syndrome.

See Section 3.3 for recommendations on who should perform surgeries, cardiac catheterization, and other procedures in these patients; Section 3.4 for recommendations on diagnostic evaluation; and Table 33 for routine testing and follow-up intervals.

Recommendation-Specific Supportive Text

1. Right-to-left shunting through septal defects or connections between the great arteries associated with subpulmonary ventricular hypertension may be diagnosed as Eisenmenger syndrome. PAH medications may be beneficial for patients with Eisenmenger syndrome; however, other conditions may cause right-to-left shunting for reasons other than shunt-related PAH and thus may require different treatment options. These other conditions include: a) severe pulmonary hypertension of other cause (e.g., thromboembolic disease, rheumatic disease), b) subpulmonary chamber outflow obstruction, c) abnormalities of subpulmonary chamber compliance, and d) vascular streaming. Accurate diagnosis is

necessary to guide therapy. For example, PAH therapies will not be beneficial if the source of right-to-left shunting is RVOT obstruction; rather, alleviation of the RVOT obstruction is the necessary treatment. Accurate diagnosis of Eisenmenger syndrome and exclusion of other potential contributors to right-to-left shunting or pulmonary hypertension by means of advanced imaging and cardiac catheterization are crucial prerequisites to optimize therapy for adults with Eisenmenger syndrome.

2. In adults with Eisenmenger syndrome associated with ASD or VSD in World Health Organization functional class III or IV, RCTs demonstrate improved 6-minute walk distance, hemodynamics, and subjective functional ability after 4 months of oral bosentan (S4.4.6.2-17). Longer-term benefit has been demonstrated through open-label extension of this initial RCT (S4.4.6.2-1) and in single-center registry cohorts (S4.4.6.2-1, S4.4.6.2-17). There may be a class effect for endothelin receptor antagonists, but others have not been studied in this population.

3. A randomized crossover trial of combination PAH therapy (PDE-5 inhibitor therapy and endothelin receptor antagonist therapy) enrolled adults with Eisenmenger syndrome or with idiopathic PAH and demonstrated improvement in systemic arterial saturation but not in functional ability or hemodynamics (S4.4.6.2-6). Use of combination PAH therapy for adults with Eisenmenger syndrome was further supported by a single-center cohort series suggesting improvement in 6-minute walk testing and hemodynamics in adults with Eisenmenger syndrome using combined PDE-5 inhibitory therapy and endothelin receptor antagonist therapy (S4.4.6.2-1, S4.4.6.2-4, S4.4.6.2-18).

4. Open-label single-center registries and cohort studies of adults with Eisenmenger syndrome, attributable to shunts other than ASD/VSD or with complex congenital heart lesions, suggest benefit in functional capacity or hemodynamics after months of endothelin receptor antagonist therapy (S4.4.6.2-1, S4.4.6.2-7). Patients with ACHD and Down syndrome have greater likelihood to develop pulmonary hypertension, and they have unique comorbidities that influence the nature of their pulmonary hypertension, the metrics used in follow-up, and the potential for benefit from as well as adverse response to therapy. Open-label single-center registries and cohorts of adults with Down syndrome and Eisenmenger syndrome suggest benefit in subjective and/or objective functional capacity after months of endothelin receptor antagonist therapy, generally as contrasted to performance before institution of endothelin receptor antagonist therapy (S4.4.6.2-8–S4.4.6.2-10). Accurate diagnosis of PAH and Eisenmenger syndrome remains essential before initiating such therapy.

5. RCTs (S4.4.6.2-16) regarding PDE-5 inhibitor therapy for adults with Eisenmenger syndrome have limitations, but are supported by multiple open-label prospective studies and information from a large single-center retrospective registry (S4.4.6.2-1, S4.4.6.2-11–S4.4.6.2-16). These studies suggest benefit in functional capacity and hemodynamics after use of either sildenafil or tadalafil at varying doses and for varying periods of follow-up. Benefit was either in comparison to subjects' performance before institution of therapy or to other adults with similar Eisenmenger syndrome anatomy and physiology who were not prescribed PDE-5 inhibitors.

4.4.7. Coronary Anomalies

Coronary abnormalities are among the most common congenital cardiovascular anomalies, surpassing in prevalence nearly all others combined. Coronary anomalies include anomalous aortic origin of a coronary artery (AAOCA), coronary fistula, and myocardial bridge. Many congenital coronary abnormalities have a benign outcome. In contrast, natural history studies of anomalous coronary artery from the PA (particularly anomalous left coronary artery from the PA) suggest poor outcome in untreated patients; similar natural history studies are lacking regarding untreated patients with AAOCA,

but other evidence raises concern. See Table 34 and Figure 5 for a diagnostic and treatment algorithm for AAOCA.

Assessment of the risk of SCD in patients with AAOCA and of the role of AAOCA in causing ischemia or symptoms is difficult because available data do not adequately capture the clinical spectrum of these anomalies. Autopsy series are available that help describe the anomalies found in patients who suffered SCD contrasted to other causes of death (S4.4.7-1–S4.4.7-5). There are surgical case series that describe findings before operation, operative anatomy and postoperative course (S4.4.7-2, S4.4.7-5–S4.4.7-8). There are imaging studies describing the anatomy and potential pathophysiological abnormalities associated with AAOCA (S4.4.7-6, S4.4.7-9–S4.4.7-11). There are surgical series describing improvement in symptoms after operation (S4.4.7-6–S4.4.7-8). There are surveys and registries that describe the heterogeneous management strategies applied to AAOCA (S4.4.7-12–S4.4.7-14). What is lacking are data proving that any particular management strategy prevents SCD. As a consequence, decisions regarding whether surgery is necessary or exercise restriction or medical therapy might be beneficial are all based on synthesizing limited data and applying to an individual patient. Clinicians commonly extrapolate to assist in medical decision-making, but the consequences of being "wrong" for a young patient with AAOCA may be perceived to be greater than for many other conditions. Consequently, there is often a clinical urge to seek a reason to do something like surgical repair, because the available data do not identify clinical features that provide reassurance that a patient is at low risk of cardiovascular events. Unfortunately, evidence demonstrating that surgical repair ameliorates SCD risk, derived from large enough cohorts followed over a sufficient period of time, is not available.

Table 34. Factors That May Relate to the Clinical Importance of AAOCA and Risk of SCD

Age	AAOCA is more commonly invoked as the cause of SCD in patients <35 y of age than in patients >35 y of age, in whom atherosclerotic coronary disease becomes a more prevalent cause. However, death has been attributed to AAOCA in patients of all ages; there does not seem to be an age beyond which the AAOCA may not be relevant, even in the setting of atherosclerotic coronary disease and other concomitant conditions (S4.4.7-1, S4.4.7-2).
Anatomy of coronary ostium and proximal coronary course	Slit-like/fish-mouth-shaped orifice, acute angle takeoff, intramural course, interarterial course and hypoplasia of the proximal coronary artery have all been proposed as reasons for symptoms, ischemia and SCD in patients with AAOCA. The slit-like orifice is more commonly seen in anomalous right coronary artery arising from the left sinus. Each of these anatomic findings offers a pathophysiological mechanism for intermittent ischemia, particularly at times of high cardiac output and/or increased aortic wall tension, such as during exercise (S4.4.7-6, S4.4.7-9–S4.4.7-11).
Anomalous origin	Left coronary artery arising from the right cusp is less common than the right coronary artery arising from the left cusp but is more often found in autopsy series of SCD (S4.4.7-1, S4.4.7-3, S4.4.7-15). This suggests that anomalous origin of the left coronary artery from the right cusp is more likely to cause SCD than anomalous origin of the right coronary artery from the left cusp. This may be due either to anatomic features that make anomalous aortic origin of the left coronary artery prone to coronary compromise or because a larger proportion of myocardium is supplied by the left coronary artery, or both.
Exercise	Autopsy series suggest a most patients die during, or in close temporal association with, exercise (S4.4.7-3–S4.4.7-5).
Ischemia	Autopsy series demonstrate myocardial fibrosis in a significant number of patients whose deaths were attributed to AAOCA, particularly in patients with anomalous left coronary artery arising from the right cusp (S4.4.7-5). Surgical series describe patients

	with ischemia or MI before surgical repair in the absence of other CAD, suggesting a relation of the coronary anomaly to the ischemia (S4.4.7-16). This suggests that had perfusion imaging been obtained before SCD, ischemia would have been found in such patients (S4.4.7-17, S4.4.7-18). However, other data indicate that a normal stress test does not preclude a SCD event, with the proviso that most of those studies used only stress ECG, rather than the more sensitive and specific modalities of nuclear perfusion imaging or stress echocardiography. In addition, postoperative studies have shown that ischemia may be found after surgical repair in the distribution not supplied by the abnormal coronary artery and may not persist on repeat testing (S4.4.7-19).
Symptoms	In autopsy and surgical series, a significant number of patients reported cardiovascular symptoms, including before SCD events (S4.4.7-4, S4.4.7-7, S4.4.7-8, S4.4.7-20, S4.4.7-21). Symptoms are more commonly reported in patients in whom the left coronary artery arises from the right sinus. Surgical series have described improvement in symptoms after surgical repair (S4.4.7-3–S4.4.7-8).

AAOCA indicates anomalous aortic origin of the coronary artery; CAD, coronary artery disease; ECG, electrocardiogram; MI, myocardial infarction; and SCD, sudden cardiac death.

4.4.7.1. Anomalous Coronary Artery Evaluation

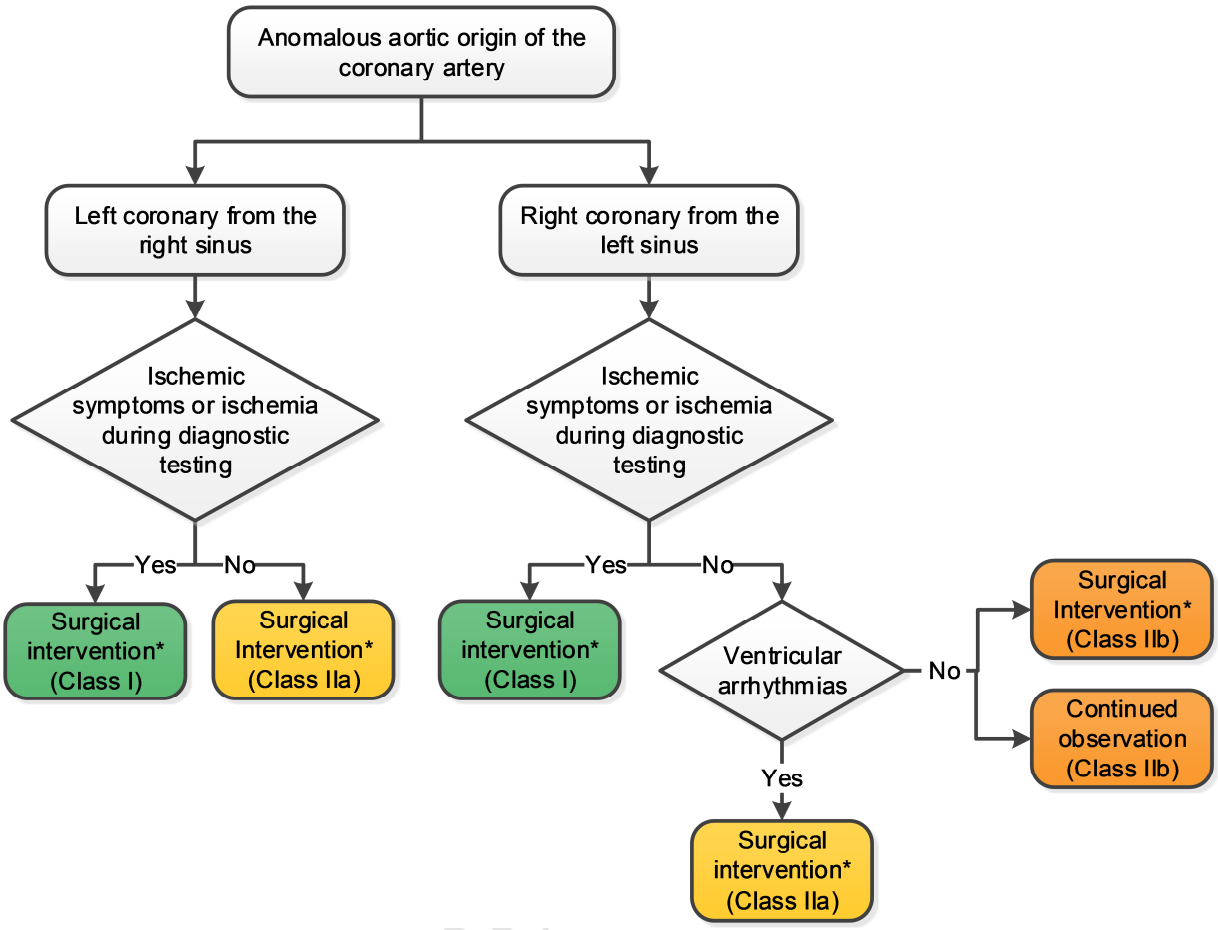
Recommendations for Anomalous Coronary Artery Evaluation Referenced studies that support recommendations are summarized in Online Data Supplement 51.		
COR	**LOE**	**Recommendations**
		Diagnostic
I	**C-LD**	**1. Coronary angiography, using catheterization, CT, or CMR, is recommended for evaluation of anomalous coronary artery (S4.4.7.1-1–S4.4.7.1-3).**
I	**C-LD**	**2. Anatomic and physiological evaluation should be performed in patients with anomalous aortic origin of the left coronary from the right sinus and/or right coronary from the left sinus (S4.4.7.1-4–S4.4.7.1-9).**

Recommendation-Specific Supportive Text

1. CTA, CMR, and catheterization can all delineate the proximal course of the coronary artery and relationship to other structures. CTA is generally preferred because it has superior spatial and temporal resolution, although CMR may also provide adequate delineation of the relationship of the coronary artery to the aorta, PA and other structures, including whether the proximal course appears to be intramural. Coronary angiography by catheterization can be helpful when there is concern about stenosis in the coronary artery or when concomitant hemodynamic evaluation for shunt assessment or intravascular ultrasonography/flow evaluation is needed.

2. Assessment of AAOCA is enhanced when the precise anatomy and physiological impact of the coronary artery anomaly are understood. As described in Table 34, the specific anomalous origin, anatomy of the orifice and proximal vessel and presence of ischemia may all influence the clinical course and thus the management options. Understanding these issues as precisely as possible will better inform clinical decisions.

Figure 5. Anomalous Aortic Origin of the Coronary Artery



*Surgical intervention to involve unroofing or coronary revascularization for patients with concomitant fixed obstruction.

4.4.7.2. Anomalous Aortic Origin of Coronary Artery

Recommendations for Anomalous Aortic Origin of Coronary Artery Referenced studies that support recommendations are summarized in Online Data Supplement 51.		
COR	**LOE**	**Recommendations**
		Therapeutic
I	**B-NR**	**1. Surgery is recommended for AAOCA from the left sinus or AAOCA from the right sinus for symptoms or diagnostic evidence consistent with coronary ischemia attributable to the anomalous coronary artery (S4.4.7.2-1–S4.4.7.2-3).**
IIa	**C-LD**	**2. Surgery is reasonable for anomalous aortic origin of the left coronary artery from the right sinus in the absence of symptoms or ischemia (S4.4.7.2-4–S4.4.7.2-6).**
IIa	**C-EO**	**3. Surgery for AAOCA is reasonable in the setting of ventricular arrhythmias.**
IIb	**B-NR**	**4. Surgery or continued observation may be reasonable for asymptomatic**

		patients with an anomalous left coronary artery arising from the right sinus or right coronary artery arising from the left sinus without ischemia or anatomic or physiological evaluation suggesting potential for compromise of coronary perfusion (e.g., intramural course, fish-mouth-shaped orifice, acute angle) (S4.4.7.2-4–S4.4.7.2-6).

Recommendation-Specific Supportive Text

1. In patients with symptoms related to AAOCA, repair of the anomaly should alleviate symptoms. In autopsy and surgical series, cardiac symptoms are more common in patients with a left coronary artery arising from the right coronary cusp. In autopsy studies of patients who died because of an anomalous coronary artery, fibrosis is a common finding, suggesting that ischemia preceded the terminal event. However, there are patients in whom a SCD event occurred despite normal stress ECG, and consequently absence of ischemia is not reassuring. Autopsy series show that many patients whose death is attributed to anomalous coronary arteries are young, thus management of patients should take age into account, with heightened concern about the risk of sudden death in younger patients (S4.4.7.2-7–S4.4.7.2-9).

2. Anomalous left coronary from the right sinus is less common than anomalous right coronary from the left sinus (S4.4.7.2-10), but anomalous left coronary artery from the right is more commonly found in autopsy series of athletes and military recruits who had nontraumatic death than right coronary from the left sinus (S4.4.7.2-1, S4.4.7.2-11–S4.4.7.2-13). The overrepresentation of the anomalous left coronary from the right sinus suggests a higher risk of SCD, particular at extremes of exertion and in patients <35 years of age.

There are some anatomic features that are thought to be associated with increased risk of compromise of coronary flow and/or SCD, including a fish-mouth-shaped or slit-like orifice, or intramural course (S4.4.7.2-14), although the slit-like orifice is more commonly encountered in a right coronary arising from the left cusp. It is difficult to quantitate the absolute risk of SCD associated with anomalous aortic origin of the left coronary from the right sinus, and data demonstrating that surgery ameliorates the SCD risk have not been published. Until studies suggest otherwise, limited data and expert consensus suggest that it is reasonable that adults with this malformation should undergo surgical unroofing unless there are extenuating circumstances that would make surgery high risk.

3. In patients with ventricular arrhythmias presumed related to ischemia caused by anomalous origin of a coronary artery, repair is an option to alleviate the ischemia and presumably mitigate the recurrence of ventricular arrhythmias. However, care should be individualized, as there may be other factors (e.g., CAD, cardiomyopathy, residual ischemia) contributing to ventricular arrhythmias that warrant continued vigilance and additional therapy.

4. Anomalous aortic origin of the right coronary from the left sinus is more common than anomalous aortic origin of the left coronary from the right sinus. The risk of SCD with the former malformation is difficult to quantitate. There is some physiological rationale to believe that asymptomatic patients without evidence of compromised blood flow would benefit from unroofing, but there are not data to demonstrate that surgical interventions alter the risk of SCD. Thus, watchful waiting may be an appropriate course as well, particularly for a patient with an anomalous right coronary arising from the left sinus.

4.4.7.3. Anomalous Coronary Artery Arising From the PA

Recommendations for Anomalous Coronary Artery Arising From the PA Referenced studies that support recommendations are summarized in Online Data Supplement 51.		
COR	**LOE**	**Recommendations**
Therapeutic		
I	**B-NR**	**1. Surgery is recommended for anomalous left coronary artery from the PA (S4.4.7.3-1–S4.4.7.3-7).**
I	**C-EO**	**2. In a symptomatic adult with anomalous right coronary artery from the PA with symptoms attributed to the anomalous coronary, surgery is recommended.**
IIa	**C-EO**	**3. Surgery for anomalous right coronary artery from the PA is reasonable in an asymptomatic adult with ventricular dysfunction or with myocardial ischemia attributed to anomalous right coronary artery from the PA.**

Recommendation-Specific Supportive Text

1. Surgery can include reimplantation of the left coronary artery directly into the aorta with or without an interposition graft. Ligation or closure of the left coronary artery at the level of the PA with coronary artery bypass grafting can also be performed, usually using the left internal mammary artery anastomosed to the left anterior descending.

2. Surgery can include reimplantation of the right coronary artery directly into the aorta with or without an interposition graft. Ligation or closure of the right coronary artery at the level of the PA with coronary artery bypass grafting can also be performed, usually using the right internal mammary artery anastomosed to the right coronary or posterior descending coronary artery.

3. Surgery to alleviate ischemia or ventricular dysfunction is reasonable if the anomalous coronary artery is thought to be the cause. Surgery can include reimplantation of the right coronary artery directly into the aorta with or without an interposition graft. Ligation or closure of the right coronary artery at the level of the PA with coronary artery bypass grafting can also be performed, usually using the right internal mammary artery anastomosed to the right coronary or posterior descending coronary artery.

4.4.8. Coronary Artery Fistula

Coronary artery fistula is an abnormal communication between a coronary artery and another cardiovascular structure, which may include a cardiac chamber, coronary sinus, superior vena cava, or PA. The incidence of coronary artery fistula is 0.1% to 0.2% in all patients undergoing coronary angiography (S4.4.8-1, S4.4.8-2). Fistulous communications may be congenital or acquired. Specific management strategies, which can include surgical repair or catheter embolization, have been controversial. In a series of 46 patients treated with surgery, predominant preoperative symptoms included angina and HF (S4.4.8-3). Importantly, postoperative myocardial infarction occurred in 11% because of low flow in the dilated coronary artery proximal to fistula closure. Late survival was also significantly reduced compared with an age-matched population. The presence of coronary artery fistula(s) requires review by a knowledgeable team that may include congenital or noncongenital cardiologists and surgeons to determine the role of medical therapy and/or percutaneous or surgical closure (S4.4.8-3).

5. Evidence Gaps and Future Directions

There are multiple challenges to developing evidenced-based care for patients with ACHD. The heterogeneity of conditions leads to small numbers of specific ACHD populations from which to derive guidelines. Additionally, lack of infrastructure to track prevalence, fragmented care systems, loss to follow-up, and changes in treatment strategies over time all contribute to the challenges of developing GDMT care (S5-1). Comprehensive multicenter and population registries and databases are needed to have adequate numbers of patients to address clinical questions. Novel study methodologies are needed to ascertain effectiveness of diagnostic and therapeutic options when each disease is sufficiently rare and events occur over sufficiently long periods that RCTs are impractical. Although there are data that patients with complex CHD have improved survival when cared for at an ACHD center, how can networks of care be developed that ensure patients get the expert care needed when there are inadequate number of ACHD cardiologists and ACHD centers? How do we ensure that patients are not lost to care as they transition from pediatric to adult cardiology? How do we ensure that patients with ACHD who would benefit from heart transplantation receive accurate listing priority? See Table 35 for a collection of high-impact research questions in ACHD.

Table 35. High-Impact Research Questions in ACHD

General	
Pathophysiology	• What are the mechanisms of heart failure that can be prevented, reversed, or treated? • Why does the systemic right ventricle fail? • Will all patients with Fontan physiology develop clinically important cirrhosis, and how can we prevent this? • Who is at risk of aortic rupture and dilation? • Are patients with manipulated coronary arteries (e.g., ASO, Ross repair) at risk of premature coronary artery disease? • What is the impact of radiation exposure on long-term health? • Can we predict who will develop pulmonary hypertension/pulmonary vascular disease?
Medical and surgical treatment	• How can we modify current CHD surgical procedures to prevent or reduce later development of heart failure and/or arrhythmias? • Which patients with ACHD can use direct oral anticoagulants instead of warfarin? • What is the best algorithm for contraception choices? • Beyond those with severe PAH, which patients will benefit from PAH therapies? • Do patients with ACHD with systemic right ventricles and HF benefit from standard therapies (beta blockers, ACE inhibitors/ARBs, aldosterone antagonist)? Which one(s)? • What medical therapies benefit patients with failing Fontan physiology? • Do asymptomatic patients with ACHD with PAH benefit from PAH-specific therapy? • Who will benefit from ventricular assist devices? • What should be the threshold(s) for aortic aneurysm surgery? • What pacing and resynchronization strategies are of most benefit, and when should they be used?
Outcomes/risk assessment	• What criteria should determine transplantation eligibility? • Which patients benefit from primary prevention ICDs? • How can we risk stratify for SCD in patients with systemic right ventricles? • What operative risk score predicts outcomes in ACHD reoperations? • What HF risk score predicts outcomes in patients with ACHD? • Is there a level of exercise where risk exceeds benefit? • What is the rate and/or risk of endocarditis?

Assessment	• Who is at high risk of neurodevelopmental abnormalities and would benefit from neuropsychiatric evaluation and treatment? • Who should be screened for anxiety and depression, what treatment is most effective, and are there differences compared with non-patients with ACHD? • What is the standard protocol for assessing right ventricular size and function by CMR imaging? • Which biomarkers are predictive of mortality and morbidity?
Disease-specific	
Coarctation of the aorta	• Which measure of hypertension—resting, exercise, or ambulatory—best predicts outcomes? • Is there an optimal antihypertensive regimen? • What should blood pressure goals be? • How often should patients be screened for thoracic aneurysm? • Should exercise-induced hypertension be treated? • What criteria warrant reintervention in recoarctation? • Is long-term outcome better with medical therapy or catheter intervention for less than severe recoarctation? • Should patients be screened for intracranial aneurysm, and if so, how often?
Ebstein anomaly	• What is the indication for surgery in the asymptomatic patient? • Who should have a Glenn shunt at the time of tricuspid valve surgery? • Should surgeons attempt tricuspid valve repair or routinely perform replacement in all patients?
TOF	• What is the optimal timing for pulmonary valve replacement in asymptomatic patients with TOF? • Do pulmonary valve replacement and ventricular tachycardia ablation decrease the risk of SCD? • Who needs a primary prevention ICD, and does this strategy reduce mortality? • Is there a role for PAH therapies in TOF? • Why does left ventricular dysfunction develop?
TGA/systemic right ventricle	• Who benefits from ACE inhibitors/ARBs/beta blockers/spironolactone? • Who needs a primary prevention ICD, and does this strategy prevent mortality? • What imaging findings predict mortality/morbidity? • In CCTGA with VSD/PS, does the double switch have better long-term outcomes than VSD closure and left ventricle–to-PA conduit? • When should tricuspid valve replacement be performed? • What is the role of cardiac resynchronization therapy in patients with systemic right ventricle?
ASO	• What are the long-term outcomes after ASO? • How should the possibility of asymptomatic coronary disease (ostial, compression) and ischemia be assessed?
Single ventricle/Fontan	• Is warfarin or aspirin beneficial in patients with a Fontan? • Are PAH therapies beneficial? • Is exercise capacity predictive of mortality? • What liver screening is appropriate and at what intervals? • How is protein-losing enteropathy best medically treated? • Why do some patients fail with preserved ejection fraction, whereas other have decreased ejection fraction? • What are the long-term outcomes of hypoplastic left heart syndrome? • What is ideal timing for heart transplantation in single ventricle Fontan patients, and should liver issues prompt earlier transplantation than might be felt necessary from a cardiac perspective?

	• Which has better long-term outcomes, the Fontan operation or bidirectional Glenn alone?
Coronary anomalies	• Does surgical intervention in anomalous aortic origin of coronary arteries improve survival?

ACE indicates angiotensin-converting enzyme; ACHD, adult congenital heart disease; ARB, angiotensin-receptor blocker; ASO, arterial switch operation; CCTGA, congenitally corrected transposition of the great arteries; CHD, congenital heart disease; CMR, cardiac magnetic resonance; ICD, implantable cardioverter-defibrillator; HF, heart failure; PA, pulmonary artery; PAH, pulmonary artery hypertension; PS, pulmonary stenosis; SCD, sudden cardiac death; TGA, transposition of the great arteries; TOF, tetralogy of Fallot; and VSD, ventricular septal defect.

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Key Words: ACC/AHA Clinical Practice Guidelines ■ arrhythmias ■ cardiac catheterization ■ cardiac defects ■ congenital heart disease ■ congenital heart surgery ■ unoperated/repaired heart defect

Appendix 1. Author Relationships With Industry and Other Entities (Relevant)—2018 AHA/ACC Guideline for the Management of Adults With Congenital Heart Disease* (February 2018)

Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness	Voting Recusals by Section†
Karen K. Stout *(Chair)*	University of Washington—Director, Adult Congenital Heart Disease Program, Professor, Internal Medicine and Pediatrics	None	None	None	None	None	None	None
Curt J. Daniels *(Vice Chair)*	The Ohio State University Heart Center and Nationwide Children's Hospital—Director, Adult Congenital Heart Disease and Pulmonary Hypertension Program, Professor, Internal Medicine and Pediatrics	None	None	None	None	• Actelion‡	None	4.1.1, 4.1.2, 4.1.3, 4.1.4, 4.1.5, 4.4.6.1, 4.4.6.2
Jamil A. Aboulhosn	UCLA Adult Congenital Heart Disease Center—Director	• Actelion • GE Medical • Edward Lifesciences§ • Medtronic	None	None	• Gore	• United Therapeutics • Actelion • Medtronic • St. Jude • Edward Lifesciences	None	4.1.1, 4.1.2, 4.1.3, 4.1.4, 4.1.5, 4.2.6, 4.3.1.1, 4.3.1.2, 4.3.5, 4.4.6.1, 4.4.6.2
Biykem Bozkurt	Baylor College of Medicine—Professor of Medicine	None	None	None	None	• Novartis	None	None

Craig S. Broberg	Oregon Health and Science University—Associate Professor of Medicine	None	None	None	None	• Actelion	None	4.1.1, 4.1.2, 4.1.3, 4.1.4, 4.1.5, 4.4.6.1, 4.4.6.2
Jack M. Colman	University of Toronto—Professor of Medicine and Obstetrics & Gynecology, Toronto Congenital Cardiac Centre for Adults and Pregnancy and Heart Disease Program; University Health Network and Mount Sinai Hospital—Senior Attending Cardiologist	None	None	None	None	None	None	None
Stephen R. Crumb	Boston Children's Hospital—Nurse Practitioner and Coordinator, COACH and Pulmonary Hypertension Programs	None	None	None	None	None	None	None
Joseph A. Dearani	Mayo Clinic—Professor of Surgery and Chair, Division of Cardiovascular Surgery	None	None	None	None	• Sorin (LivaNova)§‖ • Cormatrix‖	None	None
Stephanie Fuller	University of Pennsylvania Perelman School of Medicine—Associate Professor of Clinical Surgery	None	None	None	None	None	None	None
Michelle Gurvitz	Harvard Medical School; Brigham and Women's Hospital—Instructor of Pediatrics, Assistant Professor	None	None	None	None	None	None	None

Paul Khairy	Montreal Heart Institute Adult Congenital Center—Director; Professor of Medicine	None	None	None	None	• Boehringer Ingelheim§ • St. Jude Medical§ • Medtronic§ • Actelion§	None	4.1.1, 4.1.2, 4.1.3, 4.1.4, 4.1.5, 4.2.6, 4.3.1.1, 4.3.1.2, 4.3.5, 4.4.6.1, 4.4.6.2
Michael J. Landzberg	Boston Children's Hospital—Director, Adult Congenital Heart Service; Harvard Medical School—Associate Professor of Medicine	None	None	None	None	• Gilead • Actelion	None	4.1.1, 4.1.2, 4.1.3, 4.1.4, 4.1.5, 4.4.6.1, 4.4.6.2
Arwa Saidi	University of Florida College of Medicine—Professor, Congenital Heart Center	None	None	None	None	• Actelion§	None	4.1.1, 4.1.2, 4.1.3, 4.1.4, 4.1.5, 4.4.6.1, 4.4.6.2
Anne Marie Valente	Boston Children's Hospital, Brigham and Women's Hospital—Outpatient Director, Boston Adult Congenital Heart Disease and Pulmonary Hypertension Service; Harvard Medical School—Associate Professor of Medicine and Pediatrics	None	None	None	None	None	None	None
George F. Van Hare	Washington University School of Medicine—Director, Pediatric Cardiology; St. Louis Children's, Washington University Heart Center—Co-Director	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 ≥$5,000 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*.

*The ACHD Guideline began in March 2014. Over the initial years of the CMS Open Payment System, understandably, there have been issues related to accurate reporting of food and beverage payments. For this reason, the ACC and AHA have not considered these minor charges relevant relationships with industry.

†Writing committee members are required to recuse themselves from voting on sections to which their specific relationships with industry and other entities may apply.

‡No financial benefit.

§Significant relationship.

‖CMS reported payments to Dr. Dearani in 2016 related to research for the Sorin Group and Cormatrix; however, he disagrees with this report. The sections authored by Dr. Dearani have been reviewed, and it was affirmed that there was no implication of any influence of industry.

ACC indicates American College of Cardiology; AHA, American Heart Association; CMS, Centers for Medicare & Medicaid Services; COACH, Columbus Ohio Adult Congenital Heart; and UCLA, University of California, Los Angeles.

Appendix 2. Reviewer Relationships With Industry and Other Entities (Comprehensive)—2018 AHA/ACC Guideline for the Management of Adults With Congenital Heart Disease (February 2018)

Reviewer	Representation	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Samuel J. Asirvatham	Official Reviewer—AHA	Mayo Clinic—Professor of Medicine and Pediatrics	• Abiomed • AtriCure • Biosense Webster • Biotronik • Boston Scientific* • Medtronic • Sanofi-aventis • St. Jude Medical	None	None	None	None	None
Wendy M. Book	Official Reviewer—AHA	Emory University—Professor of Medicine and Director of Emory Adult Congenital Heart Center, Department of Medicine	None	None	None	None	• Actelion	• Defendant, congenital heart disease, 2015
Samuel S. Gidding	Official Reviewer—ACC/AHA Task Force on Clinical Practice Guidelines	Nemours Cardiac Center DuPont Hospital for Children—Chief, Division of Pediatric Cardiology	None	None	None	None	None	None

Yuli Y. Kim	Official Reviewer—AHA	University of Pennsylvania—Assistant Professor of Medicine; Children's Hospital of Philadelphia—Medical Director, Philadelphia Adult Congenital Heart Center	None	None	None	None	None	None
Geetha Raghuveer	Official Reviewer—ACC Board of Governors	Children's Mercy Hospital— Pediatric Cardiologist; University of Missouri, Kansas City School of Medicine—Professor of Pediatrics	None	None	None	None	None	None
Carole A. Warnes	Official Reviewer—ACC Board of Trustees	Mayo Clinic—Professor of Medicine	None	None	None	None	None	None
Peter J. Bartz	Organizational Reviewer—ASE	Children's Hospital of Wisconsin—Associate Professor, Medical College of Wisconsin	None	None	None	None	None	None
Mitchell I. Cohen	Organizational Reviewer—HRS	Inova Fairfax Children's Hospital—Co-Director of the Heart Center and Chief, Pediatric Cardiology	None	None	None	None	None	None
Marshall L. Jacobs	Organizational Reviewer—AATS	Johns Hopkins School of Medicine—Professor of Surgery and Director, Pediatric Heart Surgery Outcomes Research	None	None	None	None	None	None
Larry A. Latson	Organizational Reviewer—SCAI	Joe DiMaggio Children's Hospital Heart Institute—Medical Director, Pediatric and Congenital Interventional Cardiology	• Gore Medical	None	None	None	• St. Jude Medical	None

Constantine Mavroudis	Organizational Reviewer—STS	Florida Hospital for Children—Medical Director, Pediatric and Congenital Heart Center	None	None	None	None	None	None
Doff B. McElhinney	Organizational Reviewer—SCAI	Stanford University—Professor, Cardiothoracic Surgery and of Pediatrics	• Medtronic*	None	None	None	None	None
Erwin N. Oechslin	Organizational Reviewer—ISACHD	University of Toronto—Professor of Medicine; Peter Munk Cardiac Centre—Director, Adult Congenital Heart Disease Program	• Actelion	None	None	None	None	None
John K. Triedman	Organizational Reviewer—HRS	Boston Children's Hospital—Senior Associate in Cardiology; Harvard Medical School—Professor of Pediatrics	• Biosense Webster	None	None	None	None	None
Naser Ammash	Content Reviewer	Mayo Clinic—Professor of Medicine	None	None	None	None	None	None
Helmut Baumgartner	Content Reviewer	University of Muenster—Professor of Cardiology and Adult Congenital Heart Disease; University Hospital Muenster—Director, Division of Adult Congenital and Valvular Heart Disease, Department of Cardiovascular Medicine	None	None	None	None	None	None
James C. Blankenship	Content Reviewer—ACC Interventional Section Leadership Council	Geisinger Medical Center—Staff Physician and Director, Cardiac Catheterization Laboratory	None	None	None	None	• Abbott Vascular† • Boston Scientific† • GlaxoSmithKline† • Takeda Pharmaceutical†	None

Ralph G. Brindis	Content Reviewer—ACC/AHA Task Force on Clinical Practice Guidelines	Northern California Kaiser Permanente—Senior Advisor, Cardiovascular Disease; University of California, San Francisco—Clinical Professor of Medicine	None	None	None	None	None	None
Robert M. Campbell	Content Reviewer	Emory University School of Medicine, Sibley Heart Center Cardiology—Professor of Pediatrics	None	None	None	None	None	None
Lesley H. Curtis	Content Reviewer—ACC/AHA Task Force on Clinical Practice Guidelines	Duke University School of Medicine—Professor of Medicine	None	None	None	None	• Boston Scientific* • GE Healthcare* • GlaxoSmithKline* • Medtronic* • Novartis*	None
Kristi K. Fitzgerald	Content Reviewer	Nemours Cardiac Center DuPont Hospital for Children—Genetic Counselor, Division of Pediatric Cardiology	None	None	None	None	None	None
Lee A. Fleisher	Content Reviewer—ACC/AHA Task Force on Clinical Practice Guidelines	University of Pennsylvania Health System Department of Anesthesiology and Critical Care—Robert Dunning Dripps Professor of Anesthesiology	None	None	None	None	None	None
Federico Gentile	Content Reviewer—ACC/AHA Task Force on Clinical Practice Guidelines	Centro Cardiologico Gentile—Director, Cardiovascular Disease	None	None	None	None	None	None
Louise Harris	Content Reviewer	Toronto General Hospital—Professor of Medicine	• St. Jude Medical	None	None	None	None	None

Mark A. Hlatky	Content Reviewer—ACC/AHA Task Force on Clinical Practice Guidelines	Stanford University School of Medicine—Professor of Health Research and Policy, and of Cardiovascular Medicine	None	None	None	None	None	None
Craig T. January	Content Reviewer	University of Wisconsin School of Medicine and Public Health—Professor, Division of Cardiovascular Medicine	None	None	None	None	None	None
José A. Joglar	Content Reviewer—ACC/AHA Task Force on Clinical Practice Guidelines	UT Southwestern Medical Center—Professor of Internal Medicine	None	None	None	None	None	None
Thomas K. Jones	Content Reviewer	Seattle Children's Hospital—Professor of Pediatrics and Director, Cardiac Catheterization Laboratories	• Gore Medical* • Medtronic*	None	None	None	• Gore Medical* • Medtronic* • St. Jude Medical*	None
Sana M. Al-Khatib	Content Reviewer—ACC/AHA Task Force on Clinical Practice Guidelines	Duke University Medical Center—Professor of Medicine	None	None	None	None	None	None
Brian E. Kogon	Content Reviewer	Emory University School of Medicine—Associate Professor, Surgery and Surgical Director of Emory Adult Congenital Heart Center and Chief of Pediatric Cardiac Surgery	None	None	None	None	None	None

Gautam Kumar	Content Reviewer—ACC Interventional Section Leadership Council	Emory University School of Medicine, Division of Cardiology—Associate Professor of Medicine	• Abiomed	None	None	None	• OrbusNeich Medical	None
Eric V. Krieger	Content Reviewer	University of Washington—Associate Professor of Medicine and Associate Director, Adult Congenital Heart Service	• Actelion	None	None	None	None	None
Glenn N. Levine	Content Reviewer—ACC/AHA Task Force on Clinical Practice Guidelines	Baylor College of Medicine—Professor of Medicine; Michael E. DeBakey VA Medical Center—Director, Cardiac Care Unit	None	None	None	None	None	None
C. Huie Lin	Content Reviewer—SCAI	Houston Methodist DeBakey Heart & Vascular Center—Cardiologist	• Gore Medical • ACI Clinical (DSMB)	• Abiomed	None	• St. Jude Medical	None	None
Massimo Mancone	Content Reviewer—ACC AIG	Sapienza University of Rome—Cardiology Consultant	None	None	None	None	None	None
Ariane Marelli	Content Reviewer	McGill University Health Center—Professor of Medicine and Director, MAUDE Unit	None	None	None	None	None	None
Koichiro Niwa	Content Reviewer	St. Luke's International Hospital—Director, Department of Cardiology	None	None	None	None	None	None

Matthew Oster	Content Reviewer	Emory University School of Medicine—Associate Professor; Children's Healthcare of Atlanta—Director, Children's Cardiac Outcomes Research Program at Sibley Heart Center	None	None	None	None	None	None
Catherine M. Otto	Content Reviewer	University of Washington School of Medicine—Professor of Medicine, Division of Cardiology and Director, Heart Valve Clinic	None	None	None	None	None	None
Richard L. Page	Content Reviewer	University of Wisconsin School of Medicine and Public Health—Chair, Department of Medicine	None	None	None	None	None	None
James Perry	Content Reviewer	Rady Children's Hospital; University of California, San Diego—Professor of Pediatrics, Affiliate Professor of Bioengineering, and Director, Electrophysiology and Adult Congenital Heart Programs	None	None	None	None	None	None
Susan J. Pressler	Content Reviewer—ACC/AHA Task Force on Clinical Practice Guidelines	Indiana University School of Nursing—Professor and Director, Center for Enhancing Quality of Life in Chronic Illness	None	None	None	None	• Pfizer†	None
Candice K. Silversides	Content Reviewer	University of Toronto—Associate Professor	None	None	None	None	None	None

Duminda N. Wijeysundera	Content Reviewer—ACC/AHA Task Force on Clinical Practice Guidelines	University of Toronto—Assistant Professor, Department of Anesthesia and Institute of Health Policy Management and Evaluation	None	None	None	None	None	None
Ali N. Zaidi	Content Reviewer	Montefiore Einstein Center for Heart and Vascular Care—Director, Montefiore Adult Congenital Heart Disease Program; Albert Einstein College of Medicine—Associate Professor, Internal Medicine and Pediatrics	None	None	None	None	None	None
Elisa Zaragoza-Macias	Content Reviewer	PeaceHealth North Cascade Cardiology—Cardiologist	None	None	None	None	None	None

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 ≥$5,000 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. Please refer to http://www.acc.org/guidelines/about-guidelines-and-clinical-documents/relationships-with-industry-policy for definitions of disclosure categories or additional information about the ACC/AHA Disclosure Policy for Writing Committees.

*Significant relationship.
†No financial benefit.

AATS indicates American Association for Thoracic Surgery; ACC, American College of Cardiology; AHA, American Heart Association; AIG, Assembly of International Governors; ASE, American Society of Echocardiography; DSMB, Data Safety Monitoring Board; HRS, Heart Rhythm Society; ISACHD, International Society for Adult Congenital Heart Disease; MAUDE, McGill Adult Unit for Congenital Heart Disease Excellence; SCAI, Society for Cardiovascular Angiography and Interventions; and STS, Society of Thoracic Surgeons; and UT, University of Texas.

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1. Introduction

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4.4. Complex Lesions

4.4.1. Transposition of the Great Arteries

4.4.1.1. Transposition of the Great Arteries With Atrial Switch

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4.4.6. Severe PAH and Eisenmenger Syndrome

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