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2020 ESC Guidelines for the management of adult congenital heart disease

The Task Force for the management of adult congenital heart disease of the European Society of Cardiology (ESC)

Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Adult Congenital Heart Disease (ISACHD)

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Click here to access the corresponding chapter in Section 17- Congenital heart disease in children and adults

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Abbreviations and acronyms

3D	Three-dimensional
6MWT	6-minute walk test
AAOCA	Anomalous aortic origin of a coronary artery
AAOLCA	Anomalous aortic origin of the left coronary artery
ACAPA	Anomalous coronary artery from the pulmonary artery
ACE	Angiotensin-converting enzyme
ACHD	Adult congenital heart disease
AF	Atrial fibrillation
ALCAPA	Anomalous left coronary artery from the pulmonary artery
AR	Aortic regurgitation
ARB	Angiotensin II receptor blocker
ARCAPA	Anomalous right coronary artery from the pulmonary artery
AS	Aortic stenosis
ASD	Atrial septal defect
ASI	Aortic size index
AT	Atrial tachycardia
AV	Atrioventricular
AVA	Aortic valve area
AVAi	Indexed aortic valve area
AVNRT	Atrioventricular node reentrant tachycardia
AVRT	Atrioventricular reentrant tachycardia
AVSD	Atrioventricular septal defect
BAV	Bicuspid aortic valve
BNP	B-type natriuretic peptide
BSA	Body surface area
CAD	Coronary artery disease
CABG	Coronary artery bypass graft
CCT	Cardiovascular computed tomography
ccTGA	Congenitally corrected transposition of the great arteries
CHD	Congenital heart disease
CMR	Cardiovascular magnetic resonance
CoA	Coarctation of the aorta
CONCOR	CONgenital CORvitia
CPET	Cardiopulmonary exercise testing
CRT	Cardiac resynchronization therapy
DCRV	Double-chambered right ventricle
EACVI	European Association of Cardiovascular Imaging
EAT	Ectopic atrial tachycardia
ECG	Electrocardiogram
EF	Ejection fraction
EP	Electrophysiology/electrophysiological
ERA	Endothelin receptor antagonist
ESC	European Society of Cardiology

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HLHS	Hypoplastic left heart syndrome
HTAD	Heritable thoracic aortic disease
IART	Intraatrial reentrant tachycardia
ICD	Implantable cardioverter defibrillator
IE	Infective endocarditis
INR	International normalized ratio
IVC	Inferior vena cava
LA	Left atrium/atrial
L–R	Left-to-right
LV	Left ventricle/ventricular
LVEF	Left ventricular ejection fraction
LVESD	Left ventricular end systolic diameter
LVH	Left ventricular hypertrophy
LVOT	Left ventricular outflow tract
LVOTO	Left ventricular outflow tract obstruction
MAPCAs	Major aortic pulmonary collaterals
MCV	Mean corpuscular volume
mWHO	Modified World Health Organization
NOAC	Non-vitamin K antagonist oral anticoagulant
NT-pro-BNP	N-terminal-pro-B-type natriuretic peptide
NYHA	New York Heart Association
PA	Pulmonary artery
PAH	Pulmonary arterial hypertension
PAH-CHD	Pulmonary arterial hypertension associated with congenital heart disease
PAP	Pulmonary artery pressure
PDA	Patent ductus arteriosus
PDE-5	Phosphodiesterase type 5
PES	Programmed electrical stimulation
PFO	Patent foramen ovale
PH	Pulmonary hypertension
PM	Pacemaker
PR	Pulmonary regurgitation
PS	Pulmonary stenosis
PVD	Pulmonary vascular disease
PVR	Pulmonary vascular resistance
PVRep	Pulmonary valve replacement
QIs	Quality indicators
Qp:Qs	Pulmonary to systemic flow ratio
RA	Right atrium/atrial
R–L	Right-to-left
rTOF	Repaired tetralogy of Fallot
RV	Right ventricle/ventricular
RVEDVi	Right ventricular end diastolic volume indexed
RVEF	Right ventricular ejection fraction
RVESVi	Right ventricular end systolic volume indexed
RVH	Right ventricular hypertrophy
RVOT	Right ventricular outflow tract
RVOTO	Right ventricular outflow tract obstruction
RVSP	Right ventricular systolic pressure
SCD	Sudden cardiac death
SND	Sinus node dysfunction
SubAS	Subaortic stenosis
SupraAS	Supravalvular aortic stenosis
SVC	Superior vena cava
SVT	Supraventricular tachycardia
TGA	Transposition of the great arteries
TOE	Transoesophageal echocardiography
TOF	Tetralogy of Fallot
TPVI	Transcatheter pulmonary valve implantation
TR	Tricuspid regurgitation
TTE	Transthoracic echocardiography
TV	Tricuspid valve
UVH	Univentricular heart
VE/VCO2	Ventilation to carbon dioxide output
VF	Ventricular fibrillation
VKA	Vitamin K antagonist
Vmax	Maximum Doppler velocity
VSD	Ventricular septal defect
VT	Ventricular tachycardia
WHO	World Health Organization
WU	Wood units

1 Preamble

Guidelines summarize and evaluate available evidence with the aim of assisting health professionals in proposing the best management strategies for an individual patient with a given condition. Guidelines and their recommendations should facilitate decision making of health professionals in their daily practice. However, the final decisions concerning an individual patient must be made by the responsible health professional(s) in consultation with the patient and caregiver as appropriate.

A great number of guidelines have been issued in recent years by the European Society of Cardiology (ESC), as well as by other societies and organizations. Because of their impact on clinical practice, quality criteria for the development of guidelines have been established in order to make all decisions transparent to the user. The recommendations for formulating and issuing ESC Guidelines can be found on the ESC website (https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Guidelines-development/Writing-ESC-Guidelines). The ESC Guidelines represent the official position of the ESC on a given topic and are regularly updated.

In addition to the publication of Clinical Practice Guidelines, the ESC carries out the EurObservational Research Programme of international registries of cardiovascular diseases and interventions which are essential to assess, diagnostic/therapeutic processes, use of resources and adherence to Guidelines. These registries aim at providing a better understanding of medical practice in Europe and around the world, based on high-quality data collected during routine clinical practice.

Furthermore, the ESC has developed and embedded in this document a set of quality indicators (QIs), which are tools to evaluate the level of implementation of the Guidelines and may be used by the ESC, hospitals, healthcare providers and professionals to measure clinical practice as well as used in educational programmes, alongside the key messages from the guidelines, to improve quality of care and clinical outcomes.

The Members of this Task Force were selected by the ESC, including representation from its relevant ESC sub-specialty groups, in order to represent professionals involved with the medical care of

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Table 1 Classes of recommendations

Classes of recommendations	Definition	Wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended or is indicated
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
Class IIa	Weight of evidence/opinion is in favour of usefulness/efficacy.	Should be considered
Class IIb	Usefulness/efficacy is less well established by evidence/opinion.	May be considered
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended

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Table 2 Levels of evidence

Level of evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

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patients with this pathology. Selected experts in the field undertook a comprehensive review of the published evidence for management of a given condition according to ESC Committee for Practice Guidelines (CPG) policy. A critical evaluation of diagnostic and therapeutic procedures was performed, including assessment of the risk–benefit ratio. The level of evidence and the strength of the recommendation of particular management options were weighed and graded according to predefined scales, as outlined below.

The experts of the writing and reviewing panels provided declaration of interest forms for all relationships that might be perceived as real or potential sources of conflicts of interest. Their declarations of interest were reviewed according to the ESC declaration of interest rules and can be found on the ESC website (http://www.escardio.org/guidelines). This process ensures transparency and prevents potential biases in the development and review processes. Any changes in declarations of interest that arise during the writing period were notified to the ESC and updated. The Task Force received its entire financial support from the ESC without any involvement from the healthcare industry.

The ESC CPG supervises and coordinates the preparation of new Guidelines. The Committee is also responsible for the endorsement process of these Guidelines. The ESC Guidelines undergo extensive review by the CPG and external experts. After appropriate revisions the Guidelines are approved by all the experts involved in the Task

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Force. The finalized document is approved by the CPG for publication in the European Heart Journal. The Guidelines were developed after careful consideration of the scientific and medical knowledge and the evidence available at the time of their dating.

The task of developing ESC Guidelines also includes the creation of educational tools and implementation programmes for the recommendations including condensed pocket guideline versions, summary slides, booklets with essential messages, summary cards for non-specialists and an electronic version for digital applications (smartphones, etc.). These versions are abridged and thus, for more detailed information, the user should always access to the full text version of the Guidelines, which is freely available via the ESC website and hosted on the EHJ website. The National Cardiac Societies of the ESC are encouraged to endorse, adopt, translate and implement all ESC Guidelines. Implementation programmes are needed because it has been shown that the outcome of disease may be favourably influenced by the thorough application of clinical recommendations.

Health professionals are encouraged to take the ESC Guidelines fully into account when exercising their clinical judgment, as well as in the determination and the implementation of preventive, diagnostic or therapeutic medical strategies. However, the ESC Guidelines do not override in any way whatsoever the individual responsibility of health professionals to make appropriate and accurate decisions in consideration of each patient's health condition and in consultation with that patient or the patient's caregiver where appropriate and/or necessary. It is also the health professional's responsibility to verify the rules and regulations applicable in each country to drugs and devices at the time of prescription.

2 Introduction

2.1 Why do we need new Guidelines on the management of adult congenital heart disease?

Since the previous version of the Guidelines on the management of grown-up congenital heart disease (CHD) was published in 2010, new evidence has accumulated for this patient group, particularly on percutaneous interventional techniques and risk stratification with regard to timing of surgery and catheter intervention, as well as medical treatment. This made a revision of the recommendations necessary.

Since adult patients with CHD now present in increasing numbers at advanced ages, including the elderly, the term grown-up CHD no longer appears appropriate and was therefore replaced with adult CHD (ACHD) throughout the document. This is also in accordance with international literature.

2.2 Content of these Guidelines

Decision making in ACHD involves accurate diagnosis, timing of intervention, risk assessment, and selection of the most suitable type of intervention. In addition, specific aspects of medical treatment for conditions such as heart failure, pulmonary hypertension (PH), and anticoagulation are addressed.

These guidelines focus on ACHD, are oriented towards management, and for more details in the topics of endocarditis, isolated valve disease, and aortic disease, refer to the relevant separate guideline documents published by the European Society of Cardiology (ESC).

2.3 New format of the Guidelines

The new Guidelines have been adapted to facilitate their use in clinical practice and to meet the readers' demands by focusing on condensed, clearly presented recommendations. At the end of the document, *section 5* proposes topics for future research and *section 6* summarizes the key messages. For more background information please refer to the ESC Textbook of Cardiovascular Medicine.[1]

2.4 How to use these Guidelines

The Committee emphasizes that many factors ultimately determine the most appropriate treatment in individual patients within a given community. These factors include availability of diagnostic equipment, the expertise of cardiologists and surgeons, especially in the field of congenital heart surgery and percutaneous intervention, and notably, the wishes of well-informed patients. Furthermore, owing to the lack of evidence-based data in the field of ACHD, most recommendations are largely the result of expert consensus based on retrospective and prospective observational studies and registries. Therefore, deviations from these Guidelines may be appropriate in certain clinical circumstances.

2.5 What is new in the 2020 Guidelines?

Selected revised recommendations, new recommendations, and new concepts are summarized in *Table 3*.

3 General aspects

3.1 Prevalence of adult congenital heart disease

To date, the prevalence of CHD worldwide is ~9 per 1000 newborns, with substantial geographic variation.[2,3] While the prevalence of severe congenital heart defects is declining in many Western/developed countries due to foetal screening and pregnancy termination, overall prevalence on a global scale is increasing.[4] Due to medical, surgical, and technological evolutions over the past decades, >90% of individuals with CHD who are born, now survive into adulthood.[5] As a result, the prevalence of CHD in the community has increased and now by far exceeds the number of children with CHD.[6] CHD can be classified as mild, moderate, or severe (see *Table 4*).

3.2 Organization of care

When patients with CHD are approaching adulthood, they require transfer to ACHD care. This transfer should be preceded by a preparatory transition phase, which continues into adulthood according to the needs of the patient. Special healthcare organization and training programmes are required to meet the needs of this patient population.[7] Importantly, the care for ACHD patients is a lifelong process (*Figure 1*) and also requires advance care planning strategies. The ESC Working Group on Grown-up Congenital Heart Disease published a position paper on recommendations for organization of care and training in the subspecialty of ACHD in Europe.[8] The position paper refers to the previous ESC Guidelines[9] and stratified patient care into

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Table 3 Selected revised recommendations (R), new recommendations (N), and new concepts

Arrhythmia		
N	There were no formal recommendations on arrhythmia in the 2010 edition – these have now been included – for details see recommendation tables in *Sections 3.4.2 and 4.10*. Summary of the most important items: • Emphasizing the importance of understanding the cause, the mechanism of the arrhythmia, and the anatomy of the underlying CHD • Emphasizing the importance of a multidisciplinary approach for optimal arrhythmia treatment prior to, or concomitant with, percutaneous or surgical interventions • Consideration of early catheter ablation as an alternative to long-term medical treatment for symptomatic SVT and VT provided that the procedure is performed in experienced centres • Targeting VT-related anatomical isthmuses in repaired tetralogy of Fallot patients with sustained VTs before percutaneous or surgical reintervention in the RVOT, as these procedures may lead to inaccessibility of the VT substrates • Recognizing the association between bradycardia and IART and the potential benefit of PM implantation.	
Eisenmenger sydrome /pulmonary arterial hypertension		
N	It is recommended that patients with CHD and confirmed pre-capillary PH are counselled against pregnancy.	
N	Risk assessment is recommended in all patients with PAH-CHD.	
N	In low- and intermediate-risk patients with repaired simple lesions and pre-capillary PH, initial oral combination therapy or sequential combination therapy is recommended, and high-risk patients should be treated with initial combination therapy including parenteral prostanoids.	
R	Emphasize the importance of sequential PAH therapy strategy in Eisenmenger syndrome and use of 6MWT for the decision to initiate therapy.	In Eisenmenger patients with reduced exercise capacity (6MWT distance <450 m), a treatment strategy with initial endothelin receptor antagonist monotherapy should be considered followed by combination therapy if patients fail to improve.
Shunt lesions		
N	In patients with shunt lesions and non-invasive signs of PAP elevation, invasive measurement of PVR is mandatory.	
N/R	Adjusted recommendations for shunt closure (when Qp:Qs >1.5) according to calculated PVR:	
	<3 WU: class I for ASD, VSD, and PDA	
	3–5 WU: class IIa for ASD, VSD, and PDA	
	≥5 WU but decreasing to <5 WU after targeted PAH treatment: class IIb for ASD (fenestrated closure only)	
	≥5 WU for VSD and PDA (careful individual decision in expert centres); class IIb	
	≥5 WU despite targeted PAH treatment: class III for ASD.	
N	In patients with ASD and LV disease, it is recommended to perform balloon testing and carefully weigh the benefit of eliminating L–R shunt against the potential negative impact of ASD closure on outcome due to increase in filling pressure (taking closure, fenestrated closure, and no closure into consideration).	
N	Take older age into account in the decision for surgical ASD closure.	In elderly patients not suitable for device closure, it is recommended to weigh the surgical risk against the potential benefit of ASD closure.
R	Transcatheter VSD closure has become an alternative to surgery in selected patients, particularly in residual VSD.	Transcatheter VSD closure has become an alternative, particularly in residual VSDs, VSDs poorly accessible by surgery, and in muscular VSDs centrally located in the interventricular septum.
R	Specify the requirement for a congenital cardiac surgeon for partial AVSD closure.	Surgical closure is recommended in patients with significant RV volume overload and should only be performed by a congenital cardiac surgeon.
R	Specify the presence of atrial fibrillation or PH as requirements for valve repair in AVSD.	In asymptomatic patients with severe left-sided AV valve regurgitation, preserved LV function (LVESD <45 mm and/or LVEF >60%), high likelihood of successful valve repair, and low surgical risk, intervention should be considered when atrial fibrillation or systolic PAP >50 mmHg is present.
R	Specify the option of fenestrated ASD closure.	In patients with PVR ≥5 WU, fenestrated ASD closure may be considered when PVR falls below 5 WU after targeted PAH treatment and significant L–R shunt is present (Qp:Qs >1.5).
R	Include desaturation on exercise as a contraindication for ASD, VSD, AVSD, and PDA closure.	Shunt closure is not recommended in patients with severe PAH (PVR ≥5 WU) presenting with desaturation on exercise.

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Left ventricular outflow tract obstruction and aortopathies		
R	Increase the recommendation class from IIa to I in low-flow, low-gradient AS for intervention.	Intervention is indicated in patients with severe low-flow, low-gradient (mean gradient <40 mmHg) AS with reduced EF and evidence of flow (contractile) reserve excluding pseudosevere AS.
R	Lower mean Doppler gradient threshold for LVOTO intervention from 50 to 40 mmHg.	In symptomatic patients with valvular, subvalvular, or supravalvular AS and mean Doppler gradient ≥40 mmHg surgery is recommended.
R	Include BNP levels and increased PAP in the indication for intervention in valvular AS.	Intervention should be considered in asymptomatic patients with normal EF and no exercise test abnormalities (see *Section 4.5.1*) if the surgical risk is low and one of the following findings is present: • Markedly elevated BNP levels (>3-fold age- and sex-corrected normal range) confirmed by repeated measurements without other explanation. • Severe PH (systolic PAP at rest >60 mmHg confirmed by invasive measurement) without other explanation.
R	Confirm pressure gradients by invasive measurement and prefer stenting in coarctation and re-coarctation when technically feasible.	Repair of coarctation or re-coarctation (surgically or catheter based) is indicated in hypertensive patients with an increased non-invasive gradient between upper and lower limbs confirmed by invasive measurement (peak-to-peak ≥20 mmHg), with preference for catheter treatment (stenting) when technically feasible.
N	Catheter treatment (stenting) of coarctation should be considered in normotensive patients with an increased non-invasive gradient confirmed with invasive measurement (peak-to-peak ≥20 mmHg) when technically feasible.	
N	In aortopathies, aortic valve repair using the reimplantation or remodelling with aortic annuloplasty technique is recommended in young patients with Marfan syndrome or related HTAD with aortic root dilation and tricuspid aortic valves, when performed by experienced surgeons.	
N	Surgery should be considered in patients with a *TGFBR1* or *TGFBR2* mutation (including Loeys–Dietz syndrome) who have aortic root disease with maximal aortic sinus diameter ≥45 mm.	
N	In Turner syndrome, elective surgery for aneurysms of the aortic root and/or ascending aorta should be considered for women who are >16 years of age, have an ascending ASI >25 mm/m^2, and have associated risk factors for aortic dissection.	
N	In Turner syndrome, elective surgery for aneurysms of the aortic root and/or ascending aorta may be considered for women who are >16 years of age, have an ascending aortic size index >25 mm/m^2, and do not have associated risk factors for aortic dissection.	
Right ventricular outflow tract obstruction / tetralogy of Fallot /Ebstein		
R	Adjust recommendations for surgical intervention in RVOTO according to symptoms.	If surgical valve replacement is the only option, it is indicated in patients with severe stenosis who are symptomatic. If surgical valve replacement is the only option in patients with severe stenosis who are asymptomatic, it is indicated in the presence of one or more of the following: • Objective decrease in exercise capacity • Decreasing RV function and/or progressive TR to at least moderate • RVSP >80 mmHg • R–L shunting via an ASD or VSD.
R	Include preference for catheter intervention for pulmonary valve implantation in TOF.	In patients with no native outflow tract, catheter intervention (TPVI) should be preferred if anatomically feasible.
R	Specify RV dilatation in the setting of pulmonary valve replacement for TOF and for RVOT conduits.	Pulmonary valve replacement should be considered in asymptomatic patients with severe PR and/or RVOTO, in the presence of progressive RV dilation to RVESVi ≥80 mL/m^2, and/or RVEDVi ≥160 mL/m^2, and/or progression of TR to at least moderate.

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R	In case of ASDs in Ebstein anomaly, add caution about RA pressure rise or fall in cardiac output.	In the case of documented systemic embolism probably caused by paradoxical embolism, isolated device closure of ASD/PFO should be considered but requires careful evaluation before intervention to exclude induction of RA pressure increase or fall in cardiac output.
		If cyanosis (oxygen saturation at rest <90%) is the leading problem, isolated device closure of ASD/PFO may be considered but requires careful evaluation before intervention to exclude induction of RA pressure increase or fall in cardiac output.
Transposition of the great arteries		
R	Downgrade level of recommendation for AV valve repair in TGA/atrial switch from I to IIa in symptomatic patients.	In patients with severe systemic (tricuspid) AV valve regurgitation without significant ventricular systolic dysfunction (EF >40%), valve repair or replacement should be considered *regardless of symptoms.*
R	In patients with TGA/atrial switch requiring PM/ICD implantation: pay attention to the presence of baffle leaks.	In patients with a baffle leak who require a PM/ICD, closure of the baffle leak should be considered, when technically feasible, prior to insertion of transvenous leads.
N	In ccTGA, biventricular pacing should be considered in case of complete AV block or >40% ventricular pacing requirement.	
R	Revise indications for TV replacement in ccTGA, according to symptoms and systemic ventricular function. (Upgrade level of recommendation for symptomatic ccTGA patients from IIa to I).	In *symptomatic* patients with severe TR and preserved or mildly impaired systemic RV systolic function (EF >40%), TV replacement is indicated.
		In *asymptomatic* patients with severe TR and progressive systemic RV dilatation and/or mildly impaired systemic RV systolic function (EF >40%), TV replacement should be considered.
		In *symptomatic* patients with severe TR and more than mildly reduced systemic RV systolic function (EF ≤40%), TV replacement may be considered.
R	Anatomic repair (atrial + arterial switch) for ccTGA removed from the recommendations.	
Univentricular heart		
N	It is recommended that adults with unoperated or palliated UVHs undergo careful evaluation in specialized centres including multimodality imaging as well as invasive work-up to decide whether they may benefit from surgical or interventional procedures.	
Fontan circulation		
N	Sustained atrial arrhythmia with rapid AV conduction is a medical emergency and should promptly be treated with electrical cardioversion.	
N	Anticoagulation is indicated in the presence, or with a history, of atrial thrombus, atrial arrhythmias, or thromboembolic events.	
N	It is recommended that women with a Fontan circulation and any complication are counselled against pregnancy.	
N	Cardiac catheterization is recommended at a low threshold in cases of unexplained oedema, exercise deterioration, new-onset arrhythmia, cyanosis, and haemoptysis.	
N	In patients with arrhythmias, a proactive approach of electrophysiological evaluation and ablation (where appropriate) should be considered.	
N	Regular liver imaging (ultrasound, computed tomography, magnetic resonance) should be considered.	
N	Endothelin receptor antagonists and phosphodiesterase-5 inhibitors may be considered in selected patients with elevated pulmonary pressures/resistance in the absence of elevated ventricular end diastolic pressure.	
N	In selected patients with significant cyanosis, device closure of a fenestration may be considered but requires careful evaluation before intervention to exclude induction of systemic venous pressure increase or fall in cardiac output.	
Coronary artery anomalies		
N	Non-pharmacological functional imaging (e.g. nuclear study, echocardiography or CMR with physical stress) is recommended in patients with coronary anomalies to confirm/exclude myocardial ischaemia.	
A) Anomalous coronary artery from the pulmonary artery (ACAPA)		
N	Surgery is recommended in patients with ALCAPA.	
N	Surgery is recommended in patients with ARCAPA and symptoms attributable to anomalous coronary artery.	

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N	Surgery should be considered for ARCAPA in asymptomatic patients with ventricular dysfunction, or myocardial ischaemia attributable to coronary anomaly.
B) Anomalous aortic origin of a coronary artery (AAOCA)	
N	Surgery is recommended for AAOCA in patients with typical angina symptoms who present with evidence of stress-induced myocardial ischaemia in a matching territory or high-risk anatomy.
N	Surgery should be considered in *asymptomatic* patients with AAOCA (right or left) and evidence of myocardial ischaemia.
N	Surgery should be considered in *asymptomatic* patients with AAOLCA and no evidence of myocardial ischaemia but a high-risk anatomy.
N	Surgery may be considered for symptomatic patients with AAOCA even if they have neither evidence of myocardial ischaemia nor high-risk anatomy.
N	Surgery may be considered for *asymptomatic* patients with AAOLCA without myocardial ischaemia and without high-risk anatomy when they present at young age (<35 years).
N	Surgery is not recommended for AAORCA in *asymptomatic* patients without myocardial ischaemia and without high-risk anatomy.
New concepts	
	Naming (ACHD).
	Disease complexity classification.
	Staffing requirements for an ACHD expert centre.
	Emerging role of biomarkers in follow-up of ACHD.
	Detailed and specific recommendations on arrhythmia management.
	More specific and adjusted recommendations for PAH treatment.
	Recommendations on the use of anticoagulants.
	Consideration of ageing and advance care planning.
	Categories of high-risk pregnancies in accordance with the pregnancy guidelines.
	Expand Marfan syndrome section to aortopathies (and include HTAD, Turner syndrome, and bicuspid aortic disease).
	Emerging role of catheter intervention in ACHD.

6MWT = 6-minute walk test; AAOCA = anomalous aortic origin of a coronary artery; AAOLCA = anomalous aortic origin of the left coronary artery; ACAPA = anomalous coronary artery from the pulmonary artery; ACHD = adult congenital heart disease; AF = atrial fibrillation; ALCAPA = anomalous left coronary artery from the pulmonary artery; ARCAPA = anomalous right coronary artery from the pulmonary artery; AS = aortic stenosis; ASD = atrial septal defect; AV = atrioventricular; AVSD = atrioventricular septal defect; BNP = B-type natriuretic peptide; ccTGA = congenitally corrected transposition of the great arteries; CHD = congenital heart disease; CMR = cardiovascular magnetic resonance; EF = ejection fraction; HTAD = heritable thoracic aortic disease; IART = intraatrial reentrant tachycardia; ICD = implantable cardioverter defibrillator; L–R = left-to-right; LV = left ventricle/ventricular; LVEF = left ventricular ejection fraction; LVESD = left ventricular end systolic diameter; LVOT = left ventricular outflow tract; LVOTO = left ventricular outflow tract obstruction; N = new recommendation; PAH = pulmonary arterial hypertension; PAH-CHD = pulmonary arterial hypertension associated with congenital heart disease; PAP = pulmonary artery pressure; PDA = patent ductus arteriosus; PFO = patent foramen ovale; PH = pulmonary hypertension; PR = pulmonary regurgitation; PVR = pulmonary vascular resistance; Qp:Qs = pulmonary to systemic flow ratio; R = revised recommendation; RA = right atrium/atrial; R–L = right-to-left; RV = right ventricle/ventricular; RVEDVi = right ventricular end diastolic volume indexed; RVESVi = right ventricular end systolic volume indexed; RVOT = right ventricular outflow tract; RVOTO = right ventricular outflow tract obstruction; RVSP = right ventricular systolic pressure; SVT = supraventricular tachycardia; TGA = transposition of the great arteries; TGFBR = transforming growth factor beta receptor; TOF = tetralogy of Fallot; TPVI = transcatheter pulmonary valve implantation; TR = tricuspid regurgitation; TV = tricuspid valve; UVH = univentricular heart; VSD = ventricular septal defect; VT = ventricular tachycardia; WU = Wood units.

three levels: (i) patients who require care exclusively in a specialist centre, (ii) patients for whom shared care can be established with the appropriate general adult cardiac services, and (iii) patients who can be managed in non-specialist clinics (with access to specialized care if required). The proposed staff requirements for specialist centres are described in *Table 5*. The complexity of the heart defect should not be the only criterion to assign patients to a certain level of care. Although patients with complex defects can easily be assigned to a high level of care, even anatomically simple defects may require specialist care under certain circumstances [e.g. atrial septal defect (ASD) with pulmonary arterial hypertension (PAH)]. Therefore, it is recommended that all ACHD patients are seen once in a specialist centre, allowing ACHD specialists to determine the most appropriate level of care and follow-up intervals for each individual patient.[8] Networks of specialist centres with general adult care should be established for each catchment area. Indeed, with the growing population of adults with CHD, more patients will first present to general cardiologists for acute conditions, such as arrhythmia, heart failure, or endocarditis. In such cases, general cardiologists should not delay treatment in haemodynamically unstable patients but ought to liaise with the patient's ACHD centre immediately to discuss appropriate management strategies or transfer of the patient. Special attention is necessary for patients after Fontan correction presenting with arrhythmia, as even supraventricular arrhythmias are not well tolerated. Detailed advice on emergency care for ACHD patients will follow in a separate future position paper.

Transfer of adolescents to ACHD care is vital as they approach adulthood without gaps in care, and should be preceded by a preparatory transition phase with additional transition support that continues into early adulthood according to the needs of the patient.[10] Transition requires a special healthcare organization.[10,11] It is recommended that specialist ACHD centres have teams including specialist nurses, psychologists, and social workers given that anxiety, depression, or problems coping with the medical condition are well known concerns in adult patients with CHD.[12] They also play a critical role in the transition process by taking over the transitional care of patients after the transfer from paediatric cardiology. Aspects that have to be addressed by allied health professionals include mental health, psychic well-being, and quality of life.[12,13] During the ACHD

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Table 4 Classification of congenital heart disease complexity

MILD:
• Isolated congenital aortic valve disease and bicuspid aortic disease
• Isolated congenital mitral valve disease (except parachute valve, cleft leaflet)
• Mild isolated pulmonary stenosis (infundibular, valvular, supravalvular)
• Isolated small ASD, VSD, or PDA
• Repaired secundum ASD, sinus venosus defect, VSD, or PDA without residuae or sequellae, such as chamber enlargement, ventricular dysfunction, or elevated PAP.
MODERATE: (Repaired or unrepaired where not specified; alphabetical order)
• Anomalous pulmonary venous connection (partial or total)
• Anomalous coronary artery arising from the PA
• Anomalous coronary artery arising from the opposite sinus
• Aortic stenosis - subvalvular or supravalvular
• AVSD, partial or complete, including primum ASD (excluding pulmonary vascular disease)
• ASD secundum, moderate or large unrepaired (excluding pulmonary vascular disease)
• Coarctation of the aorta
• Double chambered right ventricle
• Ebstein anomaly
• Marfan syndrome and related HTAD, Turner Syndrome
• PDA, moderate or large unrepaired (excluding pulmonary vascular disease)
• Peripheral pulmonary stenosis
• Pulmonary stenosis (infundibular, valvular, supravalvular), moderate or severe
• Sinus of Valsalva aneurysm/fistula
• Sinus venosus defect
• Tetralogy of Fallot – repaired
• Transposition of the great arteries after arterial switch operation
• VSD with associated abnormalities (excluding pulmonary vascular disease) and/or moderate or greater shunt.
SEVERE: (Repaired or unrepaired where not specified; alphabetical order)
• Any CHD (repaired or unrepaired) associated with pulmonary vascular disease (including Eisenmenger syndrome)
• Any cyanotic CHD (unoperated or palliated)
• Double-outlet ventricle
• Fontan circulation
• Interrupted aortic arch
• Pulmonary atresia (all forms)
• Transposition of the great arteries (except for patients with arterial switch operation)
• Univentricular heart (including double inlet left/right ventricle, tricuspid/mitral atresia, hypoplastic left heart syndrome, any other anatomic abnormality with a functionally single ventricle)
• Truncus arteriosus
• Other complex abnormalities of AV and ventriculoarterial connection (i.e. crisscross heart, heterotaxy syndromes, ventricular inversion).

ASD = atrial septal defect; AV = atrioventricular; AVSD = atrioventricular septal defect; CHD = congenital heart disease; HTAD = heritable thoracic aortic disease; LV = left ventricle/ventricular; PA = pulmonary artery; PAP = pulmonary artery pressure; PDA = patent ductus arteriosus; VSD = ventricular septal defect.

care journey, advance care planning choices and strategies relating to end of life also require expert support.

3.3 Diagnostic work-up

Besides a thorough clinical evaluation, the medical history, including detailed information about palliative or reparative surgery and catheter-based interventions, is of critical importance in the work-up of ACHD patients. The aim of analysing patient history is to assess present and past symptoms, as well as to look for intercurrent events and any changes in medication. The most frequent symptoms reported by ACHD patients are exercise intolerance and palpitations. Self-estimated physical capacity corresponds poorly with objective measures of exercise capacity.[14] Therefore, cardiopulmonary exercise testing (CPET) has gained importance for objective assessment of exercise intolerance in both apparently asymptomatic and symptomatic patients. In addition, the patient should be questioned about his/her lifestyle to detect progressive changes in daily activity in order to limit the subjectivity of symptom analysis. In symptomatic patients, alternative causes such as anaemia, depression, weight gain, and physical deconditioning, besides the congenital defect and its sequelae or residuae, should be kept in mind and further excluded if necessary.

Clinical examination plays a major role and includes careful evaluation of any changes in auscultation findings, blood pressure, or

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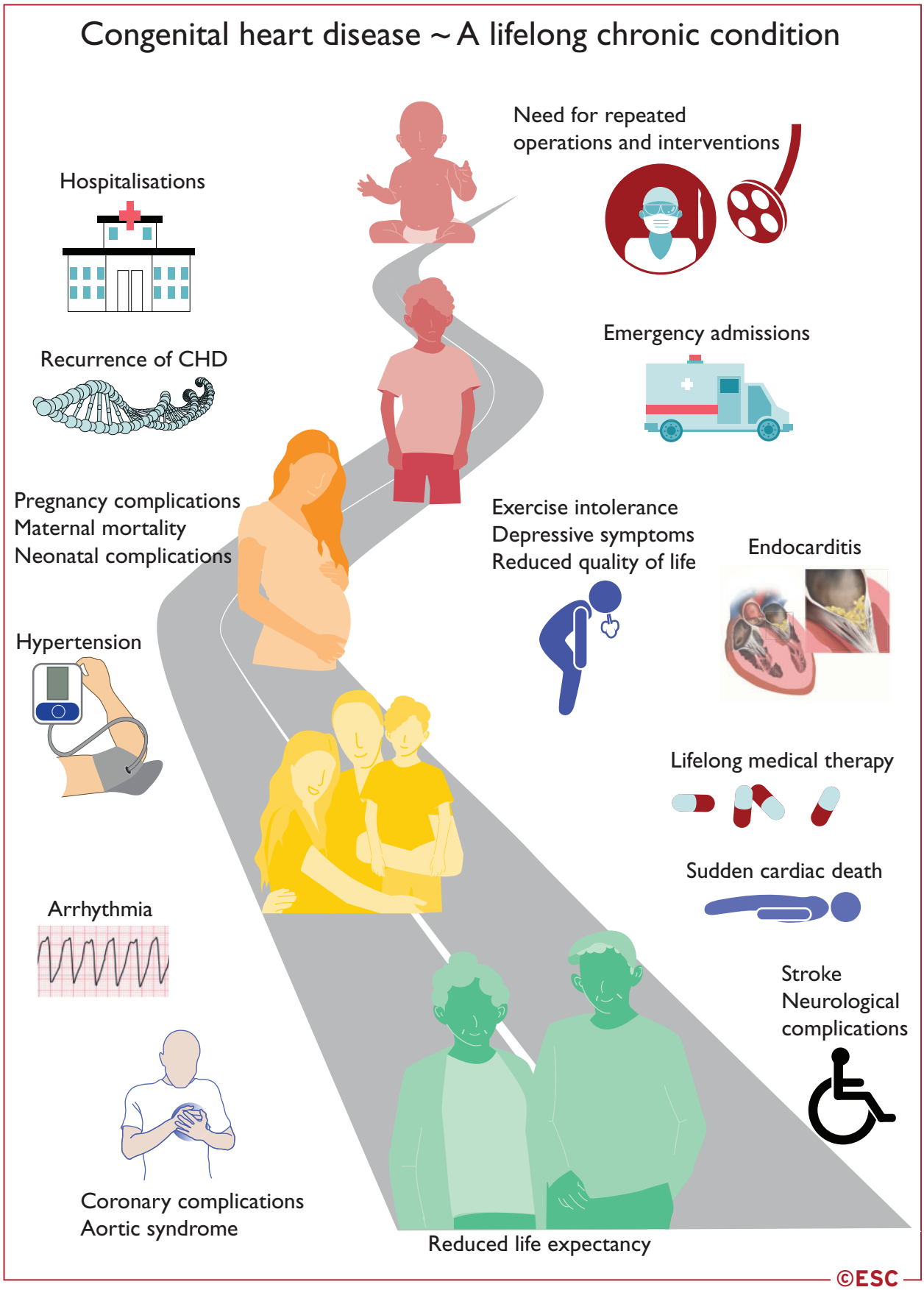


Figure 1 Central illustration. Congenital heart disease is a lifelong chronic condition.
CHD = congenital heart disease; SCD = sudden cardiac death.

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Table 5 Staff requirements for specialist ACHD centres[a]

Discipline	Required number
Adult/paediatric cardiologist with ACHD certification	≥2
ACHD imaging specialist (certified in TTE/TOE, CMR, CCT)	≥2
Congenital interventional cardiologist	≥2
CHD surgeon	≥2
Anaesthesiologist with CHD experience and expertise	≥2
Specialist nurse (if national professional nursing bodies allow specialization)	≥2
Invasive electrophysiologist with ACHD experience	≥1
Pulmonary vascular disease expert	≥1
Clinical geneticist	≥1
Psychologist	≥1
Social worker	≥1
Palliative care team	

ACHD = adult congenital heart disease; CHD = congenital heart disease; CMR = cardiovascular magnetic resonance; CCT = cardiovascular computed tomography; TOE = transoesophageal echocardiography; TTE = transthoracic echocardiography.
[a]Modified from Baumgartner *et al.*[8]

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Table 6 Indications for cardiovascular magnetic resonance imaging in ACHD patients

Indications for CMR in ACHD patients
• Quantification of RV volumes, EF (including subpulmonary RV, systemic RV, and single ventricle)
• Evaluation of RVOTO and RV–PA conduits
• Quantification of PR
• Evaluation of PAs (stenoses, aneurysms) and the aorta [aneurysm, dissection, coarctation (CCT may be superior)]
• Evaluation of systemic and pulmonary veins (anomalous connection, obstruction, coronary venous anatomy pre-procedure, etc.)
• Collaterals and arteriovenous malformations (CCT may be superior)
• Coronary anomalies and CAD (CCT is superior for intramural course, slit-like course, acute angle take-off, myocardial bridging, and plaque assessment)
• Detection and quantification of myocardial ischaemia by CMR stress perfusion
• Evaluation of intra- and extracardiac masses
• Quantification of myocardial mass (LV and RV)
• Detection and quantification of myocardial fibrosis/scar (late gadolinium enhancement, T1 mapping) tissue characterization (fibrosis, fat, iron, etc.)
• Quantification of systemic and pulmonary blood flow to calculate Qp:Qs
• Quantification of perfusion distribution to the right/left lung
• Measurement of pulmonary blood flow in patients with multiple sources of blood supply (i.e. with major aorto-pulmonary collateral arteries)

ACHD = adult congenital heart disease; CAD = coronary artery disease; CMR = cardiovascular magnetic resonance; CCT = cardiovascular computed tomography; EF = ejection fraction; LV = left ventricle/ventricular; PA = pulmonary artery; PR = pulmonary regurgitation; Qp:Qs = pulmonary to systemic flow ratio; RV = right ventricle/ventricular; RVOTO = right ventricular outflow tract obstruction.

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development of signs of heart failure. An electrocardiogram (ECG) and pulse oximetry are routinely carried out alongside clinical examination. A chest X-ray provides information on changes in heart size and configuration, as well as pulmonary vascularization. Non-invasive imaging is routinely performed by transthoracic echocardiography (TTE) involving transoesophageal echocardiography (TOE) and cardiovascular magnetic resonance (CMR) imaging where indicated. Thus, patients with CHD may particularly benefit from magnetic resonance-conditional/compatible pacemakers and defibrillators.

Echocardiography is superior to CMR in estimating pressure gradients and pulmonary artery (PA) pressure (PAP), and detecting small, highly mobile structures such as vegetations. CMR is ideal for accurate quantification of ventricular volumes, ejection fraction (EF), valvular regurgitation,[15] calculation of pulmonary and systemic blood flow, and myocardial fibrosis assessment. Cardiovascular computed tomography (CCT) with modern single or dual source scanners can be performed with dose-saving protocols and may be required for special indications — as indicated in *Table 6*. Interdisciplinary expert collaboration is important: imaging CHD experts need to respond to feedback from CHD surgeons, interventionalists, and electrophysiologists to optimize imaging contribution to care, as well as work with each other to enhance appropriate use of multimodality imaging. Advanced imaging is usually best reserved for when patients are seen in the specialist centre rather than be repeated.

Echocardiography, CMR, and CCT require staff with expertise in CHD as well as in imaging, which has training and resource implications. Within the ESC, this is recognized by a certification examination of the European Association of Cardiovascular Imaging (EACVI), separate from the standard TTE, TOE, or CMR examination, and specific to CHD.

3.3.1 Echocardiography

Echocardiography remains the first-line imaging modality.[16] M-mode, two-dimensional, and three-dimensional (3D) echocardiography are all used for imaging, whereas tissue Doppler imaging and deformation imaging, especially longitudinal strain and strain rate, are becoming integral parts of functional assessment.[17]

Echocardiography provides information on cardiac anatomy, situs (including orientation and position of the heart), connection of the atria and ventricles, heart valves, and connection of ventricles with the great arteries. For assessment of morphology and function of cardiac valves, TTE and, if necessary, TOE (nowadays often combined with 3D echocardiography), is the preferred imaging modality. This is also true for shunt lesions, such as ASDs or ventricular septal defects (VSDs): 3D echocardiography enables an en face view, which can be helpful in the assessment of the size and shape of a defect and its relation to surrounding structures.

Ventricular size, shape, volume, and EF can be measured and calculated with TTE. Signs of volume overload, in the case of a shunt or valvular regurgitation, or pressure overload, in the case of increased afterload, are detected in a good-quality TTE. Even older techniques using M-mode for measurement of tricuspid annular plane systolic

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excursion and mitral annular plane systolic excursion are still valid, especially in longitudinal follow-up. For left ventricular (LV) systolic function, 3D echocardiography, tissue Doppler imaging, and two-dimensional deformation imaging have proved to be robust tools and deserve to be integrated into clinical practice. Even accounting for newer techniques, echocardiography retains a key role in longitudinal follow-up assessment of systolic function of a right or single ventricle, although for more accurate measurements additional imaging is often needed in the form of CMR.

3.3.2 Cardiovascular magnetic resonance imaging

CMR has become an essential facility in the specialist unit. It enables 3D anatomical reconstruction, which is not restricted by body size or acoustic windows, and has rapidly improving spatial and temporal resolution.[18] CMR requires a regular heart rhythm for optimal image quality, however, diagnostic CMR studies are often achievable even in patients with irregular heart rhythms [frequent ectopy or atrial fibrillation (AF)] and metallic artefacts. CMR is the gold-standard imaging method for quantification of volumes. It may be an alternative when echocardiography cannot be obtained with sufficient quality, or used as a second method when echocardiography measurements are borderline or ambiguous. Furthermore, the lack of radiation makes it a useful tool when serial evaluations are needed (e.g. for monitoring aortic dimensions). CMR allows calculation of systemic and pulmonary blood flow in patients with multiple sources of blood supply and, in combination with invasive catheterization, of pulmonary vascular resistance (PVR). Tissue characterisation for myocardial fibrosis is a unique capability of CMR. Late gadolinium enhancement CMR for focal fibrosis and interstitial fibrosis T1 mapping imaging are increasingly being applied in ACHD for their potential diagnostic and prognostic value. However, large CHD lesion-specific studies to determine if they predict survival are ongoing.

To mitigate the low risk of nephrogenic systemic fibrosis, gadolinium contrast should be avoided in patients with a low glomerular filtration rate (<30 mL/min/1.73 m^2). It is therefore recommended that creatinine levels are checked prior to CMR. Even though clinical repercussions have not yet been seen, long-term brain deposits of gadolinium — regardless of renal function — raised concerns about cumulative lifetime doses in CHD patients who undergo serial CMR from a young age. It is preferred, therefore, that gadolinium is selectively administered in specialist centres using a macrocyclic, rather than linear chelated, gadolinium contrast, which presents a decreased risk at the lowest dose to achieve image enhancement.[19]

Adults with CHD with conventional pacemakers (PM) and defibrillators (ICD) can undergo CMR within guidelines where local support is available.[20]

3D CMR imaging can be integrated into electrophysiology (EP) procedures to inform and guide them. 3D CCT and CMR reconstructions can also be used for virtual reality rehearsal of interventions or planning from patient-specific 3D prints.

Indications for CMR are summarized in *Table 6*.

3.3.3 Cardiovascular computed tomography

CCT has high spatial resolution and rapid acquisition time; it is particularly relevant for imaging the great vessels, coronary arteries, and collateral arteries, and for parenchymal lung disease (*Table 6*). In many institutions, CCT is the preferred imaging modality in planning for transcatheter valve implantation. Ventricular size and function can be assessed, with inferior temporal resolution compared with CMR, typically with an increased radiation dose, and is therefore not used serially for this indication. Recent rapid developments have substantially reduced the amount of radiation exposure, achieving <5 mSv for a combined CCT coronary, pulmonary, and aortic angiogram. For ACHD patients, this has made CCT more attractive for specific indications such as assessment, in particular for coronary artery pathology, and detailed assessment of collaterals.[21]

CCT is particularly useful in emergency settings including dissection, pulmonary embolism, and paravalvular abscess in the setting of endocarditis, where it may have advantages over echocardiography and CMR due to being less susceptible to prosthetic valve artefact.

In patients with prosthetic valves (in situ >3 months), fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography is useful for early diagnosis of inflammation and infection at the site of the valve, and also for identifying infection at secondary sites.[22]

3.3.4 Cardiopulmonary exercise testing

Formal exercise testing has an important role in the CHD population, in which quality of life and functional capacity are key measures of the success of intervention. CPET, including assessment of objective exercise capacity (peak oxygen consumption), ventilatory efficiency [ventilation to carbon dioxide output (VE/VCO_2) slope], chronotropic and blood pressure response, as well as exercise-induced arrhythmia and desaturation, gives a broader evaluation of functional capacity and physical fitness, and has endpoints which correlate well with morbidity and mortality in ACHD patients.[23] Serial exercise testing should therefore be a part of long-term follow-up protocols. It plays an important role in the timing of interventions and reinterventions. CPET is also a useful tool for recommending the intensity of physical activity based on an individualized exercise prescription.[24] The 6-minute walk test (6MWT) is another simple test for quantification of exercise capacity; it relates to outcome in patients with PAH.

3.3.5 Cardiac catheterization

Cardiac catheterization is mainly reserved for resolution of specific anatomical and physiological questions, or for intervention. Indications include assessment of PVR, ventricular diastolic function (including constrictive and restrictive physiology), pressure gradients, shunt quantification, coronary angiography, and evaluation of extracardiac vessels such as aortic pulmonary collateral arteries when non-invasive evaluation leaves uncertainty.

In shunt lesions with Doppler echocardiographic signs of PH, catheterization — including testing of vasoreactivity — remains essential in the decision on shunt closure. Inhaled nitric oxide is the most widely used agent for this purpose. Estimation of PVR in shunt lesions requires accurate calculation of pulmonary flow using the Fick principle. This method with measured oxygen consumption allows the most accurate cardiac output quantification.

Before surgery, coronary artery imaging should be performed (by CCT or invasive coronary angiography) in men >40 years of age, postmenopausal women, and patients with signs of, or one or more risk factors for, coronary artery disease (CAD).[25]

3.3.6 Biomarkers

Different classes of biomarkers have been reported to be associated with adverse events in the CHD population, including

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neurohormones and markers of myocardial injury (high-sensitivity troponins) or inflammation (high-sensitivity C-reactive protein). Among the neurohormones, natriuretic peptides [B-type natriuretic peptide (BNP) and N-terminal-pro-BNP (NT-pro-BNP)] are best studied in ACHD patients. They carry important prognostic information, but are less useful to diagnose heart failure across different cardiac lesions due to a cut-off variability depending on the underlying defect and type of repair.[26] They are most useful in patients with biventricular circulation and least useful in patients with a Fontan circulation.[27] Serial testing of natriuretic peptides plays a role in identifying patients at risk for adverse events. Of note, natriuretic peptides may be increased in cyanotic heart disease simply due to hypoxia-induced peptide secretion.[28]

3.4 Therapeutic considerations

3.4.1 Heart failure

The development of heart failure is a common problem affecting 20–50% of the ACHD population, and is a main cause of death.[29] The incidence is increasing and is probably underestimated. Since latent signs and symptoms of heart failure might occur frequently, patients at high risk of developing heart failure require systematic follow-up and diagnostic screening.[30] Any haemodynamic abnormalities, including arrhythmias, potentially causing heart failure that can be addressed by intervention or surgery must be excluded and, if possible, treated first. In the absence of specific guidelines, ACHD practitioners follow the current guidelines for medical treatment for both heart failure and common heart failure-related comorbidities, such as diabetes mellitus, AF, central sleep apnoea, iron deficiency, and cachexia.[31] However, as the pathophysiology of cardiorespiratory dysfunction is often different from the failing circulation in patients with non-congenital (acquired) heart disease, extrapolation of results from published heart failure studies to ACHD patients are inappropriate, particularly in patients with a systemic right ventricle (RV), a failing subpulmonary ventricle, or in patients with a single ventricle physiology. The pathophysiology of ACHD heart failure with systolic ventricular dysfunction includes a broad spectrum of causes. Both systemic and subpulmonary ventricles, whether morphological left or right, single ventricles included, might be chronically overloaded by pressure and/or volume, which leads to progressive ventricular dysfunction. Altered myocardial architecture (non-compaction) and ventricular interdependence can compromise systolic ventricular function. Myocardial injury (limited myocardial protection during bypass, after ventriculotomy, and after chronic hypoxia) may occur in CHD patients. Finally, ischaemic heart disease – mainly related to ageing or congenital coronary anomalies – and persistent tachyarrhythmia might be responsible for impaired systemic and subpulmonary ventricular function.[30] The few available data on heart failure treatments, specifically in ACHD patients, are often not conclusive and derived from small patient cohorts. As a consequence, ACHD-specific recommendations are mostly based on clinical experience or position statements.[30] In a biventricular circulation, patients with an impaired systemic LV are generally treated with conventional heart failure therapy; this is also applied in symptomatic patients with a failing systemic RV. Diuretics mainly control symptoms; whether the long-term use of inhibitors of the renin–angiotensin aldosterone system or beta blockers influences clinical outcome remains unknown. Also, no long-term clinical benefit of conventional heart failure treatment has been shown in a failing subpulmonary ventricle, although diuretics might alleviate symptoms. Treatment of symptomatic patients with a failing single ventricle in a Fontan circulation, or in the case of a persistent right-to-left (R–L) shunt, should always be carefully initiated, taking the labile balance of ventricular preload and systemic afterload into account. In ACHD patients with heart failure, there are currently only a few small studies looking at the new drug sacubitril/valsartan, which was found to decrease morbidity and mortality and implemented in the therapy of chronic heart failure in recent ESC Guidelines[31], however, no recommendation can be made at this moment. Heart failure with preserved EF is also not uncommon in ACHD patients. Therapeutic recommendations should follow the general heart failure guidelines. On top of medical treatment, cardiac resynchronization therapy (CRT) has gained increasing interest for use in ACHD patients with congestive heart failure, despite little evidence on indications and outcomes. Efficacy of CRT in CHD may vary with the underlying structural and functional substrate, such as anatomy of the systemic ventricle (left, right, or functionally single), presence and degree of structural systemic atrioventricular (AV) valve regurgitation, primary myocardial disease or scarring, and type of electrical conduction delay.[32]

It is expected that the incidence of acute heart failure in ACHD patients will also increase over time due to increasing age and more complex diseases. The knowledge of correct use of inotropes, the availability of extra-corporal membrane oxygenation, and advanced bridging techniques are the minimum requirements to adequately support ACHD patients with acute heart failure; transfer to an expert centre is recommended.[33]

Heart transplantation may also be considered as a therapeutic option for end-stage heart failure. Outcome after transplant surgery is continuously improving, particularly in CHD patients, but perioperative mortality still remains higher than in other underlying diseases. This is mainly related to previous cardiac surgery, complex anatomy and pathophysiology, and comorbidities (multisystem disorder). The increased use of ventricular assist devices can bridge patients to transplantation; in selected patients, it may be an option as destination therapy. Some patients may have extreme complex anatomy or high levels of antibodies against the human leucocyte antigens and are not eligible for transplantation.

In some patients, multiorgan transplantation is required. Heart-lung transplantation is applied in CHD patients with irreversible PAH such as Eisenmenger syndrome, however, the lack of donor organs is a major limitation.

Simultaneous heart-liver transplantation is rarely done in liver failure after Fontan palliation or in patients with long-standing hepatic pressure load due to right heart failure [e.g. unrecognized Ebstein's malformation of the tricuspid valve (TV)]; experience of this kind of surgery is limited.

In all cases, timely evaluation for transplantation by ACHD heart failure specialists in a transplant centre with ACHD expertise is recommended. Advance care planning, eventually including palliative care, should be offered to all advanced heart failure patients.

3.4.2 Arrhythmias and sudden cardiac death

3.4.2.1 Arrhythmia substrates

The entire spectrum of arrhythmias may be encountered in ACHD patients. However, some congenital arrhythmia substrates are related to the malformation itself (*Table 7* and *section 4*). Longer life expectancy (in conjunction with exposure to conventional risk factors for arrhythmogenic substrates) increases the prevalence of

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Table 7 Risk estimates for arrhythmic events and bradycardias in ACHD

	Supraventricular arrhythmias			Ventricular arrythmias and SCD		Bradycardia			
Type of CHD	AVRT	IART/ EAT	AF	Sustained VT	SCD	SND		AV block	
						Congenital	Acquired	Congenital	Acquired
Secundum ASD		++	++			(+)	+		(+)
Superior sinus venosus defect		++	+				+		
AVSD/primum ASD		++	++	(+)		(+)		(+)	++
VSD		+	(+)	+	(+)[a]				+
Ebstein anomaly	+++	++	+	(+)	++[b]		++		
TOF		++	++	++	++		+		+
TGA									
Atrial switch		+++	+	++[c]	+++[b]		+++		+
Arterial switch		+		+[c]	(+)		(+)		
ccTGA	++	+	+	(+)	++[b]			+	++
Fontan operation									
Atriopulmonary connection		+++	++		+[b]		++		
Intracardiac lateral tunnel		++	+		+[b]		++		
Extracardiac conduit		+	+		+[b]		+		
Eisenmenger physiology Incompletely palliated CHD		++	++		++[d]				

Empty cells indicate that although not specifically indicated, arrhythmic events may occur (no symbol).

(+) = minimal risk + = mild risk ++ = moderate risk +++ = high risk

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AF = atrial fibrillation; ASD = atrial septal defect; AV = atrioventricular; AVRT = atrioventricular reentrant tachycardia; AVSD = atrioventricular septal defect; ccTGA = congenitally corrected transposition of the great arteries; CHD = congenital heart disease; EAT = ectopic atrial tachycardia; IART = intraatrial reentrant tachycardia; SCD = sudden cardiac death; SND = sinus node dysfunction; TGA = transposition of the great arteries; TOF = tetralogy of Fallot; VSD = ventricular septal defect; VT = ventricular tachycardia.

[a]Considering the high prevalence of VSD, the overall risk in unselected patients with VSD is considered to be minimal.

[b]SCD may be due to supraventricular arrhythmias with rapid AV conduction.

[c]VT higher estimated risk in complex dextro-TGA.

[d]Non-arrhythmic.

arrhythmias related to structural remodelling, which may occur at a younger age than in the general population, e.g. AF.

Other arrhythmias are related to the type and timing of the ACHD repair. Right atrial (RA) incisions, together with cardiac remodelling secondary to haemodynamic overload, contribute to the high prevalence of atrial tachycardias (AT) in various CHDs. Most frequently encountered is late intraatrial reentrant tachycardia (IART), in particular cavotricuspid isthmus-dependent atrial flutter. Atrial rates between 150 and 250 beats per minute may lead to rapid AV conduction, haemodynamic compromise, and sudden cardiac death (SCD). Monomorphic ventricular tachycardia (VT) also depends on the malformation (*Table 7*) and type of repair,[34,35] with the critical part of the macro-reentry circuit typically located within anatomically well-defined isthmuses bordered by surgical scars and patch material. In contrast, in patients with progressive failure of the systemic or subpulmonary ventricle, more complex EP changes may occur. These changes involve ion channel remodelling, alterations in calcium handling, and remodelling of the extracellular matrix leading to different arrythmias including less well-organized fast polymorphic VT and ventricular fibrillation (VF).[36]

3.4.2.2 Assessment in patients with suspected/documented arrhythmias and arrhythmia management

In symptomatic patients without arrhythmia documentation at presentation, evaluation depends on the frequency [Holter registration, device interrogation (if present), event recorder] and circumstances (exercise testing) of symptoms.

The usefulness of periodic evaluation beyond 12-lead ECGs (e.g. periodic Holter) in asymptomatic patients is less clear. A high

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prevalence of asymptomatic findings has been reported that rarely change management.[37]

In all patients, evaluation for a reversible cause of the arrhythmia (e.g. hyperthyroidism, inflammatory process) and new or residual haemodynamic abnormalities is important. Arrhythmias causing haemodynamic instability require immediate termination irrespective of duration/anticoagulation following current recommendations.[32] Post-conversion, sinus arrest/bradycardia may occur and availability of back-up pacing needs to be considered in patients at risk for sinus node dysfunction (SND) (*Table 7*). If IART/AF is tolerated and lasting ≥48 h, cardiac thrombus needs to be ruled out (TOE) and/or appropriate anticoagulation (>3 weeks) and pharmacological rate control needs to be initiated before cardioversion using a beta blocker or calcium channel blocker (in patients with normal systemic ventricular function and absent preexcitation).[32,37,38] Maintenance of sinus rhythm is the aim in all CHD patients.[32,37] Catheter ablation is recommended as first-line therapy and preferred over long-term pharmacological treatment, in case of amenable, circumscribed substrates, as antiarrhythmic drugs are often associated with negative inotropic and/or dromotropic effects.[32] Antiarrhythmic drugs such as class IC drugs may slow the rate of IART without blocking AV conduction allowing 1:1 conduction with worsening haemodynamics.[32] Amiodarone may be considered for AT/AF recurrence prevention in patients with CHD and systemic ventricular dysfunction, hypertrophy of systemic ventricle, or CAD, in whom catheter ablation fails or is otherwise no option. Side effects of amiodarone are frequent and it should be used with caution in cyanotic CHD, low body weight, hepatic, thyroid, or pulmonary disease, or prolonged QT interval. Long-term amiodarone therapy is not advised in young CHD patients.[32]

For optimal chronic arrhythmia management, referral to a centre with a multidisciplinary team and expertise in CHD-related arrhythmias is mandatory.[32,37] For more specifications on anticoagulation see *section 3.4.7*.

3.4.2.3 Sinus node dysfunction, atrioventricular block, and infra-hisian conduction delay

Periodic Holter for patients at risk for SND and AV block should be considered in asymptomatic patients. Chronic SND/bradycardia with ineffective atrial haemodynamics may affect atrial remodelling and facilitate IART. Patients with post-operative AV block are considered at increased risk for SCD. Accordingly, broader indications for pacemaker implantation compared with patients with structurally normal hearts have been suggested.[20,32]

In ACHD patients with a biventricular circulation and a systemic LV, indications for CRT follow standard criteria. Of note, conventional ventricular pacing rather than bundle branch block is the major cause of systemic ventricular dysfunction. Accordingly, CRT is recommended in ACHD with a systemic EF ≤35% and intrinsic narrow QRS, and an anticipated requirement for significant pacing and new device placement. Alternatively, his bundle pacing could be considered. Efficacy of CRT in ACHD may vary across defects and may depend on the individual anatomy and causes of dyssynchrony (e.g. systemic RV/single ventricle, AV valve regurgitation, scarring). In general, QRS duration alone may not be a sufficient predictor and follow-up data are limited. In addition, thoracotomy or hybrid lead implantation is often required and data on longevity of CRT are lacking.[32]

3.4.2.4 Sudden cardiac death and risk stratification

SCD related to ventricular arrhythmia is of concern (7−26% of all deaths in adults).[29,39,40] Although the incidence in the CHD population at large is relatively low (<0.1% per year), some defects place patients at higher risk, with occasional disease-specific substrates and risk factors (*Table 7*). Identifying patients at risk for SCD remains a challenge.

ICD implantation for secondary prevention of SCD and for primary prevention in patients with biventricular physiology and a systemic LV follows standard criteria.[37,41] Antiarrhythmic drugs may be used as an adjunct to an ICD in order to reduce the ventricular arrhythmia burden.[32] The benefit of ICD therapy in primary prevention for single or systemic RVs is less well established.

Accordingly, with the exception of tetralogy of Fallot (TOF), specific guidelines regarding ICD implantation for primary prevention in CHD remain elusive.[32,37] Transvenous ICD systems have been used, but in patients with limited venous access to the ventricle or intracardiac shunt, the subcutaneous ICD may be an alternative. However, not all patients are eligible due to the risk of inappropriate sensing and lack of antitachycardia and antibradycardia pacing.

The usefulness of programmed electrical stimulation (PES) in asymptomatic patients with CHD is unclear. It seems reasonable in patients with ventricular incisions and/or a substrate for ventricular reentry typically, but not exclusively, encountered in repaired TOF (rTOF). It is important to recognize other causes of SCD due to bradycardia/total AV block and bradycardia-induced ventricular arrhythmia with or without long QT, and IART/AF with rapid conduction.

Recommendations for treatment of arrhythmias in adult congenital heart disease

Recommendations	Class[a]	Level[b]
In patients with moderate and severe CHD complexity (*Table 4*) and documented arrhythmias, referral to a centre with a multidisciplinary team and expertise in ACHD patients and ACHD-related arrhythmia is indicated.	I	C
In CHD patients with documented arrhythmias or at high risk for post-procedural arrhythmias (e.g. ASD closure at older age) considered for percutaneous or surgical (re)interventions, referral to a centre with a multidisciplinary team with expertise in these interventions and in invasive treatment of arrhythmias is indicated.	I	C
In mild CHD, catheter ablation is recommended over long-term medical therapy for symptomatic, sustained recurrent SVT (AVNRT, AVRT, AT, and IART), or if SVT is potentially related to SCD (*Table 7*).	I	C
In moderate and severe CHD, catheter ablation should be considered for symptomatic, sustained recurrent SVT (AVNRT, AVRT, AT, and IART), or if SVT is potentially related to SCD (*Table 7*), provided that the procedure is performed in experienced centres.	IIa	C

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Catheter ablation is indicated as adjunctive therapy to ICDs in patients who present with recurrent monomorphic VT, incessant VT, or electrical storm not manageable by medical therapy or ICD reprogramming.	I	C
Catheter ablation should be considered for symptomatic, monomorphic sustained VT in patients for whom medical therapy is not desired, provided that the procedure is performed in experienced centres.	IIa	C
Implantable cardiac defibrillator		
ICD implantation is indicated in adults with CHD who are survivors of an aborted cardiac arrest due to VF or haemodynamically untolerated VT after evaluation to define the cause of the event and exclusion of reversible causes.	I	C
ICD implantation is indicated in adults with CHD and sustained VT after haemodynamic evaluation and repair when indicated. EP evaluation is required to identify patients in whom catheter ablation or surgical ablation may be beneficial as adjunctive treatment or in whom it may offer a reasonable alternative.	I	C
ICD implantation should be considered in adults with CHD with biventricular physiology and a systemic LV presenting with symptomatic heart failure (NYHA II/III) and EF ≤35% despite ≥ 3 months of optimal medical treatment, provided they are expected to survive substantially longer than one year with good functional status.[c]	IIa	C
ICD implantation should be considered in patients with CHD and unexplained syncope and suspicion for arrhythmia aetiology and either advanced ventricular dysfunction or inducible VT/VF at programmed electrical stimulation.	IIa	C
ICD implantation should be considered in selected TOF patients with multiple risk factors for SCD, including LV dysfunction, non-sustained, symptomatic VT, QRS duration ≥180 ms, extensive RV scarring on CMR, or inducible VT at programmed electrical stimulation.	IIa	C
ICD implantation may be considered in patients with advanced single or systemic RV dysfunction (EF systemic RV <35%) in the presence of additional risk factors.[d]	IIb	C
Pacemaker		
PM implantation should be considered in ACHD patients with bradycardia-tachycardia syndrome to prevent IART, if ablation fails or is not possible.	IIa	C
PM implantation should be considered for patients with severe CHD and sinus or junctional bradycardia (daytime heart rate <40 beats per minute or pauses >3 s).	IIa	C
PM implantation should be considered for patients with CHD and compromised haemodynamics due to sinus bradycardia or loss of AV synchrony.	IIa	C
PM implantation may be considered for patients with moderate CHD and sinus or junctional bradycardia (daytime heart rate <40 beats per minute or pauses >3 s).	IIb	C

Continued

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ACHD = adult congenital heart disease; ASD = atrial septal defect; AT = atrial tachycardia; AV = atrioventricular; AVNRT = atrioventricular node reentrant tachycardia; AVRT = atrioventricular reentrant tachycardia; CHD = congenital heart disease; CMR = cardiovascular magnetic resonance; EF = ejection fraction; EP = electrophysiology/electrophysiological; IART = intraatrial reentrant tachycardia; ICD = implantable cardioverter defibrillator; LV = left ventricle/ventricular; NYHA = New York Heart Association; PM = pacemaker; RV = right ventricle/ventricular; SCD = sudden cardiac death; SVT = supraventricular tachycardia; TGA = transposition of the great arteries; TOF = tetralogy of Fallot; VF = ventricular fibrillation; VT = ventricular tachycardia.

[a]Class of recommendation.

[b]Level of evidence.

[c]Considering the broad spectrum of ACHD with LV pathologies that may differ from acquired heart diseases, the potentially higher risk of ICD-related complications in ACHD, and the paucity of data on the benefit of ICDs for primary prevention of SCD in ACHD, a personalized approach seems appropriate.

[d]Data are sparse and risk factors may be lesion specific, including non-sustained VT, NYHA II/III, severe AV valve regurgitation, and wide QRS ≥140 ms (TGA).

3.4.3 Pulmonary hypertension

3.4.3.1 Introduction and classification

PH is an important prognostic factor in patients with CHD,[42] requiring particular attention in pregnancy[43] or prior to reparative cardiac or other major surgery. Until recently, PH was defined by an increase in invasively measured mean PAP ≥25 mmHg at rest.[44] While this has now been reduced to >20 mmHg,[45] classification as pre-capillary PH — also called PAH — additionally requires an increase in PVR ≥3 Wood units (WU) (*Table 8*).[45] This increase in resistance in this group is due to an obstructive pulmonary vasculopathy which is driven by genetic background, modifier genes, vascular shear stress, and environmental triggers.[44] It is important to separate PAH associated with CHD (PAH-CHD, in group 1 of the PH classification[44]) from conditions with an LV filling pressure >15 mmHg (post-capillary PH due to passive transmission of LV filling pressures in groups 2 and 5 of the PH classification),[44] because of the futility of PAH-targeted treatments in post-capillary PH. Clinical subtypes of PAH-CHD are PAH with congenital systemic-pulmonary shunts, Eisenmenger syndrome, repaired defects, and PAH that appears coincidental with CHD, frequently with small defects. Fontan circulation is another condition with pulmonary vascular disease (PVD) and sometimes elevated PVR. An increase in PAP in these patients is, however, more frequently caused post-capillary (increase in ventricular filling pressure and/or AV valve regurgitation). In complex CHD, PAH may be restricted to certain segments of the pulmonary vascular bed (segmental PAH).[46] This is most frequently encountered in complex pulmonary atresia with VSD.

Although PAH-CHD can occur in males and females of any age, the disease is more frequently encountered in females, and increases with biological age and age at defect closure.[47] The sex bias disappears in PAH-CHD after defect repair.[48] More recently, a nationwide CHD

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Table 8 Definitions of pulmonary hypertension subtypes and their occurrence in ACHD

Pulmonary Hypertension in Adult Congenital Heart Disease		
Definition	**Haemodynamic characteristics[a]**	**Clinical settings**
Pulmonary Hypertension (PH)	Mean PAP >20 mmHg	All
Pre-capillary PH (PAH)	Mean PAP >20 mmHg PAWP ≤15 mmHg PVR ≥3 WU	Shunt lesions prior to and after repair (including Eisenmenger syndrome) Complex CHD (including UVH, segmental PAH)
Isolated post-capillary PH	Mean PAP >20 mmHg PAWP >15 mmHg PVR <3 WU	Systemic ventricular dysfunction Systemic AV valve dysfunction Pulmonary vein obstruction Cor triatriatum
Combined pre- and post-capillary PH	Mean PAP >20 mmHg PAWP >15 mmHg PVR ≥3 WU	Settings listed under isolated post-capillary PH Settings listed under isolated post-capillary PH in combination with shunt lesions/complex CHD

ACHD = adult congenital heart disease; AV = atrioventricular; CHD = congenital heart disease; PAH = pulmonary arterial hypertension; PAP = pulmonary artery pressure; PAWP = pulmonary artery wedge pressure; PH = pulmonary hypertension; PVR = pulmonary vascular resistance; UVH = univentricular heart; WU = Wood units.
[a]The most recent definition of PH[45] lowers mean PAP from ≥25 mmHg[44] to >20 mmHg but additionally requires a PVR ≥3 WU for pre-capillary PH.

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population study reported a PAH prevalence of 3.2% in CHD patients, accounting for 100 per million in the general adult population.[47]

3.4.3.2 Diagnosis

The 2015 guidelines for the diagnosis and treatment of PH presented a haemodynamic algorithm for the diagnosis of PH, highlighting the role of right heart catheterization to differentiate pre- from post-capillary PH.[44] The algorithm has recently been modified,[45] and *Table 8* illustrates current definitions of different types of PH and the settings in which they may occur in ACHD. In this definition, mean PAP threshold is >20 instead of ≥25 mmHg in the presence of a PVR ≥3 WU to define pre-capillary PH.[45]

3.4.3.2.1 Diagnostic work-up of pulmonary hypertension in adult congenital heart disease.

The diagnostic work-up includes medical history, physical examination, lung function tests, arterial blood gas analysis, imaging (especially echocardiography), and laboratory testing (including total blood cell counts, serum iron levels, haematocrit, infectious diseases, and NT-pro-BNP measurements). In general, right heart catheterization with compartmental oximetry is required for major decisions such as start and follow-up of vasodilator therapy, pregnancy, or surgery. The threshold for invasive assessment is, however, higher in patients with Eisenmenger syndrome. Invasive haemodynamic assessment is usually not required for guiding therapeutic interventions over time. Because higher haematocrit levels lead to higher PVR, this may have to be taken into account.[49]

3.4.3.2.2 Risk assessment.

Outcomes of PAH-CHD patients have improved with the availability of new PAH therapies, advances in surgical and perioperative management, and use of a team-based, multidisciplinary approach.[44,50,51] In recent series, outcomes of PAH-CHD patients appear to be better than in idiopathic PAH,[48] but depend on the PH subset. Outcomes of PAH associated with small defects resemble the dismal outcomes of idiopathic PAH, presumably because these conditions are based on a similar vascular proliferative disorder. PAH after defect repair carries even worse prognosis.[48]

3.4.3.3 Therapeutic management of pulmonary hypertension in adult congenital heart disease

3.4.3.3.1 Expert centres.

Successful management of an ACHD patient with PH requires a multidisciplinary management team comprising experts in imaging, cardiology, respiratory medicine, haematology, infectious diseases, obstetrics, anaesthesiology, neonatology, PH, thoracic and cardiovascular surgery, nursing, and medical genetics.

3.4.3.3.2 General measures.

The main general measures are social and psychological support, vaccination, and avoidance of excessive physical stress. Follow-up visits are planned individually. Pregnancy must be avoided in all cases of pre-capillary PH. Continuous supplemental oxygen is recommended when the arterial blood oxygen pressure is consistently <60 mmHg,[44] except in Eisenmenger patients in whom it is only recommended when it produces a documented, consistent, and significant increase in oxygen saturation and improvement of symptoms.

3.4.3.3.3 Anticoagulation.

Anticoagulation with vitamin K antagonists (VKAs) in the absence of atrial arrhythmia, mechanical valves, or vascular prosthesis is not generally recommended in PAH-CHD, and has to be decided on an individual basis, e.g. large PA aneurysms with thrombus or previous thromboembolic events. No data exist on the use of non-vitamin K antagonist oral anticoagulants (NOACs). In patients with Eisenmenger syndrome, data supporting the routine use of anticoagulation are lacking, but oral anticoagulation should be considered in patients with atrial arrhythmias and may be considered in the presence of PA thrombosis or embolism and low bleeding risk. As the risk of bleeding is increased in cyanotic patients, the use of oral

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anticoagulation and antiplatelet agents should be considered carefully on a case-by-case basis.

3.4.3.3.4 Shunt repair.

Because endothelial shear triggers PH,[52] surgical/interventional repair of conditions of increased flow are conceptualized to protect the pulmonary vasculature. The threshold PVR permitting reparative surgical closure of a left-to-right (L–R) shunt without right heart failure differs for the different shunt lesions (see *sections 4.1–4.4*). However, the decision to close a shunt is made using all the available information and is not solely dependent on the haemodynamics obtained at cardiac catheterization;[53,54] the decision should only be taken in expert centres.

There is no prospective evidence that a treat-and-repair approach in patients with PAH-CHD confers long-term benefits.[44,55] No prospective data are available on the usefulness of vasoreactivity testing, closure test, or lung biopsy for assessment of operability.[53,54,56–60]

3.4.3.3.5 Pulmonary arterial hypertension-directed medical therapy. Advanced therapies benefit patients with Eisenmenger syndrome,[51] and likely also other PAH-CHD.[61,62] According to the 2015 ESC/ERS Guidelines on PH,[44] pre-capillary PH (PAH), including Eisenmenger syndrome, is a moderate- to high-risk condition and requires a proactive approach using initial[63] or sequential combination treatment,[64,65] including parenteral prostacyclins.[44] Parenteral prostaglandins work best when started early.[66] The presence of a central intravenous catheter for parenteral therapy, however, increases the risk of paradoxical embolism and infection in Eisenmenger patients and those with R–L shunt lesions. In this setting, subcutaneous or inhaled forms of administration are therefore generally preferred.

Exclusions to this rule are patients with closed or coincidental defects meeting strict criteria for vasodilator responsiveness (mainly a decrease of mean PAP >10 mmHg and below 40 mmHg acutely under nitric oxide inhalation) who may be treated with calcium channel blocker therapy only. However, such patients are extremely rare among adults with PAH-CHD. General vasoreactivity testing is not recommended in PAH-CHD.[44]

Long-term home oxygen therapy may improve symptoms but has not been shown to augment survival in Eisenmenger patients. The use of supplemental oxygen should be restricted to those cases in which it produces a documented, consistent, and significant increase in arterial oxygen saturation and improves symptoms.

Secondary erythrocytosis is beneficial for adequate oxygen transport and delivery, and routine phlebotomy should be avoided; for more details see *section 3.4.8*.

In Eisenmenger patients, the endothelin receptor antagonist (ERA) bosentan has been shown to improve 6MWT and decrease PVR after 16 weeks of treatment in World Health Organization (WHO) functional class III patients.[67] Although a beneficial effect of bosentan has been shown on exercise capacity and quality of life in this group of patients, an effect on mortality is less well documented. Long-term follow-up showed sustained improvement in symptoms. Experiences with other ERAs and the phosphodiesterase type 5 (PDE-5) inhibitors, sildenafil and tadalafil, show favourable functional and haemodynamic results in patients with PAH-CHD and Eisenmenger syndrome, with less robust evidence. Experience is limited for latest-generation PAH drugs such as macitentan, selexipag, or riociguat in the setting of CHD.[66] While patients with simple repaired lesions have been included in the landmark studies for these substances, and are likely to benefit similarly to idiopathic PAH patients, data are currently limited for Eisenmenger patients. A recent randomized controlled trial investigating efficacy of macitentan to improve 6MWT in Eisenmenger syndrome was neutral.[68] Most centres follow a sequential symptom-orientated treatment strategy in Eisenmenger syndrome, generally starting with an oral ERA or PDE-5 inhibitor and escalating therapy if symptoms persist or in the case of clinical deterioration. Should an adequate improvement in symptoms not be achieved with oral therapy, parenteral options should be considered proactively.

The effect of PAH therapy in patients with segmental PAH remains a matter of debate. While some series reported promising results, there have been cases where therapies were not tolerated.[46]

Heart-lung or lung transplantation with heart surgery is an option in special cases not responsive to medical treatment but is limited by surgical complexity and organ availability.

Recommendations for treatment of pulmonary arterial hypertension associated with congenital heart disease

Recommendations	Class[a]	Level[b]
It is recommended that patients with CHD and confirmed pre-capillary PH[c] are counselled against pregnancy.	I	C
Risk assessment is recommended in all patients with PAH-CHD.[d]	I	C
In low- and intermediate-risk patients with repaired simple lesions and pre-capillary PH, initial oral combination therapy or sequential combination therapy is recommended and high-risk patients should be treated with initial combination therapy including parenteral prostanoids.[e] [63–65]	I	A
In Eisenmenger patients with reduced exercise capacity (6MWT distance <450 m), a treatment strategy with initial endothelin receptor antagonist monotherapy should be considered followed by combination therapy if patients fail to improve.[67–69]	IIa	B

6MWT = 6-minute walk test; CHD = congenital heart disease; PAH-CHD = pulmonary arterial hypertension associated with congenital heart disease; PH = pulmonary hypertension.
[a]Class of recommendation.
[b]Level of evidence.
[c]The risk of pregnancy in patients with pre-capillary PH is very high. It may be less in pregnancies of patients with post-capillary PH, therefore, a right heart catheterization is necessary in all patients with a suspicion of pre-capillary PH to confirm the diagnosis.
[d]For details see 2015 ESC/ERS Guidelines for diagnosis and treatment of PH.[44]
[e]For details about choice of drugs and the recommended risk-adjusted treatment algorithm see 2015 ESC/ERS Guidelines for diagnosis and treatment of PH.[44]

3.4.4 Surgical treatment

Cardiac surgery in ACHD patients deserves special attention. Even small operations can carry a high risk due to the dysregulation of the delicate balance in which ACHD patients often thrive. This risk cannot be calculated using conventional surgical risk scores. The adult congenital heart surgery score was derived from the Society of

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Thoracic Surgeons Congenital Heart Surgery Database as the first evidence-based score, designed specifically for surgery in ACHD.[70] Upon evaluation, the score reached a good predictive power in ACHD, although the corresponding paediatric score performed better in children,[71] indicating that in ACHD, individual patients' comorbidities may play a more important role in determining outcomes. The ACHD mortality score, an expert-based score that accounts for comorbidities, may therefore also be considered for evaluating the risk of cardiac surgery in ACHD.[72]

Apart from the need for personalized risk assessment, understanding the specific anatomy and haemodynamics, experience with redo surgery, and special requirements in intensive care units are factors that determine short- and long-term outcomes. When ACHD patients are operated on by a congenital cardiac surgeon, outcome is proven to be superior.[73] Therefore, the strict recommendation is that all ACHD patients are operated on by a congenital cardiac surgeon in a multidisciplinary environment with expertise in ACHD. This holds true for all ACHD cardiac surgery in the present recommendations except for surgery of uncomplicated bicuspid aortic valve (BAV), heritable thoracic aortic disease (HTAD) such as Marfan syndrome, and secundum-type ASD without anomalous pulmonary venous connection and/or absence of PVD. The multidisciplinary expert environment also favours the growing interest in, and need for, hybrid procedures, where (congenital) cardiac surgeons, vascular surgeons, interventional congenital cardiologists, and electrophysiologists collaborate in technically challenging procedures.

3.4.5 Catheter intervention

Catheter-based interventions, either as stand-alone or hybrid procedures, are an appealing alternative to conventional open-heart surgery, obviating the need for redo sternotomy/thoracotomy and cardiopulmonary bypass. The most frequent percutaneous interventions are closure of shunt lesions (in particular secundum-type ASD, rarely VSD, and persistent arterial duct), fistula, or unusual collaterals; balloon dilatation of the pulmonary valve and valved grafts; balloon dilatation and/or stenting of narrowed great vessels [e.g. (re-coarctation of the aorta (CoA) and pulmonary arterial stenosis]; and transcatheter pulmonary valve implantation (TPVI). ACHD diagnosis and, in particular, interventional care should be delivered by people who are trained as CHD caregivers and are part of an ACHD care centre, where individual procedures are reviewed and discussed within a multidisciplinary team.[74] It is of particular importance that a programme performing transcatheter interventions in ACHD patients should be co-located with appropriate congenital cardiac services for the management of procedural complications. In many programmes, experienced paediatric interventional cardiologists form an important component of ACHD intervention services, but in others (e.g. those based in a separate paediatric hospital), paediatric interventionalists may be uncomfortable with the interventional management of adults with congenital cardiac problems. Therefore, full collaboration between adult and paediatric cardiology is recommended. Concentration of ACHD catheterization in a limited number of designated centres allows quality assurance as well as co-location of key cardiovascular services.[74] Minimum annual numbers of interventions per centre have been proposed in a recent recommendation paper.[74]

3.4.6 Infective endocarditis

The risk of infective endocarditis (IE) in ACHD patients is higher than in the general population, with marked variation between lesions. The 2015 ESC Guidelines on IE maintain the restriction of antibiotic prophylaxis to patients at high risk of IE undergoing at-risk dental procedures.[22] High-risk conditions are prosthetic valves, including transcatheter valves, valve repair using a prosthetic ring, previous IE, any cyanotic CHD, and any CHD repaired with prosthetic material up to 6 months after the procedure or lifelong if residual shunt or valvular regurgitation remains.

Non-specific hygiene measures should be applied in all ACHD patients: good oral and cutaneous hygiene, and aseptic measures during healthcare and any invasive procedure. Piercings and tattoos are discouraged and otherwise should be performed in optimal hygienic conditions.

All patients need to be educated about symptoms of IE and appropriate behaviour (seeking medical advice, importance of blood cultures before starting antibiotic treatment) at occurrence of such symptoms.

Recent studies confirmed the relatively high risk of IE in patients after valve surgery, particularly previous IE and bovine jugular vein conduits.[75–78] Specific awareness is needed after TPVI using a Melody valve prosthesis.[75]

3.4.7 Antithrombotic treatment

Patients with ACHD are at increased risk of thromboembolic events, but evidence on prevention is limited. In patients with IART or AF, the CHA_2DS_2-VASc and HAS-BLED scores have proven beneficial in adult patients with acquired heart disease.[38] However, as their validity in the CHD population is uncertain, the scores should only be used in combination with individually assessed risks. Traditionally, VKAs are used for thromboembolic prevention, but in general cardiology, NOACs are currently recommended in preference to VKA. Also, in the CHD population, NOACs seem similarly safe and effective, in the absence of mechanical valves or severe mitral valve stenosis.[79,80] Anticoagulation therapy is recommended in paroxysmal and persistent AF/IART in patients with moderate or severe CHD, but an individualized approach remains necessary. In patients with mild CHD, the CHA_2DS_2-VASc and HAS-BLED scores[38] should be used as per general recommendations.[81] Whether all Fontan patients benefit from anticoagulation is unclear at the moment. Bleeding risk should also be considered and weighed against thrombogenic risk, especially in cyanotic patients. For secondary prevention, anticoagulation is recommended in patients with a thromboembolic event or incidental intracardiac or intravascular thrombus (see also 2017 ESC/EACTS Guidelines on valvular heart disease and 2018 ESC Guidelines on pregnancy).

3.4.8 Management of cyanotic patients

Cyanosis is caused by R−L shunt due to an anatomical communication between the systemic and pulmonary circulation at the atrial, ventricular, or arterial level. Cyanotic heart disease comprises a heterogeneous group of lesions with different underlying anatomy and pathophysiology: normal or restricted pulmonary blood flow in the presence of an obstruction across the pulmonary outflow tract or increased pulmonary blood flow in the absence of such an obstruction which, in some defects, may result in development of PAH and

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eventually Eisenmenger syndrome (see *sections 3.4.3* and *4.15*). They may present with or without prior palliative intervention. Cyanotic patients are complex and must be followed by an ACHD specialist.

3.4.8.1 Adaptive mechanisms

Cyanosis induces adaptive mechanisms to improve oxygen transport and delivery to the tissue: secondary erythrocytosis, rightward shift of the oxyhaemoglobin dissociation curve, and increase in cardiac output.[82,83] Erythrocytosis secondary to erythropoietin stimulus is the physiological response to chronic hypoxaemia. *Compensated* erythrocytosis reflects an equilibrium and *decompensated* erythrocytosis indicates failure of an equilibrium (excessive red blood cell/haemoglobin increase and unstable, rising haematocrit with major hyperviscosity symptoms).[82,84]

3.4.8.2 Multisystem disorder

Cyanosis and secondary erythrocytosis imply profound consequences for the entire organ system:[82,84,85]

- Blood viscosity is increased and is directly related to red blood cell mass.[84]
- Haemostatic abnormalities are common and complex and are attributed to abnormalities in platelets (thrombocytopaenia and thrombasthenia), coagulation pathways, and other abnormal coagulation mechanisms. Vitamin K-dependent clotting factors and factor V are reduced, fibrinolytic activity is increased, and the largest von Willebrand multimers are depleted.
- Increased turnover of red blood cells/haemoglobin and impaired urate filtration lead to hyperuricaemia.[86] The increased concentration of unconjugated bilirubin puts cyanotic patients at risk for calcium bilirubinate gallstones.
- Severe endothelial dysfunction is evident by the striking impairment of endothelium-dependent vasodilation.[85]
- Chronic hypoxaemia, increased blood viscosity, and endothelial dysfunction affect microcirculation, myocardial function, and the function of other organ systems.

3.4.8.3 Clinical presentation and natural history

Clinical presentation includes central cyanosis, a result of an increased quantity of reduced haemoglobin (>5 g/100 mL blood), clubbing, and frequently scoliosis. The underlying anatomy/pathophysiology characterizes cardiac findings.

Mortality is significantly higher in cyanotic patients than in acyanotic patients.[87] Outcome is determined by the underlying anatomy, pathophysiology, palliative procedures, complications of cyanosis, and preventive measures.[88,89] Low platelet count, severe hypoxia, cardiomegaly, and elevated haematocrit during childhood are parameters to predict premature death and adverse events in patients with and without PVD.[90] Iron deficiency is associated with adverse late outcome;[91,92] BNP can predict outcome in Eisenmenger patients.[93,94] However, in a multicentre study,[89] only age, pre-tricuspid shunt, absence of sinus rhythm, lower oxygen saturation at rest, and presence of pericardial effusion, but not BNP, were the strongest predictors for death.

3.4.8.4 Late complications

- Hyperviscosity symptoms include headache, faintness, dizziness, fatigue, tinnitus, blurred vision, paraesthesia of fingers, toes, and lips, muscle pain, and weakness (classified moderate when they interfere with some activities, severe when they interfere with most activities).[82,83] Hyperviscosity symptoms are unlikely in an iron-replete patient with haematocrit <65%.
- Bleeding and thrombotic diathesis occur; both cause a therapeutic dilemma (risks of thrombosis and bleeding). Spontaneous bleeding is usually minor, self-limiting (dental bleeding, epistaxis, easy bruising, menorrhagia). Haemoptysis is the most common major bleeding event and is an external manifestation of an intrapulmonary haemorrhage not reflecting the extent of parenchymal bleeding (reported in up to 100% of Eisenmenger patients).[95,96] Thrombosis is caused by coagulation abnormalities, stasis of blood in dilated chambers and vessels, atherosclerosis and/or endothelial dysfunction, the presence of thrombogenic material (e.g. conduits), and arrhythmias. The haemostatic abnormalities do not protect against thrombotic complications. Laminated thrombi in large, partially calcified and aneurysmal PAs are common (up to 30%).[97–100] Female sex, low oxygen saturation, older age, biventricular dysfunction, and dilated PAs have been identified as risk factors.[97,100,101]
- Cerebrovascular infarctions are common, but underreported.[97] They may be caused by thromboembolic events (paradoxical embolism, supraventricular arrhythmia), rheological factors (microcytosis), endothelial dysfunction, and traditional atherosclerotic risk factors. The severity of secondary erythrocytosis is not in itself a risk factor.[102] Microcytosis caused by iron deficiency, due to inappropriate phlebotomies, was the strongest independent predictor for cerebrovascular events in one study.[91] Severity of cyanosis and CHD complexity are other risk factors.[97]
- Paradoxical emboli may be caused by transvenous leads or catheters.
- Iron deficiency is frequently caused by, and may be exacerbated by, inappropriate phlebotomies or heavy menstruation in female patients.
- Arrhythmias – supraventricular and ventricular.
- Infectious complications include endocarditis, cerebral abscess, and pneumonia. Fever, associated with a new or different headache, raises suspicion of a brain abscess.
- Renal dysfunction is common and is due to functional and structural abnormalities of the kidneys.
- Cholelithiasis is common and can be complicated by cholecystitis/choledocholithiasis.
- Rheumatological complications include gouty arthritis, hypertrophic osteoarthropathy, and kyphoscoliosis.[83]

3.4.8.5 Diagnostic aspects

Particular attention must be paid to hyperviscosity symptoms and bleeding/ischaemic complications. Oxygen saturation must be obtained with pulse oximetry at rest for at least 5 min, and exercise capacity should be assessed on a regular basis, preferably with a 6MWT.

Blood work must include cellular blood count, mean corpuscular volume (MCV), serum ferritin (serum iron, iron saturation, transferrin, and transferrin saturation may be required for earlier detection of iron deficiency), creatinine, serum uric acid, clotting profile, BNP/NT-pro-BNP, folic acid, and vitamin B12 in the presence of elevated MCV or normal MCV and low serum ferritin.

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3.4.8.6 Laboratory precautions

- Coagulation parameters: plasma volume is reduced due to secondary erythrocytosis; the amount of sodium citrate must be adjusted to haematocrit if haematocrit is >55%.
- Haematocrit determined with automated electronic particle counts (micro-haematocrit centrifugation) results in falsely high haematocrit due to plasma trapping.
- Glucose level can be reduced (increased in vitro glycolysis, which results from the increased number of erythrocytes).

3.4.8.7 Indications for intervention

Risk and benefit must be carefully considered and require expertise. Cyanotic patients without PAH/Eisenmenger syndrome must be periodically evaluated for any procedure that may improve quality of life and reduce morbidity, or for eligibility for physiological repair (see *section 4.15*).

3.4.8.8 Medical therapy

- Specific PAH treatment: see *section 3.4.3*.
- Arrhythmias: sinus rhythm should be maintained whenever possible. Antiarrhythmic therapy must be individualized (medications, ablation, epicardial PM/ICD). Antiarrhythmic therapy is extremely difficult; drug therapy should be initiated with particular care and generally in a hospital.
- Therapeutic phlebotomy should only be performed in the presence of moderate/severe hyperviscosity symptoms due to secondary erythrocytosis (haematocrit at least >65%), in the absence of dehydration and iron deficiency.[82] Isovolumetric fluid replacement (750–1000 mL of isotonic saline while removing 400–500 mL of blood) should be undertaken.
- Blood transfusion may be required in the presence of iron-replete anaemia (haemoglobin inadequate to oxygen saturation) and should not be based on conventional indications.
- Iron supplementation should be performed in the presence of iron deficiency (MCV <80 fL, low iron stores) and carefully followed (rebound effect).
- Routine anticoagulation/aspirin: currently available data do not support any benefit in cyanotic patients to prevent thromboembolic complications. There is, however, an increased risk of bleeding.
- Indication for anticoagulation: atrial flutter/AF (target INR 2–2.5; higher target INR in the presence of other risk factors). Note laboratory precautions: false high INR values are measured due to the high haematocrit. There are no data and only anecdotal experiences about the use of NOACs (see also *section 3.4.7*).
- Haemoptysis: requires chest computed tomography if there is an infiltrate on the chest X-ray. Bronchoscopy puts the patient at risk and seldom provides useful information. Therapy includes discontinuation of aspirin, non-steroidal anti-inflammatory agents, oral anticoagulants; treatment of hypovolaemia and anaemia; reduction of physical activity; and suppression of non-productive cough. Selective embolization of bronchial arteries may be required for refractory intrapulmonary haemorrhage/haemoptysis. Antifibrinolytic agents (e.g. inhaled tranexamic acid) are under investigation and may be a novel approach to treat haemoptysis.[103] More trials are needed.
- Hyperuricaemia: no indication to treat asymptomatic hyperuricaemia.
- Acute gouty arthritis (atypical presentation) is treated with oral or intravenous colchicine, probenecid, and anti-inflammatory drugs, with attention paid to the risk of renal failure and bleeding. Uricosuric (e.g. probenecid) or uricostatic agents (e.g. allopurinol) avoid recurrence.

3.4.8.9 Follow-up recommendations

All cyanotic patients require lifelong evaluation with follow-up visits every 6–12 months in a specialized ACHD centre in close collaboration with the family physician. Evaluation includes:

Table 9 Risk reduction strategies in patients with cyanotic congenital heart disease

Prophylactic measures are the mainstay of care to avoid complications.[83]	
The following exposures/activities should be avoided:	**Other risk reduction strategies include:**
• Pregnancy in patients with Eisenmenger syndrome and in cyanotic patients without PAH, but arterial oxygen saturation <90%	• Use of an air filter in an intravenous line to prevent air embolism
• Iron deficiency and anaemia (no routine, inappropriate phlebotomies to maintain a pre-determined haemoglobin) – treat iron deficiency and iron-deficient anaemia	• Consultation with an ACHD cardiologist before administration of any agent and performance of any surgical/interventional procedure
• Inappropriate anticoagulation	• Prompt antibiotic therapy of upper respiratory tract infections
• Dehydration	• Cautious use or avoidance of agents that impair renal function
• Infectious disease: administer influenza and pneumococcal vaccines	• Contraceptive advice at each clinic visit
• Cigarette smoking, recreational drug abuse including excessive alcohol	
• Transvenous PM/ICD leads	
• Strenuous exercise	
• Acute exposure to heat (sauna, hot tub, or hot shower) or extreme cold	
• Oestrogen-containing contraception	

CHD = congenital heart disease; ICD = implantable cardioverter defibrillator; PAH = pulmonary arterial hypertension; PM = pacemaker.

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- Comprehensive evaluation and systematic review of potential complications.
- Blood tests (see *section 3.4.8.8*)
- Education about risk reduction strategies (*Table 9*).

3.4.8.10 Additional considerations

- Air flight: commercial air travel is well tolerated.[104,105] Risk-reduction strategies include avoidance of travel- and non-travel-related stress, dehydration, alcoholic drinks, and measures to prevent deep vein thrombosis.
- Exposure to high altitude: acute exposure to high altitude (>2500 m) should be avoided. Gradual ascent up to 2500 m may be tolerated.
- Pregnancy**:** pregnancy in cyanotic patients, without PH, results in significant maternal and foetal complications and requires follow-up by a Pregnancy Heart Team. Oxygen saturation (>85%) and haemoglobin (<200 g/L) before pregnancy were the strongest predictors for live birth in one series.[106] Pregnancy should be strongly discouraged in Eisenmenger syndrome and in cyanotic patients without PAH, but an arterial oxygen saturation <90%[43] (see *section 3.5.7*).
- IE prophylaxis: recommended in all patients (see *section 3.4.6*).

3.5 Additional considerations

3.5.1 Sex differences

Women have been appropriately included in trials, and sex-stratified analyses are available to some extent. Data regarding sex difference on prevalence of CHD, morbidity, and mortality are conflicting.[76,107–110] Although no differences in mortality were noted in the CONgenital CORvitia (CONCOR) study, there were significant sex differences in morbidity (increased risk for PH for women, but lower risk for IE, aortic complications, and ICD implantation).[111] Whether these differences relate to genetic and inherent biological difference, smaller body size, or other not yet defined differences warrants further exploration.[112]

Sex differences are important for diagnostic evaluation and clinical decision making. Although recommendations are usually not sex specific, body surface area (BSA)-normalized cut-offs of aortic and cardiac chamber dimensions may correct for smaller BSA in women.[113] Personalized counselling is essential in women contemplating pregnancy, as indications for intervention in females may set lower absolute values for aortic surgery (hereditary/CHD-associated aortopathy) or for pulmonary valve replacement (PVRep) in patients with TOF.[112]

There are data showing different impacts for men than women for employment,[114] gaps in medical care,[115] and physical activity.[116] Clinical evaluation, decision making, and counselling may require tailoring to the individual to help ensure equity of outcomes.

3.5.2 Adult congenital heart disease at more advanced age

To date, ~90% of patients with mild, 75% with moderate, and 40% with complex heart defects reach the age of 60 years.[117] These proportions are expected to rise further in the upcoming decades. Hence, there is a growing population of older persons with CHD and unique healthcare needs. These older patients are characterized by more comorbidities, inherent age-related risk for arrhythmia (especially AF), accelerated ageing, acquired disease, changed responses to medication, earlier onset of geriatric syndromes (e.g. cognitive decline, immobility/falls, failure to thrive, sensory alterations), and an altered psychosocial profile.[118,119] Dedicated guidelines for older patients with CHD ought to be consulted to provide adequate care to this more vulnerable patient population.[120] The onset of acquired diseases starts early in life, therefore, prevention strategies ought to be implemented in the first decades of life (at paediatric cardiology).

3.5.3 Advance care planning and end-of-life care

Most patients, independent of defect complexity, wish to discuss life expectancy prior to being confronted with life-threatening complications.[121] Such complications may occur during high-risk interventions or reflect an uncertain illness trajectory. Timely discussion of advance care planning is a critical component of patient-centred, comprehensive care.[121,122] Initiation of this demanding conversation is difficult. Unplanned hospital admissions, ICD insertion, or functional decline can serve as a trigger for such conversations. Most patients do not start advance care planning discussions on their own and wait for the provider's initiative. The content of advance care planning discussions depends on the patient's physical and psychological health and preferences. Initially, discussion about life expectancy and treatment preferences may be all the patient wants. With deteriorating health, a holistic assessment of the patient's wishes and values, advance directives, nomination of a surrogate decision maker, and decisions regarding device therapies in ICD patients are required.

During the process of care, active disease-specific treatment may progressively become supported and eventually substituted by palliative care. Involvement of palliative care specialists can be supportive. At any time, it is important to emphasize that active disease-specific care might continue during the advance care planning process, even near the end of life, keeping in line with patients' preferences and goals. The role of palliative care and family support continues after the patient's death in managing bereavement care.[123]

Whenever possible, family members should be involved in all steps. Patient preferences can change over time and periodic re-evaluation of the patient's wishes is necessary.

3.5.4 Insurance and employment

For ACHD patients, it is often difficult to obtain life-, health-, or travel insurance, and mortgages.[124–126] If insurance is granted, patients frequently need to pay an extra charge or the heart defect as a pre-existing condition excludes them from insurance. In general, obtaining insurance or not, and the higher fee, are mostly unrelated to the complexity of the defect, the functional status of the patient, or the prognosis,[124,126] but are rather a function of the policies of insurance companies and reflect a large inter- and intra-country variation. Patients currently need to shop around, and both clinicians and patient associations may be of help. Insurability is a definite issue that should be discussed during patient counselling. Also, employment, in particular the requirements for specific professions, needs attention.[127] Starting in adolescence, choices about education should be

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made based on the possibilities to perform heavy exercise and work night shifts, and the use of specific medication such as oral anticoagulation.

3.5.5 Exercise and sports

Recommendations for exercise and sports need to be based on the underlying congenital heart defect and its potential complications, the haemodynamic and EP status of the patient, and their pre-existing fitness.[24] Counselling must consider the type of sport and the anticipated effort levels. In general, physicians have been over-conservative in their advice, especially as physical activity has well-documented benefits for fitness, psychological well-being, and social interaction, as well as a positive effect on the future risk of acquired heart disease; symptoms do not exclude physical activity. Dynamic exercise is more suitable than static exercise. In addition, in patients with known cardiac conditions, complications during exercise, including SCD, are rare.[128] Recommendations for participation in low- to high-intensity sports are discussed in the position paper of Budts *et al.*[24] Guidelines on elite sports in athletes with CHD are described in the 2020 ESC Guidelines on sports cardiology.[129] Assessment of physical exercise capacity should be done before recommending recreational exercise or sport in order to avoid intense exercise in untrained patients. Most patients with CHD can safely engage in regular, moderate physical activity. A few conditions, such as systemic ventricular systolic dysfunction, systemic ventricular outflow tract obstruction, PH, haemodynamically significant arrhythmias, or aortic dilation, warrant more caution.

3.5.6 Non-cardiac surgery

The evaluation and management of ACHD patients should follow the principles of the 2014 ESC Guidelines on non-cardiac surgery[130] and consider the specificities of CHD. Factors associated with increased risk of perioperative morbidity and mortality are cyanosis, congestive heart failure, poor general health, younger age, PH, operations on the respiratory and nervous systems, complex CHD, and urgent/emergency procedures. In patients with complex CHD (Fontan, Eisenmenger syndrome, cyanotic patients), non-cardiac surgical and interventional procedures should be performed in an expert centre.[130,131] Issues to consider are endocarditis prophylaxis, complications related to underlying haemodynamics, abnormal venous and/or arterial anatomy affecting venous and arterial access, persistent shunts, valvular disease, arrhythmias including bradyarrhythmias, erythrocytosis, pulmonary vascular disease (PVD), prevention of venous thrombosis, monitoring of renal and liver function, periprocedural anticoagulation, possible need for non-conventional drug dosing, increased prevalence of hepatitis C infection because of prior procedures and remote blood transfusions and, finally, developmental disability.

3.5.7 Pregnancy, contraception, and genetic counselling

3.5.7.1 Pregnancy and contraception

The majority of ACHD patients tolerate pregnancy well, but women with complex CHD have higher risks. Detailed ESC Guidelines on pregnancy and heart disease were published in 2018.[43]

Pre-pregnancy counselling should be provided to all women with CHD. Specialist care is best provided in a multidisciplinary team setting by the Pregnancy Heart Team. This team should have input from ACHD cardiology, obstetrics, and anaesthesia, and where necessary from other specialists, including clinical geneticists. The team should be involved in all patients with at least moderate to complex heart disease before pregnancy for timely counselling and advice during pregnancy in order to plan antenatal care, including delivery and post-partum follow-up and need for cardiac monitoring. Risk estimation should be individualized and based on the modified WHO (mWHO) classification (*Table 10*).[43]

Functional status before pregnancy, ventricular function, severity of the lesions, and history of previous cardiac events are also of prognostic value.[132] CPET performed before conception can predict maternal and neonatal outcomes. A blunted heart rate response to exercise is associated with a higher risk of maternal cardiac and neonatal adverse events.

Maternal mortality is 0–1% and heart failure complicates pregnancy in 11% of women with heart disease, with PAH being associated with the highest risks.[133,134] Cyanosis poses a significant risk to the foetus, with live birth unlikely (<12%) if oxygen saturation is <85%.[106]

Women with cardiac disease also have an increased risk of obstetric complications, including premature labour, pre-eclampsia, and postpartum haemorrhage.[135] The potential for drugs affecting the foetus should always be considered; angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs), in particular, should not be used. Women requiring oral anticoagulation deserve special attention. VKAs are teratogenic, especially at higher doses. A dose-adjusted treatment algorithm is proposed in the 2018 ESC Guidelines on pregnancy.[43]

The pregnancy duration and mode of delivery should be decided by the Pregnancy Heart Team, taking the CHD severity into account.

Contraception should be discussed in a timely fashion with specific attention to effectiveness and safety.[136] Barrier methods are safe and protect against sexually transmitted diseases, however, they only have a high contraceptive efficacy with compliant couples. Hormonal contraceptives are highly efficacious, but there are few data on their safety in the ACHD population. The combined oral contraceptive is highly effective (99.9%), but is best avoided in patients with a pre-existing thrombotic risk (cyanosis, Fontan physiology, mechanical valves, prior thrombotic events, PAH), especially as there are few data to suggest that concomitant oral anticoagulation therapy will negate this risk. Progesterone-only contraceptives, on the other hand, do not pose such a high thrombosis risk, and newer preparations available for oral administration or with intrauterine implants have a high efficacy (>95%). The risk of endocarditis after insertion of progesterone-coated intrauterine devices is probably low. However, there is a risk of vasovagal reactions (5%) at the time of insertion or removal. Patients with a fragile physiology (e.g. patients with a Fontan circulation, PH, cyanotic CHD, Eisenmenger syndrome) should have their intrauterine device inserted/removed in a safe environment (i.e. in an environment with expertise in ACHD). Female sterilization or male partner sterilization should only be considered after careful discussion, with particular reference to long-term prognosis.

Assisted reproduction has added risks above those of pregnancy alone, and consultation with an ACHD specialist must be performed before treatment. Superovulation is prothrombotic and can be complicated by ovarian hyperstimulation syndrome, with marked fluid shifts and an even greater risk of thrombosis.[137] The risk of ovarian

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Table 10 Congenital heart disease with high risk and extremely high risk for pregnancy

Significantly increased risk of maternal mortality or severe morbidity (mWHO class III) (cardiac event rate 19–27%)	Extremely high risk of maternal mortality or severe morbidity (mWHO class IV)[a] (cardiac event rate 40–100%)
Unrepaired cyanotic heart disease	Pulmonary arterial hypertension
Moderate LV impairment (EF 30–45%)	Severe LV impairment (EF <30% or NYHA class III–IV)
Systemic RV with good or mildly decreased ventricular function	Systemic RV with moderate or severely decreased ventricular function
Fontan circulation. If the patient is otherwise well and the cardiac condition uncomplicated	Fontan with any complication
Severe asymptomatic AS	Severe symptomatic AS
Moderate mitral stenosis	Severe mitral stenosis
Moderate aortic dilatation (40–45 mm in Marfan syndrome or other HTAD; 45–50 mm in BAV, 20–25 mm/m^2 in Turner syndrome)	Severe aortic dilatation (>45 mm in Marfan syndrome or other HTAD, >50 mm in BAV, >25 mm/m^2 in Turner syndrome)
Mechanical valve	Severe (re-)coarctation

AS = aortic stenosis; ASI = aortic size index; BAV = bicuspid aortic valve; CHD = congenital heart defect; EF = ejection fraction; HTAD = heritable thoracic aortic disease; LV = left ventricle/ventricular; mWHO = modified World Health Organization; NYHA = New York Heart Association; RV = right ventricle/ventricular; TOF = tetralogy of Fallot.
[a]Pregnancy should definitely be avoided in women with these conditions.
Modified from the 2018 ESC guidelines for the management of cardiovascular disease during pregnancy.[43]

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hyperstimulation syndrome can be reduced by careful cycle monitoring, using low-dose follicle-stimulating hormone in combination with a gonadotropin-releasing hormone antagonist, freezing all embryos, and only transferring a single embryo. The last option is strongly advised in women with heart disease, since conceiving a multiple pregnancy is associated with greater cardiovascular changes and more maternal and foetal complications.[138] Pregnancy and fertility treatment are contraindicated in women with mWHO classification of maternal cardiovascular risk class IV.[43] In women with mWHO class III, or those who are anticoagulated, the risk of superovulation is very high and the alternative of natural cycle *in vitro* fertilization should be considered.

Sexuality is an important element of quality of life. The few available data suggest that sexual function is a concern in both women and men and should be discussed more often.[139]

3.5.7.2 Genetic counselling and recurrence risk

Genetic counselling, whether supplemented with further genetic testing or not, should at least be considered for every ACHD patient. Demonstrating a genetic abnormality can be important to further adjust the patient's own management and is evidently also important for family planning. It is estimated that 10–30% of all structural CHD would have a genetic basis. This rate is higher in cases of associated organ disorders and familial occurrence, and lower in isolated cases. With the rapid technical progress and possibilities of genetic testing, the reliability of these tests is further improving. Naturally, genetic elaboration in each patient must be multidisciplinary, with integration of necessary clinical data and adequate interpretation of found genetic variants. A detailed consensus document on this subject, providing an algorithm for genetic testing and an overview of the main syndromes to consider, has recently been published.[140]

One of the important and specific aspects of genetic counselling is the assessment of recurrence risk, which needs consideration in both men and women. The recurrence rate of CHD in offspring ranges from 2–50% and is higher in affected women than men. The highest recurrence risks are found in single gene disorders and/or chromosomal abnormalities such as Marfan, Noonan, 22q11 deletion syndrome, and Holt-Oram syndrome. Among patients with isolated,

Table 11 Recurrence rates for various congenital heart lesions according to the sex of the affected parent[a]

	Recurrence rate (%)*	
	Women	Men
ASD	4–6	1.5–3.5
VSD	6–10	2–3.5
AVSD	11.5–14	1–4.5
PDA	3.5–4	2–2.5
CoA	4–6.5	2–3.5
Marfan/HTAD	50[b]	
LVOTO	8–18	3–4
RVOTO (PS)	4–6.5	2–3.5
Eisenmenger syndrome	6	NR
TOF	2–2.5	1.5
Pulmonary atresia/VSD	NR	NR
TGA	2[b]	
ccTGA	3–5[b]	
UVH (HLHS)	21[b]	

ASD = atrial septal defect; AVSD = atrioventricular septal defect; ccTGA = congenitally corrected transposition of the great arteries; CHD = congenital heart disease; CoA = coarctation of the aorta; HLHS = hypoplastic left heart syndrome; HTAD = heritable thoracic aortic disease; LVOTO = left ventricular outflow tract obstruction; NR = not reported; PDA = patent ductus arteriosus; PS = pulmonary stenosis; RVOTO = right ventricular outflow tract obstruction; TGA = transposition of the great arteries; TOF = tetralogy of Fallot; UVH = univentricular heart; VSD = ventricular septal defect.
*Except for Marfan syndrome, rates apply to patients with isolated cardiac lesions in whom known genetic/syndromic entities have been excluded.
[a]Modified from Pierpont *et al.*[141]
[b]Sex-specific data not available or not relevant.

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non-familial CHD, the recurrence rate varies from 1–21%,[141] according to the underlying lesion. An overview is provided in *Table 11*. Foetal echocardiography in affected couples is recommended at 19–22 weeks gestation and can be done as early as 15–16 weeks gestation.

4 Specific lesions

4.1 Atrial septal defect and anomalous pulmonary venous connection

4.1.1 Introduction and background

ASD can remain undiagnosed until adulthood. ASD types include:

- Secundum ASD (80% of ASDs; located in the region of the fossa ovalis and its surrounding).
- Primum ASD [15%; synonyms: partial AV septal defect [atrioventricular septal defect (AVSD) with communication on the atrial level only], partial AV canal; located near the crux, AV valves are typically malformed, resulting in various degrees of regurgitation (see *section 4.3*)].
- Superior sinus venosus defect [5%; located near the superior vena cava (SVC) entry, associated with partial or complete connection of right pulmonary veins to SVC/RA].
- Inferior sinus venosus defect [<1%; located near the inferior vena cava (IVC) entry].
- Unroofed coronary sinus [<1%; separation from the left atrium (LA) can be partially or completely missing].

Associated lesions include anomalous pulmonary venous connection, persistent left SVC, pulmonary valve stenosis, and mitral valve prolapse. Interatrial defects are the most frequently associated defects in Ebstein anomaly (see *section 4.9*). Treatment decisions are more complex in the latter combination. The present section deals with isolated ASD.

The shunt volume depends on RV/LV compliance, defect size, and LA/RA pressure. A simple ASD results in L–R shunt because of the higher compliance of the RV compared with the LV (relevant shunt in general with defect sizes ≥10 mm), and causes RV volume overload and pulmonary overcirculation. Reduction in LV compliance, or any condition with elevation of LA pressure (hypertension, ischaemic heart disease, cardiomyopathy, aortic and mitral valve disease), increases L–R shunt. As a consequence, an ASD may become haemodynamically more important with age. Reduced RV compliance (pulmonic stenosis, PAH, other RV disease) or TV disease may decrease L–R shunt or eventually cause shunt reversal, resulting in cyanosis.

4.1.2 Clinical presentation and natural history

Patients frequently remain asymptomatic until adulthood. However, the majority develop symptoms beyond the fourth decade including reduced functional capacity, exertional shortness of breath, and palpitations (supraventricular tachyarrhythmias), and less frequently pulmonary infections and right heart failure. Life expectancy is reduced overall, but survival is much better than previously assumed.[142] PAP can be normal, but on average increases with age. Severe PVD is nevertheless very rare (<5%); its development presumably requires additional factors and the disease course is similar to idiopathic PAH.[48] With increasing age, and with increasing PAP, tachyarrhythmias become more common (atrial flutter, AF).[143] Systemic embolism may be caused by paradoxical embolism (rare) or AF and atrial flutter.

4.1.3 Diagnostic work-up

See *section 3.3* for general principles.

Key clinical findings include fixed splitting of the second heart sound and a systolic pulmonary flow murmur. ECG typically shows an incomplete right bundle branch block and right-axis deviation (superior left-axis deviation in partial AVSD). An increased pulmonary vascularity on chest X-ray is frequently overlooked.

- Echocardiography is the first-line diagnostic technique, providing diagnosis and quantification. RV volume overload, which may be the first unexpected finding in a patient with previously undiagnosed ASD, is the key finding and best characterizes the haemodynamic relevance of the defect (preferable to the shunt ratio). Sinus venosus defects in general require TOE for accurate diagnosis (CMR/CCT is an alternative and superior in case of inferior sinus venosus defects). TOE is also required for precise evaluation of secundum defects before device closure, which should include sizing, exploration of the residual septum's morphology, the rim size and quality, exclusion of additional defects, and confirmation of a normal pulmonary venous connection. 3D echocardiography provides visualization of ASD morphology. Other key information to be provided includes PAP and tricuspid regurgitation (TR).
- CMR is rarely required but may be useful for assessment of RV volume overload, identification of inferior sinus venosus defect, quantification of pulmonary to systemic flow ratio (Qp:Qs), and evaluation of pulmonary venous connection (alternatively for the latter, use CCT).
- Cardiac catheterization is required in case of non-invasive signs of PAP elevation (calculated systolic PAP >40 mmHg or indirect signs when PAP cannot be estimated) to determine PVR.
- Exercise testing should be performed in patients with PAH to exclude desaturation.

4.1.4 Surgical/catheter interventional treatment

Indications for intervention are summarized in the *Recommendations for intervention in atrial septal defect (native and residual)* table and in *Figure 2*.

Surgical repair has low mortality (<1% in patients without significant comorbidity) and good long-term outcome when performed early (childhood, adolescence) and in the absence of PH.[144,145] Although surgical repair can be performed with very low risk, even in the elderly, comorbidities that may affect operative risk need to be considered and then risk weighed against potential benefit.

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Recommendations for intervention in atrial septal defect (native and residual)

Recommendations	Class[a]	Level[b]
In patients with evidence of RV volume overload[c] and no PAH (no non-invasive signs of PAP elevation or invasive confirmation of PVR <3 WU in case of such signs) or LV disease, ASD closure is recommended regardless of symptoms.[146,147]	I	B
Device closure is recommended as the method of choice for secundum ASD closure when technically suitable.	I	C
In elderly patients not suitable for device closure, it is recommended to carefully weigh the surgical risk against the potential benefit of ASD closure.	I	C
In patients with non-invasive signs of PAP elevation, invasive measurement of PVR is mandatory.	I	C
In patients with LV disease, it is recommended to perform balloon testing and carefully weigh the benefit of eliminating L−R shunt against the potential negative impact of ASD closure on outcome due to an increase in filling pressure (taking closure, fenestrated closure, and no closure into consideration).	I	C
In patients with suspicion of paradoxical embolism (exclusion of other causes), ASD closure should be considered regardless of size providing there is absence of PAH and LV disease.	IIa	C
In patients with PVR 3−5 WU, ASD closure should be considered when significant L−R shunt is present (Qp:Qs >1.5).	IIa	C
In patients with PVR ≥5 WU, fenestrated ASD closure may be considered when PVR falls below 5 WU after targeted PAH treatment and significant L−R shunt is present (Qp:Qs >1.5).	IIb	C
ASD closure is not recommended in patients with Eisenmenger physiology, patients with PAH and PVR ≥5 WU despite targeted PAH treatment, or desaturation on exercise.[d]	III	C

ASD = atrial septal defect; L−R = left-to-right; LV = left ventricle/ventricular; PAH = pulmonary arterial hypertension; PAP = pulmonary artery pressure; PVR = pulmonary vascular resistance; Qp:Qs = pulmonary to systemic flow ratio; RV = right ventricle/ventricular; WU = Wood units.
[a]Class of recommendation.
[b]Level of evidence.
[c]RV enlargement with increased stroke volume.
[d]There are limited data available for a precise cut-off, but by clinical experience, this would be given by a fall of arterial oxygen saturation <90%.

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Device closure has become the first choice for secundum defect closure, when feasible, based on the morphology (includes stretched diameter ≤38 mm and sufficient rim of 5 mm except towards the aorta). This is the case in ∼80% of patients. Although it cannot be assumed to be zero, several recent studies have reported no mortality. Serious complications have been observed in ≤1% of patients.[148,149] Atrial tachyarrhythmias occurring early after intervention are mostly transient. Erosion of the atrial wall, anterior mitral leaflet, or the aorta, as well as thromboembolic events, appear to be very rare.[150,151] Antiplatelet therapy is required for at least 6 months (aspirin 75 mg o.d. minimum). Potential incidence of late arrhythmias or adverse events still requires investigation. Studies comparing surgery and catheter intervention have reported similar success rates and mortality, but morbidity was lower and hospital stays shorter with catheter intervention while reintervention rate was slightly higher.[148,152]

Outcome is best with repair at age <25 years.[144,145] ASD closure after the age of 40 years appears not to affect the frequency of arrhythmia development during follow-up.[146,153] However, the patient's morbidity benefits from closure at any age (exercise capacity, shortness of breath, right heart failure), particularly when it can be done by catheter intervention.[146,153]

In patients with impaired LV function (systolic and diastolic), ASD closure may worsen heart failure. These patients must be carefully evaluated and may require pre-interventional testing (balloon occlusion with reassessment of haemodynamics) to decide between complete, fenestrated, or no closure, considering that an increase in filling pressure due to ASD closure may worsen symptoms and outcome.[154]

Patients with PH must be evaluated with particular care. Calculation of PVR is mandatory. In patients with PVR <5 WU, ASD closure has been shown to be safe and associated with a decrease in PAP and improvement of symptoms.[60,153,155] However, even in this group, the extent of improvement decreases with increasing PAP. Patients with PVR ≥5 WU are unlikely to improve[60] and likely to have an even worse outcome with complete ASD closure.[48,156] Vasoreactivity testing is not recommended when making the decision whether to close an ASD in patients with PVR ≥5 WU. It appears safer to treat PAH, re-evaluate haemodynamics during follow-up, and consider fenestrated closure only when PVR falls below 5 WU in the presence of significant L−R shunt. If this is not the case, ASD closure should be avoided.

In patients with atrial flutter/AF, cryo- or radiofrequency ablation (modified maze procedure) should be considered at the time of surgery. Device closure may restrict access to the LA for later EP interventions.

In patients of advanced age with ASDs not suitable for device closure, individual surgical risk due to comorbidities must be carefully weighed against the potential benefits of ASD closure.

4.1.5 Specific aspects of isolated anomalous pulmonary venous connections

Anomalous pulmonary venous connections do not only occur in association with ASD (typically in sinus venous defects) but can also be isolated. This results in volume overload of the right heart, with a physiological effect similar to that of an ASD, but when isolated, differs in that there is no potential for R−L shunting, and the magnitude of the L−R shunt is not exacerbated by the development of acquired left heart disease. Most common is the connection of the right upper pulmonary vein to the SVC. Other abnormal connections include right pulmonary vein(s) to the IVC ('scimitar vein', which may be associated with sequestration of the right lower lobe), left upper

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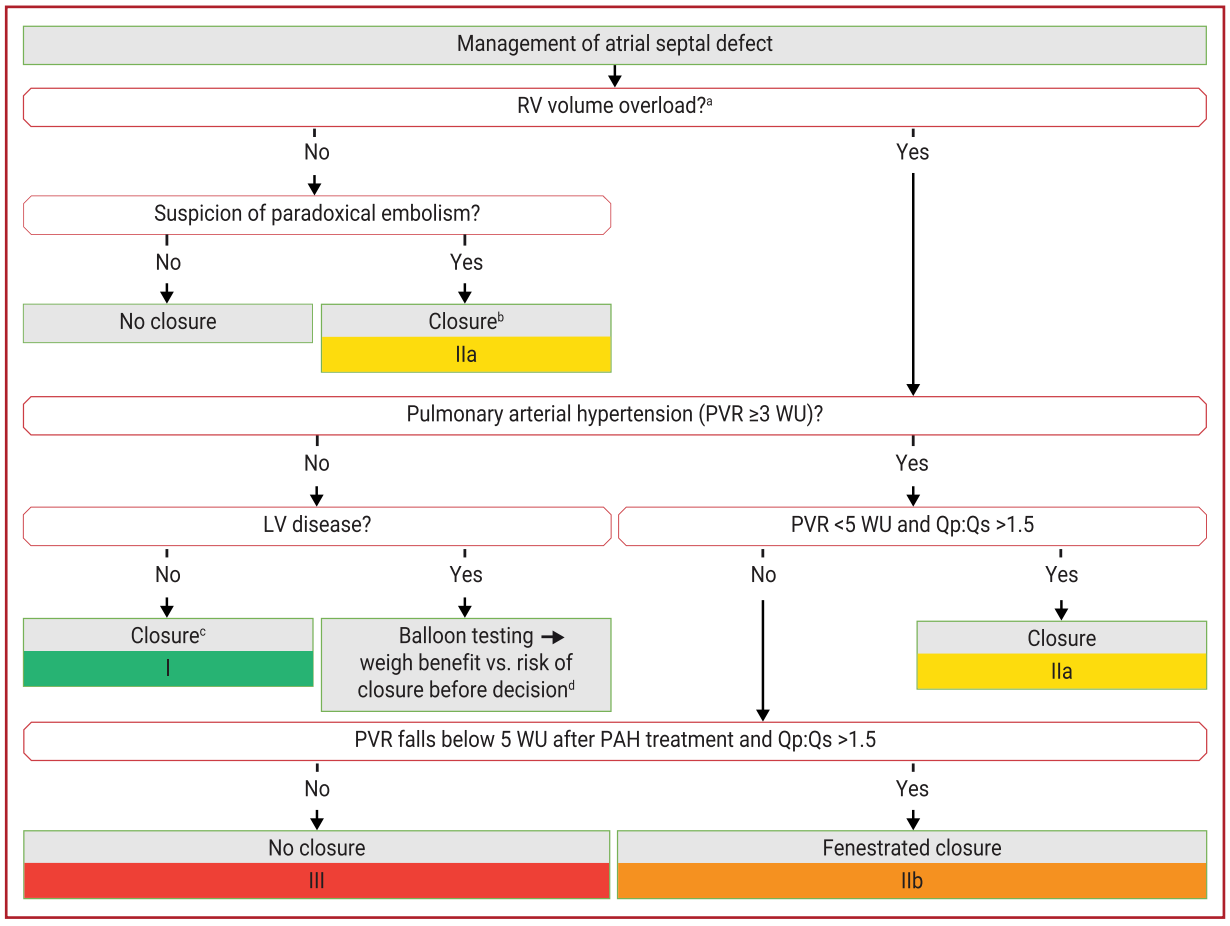


Figure 2 Management of atrial septal defect.
ASD = atrial septal defect; L—R = left-to-right; LV = left ventricle/ventricular; PAH = pulmonary arterial hypertension; PVR = pulmonary vascular resistance; Qp:Qs = pulmonary to systemic flow ratio; RV = right ventricle/ventricular; WU = Wood units.
[a]RV enlargement with increased stroke volume.
[b]Providing there is no PAH or LV disease.
[c]In elderly patients not suitable for device closure, carefully weigh surgical risk vs. potential benefit of ASD closure.
[d]Carefully weigh the benefit of eliminating L—R shunt against the potential negative impact of ASD closure on outcome due to an increase in filling pressure (taking closure, fenestrated closure, and no closure into consideration).

pulmonary vein(s) to the left innominate vein, and right upper pulmonary vein(s) connecting high on the SVC. 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, particularly in scimitar syndrome; it should only be performed by a congenital cardiac surgeon.

Indications for surgery follow the principals of recommendation for ASD closure, but technical suitability for repair and operative risk must be weighed against the potential benefit of intervention. It is unusual for a single anomalous pulmonary venous connection of only one pulmonary lobe to result in a sufficient volume load to justify surgical repair.

4.1.6 Follow-up recommendations

Follow-up evaluation should include assessment of a residual shunt, RV size and function, TR and PAP by echocardiography, and assessment of arrhythmias by history, ECG, and — only if indicated — Holter monitoring. Patients repaired at age <25 years without relevant sequelae or residua (no residual shunt, normal PAP, normal RV, no arrhythmias) do not require regular follow-up. However, patients and referring physicians should be informed about the possible late occurrence of tachyarrhythmias.

Patients with residual shunt, elevated PAP, or arrhythmias (before or after repair) and those repaired at adult age (particularly >40 years) should be followed on a regular basis, including evaluation in specialized ACHD centres (intervals depending on the severity of residual problems). After device closure, regular follow-up during the first 2 years and then, depending on results, every 3—5 years is reasonable.

Late post-operative arrhythmias after surgical repair at age <40 years are most frequently IART or atrial flutter, which can be successfully treated with radiofrequency or cryoablation. Without repair or with repair after age 40 years, AF becomes more common. In patients who undergo ASD closure aged >40 years, the prevalence of atrial arrhythmias is up to 40—60%. Access to the LA may be restricted after device closure.

SVC stenosis may occur after repair of a sinus venosus defect, as well as stenoses of redirected pulmonary veins.

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4.1.7 Additional considerations

- Exercise/sports: no restrictions in asymptomatic patients before or after intervention without PH, significant arrhythmias, or RV dysfunction; limitation to low-intensity recreational sports in PAH patients (see *section 3.5.5*).
- Pregnancy: low risk in patients without PH, although there may be an increased risk of paradoxical embolism. Patients with pre-capillary PH should be counselled against pregnancy (see *section 3.5.7*).
- IE prophylaxis: recommended for 6 months after device closure (see *section 3.4.6*).

4.2 Ventricular septal defect

4.2.1 Introduction and background

VSD is mostly diagnosed and — when indicated — treated before adulthood. Spontaneous closure is frequent in childhood. Several locations of the defect within the interventricular septum are possible, and these can be divided into four groups according to their location within the RV (nomenclature varies and synonyms are added):[157]

- Perimembranous/paramembranous/subaortic/conoventricular (most common, ~80% of VSDs; located in the membranous septum with possible extension into inlet, trabecular, or outlet septum; adjacent to tricuspid and aortic valve; so-called aneurysms of the membranous septum — i.e. tissue from the septal leaflet of the TV — are frequent and may result in partial or complete closure).
- Muscular/trabecular (up to 15—20%; completely surrounded by muscle; various locations; frequently multiple; spontaneous closure particularly frequent).
- Outlet (with or without malalignment of the outlet septum)/supracristal/subarterial/subpulmonary/infundibular/conal/doubly committed juxta-arterial [~5%; located beneath the semilunar valves in the conal or outlet septum; may be associated with progressive aortic regurgitation (AR) due to prolapse of the right aortic cusp and aneurysm of the sinus of Valsalva].
- Inlet/AV canal/AVSD type (inlet of the ventricular septum immediately inferior to the AV valve apparatus; associated with a common AV valve; may be associated with AV septal malalignment and straddling TV; typically occurring in Down syndrome).

Often there is one single defect, but multiple defects do occur. VSD is also a common component of complex anomalies, such as TOF, transposition of the great arteries (TGA), and congenitally corrected TGA (ccTGA). Spontaneous closure occurs mainly during childhood and is uncommon in outlet defects.[158]

The direction and magnitude of the shunt are determined by PVR and systemic vascular resistance, the size of the defect, LV/RV systolic and diastolic function, and the presence of right ventricular outflow tract (RVOT) obstruction (RVOTO) and left ventricular outflow tract (LVOT) obstruction (LVOTO).

4.2.2 Clinical presentation and natural history

The usual clinical presentations in adults include:

- VSD operated on in childhood, without residual VSD and no PH.
- VSD operated on in childhood, with residual VSD. The residual shunt size determines the degree of LV volume overload and the development of PH.
- Small VSD with insignificant L—R shunt, without LV volume overload or PH (restrictive VSD), which was not considered for surgery in childhood.
- VSD with L—R shunt, PH (various degrees), and various degrees of LV volume overload (rare).
- VSD with R—L shunt (Eisenmenger syndrome): large, non-restrictive, VSD with originally large L—R shunt and development of severe PVD eventually resulting in shunt reversal (cyanosis; see *sections 3.4.3* and *3.4.8*).

A large majority of patients with a VSD that has been closed entirely in childhood (spontaneously or surgically), or patients with a small VSD who were either never operated on or who had a residual defect after surgical repair with no LV volume overload on echocardiography, usually remain asymptomatic and do not require further surgery.[159] However, an unknown percentage of patients with a small residual VSD develop problems later in life.[160] Survival 40 years after closure appears to remain slightly lower than in the general population.[161]

Several possible problems may occur with advancing age:

- A double-chambered RV (DCRV) can develop over time, mostly in perimembranous defects, and may be a result of the jet lesion of the RV endothelium caused by the high-velocity VSD jet.
- In the case of an outlet (supracristal) VSD (less commonly perimembranous), there is a risk for prolapse of the right coronary (or non-coronary) cusp of the aortic valve, resulting in progressive AR and formation of a sinus of Valsalva aneurysm.
- Arrhythmias can occur, but are less frequent than in other forms of CHD[162].
- Complete heart block — rare nowadays — was not uncommon in the earlier years of cardiac smurgery, so can occur, especially in older patients. These patients usually require lifelong pacing.
- Late LV dysfunction and heart failure.
- Endocarditis.

4.2.3 Diagnostic work-up

See *section 3.3* for general principles.

Specific clinical findings include a holosystolic murmur over the third to fourth left intercostal space, and a precordial thrill may be felt.

- Echocardiography is the key diagnostic technique, in general providing the diagnosis and assessment of disease severity. Key findings to provide are location, number, and size of defects, severity of LV volume overload, and estimated PAP. AR due to prolapse of the right or non-coronary cusp must be checked for, especially in the case of outlet (supracristal) and high perimembranous VSDs. DCRV and sinus of Valsalva aneurysm must be excluded.
- CMR can serve as an alternative if echocardiography is insufficient, particularly for assessment of LV volume overload and shunt quantification.
- Cardiac catheterization is required in case of non-invasive signs of PAP elevation (calculated systolic PAP >40 mmHg or indirect signs when PAP cannot be estimated) to determine PVR.
- Exercise testing should be performed in patients with PAH to exclude desaturation.

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4.2.4 Surgical/catheter interventional treatment

Indications for intervention are summarized in the *Recommendations for intervention in ventricular septal defect (native and residual)* table and in *Figure 3*.

Surgical closure can be performed with low operative mortality (1–2%) and good long-term results.[163] Transcatheter closure has become an alternative, particularly in residual VSDs, in VSDs that are poorly accessible for surgical closure, and in muscular VSDs that are located centrally in the interventricular septum. In perimembranous VSD, it has been shown to be feasible. Whether the risk of complete AV block and entrapment of TV tissue leading to TR, or the risk of AR that has been observed in children, is relevant in adults undergoing interventional closure of a perimembranous VSD remains to be seen.

Patients eligible for VSD closure at adult age are rare. Most patients have either small VSDs with insignificant shunt or have already developed PH. The latter must be evaluated with particular caution. Patients with shunt closure and persistent/progressive PAH appear to have a particularly poor outcome.[48]

Recommendations for intervention in ventricular septal defect (native and residual)

Recommendations	Class[a]	Level[b]
In patients with evidence of LV volume overload[c] and no PAH (no non-invasive signs of PAP elevation or invasive confirmation of PVR <3 WU in case of such signs), VSD closure is recommended regardless of symptoms.	I	C
In patients with no significant L–R shunt, but a history of repeated episodes of IE, VSD closure should be considered.	IIa	C
In patients with VSD-associated prolapse of an aortic valve cusp causing progressive AR, surgery should be considered.	IIa	C
In patients who have developed PAH with PVR 3–5 WU, VSD closure should be considered when there is still significant L–R shunt (Qp:Qs >1.5).	IIa	C
In patients who have developed PAH with PVR ≥5 WU, VSD closure may be considered when there is still significant L–R shunt (Qp:Qs >1.5), but careful individual decision in expert centres is required.	IIb	C
VSD closure is not recommended in patients with Eisenmenger physiology and patients with severe PAH (PVR ≥5 WU) presenting with desaturation on exercise.[d]	III	C

AR = aortic regurgitation; IE = infective endocarditis; L–R = left-to-right; LV = left ventricle/ventricular; PAH = pulmonary arterial hypertension; PAP = pulmonary artery pressure; PVR = pulmonary vascular resistance; Qp:Qs = pulmonary to systemic flow ratio; VSD = ventricular septal defect; WU = Wood units.
[a]Class of recommendation.
[b]Level of evidence.
[c]LV enlargement with increased stroke volume.
[d]There are limited data available for a precise cut-off, but by clinical experience, this would be given by a fall of arterial oxygen saturation <90%.

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4.2.5 Follow-up recommendations

Development of AR or TR, degree of (residual) shunt, LV dysfunction, elevation of PAP, or development of DCRV, should be excluded or assessed if present by echocardiography.

Possible development of complete AV block requires attention (patients who develop bifascicular block or transient trifascicular block after VSD closure are at risk in later years for the development of complete AV block).

Patients with more than small residual VSD, valvular lesions, or haemodynamic impairment (LV dysfunction or PAH) should be seen every year, including evaluation in specialized ACHD centres. In patients with a small VSD (native or residual, normal LV, normal PAP, asymptomatic) and no other lesion, 3–5-year intervals may be reasonable. After device closure, regular follow-up during the first 2 years and then, depending on the results, every 2–5 years is reasonable. After surgical closure without residual abnormality, 5-year intervals may be reasonable.

4.2.6 Additional considerations

- Exercise/sports: no restrictions are required in patients after VSD closure, or with small VSD without PH, significant arrhythmias, or LV dysfunction. Patients with PAH must limit themselves to low-intensity recreational activity/sports (see *section 3.5.5*).
- Pregnancy: patients with pre-capillary PH (PAH) should be counselled against pregnancy. The risk is low in asymptomatic patients with normal LV and no PAH (see *section 3.5.7*).
- IE prophylaxis: recommended only for high-risk patients (see *section 3.4.6*).

4.3 Atrioventricular septal defect

4.3.1 Introduction and background

An AVSD (AV canal or endocardial cushion defect) is characterized by the presence of a common AV junction. The partial AVSD usually has a defect only at the atrial level (primum ASD) or, in rare cases, only at the ventricular level. The anterior and posterior bridging leaflets are fused centrally, creating separate left- and right-sided orifices. In a complete AVSD, the central fusion is not present and there is only one orifice. A complete AVSD (complete AV canal) has a septal defect in the crux of the heart, extending into both the interatrial and interventricular septum (non-restrictive inlet VSD). The AV node is positioned posterior and inferior to the coronary sinus. The bundle of His and the left bundle branch are displaced posteriorly. This accounts for an abnormal activation sequence of the ventricles (prolongation of AV conduction time, left-axis deviation) and is important to recognize during EP studies and catheter ablation.

Most complete AVSDs occur in Down syndrome patients (>75%), and most partial AVSDs occur in non-Down syndrome patients (>90%). AVSD may occur in association with TOF and other forms of complex CHD. An AVSD with unequal position of the common AV valve above the ventricles is accompanied by a variable degree of ventricular hypoplasia (unbalanced AVSD). The following recommendations apply to balanced AVSDs.

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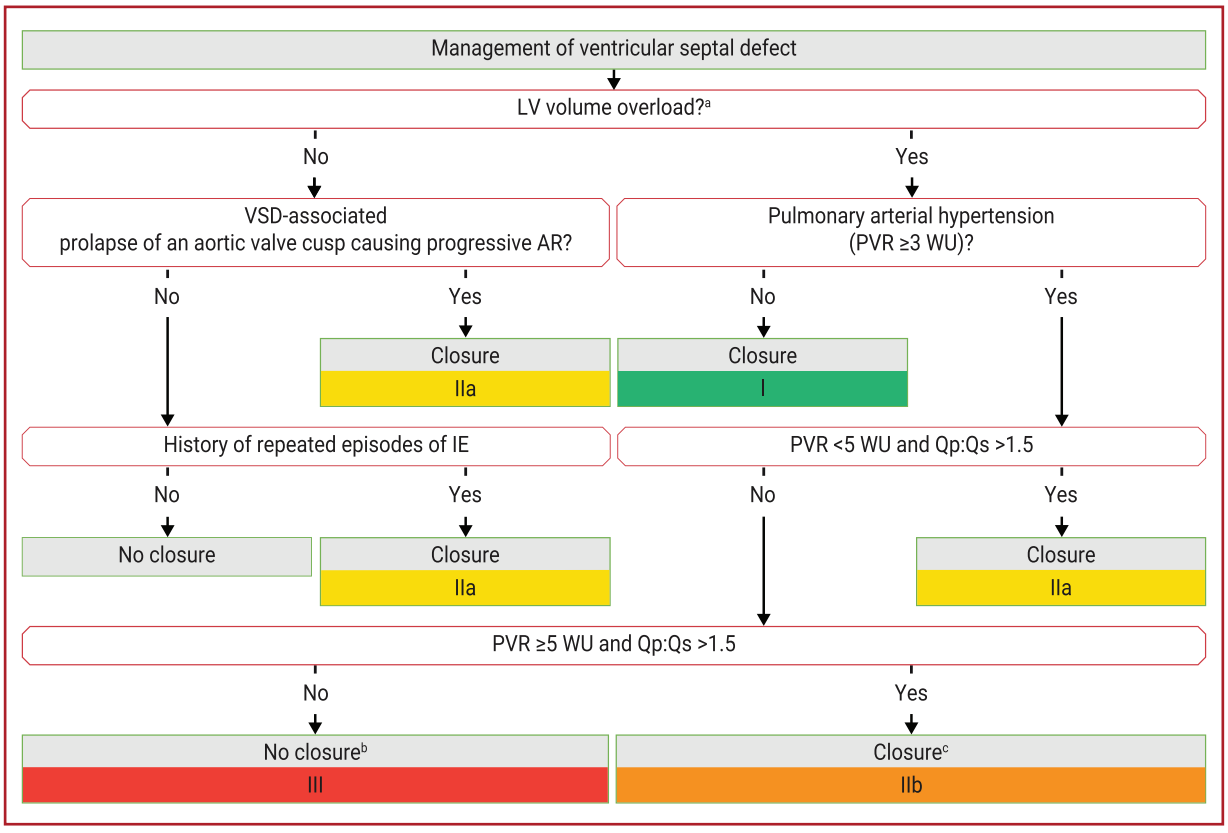


Figure 3 Management of ventricular septal defect.
AR = aortic regurgitation; IE = infective endocarditis; LV = left ventricle/ventricular; Qp:Qs = pulmonary to systemic flow ratio; PAH = pulmonary artery hypertension; PVR = pulmonary vascular resistance; VSD = ventricular septal defect; WU = Wood units.
[a]LV enlargement with increased stroke volume.
[b]Includes all patients with desaturation at rest (Eisenmenger physiology) or on exercise.
[c]Careful individual decision in expert centres is required.

4.3.2 Clinical presentation and natural history

Clinical presentation depends on the presence and size of the ASD and VSD and competence of the left-sided AV valve. Symptoms are not specific for an AVSD and are caused by intracardiac shunting (L–R, R–L, or bidirectional), PH, AV valve regurgitation, ventricular dysfunction, or LVOTO. Exercise intolerance, dyspnoea, arrhythmia, and cyanosis may be present. LVOTO (subvalvular) may be present or develop over time. Complete AV block may develop late.

The history of unoperated complete AVSD is that of Eisenmenger syndrome unless the VSD is only small (see *sections 3.4.3* and *3.4.8*).

Unrepaired primum ASD (partial AVSD) is not uncommon in adults. The presenting clinical symptoms are that of an L–R shunt at the atrial level (see *section 4.1*) and/or that of left-sided AV valve regurgitation ('cleft'). Patients may still be asymptomatic, but symptoms tend to increase with age; most adults are symptomatic by 40 years of age.

4.3.3 Diagnostic work-up

See *section 3.3* for general principles.

Clinical findings depend on the individual variant (see *sections 4.3.1* and *4.3.2*).

- Echocardiography is the key diagnostic technique. It provides assessment of each anatomic component of the AVSD, of the AV valves and their connections, the severity and exact substrate of AV valve regurgitation, the magnitude and direction of intracardiac shunting, LV and RV function, PAP, and assessment of the presence/absence of LVOTO.
- CMR is indicated when additional quantification of ventricular volumes and function, AV valve regurgitation, or intracardiac shunting is required for decision making.
- Cardiac catheterization is required in case of non-invasive signs of PAP elevation (calculated systolic PAP >40 mmHg or indirect signs when PAP cannot be estimated) to determine PVR.
- Exercise testing should be performed in patients with PAH to exclude desaturation.

4.3.4 Surgical/catheter interventional treatment

Catheter closure of AVSDs is not feasible, and intervention is therefore surgical (defect closure, valve repair). In cases of residual interatrial or interventricular communications, endocardial pacing causes an elevated risk of paradoxical emboli; this should be taken into account when pacing is indicated. Epicardial pacing may be required. The expertise of a congenital cardiac surgeon is recommended for all kinds of AVSD defect closures and AV valve repairs.

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Recommendations for intervention in atrioventricular septal defect

Recommendations	Class[a]	Level[b]
Complete AVSD		
Surgical repair is not recommended in patients with Eisenmenger physiology, and patients with PAH (PVR ≥5 WU) presenting with desaturation on exercise.[c]	III	C
For recommendations on intervention see also recommendations for intervention in VSD (*section 4.2*).		
Partial AVSD (primum ASD)		
Surgical closure is recommended in patients with significant RV volume overload and should only be performed by a congenital cardiac surgeon.	I	C
For further details see recommendations for intervention in ASD (*section 4.1*).		
AV valve regurgitation		
Valve surgery, preferably AV valve repair, is recommended in symptomatic patients with moderate to severe AV valve regurgitation and should be performed by a congenital cardiac surgeon.	I	C
In asymptomatic patients with severe left-sided AV valve regurgitation, valve surgery is recommended when LVESD ≥45 mm[d] and/or LVEF ≤60% provided other causes of LV dysfunction are excluded.	I	C
In asymptomatic patients with severe left-sided AV valve regurgitation, preserved LV function (LVESD <45 mm[d] and/or LVEF >60%), high likelihood of successful valve repair, and low surgical risk, intervention should be considered when atrial fibrillation or systolic PAP >50 mmHg is present.	IIa	C
Left ventricular outflow tract obstruction		
See recommendations for intervention in SubAS (*section 4.5.3*).		

ASD = atrial septal defect; AV = atrioventricular; AVSD = atrioventricular septal defect; LV = left ventricle/ventricular; LVEF = left ventricular ejection fraction; LVESD = left ventricular end systolic diameter; LVOTO = left ventricular outflow tract obstruction; PAH = pulmonary artery hypertension; PAP = pulmonary artery pressure; PVR = pulmonary vascular resistance; RV = right ventricle/ventricular; SubAS = subaortic stenosis; VSD = ventricular septal defect; WU = Wood units.

[a]Class of recommendation.

[b]Level of evidence.

[c]There are limited data available for a precise cut-off, but by clinical experience, this would be given by a fall of arterial oxygen saturation <90%.

[d]Cut-off refers to average-sized adults and may require adaption in patients with unusually small or large stature.

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4.3.5 Follow-up recommendations

Lifelong regular follow-up of all patients with an AVSD, operated and unoperated, is recommended, including evaluation in specialized ACHD centres. Particular attention should be paid to residual shunt, AV valve malfunction, LV and RV enlargement and dysfunction, PAP elevation, LVOTO, and arrhythmias.[164] The frequency of outpatient visits depends on the presence and severity of residual abnormalities. A patient with a surgically repaired AVSD without significant residual abnormalities should be seen at least every 2–3 years. In the case of residual abnormalities, the intervals should be shorter.

Indications for reoperation for residual abnormalities are comparable with the indications for primary surgery. In operated patients, the most frequently occurring problem is left-sided AV valve regurgitation.[165,166] It has to be emphasized that these valves are different from mitral valves and more difficult to repair. Left-sided AV valve stenosis (most often a result of previous repair) that causes symptoms should be operated on.

4.3.6 Additional considerations

- Exercise/sports: for most patients with uncomplicated, repaired AVSD, physical activity does not need restriction. Many will, however, have subnormal exercise performance when measured objectively. Patients with important residual problems require individual recommendations (see *section 3.5.5*).
- Pregnancy: well tolerated in patients with complete repair and no significant residual lesions. An unoperated partial AVSD increases the risk of paradoxical embolization. Patients with pre-capillary PH should be counselled against pregnancy. As a rule, patients with residual left-sided AV valve regurgitation, who have no indication for surgery, tolerate pregnancy relatively well, although arrhythmias and worsening of AV valve regurgitation may occur[167] (see *section 3.5.7*).
- IE prophylaxis: recommended only for high-risk patients (see *section 3.4.6*).

4.4 Patent ductus arteriosus

4.4.1 Introduction and background

Patent ductus arteriosus (PDA) is the persistent communication between the proximal left PA and the descending aorta just distal to the left subclavian artery. It can be associated with a variety of CHD lesions, however, in adults, it is usually an isolated finding.

PDA originally results in L–R shunt and LV and LA volume overload. In moderate and large PDA, PAP is elevated. In patients who reach adulthood with a moderate PDA, either LV volume overload or PAH may be predominant. Adult patients with a large PDA have, in general, developed Eisenmenger physiology.

4.4.2 Clinical presentation and natural history

Presentations of adult patients with PDA include:

- Small duct with no LV volume overload (normal LV) and normal PAP (generally asymptomatic).
- Moderate PDA with predominant LV volume overload: large LV with normal or reduced function (may present with left heart failure).
- Moderate PDA with predominant PAH: pressure-overloaded RV (may present with right heart failure).
- Large PDA: Eisenmenger physiology with differential hypoxaemia and differential cyanosis (lower extremities cyanotic, sometimes left arm too); see *sections 3.4.3* and *3.4.8*.

Aneurysm formation of the duct is a very rare complication.

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4.4.3 Diagnostic work-up

See *section 3.3* for general principles.

Specific clinical findings include a continuous murmur that disappears with development of Eisenmenger syndrome (for differential cyanosis, see *section 4.4.2*; oxygen saturation should be measured at the upper and lower extremities).

- Echocardiography is the key diagnostic technique and provides the diagnosis (may be difficult in patients with Eisenmenger physiology), the degree of LV volume overload, PAP, PA size, and right heart changes.
- CMR is indicated when additional quantification of LV volumes and quantification of shunt (Qp:Qs) is needed.
- CMR/CCT can further evaluate the anatomy where required.
- Cardiac catheterization is required in the case of non-invasive signs of PAP elevation (calculated systolic PAP >40 mmHg or indirect signs when PAP cannot be estimated) to determine PVR. Measurement of pulmonary blood flow is challenging in this setting. Measurement of oxygen saturation in both left and right PAs is mandatory.
- Exercise testing should be performed in patients with PAH to exclude desaturation of lower limbs.

4.4.4 Surgical/catheter interventional treatment

Indications for intervention are summarized in the *Recommendation for intervention in patent ductus arteriosus* table and in *Figure 4*.

Recommendations for intervention in patent ductus arteriosus

Recommendations	Class[a]	Level[b]
In patients with evidence of LV volume overload[c] and no PAH (no non-invasive signs of PAP elevation or invasive confirmation of PVR <3 WU in case of such signs), PDA closure is recommended regardless of symptoms.	I	C
Device closure is recommended as the method of choice when technically suitable.	I	C
In patients who have developed PAH with PVR 3–5 WU, PDA closure should be considered when there is still significant L–R shunt (Qp:Qs >1.5).	IIa	C
In patients who have developed PAH with PVR ≥5 WU, PDA closure may be considered when there is still significant L–R shunt (Qp:Qs >1.5) but careful individual decision in expert centres is required.	IIb	C
PDA closure is not recommended in patients with Eisenmenger physiology and patients with lower limb desaturation on exercise.[d]	III	C

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L–R = left-to-right; LV = left ventricle/ventricular; PAH = pulmonary arterial hypertension; PAP = pulmonary artery pressure; PDA = patent ductus arteriosus; PVR = pulmonary vascular resistance; Qp:Qs = pulmonary to systemic flow ratio; WU = Wood units.

[a]Class of recommendation.

[b]Level of evidence.

[c]LV enlargement with increased stroke volume.

[d]There are limited data available for a precise cut-off, but by clinical experience, this would be given by a fall of arterial oxygen saturation <90%.

In adults, calcification of the PDA may cause a problem for surgical closure. Device closure is the method of choice, even if cardiac operations are indicated due to other concomitant cardiac lesions, and can be successfully performed in the vast majority of adults with a very low complication rate.[168–170] Surgery is reserved for the rare patient with a duct too large for device closure or with unsuitable anatomy such as aneurysm formation.

4.4.5 Follow-up recommendations

Echocardiographic evaluation should include LV size and function, PAP, residual shunt, and associated lesions.

Patients with no residual shunt, normal LV, and normal PAP do not require regular follow-up after 6 months.

Patients with LV dysfunction and patients with residual PAH should be followed at intervals of 1–3 years, depending on severity, including evaluation in specialized ACHD centres.

4.4.6 Additional considerations

- Exercise/sports: no restrictions in asymptomatic patients before or after intervention without PH; limitation to low-intensity sports in PAH patients.
- Pregnancy: no significantly increased risk for patients without PH. Patients with pre-capillary PH should be counselled against pregnancy (see *section 3.5.7*).
- IE prophylaxis: limited to high-risk patients (see *section 3.4.6*).

4.5 Left ventricular outflow tract obstruction

4.5.1 Valvular aortic stenosis

4.5.1.1 Introduction and background

The most common cause for congenital valvular aortic stenosis (AS) is BAV. Up to 80% of patients with a BAV will develop ascending aortic dilatation, which is discussed in *section 4.7.2*. For the management of AR associated with BAV, see the 2017 ESC/EACTS Guidelines on the management of valvular heart disease.[25]

4.5.1.2 Clinical presentation and natural history

Patients frequently remain asymptomatic for many years. Progression of stenosis varies and depends on initial severity, degree of calcification, age, and atherosclerotic risk factors. In BAV, progression is faster in those patients with greater closure-line eccentricity and an anteroposterior-oriented line of closure.

Prognosis is good and sudden death is rare in asymptomatic patients with good exercise tolerance, even when stenosis is severe.[171]

Once symptoms (angina pectoris, dyspnoea, or syncope) occur, the prognosis deteriorates rapidly. In patients with BAV, cardiac mortality has been reported to be 0.3% per patient-year of follow-up, the frequency of aortic dissection 0.03%, and endocarditis 0.3%. Dilated aortic sinuses and/or ascending aorta have been found in 45% of patients after 9 years of follow-up.[172]

4.5.1.3 Diagnostic work-up

See *section 3.3* for general principles. Diagnostic criteria for degree of AS are summarized in *Table 12*.

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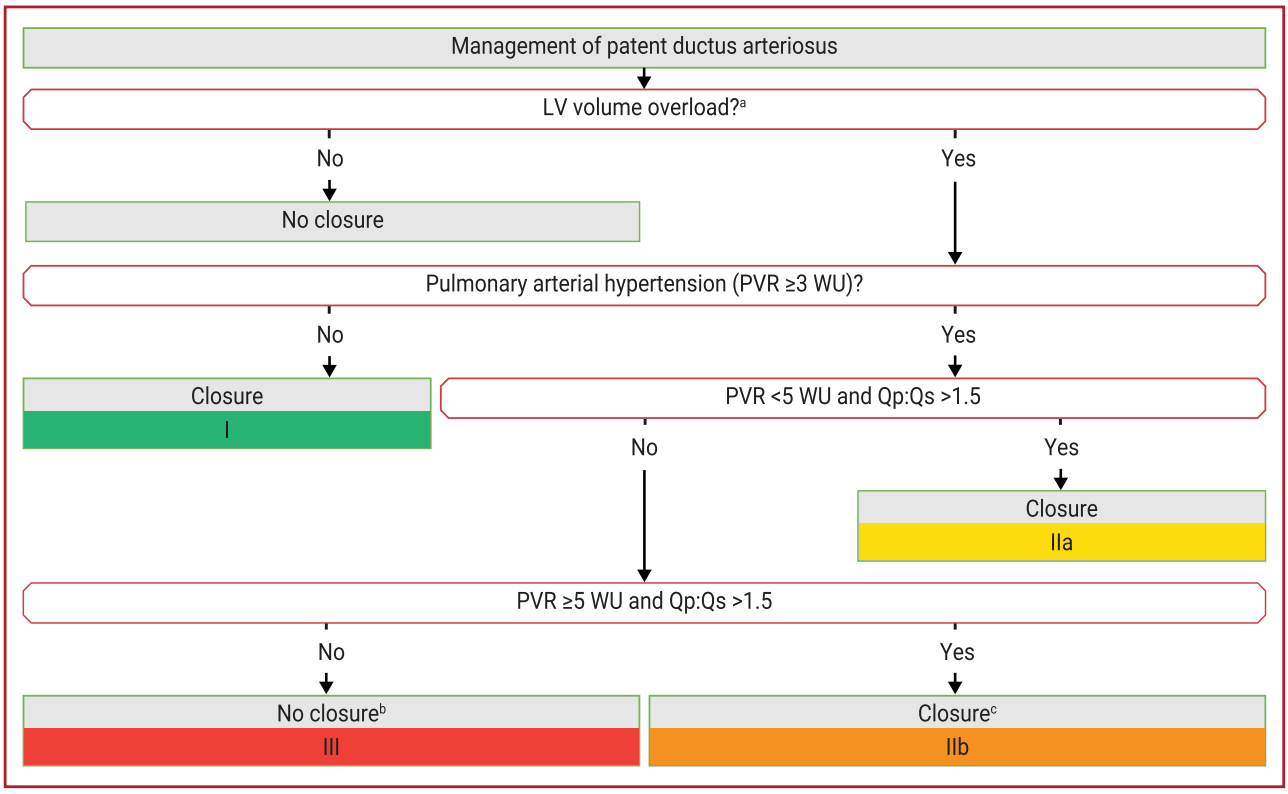


Figure 4 Management of patent ductus arteriosus.
LV = left ventricle/ventricular; Qp:Qs = pulmonary to systemic flow ratio; PAH = pulmonary artery hypertension; PDA = patent ductus arteriosus; PVR = pulmonary vascular resistance; WU = Wood units.
[a]LV enlargement with increased stroke volume.
[b]Includes all patients with lower limb desaturation at rest (Eisenmenger physiology) or on exercise.
[c]Careful individual decision in expert centres is required.

Specific clinical findings include the typical systolic ejection murmur over the aortic valve, radiating into the carotid arteries. An ejection click can be heard and a thrill may be palpable. The ECG may show LV hypertrophy (LVH) with or without strain. In patients diagnosed with a BAV, CoA should be excluded (see *section 4.6*).

- Echocardiography is the gold standard for the diagnosis of AS and for assessing the degree of calcification, LV function, LVH, and associated lesions including ascending aortic dilatation. With Doppler echocardiography, the degree of AS severity is determined from transvalvular peak velocity (V_{max}), mean gradient, and continuity equation-calculated aortic valve area (AVA). For more details, see recent recommendations for the echocardiographic assessment of AS.[173]
- TOE may occasionally provide more anatomical details about valve dysfunction or AVA planimetry in non-calcified valves.
- Exercise testing is recommended in asymptomatic patients, particularly in moderate-to-severe AS, to confirm asymptomatic status and evaluate exercise tolerance, blood pressure response, and arrhythmias for risk stratification and timing of surgery.
- Low-dose dobutamine or exercise stress echocardiography is helpful in AS with reduced stroke volume and impaired LV function (classical low-flow, low-gradient AS).[173]

Table 12 Diagnostic criteria for degree of aortic stenosis severity[173]

	Mild AS	Moderate AS	Severe AS
V_{max} (m/s)[a]	2.6–2.9	3.0–3.9	≥4.0
Mean gradient (mmHg)[a]	<20	20–39	≥40
AVA (cm^2)	>1.5	1.0–1.5	<1.0
AVAi (cm^2/m^2 BSA)	>0.85	0.60–0.85	<0.60
LVOT velocity/aortic valve velocity	>0.50	0.25–0.50	<0.25

AS = aortic stenosis; AVA = aortic valve area; AVAi = indexed aortic valve area; BSA = body surface area; LVOT = left ventricular outflow tract; V_{max} = maximum Doppler velocity.
[a]At normal transvalvular flow.

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- CMR/CCT, despite having potential for assessing AS, is mainly required to assess dilation of the ascending aorta, in cases where measurement is unreliable with echocardiography.
- CCT has become particularly important for the quantification of valve calcification when assessing AS severity in low-gradient AS, although it should be noted that aortic valve

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Recommendations for intervention in valvular aortic stenosis

Recommendations	Class[a]	Level[b]
Symptomatic patients with aortic valve stenosis		
In symptomatic patients with severe high-gradient AS (mean gradient ≥40 mmHg), intervention is recommended.[25,171,174,175]	I	B
Intervention is indicated in symptomatic patients with severe low-flow, low-gradient (mean gradient <40 mmHg) AS with reduced EF and evidence of flow (contractile) reserve excluding pseudosevere AS.	I	C
Asymptomatic patients with severe aortic valve stenosis		
Intervention is indicated in asymptomatic patients with severe AS and an abnormal exercise test showing symptoms on exercise clearly related to AS.	I	C
Intervention is indicated in asymptomatic patients with severe AS and systolic LV dysfunction (LVEF <50%) not due to another cause.	I	C
Intervention should be considered in asymptomatic patients with severe AS when they present with a fall in blood pressure below baseline during exercise testing.	IIa	C
Intervention should be considered in asymptomatic patients with normal EF and none of the above-mentioned exercise test abnormalities if the surgical risk is low and one of the following findings is present: • Very severe AS defined by a V_{max} >5.5 m/s. • Severe valve calcification and a rate of V_{max} progression ≥0.3 m/s/year. • Markedly elevated BNP levels (>3-fold age- and sex-corrected normal range) confirmed by repeated measurements without other explanation. • Severe PH (systolic PAP at rest >60 mmHg confirmed by invasive measurement) without other explanation.	IIa	C
Concomitant aortic valve surgery at the time of other cardiac/ascending aorta surgery		
Surgery is recommended when patients with severe AS undergo surgery of the ascending aorta or of another valve, or CABG.	I	C
Patients with moderate AS undergoing CABG surgery or surgery of the ascending aorta or another valve should be considered for additional valve replacement.	IIa	C

AS = aortic stenosis; BNP = B-type natriuretic peptide; CABG = coronary artery bypass graft; EF = ejection fraction; LV = left ventricle/ventricular; LVEF = left ventricular ejection fraction; PAP = pulmonary artery pressure; PH = pulmonary hypertension; V_{max} = maximum Doppler velocity.
[a]Class of recommendation.
[b]Level of evidence.

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stenosis in young patients is not necessarily associated with significant calcification.
- Cardiac catheterization is only required if non-invasive evaluation yields uncertain results, for evaluation of coronary arteries, or when percutaneous balloon angioplasty is considered.

4.5.1.4 Medical therapy

Symptomatic patients require urgent surgery. Medical treatment for AS-related heart failure is reserved for non-operable patients. Neither statin treatment, nor any other medical treatment, has so far been shown to retard progression of AS.

4.5.1.5 Surgical/catheter interventional treatment

Indications for intervention are summarized in the *Recommendations for intervention in valvular aortic stenosis table* and in *Figure 5*.

In selected adolescents and young adults with non-calcified valves, balloon valvuloplasty may be considered. This may be the case in haemodynamically unstable patients as a bridge to surgery or to delay valve replacement in women with anatomically suitable valves and desire of pregnancy. In patients with calcified valves, the treatment of choice is valve replacement. Mechanical valves are more durable than biological valves or homografts but require lifelong anticoagulation. The Ross procedure (two-valve operation) has been suggested for patients of childbearing age and for those wanting to avoid anticoagulation. Progressive degeneration of the homograft after the Ross procedure is the most frequent reason for reintervention during follow-up. Transcatheter pulmonary valve implantation has become an alternative technique for surgical treatment of the degenerated pulmonary valve. Transcatheter aortic valve implantation currently has no place in the treatment of congenital AS, except in very rare cases with high surgical risk, when technically feasible.

4.5.1.6 Follow-up recommendations

Lifelong and regular follow-up is required, and the intervals depend upon the degree of stenosis severity. It is also necessary after valve intervention at minimum yearly intervals.

Echocardiographic imaging of the aortic valve and aortic root to determine progression of valve stenosis and aortic dilation is mandatory. CMR or CCT of the aorta is recommended in patients with a native BAV, patients with a history of isolated valve replacement where the ascending aorta is not well visualized on TTE, and in patients with root/ascending diameters >40mm.[176]

4.5.1.7 Additional considerations

- Exercise/sports: patients with severe symptomatic and asymptomatic AS, and those with moderate stenosis due to BAV and dilated aorta, should avoid isometric exercise and high-intensity sports. In mild and moderate AS, more intensive physical activity is allowed. A prior exercise test to guide counselling is recommended.[24]
- Pregnancy: contraindicated in severe symptomatic AS. Treatment by either balloon valvuloplasty or surgery should be performed before conception. In asymptomatic patients with severe AS and a normal exercise test, pregnancy may be possible in selected patients. The aorta requires particular attention as BAV-related

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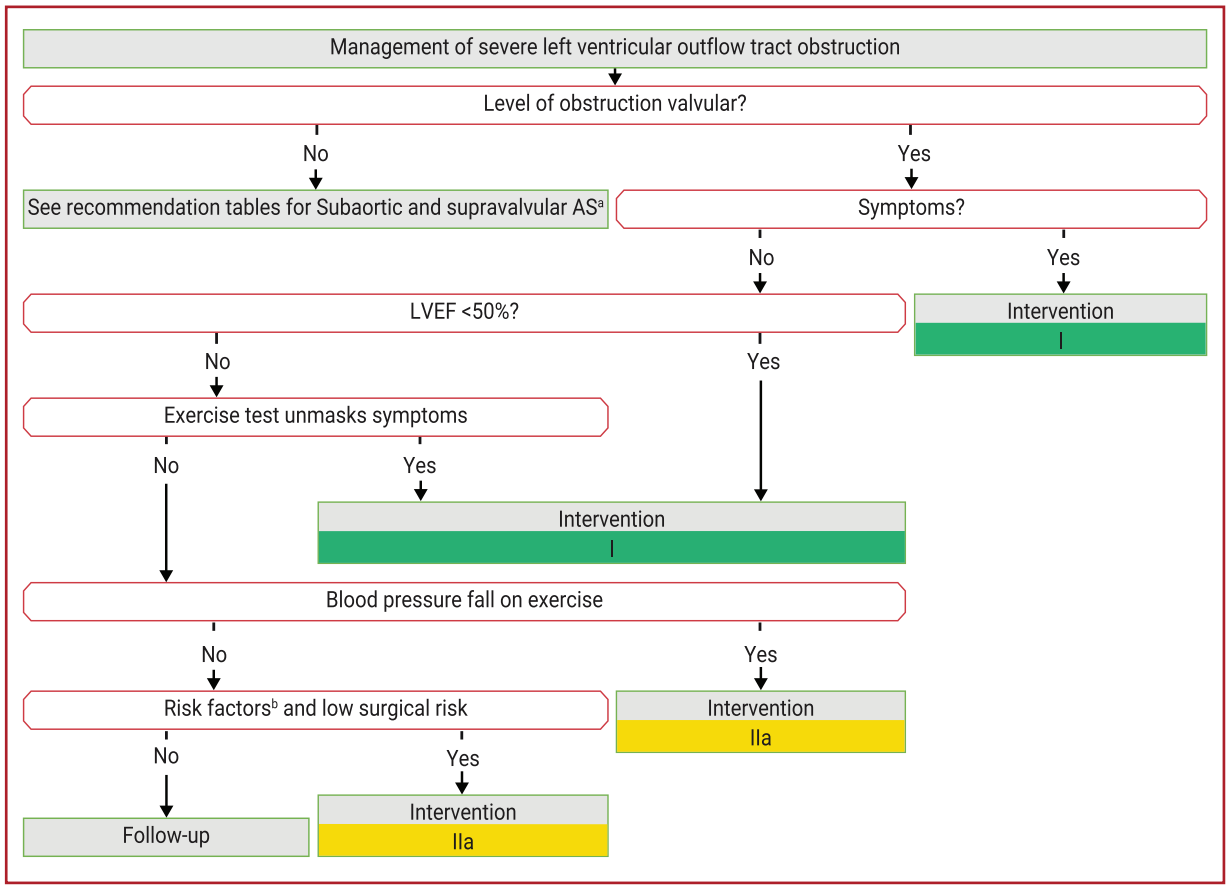


Figure 5 Management of severe left ventricular outflow tract obstruction.
AS = aortic stenosis; LVEF = left ventricular ejection fraction; LVOTO = left ventricular outflow tract obstruction; PAP = pulmonary artery pressure; PH = pulmonary hypertension; SubAS = subaortic stenosis SupraAS = supravalvular aortic stenosis.
[a]See *Section 4.5*. There are fundamental differences in management decisions compared to valvular AS, particularly because a valve substitute with its consequences is generally not required.
[b]Peak velocity >5.5m/s; severe calcification + peak velocity progression ≥0.3 m/s/y; markedly elevated neurohormones (>3-fold age- and sex-corrected normal range); severe PH (systolic PAP >60 mmHg without other explanation).

aortic dilation may be induced and progress during and after pregnancy; there is a risk of dissection (see *section 3.5.7*).
- IE prophylaxis: recommended only for high-risk patients (see *section 3.4.6*).

4.5.2 Supravalvular aortic stenosis

4.5.2.1 Introduction and background

Supravalvular AS (SupraAS) may occur as a characteristic feature of Williams–Beuren syndrome or be isolated/familial, which are respectively caused by deletion of the elastin gene located on chromosome 7q11.23 or a mutation in this same gene. These genetic defects lead to obstructive arteriopathy of varying severity, which is most pronounced at the sinotubular junction.[177]

SupraAS may also be encountered in the setting of familial homozygous hypercholesterolaemia.[178] SupraAS occurs as a localized fibrous diaphragm just distal to the coronary ostia or, most commonly, as an external hourglass deformity with a corresponding luminal narrowing of the aorta, or as diffuse stenosis of the ascending aorta. It may be associated with aortic valve abnormalities, hypoplasia of the entire aorta, involvement of coronary ostia, or stenosis of major branches of the aorta or PAs.

4.5.2.2 Clinical presentation and natural history

The majority of patients present in childhood with symptoms of either outflow obstruction or myocardial ischaemia. While progression of SupraAS is rare in adulthood, adults remain at risk for cardiac complications.[179] Sudden death occurs rarely, but it is more common in SupraAS with Williams–Beuren syndrome, with diffuse peripheral PA stenosis, or with CAD, particularly related to anaesthetic procedures.

4.5.2.3 Diagnostic work-up

See *section 3.3* for general principles.

Auscultation typically reveals a loud systolic ejection murmur best heard at the left lower sternal border without associated ejection click or diastolic murmur of AR.

- Echocardiography enables the anatomic diagnosis of SupraAS when the acoustic window allows. Doppler echocardiography provides pressure gradients, but these may over- or underestimate the actual pressure drop across the obstruction. TOE allows good visualization of the coronary ostia and 3D TOE can be used for detailed evaluation of the stenotic region.[180]
- For exercise testing, see valvular AS (*section 4.5.1*).

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- CMR/CCT is useful for detailed evaluation of supravalvular anatomy, in particular, when multilevel LVOTO is present or for (pre-operative) assessment of coronary artery anatomy and other aortic or aortic branch lesions (e.g. carotid and renal artery stenosis), and central and branch PAs.
- Cardiac catheterization: haemodynamic assessment is recommended when non-invasive quantification remains uncertain.
- Genetic evaluation, with counselling and subsequent testing using micro-array techniques to diagnose Williams–Beuren syndrome and sequencing of the elastin gene in non-syndromic presentations, is useful.

4.5.2.4 Surgical/catheter interventional treatment

Surgery is the primary treatment: the operative mortality rate for fibrous diaphragm and hourglass deformity is <5%. Since the coronary arteries are under high pressure, surgery might be considered earlier than in patients with valvular AS, particularly when no valve substitute is required. Following operative repair, the survival rate has been reported to be 80–85% at 20 years.[181] AR may be present in ~25% of patients, but usually it is not progressive after surgical relief of SupraAS.

Recommendations for intervention in supravalvular aortic stenosis

Recommendations	Class[a]	Level[b]
In patients with symptoms (spontaneous or on exercise test) and mean Doppler gradient ≥40 mmHg, surgery is recommended.	I	C
In patients with mean Doppler gradient <40 mmHg, surgery is recommended when one or more of the following findings are present: • Symptoms attributable to obstruction (exertional dyspnoea, angina, syncope). • LV systolic dysfunction (EF <50% without other explanation). • Surgery required for significant CAD or valvular disease.	I	C
Patients with mean Doppler gradient ≥40 mmHg[c] – but without symptoms, LV systolic dysfunction, LVH, or abnormal exercise test – may be considered for repair when the surgical risk is low.	IIb	C

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CAD = coronary artery disease; EF = ejection fraction; LV = left ventricle/ventricular; LVH = left ventricular hypertrophy.
[a]Class of recommendation.
[b]Level of evidence.
[c]Doppler-derived gradients may overestimate the obstruction and may need confirmation by left heart catheterization.

4.5.2.5 Follow-up recommendations

Lifelong and regular follow-up, including echocardiography, is required to determine progression of obstruction (rare), LV size/function, and development of symptoms, as well as after surgery to detect late restenosis, development of aneurysm (CMR/CCT), and the occurrence or progression of CAD. Follow-up should include evaluation in specialized ACHD centres.

4.5.2.6 Additional considerations

- Exercise/sports: see valvular AS (*section 4.5.1*).
- Pregnancy: See valvular AS (*section 4.5.1*). Male and female patients with Williams–Beuren syndrome and elastin gene mutations have a 50% transmission risk (family screening recommended).
- IE prophylaxis: recommended only for high-risk patients (see *section 3.4.6*).

4.5.3 Subaortic stenosis

4.5.3.1 Introduction and background

Subaortic stenosis (SubAS) occurs as an isolated lesion, but is frequently associated with aortic valve disease, VSD, AVSD, or Shone complex (multilevel left heart obstruction). It may also develop after repair of these lesions. It is caused by a fibrous ridge/ring in the LVOT proximal to the aortic valve or as a fibromuscular narrowing. SubAS has to be differentiated from obstructive hypertrophic cardiomyopathy.

4.5.3.2 Clinical presentation and natural history

The clinical course is highly variable. The presence of associated CHD, particularly a VSD, is related with SubAS progression; age seems not to play a role in disease. AR is frequent but rarely haemodynamically significant or progressive.[182] Although infrequent, sudden death has been reported in SubAS patients.

4.5.3.3 Diagnostic work-up

See *section 3.3* for general principles.

Clinical findings mainly include a systolic ejection murmur at the left sternal border without systolic ejection click. A diastolic murmur refers to AR.

- Echocardiography visualizes LVOT anatomy, associated aortic valve abnormality, degree of AR, LV function, LVH, and associated lesions. With Doppler echocardiography, the severity of the subvalvular obstruction is determined, but Doppler-derived gradients may overestimate the obstruction and may require confirmation by cardiac catheterization. Occasionally, TOE is necessary to better demonstrate the membrane or ring. 3D TOE can be helpful to characterize the complex LVOT anatomy and estimate the area of obstruction by planimetry.
- CMR may be useful to characterize complex LVOTO anatomies, especially in patients with poor acoustic window.

4.5.3.4 Surgical/catheter interventional treatment

Surgical treatment is the only effective intervention and involves a complete resection of the fibrous ridge/ring and parts of the muscular base along the left septal surface. Fibromuscular or tunnel-type SubAS requires more extensive resection or a Konno procedure. Surgical results are good, but restenosis may occur. In patients with low surgical risk and morphologically well suited to repair, the threshold for intervention is lower than in aortic valve stenosis since no valve implant is required. In the case of moderate or severe AR, the aortic valve must be repaired or replaced at the time of surgery.

4.5.3.5 Follow-up recommendations

Lifelong regular follow-up, including echocardiography, is required in the non-operated state to determine progression of obstruction, AR, and LV hypertrophy, function, and size. Regular post-operative follow-

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up is also necessary to detect and observe late restenosis, progressive AR, and complications such as arrhythmias, heart block, and iatrogenic VSD. Follow-up should include evaluation in specialized ACHD centres, and the frequency is related to the expected disease progression.

Recommendations for intervention in subaortic stenosis

Recommendations	Class[a]	Level[b]
In symptomatic patients (spontaneous or on exercise test) with a mean Doppler gradient ≥40 mmHg[c] or severe AR, surgery is recommended.	I	C
Asymptomatic patients should be considered for surgery when one or more of the following findings are present: • Mean gradient <40 mmHg but LVEF <50%. • AR is severe and LVESD >50 mm (or 25 mm/m^2 BSA) and/or EF <50%[d]. • Mean Doppler gradient is ≥40 mmHg[c] and marked LVH present. • Mean Doppler gradient is ≥40 mmHg[c] and there is a fall in blood pressure below baseline on exercise.	IIa	C
Asymptomatic patients may be considered for surgery when one or more of the following findings are present: • Mean Doppler gradient is ≥40 mmHg,[c] LV is normal (EF >50% and no LVH), exercise testing is normal, and surgical risk is low. • Progression of AR is documented and AR becomes more than mild (to prevent further progression).	IIb	C

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AR = aortic regurgitation; BSA = body surface area; EF = ejection fraction; ESC = European Society of Cardiology; LV = left ventricle/ventricular; LVEF = left ventricular ejection fraction; LVESD = left ventricular end systolic diameter; LVH = left ventricular hypertrophy.
[a]Class of recommendation.
[b]Level of evidence.
[c]Doppler-derived gradients may overestimate the obstruction and may need confirmation by cardiac catheterization.
[d]See 2017 ESC Guidelines on the management of valvular heart disease.[25]

4.5.3.6 Additional considerations

- Exercise/sports: see valvular AS (*section 4.5.1*).
- Pregnancy: only contraindicated in severe, symptomatic SubAS where surgery should be performed before pregnancy (even in asymptomatic severe SubAS, surgery should be considered) (see *section 3.5.7*).
- IE prophylaxis: recommended only for high-risk patients (see *section 3.4.6*).

4.6 Coarctation of the aorta

4.6.1 Introduction and background

CoA is considered as part of a generalized arteriopathy, and not only as narrowing of the aorta. It occurs as a discrete stenosis or as a long, hypoplastic aortic (arch) segment. Typically, CoA is located in the area where the ductus arteriosus inserts, and only in rare cases occurs ectopically (ascending, descending, or abdominal aorta).

Associated lesions include BAV (up to 85%), ascending aortic aneurysm, SubAS, or SupraAS, (supra)mitral valve stenosis (including parachute mitral valve), Shone complex, or complex congenital heart defects. CoA can be associated with Turner syndrome and Williams–Beuren syndrome. Extracardiac vascular anomalies have been reported in CoA patients including anomalous origin of the right subclavian artery (in 4–5% of cases), collateral arterial circulation, and intracerebral aneurysms (in up to 10%).

4.6.2 Clinical presentation and natural history

Signs and symptoms depend on the severity of CoA. Patients with severe CoA usually present with signs and symptoms early in life, while particularly mild cases may not become evident until adulthood, where CoA is detected in the work-up of arterial hypertension.

Key symptoms may include headache, nosebleeds, dizziness, tinnitus, shortness of breath, abdominal angina, claudication, and cold feet.

Patients with CoA who reach adolescence demonstrate very good long-term survival up to age 60 years. Long-term morbidity is common, however, largely related to aortic complications and longstanding hypertension.[183]

The natural course may be complicated by left heart failure, intracranial haemorrhage (from berry aneurysm), IE, aortic rupture/dissection, premature coronary and cerebral artery disease, and associated heart defects.

4.6.3 Diagnostic work-up

See *section 3.3* for general principles.

Office blood pressure measurement in the upper and lower extremities are the primary studies required in all coarctation patients. A blood pressure gradient between upper and lower extremities (systolic ≥20 mmHg) indicates significant CoA. Weak or absent pulses in the lower extremities or radiofemoral pulse delay also indicate significant coarctation.

- Ambulatory blood pressure measurements (right arm) are recommended to detect/confirm arterial hypertension (24-h mean systolic >130 mmHg and/or diastolic >80 mmHg).
- Other findings consist of a suprasternal thrill (proximal obstruction), an interscapular (systolic) murmur, or continuous murmurs (due to collateral vessels). In the case of a pinpoint CoA, murmurs may be completely absent.
- Chest X-ray findings may be characterized by rib notching of the third and fourth (to the eighth) ribs due to the collaterals.
- Echocardiography provides information regarding site, structure, and extent of CoA, LV function and LVH, associated cardiac abnormalities, and aortic and supra-aortic vessel diameters. Doppler gradients are not useful for quantification, neither in native nor in post-operative coarctation. In the presence of extensive collateral arteries, gradients are not reliable and are often underestimated. After surgical repair or stenting, increased systolic flow rates may develop, even in the absence of significant narrowing, due to decreased/absent aortic compliance and

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Doppler-related pressure recovery. The gradient is then overestimated. A diastolic tail in the descending aorta and diastolic forward flow in the abdominal aorta are findings of significant (re-)CoA.

- CMR and CCT, including 3D reconstruction, are the preferred non-invasive techniques to evaluate the entire aorta in adolescents and adults. Both depict site, extent, and degree of the aortic narrowing, the aortic arch and head and neck vessels, the pre- and post-stenotic aorta, and collaterals. Both methods detect complications such as aneurysms, false aneurysms, restenosis, or residual stenosis.[184]
- Imaging of intracerebral vessels is indicated in the case of symptoms and/or clinical manifestations of aneurysms/rupture.
- Cardiac catheterization with manometry (a peak-to-peak gradient ≥20 mmHg) indicates a haemodynamically significant CoA in the absence of well-developed collaterals and is performed in the setting of interventional treatment. It should be noted that, in patients under general anaesthesia, invasive measurement of gradient may be underestimated.

4.6.4 Surgical/catheter interventional treatment

Indications for intervention are summarized in the *Recommendations for intervention in coarctation and re-coarctation of the aorta* table and in *Figure 6*.

In native CoA, as well as re-coarctation with appropriate anatomy, stenting has become the first-choice treatment in many ACHD centres.[185] The use of covered stents is preferred because of lower short- and long-term complication rates.[186] Biodegradable stents are in development but are mainly applied in children when the aorta is still expected to grow.

Balloon angioplasty in adults is only indicated for re-dilatation of previously stented aortas.

While paediatric surgical techniques include resection and end-to-end anastomosis, resection and extended end-to-end anastomosis, prosthetic patch aortoplasty, subclavian flap aortoplasty, interposition of a (tube) graft, and bypass tube (jump) grafts, only the latter two are generally feasible in adults. Ascending-to-descending aorta conduits may be preferable in adults with difficult anatomy. Although the surgical risk in simple CoA may currently be <1%, it increases significantly beyond the age of 30–40 years. Spinal cord injury has become extremely rare.[187]

As coarctation is not a localized disease of the aorta, associated lesions that may require structural interventions have to be considered:

- Associated significant aortic valve stenosis or regurgitation (BAV).
- Aneurysm of the ascending aorta with a diameter >50 mm or rapid progression of diameter.
- Aneurysm and false aneurysms at the previous CoA site.
- Symptomatic or large aneurysms of the circle of Willis.

Treatment should be performed in centres with extensive experience in the treatment of CHD.

Recommendations for intervention in coarctation and re-coarctation of the aorta

Recommendations	Class[a]	Level[b]
Repair of coarctation or re-coarctation (surgically or catheter based) is indicated in hypertensive patients[c] with an increased non-invasive gradient between upper and lower limbs confirmed with invasive measurement (peak-to-peak ≥20 mmHg) with preference for catheter treatment (stenting), when technically feasible.	I	C
Catheter treatment (stenting) should be considered in hypertensive patients[c] with ≥50% narrowing relative to the aortic diameter at the diaphragm, even if the invasive peak-to-peak gradient is <20 mmHg, when technically feasible.	IIa	C
Catheter treatment (stenting) should be considered in normotensive patients[c] with an increased non-invasive gradient confirmed with invasive measurement (peak-to-peak ≥20 mmHg), when technically feasible.	IIa	C
Catheter treatment (stenting) may be considered in normotensive patients[c] with ≥50% narrowing relative to the aortic diameter at the diaphragm, even if the invasive peak-to-peak gradient is <20 mmHg, when technically feasible.	IIb	C

[a]Class of recommendation.
[b]Level of evidence.
[c]Right arm ambulatory blood pressure monitoring should be considered for the diagnosis of hypertension.

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4.6.5 Follow-up recommendations

Residua, sequelae, and complications are listed below:

- Arterial hypertension at rest or during exercise is common, even after successful treatment, and is an important risk factor for premature CAD, ventricular dysfunction, and rupture of aortic or cerebral aneurysms.[188]
- The geometry of the arch (gothic, crenel, normal) and smaller aortic size in the stented region may play a role in the development of hypertension. Right arm 24-h ambulatory blood pressure measurement better detects hypertension than a one-off measurement.[189] The significance of isolated, exercise-induced hypertension is a matter of debate.
- An increased pressure gradient (systolic ≥20 mmHg) between upper and lower extremities indicates re-coarctation and warrants invasive assessment for confirmation and treatment.
- Medical treatment of arterial hypertension should follow the 2018 ESC/ESH Guidelines.[190]
- Recurring or residual CoA may induce or aggravate systemic arterial hypertension and its complications.
- Aneurysms of the ascending aorta or at the intervention site present a risk of rupture and death. Patch repairs (e.g. with Dacron) are at particular risk of repair-site aneurysms, while

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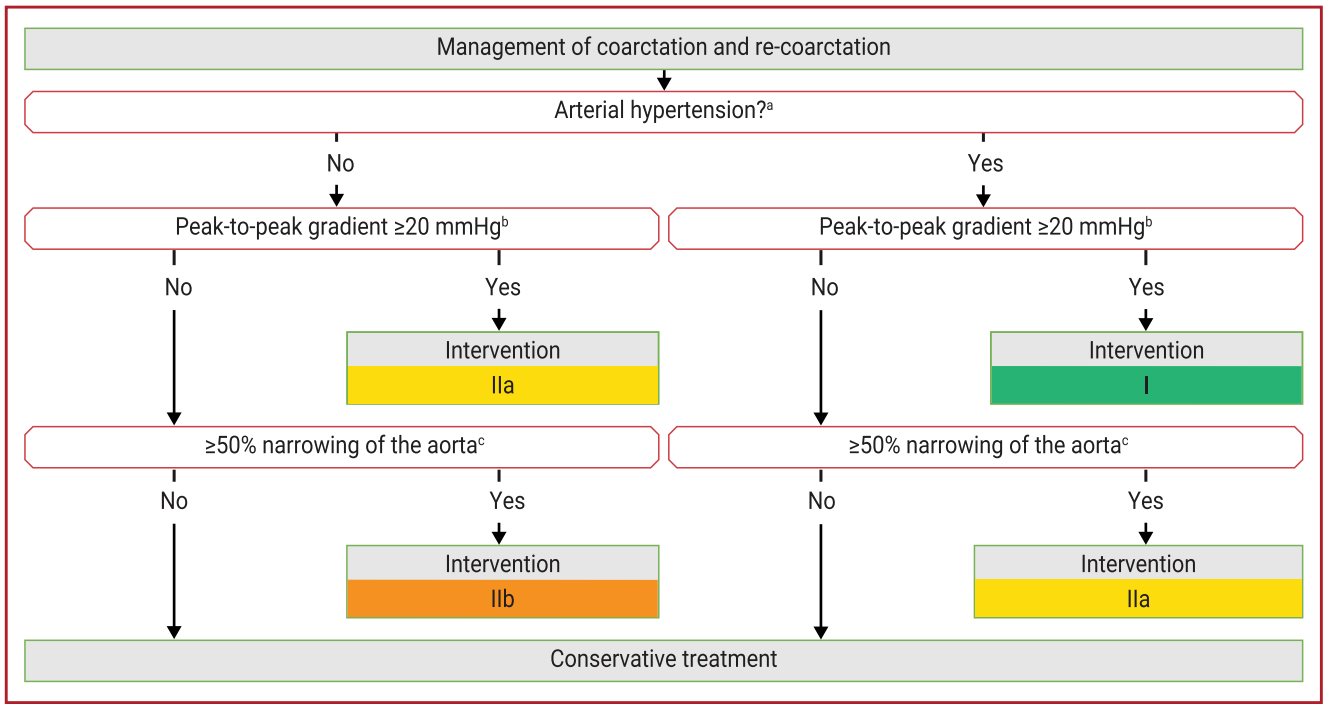


Figure 6 Management of coarctation and re-coarctation of the aorta.
CoA = coarctation of the aorta.
[a]Right arm ambulatory blood pressure should be considered for diagnosis.
[b]Invasively confirmed measurement.
[c]Relative to the aortic diameter at the diaphragm.

interposition grafts are at particular risk of false aneurysms,[191] and both should be imaged on a regular basis.

- Attention is required for BAV, mitral valve disease, premature CAD, and berry aneurysms of the circle of Willis (routine screening in asymptomatic patients is not recommended).

All CoA patients require regular follow-up at least every year. Imaging of the aorta (preferably with CMR) is required to document post-repair or post-interventional anatomy and complications (restenosis, aneurysm, false aneurysm formation). Recommended imaging intervals are commonly every 3–5 years but also depend on baseline pathology.

4.6.6 Additional considerations

- Exercise/sports: patients without residual obstruction, who are normotensive at rest and with exercise, can usually lead normally active lives without restriction. Patients with arterial hypertension, residual obstruction, or other complications should avoid heavy isometric exercises in proportion to the severity of their problems.
- Pregnancy: after successful treatment of CoA, many women tolerate pregnancy without major problems.[43] In particular, women with unrepaired CoA – but also those after repair with arterial hypertension, residual CoA, or aortic aneurysms – have an increased risk of aortic rupture and rupture of a cerebral aneurysm during pregnancy and delivery. An excess of miscarriages and hypertensive disorders has been reported[192] (see *section 3.5.7*).
- IE prophylaxis: recommended only for high-risk patients (see *section 3.4.6*).

4.7 Aortopathies

4.7.1 Marfan syndrome and related heritable thoracic aortic diseases

4.7.1.1 Introduction and background

Marfan syndrome is the prototype of syndromic HTAD entities, comprising a clinically and genetically heterogeneous group of disorders with aneurysm or dissection of the thoracic aorta as the common denominator. Both syndromic and non-syndromic (or isolated) forms of HTAD are part of the clinical spectrum, with notable clinical overlap between the various entities.

For more details on the various syndromes, please refer to the 2014 ESC Guidelines on aortic disease[193] and a consensus document on genetic testing in ACHD/HTAD.[140] Since most children with mainly syndromic forms of HTAD will be transferred to ACHD units at adult age, these Guidelines focus on specific cardiovascular complications. Marfan syndrome is considered as the model disease – other syndromes are mentioned in case of important differences from Marfan syndrome.

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4.7.1.2 Clinical presentation and natural history

Although thoracic aortic disease — either aneurysms detected by screening or dissection in an emergency setting — is the principal characteristic in Marfan syndrome /HTAD, extra-aortic features in the skeletal/ocular organ system may be the key to diagnosis in some patients.

Prognosis in all HTAD entities is mainly determined by progressive dilation of the aorta, leading to aortic dissection or rupture. Prognosis varies according to the underlying genetic defect. The average age at death in untreated Marfan syndrome patients is <40 years, but can approach that of the general population in patients in whom the diagnosis is known and who are properly managed.[29,194] More rare cardiovascular causes of death include heart failure and SCD.[29]

In Marfan syndrome, the major determinant of type A aortic dissection is the aortic root diameter with increased risk of rupture ≥50 mm.[195] Other risk factors include family history of aortic dissection at low diameter,[193] aortic root growth rate, pregnancy, and hypertension. Increasing evidence for gene-based differences in aortic risk are emerging and need to be considered. Other parts of the aorta — or in the case of some entities, major branching vessels — may also dilate or dissect.

The presence of significant aortic, tricuspid, or mitral regurgitation — usually related to valve prolapse — may lead to symptoms of ventricular volume overload. However, LV disease may also occur independently of valvular dysfunction and this may be associated with arrhythmia. Mitral valve prolapse in patients with Marfan syndrome manifests early and progresses to severe regurgitation, need for surgery, and IE earlier than idiopathic mitral valve prolapse.[196]

4.7.1.3 Diagnostic work-up

Early identification and establishment of the correct diagnosis is critical since prophylactic surgery can prevent aortic dissection and rupture. This requires a multidisciplinary team approach with integration of clinical and genetic findings.[197] The diagnosis of Marfan syndrome is based on the Ghent criteria, with aortic root aneurysm/dissection and ectopia lentis as cardinal features.[198] Criteria for the other HTAD entities are less well defined.

Gene panel testing is meaningful for confirmation of the diagnosis and to guide management. Mutation pick-up rate in syndromic forms is higher (>90%) than in non-syndromic entities (20−30%).[199] Once a pathogenic variant is identified, presymptomatic genetic screening of family members is mandatory to allow early and appropriate management.

- Echocardiographic assessment of the aortic root should include measurements at the annulus, sinus, sinotubular junction, distal ascending, arch, and descending thoracic aortic levels. In adults, measurement at end diastole using the leading-to-leading edge principle is recommended. The values obtained should be corrected for the individual's age, sex, and body size using standardized nomograms.[200,201] Valvular morphology (mitral valve prolapse, BAV) and function must be assessed, as well as the presence of a PDA. LV dimension and function should be addressed according to standard recommendations.
- CMR or CCT angiography from head to pelvis should be performed in every patient at baseline, providing imaging of the entire aorta and branching vessels. In addition to measuring aortic diameters, information on aortic/vertebral artery tortuosity is important for diagnostic and prognostic purposes.[202,203]
- Holter monitoring should be performed in symptomatic patients, as ventricular arrhythmias, conduction disturbances, and SCD can occur.

4.7.1.4 Medical therapy

Although no reduction in mortality or dissection rate has been established in any trial, beta blockers remain the mainstay for medical treatment in Marfan/HTAD patients, reducing wall shear stress and aortic growth rate.[204] Rigorous antihypertensive medical treatment aimed at a 24-h ambulatory systolic blood pressure <130 mmHg (110 mmHg in patients with aortic dissection) is important, although there are no data to establish outright blood pressure thresholds. ARBs did not prove to have a superior effect when compared with beta blockers or in addition to beta blockers in several trials, but may be considered as an alternative in patients intolerant to beta blockers.[205,206] Medical treatment should be continued after surgery.

Ongoing meta-analyses of medical treatment trials may help define subgroups — based on genetic and clinical data — who benefit from specific treatment.[207] Since no medical trials have been conducted in non-Marfan HTAD, medical treatment is usually adopted from Marfan data.

4.7.1.5 Surgical treatment

Indications for intervention are summarized in the Recommendations for aortic surgery in aortopathies table.

Prophylactic aortic root surgery is the only definitive treatment for the prevention of aortic dissection in Marfan syndrome and related HTADs. In patients with anatomically normal aortic valves and low-grade regurgitation, a valve-sparing aortic root replacement by a Dacron prosthesis and reimplantation of the coronary arteries into the prosthesis (David procedure) has become the preferred surgical procedure with good long-term outcome, including in Marfan patients.[193,208] Composite graft replacement, usually with a mechanical valve, is a more durable alternative but does require lifelong anticoagulation. The decision on which technique to use should be made on an individual basis, and patient preferences and surgical experience should be taken into account.[209]

Marfan and related HTADs are associated with a risk of re-dissection and recurrent aneurysm in the distal aorta, especially in patients with previous dissection.[210,211] With improved life expectancy, these complications now occur more frequently. Open aortic surgery remains the reference method for treatment of distal aortic disease, although hybrid procedures with endovascular stenting — where proximal and distal landing is possible in a Dacron tube — could be considered in selected cases.

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4.7.1.6 Follow-up recommendations

Lifelong and regular multidisciplinary follow-up at an expert centre is required. Echocardiography and CCT/CMR are the principal examinations.

4.7.1.7 Additional considerations

- Exercise/sports: patients should be advised to avoid exertion at maximal capacity, competitive, contact, and isometric sports. Risk estimation based on aortic size has been suggested by Budts *et al.*[24]
- Pregnancy: in genetically confirmed Marfan/HTAD, there is a 50% transmission risk for both men and women. Proper and timely genetic counselling is needed. Women with an aortic root diameter >45 mm are strongly discouraged from becoming pregnant without prior repair because of the increased risk of dissection.[43] An aortic root diameter <40 mm rarely presents a problem, although a completely safe diameter does not exist. With an aortic root 40–45 mm, previous aortic growth and family history are important factors when considering repair prior to pregnancy. After repair of the ascending aorta, Marfan patients remain at risk for dissection of the residual aorta (see *section 3.5.7*).
- IE prophylaxis: recommended only for high-risk patients (see *section 3.4.6*).

4.7.2 Bicuspid aortic disease

Depending on the reported series, 20–84% of patients with a BAV will develop ascending aortic dilatation,[212] indicating that BAV should be regarded as part of a spectrum of valvluo-aortopathy and that bicuspid aortic disease may be a more appropriate term. Although the relative contribution of intrinsic/genetic wall abnormalities and altered haemodynamics remains debated, both factors are probably involved.

In the absence of significant valvular dysfunction, aortic dilatation in the setting of bicuspid aortic disease typically evolves asymptomatically. With increasing diameters, however, the risk for acute aortic dissection rises. Compared with the general population, the dissection incidence in bicuspid aortic disease patients is eight times higher, which is in absolute numbers still a low risk (31/100 000 patient years)[172,176,213] and much lower than in Marfan/HTAD. Observational studies indicate that the clinical outcome in bicuspid aortic disease patients is more similar to that of the general population with aneurysms and represents a more benign aortopathy than Marfan/HTAD.[176,214]

CoA is associated with an increased risk for dissection.[215]

For diagnostic work-up see section *4.7.1.3*.

To this date, no evidence for medical treatment of aortic dilatation in the setting of bicuspid aortic disease is available, but it may be reasonable to consider beta blockers or ARBs as first-line treatment for arterial hypertension.

Indications for intervention are summarized in the *Recommendations for aortic surgery in aortopathies* table.

Familial occurrence of BAV has clearly been established with rates of 5–10% in first-degree relatives in various studies.[216] Echocardiographic screening in first-degree relatives of BAV patients is recommended and may be appropriate, particularly in boys, in athletes, and if hypertension is present. Rare pathogenic variants in a number of genes account for <5% of all bicuspid aortic disease cases and routine genetic testing in this setting is not indicated but may be considered in familial cases.[140]

There are no data on the risk for dissection related to pregnancy in women with a dilated aorta. According to the 2018 ESC Guidelines for the management of cardiovascular disease during pregnancy,[43] women should be counselled against pregnancy when the aortic diameter is >50 mm.

For treatment of AR, see 2017 ESC/EACTS Guidelines on the management of valvular heart disease.[25]

4.7.3 Turner syndrome

Turner syndrome is caused by a partial or complete monosomy of the X-chromosome and occurs in 1 in 2500 live-born females.[217] Turner syndrome is associated with short stature, delayed puberty, ovarian dysgenesis, hypergonadotropic hypogonadism, infertility, congenital malformations of the heart, diabetes mellitus, osteoporosis, and autoimmune disorders. CHD, occurring in approximately 50% of women with Turner syndrome, includes a high incidence of BAV, CoA, partial anomalous pulmonary venous connection, left SVC, elongated transverse aortic arch, dilatation of the brachiocephalic arteries, and aortic dilatation. Given this high prevalence of abnormalities, every woman with Turner syndrome should be seen by a cardiologist at least once.[217] Even in the absence of CHD, all individuals with Turner syndrome have a generalized arteriopathy and Turner syndrome alone is an independent risk factor for thoracic aortic dilation. Aortic dissection (both type A and type B) occurs in approximately 40 per 100 000 person-years compared with 6 per 100 000 person-years in the general population.[218]

For diagnostic work-up see section *4.7.1.3*.

Indications for intervention are summarized in the *Recommendations for aortic surgery in aortopathies* table.

With advances in assisted reproductive technology and oocyte donation, an increasing number of women with Turner syndrome are now able to become pregnant. The presence of aortic dilatation and CHD increases the risks of pregnancy and Turner syndrome women are also at increased risk of hypertensive disorders, including pre-eclampsia. All women with Turner syndrome should be counselled about the increased cardiovascular risk of pregnancy and fertility treatment.[43]

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Recommendations for aortic surgery in aortopathies

Recommendations	Class[a]	Level[b]
Marfan syndrome and HTAD		
Aortic valve repair, using the reimplantation or remodelling with aortic annuloplasty technique, is recommended in young patients with Marfan syndrome or related HTAD with aortic root dilation and tricuspid aortic valves, when performed by experienced surgeons.	I	C
Surgery is indicated in patients with Marfan syndrome who have aortic root disease with a maximal aortic sinus diameter ≥50 mm.[c]	I	C
Surgery should be considered in patients with Marfan syndrome who have aortic root disease with maximal aortic sinus diameter ≥45 mm[c] and additional risk factors.[d]	IIa	C
Surgery should be considered in patients with a *TGFBR1* or *TGFBR2* mutation (including Loeys–Dietz syndrome) who have aortic root disease with maximal aortic sinus diameter ≥45mm.[c]	IIa	C
Bicuspid aortic disease		
Aortic surgery should be considered if the ascending aorta is: • ≥50 mm in the presence of a bicuspid valve with additional risk factors[e] or coarctation. • ≥55 mm for all other patients.	IIa	C
Turner syndrome		
Elective surgery for aneurysms of the aortic root and/or ascending aorta should be considered for women with Turner syndrome who are >16 years of age, have an ascending aortic size index >25 mm/m^2, and have associated risk factors for aortic dissection.[f]	IIa	C
Elective surgery for aneurysms of the aortic root and/or ascending aorta may be considered for women with Turner syndrome who are >16 years of age, have an ascending aortic size index >25 mm/m^2, and do not have associated risk factors for aortic dissection.[f]	IIb	C

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AR = aortic regurgitation; BAV = bicuspid aortic valve; ECG = electrocardiogram; BSA = body surface area; CoA = coarctation of the aorta; HTAD = heritable thoracic aortic disease.
[a]Class of recommendation.
[b]Level of evidence.
[c]At the extreme ends of the BSA range, recommended cut-offs may require appropriate adjustment.
[d]Family history of aortic dissection at a low diameter (or personal history of spontaneous vascular dissection), progressive AR, desire for pregnancy, uncontrolled hypertension, and/or aortic size increase >3 mm/year (on repeated measurements using the same ECG-gated imaging technique measured at the same level of the aorta with side-by-side comparison and confirmed by another technique).
[e]Family history of dissection at a low diameter, desire for pregnancy, systemic hypertension, and/or size increase >3 mm/year (on repeated measurements using the same ECG-gated imaging technique, measured at the same level of the aorta with side-by-side comparison and confirmed by another technique).
[f]BAV, elongation of the transverse aorta, CoA, and/or hypertension.

4.8 Right ventricular outflow tract obstruction

4.8.1 Introduction and background

RVOTO can occur at the sub-infundibular, infundibular, valvular, or supravalvular levels.

- Sub-infundibular stenosis, or DCRV, is commonly associated with a VSD. It is caused by narrowing between prominent and hypertrophied muscle bands or ridges that separate the hypertrophied, high-pressure inlet and apical portions from a low-pressure, non-hypertrophied and non-obstructive infundibular portion of the RV.[219]
- Infundibular stenosis usually occurs in combination with other lesions, particularly VSD, TOF, and secondary to valvular pulmonary stenosis (PS) (reactive myocardial hypertrophy). At the infundibular level, and to some extent the sub-infundibular level, the obstruction tends to be dynamic, meaning that the orifice narrows during systole.
- Valvular PS is usually an isolated lesion. Mainly due to intrinsic wall abnormalities, and independent of haemodynamics, dilation of the PA may occur. Most often, there is a typical dome-shaped pulmonary valve with a narrow central opening but a preserved mobile valve base. A dysplastic pulmonary valve, with poorly mobile cusps and myxomatous thickening, is less common (15–20%; even less in untreated adults) and frequently part of Noonan syndrome. In adults, a stenotic pulmonary valve may calcify late in life.
- Supravalvular PS, or pulmonary arterial stenosis, is caused by narrowing of the main pulmonary trunk, pulmonary arterial bifurcation, or pulmonary branches. It seldom occurs in isolation, and may occur in Williams–Beuren syndrome, Noonan syndrome, congenital rubella syndrome, or Alagille syndrome. The stenosis may be located in the main branches or more peripherally; it may be discrete or diffuse (hypoplastic) or there may be frank occlusion, and it may occur as single or multiple stenoses. Stenosis may be secondary to previous placement of a PA band or at a previous shunt site. A diameter narrowing ≥50% is usually considered to be significant and would be expected to have a pressure gradient and result in hypertension in the proximal PA.

4.8.2 Clinical presentation and natural history

- Sub-infundibular/infundibular: adult patients with DCRV may be asymptomatic or they may present with dyspnoea, chest discomfort, dizziness, or syncope during exertion. The degree of obstruction is progressive over time.[220]
- Valvular: patients with mild-to-moderate valvular PS are usually asymptomatic. Mild valvular PS in unoperated adults is usually not progressive.[221] Moderate PS can progress at the valvular level (calcification) or at the subvalvular level due to reactive myocardial hypertrophy. Patients with severe stenosis may present with dyspnoea and reduced exercise capacity and have a worse prognosis.
- Supravalvular: patients may be asymptomatic or have symptoms of dyspnoea and reduced exercise capacity. They are usually recognized in the context of certain syndromes or in patients referred for suspicion of PH. Peripheral PA stenosis may progress in severity.

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4.8.3 Diagnostic work-up

See *section 3.3* for general principles.

Clinical findings include a harsh systolic murmur across the obstruction and wide splitting of the second heart sound. In peripheral PS, the systolic murmur is typically heard over the lung fields.

- Echocardiography: size, shape, and function of the RV can be assessed and the exact position/level of the RVOTO can be visualized, as well as pulmonary valve, main PA, and proximal PA branches. For quantification of RV sizes, volumes, and EF, CMR is a more robust and more reliable technique. Doppler ultrasound is used for measurements of flow velocities across an obstruction to assess severity. Correlation between flow velocities and pressure gradients is only good in the case of discrete stenosis, e.g. isolated valvular PS. In the presence of normal RV function and normal transvalvular flow, RVOTO is considered mild when the peak gradient across the obstruction is <36 mmHg, moderate if 36–64 mmHg, and severe when the gradient is >64 mmHg. If the narrowing is elongated, or if more than one stenosis is present in series (e.g. subvalvular and valvular), application of the Bernoulli equation will lead to an overestimation of the pressure gradient. Doppler flow velocity of TR then gives a more reliable estimation of RV pressures – and with that, severity of the RVOTO – than the flow velocity across the RVOTO. Gradients only represent severity of an obstruction if a good systolic RV function is present. In a low-flow, low-gradient situation, it is very difficult to assess severity of a RVOTO.[222]
- CMR and CCT frequently provide additional important information identifying the level(s) of obstruction, including at the subinfundibular (DCRV), conduit, or branch PA levels, and assessment of RV volumes, pulmonary annulus, outflow tract and artery dimensions, and differential pulmonary blood flow. CMR and CCT are the methods of choice for visualization of pulmonary dilation and peripheral PS.
- Cardiac catheterization may be required to confirm the extent, severity, and level of obstruction (e.g. DCRV).

4.8.4 Surgical/catheter interventional treatment

Catheter-based balloon valvotomy is recommended for patients with non-dysplastic valvular PS and with peripheral PS (often with stent implantation).[223] Surgery is recommended for patients with sub-infundibular or infundibular PS and hypoplastic pulmonary annulus, with dysplastic pulmonary valves, and for patients with associated lesions which need a surgical approach, such as severe pulmonary regurgitation (PR) or severe TR. Peripheral PS can rarely be addressed with surgery.

Both surgical and catheter interventions should only be performed in centres specialized in CHD.

In patients with subvalvular, valvular, and supravalvular PS, a markedly dilated pulmonary trunk may be present. Rupture is extremely rare in these low-pressure, highly elastic vessels and these pulmonary aneurysms generally do not require intervention.[224]

For RV–PA conduit, see *section 4.14*.

Indications for intervention are summarized in the *Recommendations for intervention in right ventricular outflow tract obstruction* table and in *Figure 7*.

Recommendations for intervention in right ventricular outflow tract obstruction

Recommendations	Class[a]	Level[b]
In valvular PS, balloon valvuloplasty is the intervention of choice, if anatomically suitable.	I	C
Provided that no valve replacement is required, RVOTO intervention at any level is recommended regardless of symptoms when the stenosis is severe (Doppler peak gradient is >64 mmHg[c]).	I	C
If surgical valve replacement is the only option, it is indicated in patients with severe stenosis who are symptomatic.[d]	I	C
If surgical valve replacement is the only option[d] in patients with severe stenosis who are asymptomatic, it is indicated in the presence of one or more of the following. • Objective decrease in exercise capacity. • Decreasing RV function and/or progression of TR to at least moderate. • RVSP >80 mmHg. • R–L shunting via an ASD or VSD.	I	C
Intervention in patients with a Doppler peak gradient <64 mmHg should be considered in the presence of one or more of the following. • Symptoms related to PS. • Decreasing RV function and/or progressive TR to at least moderate. • R–L shunting via an ASD or VSD.	IIa	C
Peripheral PS, regardless of symptoms, should be considered for catheter interventional treatment if >50% diameter narrowing, and RVSP >50 mmHg, and/or related reduced lung perfusion is present.	IIa	C

ASD = atrial septal defect; PS = pulmonary stenosis; R–L = right-to-left; RV = right ventricle/ventricular; RVOTO = right ventricular outflow tract obstruction; RVSP = right ventricular systolic pressure; TR = tricuspid regurgitation; VSD = ventricular septal defect.

[a]Class of recommendation.

[b]Level of evidence.

[c]RVSP estimated from TR velocity should confirm severe PS.

[d]The threshold for intervention is higher when a valve substitute is required because long-term risks, such as endocarditis and re-intervention for prosthetic valve failure, need to be taken into account.

4.8.5 Follow-up recommendations

Patients with RVOTO need lifelong follow-up with regular echocardiographic imaging. The frequency of follow-up depends on the severity of the lesion, but most patients will need a yearly visit, including evaluation in specialized ACHD centres except for patients with mild or well repaired valvular stenosis. After surgical or catheter intervention, a residual PR may need reintervention later in life for patients who become symptomatic or when progressive RV dilatation or dysfunction occurs (see *section 4.10*). Patients with mild valvular or mild residual PS need to be seen only once in 5 years.

4.8.6 Additional considerations

- Exercise/sports: no restrictions for patients with mild (residual) PS. Patients with moderate PS should avoid high-intensity and

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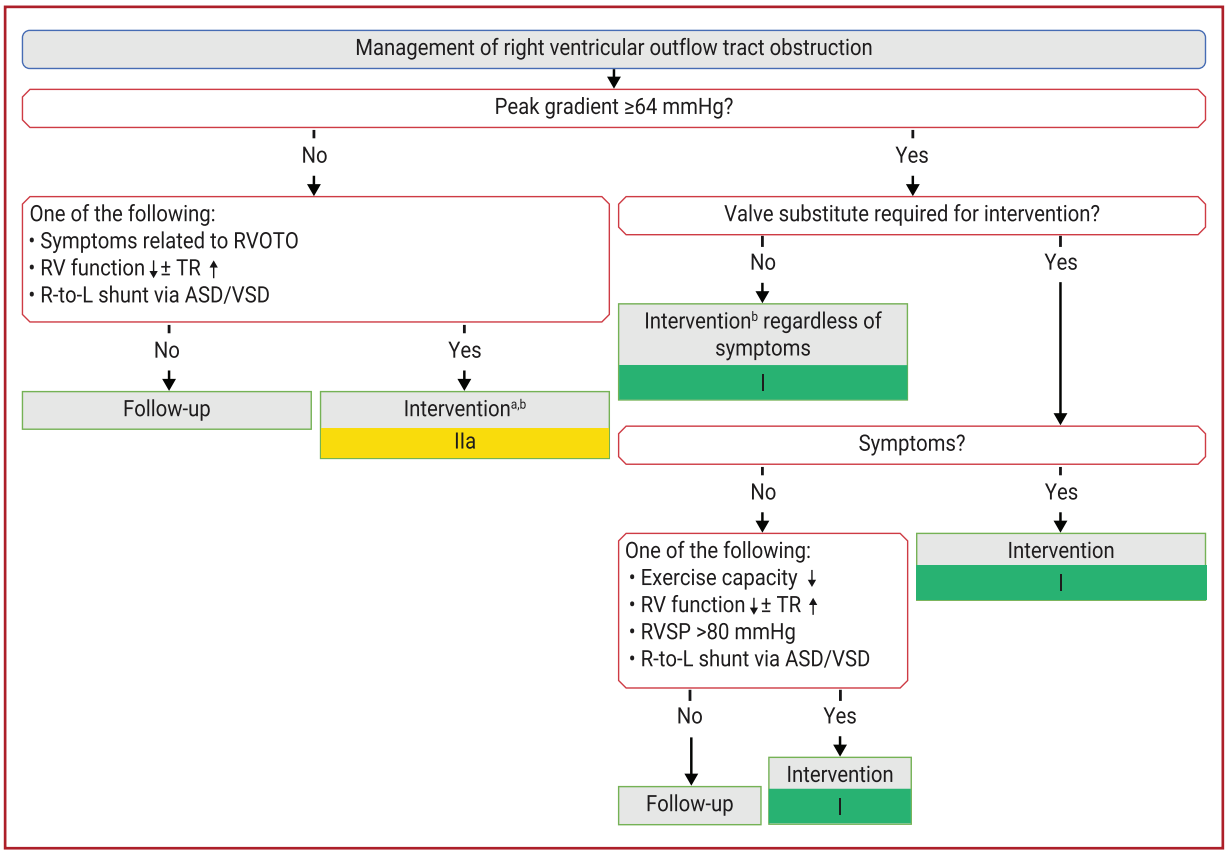


Figure 7 Management of right ventricular outflow tract obstruction.
ASD = atrial septal defect; PS = pulmonary stenosis; R–L = right-to-left; RV = right ventricle/ventricular; RVOTO = right ventricular outflow tract obstruction; RVSP = right ventricular systolic pressure; TR = tricuspid regurgitation; VSD = ventricular septal defect.
[a]In peripheral PS, regardless of symptoms, catheter interventional treatment should be considered if >50% diameter narrowing and RVSP >50 mmHg and/or related reduced lung perfusion is present.
[b]In valvular PS, balloon valvuloplasty is the intervention of choice if anatomically suitable.

static sports. Patients with severe PS should be restricted to low-intensity sports.

- Pregnancy: well tolerated unless the RVOTO is extremely severe or unless RV failure is a major issue. Transcatheter balloon valvotomy can be performed during pregnancy but is rarely necessary (see *section 3.5.7*).
- IE prophylaxis: recommended only for high-risk patients (see *section 3.4.6*).

4.9 Ebstein anomaly

4.9.1 Introduction and background

Ebstein anomaly is characterized by abnormally formed and apically displaced leaflets of the TV. The anterior leaflet usually originates at the annular level but is enlarged and sail-like, while the septal and posterior leaflets are displaced towards the RV apex and often tethered to the endocardium.

The apical displacement of the TV means that the right heart consists of a morphological RA, an atrialized portion of the RV, and the remaining functional RV; the TV is often regurgitant.

The most frequently associated anomalies include a shunt at the atrial level [secundum ASD or patent foramen ovale (PFO)] and (concealed) accessory pathways, including Mahaim-type pathways. Multiple accessory pathways in conjunction with AT and AF are associated with SCD. Ebstein-like anomaly of the systemic TV is present in one-third of ccTGA.

Haemodynamic changes depend on the severity of the TV dysfunction, the degree of atrialization of the RV, contractility of the remaining functional RV and the systemic ventricle, type and severity of concomitant anomalies, and arrhythmias.

The pathophysiology is characterized by systolic regurgitation of blood from the functional RV, across the TV, and into the atrialized ventricle or RA, which tend to dilate. An interatrial connection permits a L–R shunt or, especially during exercise, a R–L shunt. Ebstein anomaly may result in a chronically low systemic cardiac output.

4.9.2 Clinical presentation and natural history

The clinical presentation ranges from trivial symptoms to the presentation of a profound cyanotic heart defect. Patients with mild forms can be asymptomatic over decades until they are diagnosed. Typical complications include high-grade TR, RV dysfunction, RV failure, liver cirrhosis, cerebral abscesses, paradoxical embolism, pulmonary embolism, tachyarrhythmias, SCD, and IE. Key symptoms are arrhythmias [atrioventricular reentrant tachycardia (AVRT) is most

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common], dyspnoea, fatigue, poor exercise tolerance, chest pain, and peripheral and/or central cyanosis.

4.9.3 Diagnostic work-up

See *section 3.3* for general principles.

Clinical findings may include cyanosis and hepatomegaly. Auscultation findings include a widely split first sound and second sound, serial clicks, third and fourth sound, and a systolic murmur from TR. ECG may show RA hypertrophy, a prolonged PR interval, right bundle branch block (often with a splintered QRS complex), deep Q in II, III, aVF, and V1–V4, pre-excitation, low voltage, multiple pathways (AVRT), and supraventricular and ventricular arrhythmias.

- Chest X-ray is helpful to follow changes in the heart's size.
- Echocardiography provides information on: anatomy and function of the TV; apical distal displacement of the septal or posterior leaflet (in adults ≥0.8 cm/m^2 BSA); size of the anterior leaflet; tethering of the septal or posterior TV leaflet on the septum or ventricular wall; size and function of the different cardiac sections (RA, atrialized ventricle, remaining functional RV, and LV); and RVOTO and associated lesions.
- CMR has value with regards to prognostication[225], and for evaluation before and after surgery, as it offers unrestricted views for assessment and quantification of the dilated right heart, RV function, and TV function.

4.9.4 Surgical/catheter interventional treatment

Clinical symptoms determine the treatment. Conservative therapy can alleviate symptoms temporarily and create a beneficial basis for the following operation.[226] Oral anticoagulation is recommended for patients with a history of paradoxical embolism or AF. In the presence of an increased thromboembolic risk or a R–L shunt, oral anticoagulation may be considered. Symptomatic rhythm disorders can be treated conservatively or, preferably, with EP intervention.[227] Transcatheter access to right-sided accessory pathways and the slow pathway in AV node reentry may be hindered by TV surgery, such that it may be reasonable to assess for arrhythmia substrates and proceed with catheter ablation, if identified, before surgery. Occasionally, there may be an indication to close the atrial communication in isolation. However, this needs to be discussed carefully, as it may lead to a further increase in right heart pressures and a decrease in systemic cardiac output. Surgical repair remains challenging and should only be performed by surgeons with specific experience in this lesion. TV repair, if feasible, is preferred over TV replacement (with closure of an associated interatrial communication). If the RV is too small for repair or RV dysfunction has developed, an additional bidirectional cavopulmonary (Glenn) anastomosis may be considered in adults with preserved LV function when LA pressure and LV end diastolic pressure are not elevated.[228] In patients with failed repair, or in severe biventricular dysfunction, heart transplantation may be the only option.

The previously high operative mortality (>25%) has fallen to <6% in specialized centres. Over 90% of patients operated on by an experienced surgeon survive >10 years, many in functional class I or II. Late fatalities are probably due to arrhythmias. In a large series, survival free of late reoperation was 86%, 74%, 62%, and 46% at 5, 10, 15, and 20 years, respectively.[229]

Recommendations for intervention in Ebstein anomaly

Recommendations	Class[a]	Level[b]
Indications for surgery		
Surgical repair is recommended in patients with severe TR and symptoms or objective deterioration of exercise capacity.	I	C
It is recommended that surgical repair is performed by a congenital surgeon with specific experience in Ebstein surgery.	I	C
If there is an indication for TV surgery, ASD/PFO closure is recommended at the time of valve repair if it is expected to be haemodynamically tolerated.	I	C
Surgical repair should be considered regardless of symptoms in patients with progressive right heart dilation or reduction of RV systolic function.	IIa	C
Indications for catheter intervention		
In patients with symptomatic arrhythmias, or pre-excitation on the ECG, electrophysiologic testing followed by ablation therapy, if feasible, or surgical treatment of the arrhythmias in the case of planned heart surgery is recommended.	I	C
In the case of documented systemic embolism, probably caused by paradoxical embolism, isolated device closure of ASD/PFO should be considered but requires careful evaluation before intervention to exclude induction of RA pressure increase or fall in cardiac output.	IIa	C
If cyanosis (oxygen saturation at rest <90%) is the leading problem, isolated device closure of ASD/PFO may be considered but requires careful evaluation before intervention to exclude induction of RA pressure increase or fall in cardiac output.	IIb	C

ASD = atrial septal defect; ECG = electrocardiogram; PFO = patent foramen ovale; RA = right atrium/atrial; RV = right ventricle/ventricular; TR = tricuspid regurgitation; TV = tricuspid valve.
[a]Class of recommendation.
[b]Level of evidence.

4.9.5 Follow-up recommendations

Regular follow-up (at least yearly) is required in all patients in specialized ACHD centres. Typical post-operative residual anomalies to look for are persisting or new TR, the usual complications after valve replacement, failure of RV or LV, residual atrial shunts, arrhythmias, and higher-grade AV blocks.

Reintervention may become necessary for recurrent TR and failure of prosthetic valves.

4.9.6 Additional considerations

- Exercise/sports: patients without residual anomalies can usually lead normally active lives without restriction, except for extensive static

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sports. Patients with more than mild TR, ventricular dysfunction, shunting, arrhythmias, or other complications should avoid heavy isometric exercises, in proportion to the severity of their problems.
- Pregnancy: asymptomatic females with good ventricular function may tolerate pregnancy well. There is a certain risk of RV failure, arrhythmia, and paradoxical embolism. Pregnancy will be of higher risk in the presence of significant cyanosis, serious arrhythmia, and right heart failure (see *section 3.5.7*).
- IE prophylaxis: recommended only for high-risk patients (see *section 3.4.6*).

4.10 Tetralogy of Fallot

4.10.1 Introduction and background

TOF is characterized by the following four features: a non-restrictive VSD; overriding aorta (but <50%); infundibular, valvular, supravalvular RVOTO and/or branch PA stenosis; and consequent RV hypertrophy (RVH). TOF populations can be subdivided into syndromic patients (~20%, such as: microdeletion 22q11, trisomy 21, Alagille, Noonan, Williams, and Klippel Feil) and non-syndromic patients (which represent the vast majority).[230] The standardized mortality rate among patients with repaired TOF is almost twice as high as among patients with simple defects (ASD and VSD).[231]

4.10.2 Clinical presentation and natural history

Surgical repair of TOF has evolved over time, with relief of the RVOTO usually involving infundibulotomy, resection of obstructive muscle bundles, and the use of a patch to enlarge the pathway from the RV to the PAs. In some patients, a palliative shunt procedure – in order to increase pulmonary blood flow – has been performed before repair. Common complications in adulthood are:

- PR: significant PR is almost always encountered following a transannular patch repair. PR is usually well tolerated for years. Severe chronic PR, however, eventually leads to symptomatic RV dilation and dysfunction.[232] The severity of PR and its deleterious long-term effects are augmented by co-existing distal PA stenoses or PAH.
- Residual RVOTO can occur at the infundibulum, at the level of the pulmonary valve and main pulmonary trunk, and into the branches of the left and right PA. Elevated RV pressure and RVH have been described as independent risk factors for poor outcome and a decreased exercise performance, despite smaller RV volumes[233].
- Residual VSD can be due to partial patch dehiscence or failure of complete closure at the time of surgery; it may lead to LV volume overload.
- Aortic complications may occur many years after the initial surgical repair and include progressive aortic dilation and AR (rarely aortic dissection). The underlying mechanism is incompletely understood, and may include ascending aorta dilation, abnormal aortic elasticity, or type of surgical repair[234].
- RV and LV dysfunction/heart failure: RV dilation is usually due to residual longstanding free PR ± RVOTO. Significant TR may occur as a consequence of RV dilation, which begets more RV dilation. LV dilatation may result from longstanding palliative arterial shunts, residual VSDs, and/or AR. Both RV and LV dysfunction may be due to longstanding cyanosis before repair and/or inadequate myocardial protection during repair, adverse ventricular–ventricular interactions, electromechanical dyssynchrony,[235,236] and coronary artery abnormalities. A reduced LV free wall longitudinal strain has been reported despite preserved LVEF.[237] The incidence of clinical heart failure, with its typical signs and symptoms, increases significantly with age.[238] Underlying mechanisms may also be: damage to myocardium, sequelae from surgical repair strategies, or electrical conduction abnormalities. Management strategies effective in acquired heart disease are frequently applied in these patients, although its effectiveness for RV failure remains uncertain.[239]
- Atrial/ventricular arrhythmias and SCD: arrhythmias and sudden death are important late complications. The estimated lifetime prevalence of atrial arrhythmias is 20%. IART involving the cavotricuspid isthmus and RA incision are related to RA enlargement, whereas AF is facilitated by LA dilatation. Ventricular arrythmias encompass polymorphic VT/VF, typically related to severely impaired RV and LV function, and monomorphic sustained VT, which are particularly relevant in rTOF.[34] Although both polymorphic VT/VF and monomorphic VT can lead to SCD, with a reported frequency of 1–3.5% in retrospective studies,[32] the different underlying ventricular arrhythmia substrates need to be recognized for risk stratification and treatment. LV systolic or diastolic dysfunction, and ventricular and atrial tachyarrhythmias are predictive of death and sustained VT in adults with rTOF.[240] Possible risk factors associated with any ventricular arrhythmia and SCD in rTOF are QRS duration ≥180 ms, LV systolic or diastolic dysfunction, and inducible VT at EP testing. Older age at PVRep and pre-PVRep RVH and dysfunction may be predictive of shorter time to post-operative death and sustained ventricular arrhythmia.[241] The dominant substrates for monomorphic VT are anatomically defined isthmuses, bordered by unexcitable tissue. Isthmus dimension and conduction properties can be evaluated by catheter mapping and likely determine susceptibility to arrhythmias. Targeting the anatomical isthmuses by catheter ablation has been highly effective to control VT.[242] Whether catheter mapping can contribute to individualized risk stratification requires further investigation.
- Endocarditis can be encountered after both surgical and percutaneous PVRep. Valve-containing prosthetics are an important independent risk factor for IE in the short- and long-term after implantation, whereas non-valve-containing prosthetics are a risk factor only during the first 6 months after implantation.[76]

A schematic overview of long-term complications after repair of TOF is provided in *Figure 8*.

4.10.3 Diagnostic work-up of repaired patients

See *section 3.3* for general principles.

- Clinical findings mostly include a wide split in the second heart sound. A low-pitched early ending diastolic murmur suggests severe PR. A long, loud ejection systolic murmur indicates RVOTO, a high-pitched diastolic murmur indicates AR, and a pansystolic murmur indicates a residual VSD.

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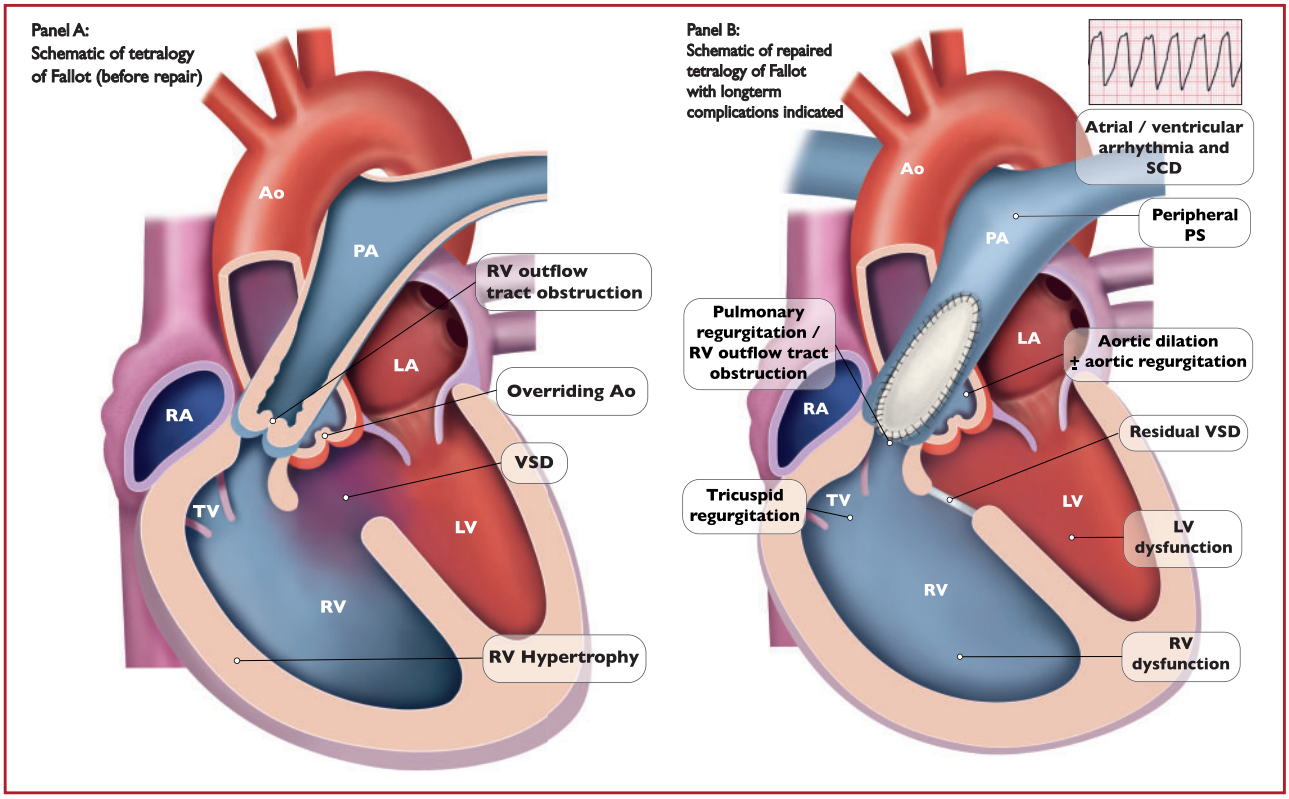


Figure 8 Management of repaired tetralogy of Fallot: long-term complications to address during follow-up.
Ao = aorta; LV = left ventricle; RV = right ventricle; PA = Pulmonary artery; TV = tricuspid valve; RA = right atrium; RV = right ventricular; LA = left atrium; PA = pulmonary artery; PS = pulmonary stenosis; SCD = sudden cardiac death; VSD = ventricular septal defect.

- ECG often shows complete right bundle branch block dependent on the surgical approach. The QRS width may also be influenced by the degree of RV dilation.
- Echocardiography provides assessment of residual RVOTO and PR, residual VSD, RV and LV size and function,[241] TR, RV pressure, aortic root size, and AR. Strain measurements are helpful in quantifying the degree of electromechanical dyssychrony.[243]
- CMR is the method of choice for assessment of RV volume and function; PR; size, shape, and expansion of the PAs; infundibulum; the ascending aorta; the position of great vessels or conduits in relation to the sternum (resternotomy); and evaluation for residual shunt (Qp:Qs). Late gadolinium enhancement demonstrates fibrosis, the extent of which relates to other risk factors for VT and SCD.[244] T1 mapping may have an emerging role.
- CCT provides information on coronary arteries (particularly important for the assessment of the spatial relationship with the RVOT prior to TPVI or surgery), the extent of conduit calcification (percutaneous valve anchoring), and the presence of major aortic pulmonary collaterals (MAPCAs). CCT may also be considered as an alternative for RV quantification in patients unable to undergo CMR.
- CPET assists timing of reintervention and provides prognostic information.[23]
- Holter monitoring, event recorder, and EP evaluation are required for selected patients (high risk, suspected or clinical arrhythmia, and/or before RVOT reoperation). Inducible sustained VT carries prognostic value for clinical VT and SCD.[245]
- Cardiac catheterization should be restricted to patients undergoing catheter-based interventions (i.e. relief of distal PA stenosis, transcatheter valve implantation) and when non-invasive evaluation is inconclusive. Before surgery, coronary angiography may visualize the coronary arteries, which is important to assess the spatial relationship with the RVOT prior to TPVI.

4.10.4 Late surgical/catheter interventional treatment

PVRep and/or relief of RVOTO can be performed with low mortality risk in patients without heart failure and/or advanced ventricular dysfunction.[246] PR is the most frequent reason for consideration of surgery. Optimal timing remains challenging. Longitudinal data are more important than single measurements to assist timing for reintervention.[247] Normalization of RV size after reintervention becomes unlikely as soon as the end systolic index exceeds 80 mL/m^2 and the end diastolic volume index exceeds 160 mL/m^2,[248–250] but this cut-off for reintervention may not correlate with clinical benefit. A recent meta-analysis demonstrated that PVRep can improve symptoms and reduce RV volume, but a survival benefit still needs to be shown.[251]

Distal PA stenosis must be addressed, either at the time of surgery (including intra-operative stenting) or with a percutaneous approach. A biological pulmonary valve (xenograft or homograft) seems to have a mean lifespan of 10–20 years,[248,252,253] and future replacement could be performed by transcatheter valve-in-valve

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procedures. There is little experience with mechanical valves in this setting and there is concern about adequate anticoagulation.

Indications for TV annuloplasty, closure of residual VSDs, and/or aortic root dilation/AR surgery should also be addressed at the time of surgery. The indication for aortic root surgery does not differ from the general population.[254]

TPVI techniques have become an alternative to open heart surgery primarily in patients with RVOT conduit stenosis/regurgitation, but also in selected patients with native RVOT regurgitation/stenosis. TPVI, when technically feasible, provides outcomes comparable to surgical PVRep and is intended to extend the lifetime of a conduit, hence reducing the number of reoperations during a patient's lifetime.[255] Stent fracture – the initially most common complication – has become less of a problem with careful preparation of the 'landing zone' using additional stents. Best long-term results were reported when a residual gradient of <15 mmHg could be achieved.[256] Uncommon complications, occurring in <2% of patients, include conduit rupture and coronary artery compression. The risk of endocarditis after TPVI remains a concern with an annual incidence rate of 2–3%.[257,258] Since coronary artery compression may be life-threatening, a balloon test to exclude potential coronary artery compression must be performed prior to TPVI, although this test carries a risk for conduit rupture. In case of severe circumscript conduit calcification, TPVI should only be performed if a CCT scan shows sufficient distance between the conduit and the coronary arteries. The strong link between slowly conducting anatomical isthmuses and sustained monomorphic VT, and the potential loss of accessibility to the anatomical isthmus by catheter ablation after surgical PVRep or after transcutaneous insertion of valves in patch augmented RVOTs, has important implications for patients who undergo reinterventions.[259] Whether pre-interventional mapping and preventive ablation of slowly conducting anatomical isthmuses before or during intervention in patients *without* documented spontaneous sustained VT is beneficial is under investigation.

Recommendations for intervention after repair of tetralogy of Fallot

Recommendations	Class[a]	Level[b]
PVRep is recommended in symptomatic patients with severe PR[c] and/or at least moderate RVOTO.[d]	I	C
In patients with no native outflow tract,[e] catheter intervention (TPVI) should be preferred if anatomically feasible.	I	C
PVRep should be considered in asymptomatic patients with severe PR and/or RVOTO when one of the following criteria is present. • Decrease in objective exercise capacity. • Progressive RV dilation to RVESVi ≥80 mL/m^2, and/or RVEDVi ≥160 mL/m^2 [f], and/or progression of TR to at least moderate. • Progressive RV systolic dysfunction. • RVOTO with RVSP >80 mmHg.	IIa	C
VSD closure should be considered in patients with residual VSD and significant LV volume overload or if the patient is undergoing pulmonary valve surgery.	IIa	C
In patients with sustained VT who are undergoing surgical PVRep or transcutaneous valve insertion, pre-operative catheter mapping and transsection of VT-related anatomical isthmuses before or during the intervention should be considered.	IIa	C
Electrophysiologic evaluation, including programmed electrical stimulation, should be considered for risk stratification for SCD in patients with additional risk factors (LV/RV dysfunction; non-sustained, symptomatic VT; QRS duration ≥180 ms, extensive RV scarring on CMR).	IIa	C
ICD implantation should be considered in selected TOF patients with multiple risk factors for SCD, including LV dysfunction, non-sustained, symptomatic VT, QRS duration ≥180 ms, extensive RV scarring on CMR, or inducible VT at programmed electrical stimulation.	IIa	C
Catheter ablation or concomitant surgical ablation for symptomatic monomorphic sustained VT may be considered in those with a preserved biventricular function as an alternative to ICD therapy, provided that the procedure is performed in highly experienced centres and that established ablation endpoints have been reached (e.g. non-inducibility, conduction block across ablation lines).	IIb	C

CMR = cardiovascular magnetic resonance; ICD = implantable cardioverter defibrillator; LV = left ventricle/ventricular; PR = pulmonary regurgitation; PVRep = pulmonary valve replacement; RV = right ventricle/ventricular; RVESVi = right ventricular end systolic volume indexed; RVEDVi = right ventricular end diastolic volume indexed; RVOT = right ventricular outflow tract; RVOTO = right ventricular outflow tract obstruction; RVSP = right ventricular systolic pressure; SCD = sudden cardiac death; TOF = tetralogy of Fallot; TPVI = transcatheter pulmonary valve implantation; TR = tricuspid regurgitation; VSD = ventricular septal defect; VT = ventricular tachycardia.
[a]Class of recommendation.
[b]Level of evidence.
[c]Regurgitant fraction by CMR >30–40%.
[d]Peak velocity >3 m/s.
[e]Patients with previous RVOT surgery using homografts, bovine jugular vein grafts, bioprostheses/conduits.
[f]Confirmed by repeated measurements.

4.10.5 Indications for electrophysiological testing and implantable cardioverter defibrillator

An ICD should be implanted for secondary prevention of SCD (patients with cardiac arrest or sustained VT) (IC recommendation). ICD implantation for primary prevention remains controversial, and no ideal risk stratification scheme has so far been developed. Patients with unexplained syncope and impaired ventricular function or other risk factors for SCD should undergo haemodynamic and EP evaluation. In the absence of a reversible cause, ICD implantation should be considered (see *section 3.4.2*).[260,261]

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4.10.6 Follow-up recommendations

All patients with TOF should have periodic cardiac follow-up in a specialized ACHD centre, which — in most patients — should be done annually. Follow-up evaluation needs to look for the complications listed in *section 4.10.2*. All patients should have CMR at regular intervals, dependent on the pathology found.

4.10.7 Additional considerations

- Exercise/sports: there are no restrictions in asymptomatic repaired patients with good haemodynamics. Patients at high risk for clinical arrhythmia/SCD, patients with advanced biventricular dysfunction, and patients with marked ascending aortopathy should be limited to low-intensity activity/sports and avoid isometric exercise.
- Pregnancy: in unrepaired patients constitutes a considerable risk of maternal and foetal complications and death. The risk of pregnancy in repaired patients depends on their haemodynamic status (low in patients with good haemodynamics). In patients with significant residual lesions, there is a risk of arrhythmia and right heart failure. Pregnancy is unlikely to have an adverse long-term effect on cardiovascular function[262] (see *section 3.5.7*).
- IE prophylaxis: recommended only for high-risk patients (see *section 3.4.6*).

4.11 Pulmonary atresia with ventricular septal defect

4.11.1 Introduction and background

Adult patients with pulmonary atresia with VSD are a heterogeneous population in terms of underlying anatomy, physiology, and previous interventions. Pulmonary atresia + VSD patients share the intracardiac anatomy of TOF but lack a direct communication between the RV and PAs. Microdeletion 22q11.2 is common (facial anomalies, nasal speech, and developmental delay).[263] PA supply varies in pulmonary atresia + VSD, and determines both clinical presentation and management (the complexity of the pulmonary vascular bed may make repair unattractive or impossible).

Patients with discordant cardiac connections and/or a single ventricle physiology and their management will be discussed in the appropriate sections.

There are three patterns of PAs:

- Unifocal with confluent, good-sized PAs supplied by a PDA.
- Multifocal, with confluent but hypoplastic PAs ('seagull' appearance) supplied by multiple MAPCAs.
- Multifocal with non-confluent or absent PAs supplied by MAPCAs.

Surgical management is a heavily debated topic due to the lack of consensus on the optimal treatment.

Patients with confluent, good-sized PAs and a pulmonary trunk (usually with valvular atresia) are suitable for a Fallot-like repair using a transannular patch. Patients with good-sized PAs but without a pulmonary trunk should undergo repair with a RV—PA conduit. Patients with confluent but hypoplastic PAs often require an arterial shunt or reconstruction of the RVOT (without VSD closure), which may enhance PA growth, and then be reviewed at a later stage for repair using a valved conduit. Patients with non-confluent PAs with adequate, but not excessive, pulmonary blood flow in infancy can survive into adulthood without surgery. There are proponents of a staged unifocalization approach for this latter challenging group of infants, ultimately aiming for a conduit repair.[264]

4.11.2 Clinical presentation and natural history

At adult age, clinical presentation for repaired patients is similar to those with TOF (see *sections 4.10* and *4.14*). Unrepaired patients present with exertional dyspnoea, fatigue, and progressive chronic cyanosis, due to decreased pulmonary blood flow from collateral stenosis, PA stenosis, increased PVR, or increasing ventricular end diastolic pressures.[265] Cyanosis will eventually lead to multiorgan involvement (see *section 3.4.8*). A number of complications may occur in unrepaired patients:

- Haemoptysis may be due to rupture of usually small collateral vessels and/or small PA thrombosis.
- Chronic heart failure is usually multifactorial and may be due to chronic cyanosis, early excessive pulmonary blood flow, increased PVR, RV dysfunction, AR, and other causes.
- Progressive dilation of the ascending aorta with increasing AR (rarely aortic dissection).
- Endocarditis can be particularly compromising in patients with limited cardiovascular reserve and those with significant cyanosis.
- Arrhythmia and SCD are not uncommon.
- Segmental PAH.[46]

4.11.3 Diagnostic work-up

See *section 3.3* for general principles.

- Clinical findings: cyanosis in unrepaired patients may be profound, even with minimal physical effort. Continuous murmurs at the back suggest MAPCAs. ECG findings include right-axis deviation and RVH. Chest X-ray may show a boot-shaped cardiac contour ('empty PA bay') with abnormal, decreased pulmonary vascularity (alternating with some areas of increased vascularity through large MAPCAs).
- Echocardiography: findings in repaired patients depend on the type of repair (see *sections 4.10* and *4.14*). For unrepaired patients, absence of direct flow from the RV to PA, with continuous flow on multiple sites on colour Doppler from the MAPCAs, may be seen. 3D echocardiography can further aid in delineating anatomic pathology and biventricular size and function. TOE is useful in certain patients to evaluate valve anatomy when transthoracic imaging is challenging or when IE is suspected.[266]
- CMR, CCT, and cardiac catheterization are required to determine sources of pulmonary blood supply and size of PAs, to assess MAPCAs, and obtain haemodynamics. In repaired patients, CMR is used for requirements similar to patients with TOF [for RV volumes and function, PR, size, shape, and expansion of the PAs, and the size of the ascending aorta, and for residual shunt (Qp:Qs)]. 3D rotational angiography and 3D overlay imaging, as

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well as X-ray and magnetic resonance imaging fusion, aid in precision assessment.[267]

4.11.4 Surgical/catheter interventional treatment

For follow-up and intervention in patients with Fallot-like repair with transannular patch, see *section 4.10*; for patients with repair using a valved RV–PA conduit, see *section 4.14*.

Patients with pulmonary atresia + VSD surviving unrepaired to adulthood, or with previous palliative procedures, may actually benefit from modern surgical or interventional procedures.[268,269] Patients with good-sized confluent PAs and those with large MAPCAs anatomically suitable for unifocalization, who have not developed severe PVD due to protecting stenosis, should be considered for surgery. Many unrepaired patients may, however, not be suitable for further surgery, mainly because of the complexity of their pulmonary vasculature. It is important to appreciate that while cardiac surgery may improve clinical status or prognosis (the latter is purely speculative), it is also a major cause of mortality.

Catheter intervention may include balloon dilation/stenting of collateral vessels to enhance pulmonary blood flow.[270] On the other hand, patients with severe haemoptysis may require coiling of ruptured collateral vessels.

Survival depends on the complexity of the pulmonary malformations and the results of surgical repair. Survival in palliated patients is significantly lower and has been reported as 60% at 20-year follow-up. Heart-lung transplantation could possibly be an option for highly selected individuals.

4.11.5 Follow-up recommendations

Patients with pulmonary atresia + VSD should have periodic follow-up in a specialized ACHD centre (at least once a year). For the management of cyanosis-related multiorgan involvement, see *section 3.4.8*.

Patients with segmental PAH may be considered for targeted PAH therapy; see *section 3.4.3*.[271,272]

Symptoms such as dyspnoea, increasing cyanosis, change in the shunt murmur, heart failure, or arrhythmias warrant special attention and should necessitate an earlier review and assessment for intervention.

4.11.6 Additional considerations

- Exercise/sports: those with excellent haemodynamics should be encouraged to exercise regularly, avoiding only extreme isometric exercise. Those with less optimal haemodynamics will be more functionally limited. Extremes of exertion should be avoided, but regular low-intensity physical activity (walking, swimming, even cycling) should be encouraged.
- Pregnancy: the risk of pregnancy in repaired patients with good haemodynamics and no history of arrhythmias is low. The risk increases with hypoxaemia, PAH, ventricular dysfunction, heart failure symptoms, and arrhythmias (see *section 3.5.7*). As microdeletion 22q11 is fairly common with this defect, patients should be checked before pregnancy.
- IE prophylaxis: recommended only for high-risk patients (including all unrepaired patients; see *section 3.4.6*).

4.12 Transposition of the great arteries

4.12.1 Introduction and background

TGA is characterized by AV concordance and ventriculo-arterial discordance: the aorta originates from the RV, the PA from the LV. TGA is called simple in the absence of associated congenital anomalies; TGA is called complex in the presence of associated anomalies: VSD (~45%), LVOTO (~25%), and CoA (~5%). Long-term outcome of complex TGA is, regardless of the type of surgical repair, worse than that of simple TGA.

The aetiology of TGA is unknown and the pathogenesis is controversial. Familial occurrence exists but is very rare. There is a 2:1 male preponderance.

Natural history is extremely poor and survival to adult life without surgical repair is the exception. Surgical techniques have evolved: atrial switch transitioned to arterial switch procedure, and complex TGAs are often operated upon using a Rastelli-type repair.

A schematic overview of surgical techniques and their long-term complications in TGA is provided in *Figure 9*.

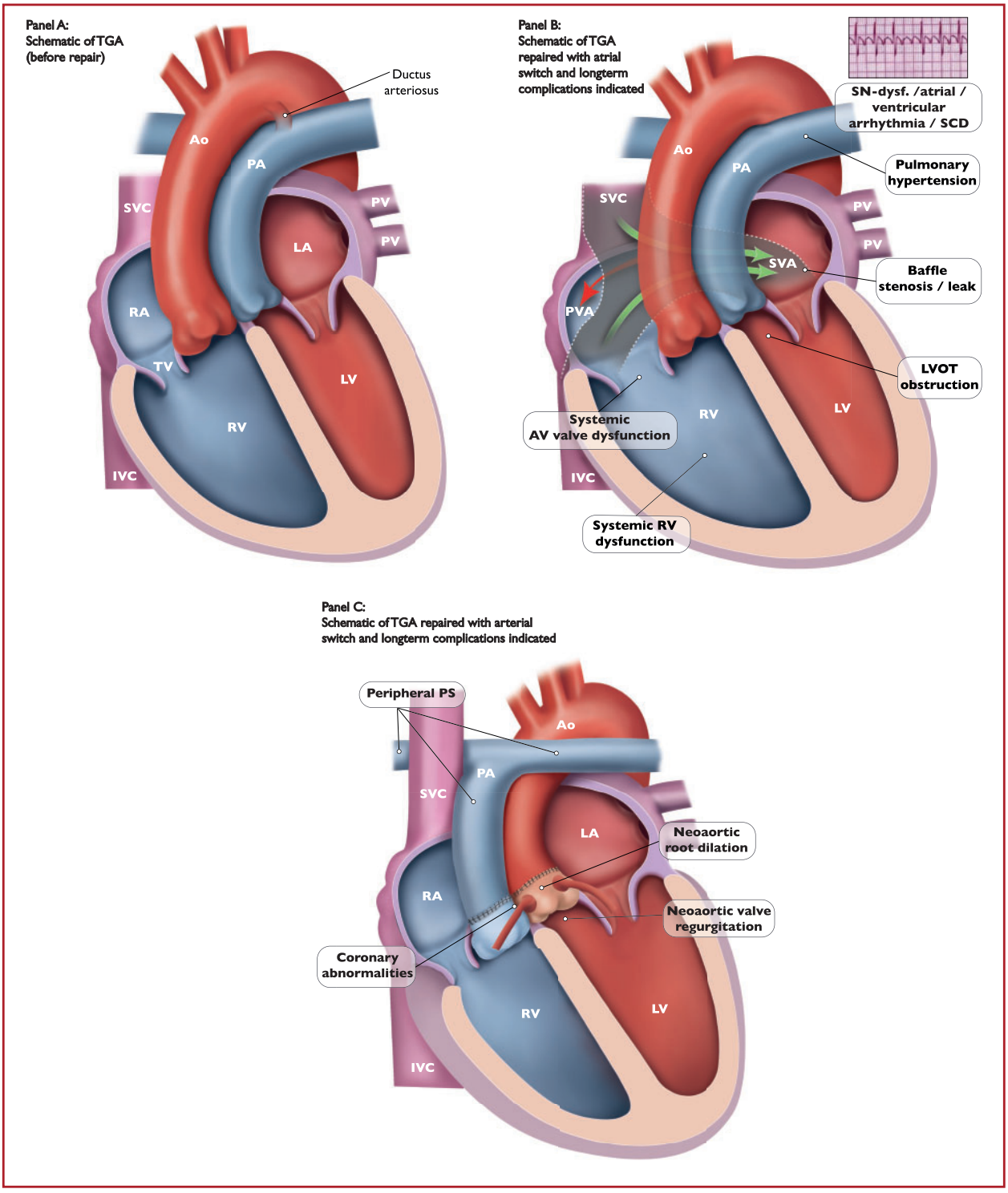
4.12.2 Atrial switch operation

4.12.2.1 Clinical presentation after atrial switch

Older adults with a simple TGA have a Mustard or Senning atrial switch procedure. The most common complications are:

- Systemic RV dysfunction and failure.
- Secondary progressive TR (systemic AV valve).
- Bradycardia and chronotropic incompetence due to loss of sinus rhythm; AV conduction is usually intact.
- Supraventricular tachyarrhythmia, typically cavotricuspid isthmus-dependent flutter, followed by macro-reentry circuit related to surgical incisions/scars; AF may occur at older age. High heart rates are often haemodynamically poorly tolerated because of the inability to increase preload, a consequence of the (restrictive) atrial baffles. Bradycardia due to SND can promote AT.
- Ventricular tachyarrhythmias: primary polymorphic VT or VF due to poor ventricular function and heart failure-related mechanism, or monomorphic VT due to scar/incision/patch-related reentry in repaired complex TGA; secondary VT or VF, preceded by supraventricular tachycardia (SVT) with rapid conduction and consecutive myocardial ischaemia due to the very low stroke volume associated with the SVT.
- Baffle stenosis, either superior baffle (most common) or inferior baffle obstruction.
- Baffle leakage, with either L–R shunt giving rise to pulmonary overflow or R–L shunting in the presence of distal flow obstruction, with cyanosis or paradoxical embolism.
- Pulmonary veins/venous atrial obstruction, most often at the site where the pulmonary veins connect to the pulmonary venous atrium/RA.

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Figure 9 Management of transposition of the great arteries: long-term complications to address during follow-up.
Ao = aorta; AV = atrioventricular; IVC = inferior caval vein; LA = left atrium; LV = left ventricle; LVOT = left ventricular (subpulmonary) outflow tract; PS = pulmonary stenosis (supravalvular/pulmonary artery branch); PV = pulmonary vein; PVA = pulmonary venous atrium; RA = right atrium; RV = right ventricle; SCD = sudden cardiac death; SN-dysf. = sinus node dysfunction; SVA = systemic venous atrium; SVC = superior vena cava; TV = tricuspid valve.

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- LVOTO can develop due to bulging of the interventricular septum towards the low-pressure subpulmonic LV, frequently associated with systolic anterior motion of the mitral valve.
- PH can become manifest, sometimes decades after the atrial switch procedure; it is usually post-capillary[273] but PAH may be present too.
- Death due to heart failure or sudden death, probably caused by arrhythmia.

In larger series with follow-up of up to 40 years, survival is 60–75%.[274,275] Event-free survival is as low as 20%.[276,277] Exercise capacity is usually reduced by inadequate increase in cardiac output: chronotropic incompetence, reduced preload resulting from the relatively narrowed and/or non-compliant baffles – inherent to the atrial switch operation – and diminished RV function.

4.12.2.2 Diagnostic work-up

See section 3.3 *for general principles.*

Clinical evaluation must include looking for signs of venous congestion. A swollen head and neck are a sign of superior baffle obstruction. Oedema of the legs, varices, hepatomegaly, and liver cirrhosis are seen in inferior baffle obstruction. Stenosis, even complete obstruction, can be asymptomatic due to an effective bypass circulation provided by the azygos or hemiazygos vein.

An ejection-type systolic murmur suggests subpulmonary outflow tract obstruction, and a systolic regurgitant-type murmur suggests regurgitation of the systemic TV. ECG findings include RVH and, not uncommonly, narrow QRS escape rhythm, without visible P waves.

- Echocardiography is the first-line diagnostic modality, providing information on size and systolic function of the subpulmonic and systemic ventricles, subpulmonary outflow tract obstruction, TR, leakage or obstruction of the atrial baffles, and assessment of pulmonary venous return. Signs of PH are often subtle – decreased flattening of the interventricular septum in systole and an abnormally wide PA – and can be difficult to recognize. Suspicion of PH dictates diagnostic heart catheterization to exclude/confirm PH as it may impact management. Contrast echocardiography can demonstrate baffle leakage – present in up to 50% in non-selected and asymptomatic patients – or baffle obstruction.[278] Injection of contrast into the upper limbs frequently misses a leak in the inferior systemic venous baffle; this can only be excluded by injection into one of the femoral veins. TOE is useful for evaluation of baffles.
- CMR provides more reliable and more robust quantitative assessment of systemic RV systolic function than echocardiography, and of patency of the atrial baffles. Size of the great arteries can be measured reliably; an abnormally wide PA and/or large subpulmonary LV may indicate PH. Shunt related to baffle leak can be quantified (Qp:Qs). Small baffle leaks not leading to a relevant shunt are difficult to detect with CMR (contrast echocardiography is superior). Late gadolinium enhancement in the systemic RV predicts clinical outcome.[279]
- Exclusion of superior baffle stenosis or baffle leak (and treatment) is essential before PM/ICD implantation or placing new/additional pacemaker wires through the superior baffle. An alternative to CMR and CCT for assessment of the superior baffle is contrast injection in the right arm and fluoroscopy.
- CPET is important in longitudinal follow-up for serial assessment of exercise capacity and chronotropic incompetence. It also can 'unmask' baffle leakage (desaturation) that is asymptomatic at rest.
- Holter monitoring, event recorder, and EP testing are indicated for selected patients if bradycardia and/or tachyarrhythmias are suspected.
- Cardiac catheterization is indicated when non-invasive assessment is inconclusive or when suspicion of PH requires evaluation (see *section 3.3.5*).

4.12.2.3 Medical treatment

- Systemic RV systolic dysfunction: there are no data to support the hypothesis that ACE inhibitors, ARBs, beta blockers, or aldosterone antagonists – alone or in combination – improve outcome.[280] No solid recommendation can currently be made.
- Systemic RV failure: in the case of overt heart failure, diuretics relieve symptoms. Although no benefit has been demonstrated for conventional heart failure medical therapy in patients with systemic RVs, more symptomatic patients may benefit from prescription of 'classical' heart failure medication.
- Arrhythmia: drugs that lower heart rate should be used with caution, since after atrial switch, patients are prone to bradycardia and SND.
- PH: the exact mechanism of PH must be elucidated before consideration of medical treatment. Post-capillary PH late after atrial switch operation seems to be most common, with the consequence that specific pulmonary vasodilator therapy is contraindicated but pre-capillary PH may be present, too. Thus, careful haemodynamic evaluation is crucial.

4.12.2.4 Surgical/catheter interventional treatment

Electrophysiology testing, ablation, cardiac resynchronization therapy, and implantable cardioverter defibrillators.

General principles, also valid for patients with the atrial switch procedure, are discussed in *section 3.4.2*.[32,37]

- EP studies and interventions are complicated because baffles interfere with normal access to the atria. The dominant mechanism of supraventricular arrhythmias is cavotricuspid isthmus atrial flutter, often requiring baffle puncture to achieve isthmus block. Alternatively, remote magnetic navigation can be used for retrograde access to the pulmonary venous atrium. Conventional retrograde transaortic route access in adults is usually not successful to achieve isthmus block. TOE guidance is recommended when puncture of a baffle is indicated. Programmed electrical stimulation for risk stratification is not useful.
- Pacemakers: see *section 3.4.2*.

Indications for intervention are summarized in the *Recommendations for surgical and catheter intervention in TGA after atrial switch operation* table.

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Recommendations for intervention in transposition of the great arteries after atrial switch operation

Recommendations	Class[a]	Level[b]
Indications for surgical intervention		
In *symptomatic* patients with pulmonary venous atrium obstruction, surgical repair (catheter intervention rarely possible) is recommended.	I	C
In *symptomatic* patients with baffle stenosis not amenable to catheter intervention, surgical repair is recommended.	I	C
In *symptomatic* patients with baffle leaks not amenable to catheter-based closure, surgical repair is recommended.	I	C
In patients with severe systemic (tricuspid) AV valve regurgitation, without significant ventricular systolic dysfunction (EF >40%), valve repair or replacement should be considered, *regardless of symptoms*.	IIa	C
PA banding in adults, as LV training with subsequent arterial switch procedure, is not recommended.	III	C
Indications for catheter intervention		
In *symptomatic* patients with baffle stenosis, stenting is recommended when technically feasible.	I	C
In *symptomatic* patients with baffle leaks and cyanosis at rest or during exercise, or with strong suspicion of paradoxical emboli, stenting (covered) or device closure is recommended when technically feasible.	I	C
In patients with baffle leaks and symptoms due to L–R shunt, stenting (covered) or device closure is recommended when technically feasible.	I	C
In *asymptomatic* patients with baffle leaks with substantial ventricular volume overload due to L–R shunt, stenting (covered) or device closure should be considered when technically feasible.	IIa	C
In patients with a baffle leak who require a PM/ICD, closure of the baffle leak with a covered stent should be considered, when technically feasible, prior to insertion of transvenous leads.	IIa	C
In *asymptomatic* patients with baffle stenosis, stenting may be considered when technically feasible.	IIb	C

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AV = atrioventricular; EF = ejection fraction; ICD = implantable cardioverter defibrillator; L–R = left-to-right; LV = left ventricle/ventricular; PA = pulmonary artery; PM = pacemaker.
[a]Class of recommendation.
[b]Level of evidence.

4.12.3 Arterial switch operation

4.12.3.1 Clinical presentation after arterial switch

Young adults with a simple TGA will probably have had an arterial switch operation. The most common complications are:

- Neo-aortic root dilatation, resulting in AR.
- Supravalvular PS and pulmonary branch stenosis (unilaterally or bilaterally), a consequence of the position of the pulmonary bifurcation anterior to the ascending aorta in the Lecompte technique and the dilatation of the neo-aortic root.
- LV dysfunction and ventricular arrhythmias are rare but may occur; both may be related to problems with the coronary arteries,[281] which were reimplanted in the neo-aorta.
- Acute angle of the aortic arch, which may lead to functional obstruction and hypertension.

Survival up to 30 years is excellent (>90% of hospital survivors[282]) and event-free survival is fair (60–80%[283–285]). A large majority of these patients are asymptomatic. As a rule, exercise capacity is mildly reduced, but it can be normal. The incidence of late coronary artery-related problems is reported to be very low,[286,287] which makes it questionable whether routine screening of coronary arteries is justified.

4.12.3.2 Diagnostic work-up

See section 3.3 *for general principles. Clinical findings of AR or PS may be present.*

- Echocardiography is the key diagnostic modality, providing information on LV function (global and regional); stenosis at the arterial anastomotic sites, most commonly PS; neo-aortic valve regurgitation; dimension of the neo-aortic root and proximal ascending aorta; and the acute angulation of the aortic arch. RV systolic function can be assessed and, if possible, peak RV systolic pressure (RVSP) should be measured (TR velocity). Due to its position: far anteriorly and just behind the sternum, echocardiographic visualization of the bifurcation and both branches is rarely possible.
- Stress echocardiography is used to assess stress-induced wall-motion abnormalities.
- CMR provides more reliable quantitative assessment of ventricular volumes, EF, and neo-aortic dilatation or regurgitation. Pulmonary trunk and branches can be visualized, together with their relation to the (dilated) neo-aortic root. Flow distribution between left and right lung can be calculated. Stress CMR is an alternative technique to assess myocardial perfusion and possible coronary artery compromise, where clinically indicated.
- CCT is the preferred technique for non-invasive imaging of coronary arteries, including the ostia, when stenosis is suspected. The reported low incidence of coronary-related problems makes it questionable whether routine screening for coronary artery pathologies (with whatever modality) can be justified.[286,287]
- Nuclear techniques are no longer used as first-choice imaging modality but may still have a role if other techniques are not available or lead to inconclusive or contradictory results.
- Cardiac catheterization, including coronary angiography, is indicated in the case of LV dysfunction and suspicion of myocardial ischaemia. In the case of severe pulmonary branch stenosis and

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inconclusive non-invasive assessment or suspected PAH, cardiac catheterization is indicated.

4.12.3.3 Surgical/catheter interventional treatment

Indications for intervention are summarized in the *Recommendations for interventions in TGA after arterial switch operation* table.

Recommendations for intervention in transposition of the great arteries after arterial switch operation

Recommendations	Class[a]	Level[b]
Stenting or surgery (depending on substrate) is recommended for coronary artery stenosis causing ischaemia.	I	C
Neo-aortic root surgery should be considered when the neo-aortic root is >55 mm, providing average adult stature (for neo-aortic valve replacement for severe neo-aortic AR see valvular heart disease guidelines with special considerations[c]).	IIa	C
Stenting should be considered for PA branch stenosis, regardless of symptoms, if >50% diameter narrowing and RVSP >50 mmHg and/or related reduced lung perfusion are present.	IIa	C

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AR = aortic regurgitation; ESC = European Society of Cardiology; PA = pulmonary artery; RVSP = right ventricular systolic pressure.
[a]Class of recommendation.
[b]Level of evidence.
[c]When applying the 2017 ESC/EACTS valvular heart disease Guidelines[25] for the decision to operate, it has to be taken into account that this is a reoperation and technically more difficult.

RVOTO can be subvalvular, valvular (both rare), or supravalvular (most common). Indications for treatment are similar to those described in *section 4.8*, but different anatomies may require different approaches.

4.12.4 Rastelli-type operation

4.12.4.1 Clinical presentation after Rastelli-type repair

Adults with TGA, VSD, and PS (complex transposition) have often had a Rastelli-type repair. The VSD patch directs blood from the LV to the aorta and the RV is connected to the PA with a valved conduit. Variants of the Rastelli technique, sharing the same principle, are the réparation à l'etage ventriculaire and Nikaidoh techniques.

Common complications are:

- Stenosis or regurgitation of the valved conduit between the RV and the PA.
- LVOTO, i.e. obstruction of the flow from the LV to the aorta.
- Residual VSD.
- AR.
- LV dysfunction.
- Arrhythmias, both ventricular and supraventricular.
- Endocarditis of the valved conduit.
- Death, either sudden (arrhythmia) or due to heart failure.

The few long-term outcome studies report 20-year survival <60% and 20-year event-free survival 20–30%. Replacement of the conduit between the RV and PA is the most common indication for reoperation. Relief of LVOTO is the second most common, followed by closure of a residual VSD.[288] Endocarditis of the valved conduit is relatively common.

Exercise capacity is mildly to substantially diminished. Repeat reintervention, surgical or percutaneous, is the fate of most patients with a Rastelli-type repair.

4.12.4.2 Diagnostic work-up

See *section 3.3* for general principles.

Clinical findings may suggest conduit stenosis, residual VSD, TR, mitral regurgitation, or AR.

- Echocardiography: the connection between the posteriorly positioned LV and the anteriorly positioned (due to the TGA) aortic valve, aortic valve function, and aortic root diameters should be assessed. The anatomy and function of the conduit between the RV and the pulmonary trunk must be visualized and assessed with Doppler interrogation. RV pressure assessed with Doppler measurement of TR jet velocity is of particular importance because the Doppler technique often overestimates the pressure gradient across the RV–PA conduit.
- CMR provides a more robust quantification of LV and RV volumes, aortic diameters, and EF. The RV–PA conduit, often difficult to visualize by echocardiogram, and peripheral PAs can be readily seen and measured with CMR. In the presence of a residual VSD, Qp:Qs can be calculated.
- Cardiac catheterization may be required for haemodynamic assessment of conduit stenosis. Angiography can be helpful for assessing the level of stenosis and peripheral PA stenosis.

4.12.4.3 Surgical/catheter interventional treatment

For indications for treatment of conduit stenosis, see *section 4.14*.

If L–R shunting through a residual VSD causes symptoms or substantial LV volume overload, surgical/catheter treatment should be performed (IC recommendation).

4.12.5 Follow-up recommendations (irrespective of type of repair)

All patients with TGA, regardless of the type of operation, should be seen at least annually in a specialized ACHD centre, with attention given to the specific issues previously described (*see sections 4.12.2.1, 4.12.3.1 and 4.12.4.1*).

4.12.6 Additional considerations (irrespective of type of repair)

- Exercise/pregnancy/IE prophylaxis: see *sections 3.4.6, 3.5.5* and *3.5.7*.

4.13 Congenitally corrected transposition of the great arteries

4.13.1 Introduction and background

ccTGA, or discordant atrio-ventricular and ventriculo-arterial connections, is uncommon. The ventricles are inverted, with the aorta arising anteriorly from the RV (usually on the left side) and the PA arising posteriorly from the LV (usually on the right side). The abnormal connections in 'double' discordance may be present in hearts

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with usual or mirror-image atrial arrangement. Abnormal base-apex orientation, especially dextrocardia (apex of the heart pointed to the right), is common (20%). Associated lesions are common (80–90%): VSD (70%), PS (40%), dysplastic systemic TV (e.g. Ebstein-like malformation).

The position of the AV node (sometimes multiple AV nodes), and the course of the bundle of His, are often abnormal and lead to AV conduction abnormalities. The anterior and lateral displacement of a fragile His bundle is important to recognize during EP studies and catheter interventions.

4.13.2 Clinical presentation and natural history

The natural history and clinical presentation are determined by associated malformations. Patients with associated lesions reaching adulthood have either been operated upon [closure of VSD, relief of PS or (rarely) TV repair or replacement] or have a balanced physiology. Patients with isolated ccTGA rarely develop complications before adulthood.

Late complications are:

- Systemic RV dysfunction and failure.
- Progressive TR (systemic AV valve).
- LVOTO.
- Complete AV block (2% loss of AV conduction per year); it is more common after VSD repair and/or TV replacement and may occur during pregnancy.
- VTs (extremely rare).

Life expectancy is reduced: ~50% of patients with associated lesions were alive at the age of 40 years; without associated lesions, ~50% of patients were alive at the age of 60 years. Patients die from congestive heart failure or die suddenly, presumably due to VT/VF, regardless of the presence of advanced heart failure.

4.13.3 Diagnostic work-up

See *section 3.3* for general principles.

- Clinical findings may include murmurs of TR, VSD, and/or PS.
- ECG may reveal a prolonged PR interval or a complete heart block. Early septal activation from right to left may cause deep Q waves in II, III, aVF, and V1–V3. Reversal of the normal precordial progression may be seen as a QR pattern in V1 and rS in V6. Wolff–Parkinson–White syndrome is present in 2–4% of patients.
- Chest X-ray may show an abnormally straight left heart border due to the leftward and anterior position of the ascending aorta, dextroposition with apex to the right (20%), or mesocardia (relatively common).
- Echocardiography is the key diagnostic modality, demonstrating double discordance and identifying associated anomalies (Ebstein-like malformation of the TV and TR, VSD, LVOTO, and PS). Systolic RV and LV function and severity of TR can be qualitatively assessed.
- CMR provides intracardiac and great vessel anatomy and is indicated for quantification of ventricular volumes, mass, and EF, especially since echocardiographic assessment of systolic function in systemic RVs is difficult and less reliable.
- Holter monitoring, event recorder, and EP testing may be indicated for detection of arrhythmias, progressive AV block, and for risk assessment for SCD.
- Cardiac catheterization is indicated when non-invasive assessment is inconclusive, or PH requires evaluation (see *section 3.4.5*).

4.13.4 Medical treatment

There are no data to support the hypothesis that ACE inhibitors, ARBs, beta blockers or aldosterone antagonists, alone or in combination, improve outcome.[280] Routine prescription of these medications to prevent heart failure/improve outcome is not recommended.

- Diuretics may provide relief of symptoms if overt heart failure is present. Although there is no proven benefit from heart failure medical therapy, in terms of outcome in patients with systemic RVs, 'classical' heart failure medications or ARBs may provide some benefit in more symptomatic patients.[289] A systemic RV morphology is not a contraindication for a ventricular assist device. The coarse trabecularization of the RV apex may deserve special consideration, since it may block the inflow cannula. Selective myomectomy should be considered.

4.13.5 Surgical/catheter interventional treatment

Catheter intervention may be recommended for PA stenosis or conduit stenosis, which can be dilated or stented. However, a residual LVOTO may have a beneficial effect on the dilated subaortic RV and subaortic AV (tricuspid) valve regurgitation because of the septal shift. If complete heart block occurs, AV sequential pacing is the standard. Fixation of the pacemaker wire in the smooth-walled LV is difficult and requires a screw-in electrode. There are some data suggesting that biventricular pacing with a second ventricular wire through the (normally connecting) coronary sinus behind the subaortic RV may lead to a better preservation of RV systolic function than LV pacing alone.[290]

Recommendations for intervention in congenitally corrected transposition of the great arteries

Recommendations	Class[a]	Level[b]
In *symptomatic* patients with severe TR and preserved or mildly impaired systemic RV systolic function (EF >40%), TV replacement is indicated.	I	C
In *asymptomatic* patients with severe TR and progressive systemic RV dilatation and/or mildly impaired systemic RV systolic function (EF >40%), TV replacement should be considered.	IIa	C
Biventricular pacing should be considered in case of complete AV block or >40% ventricular pacing requirement.	IIa	C
In *symptomatic* patients with severe TR and more than mildly reduced systemic RV systolic function (EF ≤40%), TV replacement may be considered.	IIb	C

AV = atrioventricular; EF = ejection fraction; RV = right ventricle/ventricular; TR = tricuspid regurgitation; TV = tricuspid valve.
[a]Class of recommendation.
[b]Level of evidence.

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The most challenging questions are TR, RV dysfunction, and when to implant a TV and/or an ICD. In contrast to the situation in the paediatric age group, in which double switch is an established treatment option in case of systemic RV failure, this approach is very rarely successful in adults.

Systemic AV valve (tricuspid) regurgitation is frequently the focus of surgical treatment. Repair is rarely feasible and, as a rule, valve replacement is the treatment of choice. Pre-operative systemic RVEF ≤40%, PAP >50 mmHg, AF, and New York Heart Association (NYHA) class III to IV are associated with late mortality.[291]

4.13.6 Follow-up recommendations

Patients with ccTGA need lifelong follow-up in a specialized ACHD centre at annual intervals, particularly because of conduction disturbances and subaortic ventricular and subaortic AV valve dysfunction. For arrhythmias, see *section 3.4.2*.

4.13.7 Additional considerations

- Exercise/sports: symptomatic patients with ccTGA and preserved RVEF should avoid high-intensity sports and preferably not do more than moderate-static and moderate-intensity sports. Patients with significant associated lesions and/or decreased subaortic RV function should be restricted to low-static and low-intensity sports.
- Pregnancy: risk depends on functional status, ventricular function, systemic AV valve function, presence of arrhythmias (especially AV block), and associated lesions (see *section 3.5.7*).

4.14 Right ventricular to pulmonary artery conduit

4.14.1 Introduction and background

Conduits establish the continuity between the RV and the PA in complex defects when the native outflow tract is not amenable to reconstruction, including pulmonary atresia, common arterial trunk, TOF, absent pulmonary valve syndrome, Rastelli procedure, and Ross operation.

Types of conduits include valved [pulmonary or aortic homograft, bioprosthetic valves, bovine jugular vein conduits (Contegra)] and non-valved conduits. There is no ideal conduit. Limited durability implicates early reoperation. Predictors for conduit failure are sterilization/preservation process, smaller conduit, conduit type, younger age at implantation, PA stenosis, and diagnosis of transposition.[269,292,293] Freedom from reoperation for conduit failure at 20 years was reported at 32% and 40%.[269,292]

Complications include outgrowth, progressive obstruction with and without regurgitation, endocarditis, and aneurysms or pseudoaneurysms.

Clinical presentation may include exertional dyspnoea, palpitations, syncope, and SCD.

4.14.2 Diagnostic work-up

See *section 3.3* for general principles.

Clinical findings may include a precordial thrill, prominent A wave of the jugular veins, and systolic murmur. Conduit calcification may be seen on chest X-ray.

- Echocardiography is the first-line diagnostic tool providing size, shape, and function of both ventricles, PR, TR, and associated lesions. Gradients across the conduit may be difficult to measure and unreliable. RV pressure derived from TR velocity should be used to assess conduit stenoses.
- CMR is used to quantify conduit stenosis and/or regurgitation, RV volumes and mass, and to assess PAs.
- CMR/CCT is helpful for coronary artery anatomy and proximity of the RV/conduit, and other structures to the retro sternum.
- Catheterization with haemodynamic assessment is always required if intervention is considered. Angiography provides information on the level of stenosis, peripheral PA stenoses, and coronary anatomy (anomalies/abnormal course).

4.14.3 Surgical/catheter interventional treatment

Balloon dilation/stent implantation have been reported to be safe and to prolong the lifespan of failing conduits.[294,295] Percutaneous pulmonary valve implantation has now become the treatment of choice for dysfunctional valves, if technically feasible. Current exclusions for TPVI include occluded systemic veins, active infection, unsuitable outflow tract morphology, and unfavourable coronary anatomy (compression by the expanded implant). Surgery is preferred when additional interventions are considered (tricuspid annuloplasty). Longitudinal data are more important for timing of reintervention than single measurements.

Recommendations for intervention in right ventricular to pulmonary artery conduits

Recommendations	Class[a]	Level[b]
Symptomatic patients with RVSP >60 mmHg (may be lower in case of reduced flow) and/or severe PR[c] should undergo intervention with preference for catheter intervention (TPVI) if anatomically feasible.	I	C
Asymptomatic patients with severe RVOTO and/or severe PR should be considered for intervention, preferably catheter intervention (TPVI) if anatomically feasible, when at least one of the following criteria is present: • Decrease in objective exercise capacity (CPET). • Progressive RV dilation to RVESVi ≥80 mL/m^2, and/or RVEDVi ≥160 mL/m^2, and/or progression of TR to at least moderate. • Progressive RV systolic dysfunction. • RVSP >80 mmHg.	IIa	C

CPET = cardiopulmonary exercise testing; CMR = cardiovascular magnetic resonance; PR = pulmonary regurgitation; RV = right ventricle/ventricular; RVEDVi = right ventricular end diastolic volume indexed; RVESVi = right ventricular end systolic volume indexed; RVOTO = right ventricular outflow tract obstruction; RVSP = right ventricular systolic pressure; TPVI = transcatheter pulmonary valve implantation; TR = tricuspid regurgitation.
[a]Class of recommendation.
[b]Level of evidence.
[c]Regurgitant fraction by CMR >30–40%.

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4.14.4 Follow-up recommendations

Regular follow-up in a specialized ACHD centre at least every year is recommended. Special attention should be given to exercise capacity (CPET), RVSP (conduit gradient), RV function, TR, and arrhythmias.

4.14.5 Additional considerations

- Exercise/sports: no restrictions are required in asymptomatic patients with mild obstruction. High-risk patients with high RV pressure must limit themselves to low-intensity activity/sports and avoid isometric exercise. Other patients should limit themselves according to symptoms.
- Pregnancy: maternal and foetal risks are driven by the underlying congenital heart defect and severity of RVOTO, arrhythmia, and heart failure (see *section 3.5.7*).
- IE prophylaxis: recommended in all patients (see *section 3.4.6*).

4.15 Univentricular heart

This section deals with unoperated and palliated univentricular heart (UVH). For patients after Fontan operation see *section 4.16*.

4.15.1 Introduction and background

The term 'UVH' summarizes a variety of malformations where either the RV or LV is missing or, if present, is hypoplastic and thus not amenable for biventricular repair, such as:

- Tricuspid atresia.
- Hypoplastic right heart syndrome variants, e.g. pulmonary atresia with intact ventricular septum variants.
- Hypoplastic left heart syndrome (HLHS) variants, including mitral atresia.
- Double-inlet LV.
- Double-inlet RV.
- Extreme forms of unbalanced complete AV septal defects.
- Single ventricle with undefined morphology.

These malformations are always associated with additional intra- and/or extracardiac lesions such as:

- ASD, VSD, AVSD, PDA.
- AS (valvular, subvalvular).
- Aortic arch anomalies: hypoplasia, interruption, coarctation.
- PS (valvular, subvalvular), pulmonary atresia.
- PA anomalies: peripheral stenosis, hypoplasia, one-sided absence.
- Discordant connections, malposition of the great arteries.
- AV valve stenosis, regurgitation, overriding, straddling.
- LA or RA isomerism, abnormal systemic or pulmonary venous connections.
- Left SVC, absent innominate vein, absent right SVC, absent infrahepatic IVC with azygos or hemiazygos continuity.
- Aortic-to-pulmonary collateral arteries.
- Polysplenia or asplenia.

Detailed anatomic description is beyond the scope of these guidelines and can be found in textbooks. Owing to the lack of data, recommendations are mainly based on expert consensus.[296–300] When presenting as adults, the vast majority of patients with these conditions will have undergone previous palliation with some type of systemic-to-PA shunt, cavopulmonary connection (Glenn), or now preferably a Fontan operation or one of its modifications; the latter is covered in *section 4.16*.

Two different haemodynamic situations can be identified:

- No anatomic restriction to pulmonary blood flow: if pulmonary circulation remains unmodified (i.e. no surgery), many patients will die in childhood due to intractable heart failure. Those who survive this period will have developed severe PVD. This will be a main determinant of long-term outcome. Many will have had pulmonary banding to restrict pulmonary blood flow in early childhood. An effective banding will protect against PVD, while allowing enough pulmonary blood flow to limit the degree of cyanosis. A banding that is too loose will result in pulmonary overflow and PVD despite the banding. If the banding is too tight, pulmonary blood flow will be extremely limited, resulting in severe cyanosis.
- Obstruction to pulmonary blood flow (frequently valvular and/or subvalvular PS or atresia): sometimes the obstruction is such that the pulmonary circulation is adequate (not excessive, thus avoiding development of PH, and not too restricted, thus without extreme cyanosis). These balanced situations are the exception but allow survival into adulthood without having surgery. Most patients have a very restricted pulmonary blood flow, necessitating a systemic-to-PA shunt operation in childhood – most commonly Blalock–Taussig (subclavian to PA), rarely Waterston or Potts (ascending or descending aorta to PA, respectively). If a systemic-to-PA shunt is too large, pulmonary overflow will result in PVD at adult age. If the shunt is too small, patients will be extremely cyanotic. Beyond infancy, an anastomosis between the SVC and PA is a possibility: the classical Glenn anastomosis to the right PA (historical) or an end-to-side anastomosis with the PA, creating a bidirectional cavopulmonary anastomosis. An adequate shunt will lead to a balanced situation.

4.15.2 Clinical presentation and natural history

Depending on the extent of pulmonary blood flow, presence or absence of PVD, and ventricular function, patients may present with various degrees of cyanosis and congestive heart failure. Exercise ability is generally substantially reduced (with exceptions); complete AV block, arrhythmias (supraventricular, but also ventricular, SCD not unusual), stroke, brain abscess, and thromboembolism can occur. Endocarditis is relatively common in this population. For more details, see *section 3.4.8*.

Cyanosis is typically present in patients with UVH without a Fontan operation. Arterial oxygen saturation commonly ranges from 75–85% but may, in exceptional cases with ideally balanced circulations, reach values >90%.

Patients may present with progressive obstruction towards the aorta. This will lead to ventricular hypertrophy and, eventually, to reduced cardiac output. Progressive obstruction towards the PA will cause progressive cyanosis. In Glenn patients, worsening cyanosis may also be due to development of pulmonary arteriovenous malformations or IVC-to-SVC collaterals.

The UVH has to accommodate both systemic and pulmonary venous return. This chronic volume overload will lead to a high likelihood of ventricular failure relatively early in life. AV valve regurgitation may develop or progress, if present previously. The already

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diminished exercise capacity will deteriorate further. Eventually, overt heart failure may develop, in addition to the cyanosis.

In rare cases, with a well-balanced haemodynamic situation, ventricular dysfunction does not develop, and survival until the fifth, sixth, and even seventh decade has been reported.

4.15.3 Diagnostic work-up

See *section 3.3* for general principles.

Clinical findings include central cyanosis, clubbing of fingers and toes, and often an asymmetric chest with a precordial heave at the side where the heart lies in the chest. Scoliosis is a common problem. The second heart sound is typically single, but the rest of the auscultation depends on the associated abnormalities. ECG may reveal rhythm or conduction disturbances. Atrial reentrant tachycardia with 2:1 block and only modest tachycardia may be easily overlooked.

- TTE is the key diagnostic technique, providing information on anatomy and monitoring of cardiac function during follow-up. The segmental approach is required in the echocardiographic examination; UVHs are always complex and can present with a wide range of abnormalities in situs, orientation, and connections.
  Fundamental TTE parameters/issues/items in the diagnosis of UVHs are:
  - Abdominal and atrial situs.
  - Position of the heart in the chest and position of the apex.
  - Veno-atrial, AV, and ventriculo-arterial connections.
  - Morphological and haemodynamic information has to be obtained on the entire heart.
  - Exact anatomy of the ventriculo-arterial connection and its functional status has to be assessed, with special focus on obstruction towards the aorta or pulmonary vascular bed.
  - AV valve function should be evaluated, with special focus on regurgitation.
  - Ventricular function/hypertrophy.
  - ASD/VSD type, size, number, location.
  - Ascending aorta, aortic arch, and descending aorta; detect/exclude coarctation.
  - PAs – common trunk, branches, and sources of pulmonary blood supply.
  - Visualization of shunts (Blalock–Taussig, Waterston, etc.).

  TOE may be indicated in cases of inadequate TTE images.
- CMR is the imaging modality of choice for extracardiac anatomy, including veno-atrial and ventriculo-arterial connections (CCT is an alternative). Detailed morphological information of intracardiac anatomy can also be obtained. CMR is also the method of choice for quantification of ventricular volumes, EF, and relative distribution of blood flow in the left and right lungs.
- Cardiac catheterization is required when intervention is considered for haemodynamic assessment, in particular PAP and transpulmonary gradient (PVR is often difficult to assess in this setting). It is mandatory when patients are evaluated for a Fontan operation. Evaluation of systemic-to-PA or Glenn shunts – and their sequelae (stenosis of the pulmonary branches) and other vascular anomalies (arteriovenous collateral vessels, fistulas, etc.) – may also require catheterization.

Special considerations and recommendations for intervention in univentricular heart

Recommendations	Class[a]	Level[b]
It is recommended that adults with unoperated or palliated UVHs undergo careful evaluation in specialized centres, including multimodality imaging as well as invasive work-up to decide whether they may benefit from surgical or interventional procedures.	I	C
Only well-selected symptomatic cyanotic patients, after careful evaluation [low pulmonary vascular resistances, adequate function of the AV valve(s), preserved ventricular function], should be considered candidates for a Fontan circulation.	IIa	C
Patients with increased pulmonary blood flow – unlikely at adult age – should be considered for PA banding or tightening of a previously placed band.	IIa	C
Patients with severe cyanosis and decreased pulmonary blood flow, but without elevated PVR or PAP, should be considered for a bidirectional Glenn shunt.	IIa	C
Patients with severe cyanosis and decreased pulmonary blood flow not suitable for a Glenn shunt may be considered for a systemic-to-PA shunt.	IIb	C
Heart transplantation and heart-lung transplantation should be considered when there is no conventional surgical option in patients with poor clinical status.	IIa	C

AV = atrioventricular; PA = pulmonary artery; PAP = pulmonary artery pressure; PVR = pulmonary vascular resistance; UVH = univentricular heart.
[a]Class of recommendation.
[b]Level of evidence.

Interventional treatment, such as pulmonary valvotomy to increase pulmonary blood flow in cases of severe PS, is debatable.

If the clinical situation is stable, the (frequently high) risk of any type of surgical intervention should be weighed very carefully against the possible benefit.

A Fontan operation can only be considered in very well selected patients (see *section 4.16*). For patients with severe cyanosis, with decreased pulmonary blood flow without elevated PVR, a bidirectional Glenn shunt (SVC-to-PA) can be an option. If a systemic-to-pulmonary shunt (e.g. arteriovenous axillary fistula or systemic artery pulmonary shunt) is the only option (bidirectional Glenn shunt not sufficient or PAP not low enough for this shunt), the benefit of increased pulmonary blood flow should be weighed against increased volume load to the systemic ventricle.

For transplantation, previous sternotomies/thoracotomies, aorto-pulmonary collaterals, and the multisystem nature of cyanotic CHD are technical and medical challenges and limit the outcome.

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4.15.4 Conservative management

See *sections 3.4.3* and *3.4.8* for haematological management and the role of targeted therapy in PVD.

4.15.5 Follow-up recommendations

Regular evaluation is required in a specialized ACHD centre.

Frequency is individualized, but at least yearly, with physical examination, measurement of oxygen saturation, laboratory tests (haematological indices, iron status, liver function, kidney function, etc.), ECG, X-ray, and echocardiography (see also *section 3.4.8*).

CMR and an exercise test are required at least once at adult age and at further intervals timed according to baseline findings.

4.15.6 Additional considerations

- Exercise/sports: as a rule, patients do not have an elevated risk of death during exercise, but they do have a substantially reduced exercise capacity. Recreational sports can be considered at a symptom-limited level.
- Pregnancy: contraindicated in patients with severely reduced pulmonary blood flow or with severe PVD, or if ventricular function is poor. Cyanosis poses a significant risk to the foetus, with a live birth unlikely (<12%) if oxygen saturation is <85%[106] (see *section 3.5.7*).
- For contraception, a combined oral contraceptive pill must be avoided because of the risk of thrombogenicity and thromboembolism. Progestogen-only pills and progestogen-eluting intrauterine devices or implantation systems provide safe contraception with a smaller cardiovascular risk.
- IE prophylaxis: indicated in all patients (see *section 3.4.6*).

4.16 Patients after Fontan operation

4.16.1 Introduction and background

The Fontan operation was introduced in 1968 and has become the definitive treatment for suitable patients with a range of cardiac malformations characterized by a single functional ventricle (see *section 4.15*). Surgery consists of the separation of the systemic and pulmonary venous returns without a subpulmonary ventricle and restores them to being 'in series'. Since its introduction, a number of modifications have been made to the original procedure, designed to streamline the systemic venous return to the PAs. Currently, the total cavopulmonary connection has replaced the atriopulmonary connection (RA appendage to PA), with either an intracardiac or extracardiac conduit between the IVC and the PA, together with an SVC-to-PA anastomosis (bidirectional Glenn).[301] This circulation is frequently established in two stages. Adults with HLHS remain a small but expanding group of patients. The first data in adulthood describe a considerable prevalence of major adverse cardiovascular events and it appears that HLHS patients are more prone to complications than general Fontan patients, warranting closer follow-up and assessment.[302]

The natural history and outcome of other palliations for hearts with a 'single ventricle' are poor, so that the Fontan is usually undertaken in all patients in whom the haemodynamics are suitable. It is now appreciated that the operative mortality and subsequent outcome depend on the suitability of the circulation and adherence to defined criteria. Strict selection gives the best early and late results, with operative mortality of <5% in modern series and includes low PVR and PAP (mean <15 mmHg), preserved ventricular function, adequate PA size, no relevant AV valve regurgitation, and normal rhythm. A 'fenestration' has been performed in selected or all cases by some centres to allow for shunting of deoxygenated blood to the systemic circulation at atrial level, aiming to improve the cardiac output at the expense of cyanosis.[303] Fontan operation, when considered late in adults, is not always the palliation of choice because of the limited long-term outcome.

4.16.2 Clinical presentation and natural history

The lack of a subpulmonary ventricle results in chronic systemic venous hypertension, markedly altered pulmonary haemodynamics, and a chronically 'preload-deprived' ventricle. A number of important problems have emerged during long-term follow-up. Although 10-year survival may approach 90%, it should be appreciated that a premature decline in cardiovascular performance, with reduced survival, is inevitable even in the best Fontan patients.[304] Important haemodynamic issues contributing to late Fontan failure include a progressive decline in systemic ventricular function, AV valve regurgitation, a rise in PVR, atrial enlargement, pulmonary venous obstruction, progressively restrictive subaortic VSD, and the consequences of chronic systemic venous hypertension including hepatic congestion and dysfunction.[305] Further complications include atrial and PA thrombus formation, development of pulmonary arteriovenous malformations, systemic arterial-to-pulmonary venous or systemic arterial-to-pulmonary arterial connection, and systemic-to-pulmonary venous collaterals.

After the Fontan operation, the majority of patients do well during childhood and adolescence, although exercise capacity is reduced when measured objectively. However, clinical complications may subsequently develop, with a progressive decline in exercise performance and heart failure, cyanosis, chronic venous insufficiency, and development of important arrhythmias, especially in patients with a classical Fontan operation.[306] By 10 years after a Fontan operation, ~20% of patients have supraventricular tachyarrhythmias (including typically IART and atrial flutter, but also AF and focal AT).[307] Bradycardia due to SND may facilitate occurrence of AT. The incidence of AT is lower after total cavopulmonary connection than atriopulmonary connection, and lower after extracardiac conduit than intracardiac conduit.[308] Atrial tachyarrythmias with rapid conduction are associated with SCD.

The spectrum of Fontan-associated liver disease is wide and includes both hepatic congestion and severe fibrosis, with signs of portal hypertension and hyperenhancing nodules as well as hepatocellular carcinoma.[309]

Protein-losing enteropathy is a rare but important complication and results in peripheral oedema, pleural effusions, and ascites. It can be diagnosed by documentation of low serum albumin and elevated

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α1-antitrypsin levels in the stool.[310] It has traditionally been associated with a very poor prognosis (5-year survival <50%) but a more recent study reported a 5-year survival of 88%; however, treatment remains challenging.[311] Plastic bronchitis and lymphatic system dysfunction may further complicate prognosis.

For more details, see a recently published extensive review.[312]

4.16.3 Diagnostic work-up

See *section 3.3* for general principles.

Clinical findings include commonly mild, non-pulsatile jugular venous distension. Significant jugular venous distension and hepatomegaly, however, raise suspicion of Fontan obstruction or ventricular failure. ECG frequently shows junctional rhythm or atrial arrhythmias. Pleural effusion on chest X-ray raises suspicion of protein-losing enteropathy.

- Echocardiography is the first-line diagnostic tool, providing information on ventricular and valve function. To image the Fontan pathway, TOE or other imaging modalities are generally required.
- Annual blood tests should include haematology, serum albumin, and liver and renal function. When protein losing enteropathy is suspected, α1-antitrypsin clearance must be calculated.
- CMR is helpful for evaluation of the Fontan pathway, collaterals, and pulmonary veins (e.g. right pulmonary vein obstruction by enlarged RA) and for thrombus, all of which CCT can also provide. CCT requires experience to mitigate streaming artefact and false positive diagnosis of thrombus. CMR is regularly performed for ventricular volumes, Fontan pathway patency and flows, to evaluate AV valve regurgitation, subaortic obstruction, myocardial fibrosis, and for detection of thrombus.
- As liver dysfunction, liver cirrhosis, and hepatocellular carcinoma have been recognized as typical complications in this setting, regular liver imaging (ultrasound, computed tomography, magnetic resonance) and laboratory assessment should be performed.
- Cardiac catheterization should be performed at a low threshold in cases of unexplained oedema, exercise deterioration, new-onset arrhythmia, cyanosis, and haemoptysis. It provides information on ventricular and valvular function, haemodynamics including PVR, and Fontan obstruction and anomalous vascular connections (see *section 4.16.2*). Integration with CMR for flows (cardiac output) may allow more precise measurement of PVR.

4.16.4 Medical treatment

- Anticoagulation: right atrial blood stasis and disturbed coagulation may predispose to thrombosis. The potential for subclinical, recurrent pulmonary embolism (eventually leading to a rise in PVR) and systemic embolism have led to a recommendation, by some, for lifelong anticoagulation. There is, however, no evidence of benefit, and practice varies between centres. Anticoagulation is indicated in the presence, or with a history, of atrial thrombus, atrial arrhythmias, or thromboembolic events. Although NOACs have been reported to be safe in selected Fontan patients,[79] robust prospective efficacy data are lacking and thus these drugs cannot currently be recommended as standard therapy.
- Antiarrhythmic therapy: loss of sinus rhythm may precipitate rapid haemodynamic decline and atrial arrhythmias. Sustained atrial arrhythmia with rapid AV conduction should be considered a medical emergency. Electrical cardioversion is the mainstay of treatment, as drug therapy is often ineffective. Amiodarone may be effective in preventing recurrence, but it has many long-term side effects. Sotalol can be an alternative. There should be a low threshold for radiofrequency ablation, although these are difficult arrhythmias to treat in the catheterization laboratory.[313] Antitachycardia atrial PMs may assist. If AV pacing is required, this will need an epicardial approach. Occurrence of arrhythmias should prompt haemodynamic evaluation. In addition, a proactive approach of EP evaluation and ablation therapy (where appropriate) should be considered, including Fontan conversion with concomitant arrhythmia surgery. ICD therapy may be considered in selected patients. See *section 3.4.2*.
- Therapy of protein losing enteropathy: medical therapy remains challenging and various treatments have been proposed (after exclusion of haemodynamic problems) including salt restriction, high protein diet, diuretics, ACE inhibitors (may be poorly tolerated), steroids, albumin infusion, chronic subcutaneous heparin, creation of a fenestration (by interventional catheter), and eventually, consideration of transplantation.
- Pulmonary vasodilators: ERAs and PDE-5 inhibitors may be considered in selected patients with elevated pulmonary pressure/resistance in the absence of elevated ventricular end diastolic pressure. Data on the routine use of these medications in Fontan patients are limited at present. A randomized trial of the ERA bosentan has demonstrated significantly improved cardiopulmonary exercise capacity in 75 adults with Fontan physiology.[314]

4.16.5 Surgical/interventional treatment

Patients with a 'failing Fontan' (with a combination of intractable arrhythmia, right atrial dilation, worsening AV valve regurgitation, deterioration of ventricular function, and/or atrial thrombus) should be considered for surgery.[315] While patients with failing systemic ventricular function may benefit from heart transplantation (performed in experienced settings), patients with preserved systemic ventricular function, atrial arrhythmia, and impaired flow dynamics in the Fontan pathway may benefit from conversion to extracardiac total cavopulmonary connection and concomitant cryoablation.[316] The latter has provided good early results in a very experienced setting, but is associated with surgical mortality and ongoing morbidity, with the need for both continued drug therapy and pacemaker implantation in the majority of cases.[317] If performed late, conversion may be less likely to result in a good outcome, and cardiac transplantation may be required. However, the best timing for a conversion remains a matter of uncertainty. In selected adult patients, it may be appropriate to consider device closure of a fenestration if there is significant cyanosis, but this may also worsen the patient's condition. Catheter intervention may also be required in the case of flow obstruction, or anomalous vascular connections.

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Special considerations and recommendations for intervention after Fontan operation

Recommendations	Class[a]	Level[b]
Sustained atrial arrhythmia with rapid AV conduction is a medical emergency and should be promptly treated with electrical cardioversion.	I	C
Anticoagulation is indicated in the presence, or with a history, of atrial thrombus, atrial arrhythmias, or thromboembolic events.	I	C
It is recommended that women with a Fontan circulation and any complication are counselled against pregnancy.	I	C
Cardiac catheterization is recommended at a low threshold in cases of unexplained oedema, exercise deterioration, new-onset arrhythmia, cyanosis, and haemoptysis.	I	C
In patients with arrhythmias, a proactive approach of electrophysiologic evaluation and ablation (where appropriate) should be considered.	IIa	C
Regular liver imaging (ultrasound, computed tomography, magnetic resonance) should be considered.	IIa	C
Endothelin receptor antagonists and phosphodiesterase-5 inhibitors may be considered in selected patients with elevated pulmonary pressure/resistance in the absence of elevated ventricular end diastolic pressure.	IIb	C
In selected patients with significant cyanosis, device closure of a fenestration may be considered but requires careful evaluation before intervention to exclude induction of systemic venous pressure increase or fall in cardiac output.	IIb	C

AV = atrioventricular.
[a]Class of recommendation.
[b]Level of evidence.

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4.16.6 Follow-up recommendations

As a result of these many complex issues, the care of Fontan patients is one of the major challenges for ACHD practitioners. All Fontan patients should be followed in specialized ACHD centres, usually at least annually, with echocardiography, ECG, blood tests, and exercise testing. Intervals for CMR and hepatic ultrasound (or computed tomography) must be decided on an individual basis. For adults, it appears reasonable to perform a baseline hepatic assessment with magnetic resonance imaging at the first visit to guide the frequency and mode of follow-up based on the degree of pre-existing hepatic changes. In addition, yearly follow-up hepatic assessments including, for example, liver ultrasound and alpha-fetoprotein measurement, should be considered after consultation with local hepatology services.

Comprehensive assessment is mandatory for patients with manifestations of the 'failing Fontan' complex, with particular care to exclude even minor obstructions to cavopulmonary flow and pulmonary venous return, which may have a major haemodynamic impact.

4.16.7 Additional considerations

- Exercise/sports: after Fontan operation, patients have significantly reduced exercise capacity as part of their circulation. However, moderate symptom-limited aerobic exercise is to be recommended according to current recommendations to improve musculatory strength and quality of life.[24]
- Pregnancy: patients with a Fontan circulation and any complication should be advised against pregnancy. Successful pregnancy is possible in selected patients, although with significant maternal morbidity, especially heart failure and arrhythmia, but also thromboembolic complications. Therapeutic anticoagulants should be considered, balanced against the risk of bleeding, which is also higher in these patients. Intensive monitoring, including after delivery, is mandatory. There is a high miscarriage rate of 27–55% and a high rate of prematurity and intrauterine growth restriction. Whether pregnancy with its volume loading has an adverse effect on the long-term outcome of women with a single ventricle remains to be elucidated.
- IE prophylaxis: only recommended in patients with a recent redo Fontan (<6 months), cyanosis, a prosthetic valve, residual patch leak, or prior endocarditis.

4.17 Coronary anomalies

4.17.1 Introduction and background

Coronary anomalies include anomalous aortic origin of a coronary artery (AAOCA), anomalous coronary artery from the PA (ACAPA), and coronary fistulae.

4.17.1.1 Anomalous coronary artery from the pulmonary artery

Although many congenital coronary anomalies are benign, natural history studies of anomalous left coronary artery from the PA (ALCAPA) document poor outcome if untreated.[318] ACAPA results in low oxygen levels in the coronary artery, coronary steal syndrome, and myocardial ischaemia. ALCAPA can present as a silent or symptomatic myocardial infarction, LV dysfunction, VTs, or even SCD. Patients may also primarily present with volume overload due to L–R shunt causing heart failure symptoms. However, anomalous right coronary artery from the PA (ARCAPA) has frequently been diagnosed incidentally. Dual coronary system repair, including coronary button transfer with or without an interposition graft, is preferred. A coronary artery bypass graft (CABG) with closure of the ACAPA should be reserved for those in whom coronary transfer is not feasible.

4.17.1.2 Anomalous aortic origin of a coronary artery

Natural history studies are lacking regarding untreated patients with AAOCA. The debate about management is ongoing, in particular in patients with an interarterial course of an anomalous coronary artery. Risk assessment for SCD is difficult because of the lack of data. Autopsy series show that most patients are young (<35 years) and die during, or shortly after, exercise. Myocardial fibrosis has been demonstrated, suggesting myocardial ischaemia may play a role. Left coronary artery arising from the opposite (right) sinus is less

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common, but more malignant than the right coronary artery from the left sinus. High orifice, ostial stenosis, slit-like/fish-mouth-shaped orifice, acute-angle take-off, intramural course and its length, or inter-arterial course and hypoplasia of the proximal coronary artery have been associated with myocardial ischaemia and have all been proposed as risk factors.[319–322]

Risk stratification must also include age (<35 years) and level of exercise (e.g. competitive sports). There is very limited evidence that surgery in asymptomatic middle-aged patients provides any survival benefit or modifies the SCD risk.[323,324]

4.17.1.3 Coronary artery fistulae

A coronary artery fistula, whether congenital or acquired, is an abnormal connection between a coronary artery and cardiac chamber or vessel. Small fistulae have a good prognosis without treatment. Medium or large fistulae are associated with long-term complications (angina, myocardial infarction, arrhythmias, heart failure, and endocarditis). The presence of symptoms, complications, and a significant shunt are the main indications for percutaneous or surgical closure.

4.17.2 Diagnostic evaluation

CCT is the preferred technique for the evaluation of high-risk anatomy, including features such as an intramural course and orifice anomalies (slit-like orifice, acute-angle take-off, orifice >1 cm above the sinotubular junction).

Assessment of physical stress-induced ischaemia using advanced imaging modalities is the key to decision making.

Recommendations for the management of patients with anomalous coronary arteries

Recommendations	Class[a]	Level[b]
Non-pharmacological functional imaging (e.g. nuclear study, echocardiography, or CMR with physical stress) is recommended in patients with coronary anomalies to confirm/exclude myocardial ischaemia.	I	C
Anomalous coronary arteries from the pulmonary artery		
Surgery is recommended in patients with ALCAPA.	I	C
Surgery is recommended in patients with ARCAPA and symptoms attributable to anomalous coronary artery.	I	C
Surgery should be considered for ARCAPA in asymptomatic patients with ventricular dysfunction, or myocardial ischaemia attributable to coronary anomaly.	IIa	C
Anomalous aortic origin of the coronary artery		
Surgery is recommended for AAOCA in patients with typical angina symptoms who present with evidence of stress-induced myocardial ischaemia in a matching territory or high-risk anatomy.[c]	I	C
Surgery should be considered in *asymptomatic* patients with AAOCA (right or left) and evidence of myocardial ischaemia.	IIa	C
Surgery should be considered in *asymptomatic* patients with AAOLCA and no evidence of myocardial ischaemia but a high-risk anatomy.[c]	IIa	C
Surgery may be considered for symptomatic patients with AAOCA even if there is no evidence of myocardial ischaemia or high-risk anatomy.[c]	IIb	C
Surgery may be considered for *asymptomatic* patients with AAOLCA without myocardial ischaemia and without high-risk anatomy[c] when they present at young age (<35 years).	IIb	C
Surgery is not recommended for AAORCA in asymptomatic patients without myocardial ischaemia and without high-risk anatomy.[c]	III	C

AAOCA = anomalous aortic origin of a coronary artery; AAOLCA = anomalous aortic origin of the left coronary artery; AAORCA = anomalous aortic origin of the right coronary artery; ALCAPA = anomalous left coronary artery from the pulmonary artery; ARCAPA = anomalous right coronary artery from the pulmonary artery; CMR = cardiovascular magnetic resonance.
[a]Class of recommendation.
[b]Level of evidence.
[c]High-risk anatomy includes features such as an intramural course and orifice anomalies (slit-like orifice, acute-angle take-off, orifice >1 cm above the sinotubular junction).

4.17.3 Surgical treatment

Indications for surgery are summarized in the Recommendations for the management of patients with anomalous coronary arteries table.

5 Quality indicators

The overall aim of this new edition of the ESC Clinical Practice Guidelines for ACHD is to assist caregivers in their daily practice for the benefit of patients. In a next step, it is important to analyse the adaptation of, and the adherence to, these Guidelines in practice, a process that can be envisaged using Quality Indicators (QIs).

QIs are sets of measures that enable the quantification of adherence to Guideline recommendations and provide a mechanism for measuring opportunities to improve cardiovascular care and outcomes.[325] QIs show important differences from Clinical Practice Guidelines. For instance, the latter are recommendations for care to apply prospectively to individual patients, whereas QIs are applied retrospectively to a group of patients to assess if a care process was delivered or not.[325]

QIs are derived from evidence, feasible, concretely interpretable, and usable.[326] The goal of QIs is to improve quality of health care, and they have been increasingly used by health authorities, professional organisations, healthcare payers, as well as the public.[327–329]

The process of development and defining QIs for the management of specific ACHD items has been initiated during the Guideline writing process and results will be published later in a dedicated document.

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6 Gaps in evidence

6.1 General aspects

6.1.1 Organization of care and patient evaluation

- Congenital heart defects are arbitrarily classified into lesions of different complexities (mild, moderate, severe; *Table 4*). The validity of this classification for clinical management and risk stratification remains to be investigated in large registries.
- Minimal volumes of patients under care at each ACHD expert centre, and the necessary staff resources for an optimal outcome, need to be defined.
- Relevant outcome measures, over and above mortality, need to be determined to measure quality of care.
- The role of neurohormones to estimate disease severity and timing of interventions is not yet fully established and needs to be defined.

6.1.2 Heart failure

- The pathophysiology/mechanism of heart failure, especially in those with a systemic RV and Fontan circulation, is incompletely understood and needs further study to find better ways for prevention and treatment.
- Indications for application of standard heart failure treatment in both acute and chronic settings need to be better defined.
- The prediction and course of heart failure needs to be better defined to improve indications and timing of ventricular assist device/transplantation.
- Large-scale collaborative international prospective registries on medical and device therapy in ACHD are needed and support for the set up and practical implementation is required.

6.1.3 Arrhythmia

- Dedicated scoring systems to assess the indication for anticoagulation in the setting of atrial arrhythmias are needed for moderate and complex CHD.
- Targeting slow-conducting anatomical isthmuses by catheter ablation has been highly effective to control monomorphic VT in repaired tetralogy of Fallot. Whether catheter mapping can contribute to individualized risk stratification in patients without spontaneous VTs in repaired tetralogy of Fallot and related defects requires further research.
- The potential loss of accessibility to slow-conducting anatomical isthmuses by catheter ablation after re-valving rTOF and related defects is of concern. Whether patients without documented VT benefit from preventive ablation before or during re-valving should be studied.
- Indications for pacing and CRT in ACHD patients are mainly derived from adults with anatomically normal hearts with ischaemic or dilated cardiomyopathy and are not adapted to the diversity of structural and functional CHD substrates. The selection of CRT candidates, CRT application, and optimal pacing sites for the different CHD substrates requires further research.

6.1.4 Pulmonary arterial hypertension

- The impact of medical PAH therapy on survival of patients with Eisenmenger syndrome requires further study.
- The role of upfront combination therapy in PAH-CHD requires further attention.
- Limited experience is available for prostacyclin therapy in patients with PAH-CHD and needs further investigation.

6.1.5 Cyanotic patients

- The benefit of routine anticoagulation, in the absence of any strong risk factor for thromboembolic complications (e.g. atrial arrhythmias), is controversial and requires further study.

6.2 Specific lesions

6.2.1 Shunt lesions

- Late outcome after device closure requires further study, particularly of arrhythmias.
- The impact of shunt closure on long-term outcome of patients with PAH remains an area of uncertainty; further research is required to better define the thresholds for treatment recommendations.

6.2.2 Left ventricular outflow tract obstruction and coarctation

- The optimal timing of intervention in asymptomatic severe LVOTO requires further study.
- Transcatheter aortic valve implantation is rapidly evolving; its role in ACHD needs further refinement.
- According to the 2018 ESC Guidelines for the management of arterial hypertension,[190] definitions of hypertension in patients with repaired CoA are the same as in general arterial hypertension and patients should be managed according to the general guidelines: evidence for this strategy is lacking and prospective studies are required.

6.2.3 Aortopathies

- Estimation of the risk for aortic dissection and definition of the threshold for prophylactic surgery in HTAD based on diameter alone is suboptimal and calls for a more personalized approach. Whether the type of underlying gene defect is helpful in this stratification requires further study.
- Current prophylactic treatment regimens in HTAD patients include beta blockers and ARBs. Either in monotherapy or combined, neither one prevents further growth of the aorta. The search for new and better treatment targets should continue.

6.2.4 Right ventricular outflow tract obstruction

- Criteria for concomitant TV repair at the time of RVOT surgery require refinement.
- The identification of patients with low-gradient RVOTO who have severe stenosis and would benefit from intervention requires improvement.
- The criteria for identification of RVOTO patients who would benefit from reintervention for residual PR requires further research.
- The role of an EP study for risk stratification for SCD is controversial in patients with rTOF and needs further study.

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6.2.5 Ebstein anomaly

- The identification of asymptomatic Ebstein patients with severe TR who would benefit from TV surgery requires further improvement.
- The identification of Ebstein patients at risk for late life-threatening arrhythmias needs to be improved.

6.2.6 Tetralogy of Fallot

- Optimal timing of PVRep for asymptomatic patients with significant PR needs to be further improved.
- Long-term follow-up studies after TPVI are required to increase knowledge about valve durability, consequences of stent fractures, and occurrence of endocarditis.
- The identification of rTOF patients at risk for late life-threatening arrhythmias, who would benefit from ICD implantation as primary prevention, needs to be improved.
- The effect of medical treatment on RV dilatation and/or dysfunction in rTOF patients needs to be established.

6.2.7 Transposition of the great arteries

- The potential benefit of classical heart failure medical therapy and biventricular pacing in patients with a systemic RV after an atrial switch procedure requires further study.
- Risk stratification for SCD and indications for primary ICD implantation after atrial switch require refinement.
- After an arterial switch procedure, the risk of dissection/rupture of neo-aortic root aneurysms requires further study to refine the recommendations for prophylactic surgery.
- Long-term follow-up after arterial switch is required to study the risk for development of CAD after reimplantation of the coronary arteries into the neo-aortic root.

6.2.8 Congenitally corrected transposition of the great arteries

- The definition of optimal timing for TV replacement in patients with severe asymptomatic TR requires more data.
- The potential benefit of pulmonary banding for the preservation of systemic ventricular function requires further study.

6.2.9 Univentricular heart and Fontan operation

- The role of medication, including pulmonary vasodilators, in Fontan patients is not clear and requires further study.
- The effects of pregnancy on long-term maternal outcome must be better established.
- Physiological determinants of long-term outcome in Fontan patients, including the role of the lymphatic system, requires more research.

6.2.10 Coronary anomalies

- Identification of adult patients with coronary anomalies (AAOCA, ACAPA) who are at risk for SCD, and for whom surgery provides benefit at adult age, requires further research.

7 Key messages

7.1 General aspects

7.1.1 Organization of care and patient evaluation

- Special structural and organizational healthcare requirements are necessary to meet the needs of ACHD patients.
- Multimodality imaging is key for adequate assessment of overall anatomy and ventricular and valvular function, and quantification of blood flow, including perfusion distribution.
- Objective exercise testing is an important tool for determining the timing of interventions and reinterventions.
- Cardiac catheterization remains key for the assessment of haemodynamics, in particular, PAP and vascular resistance.

7.1.2 Heart failure

- The key treatment for heart failure in ACHD patients remains its prevention by optimizing haemodynamics and heart rhythm. This requires systematic follow-up in specialized centres to facilitate timely intervention.
- In a biventricular circulation, standard heart failure treatment can be extrapolated to ACHD patients with a systemic LV and may be applied in patients with a systemic RV, although it remains uncertain whether the known benefits of treating a failing LV can be expected. Pathophysiology of patients with an atrial switch, and especially with a UVH and Fontan palliation, differs markedly from a 'regular circulation' and standard heart failure therapy has to be applied cautiously.
- Timely referral and consultation with ACHD and heart failure specialists in a centre with a transplant service and ACHD expertise is recommended, especially in those with moderate and severe complexity CHD.

7.1.3 Arrhythmia

- In all patients, evaluation for a reversible cause of an arrhythmia and for new or residual haemodynamic abnormalities should be performed.
- Maintenance of sinus rhythm is the aim in most ACHD patients.
- For optimal chronic arrhythmia management, referral to a centre with a multidisciplinary team and expertise in ACHD-related arrhythmias is mandatory.
- Patients with documented arrhythmias or at high risk for post-procedural arrhythmias considered for percutaneous or surgical (re)interventions should be discussed in a multidisciplinary team with expertise in interventions *and* invasive treatment of arrhythmias.

7.1.4 Pulmonary arterial hypertension

- PAH in CHD is a progressive disease with poor prognosis.
- High suspicion of PAH, and regular assessment for the presence of PAH in patients with shunt lesions, after defect closure is recommended.
- Proactive treatment is required in all PAH patients, including those with Eisenmenger syndrome.
- Women with CHD and confirmed pre-capillary PH should be counselled against pregnancy.

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7.1.5 Cyanotic patients

- Cyanotic patients present with a multisystem disorder and are at risk for both bleeding and thrombotic complications, causing a therapeutic dilemma.
- Routine phlebotomies must be avoided as they put patients at risk for iron-deficient anaemia and cerebrovascular complications. Therapeutic phlebotomy is only indicated in the presence of moderate/severe hyperviscosity symptoms.
- Cyanotic patients have a very balanced, but fragile, pathophysiology and any intervention puts the patient at high risk; all interventions must therefore be performed in an ACHD expert centre.
- Prophylactic measures are the mainstay of care to prevent and avoid complications.

7.2 Specific lesions

7.2.1 Shunt lesions

- Treatment decisions require careful evaluation of ventricular volume overload and pulmonary circulation.
- In patients with non-invasive signs of elevated PAP, heart catheterization with assessment of PVR is mandatory.
- In the presence of PVR ≥5 WU, ASD closure should be avoided. VSD and PDA closure may only be considered in selected patients with significant shunt after careful evaluation in an ACHD and PH expert centre.
- Device closure is the treatment of choice when technically feasible.

7.2.2 Left ventricular outflow tract obstruction

- The strongest indications for surgery remain symptoms and LV dysfunction.
- Exercise testing should be performed in patients with severe obstruction who do not report symptoms in order to confirm asymptomatic status.
- In congenital valvular AS, associated aortic disease (ascending aortic dilatation and/or CoA) needs to be excluded.

7.2.3 Aortic coarctation

- Correct blood pressure measurement (right arm, ambulatory) is essential in the follow-up of patients with CoA.
- The decision to (re)intervene depends on blood pressure, gradient, and stenosis morphology.
- Stenting is the treatment of choice when technically feasible.

7.2.4 Aortopathies

- Lifelong surveillance is essential in all HTAD patients and should include imaging of the entire aorta, as well as assessment of valvular and myocardial function.
- The aortic diameter at which surgery should be performed depends on the underlying disease and presence of risk factors.

7.2.5 Right ventricular outflow tract obstruction

- RVOTO may be overestimated by the flow velocity across the obstruction, particularly when the narrowing is elongated, or stenosis is present in series (e.g. subvalvular and valvular). Therefore, cross-checking with RV pressure estimated from TR velocity is required.
- Catheter intervention is the treatment of choice for patients with non-dysplastic valvular PS (balloon valvuloplasty) and with peripheral PS (often with stent implantation).
- The indication for intervention is more restrictive whenever a valve substitute is required because of its long-term implications for complications and requirement for reintervention.

7.2.6 Ebstein anomaly

- Timing of surgery remains challenging and this operation should only be performed by surgeons with specific experience in this lesion.
- Valve repair is the preferred technique whenever feasible.

7.2.7 Tetralogy of Fallot

- Significant PR and/or RVOTO, RV and LV dysfunction, and arrhythmias are common long-term complications.
- Possible risk factors associated with any ventricular arrhythmia and SCD in rTOF are QRS duration >180 ms, LV systolic or diastolic dysfunction, RV dysfunction, inducible VT at programmed electrical stimulation, and history of atrial arrhythmia.
- The optimal timing for intervention in asymptomatic severe PR remains challenging. Normalization of RV size becomes unlikely when the end diastolic volume index exceeds 160 mL/m^2, but this cut-off for reintervention may not correlate with clinical benefit.
- TPVI has become the treatment of choice for RVOT reintervention when anatomically feasible.

7.2.8 Transposition of the great arteries

- Systemic ventricular failure, secondary systemic AV valve regurgitation, arrhythmia, and baffle stenosis and/or leakage are common long-term complications that need to be addressed after atrial switch operation.
- Outcome of morbidity has markedly improved with introduction of the arterial switch operation. Dilatation of the neo-aortic root with or without significant regurgitation of the neo-aortic valve, supravalvular PS, and pulmonary branch stenosis mostly occur during infancy, but may need reintervention during adulthood.
- New LV systolic dysfunction and/or arrhythmias after arterial switch require full evaluation, including exclusion of ostial/proximal stenoses of the reimplanted coronary arteries.
- Failure of the RV-to-PA conduit (stenosis, regurgitation, or both) is the predominant long-term complication requiring reintervention after the Rastelli operation.

7.2.9 Congenitally corrected transposition of the great arteries

- Systemic RV failure, systemic AV valve regurgitation, AV block, and atrial arrhythmia are common late complications.
- Systemic AV valve regurgitation is an important driver of late outcome and, when severe, should be addressed before systemic RV function becomes impaired.

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7.2.10 Univentricular heart and Fontan operation

- Although quality of life is well preserved in many Fontan patients, all require regular intensive follow-up at an ACHD expert centre as they are at risk of developing multiple severe complications including arrhythmia, heart failure, hepatic disease, and protein-losing enteropathy.
- Low pulmonary artery pressure is mandatory for a good functioning Fontan circulation and a low threshold for invasive haemodynamic assessment is recommended when dysfunction is suspected, or complications occur.
- Arrhythmias are poorly tolerated and require immediate action.
- Pregnancy is feasible in selected patients with well-functioning Fontan circulation but there is a high risk of miscarriage and pregnancy should be managed in an ACHD expert centre.
- Surveillance for liver problems is mandatory in all Fontan patients.

7.2.11 Coronary anomalies

- CCT is the preferred technique for the evaluation of high-risk anatomy including features such as an intramural course and orifice anomalies (slit-like orifice, acute-angle take-off, orifice >1 cm above the sinotubular junction).
- Assessment of stress-induced ischaemia, by means of advanced imaging modalities with physical stress, is the key for decision making.
- In patients with coronary fistulae, the presence of symptoms, complications, and a significant shunt are the main indications for percutaneous or surgical closure.

8 'What to do' and 'what not to do' messages from the Guidelines

Recommendations	Class[a]	Level[b]
Treatment of arrhythmias in adult congenital heart disease		
In patients with moderate and severe CHD complexity (*Table 4*) and documented arrhythmias, referral to a centre with a multidisciplinary team and expertise in ACHD patients and ACHD-related arrhythmia is indicated.	I	C
In CHD patients with documented arrhythmias or at high risk for post-procedural arrhythmias (e.g. ASD closure at older age) considered for percutaneous or surgical (re)interventions, referral to a centre with a multidisciplinary team with expertise in these interventions and in invasive treatment of arrhythmias is indicated.	I	C
In mild CHD, catheter ablation is recommended over long-term medical therapy for symptomatic, sustained recurrent SVT (AVNRT, AVRT, AT, and IART), or if SVT is potentially related to SCD (*Table 7*).	I	C
Catheter ablation is indicated as adjunctive therapy to ICDs in patients who present with recurrent monomorphic VT, incessant VT, or electrical storm not manageable by medical therapy or ICD reprogramming.	I	C
ICD implantation is indicated in adults with CHD who are survivors of an aborted cardiac arrest due to VF or haemodynamically untolerated VT after evaluation to define the cause of the event and exclusion of reversible causes.	I	C
ICD implantation is indicated in adults with CHD and sustained VT after haemodynamic evaluation and repair when indicated. EP evaluation is required to identify patients in whom catheter ablation or surgical ablation may be beneficial as adjunctive treatment or in whom it may offer a reasonable alternative.	I	C
Treatment of pulmonary arterial hypertension associated with congenital heart disease		
It is recommended that patients with CHD and confirmed pre-capillary PH are counselled against pregnancy.	I	C
Risk assessment is recommended in all patients with PAH-CHD.	I	C
In low- and intermediate-risk patients with repaired simple lesions and pre-capillary PH, initial oral combination therapy or sequential combination therapy is recommended and high-risk patients should be treated with initial combination therapy including parenteral prostanoids.	I	A
Atrial septal defect (native and residual)		
In patients with evidence of RV volume overload and no PAH (no non-invasive signs of PAP elevation or invasive confirmation of PVR <3 WU in case of such signs) or LV disease, ASD closure is recommended regardless of symptoms.	I	B
Device closure is recommended as the method of choice for secundum ASD closure when technically suitable.	I	C
In elderly patients not suitable for device closure, it is recommended to carefully weigh the surgical risk against the potential benefit of ASD closure.	I	C
In patients with non-invasive signs of PAP elevation, invasive measurement of PVR is mandatory.	I	C
In patients with LV disease, it is recommended to perform balloon testing and carefully weigh the benefit of eliminating L–R shunt against the potential negative impact of ASD closure on outcome due to an increase in filling pressure (taking closure, fenestrated closure, and no closure into consideration).	I	C
ASD closure is not recommended in patients with Eisenmenger physiology, patients with PAH and PVR ≥5 WU despite targeted PAH treatment, or desaturation on exercise.	III	C

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Ventricular septal defect (native and residual)		
In patients with evidence of LV volume overload and no PAH (no non-invasive signs of PAP elevation or invasive confirmation of PVR <3 WU in case of such signs), VSD closure is recommended regardless of symptoms.	I	C
VSD closure is not recommended in patients with Eisenmenger physiology and patients with severe PAH (PVR ≥5 WU) presenting with desaturation on exercise.	III	C
Atrioventricular septal defect		
Surgical repair is not recommended in patients with Eisenmenger physiology and patients with PAH (PVR ≥5 WU) presenting with desaturation on exercise.	III	C
Surgical closure is recommended in patients with significant RV volume overload and should only be performed by a congenital cardiac surgeon.	I	C
Valve surgery, preferably AV valve repair, is recommended in symptomatic patients with moderate to severe AV valve regurgitation and should be performed by a congenital cardiac surgeon.	I	C
In asymptomatic patients with severe left-sided AV valve regurgitation, valve surgery is recommended when LVESD ≥45 mm and/or LVEF ≤60% provided other causes of LV dysfunction are excluded.	I	C
Patent ductus arteriosus		
In patients with evidence of LV volume overload and no PAH (no non-invasive signs of PAP elevation or invasive confirmation of PVR <3 WU in case of such signs), PDA closure is recommended regardless of symptoms.	I	C
Device closure is recommended as the method of choice when technically suitable.	I	C
PDA closure is not recommended in patients with Eisenmenger physiology and patients with lower limb desaturation on exercise.	III	C
Valvular aortic stenosis		
Intervention is recommended in all symptomatic patients with severe high-gradient AS (mean gradient ≥40 mmHg).	I	B
Intervention is indicated in patients with severe low-flow, low-gradient (mean gradient <40 mmHg) AS with reduced EF and evidence of flow (contractile) reserve excluding pseudosevere AS.	I	C
Intervention is indicated in asymptomatic patients with severe AS and an abnormal exercise test showing symptoms on exercise clearly related to AS.	I	C
Intervention is indicated in asymptomatic patients with severe AS and systolic LV dysfunction (LVEF <50%) not due to another cause.	I	C
Surgery is recommended when patients with severe AS undergo surgery of the ascending aorta or of another valve, or CABG.	I	C
Supravalvular aortic stenosis		
In patients with symptoms (spontaneous or on exercise test) and mean Doppler gradient ≥40 mmHg, surgery is recommended.	I	C
In patients with mean Doppler gradient <40 mmHg, surgery is recommended when one or more of the following findings are present: • Symptoms attributable to obstruction (exertional dyspnoea, angina, syncope). • LV systolic dysfunction (EF <50% without other explanation). • Surgery required for significant CAD or valvular disease.	I	C
Subaortic stenosis		
In symptomatic patients (spontaneous or on exercise test) with a mean Doppler gradient ≥40 mmHg or severe AR, surgery is recommended.	I	C
Coarctation and re-coarctation of the aorta		
Repair of coarctation or re-coarctation (surgically or catheter based) is indicated in hypertensive patients with an increased non-invasive gradient between upper and lower limbs confirmed with invasive measurement (peak-to-peak ≥20 mmHg) with preference for catheter treatment (stenting) when technically feasible.	I	C
Aortic surgery in aortopathies		
Aortic valve repair, using the reimplantation or remodelling with aortic annuloplasty technique, is recommended in young patients with Marfan syndrome or related HTAD with aortic root dilation and tricuspid aortic valves when performed by experienced surgeons.	I	C
Surgery is indicated in patients with Marfan syndrome who have aortic root disease with a maximal aortic sinus diameter ≥50 mm.	I	C

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Right ventricular outflow tract obstruction		
In valvular PS, balloon valvuloplasty is the intervention of choice, if anatomically suitable.	I	C
Provided that no valve replacement is required, RVOTO intervention at any level is recommended regardless of symptoms when the stenosis is severe (Doppler peak gradient is >64 mmHg).	I	C
If surgical valve replacement is the only option, it is indicated in patients with severe stenosis who are symptomatic.	I	C
If surgical valve replacement is the only option in patients with severe stenosis who are asymptomatic, it is indicated in the presence of one or more of the following: • Objective decrease in exercise capacity. • Decreasing RV function and/or progression of TR to at least moderate. • RVSP >80 mmHg. • R−L shunting via an ASD or VSD.	I	C
Ebstein anomaly		
Surgical repair is recommended in patients with severe TR and symptoms or objective deterioration of exercise capacity.	I	C
It is recommended that surgical repair is performed by a congenital surgeon with specific experience in Ebstein surgery.	I	C
If there is an indication for TV surgery, ASD/PFO closure is recommended at the time of valve repair if it is expected to be haemodynamically tolerated.	I	C
In patients with symptomatic arrhythmias or pre-excitation on the ECG, electrophysiologic testing followed by ablation therapy, if feasible, or surgical treatment of the arrhythmias in the case of planned heart surgery is recommended.	I	C
After repair of tetralogy of Fallot		
PVRep is recommended in symptomatic patients with severe PR and/or at least moderate RVOTO.	I	C
In patients with no native outflow tract, catheter intervention (TPVI) should be preferred if anatomically feasible.	I	C
Transposition of the great arteries after atrial switch operation		
In *symptomatic* patients with pulmonary venous atrium obstruction, surgical repair (catheter intervention rarely possible) is recommended.	I	C
In *symptomatic* patients with baffle stenosis not amenable to catheter intervention, surgical repair is recommended.	I	C
In *symptomatic* patients with baffle leaks not amenable to catheter-based closure, surgical repair is recommended.	I	C
PA banding in adults, as LV training with subsequent arterial switch procedure, is not recommended.	III	C
In *symptomatic* patients with baffle stenosis, stenting is recommended when technically feasible.	I	C
In *symptomatic* patients with baffle leaks and cyanosis at rest or during exercise, or with strong suspicion of paradoxical emboli, stenting (covered) or device closure is recommended when technically feasible.	I	C
In patients with baffle leaks and symptoms due to L−R shunt, stenting (covered) or device closure is recommended when technically feasible.	I	C
Transposition of the great arteries after arterial switch operation		
Stenting or surgery (depending on substrate) is recommended for coronary artery stenosis causing ischaemia.	I	C
Congenitally corrected transposition of the great arteries		
In *symptomatic* patients with severe TR and preserved or mildly impaired systemic RV systolic function (EF >40%), TV replacement is indicated.	I	C
Right ventricular to pulmonary artery conduits		
Symptomatic patients with RVSP >60 mmHg (may be lower in case of reduced flow) and/or severe PR should undergo intervention with preference for catheter intervention (TPVI) if anatomically feasible.	I	C
Univentricular heart		
It is recommended that adults with unoperated or palliated UVHs undergo careful evaluation in specialized centres, including multimodality imaging as well as invasive work-up to decide whether they may benefit from surgical or interventional procedures.	I	C
After Fontan operation		
Sustained atrial arrhythmia with rapid AV conduction is a medical emergency and should be promptly treated with electrical cardioversion.	I	C
Anticoagulation is indicated in the presence, or with a history, of atrial thrombus, atrial arrhythmias, or thromboembolic events.	I	C
It is recommended that women with a Fontan circulation and any complication are counselled against pregnancy.	I	C
Cardiac catheterization is recommended at a low threshold in cases of unexplained oedema, exercise deterioration, new-onset arrhythmia, cyanosis, and haemoptysis.	I	C

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Anomalous coronary arteries		
Non-pharmacological functional imaging (e.g. nuclear study, echocardiography, or CMR with physical stress) is recommended in patients with coronary anomalies to confirm/exclude myocardial ischaemia.	I	C
Anomalous coronary arteries from the pulmonary artery		
Surgery is recommended in patients with ALCAPA.	I	C
Surgery is recommended in patients with ARCAPA and symptoms attributable to anomalous coronary artery.	I	C
Anomalous aortic origin of the coronary artery		
Surgery is recommended for AAOCA in patients with typical angina symptoms who present with evidence of stress-induced myocardial ischaemia in a matching territory or high-risk anatomy.	I	C
Surgery is not recommended for AAORCA in asymptomatic patients without myocardial ischaemia and without high-risk anatomy.	III	C

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AAOCA = anomalous aortic origin of a coronary artery; AAORCA anomalous aortic origin of the right coronary artery; ACHD = adult congenital heart disease; ALCAPA = anomalous left coronary artery from the pulmonary artery; ARCAPA = anomalous right coronary artery from the pulmonary artery; AR = aortic regurgitation; AS = aortic stenosis; ASD = atrial septal defect; AT = atrial tachycardia; AV = atrioventricular; AVNRT = atrioventricular node reentrant tachycardia; AVRT = atrioventricular reentrant tachycardia; AVSD = atrioventricular septal defect; CABG = coronary artery bypass graft; CAD = coronary artery disease; CHD = congenital heart disease; CMR = cardiovascular magnetic resonance; ECG = electrocardiogram; EF = ejection fraction; EP = electrophysiology/electrophysiological; HTAD = heritable thoracic aortic disease; IART= intraatrial reentrant tachycardia; ICD = implantable cardioverter defibrillator; L–R = left-to-right; LV = left ventricle/ventricular; LVEF = left ventricular ejection fraction; LVESD = left ventricular end systolic diameter; PAH = pulmonary arterial hypertension; PAP = pulmonary arterial pressure; PAH-CHD = pulmonary arterial hypertension associated with congenital heart disease; PDA = patent ductus arteriosus; PFO = patent foramen ovale; PH = pulmonary hypertension; PR = pulmonary regurgitation; PS = pulmonary stenosis; PVR = pulmonary vascular resistance; PVRep = pulmonary valve replacement; R–L = right-to-left; RV = right ventricle/ventricular; RVOTO = right ventricular outflow tract obstruction; RVSP = right ventricular systolic pressure; SCD = sudden cardiac death; SVT = supraventricular tachycardia; TPVI = transcatheter pulmonary valve implantation; TR = tricuspid regurgitation; TV = tricuspid valve; UVH = univentricular heart; VF = ventricular fibrillation; VSD = ventricular septal defect; VT = ventricular tachycardia; WU = Wood units;

[a]Class of recommendation.

[b]Level of evidence.

9 Appendix

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