ESC Guidelines for the Management of Grown-up Congenital Heart Disease (GUCH)

(Version 2010)

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

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ESC Guidelines for the management of grown-up congenital heart disease (GUCH)

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European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

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Classes of recommendations

- Evidence and/or general agreement that a given treatment or procedure *is beneficial, useful and effective.*
- Conflicting evidence and/or divergence of opinion about the usefulness/efficacy of the given treatment or procedure:
  - Weight of opinion/evidence is in favour of usefulness/efficacy.
  - Usefulness/efficacy is less well established by evidences/opinion.
- Evidence and/or general agreement that the given treatment or procedure *is not useful/effective and in some cases may be harmful.*

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Levels of evidence

- Data derived from *multiple* randomized clinical trials or *meta-analyzes*.
- Data derived from *a single* randomized clinical trial or large-non randomized studies.
- Consensus of opinion of the experts and/or small studies, restropective studies, registries.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Basic Patient Assessment

Thorough clinical evaluation is crucial for management of GUCH!!

- **Patient history**
  - Assess present and past symptoms.
  - Look for intercurrent events and changes in medication.
  - Question lifestyle to detect progressive changes in daily activity.
- **Clinical examination**
  Plays a major role and includes, during follow-up, careful evaluation with regard to any changes in auscultation findings, bood pressure and development of signs of heart failure.
- **Electrocardiogram (ECG) and pulse oximetry**
  Routinely carried out alongside clinical examination.
- **Chest x-ray**
  No longer performed routinely but rather on indication - nevertheless helpful for longterm FU (heart size/configuration, pulm. vascularis.).

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Echocardiography in GUCH (1)

- In general first line investigation.
- Provides in most instancies, information on the basic cardiac anatomy including heart position and orientation, venous return, connection of the atria and ventricles, and origin of the great arteries.
- Allows evaluation of the morphology of cardiac chambers, ventricular function, valve morphology and function, detection and evaluation of shunts.
- Assessment of ventricular volume overload (increase in enddiastolic volume and stroke volume) and pressure overload (hypertrophy and increase in ventricular pressure) are of major importance.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Echocardiography in GUCH (2)

- Doppler echocardiographic information includes detection and evaluation of valvular regurgitation, hemodymanic data such as gradients across obstructions and right ventricular (RVP) and pulmonary artery pressure (PAP) as well as flow calculations.
- Limitations:
  - highly investigator dependent,
  - assessment of ventricular volumes and function may be complicated by geometry and regional incoordination (systemic and non-syst. RVs and univentricular hearts!),
  - Doppler gradients may sometimes be misleading, particularly in RVOTO, coarctation, stenoses in series,
  - venous return, great arteries may be difficult to image.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Cardiac Magnetic Resonance (CMR)

- CMR has become increasingly important in evaluation and management of GUCH and is an essential facility in the specialist unit.
- Enables excellent three-dimensional anatomical reconstruction.
- Not restricted by body size and acoustic window.
- Many patients, in particular those with moderately and severly complex disease benefit from CMR. Indications for repeat studies and time intervals depend on individual findings of the first study.

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Indications for CMR in GUCH (1)

- **Alternative to echo when both techniques can provide similar information but when echo cannot be obtained with sufficient quality** (CMR can provide most information yielded by echo, however, echo is superior in estimating gradients, PAP and detecting small, highly mobile structures such as vegetations).
- Second method when echo measurements are borderline or ambiguous:
  - LV volume and LVEF, particularly in the setting of volume overload,
  - quantification of valvular regurgitation.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Indications for CMR in GUCH (2)

Indications where CMR is superior to echo and should be regularly used when the information is essential for patient management.

Quantification of RV volumes and EF (Tetralogy of Fallot, systemic RV, etc)	Evaluation of collaterals and arteriovenous malformations (CT)
Evaluation of RVOTO and RV-PA conduits	Coronary artery anomalies and disease (CT angio is superior!)
Quantification of pulmonary regurgitation	Evaluation of intracardiac and extracardiac masses
Evaluation of pulmonary arteries (stenoses, aneurysms)	Quantification of myocardial mass (LV and RV)
Evaluation of the aorta (aneurysms, dissection, coarctaion)	Detection and quantification of myocardial fibrosis / scar (LE)
Evaluation of systemic and pulm. veins (anomalous connection, obstr.)	Tissue characterisation (fibrosis, fat, iron, etc)

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Computed Tomography (CT) in GUCH

- Increasing role in imaging of GUCH patients.
- Excellent spatial resolution.
- Rapid acquisition time.
- Particularly good for imaging arteries and veins, particularly superior to CMR for epicardial coronary arteries, collaterals, AV malformations.
- Ventricular size and function can be assessed but with inferior temporal resolution compared to CMR.
- Major drawback compared to CMR: radiation.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Cardiopulmonary Exercise Testing (CPET)

- CPET, including assessment of:
  - objective exercise capacity (time, max. oxygen uptake),
  - ventilation efficiency (VE/VCO_2 slope),
  - chronotropic and blood pressure response,
  - exercise induced arrhythmia.

  gives a broad evaluation of function and fitness.
- CPET has endpoints correlating well with mortality and morbidity.
- Serial testing should be part of long-term FU protocols and interventional trials.
- Plays an important role in the timing of intervention and re-intervention.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Cardiac Catheterization in GUCH

Now reserved for resolution of specific anatomical and physiologic questions or for intervention

- **Indications for diagnosic catheterization include:**
  - assessment of PAP, PVR, particularly in shunt lesions when non-invas. estimated PAP > 50% systemic pressure and in complex CHD,
  - testing of vasoreactivity may be required for decision to intervene (oxygen has been traditionally used, nitric oxide may be preferable),
  - LV and RV diastolic function, pressure gradients and shunt quantification when non-invasive evaluation remains uncertain,
  - coronary angiography before surgery in men > 40 yrs, postmeno-pausal women and pts. with signs of or risk factors for CAD,
  - evaluation of extracardiac vessels such as aortic-pulmonary collateral arteries, etc.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Medical Heart Failure (HF) Therapy in GUCH

- Frequent problem in the GUCH population.
- In general current HF treatment recommendations are also followed in GUCH patients.
- However, as pathophysiology of cardiorespiratory dysfunction is often very different from the failing “normal” circulation, extrapolation of results from published studies to GUCH patients may be difficult particularly in settings such as TGA with atrial switch or a Fontan circulation (available data limited by small number of patients and conflicting results).
- Cardiac resynchronisation therapy has gained increasing interest. However, there is, as yet, little evidence to define indications and outcomes.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Arrhythmias in GUCH

- Frequent cause of morbidity and mortality and main reason for hospitalisation.
- Risk stratification and treatment are often different from those applied to the normally formed heart.
- Onset of arrhythmias may be a sign of haemodynamic decompensation.
- The risk associated with arrhythmias may be amplified in the presence of the frequently abnormal underlying circulation.
- Catheter ablation requires specific experience and skill; results are generally worse in GUCH patients but nevertheless preferred treatment where feasible.
- Antiarrhythmic drugs are frequently poorly tolerated.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Sudden Cardiac Death (SCD) in GUCH

- SCD is of particular concern in GUCH patients.
- Five defects with greatest known risk:
  - repaired Tetralogy of Fallot,
  - TGA with atrial switch,
  - congenitally corrected TGA,
  - Aortic Stenosis,
  - Univentricular hearts.
- Unexplained syncope is a warning event requiring careful evaluation of arrhythmia.
- Although various risk factors have been defined, algorithms for risk assessement and indications for ICD implantation have so far not been well established.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

General Indications for EP and ICD Implantation in GUCH

- ICD implantation is indicated in survivors of cardiac arrest after exclusion of reversible causes.
- Patients with spontaneous sustained VT should undergo invasive haemodynamic and EP evaluation. Recommended therapy includes catheter ablation or surgical resection to eliminate VT. If that is not successful, ICD implantation is recommended.
- Invasive haemodynamic and EP evaluation is reasonable in patients with unexplained syncope and impaired ventricular function. In the absence of a defined and reversible cause, ICD implantation is reasonable.
- EP testing may be considered for patients with ventricular couplets or non-sustained VT to determine the risk of sustained VT.

Class[a]	Level[b]
I	B
I	C
IIa	B
IIb	C

a = class of recommendation. b = level of evidence.
EP = electrophysiology; ICD = implanted cardioverter defibrillator; VT = ventricular tachycardia

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Prophylaxis of Infective Endocarditis (IE)

- Good oral hygiene and regular dental review are crucial.
- Aseptic measures are mandatory during manipulation of venous catheters and during any invasive procedure.
- GUCH patients should be discouraged from getting piercings and tattoos.
- Antibiotic prophylaxis is currently only recommended for the patients with the highest risk of IE undergoing the highest risk procedures (only for dental procedures requiring manipulation of the gingival or periapical region of the teeth or perforation of the oral mucosa).

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Prophylaxis of Infective Endocarditis (IE)

Class	Level
IIa	C

- Antiobiotic prophylaxis of IE includes the following patient groups:
  - patients with prosthetic valve or prosthetic material used for cardiac valve repair,
  - patients with previous IE,
  - following patients with congenital heart disease (CHD):
    a. cyanotic CHD, without repair, or with residual defects, palliative shunts or conduits,
    b. CHD after repair with prosthetic material whether placed by surgery or by percutaneous technique, up to 6 months after the procedure (until endothelialisation),
    c. when a residual defect persists at the site of implantation of a prosthetic material.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Pregnancy in GUCH

- Many GUCH patients tolerate pregnancy well.
- Careful risk assessment and specialist care provided in a multi-disciplinary team setting are crucial.
- Timely counselling should be an essential component of the service provided. The team should be involved early in pregnancy in order to plan antenatal care, including delivery and post-partum follow-up.
- High risk patients include:
  - severe PAH (Eisenmenger patients and others),
  - severe left heart outflow/inflow obstruction,
  - poor systemic ventricular function (EF< 40%),
  - aortic root dilatation in Marfan's and similar syndromes,
  - cyanosis (oxygen saturation is < 85%),
  - mechanical valve prosthesis.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Atrial Septal Defect
Diagnostic Work-up

- **Echocardiography**
  Key diagnostic technique providing diagnosis and quantification (RV volume overload):
  - TEE for precise evaluation of secundum defects prior to device closure (size, residual septal morphology, rim size and quality, exclusion of additional defects and confirmation of normal pulmonary venous connection) and of sinus venosus defects,
  - Other key inform. to be provided includes PAP and TR.
- **CMR/CT**
  If echo is insufficient, particularly for RV volume overload and pulmonary venous connection.
- **Cardiac catheterization**
  Estimation of PVR when echo PAP > 50% of systemic pressure.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Indications for Intervention in Atrial Septal Defect

- Patients with significant shunt (signs of RV volume overload) and PVR < 5 WU should undergo ASD closure regardless of symptoms.
- Device closure is the method of choice for secundum ASD closure when applicable.
- All ASDs regardless of size in patients with suspicion of paradoxical embolism (exclusion of other causes) should be considered for intervention.
- Patients with PVR ≥ 5 WU but < 2/3 SVR or PAP < 2/3 systemic pressure (baseline or when challenged with vasodilators, preferably nitric oxide, or after targered PAH therapy) and evidence of net L-R shunt (Qp:Qs > 1.5) may be considered for intervention.
- ASD closure must be avoided in patients with Eisenmenger physiology.

Class[a]	Level[b]
I	B
I	C
IIa	C
IIb	C
III	C

a = class of recommendation. b = level of evidence.
ASD = atrial septal defect; L-R shunt = left-to-right shunt; PAH = pulmonary arterial hypertension; PAP = pulmonary artery pressure; PVR = pulmonary vascular resistance; Qp:Qs = pulmonary to systemic flow ratio; SVR = systemic vascular resistance; WU = Wood units.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Atrial Septal Defect
Follow-up

- **FU evaluation** shoud include assessment of a residual shunt, RV size and function, TR and PAP by echocardiography as well as of arrhythmias by history, ECG and only if indicated (not routinley) Holter.
- Late post-op. **arrhythmias** after surgical repair at age < 40 years are most frequently intraatrial reentrant tachycardia or atrial flutter which can be successfully treated with radiofrequency ablation. With or without repair after 40 years, atrial fibrillation becomes more common (oral anticoagulation!).
- Patients repaired < 25 yrs without relevant sequelae or residuae do not require regular FU; the others should be followed on a regular basis including evaluation in specialized GUCH centers.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Ventricular Septal Defect
Diagnostic Work-up

- **Echocardiography**
  Key diagnostic technique providing diagnosis and quantification (LV volume overload).

  Key findings to provide are location, number and size of defects, severity of LV volume overload and PAP.

  Check for AR due to prolapse of the right or non-coronary cusp (especially in outlet/supracristal and high perimembranous VSDs) and for DCRV.
- **CMR**
  If echo is insufficient, particularly for assessment of LV volume overload and shunt quantification.
- **Cardiac catheterization**
  Estimation of PVR when echo PAP > 50% of systemic pressure.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Indications for Intervention in Ventricular Septal Defect

	Class[a]	Level[b]
• Patients with symptoms that can be attributed to L-R shunting through the (residual) VSD and who have no severe pulmonary vascular disease (see below) should undergo surgical VSD closure.	I	C
• Asymptomatic patients with evidence of LV volume overload attributable to the VSD should undergo surgical VSD closure.	I	C
• Patients with a history of IE should be considered for surgical VSD closure.	IIa	C
• Patients with VSD associated prolapse of an aortic valve cusp causing progressive AR should be considered for surgery.	IIa	C
• Patients with VSD and PAH should be considered for surgery when there is still net L-R shunt (Qp:Qs > 1.5) present and PAP or PVR are < 2/3 of systemic values (baseline or when challenged wich vasodilators, preferably nitric oxide, or after targered PAH therapy).	IIa	C
• Surgery must be avoided in Eisenmerger VSD and when exercise induced desaturation is present.	III	C
• If the VSD is small, not subarterial, does not lead to LV volume overload or pulmonary hypertension and there is no history of IE, surgery should be avoided.	III	C

AR = aortic regurgitation; IE = infective endocarditis; LV = left ventricle; PAH = pulmonary arterial hypertension; L-R shunt = left-to-right shunt; PVR = pulmonary vascular resistance; Qp:Qs = pulmonary to systemic flow ratio; VSD = ventricular septal defect.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Ventricular Septal Defect
Follow-up

- **FU evaluation** shoud include assessment of AR, TR, degree of (residual) shunt, LV dysfunction, elevation of PAP, development of DCRV and development of discrete subaortic stenosis 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).
- Patients with LV dysfunction, residual shunt, PAH, AR, RVOT or LVOT obstruction should be seen *every year*, small VSDs *in 3-5 year intervals*; after device closure: regular follow-up *until 2 years* and then depending on the result *every 2-4 years* is recommended. After surgical closure without residual abnormality *5-year intervals*.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Atrioventricular Septal Defect (AVSD)
Diagnostic Work-up

- **Echocardiography**
  Key diagnostic technique providing assessment of each anatomic component of the AVSD, of the AV-valves and their connections (straddling; overriding) and the severity and exact substrate of AV valve regurgitation, the magnitude and direction of intracardiac shunting, LV and RV function, PAP and the assessment of presence/absence of sub-aortic stenosis.
- **CMR**
  Indicated when additional quantification of ventricular volumes and function or intracardiac shunting is required for decision making.
- **Cardiac catheterization**
  Estimation of PVR when echo PAP > 50% of systemic pressure.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Indications for Intervention in Atrioventricular Septal Defect

	Class[a]	Level[b]
Complete AVSD		
• Cardiac surgery must be avoided in patients with Eisenmenger physiology. In case of doubt, PVR testing is recommended.	III	C
• For indication of intervention see also VSD.		
Partial AVSD		
• Surgical closure should be performed in case of significant volume overload of the RV. For further details see ASD.	I	C
AV valve regurgitation		
• Symptomatic patients with moderate to severe AV valve regurgitation should undergo valve surgery, preferably AV valve repair.	I	C
• Asymptomatic patients with moderate or severe left-sided valve regurgitation and LVESD > 45 mm and/or impaired LV function (LVEF < 60%) should undergo valve surgery when other causes of LV dysfunction are excluded.	I	B
• Surgical repair should be considered in asymptomatic patients with moderate or severe left-sided AV valve regurgitation who have signs of volume overload of the LV and a substrate of regurgitation that is very likely to be amenable for surgical repair.	IIa	C
SubAS		
• See LVOTO.	-	-

ASD = atrial septal defect; AV = atrioventricular; AVSD = atrioventricular septal defect; LV = left ventricle; LVEF = left ventricular ejection fraction; LVESD = left ventricular end-systolic diameter; PVR = pulmonary vascular resistance; RV = right ventricle; SubAS = subaortic stenosis; VSD = ventricular septal defect.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

AVSD
Follow-up

- **FU evaluation** should pay particular attention to residual shunt, AV valve malfunction, LV and RV enlargement and dysfunction, PAP elevation, subaortic stenosis and arrhythmias.

- Life-long regular follow-up of all patients, operated and non operated, with an AVSD is recommended including evaluation in specialized GUCH centers. The frequency of outpatient visits depends on the presence and severity of residual abnormalities. A surgically repaired AVSD without significant residual abnormalities should be seen at least every 2 to 3 years. In case of residual abnormalities, the intervals should be shorter.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Patent Ductus Arteriosus (PDA)
Diagnostic Work-up

- **Echocardiography**
  Key diagnostic technique providing the diagnosis (may be difficult in pts. with Eisenmenger physiology), the degree of LV volume overload, PAP, PA size and right heart changes.
- **CMR**
  Indicated when additional quantification of LV volumes or evaluation of PA anatomy are required.
- **Cardiac catheterization**
  Estimation of PVR when echo PAP > 50% of systemic pressure.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Indications for Intervention in Patent Ductus Arteriosus

	Class[a]	Level[b]
• PDA should be closed in patients with signs of LV volume overload.	I	C
• PDA should be closed in patients with PAH but PAP < 2/3 of systemic pressure or PVR < 2/3 of SVR.	I	C
• Device closure is the method of choice where technically suitable.	I	C
• PDA closure should be considered in patients with PAH and PAP > 2/3 of systemic pressure or PVR > 2/3 of SVR but still net L-R shunt (Qp:Qs > 1.5) or when testing (preferably with nitric oxide) or treatment demonstrates pulmonary vascular reactivity.	IIa	C
• Device closure should be considered in small PDAs with continuous murmur (normal LV and PAP).	IIa	C
• PDA closure should be avoided in silent duct (very small, no murmur).	III	C
• PDA closure must be avoided in PDA Eisenmerger or patients with severe PAH and exercice induced lower limb desaturation.	III	C

a = class of recommendation. b = level of evidence.
L-R shunt = left-to-right shunt; LV = left ventricle; PAH = pulmonary arterial hypertension; PAP = pulmonary artery pressure; PDA = patent ductus arteriosus; PVR = pulmonary vascular resistance; Qp:Qs = pulmonary to systemic flow ratio; SVR = systemic vascular resistance.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Patent Ductus Arteriosus
Follow-up

- **FU evaluation.** 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 with 1-3 years intervals depending on severity, including evaluation in specialized GUCH centers.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Valvular AS
Diagnostic Work-up

- **Echocardiography**
  Gold standard for diagnosis, degree of calcification, LV function, LVH and associated lesions. With Doppler echocardiography severity of AS is determined from transvalvular peak velocity (Vmax), mean gradient and continuity equation calculated effective orifice area.

  TEE may occasionally be helpful to planimeter AVA.

  Low dose dobutamine echo is helpful in low flow AS.
- **Exercise testing**
  In asympt. pts. to confirm asympt. status, evaluate exercise tolerance, blood pressure response and arrhythmias for timing of surgery.
- **CMR/CT**
  Mainly required to quantify aortic dilation.
- **Catheterization**
  Only if echo results are uncertain.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Diagnostic Criteria for Degree of Aortic Stenosis Severity

	Mild AS	Moderate AS	Severe AS
V max (m/sec)*	2.0 - 2.9	3.0 - 3.9	≥ 4.0
Mean gradient (mmHg)*	< 30	30 - 49	≥ 50
AVA (cm^2)	> 1.5	1.0 - 1.5	< 1.0
AVAi (cm^2/m^2 BSA)	≥ 1.0	0.6 - 0.9	< 0.6

AS = aortic stenosis; AVA = aortic valve area; AVAi = indexed AVA; BSA = body surface area.
V max = peak transvalvular velocity.
*at normal transvalvular flow.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Indications for Intervention in Valvular Aortic Stenosis (1)

	Class[a]	Level[b]
• Patients with severe AS and any valve related symptoms (AP, dyspnoea, syncope) should undergo valve replacement.	I	B
• Asymptomatic patients with severe AS should undergo surgery when they develop symptoms during exercise testing.	I	C
• Regardless of symptoms, surgery should be performed when systolic LV dysfunction is present in severe AS (LVEF < 50%), unless it is due to other causes.	I	C
• Regardless of symptoms, surgery should be performed when patients with severe AS undergo surgery of the ascending aorta or of another valve or coronary artery bypass grafting.	I	C
• Regardless of symptoms, aortic surgery should be considered if the ascending aorta is greater than 50 mm (27.5 mm/m^2 BSA) and no other indications for cardiac surgery are present.	IIa	C
• Asymptomatic patients with severe AS should be considered for surgery when they present with a fall in blood pressure below baseline during exercice testing.	IIa	C

a = class of recommendation. b = level of evidence.
AP = angor pectoris; AS = aortic stenosis; BSA = body surface area; LV = left ventricle; LVEF = ventricular ejection fraction.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Indications for Intervention in Valvular Aortic Stenosis (2)

	Class[a]	Level[b]
• Asymptomatic patients with severe AS and moderate-to-severe calcification and a rate of peak velocity progression of ≥ 0.3 m/sec/year should be considered for surgery.	IIa	C
• Patients with moderate AS undergoing coronary artery bypass surgery or surgery of the ascending aorta or another valve should be considered for additional valve replacement.	IIa	C
• Severe AS with low gradient (< 40 mmHg) and LV dysfunction with contractile reserve should be considered for surgery.	IIa	C
• Severe AS with low gradient (< 40 mmHg) and LV dysfunction without contractile reserve may be considered for surgery.	IIb	C
• Asymptomatic patients with severe AS and excessive LV hypertrophy (≥ 15 mm), unless this is due to hypertension, may be considered for surgery.	IIb	C

a = class of recommendation. b = level of evidence.
AP = angor pectoris; AS = aortic stenosis; BSA = body surface area; LV = left ventricle; LVEF = ventricular ejection fraction.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Valvular Aortic Stenosis
Follow-up

- Lifelong and regular follow-up is required, the intervals depend upon the degree of severity of stenosis. It is also necessary after valve intervention at yearly intervals.
- Echocardiographic evaluation of the aortic valve, LV, mitral valve, PAP and imaging of aortic root to determine progression of valve stenosis and aortic dilation are mandatory.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Supravalvular AS
Diagnostic Work-up

- **Echocardiography**
  Provides diagnosis and pressure gradients but these may overestimate the actual pressure drop across the stenosis.
- **Exercise testing**
  In asympt. pts. to confirm asympt. status, evaluate exercise tolerance, blood pressure response and arrhythmias for timing of surgery.
- **CMR/CT**
  Provide a precise anatomic definition of the lesion itself and identify additional lesions in the aorta, and its branches (carotid and renal artery stenosis) and pulmonary arteries. CT provides evaluation of coronary arteries.
- **Catheterization**
  Only if echo results are uncertain.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Indications for Intervention in Supravalvular Aortic Stenosis

	Class[a]	Level[b]
• Patients with symptoms (spontaneous or on exercise test) and mean Doppler gradient ≥ 50 mmHg should undergo surgery.	I	C
• Patients with mean Doppler gradient < 50 mmHg should undergo surgery when they have:		
– symptoms attributable to obstruction (exertional dyspnoea, angina, syncope) and/or,	I	C
– LV systolic dysfunction (without other explanation),	I	C
– severe LVH, attributable to obstruction (not related to hypertension),	I	C
– when surgery for significant CAD is required.	I	C
• Patients with mean Doppler gradient ≥ 50 mmHg* but without symptoms, LV systolic dysfunction, LVH or abnormal exercise test may be considered for repair when the surgical risk is low.	IIb	C

a = class of recommendation. b = level of evidence.
*Doppler derived gradients may overestimate the obstruction and may need confirmation by left heart catheterization.
CAD = coronary artery disease; LV = left ventricle; LVH = ventricular hypertrophy.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Supravalvular Aortic Stenosis
Follow-up

- 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/CT) and the occurrence or progression of CAD.

  Follow-up should include evaluation in specialized GUCH centers.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Subaortic Stenosis
Diagnostic Work-up

- **Echocardiography**
  Visualizes LVOT anatomy, associated aortic valve abnormality, amount of AR, LV function, LVH and associated lesions. With Doppler echocardiography severity of subvalvular obstruction is determined, but Doppler derived gradients may overestimate the obstruction and may need confirmation by cardiac catheterization.

  Occasionally TEE is necessary to demonstrate the membrane. Three-dimensional TEE can be helpful to characterize the complex LVOT anatomy.
- **CMR**
  May be helpful for evaluation of complex LVOT anatomy and quantification of AR.
- **Catheterization**
  Only if echo results are uncertain.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Indications for Intervention in Subaortic Stenosis

	Class[a]	Level[b]
• Symptomatic patients (spontaneous or on exercise test) with a mean Doppler gradient ≥ 50 mmHg* or severe AR should undergo surgery.	I	C
• Asymptomatic patients should be considered for surgery when:		
– LVEF is < 50% (gradient may be < 50 mmHg due to low flow),	IIa	C
– AR is severe and LVESD > 50 mm (or 25 mm/m^2 BSA) and/or EF < 50%**,	IIa	C
– mean Doppler gradient is ≥ 50 mmHg* and LVH marked,	IIa	C
– mean Doppler gradient is ≥ 50 mmHg* and blood pressure response is abnormal on exercise testing.	IIa	C
• Asymptomatic patients may be considered for surgery when:		
– mean Doppler gradient is ≥ 50 mmHg*, LV normal, exercise testing normal and surgical risk low,	IIb	C
– progression of AR is documented and AR becomes more than mild (to prevent further progression).	IIb	C

a = class of recommendation. b = level of evidence. *Doppler derived gradients may overestimate the obstruction and may need confirmation by cardiac catheterization.
**See ESC guidelines on the management of valvular heart disease. 35
AR = aortic regurgitation; BSA = body surface area; EF = ejection fraction; LV = left ventricle; LVEF = left ventricular ejection fraction; LVESD = left ventricular end systolic diameter; LVH = left ventricular hypertrophy.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Subortic Stenosis
Follow-up

- Lifelong, regular follow-up, including echocardiography is required in the non-operated state to determine progression of obstruction, AR, and LV function and size.
- Regular postoperative follow-up is necessary to detect late restenosis (frequent especially in isolated forms and surgical treatment in childhood), progressive AR, complications such as arrhythmias, heart block and iatrogenic VSD. Follow-up should include evaluation in specialized GUCH centers.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Coarctation (CoA)
Diagnostic Work-up

- **Echocardiography**
  Provides information regarding site, structure, and extent of CoA, LV function and LVH, associated cardiac abnormalities, and aortic and supraaortic vessel diameters. Doppler gradients are not useful for quantification. A diastolic "run-off"-phenomenon, is presumably the most reliable sign of significant coarctation or recoarctation.
- **CMR/CT**
  Preferred non-invasive techniques to evaluate the entire aorta, depicting site, extent and degree of the aortic narrowing, the aortic arch, the pre- and post-stenotic aorta, aneurysm and collaterals.
- **Catheterization**
  With haemodynamic assessment is still the "gold standard" for CoA evaluation in many centers.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Indications for Intervention in Coarctation of the Aorta

- All patients with a non-invasive pressure difference > 20 mmHg between upper and lower limbs, regardless of symptoms but with upper limb hypertension (> 140/90 mmHg in adults), pathologic blood pressure response during exercice, or significant LVH should have intervention.
- Independent of the pressure gradient, hypertensive patients with ≥ 50% aortic narrowing relative to the aortic diameter at the diaphragm level (on CMR, CT or invasive angiography) should be considered for intervention.
- Independent of the pressure gradient and presence of hypertension, patients with ≥ 50% aortic narrowing relative to the aortic diameter at the diaphragm level (on CMR, CT or invasive angiography) may be considered for intervention.

Class[a]	Level[b]
I	C
IIa	C
IIb	C

a = class of recommendation. b = level of evidence.
CMR = cardiac magnetic resonance; CoA = coarctation of the aorta; CT = computed tomography; LVH = left ventricular hypertrophy.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Coarctation
Follow-up

- All pts. require regular follow-up at least every second year including evaluation in specialized GUCH centers. Imaging of the aorta (preferably with CMR) is required. Imaging intervals depend on baseline pathology.
- Residua, sequelae and complications include:
  - arterial hypertension at rest or during exercise,
  - recurring or residual CoA may induce or aggravate systemic arterial hypertension,
  - aneurysms of the ascending aorta or at the intervention site (risk of rupture and death),
  - attention is required for BAV, mitral valve disease, premature CAD, berry aneurysms of the circle of Willis (currently, no routine screening is recommend).

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Marfan's Syndrom
Diagnostic Work-up

- Currently, the diagnosis of Marfan syndrome is primarily based on clinical manifestations but in the most recently revised nosology a more prominent role is assigned to molecular genetic testing.
- **Echocardiography**
  Provides aortic root measurements including max. diameter, aortic ring, sinus, sinotubular junction and distal ascending aorta, LV size and function, aortic valve morphology, Aortic regurgitation, Mitral and/or tricuspid valve prolapse and regurgitation.
- **CMR/CT**
  Should be performed in every patient providing imaging of the entire aorta including aortic dimensions beyond the root.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Marfan's Syndrom
Medical Therapy

- Beta-blockers (currently standard of care) might reduce the rate of aortic dilatation and might improve survival, at least in adults.
- Rigorous antihypertensive medical treatment, aiming at a systolic blood pressure less than 120 mmHg, and 110 mmHg in patients with aortic dissection, is important.
- The angiotensin II receptor 1 blocker losartan is potentially useful because it leads to TGFβ antagonism. Clinical trials are presently ongoing to evaluate its beneficial effect. They must be awaited before definite recommendations.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Indications for Aortic Surgery in Marfan Syndrome

- Patients should undergro surgery when aortic root maximal diameter is:
  - > 50 mm
  - 46-50 mm with:
    - family history of dissection or,
    - progressive dilation > 2 mm/year as confirmed by repeated measurement or,
    - severe AR or Mr or,
    - desire of pregnancy.
- Patients should be considered for surgery when other parts of the aorta > 50 mm or dilation is progressive.

Class[a]	Level[b]
I	C*
I	C
I	C
I	C
I	C
IIa	C

a = class of recommendation. b = level of evidence.
* ESC guidelines for valvular heart disease are slightly more strict, recommending only one diameter (45 mm) regardless of other findings. In small individuals, the use of an indexed diameter adjusted for BSA of 2.75 cm/m² should probably be used.
AR = aortic regurgitation; MR = mitral regurgitation.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Marfan Syndrome
Follow-up

- Lifelong and regular follow-up requires involvement of specialists with ample expertise in a specialized center. Echocardiographic imaging of the aortic root and CMR-imaging (or CT if CMR is contraindicated) of the entire aorta is of critical importance, especially if a dissection persists. Valvular regurgitation and ventricular function can be followed by means of echocardiography.
- Stable patients need a yearly visit with echocardiography, CMR of the entire aorta at baseline and repeated at least once in 5 years if the aortic size beyond the root is normal. In case of aneurysm formation beyond the root, CMR should be repeated at least yearly.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Right Ventricular Outflow Tract Obstruction (RVOTO) Diagnostic Work-up (1)

- **Echocardiography**
  First line diagnostic technique providing visualization of the level of RVOTO, pulmonary valve anatomy, RVH and co-existing lesions. Doppler echo-cardiography provides the gradient across obstruction, presence and severity of PR and TR and RV systolic pressure. Doppler gradients may be unreliable in patients with tubular stenosis and in patients with stenoses in series (subvalvular and valvular). In patients with double chambered RV the peak gradient may lead to underestimation of stenosis, because sampling of flow may not be axial.
- **Severity**
  Mild (peak gradient < 36 mmHg, peak velocity < 3 m/s), moderate (36 to 64 mmHg; 3-4 m/s), severe (> 64 mmHg, peak velocity > 4 m/s). Since Doppler measurements may be unreliable (see above), TR velocity with estimation of RV pressure should always be used in addition when assessing severity.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Right Ventricular Outflow Tract Obstruction (RVOTO) Diagnostic Work-up (2)

- **CMR (and CT)**
  Helpful in identifying the level(s) of obstruction, particularly at sub-infundibular, conduit or branch pulmonary artery levels and assessment of the RV. Methods of choice for visualisation of pulmonary artery dilation and peripheral PS.
- **Nuclear techniques**
  May reveal perfusion abnormalities in different lung segments in case of peripheral PS (can also be measured by CMR).
- **Cardiac catheterization**
  May be required to confirm the extent, severity and level of obstruction (f.e. DCRV).

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Indications for Intervention in Right Ventricular Outflow Tract Obstruction

	Class[a]	Level[b]
• RVOTO at any level should be repaired regardless of symptoms when Doppler peak gradient is > 64 mmHg (peak velocity > 4 m/s), provided that RV function is normal and no valve substitute is required.	I	C
• In valvular PS, balloon valvotomy should be the intervention of choice.	I	C
• In asymptomatic patients in whom balloon valvotomy is ineffective and surgical valve replacement is the only option, surgery should be performed in the presence of a systolic RVP > 80 mmHg (TR velocity > 4.3 m/sec).	I	C
• Intervention in patients with gradient < 64 mmHg should be considered in the presence of symptoms related to PS or decreased RV function or double chambered RV (which is usually progressive) or important arrhythmias or right-to-left shunting via an ASD or VSD.	IIa	C
• Peripheral PS, regardless of symptoms, should be considered for repair if > 50% diameter narrowing and RV systolic pressure > 50 mmHg and/or lung perfusion abnormalities are present.	IIa	C

a = class of recommendation. b = level of evidence.
ASD = atrial septal defect; PS = pulmonary stenosis; RV = right ventricle; RVOTO = right ventricular outflow tract obstruction; RVP = right ventricular pressure; TR = tricuspid regurgitation; VSD = ventricular septal defect.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

RVOTO
Follow-up

- Patients with RVOT obstruction need life-long follow-up with regular echocardiographic imaging. The frequency of follow-up visits depends on the severity of the lesion, but most patients will need a yearly visit including evaluation in specialized GUCH centers.

  Patients with mild valvular or mild residual PS need to be seen only once in 5 years.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Ebstein's Anomaly
Diagnostic Work-up

- **Echocardiography**
  Key diagnostic technique providing anatomy and function of the tricuspid valve, apical distal displacement of the septal or posterior leaflet (in adults ≥ 0,8 cm/m^2 body surface area), size of the anterior leaflet, "tethering" of the septal or posterior tricuspid valve leaflet on the septum or ventricular wall, size and function of the different cardiac sections (right atrium, atrialised ventricle, remaining functional RV, LV), RVOTO and associated lesions.

- **CMR**
  Has value with regard to evaluation for surgery as it offers unrestricted views for assessment of the dilated right heart, RV function and the tricuspid valve.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Indications for Intervention in Ebstein's Anomaly

	Class[a]	Level[b]
Indications for surgical repair		
• In patients with more than moderate TR and symptoms (NYHA class > II or arrhythmias) or deteriorating exercise capacity measured by CPET.	I	C
• If there is also an indication for tricuspid valve surgery, then ASD/PFO closure should be performed surgically at the time of valve repair.	I	C
• Surgical repair should be considered regardless of symptoms in patients with progressive right heart dilation or reduction of RV systolic function and/or progressive cardiomegaly on chest x-ray.	IIa	C
Indications for catheter intervention		
• Patients with relevant arrhythmias should undergo electrophysiologic testing followed by ablation therapy, if feasible, or surgical treatment of the arrhythmias in the case of planned heart surgery.	I	C
• In the case of documented systemic embolism likely caused by paradoxical embolism, isolated device closure of ASD/PFO should be considered.	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.	IIb	C

a = class of recommendation. b = level of evidence.
ASD = atrial septal defect; CPET = cardiopulmonary exercise testing; NYHA = New York Heart Association; PFO = patent foramen ovale; RV = right ventricle; TR = tricuspid regurgitation; VSD = ventricular septal defect.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Ebstein's Anomaly
Follow-up

- Regular follow-up (at least yearly) is required in all patients in specialized GUCH centers.
- Typical postoperative 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 heart blocks.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Tetralogy of Fallot after repair
Diagnostic Work-up

- **Echocardiography**
  First line diagnostic technique providing the assessment of residual RVOTO and PR, residual VSD, RV and LV size and function, TR (RVP), aortic root size and AR.
- **CMR (CT)**
  Method of choice for assessment of RV volume and function, PR, size, shape and expansion of the PAs, the ascending aorta and the position of great vessels or conduits in relations to the sternum (resternotomy).
- **CPET**
  Assists timing of re-intervention, carries prognostic info.
- **Holter monitoring, event recorder**
  Required for selected patients (high-risk, investigated for suspected or clinical arrhythmia)
- **Cardiac catheterization**
  Restricted to patients undergoing catheter based interventions (i.e. relief of distal PA stenosis, percutaneous valve implantation) and when noninvasive evaluation is inconclusive.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Indications for Intervention After Repair of Tetralogy of Fallot

	Class[a]	Level[b]
• Aortic valve replacement should be performed in patients with severe AR with symptoms or signs of LV dysfunction.	I	C
• PVRep should be performed in symptomatic patients with severe PR and/or stenosis (RV systolic pressure > 60 mmHg, TR velocity > 3.5 m/sec).	I	C
• PVRep should be considered in asymptomatic patients with severe PR and/or PS when at least one of the following criteria is present: – decrease in objective exercise capacity (CPET), – progressive RV dilation, – progressive RV systolic dysfunction, – progressive TR (at least moderate), – RVOTO with RV systolic pressure > 80 mmHg (TR velocity > 4.3 m/sec), – sustained atrial/ventricular arrhythmias.	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

a = class of recommendation. b = level of evidence.
AR= aortic regurgitation; LV = left ventricle; PR = pulmonary regurgitation; PVRep = pulmonary valve replacement; RV = right ventricle; RVOTO = right ventricular outflow tract obstruction; TR = tricuspid regurgitation; VSD = ventricular septal defect.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Tetralogy of Fallot after repair
Indications for EP Testing and ICD

- EP testing and/or ablation must be considered for symptomatic patients with suspected or documented clinical (atrial or ventricular), arrhythmia.
- For ICD: *see general recommendations.*

  ICD implantation for primary prevention remains controversial and no ideal risk stratification scheme has so far been developed.
- Risk markers: right and/or left ventricular dysfunction, extensive ventricular fibrosis (on CMR), QRS ≥ 180 msec, significant PR, non-sustained VT on Holter monitoring, inducible VT at EP testing, long-lasting palliative shunts, older age at time of repair.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Tetralogy of Fallot after repair
Follow-up (1)

All patients should have regular follow-up in a specialized GUCH center, in general annually

Late complications to look for:

- **Pulmonary regurgitation (PR):** significant PR is almost always encountered following a transannular patch repair. May eventually lead to symptomatic RV dilation and dysfunction.
- **Residual RVOTO:** can occur at the infundibulum, at the level of the pulmonary valve and main pulmonary trunk, distally, beyond the bifurcation and occasionally into the branches of the left and right PAs.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Tetralogy of Fallot after repair
Follow-up (2)

Late complications to look for (cont'd) **:**

- **RV dilatation and dysfunction:** usually due to residual long standing free PR ± RVOTO. Significant **TR** may occur as a consequence of RV dilation.
- **Residual VSD:** may lead to LV volume overload.
- **Aortic root dilatation with AR:** commonly leads to AR and rarely to aortic dissection.
- **LV dysfunction:** may (among other causes) result from an adverse ventricular-ventricular interaction (PR).
- **Atrial/ventricular tachycardia:** is related to progressive haemodynamic problems and/or surgical scarring.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

TGA + atrial switch (Mustard/Senning) Diagnostic Work-up

- **Echocardiography**
  First line diagnostic technique providing systemic and sub-pulmonary ventricular size and function, sub-pulmonary outflow tract obstruction, TR, leakage or obstruction of the atrial baffles and assessment of pulmonary venous return. SVC stenosis is, however, mostly difficult to assess and may require TEE. *Contrast echo* is helpful for baffle leakage or stenosis.
- **CMR (CT)**
  Indicated for assessment of systemic RV function and patency of the atrial baffles.
- **Holter monitoring, event recorder**
  Required for selected patients (high-risk, investigated for suspected or clinical arrhythmia).
- **Cardiac catheterization**
  Indicated when non-invasive assessment is inconclusive or PAH requires evaluation.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Indications for Intervention in Transposition of the Great Arteries After Atrial Switch (1)

Indications for surgical intervention

	Class[a]	Level[b]
• Valve repair or replacement should be performed in patients with severe symptomatic systemic (tricuspid) AV valve regurgitation without significant ventricular dysfunction (RVEF ≥ 45%).	I	C
• Significant systemic ventricular dysfunction, with or without TR, should be treated conservatively or eventually with cardiac transplantation.	I	C
• LVOTO if symptomatic or if LV function deteriorates should be treated surgically.	I	C
• In *symptomatic* pulmonary venous obstruction surgical repair (catheter intervention rarely possible) should be performed.	I	C
• *Symptomatic* patients with baffle stenosis not amenable for catheter intervention should be treated surgically.	I	C
• *Symptomatic* patients with baffle leaks not amenable for catheter intervention should be treated surgically.	I	C
• Valve repair or replacement should be considered for severe asymptomatic systemic (tricuspid) AV valve regurgitation without significant ventricular dysfunction (RVEF ≥ 45%).	IIa	C
• Pulmonary artery banding in adult patients, to create septal shift, or a left ventricular training with subsequent arterial switch, is currently experimental and should be avoided.	III	C

a = class of recommendation. b = level of evidence. AV = atrioventricular; L-R shunt = left-to-right shunt; LV = Left ventricle; LVOTO = left ventricular outflow tract obstruction; RVEF = right ventricular ejection fraction; TR = tricuspid regurgitation.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Indications for Intervention in Transposition of the Great Arteries After Atrial Switch (2)

Indications for catheter intervention

	Class[a]	Level[b]
• Stenting should be performed in *symptomatic* patients with baffle stenosis.	I	C
• Stenting (covered) or device closure should be performed in *symptomatic* patients with baffle leaks and substantial cyanosis at rest or during exercice.	I	C
• Stenting (covered) or device closure should be performed in patients with baffle leaks and symptoms due to L-R shunt.	I	C
• Stenting (covered) or device closure should be considered in *asymptomatic* patients with baffle leaks with substantial ventricular volume overload due to L-R shunt.	I	C
• Stenting should be considered in *asymptomatic* patients with baffle stenosis who require a PM treatment.	IIa	C
• Stenting may be considered in other *asymptomatic* patients with baffle stenosis.	IIb	C

a = class of recommendation. b = level of evidence.
AV = atrioventricular; L-R shunt = left-to-right shunt; LV = Left ventricle; LVOTO = left ventricular outflow tract obstruction; PM = pacemaker; RVEF = right ventricular ejection fraction; TR = tricuspid regurgitation.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

TGA + atrial switch (Mustard/Senning)
EP Testing, Ablation and ICD

- These procedures are complicated by the fact that the atria are not normally accessible for catheters and “normal” EP procedures because of the course of the baffles and should only be done in specialized centers with specific expertise.
- Patients are at increased risk of SCD.

  Atrial tachyarrhythmia, impaired systemic RV function and QRS duration ≥ 140 msec have been reported to be risk factors.

See general recommendations for ICD implantation.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

TGA + atrial switch (Mustard/Senning) Follow-up

All patients should be seen at least annually in a specialized center

Frequent complications to look for:

- Dysfunction of the systemic RV.
- TR: often develops as sign of RV dilation and progresses.
- Tachy-arrhythmias: atrial flutter is most typical, but atrial fibrillation and all other types of SVT can occur. VT and VF are reported, associated with SCD. Brady-arrhythmias: ongoing loss of sinus node function frequently necessitates pacemaker therapy.
- Baffle (intra-atrial tunnel) leaks: may cause left-to-right or right-to-left shunt.
- Obstruction of systemic venous and/or pulmonary venous drainage.
- Sub-pulmonary outflow tract obstruction: can occur due to leftward bulging of the interventricular septum (systemic ventricle may benefit).

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

TGA + arterial switch
Diagnostic Work-up (1)

- **Echocardiography**
  Key diagnostic technique providing LV function (global and regional), stenosis at the arterial anastomotic sites, most commonly PS, neoaortic valve regurgitation, dimension of the ascending aorta and the acute angulation of the aortic arch. The pulmonary trunk, the bifurcation and both branches should be evaluated for the presence, localisation and severity of stenoses. RV function should be judged and systolic pressures should be estimated (TR velocity). Stress echo can unmask LV dysfunction and detect provocable myocardial ischemia.

- **CMR**
  Evaluation of the aorta, pulmonary branch stenosis and flow distribution between left and right lung.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

TGA + arterial switch
Diagnostic Work-up (2)

- **CT**
  Might be used for non-invasive imaging of coronary arteries, including the ostia, in case of suspicion of stenosis and as an alternative for CMR.
- **Cardiac catheterization**
  Including coronary angiography is indicated in case of LV dysfunction and suspicion of myocardial ischaemia.
- **Nuclear techniques** can be used for evaluation of coronary perfusion in case of suspicion of myocardial ischaemia and a lung perfusion test is recommended in case of pulmonary branch stenosis.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Indications for Intervention in Transposition of the Great Arteries After Arterial Switch Operation

	Class[a]	Level[b]
• Stenting or surgery (depending on substrate) should be performed for coronary artery stenosis causing ischaemia.	I	C
• Surgical repair of RVOTO should be performed in symptomatic patients with RV systolic pressure > 60 mmHg (TR velocity > 3.5 m/sec).	I	C
• Surgical repair of RVOTO should be performed regardless of symptoms when RV dysfunction develops (RVP may then be lower).	I	C
• Surgical repair should be considered in asymptomatic patients with RVOTO and systolic RVP > 80 mmHg (TR velocity > 4.3 m/sec).	IIa	C
• Aortic root surgery should be considered when the (neo-)aortic root is larger than 55 mm, providing average adult stature (for aortic valve replacement for severe AR see guidelines for AR).	IIa	C
• Stenting or surgery (depending on substrate) should be considered for peripheral PS, regardless of symptoms, if > 50% diameter narrowing and RV systolic pressure > 50 mmHg and/or lung perfusion abnormalities.	IIa	C

a = class of recommendation. b = level of evidence.
AR = aortic regurgitation; AV = atrioventricular; RV = right ventricle; RVP = right ventricular pressure; RVOTO = right ventricular outflow tract obstruction; TR = tricuspid regurgitation.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

TGA + arterial switch
Follow-up

All patients should be seen at least annually in a specialized GUCH center

Frequent complications to look for:

- LV dysfunction and arrhythmias: both may be related to coronary artery problems (re-implanted ostia).
- Dilatation of the proximal part of the ascending aorta resulting in AR.
- Supravalvular PS, pulmonary branch stenosis (unilaterally or bilaterally).

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Congenitally corrected TGA
Diagnostic Work-up

- **Echocardiography**
  Key diagnostic technique demonstrating double discordance. It is important to identify associated anomalies, particularly AV valve abnormalities (Ebstein-like malformation) and regurgitation, VSD, LVOTO and PS. Systolic function of the systemic (subaortic) ventricle and severity of AV valve regurgitation can be qualitatively assessed.
- **CMR**
  Provides intracardiac and great vessel anatomy and is indicated for quantification of ventricular volumes, mass and ejection fraction when required.
- **Holter monitoring, event recorder and EP testing** are required for selected patients (high-risk, investigated for suspected or clinical arrhythmia).
- **Cardiac catheterization** is indicated when non-invasive assessment is inconclusive.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Indications for Intervention in Congenitally Corrected Transposition of the Great Arteries

- Systemic AV valve (tricuspid valve) surgery for severe regurgitation should be considered before systemic (subaortic) ventricular function deteriorates (before RVEF < 45%).
- Anatomic repair (atrial switch + arterial switch or Rastelli when feasible in case of non-restrictive VSD) may be considered when LV is functioning at systemic pressure.

Class[a]	Level[b]
IIa	C
IIb	C

a = class of recommendation. b = level of evidence.
AV = atrioventricular; LV = left ventricle; RVEF = right ventricular ejection fraction; VSD = ventricular septal defect.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Congenitally corrected TGA (cc TGA)
Follow-up

- Patients with ccTGA need life-long follow-up in a specialized GUCH center with annual intervals particularly because of conduction disturbances (AV block), systemic ventricular and systemic AV valve dysfunction.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Special Considerations and Indications for Intervention in Univentricular Hearts

	Class[a]	Level[b]
• Only well-selected patients after careful evaluation (low pulmonary vascular resistances, adequate function of the AV valve(s), preserved ventricular function) should be considered as candidates for a Fontan operation.	IIa	C
• Patients with increased pulmonary blood floow - unlikely at adult age -should be considered for PA banding or tightening of a previously placed band.	IIa	c
• Patients with severe cyanosis, with decreased pulmonary blood flow without elevated PVR, should be considered for a bidirectional Glenn shunt.	IIa	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

a = class of recommendation. b = level of evidence.
AV = atrioventricular; PA =pulmonary artery; PVR = pulmonary vascular resistance.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Patients after Fontan Operation
Diagnostic Work-up

- **Echocardiography**
  First line diagnostic tool providing ventricular and valve function. To image the Fontan pathway TEE or other imaging modalities are generally required.
- **Annual blood controls** should include haematology, serum albumin, liver and renal function. In case of suspicion of PLE α1-antitrypsin clearance must be calculated.
- **CMR**
  Is particularly helpful for evaluation of the Fontan pathway, collaterals and pulmonary veins (f.e. right pulmonary vein obstruction by enlarged right atrium) and differential pulmonary flow.
  Hepatic evaluation by ultrasound (and CT) is important (fibrosis, cirrhosis, cancer).
- **Cardiac catheterization** should be performed at a low threshold in case of unexplained oedema, exercise deterioration, new onset arrhythmia, cyanosis and haemoptysis. It provides ventricular and valvular function, haemodynamics including PVR and Fontan obstruction and anomalous vascular connections.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Patients after Fontan Operation
Medical Therapy (1)

- **Anticoagulation**
  - Right atrial blood stasis and disturbed coagulation may predispose to thrombosis.
  - The potential for sub clinical, recurrent pulmonary embolism leading to a rise in PVR has led to a recommendation by some groups for life-long anticoagulation. There is, however no evidence for benefit and practise varies among centers.
  - Anticoagulation is definitely indicated in the presence of atrial/ Fontan pathway/PA thrombus, atrial arrhythmias or thrombo-embolic events.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Patients after Fontan Operation
Medical Therapy (2)

- **Antiarrhythmic therapy:**
  - loss of sinus rhythm may precipitate rapid haemodynamic decline and sustained arrhythmia 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 arrhythmias are difficult to treat in the catheterization laboratory,
  - anti-tachycardia atrial pacemakers may assist,
  - if AV pacing is required, this will need an epicardial approach,
  - occurrence of arrhythmias should prompt haemodynamic evaluation.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Patients after Fontan Operation
Medical Therapy (3)

- **Medical therapy of protein loosing enteropathy (PLE):**
  - 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),
    - eventually consideration of transplantation.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Patients after Fontan Operation
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.
- Conversion of an atrial-pulmonary connection to a more “energy efficient” TCPC, together with arrhythmia surgery, 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.
- If performed late, conversion may become less likely to result in a good outcome and cardiac transplantation may rather be required. However, the best timing for a conversion remains a matter of uncertainty.
- Catheter intervention may be required for closure of a fenestration, in the case of flow obstruction or anomalous vascular connections.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Patients after Fontan Operation
Follow-up

- After Fontan operation patients should be followed in specialized GUCH centers, usually at least annually including:
  - echo,
  - ECG,
  - blood controls and,
  - exercise testing.

  Intervals for CMR and hepatic ultrasound (CT) must be decided on an individual basis.
- Comprehensive assessment is mandatory for patients with manifestations of the “failing Fontan” complex, with particular care to exclude even minor obstructions to cavo-pulmonary and pulmonary venous return which may have major haemodynamic impact.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

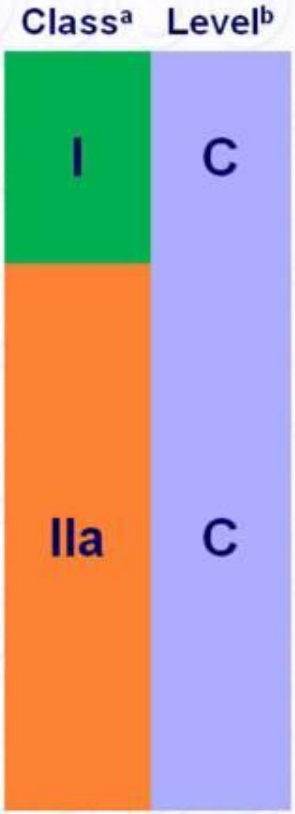
RV – PA Conduits
Diagnostic Work-up

- **Echocardiography**
  First line diagnostic tool providing size and function of both ventricles, PR, TR and associated lesions. Gradients across the conduit may be difficult to measure and not reliable. RV pressure derived from TR velocity should be used to assess conduit stenoses.
- **CMR and CT**
  May be required to image the conduit (level of stenosis), pulmonary artery and coronary artery anatomy, for the assessment of the RV and severity of PR. Before re-sternotomy, the relationship between the conduit/RV and the inner layer of the sternum must be evaluated.
- **Cardiac catheterization** always required if intervention considered.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Indications for Intervention in Patients With Right Ventricular to Pulmonary Artery Conduits

- Symptomatic patients with RV systolic pressure > 60 mmHg (TR velocity > 3.5 m/sec; may be lower in case of reduced flow) and/or moderate/severe PR should undergo surgery.
- Asymptomatic patients with severe RVOTO and/or severe PR should be considered for surgery when at least one of the following criteria is present:
  - decrease in exercise capacity (CPET),
  - progressive RV dilation,
  - progressive RV systolic dysfunction,
  - progressive TR (at least moderate),
  - RV systolic pressure > 80 mmHg (TR velocity > 4.3 m/sec),
  - sustained atrial/ventricular arrhythmias.



a = class of recommendation. b = level of evidence.
CPET = cardiopulmonary exercise testing; PR = pulmonary regurgitation; RV = right ventricle; RVOTO = right ventricular outflow tract obstruction; TR = tricuspid regurgitation.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

RV – PA conduits
Follow-up

- Regular follow-up in a spezialized GUCH center is recommended at least every 12 months.
- Special attention should be given to exercise capacity (CPET), RV systolic pressure (conduit gradient), RV function, TR and arrhythmias.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Recommendations for Targeted Pulmonary Arterial Hypertension Therapy in Congenital Heart Disease

- Targeted PAH therapy in CHD should only be performed in specialized centers.
- The ERA bosentan should be initiated in WHO-FC III* patients with Eisenmenger syndrome.
- Other ERAs, phosphodiesterase type-5 inhibitors and prostanoids should be considered in WHO-FC III* patients with Eisenmenger syndrome.
- Combination therapy may be considered in WHO-FC III patients with Eisenmenger syndrome.
- The use of calcium channel blockers should be avoided in patients with Eisenmenger syndrome.

Class[a]	Level[b]
I	C
I	B
IIa	C
IIb	C
III	C

a = class of recommendation. b = level of evidence.
*Although recent data support the use of ERA such as bosentan also in WHO-FC II, in pts with idiopathic PAH and PAH associated with connective tissue diseases such data are currently not available for Eisenmenger pts. Because of marked differences in the natural history between these groups, the results cannot simply be applied to GUCH and further studies are required before recommendations.
ERA = endothelin receptor antagonist; PAH = pulmonary arterial hypertension;
WHO-FC = World Health Organization - functional class.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Cyanotic Patients
Late Complications (1)

- **Hyperviscosity symptoms**
  Headache, faintness, dizziness, fatigue, tinnitus, blurred vision, paresthesia of fingers, toes and lips, muscle pain and weakness (unlikely in an iron-replete patient with haematocrit < 65%!!).
- **Bleeding**
  Dental bleeding, epistaxis, menorrhagia, haemoptysis (most common major bleeding and external manifestation of an intrapulmonary haemorrhage not reflecting the extent of parenchymal bleeding).
- **Thrombosis**
  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.
- **Iron deficiency**
  Is frequently caused by inappropriate phlebotomies.
- **Arrhythmias**
  Supra-ventricular and ventricular.
- **Cholelithiasis**
  Can be complicated by cholecystitis/choledocholithiasis.

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Cyanotic Patients
Late Complications (2)

- **Cerebrovascular accidents**
  May be caused by thromboembolic events (paradoxical emboli), rheologic factors (microcytosis), endothelial dysfunction and 'traditional' atherosclerotic risk factors. The severity of secondary erythrocytosis *per se* is not a risk factor; microcytosis caused by iron deficiency, due to inappropriate phlebotomies, is a strong independent predictor for cerebrovascular events.
- **Paradoxical emboli**
  May be caused by supraventricular arrhythmias or transvenous leads or catheters.
- **Infectious complications**
  Endocarditis, cerebral abscess, pneumonia.
- **Renal dysfunction**
  Is common and due to functional and structural abnormalities of the kidneys.
- **Rheumatologic complications**
  Include gouty arthritis, hypertrophic osteoarthropathy, kyphoscoliosis.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Cyanotic Patients
Diagnostic Work-up

- Oxygen saturation must be obtained with pulse oximetry at rest for at least 5 minutes.
- Exercise capacity should be assessed on a regular basis preferably with a 6-minute walk test.
- *Blood work* should include cellular blood count (MCV), serum ferritin (serum iron, transferrin and transferrin saturation may be required for earlier detection of iron deficiency), creatinine, serum uric acid, clotting profile and BNP or pro-BNP. Folic acid and vitamin B12 in the presence of elevated MCV or normal MCV and low serum ferritin.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Cyanotic Patients
Medical Therapy (1)

- For targeted PAH treatment see special table.
- **Arrhythmias.** Sinus rhythm should be maintained whenever possible. Drug therapy should be initiated with particular care and generally in-hospital. Transvenous leads must be avoided.
- **Therapeutic phlebotomy** should only be performed in the presence of moderate/severe hyperviscosity symptoms due to secondary erythrocytosis (haematocrit > 65%), in the absence of dehydration and iron deficiency. Isovolumic fluid replacement (750 to 1000 mL of isotonic saline while removing 400 to 500 mL of blood).
- **Blood transfusion** may be required in the presence of iron replete anemia (haemoglobin inadequate to oxygen saturation).
- **Iron supplementation** should be performed in the presence if iron deficiency (MCV < 80 fL) 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.

European Heart Journal 2010; doi:10.1093/eurhearj/ehq249

Cyanotic Patients
Medical Therapy (2)

- **Indication for anticoagulation:** atrial flutter/fibrillation (target INR 2 - 2.5; higher target INR in the presence of a mechanical valve).
- **Haemoptysis:** requires chest x-ray followed by chest CT scan if there is an infiltrate. Bronchoscopy poses the patient at risk and provides seldom useful information. Therapy includes discontinuation of aspirin, nonsteroidal anti-inflammatory agents and oral anticoagulants; treatment of hypovolemia and anaemia; reduction of physical activity and suppression of nonproductive cough. Selective embolization of bronchial arteries may be required for refractory intrapulmonary haemorrhage/haemoptysis.
- **Hyperuricaemia:** No indication to treat asymptomatic hyperuricaemia.
- **Acute gouty arthritis** is treated with oral or intravenous colchizine, probenecid and anti-inflammatory drugs with attention to the risk of renal failure and bleeding. Uricosuric (e.g. probenecid) or uricostatic agents (e.g. allopurinol) avoid recurrence.
- **Life-long follow-up** with visits every 6 to 12 months in a specialized GUCH center are required.

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Risk Reduction Strategies in Patients With Cyanotic Congenital Heart Disease (1)

Prophylactic measures are the mainstay of care to avoid complications

- **The following exposures/activities should be avoided:**
  - pregnancy,
  - iron deficiency and anaemia (no routine, inappropriate phlebotomies to maintain a predetermined haemoglobin),
  - dehydration,
  - infectious disease: annual influenza vaccination, pneumovax (every 5 years),
  - cigarette smoking, recreational drug abuse including alcohol,
  - transvenous PM/ICD leads,
  - strenuous exercice,
  - acute exposure to heat (sauna, hot tub/shower).

GUCH = grown-up congenital heart disease; ICD = implantable cardioverter defibrillator; PM = pacemaker.

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Risk Reduction Strategies in Patients With Cyanotic Congenital Heart Disease (2)

Prophylactic measures are the mainstay of care to avoid complications

- **Other risk reduction strategies include:**
  - use of an air filter in an intravenous line to prevent air embolism,
  - consultation of a GUCH cardiologist before administration of any agent and performance of any surgical/interventional procedure,
  - prompt therapy of upper respiratory tract infections,
  - cautious use or avoidance of agents impairing renal function,
  - contraceptive advice.

GUCH = grown-up congenital heart disease; ICD = implantable cardioverter defibrillator; PM = pacemaker.

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