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2017 ESC/EACTS Guidelines for the management of valvular heart disease

The Task Force for the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

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For the Web Addenda which include background information and detailed discussion of the data that have provided the basis for the recommendations see https://academic.oup.com/ejcts/article-lookup/doi/10.1093/ejcts/ezx324#supplementary-data.

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ABBREVIATIONS AND ACRONYMS

ΔPm	Mean transvalvular pressure gradient
2D	Two-dimensional
3D	Three-dimensional
ABC	Age, biomarkers, clinical history
ACE	Angiotensin-converting enzyme
ACS	Acute coronary syndrome
ARB	Angiotensin receptor blocker
AVA	Aortic valve area
BAV	Balloon aortic valvuloplasty
BNP	B-type natriuretic peptide
BSA	Body surface area
CABG	Coronary artery bypass grafting
CAD	Coronary artery disease
CI	Contra-indication(s)
CMR	Cardiovascular magnetic resonance
CPG	Committee for Practice Guidelines cardiac resynchronization therapy
CT	Computed tomography
EACTS	European Association for Cardio-Thoracic Surgery
ECG	Electrocardiogram
EDV	End-diastolic velocity
EROA	Effective regurgitant orifice area
ESC	European Society of Cardiology
EuroSCORE	European System for Cardiac Operative Risk Evaluation
INR	International normalized ratio
IV	Intravenous
LA	Left atrium/left atrial
LMWH	Low-molecular-weight heparin
LV	Left ventricle/left ventricular
LVEDD	Left ventricular end-diastolic diameter
LVEF	Left ventricular ejection fraction
LVESD	Left ventricular end-systolic diameter
LVOT	Left ventricular outflow tract
MSCT	Multislice computed tomography
NOAC	Non-vitamin K antagonist oral anticoagulant
NYHA	New York Heart Association
PCI	Percutaneous coronary intervention
PISA	Proximal isovelocity surface area
PMC	Percutaneous mitral commissurotomy
RV	Right ventricle/right ventricular
SAVR	Surgical aortic valve replacement
SPAP	Systolic pulmonary arterial pressure
STS	Society of Thoracic Surgeons
SVi	Stroke volume index
TAVI	Transcatheter aortic valve implantation
TOE	Transoesophageal echocardiography
TTE	Transthoracic echocardiography
TVI	Time–velocity interval
UFH	Unfractionated heparin
VHD	Valvular heart disease
VKA	Vitamin K antagonist
V_{max}	Peak transvalvular velocity

1. PREAMBLE

Guidelines summarize and evaluate available evidence with the aim of assisting health professionals in selecting 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) and by the European Association for Cardio-Thoracic Surgery (EACTS) as well as by other societies and organisations. Because of the 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). ESC Guidelines represent the official position of the ESC on a given topic and are regularly updated.

Members of this Task Force were selected by the ESC and EACTS to represent professionals involved with the medical care of 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 and approved by the EACTS. 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 in Tables 1 and 2.

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. These forms were compiled into one file and can be found on the ESC website (http://www.escardio.org/guidelines). Any changes in declarations of interest that arise during the writing period were notified to the ESC and EACTS and updated. The Task Force received its entire financial support from the ESC and EACTS 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, and in this case by EACTS-appointed experts. After appropriate revisions the Guidelines are approved by all the experts involved in the Task Force. The finalized document is approved by the CPG and EACTS for publication in the European Heart Journal and in the European Journal of Cardio-Thoracic Surgery. 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/EACTS 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, if needed, one should always refer to the full text version, which is freely available via the ESC website and hosted on the EHJ website. The National Societies of the ESC are encouraged to endorse, 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.

Table 1: Classes of recommendations

Classes of recommendations	Definition	Suggested wording to use
Class I	**Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.**	**Is recommended/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**

Surveys and registries are needed to verify that real-life daily practice is in keeping with what is recommended in the guidelines, thus completing the loop between clinical research, writing of guidelines, disseminating them and implementing them into clinical practice.

Health professionals are encouraged to take the ESC/EACTS 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/EACTS 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 to drugs and devices at the time of prescription.

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.**

2. INTRODUCTION

2.1. Why do we need new guidelines on valvular heart disease?

Since the previous version of the guidelines on the management of VHD was published in 2012, new evidence has accumulated, particularly on percutaneous interventional techniques and on risk stratification with regard to timing of intervention in VHD. This made a revision of the recommendations necessary.

2.2. Content of these guidelines

Decision making in VHD involves accurate diagnosis, timing of intervention, risk assessment and, based on these, selection of the most suitable type of intervention. These guidelines focus on acquired VHD, are oriented towards management and do not deal with endocarditis or congenital valve disease, including pulmonary valve disease, as separate guidelines have been published by the ESC on these topics.

2.3. New format of the guidelines

The new guidelines have been adapted to facilitate their use in clinical practice and to meet readers' demands by focusing on condensed, clearly represented recommendations. At the end of each section, *Key points* summarize the essentials. *Gaps in evidence* are listed to propose topics for future research. The guideline document is harmonized with the simultaneously published chapter on VHD of the ESC Textbook of Cardiology, which is freely available by Internet access (https://academic.oup.com/eurheartj/article-lookup/doi/10.1093/eurheartj/ezx324#supplementary-data).

The guidelines and the textbook are complementary. Background information and detailed discussion of the data that have provided the basis for the recommendations can be found in the relevant book chapter.

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 the availability of diagnostic equipment, the expertise of cardiologists and surgeons, especially in the field of valve repair and percutaneous intervention and, notably, the wishes of well-informed patients. Furthermore, owing to the lack of evidence-based data in the field of VHD, most recommendations are largely the result of expert consensus opinion. Therefore, deviations from these guidelines may be appropriate in certain clinical circumstances.

3. GENERAL COMMENTS

The aims of the evaluation of patients with VHD are to diagnose, quantify and assess the mechanism of VHD as well as its consequences. Decision making for intervention should be made by a 'Heart Team' with a particular expertise in VHD, comprising cardiologists, cardiac surgeons, imaging specialists, anaesthetists and, if needed, general practitioners, geriatricians and heart failure, electrophysiology or intensive care specialists. The 'Heart Team' approach is particularly advisable in the management of high-risk patients and is also important for other subsets, such as asymptomatic patients where the evaluation of valve reparability is a key component in decision making. The essential questions in the evaluation of a patient for valvular intervention are summarized in Table 3.

Table 3: Essential questions in the evaluation of patients for valvular intervention

Questions
• How severe is VHD?
• What is the aetiology of VHD?
• Does the patient have symptoms?
• Are symptoms related to valvular disease?
• Are any signs present in asymptomatic patients that indicate a worse outcome if the intervention is delayed?
• What are the patient's life expectancy[a] and expected quality of life?
• Do the expected benefits of intervention (versus spontaneous outcome) outweigh its risks?
• What is the optimal treatment modality? Surgical valve replacement (mechanical or biological), surgical valve repair, or catheter intervention?
• Are local resources (local experience and outcome data for a given intervention) optimal for the planned intervention?
• What are the patient's wishes?

VHD: valvular heart disease.
[a]Life expectancy should be estimated according to age, sex, comorbidities, and country-specific life expectancy.

3.1 Patient evaluation

Precise evaluation of the patient's history and symptomatic status as well as proper physical examination, in particular auscultation and search for heart failure signs, are crucial for the diagnosis and management of VHD. In addition, assessment of the extracardiac condition—comorbidities and general condition—require particular attention.

3.1.1 Echocardiography. Following adequate clinical evaluation, echocardiography is the key technique used to confirm the diagnosis of VHD as well as to assess its severity and prognosis. It should be performed and interpreted by properly trained personnel [1].

Echocardiographic criteria for the definition of severe valve stenosis and regurgitation are addressed in specific documents [2–4]. Recommendations for stenotic lesions are indicated in the corresponding sections and quantification of regurgitant lesions is summarized in Table 4. An integrated approach including various criteria is strongly recommended instead of referring to single measurements. Echocardiography is also key to assess valve morphology and function as well as to evaluate the feasibility and indications of a specific intervention.

Indices of left ventricular (LV) enlargement and function are strong prognostic factors. Pulmonary artery pressure should be estimated as well as right ventricular (RV) function [5]. Transoesophageal echocardiography (TOE) should be considered when transthoracic echocardiography (TTE) is of suboptimal quality or when thrombosis, prosthetic valve dysfunction or endocarditis is suspected. Intraprocedural TOE is used to guide percutaneous mitral and aortic valve interventions and to monitor the results of all surgical valve operations and percutaneous valve implantation or repair.

3.1.2 Other non-invasive investigations.

3.1.2.1 Stress testing. The primary purpose of exercise testing is to unmask the objective occurrence of symptoms in patients who claim to be asymptomatic or have non-specific symptoms, and is especially useful for risk stratification in aortic stenosis [8]. Exercise testing will also determine the level of recommended physical activity, including participation in sports.

Exercise echocardiography may identify the cardiac origin of dyspnoea. The prognostic impact has been shown mainly for aortic stenosis and mitral regurgitation [9].

The search for flow reserve (also called 'contractile reserve') using low-dose dobutamine stress echocardiography is useful for assessing aortic stenosis severity and for operative risk stratification in low-gradient aortic stenosis with impaired LV function as well as to assess the potential of reverse remodelling in patients with heart failure and functional mitral regurgitation after a mitral valve procedure [10, 11].

3.1.2.2 Cardiac magnetic resonance. In patients with inadequate echocardiographic quality or discrepant results, cardiac magnetic resonance (CMR) should be used to assess the severity of valvular

Table 4: Echocardiographic criteria for the definition of severe valve regurgitation: an integrative approach (adapted from Lancellotti *et al.* [2, 6, 7])

	Aortic regurgitation	Mitral regurgitation		Tricuspid regurgitation
Qualitative				
Valve morphology	Abnormal/flail/large coaptation defect	Flail leaflet/ruptured papillary muscle/ large coaptation defect		Abnormal/flail/large coaptation defect
Colour flow regurgitant jet	Large in central jets, variable in eccentric jets[a]	Very large central jet or eccentric jet adhering, swirling, and reaching the posterior wall of the LA		Very large central jet or eccentric wall impinging jet[a]
CW signal of regurgitant jet	Dense	Dense/triangular		Dense/triangular with early peaking (peak <2 m/s in massive TR)
Other	Holodiastolic flow reversal in descending aorta (EDV >20 cm/s)	Large flow convergence zone[a]		–
Semiquantitative				
Vena contracta width (mm)	>6	≥7 (>8 for biplane)[b]		≥7[a]
Upstream vein flow[c]	–	Systolic pulmonary vein flow reversal		Systolic hepatic vein flow reversal
Inflow	–	E-wave dominant ≥1.5 m/s[d]		E-wave dominant ≥1 m/s[e]
Other	Pressure half-time <200 ms[f]	TVI mitral/TVI aortic >1.4		PISA radius >9 mm[g]
Quantitative		Primary	Secondary[h]	
EROA (mm^2)	≥30	≥40	≥20	≥40
Regurgitant volume (mL/beat)	≥60	≥60	≥30	≥45
+ enlargement of cardiac chambers/vessels	LV	LV, LA		RV, RA, inferior vena cava

CW: continuous wave; EDV: end-diastolic velocity; EROA: effective regurgitant orifice area; LA: left atrium/atrial; LV: left ventricle/ventricular; PISA: proximal isovelocity surface area; RA: right atrium/right atrial; RV: right ventricle; TR: tricuspid regurgitation; TVI: time–velocity integral.
[a]At a Nyquist limit of 50–60 cm/s.
[b]For average between apical four- and two-chamber views.
[c]Unless other reasons for systolic blunting (atrial fibrillation, elevated atrial pressure).
[d]In the absence of other causes of elevated LA pressure and of mitral stenosis.
[e]In the absence of other causes of elevated RA pressure.
[f]Pressure half-time is shortened with increasing LV diastolic pressure, vasodilator therapy, and in patients with a dilated compliant aorta, or lengthened in chronic aortic regurgitation.
[g]Baseline Nyquist limit shift of 28 cm/s.
[h]Different thresholds are used in secondary mitral regurgitation where an EROA >20 mm^2 and regurgitant volume >30 ml identify a subset of patients at increased risk of cardiac events.

lesions, particularly regurgitant lesions, and to assess ventricular volumes, systolic function, abnormalities of the ascending aorta and myocardial fibrosis. CMR is the reference method for the evaluation of RV volumes and function and is therefore particularly useful to evaluate the consequences of tricuspid regurgitation [12].

3.1.2.3 Computed tomography. Multislice computed tomography (MSCT) may contribute to evaluation of the severity of valve disease, particularly in aortic stenosis [13, 14] and of the thoracic aorta. MSCT plays an important role in the workup of patients with VHD considered for transcatheter intervention, in particular transcatheter aortic valve implantation (TAVI), and provides valuable information for pre-procedural planning. Owing to its high negative predictive value, MSCT may be useful to rule out coronary artery disease (CAD) in patients who are at low risk of atherosclerosis.

3.1.2.4 Cinefluoroscopy. Cinefluoroscopy is particularly useful for assessing the kinetics of the occluders of a mechanical prosthesis.

3.1.2.5 Biomarkers. B-type natriuretic peptide (BNP) serum levels are related to New York Heart Association (NYHA) functional class and prognosis, particularly in aortic stenosis and mitral regurgitation [15]. Natriuretic peptides may be of value for risk stratification and timing of intervention, particularly in asymptomatic patients.

3.1.3 Invasive investigations.

3.1.3.1 Coronary angiography. Coronary angiography is indicated for the assessment of CAD when surgery or an intervention is planned, to determine if concomitant coronary revascularization is indicated (see following table of recommendations) [16]. Alternatively, coronary computed tomography (CT) can be used to rule out CAD in patients at low risk for the condition.

Management of CAD in patients with VHD (adapted from Windecker *et al.* [16])

Recommendations	Class[a]	Level[b]
Diagnosis of CAD		
Coronary angiography[c] is recommended before valve surgery in patients with severe VHD and any of the following: • history of cardiovascular disease • suspected myocardial ischaemia[d] • LV systolic dysfunction • in men >40 years of age and postmenopausal women • one or more cardiovascular risk factors.	I	C
Coronary angiography is recommended in the evaluation of moderate to severe secondary mitral regurgitation.	I	C
CT angiography should be considered as an alternative to coronary angiography before valve surgery in patients with severe VHD and low probability of CAD or in whom conventional coronary angiography is technically not feasible or associated with a high risk.	IIa	C
Indications for myocardial revascularization		
CABG is recommended in patients with a primary indication for aortic/mitral valve surgery and coronary artery diameter stenosis ≥70%.[e]	I	C
CABG should be considered in patients with a primary indication for aortic/mitral valve surgery and coronary artery diameter stenosis ≥50–70%.	IIa	C
PCI should be considered in patients with a primary indication to undergo TAVI and coronary artery diameter stenosis >70% in proximal segments.	IIa	C
PCI should be considered in patients with a primary indication to undergo transcatheter mitral valve interventions and coronary artery diameter stenosis >70% in proximal segments.	IIa	C

CABG: coronary artery bypass grafting; CAD: coronary artery disease; CT: computed tomography; LV: left ventricular; MSCT: multislice computed tomography; PCI: percutaneous coronary intervention; TAVI: transcatheter aortic valve implantation; VHD: valvular heart disease.

[a]Class of recommendation.

[b]Level of evidence.

[c]MSCT may be used to exclude CAD in patients who are at low risk of atherosclerosis.

[d]Chest pain, abnormal non-invasive testing.

[e]≥50% can be considered for left main stenosis.

3.1.3.2 Cardiac catheterization. The measurement of pressures and cardiac output or the assessment of ventricular performance and valvular regurgitation by ventricular angiography or aortography is restricted to situations where non-invasive evaluation is inconclusive or discordant with clinical findings. When elevated pulmonary pressure is the only criterion to support the indication for surgery, confirmation of echo data by invasive measurement is recommended.

3.1.4 Assessment of comorbidity. The choice of specific examinations to assess comorbidity is directed by the clinical evaluation.

3.2 Risk stratification

Risk stratification applies to any sort of intervention and is required for weighing the risk of intervention against the expected natural history of VHD as a basis for decision making. Most experience relates to surgery and TAVI. The EuroSCORE I (http://www.euroscore.org/calc.html) overestimates operative mortality and its calibration of risk is poor. Consequently, it should no longer be used to guide decision making. The EuroSCORE II and the Society of Thoracic Surgeons (STS) score (http://riskcalc.sts.org/stswebriskcalc/#/) more accurately discriminate high- and low-risk surgical patients and show better calibration to predict postoperative outcome after valvular surgery [17, 18]. Scores have major limitations for practical use by insufficiently considering disease severity and not including major risk factors such as frailty, porcelain aorta, chest radiation etc. While EuroSCORE I markedly overestimates 30-day mortality and should therefore be replaced by the better performing EuroSCORE II in this regard, it is nevertheless provided in this document for comparison, as it has been used in many TAVI studies/registries and may still be useful to identify the subgroups of patients for decision between intervention modalities and to predict 1-year mortality. Both scores have shown variable results in predicting the outcomes of intervention in TAVI but are useful for identifying low-risk patients for surgery. New scores have been developed to estimate the risk of 30-day mortality in patients undergoing TAVI, with better accuracy and discrimination, albeit with numerous limitations [19, 20].

Experience with risk stratification is being accumulated for other interventional procedures, such as mitral edge-to-edge repair. It remains essential not to rely on a single risk score figure when assessing patients or to determine unconditionally the indication and type of intervention. Patient's life expectancy, expected quality of life and patient preference should be considered, as well as local resources. The futility of interventions in patients unlikely to benefit from the treatment has to be taken into consideration, particularly for TAVI and mitral edge-to-edge repair [21]. The role of the Heart Team is essential to take all of these data into account and adopt a final decision on the best treatment strategy. Finally, the patient and family should be thoroughly informed and assisted in their decision on the best treatment option [22].

3.3 Special considerations in elderly patients

Poor mobility, as assessed by the 6-minute walk test, and oxygen dependency are the main factors associated with increased mortality after TAVI and other VHD treatments [23, 24]. The combination of severe lung disease, postoperative pain from sternotomy or thoracotomy and prolonged time under anaesthesia in patients undergoing traditional surgical aortic valve replacement (SAVR) may contribute to pulmonary complications. There is a

gradual relationship between the impairment of renal function and increased mortality after valvular surgery, TAVI and transcatheter mitral edge-to-edge repair [25], especially when glomerular filtration rate is < 30 ml/min. Coronary, cerebrovascular and peripheral artery disease have a negative impact on early and late survival after surgery and TAVI [22].

Besides specific organ comorbidities, there is growing interest in the assessment of frailty, an overall marker of impairment of functional, cognitive and nutritional status. Frailty is associated with increased morbidity and mortality after surgery and TAVI [26]. The assessment of frailty should not rely on a subjective approach, such as the 'eyeball test', but rather on a combination of different objective estimates. Several tools are available for assessing frailty [23, 26, 27].

3.4 Endocarditis prophylaxis

Antibiotic prophylaxis should be considered for high-risk procedures in patients with prosthetic valves, including transcatheter valves, or with repairs using prosthetic material and those with previous episodes of infective endocarditis [28]. Recommendations regarding dental and cutaneous hygiene and strict aseptic measures during any invasive procedures are advised in this population. Antibiotic prophylaxis should be considered in dental procedures involving manipulation of the gingival or periapical region of the teeth or manipulation of the oral mucosa [28].

3.5 Prophylaxis for rheumatic fever

Prevention of rheumatic heart disease should preferably be oriented towards preventing the first attack of acute rheumatic fever. Antibiotic treatment of group A *Streptococcus* sore throat is key in primary prevention. In patients with rheumatic heart disease, secondary long-term prophylaxis against rheumatic fever is recommended. Lifelong prophylaxis should be considered in high-risk patients according to the severity of VHD and exposure to group A *Streptococcus* [29–31].

3.6 Concept of the Heart Team and heart valve centres

The main purpose of heart valve centres as centres of excellence in the treatment of VHD is to deliver better quality of care. This is achieved through greater volumes associated with specialization of training, continuing education and clinical interest. Specialization will also result in timely referral of patients before irreversible adverse effects occur and evaluation of complex VHD conditions. Techniques with a steep learning curve may be performed with better results in hospitals with high volumes and more experience [32]. These main aspects are presented in Table 5.

A heart valve centre should have structured training programmes [32]. Surgeons and cardiologists performing any valve intervention should undergo focused training as part of their basic local board certification training. Learning new techniques should take place through mentoring to minimize the effects of the 'learning curve'.

The relationship between case volume and outcomes for surgery and transcatheter interventions is complex but should not be denied [33–35]. However, the precise numbers of procedures per individual operator or hospital required to provide high-quality care remain controversial and more scientific data are required before solid recommendations can be provided. Nevertheless, standards for provision of cardiac surgery that constitute the minimal core requirements have been released [36]. Experience in the full spectrum of surgical procedures—including valve replacement; aortic root surgery; mitral, tricuspid and aortic valve repair; repair of complicated valve endocarditis such as root abscess; treatment of atrial fibrillation as well as surgical myocardial revascularization—must be available. The spectrum of interventional procedures in addition to TAVI should include mitral valvuloplasty, mitral valve repair (edge-to-edge), closure of atrial septal defects, closure of paravalvular leaks and left atrial (LA) appendage closure as well as percutaneous coronary intervention (PCI). Expertise in interventional and surgical management of vascular diseases and complications must be available. Comprehensive recording of performance and patient outcome data at the level of the given heart valve centre is essential, as well as participation in national or ESC/EACTS registries.

Table 5: Recommended requirements of a heart valve centre (modified from Chambers *et al.* [32])

Requirements
Multidisciplinary teams with competencies in valve replacement, aortic root surgery, mitral, tricuspid and aortic valve repair, as well as transcatheter aortic and mitral valve techniques including reoperations and reinterventions. The Heart Teams must meet on a regular basis and work with standard operating procedures.
Imaging, including 3D and stress echocardiographic techniques, perioperative TOE, cardiac CT, MRI, and positron emission tomography-CT.
Regular consultation with community, other hospitals, and extracardiac departments, and between non-invasive cardiologists and surgeons and interventional cardiologists.
Back-up services including other cardiologists, cardiac surgeons, intensive care and other medical specialties.
Data review: • Robust internal audit processes including mortality and complications, repair rates, durability of repair, and reoperation rate with a minimum of 1-year follow-up. • Results available for review internally and externally. • Participation in national or European quality databases.

3D: three-dimensional; CT: computed tomography; MRI: magnetic resonance imaging; TOE: transoesophageal echocardiography.

3.7 Management of associated conditions

3.7.1 Coronary artery disease. The use of stress tests to detect CAD associated with severe valvular disease is discouraged because of their low diagnostic value and potential risks. A summary of the management of associated CAD is given in section 3.1.3.1 (see table of recommendations on the management of CAD in patients with VHD) and is detailed in specific guidelines [16].

3.7.2 Atrial fibrillation. Non-vitamin K antagonist oral anticoagulants (NOACs) are approved only for non-valvular atrial fibrillation, but there is no uniform definition of this term [37]. Recent subgroup analyses of randomized trials on atrial fibrillation support the use of rivaroxaban, apixaban, dabigatran and edoxaban in patients with aortic stenosis, aortic regurgitation or mitral regurgitation presenting with atrial fibrillation [38–41]. The use of NOACs is discouraged in patients who have atrial fibrillation associated with moderate to severe mitral stenosis, given the lack of data and the particularly high thromboembolic risk. Despite the absence of data, NOACs may be used in patients who have atrial fibrillation associated with an aortic bioprosthesis >3 months after implantation but are strictly contraindicated in patients with any mechanical prostheses [42, 43].

Surgical ablation of atrial fibrillation combined with mitral valve surgery is effective in reducing the incidence of atrial fibrillation, but at the expense of more frequent pacemaker implantation, and has no impact on short-term survival [44]. Surgical ablation should be considered in patients with symptomatic atrial fibrillation and may be considered in patients with asymptomatic atrial fibrillation if feasible with minimal risk. The decision should factor in other important variables, such as age, the duration of atrial fibrillation and LA size. Surgical excision or external clipping of the LA appendage may be considered combined with valvular surgery, although there is no evidence that it decreases thromboembolic risk. For patients with atrial fibrillation and risk factors for stroke, long-term oral anticoagulation is currently recommended, although surgical ablation of atrial fibrillation and/or surgical LA appendage excision or exclusion may have been performed [37]. Recommendations for the management of atrial fibrillation in VHD are summarized in the following table.

Key points

- Precise evaluation of the patient's history and symptomatic status as well as proper physical examination are crucial for the diagnosis and management of VHD.
- Echocardiography is the key technique to diagnose VHD and assess its severity and prognosis. Other non-invasive investigations such as stress testing, CMR, CT, fluoroscopy and biomarkers are complementary, and invasive investigation beyond preoperative coronary angiography is restricted to situations where non-invasive evaluation is inconclusive.
- Risk stratification is essential for decision making to weigh the risk of intervention against the expected natural history of VHD.
- Decision making in elderly patients requires special considerations, including life expectancy and expected quality of life, with regards to comorbidities and general condition (frailty).
- Heart valve centres with highly specialized multidisciplinary teams, comprehensive equipment and sufficient volumes of procedures are required to deliver high-quality care and provide adequate training.
- NOACs may be used in patients with atrial fibrillation and aortic stenosis, aortic regurgitation, mitral regurgitation or aortic bioprostheses >3 months after implantation but are contraindicated in mitral stenosis and mechanical valves.

Gaps in evidence

- Better tools for risk stratification need to be developed, particularly for the decision between surgery and catheter intervention and for the avoidance of futile interventions.

Management of atrial fibrillation in patients with VHD

Recommendations	Class[a]	Level[b]
Anticoagulation		
NOACs should be considered as an alternative to VKAs in patients with aortic stenosis, aortic regurgitation and mitral regurgitation presenting with atrial fibrillation [38–41].	IIa	B
NOACs should be considered as an alternative to VKAs after the third month of implantation in patients who have atrial fibrillation associated with a surgical or transcatheter aortic valve bioprosthesis.	IIa	C
The use of NOACs is not recommended in patients with atrial fibrillation and moderate to severe mitral stenosis.	III	C
NOACS are contraindicated in patients with a mechanical valve [45].	III	B
Surgical interventions		
Surgical ablation of atrial fibrillation should be considered in patients with symptomatic atrial fibrillation who undergo valve surgery [37].	IIa	A
Surgical ablation of atrial fibrillation may be considered in patients with asymptomatic atrial fibrillation who undergo valve surgery, if feasible, with minimal risk.	IIb	C
Surgical excision or external clipping of the LA appendage may be considered in patients undergoing valve surgery [46].	IIb	B

LA: left atrial; NOAC: non-vitamin K antagonist oral anticoagulant; VHD: valvular heart disease; VKA: vitamin K antagonist.
[a]Class of recommendation.
[b]Level of evidence.

- Minimum volumes of procedures per operator and per hospital that are required to achieve optimal treatment results need to be defined.
- The safety and efficacy of NOACs in patients with surgical or transcatheter bioprostheses in the first 3 months after implantation should be studied.

4. AORTIC REGURGITATION

Aortic regurgitation can be caused by primary disease of the aortic valve cusps and/or abnormalities of the aortic root and ascending aortic geometry. Degenerative tricuspid and bicuspid aortic regurgitation are the most common aetiologies in Western countries, accounting for approximately two-thirds of the underlying aetiology of aortic regurgitation in the Euro Heart Survey on VHD [47]. Other causes include infective and rheumatic endocarditis. Acute severe aortic regurgitation is mostly caused by infective endocarditis and less frequently by aortic dissection.

4.1 Evaluation

4.1.1 Echocardiography. Echocardiography (TTE/TOE) is the key examination to describe valve anatomy, quantify aortic regurgitation, evaluate its mechanisms, define the morphology of the aorta and determine the feasibility of valve-sparing aortic surgery or valve repair [48, 49].

Essential aspects of this evaluation include:

- Assessment of valve morphology: tricuspid, bicuspid, unicuspid or quadricuspid valve.
- Determination of the direction of the aortic regurgitation jet in the long-axis view (central or eccentric) and its origin in the short-axis view (central or commissural).
- Identification of the mechanism, following the same principle as for mitral regurgitation: normal cusps but insufficient coaptation due to dilatation of the aortic root with central jet (type 1), cusp prolapse with eccentric jet (type 2) or retraction with poor cusp tissue quality and large central or eccentric jet (type 3) [48].
- Quantification of aortic regurgitation should follow an integrated approach considering all qualitative, semi-quantitative and quantitative parameters [2, 6] (Table 4).
- Measurement of LV function and dimensions. Indexing LV diameters for body surface area (BSA) is recommended in patients with small body size (BSA <1.68 m^2) [50]. New parameters obtained by three-dimensional (3D) echocardiography, tissue Doppler and strain rate imaging may be useful, particularly in patients with borderline left ventricular ejection fraction (LVEF), where they may help in the decision for surgery [51].
- Measurement of the aortic root and ascending aorta in the 2-dimensional (2D) mode at four levels: annulus, sinuses of Valsalva, sinotubular junction and tubular ascending aorta [52]. Measurements are taken in the parasternal long-axis view from leading edge to leading edge at end diastole, except for the aortic annulus, which is measured in mid systole. As it will have surgical consequences, it is important to differentiate three phenotypes of the ascending aorta: aortic root aneurysms (sinuses of Valsalva >45 mm), tubular ascending aneurysm (sinuses of Valsalva <40–45 mm) and isolated aortic regurgitation (all diameters <40 mm). The calculation of indexed values has been recommended to account for body size [53].
- Definition of the anatomy of the aortic valve cusps and assessment of valve reparability should be provided by preoperative TOE if aortic valve repair or a valve-sparing surgery of the aortic root is considered.
- Intraoperative evaluation of the surgical result by TOE is mandatory in patients in whom the aortic valve is preserved or repaired in the procedure.

4.1.2 Computed tomography and cardiac magnetic resonance. CMR should be used to quantify the regurgitant fraction when echocardiographic measurements are equivocal. In patients with aortic dilatation, gated MSCT is recommended to assess the maximum diameter. CMR can be used for follow-up, but indication for surgery should preferably be based on CT measurements. Different methods of aortic measurements have been reported and this may result in diameter discrepancies of 2–3 mm that could influence therapeutic management. To improve reproducibility, it is recommended to measure diameters using the inner-inner edge technique at end diastole on the strictly transverse plane by double oblique reconstruction perpendicular to the axis of blood flow of the corresponding segment. Diameters at the annulus, sinus of Valsalva, sinotubular junction, tubular ascending aorta and aortic arch level should be reported. Maximum root diameter should be taken from sinus to sinus rather than sinus to commissure diameter, as it correlates more closely to long-axis leading edge to leading edge echo maximum diameters [54, 55].

4.2 Indications for intervention

Acute aortic regurgitation may require urgent surgery. It is primarily caused by infective endocarditis and aortic dissections. Specific guidelines deal with these entities [28, 56]. The indications for intervention in chronic aortic regurgitation are summarized on the next page (recommendations on indications for surgery in severe aortic regurgitation and aortic root disease) and in Figure 1 and may be related to symptoms, status of the LV or dilatation of the aorta.

In symptomatic patients, surgery is recommended irrespective of the LVEF value, except for extreme cases, as long as aortic regurgitation is severe and the operative risk is not prohibitive [57]. In asymptomatic patients with severe aortic regurgitation, impairment of LV function (ejection fraction ≤50%) and LV enlargement with an LV end-diastolic diameter (LVEDD) >70 mm or left ventricular end-systolic diameter (LVESD) >50 mm are associated with worse outcome and surgery should therefore be pursued when these cut-offs are reached [58]. In patients with small body size, LVESD should be related to BSA and a cut-off of 25 mm/m^2 BSA appears to be more appropriate [50]. In patients not reaching the thresholds for surgery, close follow-up is needed and exercise testing should be performed to identify borderline symptomatic patients. In truly asymptomatic patients, regular assessment of LV function and physical condition are crucial to identify the optimal time for surgery. A rapid progression of ventricular dimensions or decline in ventricular function on serial testing is a reason to consider surgery.

In patients with a dilated aorta, the rationale for surgery has been best defined in patients with Marfan syndrome and root

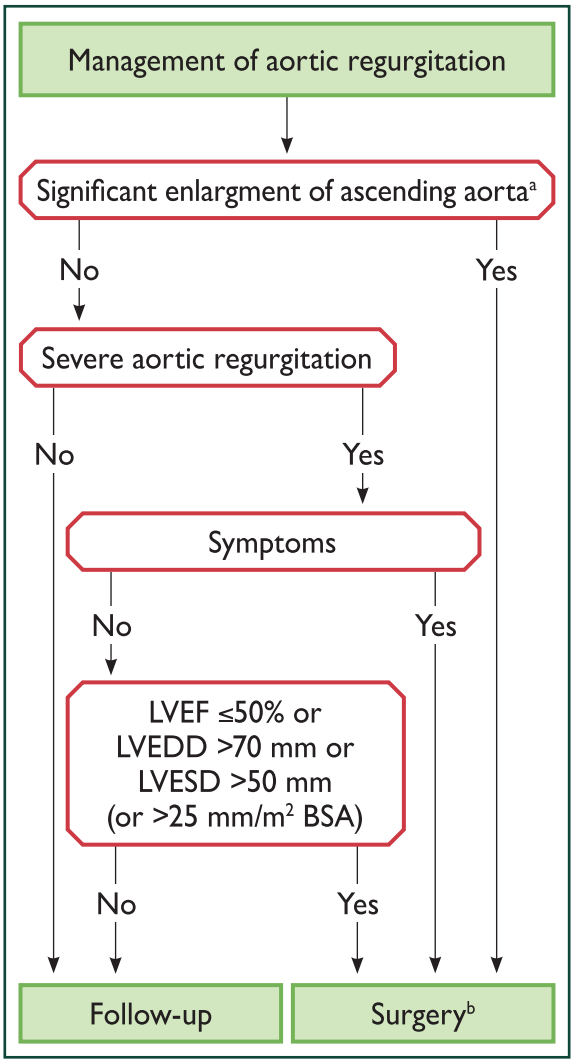

Figure 1: Management of aortic regurgitation. AR: aortic regurgitation; BSA: body surface area; LVEDD: left ventricle end-diastolic diameter; LVEF: left ventricular ejection fraction; LVESD: left ventricle end-systolic diameter.
[a]See table of recommendations on indications for surgery in severe aortic regurgitation and aortic root disease for definition.
[b]Surgery should also be considered if significant changes in LV or aortic size occur during follow-up (see table of recommendations on indications for surgery in severe aortic regurgitation and aortic root disease in section 4.2).

dilation [59]. Root aneurysms need to have root replacement, with or without preservation of the native aortic valve, but definitely with coronary reimplantation. In contrast, tubular ascending aortic aneurysms require only a supracommissural tube graft replacement without coronary reimplantation. In patients with aortic diameters borderline for aortic surgery, the family history, age and anticipated risk of the procedure should be taken into consideration. In individuals with a bicuspid aortic valve and no significant valve regurgitation, prophylactic surgery should be considered with aortic diameters ≥55 mm or ≥ 50 mm when additional risk factors or coarctation are present (see table of recommendations on indications for surgery in severe aortic regurgitation and aortic root disease). Surgery is indicated in all patients with Marfan syndrome and a maximal aortic diameter ≥50 mm. In patients with Marfan syndrome and additional risk factors and in patients with a *TGFBR1* or *TGFBR2* mutation (including Loeys–Dietz syndrome),

Indications for surgery in (A) severe aortic regurgitation and (B) aortic root disease (irrespective of the severity of aortic regurgitation)

Indications for surgery	Class[a]	Level[b]
A. Severe aortic regurgitation		
Surgery is indicated in symptomatic patients [57, 58, 66, 67].	I	B
Surgery is indicated in asymptomatic patients with resting LVEF ≤50% [57, 58].	I	B
Surgery is indicated in patients undergoing CABG or surgery of the ascending aorta or of another valve.	I	C
Heart Team discussion is recommended in selected patients[c] in whom aortic valve repair may be a feasible alternative to valve replacement.	I	C
Surgery should be considered in asymptomatic patients with resting ejection fraction >50% with severe LV dilatation: LVEDD >70 mm or LVESD >50 mm (or LVESD >25 mm/m^2 BSA in patients with small body size) [58, 66].	IIa	B
B. Aortic root or tubular ascending aortic aneurysm[d] (irrespective of the severity of aortic regurgitation)		
Aortic valve repair, using the reimplantation or remodelling with aortic annuloplasty technique, is recommended in young patients 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 ascending aortic diameter ≥50 mm.	I	C
Surgery should be considered in patients who have aortic root disease with maximal ascending aortic diameter: • ≥45 mm in the presence of Marfan syndrome and additional risk factors[e] or patients with a *TGFBR1* or *TGFBR2* mutation (including Loeys–Dietz syndrome).[f] • ≥50 mm in the presence of a bicuspid valve with additional risk factors[e] or coarctation. • ≥55 mm for all other patients.	IIa	C
When surgery is primarily indicated for the aortic valve, replacement of the aortic root or tubular ascending aorta should be considered when ≥45 mm, particularly in the presence of a bicuspid valve.[g]	IIa	C

BSA: body surface area; CABG: coronary artery bypass grafting; CT: computed tomography; ECG: electrocardiogram; LV: left ventricular; LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameter.
[a]Class of recommendation.
[b]Level of evidence.
[c]Patients with pliable non-calcified tricuspid or bicuspid valves who have a type I (enlargement of the aortic root with normal cusp motion) or type II (cusp prolapse) mechanism of aortic regurgitation [6, 48, 49].
[d]For clinical decision making, dimensions of the aorta should be confirmed by ECG-gated CT measurement.
[e]Family history of aortic dissection (or personal history of spontaneous vascular dissection), severe aortic regurgitation or mitral regurgitation, desire for pregnancy, systemic 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).
[f]A lower threshold of 40 mm may be considered in women with low BSA, in patients with a *TGFBR2* mutation or in patients with severe extra-aortic features [60].
[g]Considering age, BSA, aetiology of the valvular disease, presence of a bicuspid aortic valve and intraoperative shape and thickness of the ascending aorta.

surgery should be considered at a maximal aortic diameter ≥45 mm [60]. In the latter group, women with low BSA, patients with a *TGFBR2* mutation or patients with severe extra-aortic features appear to be at particularly high risk and surgery may be considered already at a lower threshold of 40 mm [60]. In aortic roots ≥55 mm, surgery should be considered irrespective of the degree of aortic regurgitation and type of valve pathology [61]. For patients who have an indication for aortic valve surgery, an aortic diameter ≥45 mm is considered to indicate concomitant surgery of the aortic root or tubular ascending aorta. The patient's stature, the aetiology of the valvular disease (bicuspid valve) and the intraoperative shape and wall thickness of the ascending aorta should be taken into account for individual decisions.

Although valve replacement is the standard procedure in the majority of patients with aortic regurgitation, valve repair or valve-sparing surgery should be considered in patients with pliable non-calcified tricuspid or bicuspid valves who have a type I (enlargement of the aortic root with normal cusp motion) or type II (cusp prolapse) mechanism of aortic regurgitation [6, 48, 49]. In experienced centres, valve-sparing root replacement and valve repair, when feasible, yield good long-term results with low rates of valve-related events as well as better quality of life [62–65]. The choice of the surgical procedure should be adapted to the experience of the team, the presence of an aortic root aneurysm, characteristics of the cusps, life expectancy and desired anticoagulation status. Patients in whom the Heart Team identifies the aortic valve to be repairable should be referred to appropriate surgical teams for the procedure.

4.3 Medical therapy

Medical therapy can provide symptomatic improvement in individuals with chronic severe aortic regurgitation in whom surgery is not feasible. In patients who undergo surgery but continue to suffer from heart failure or hypertension, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs) and beta-blockers are useful [68, 69].

In patients with Marfan syndrome, beta-blockers and/or losartan may slow aortic root dilatation and reduce the risk of aortic complications and should be considered before and after surgery [70–72]. By analogy, while there are no studies that provide evidence, it is common clinical practice to advise beta-blocker or losartan therapy in patients with bicuspid aortic valve if the aortic root and/or ascending aorta is dilated.

Women with Marfan syndrome and an aortic diameter >45 mm are strongly discouraged from becoming pregnant without prior repair because of the high risk of dissection. Although an aortic diameter <40 mm is rarely associated with aortic dissection, a completely safe diameter does not exist. With an aorta between 40 and 45 mm, previous aortic growth and family history are important for advising pregnancy with or without aortic repair [73]. Although the actual risk of dissection is not well-documented in the setting of bicuspid valves, counselling against pregnancy is recommended in the setting of aortic diameters >50 mm [74].

The level of physical and sports activity in the presence of a dilated aorta remains a matter of clinical judgement in the absence of evidence. Current guidelines are very restrictive, particularly regarding isometric exercise, to avoid a catastrophic event [75]. This attitude is clearly justified in the presence of connective tissue disease.

Given the family risk of thoracic aortic aneurysms, screening and referral for genetic testing of the patient's first-degree relatives with appropriate imaging studies is indicated in patients with connective tissue disease. For patients with bicuspid valves it is appropriate to have an echocardiographic screening of first-degree relatives.

4.4 Serial testing

All asymptomatic patients with severe aortic regurgitation and normal LV function should be seen for follow-up at least every year. In patients with a first diagnosis, or if LV diameter and/or ejection fraction show significant changes or come close to thresholds for surgery, follow-up should be continued at 3–6-month intervals. In inconclusive cases, BNP may be helpful, as its elevation during follow-up has been related to deterioration of LV function [76]. Patients with mild to moderate aortic regurgitation can be reviewed on a yearly basis and echocardiography performed every 2 years.

If the ascending aorta is dilated (>40 mm) it is recommended to perform CT or CMR. Follow-up assessment of the aortic dimension should be performed using echocardiography and/or CMR. Any increase >3 mm should be validated by CT angiography/CMR and compared to baseline data.

4.5 Special patient populations

If aortic regurgitation requiring surgery is associated with severe mitral regurgitation, both should be addressed during the same operation.

In patients with moderate aortic regurgitation who undergo coronary artery bypass grafting (CABG) or mitral valve surgery, the decision to treat the aortic valve is controversial, as data show that progression of moderate aortic regurgitation is very slow in patients without aortic dilatation [77]. The Heart Team should decide based on the aetiology of aortic regurgitation, other clinical factors, the life expectancy of the patient and the patient's operative risk.

Key points

- The evaluation of aortic regurgitation requires consideration of valve morphology and the mechanism and severity of regurgitation, including careful assessment of aortic dilatation.
- In asymptomatic patients with severe aortic regurgitation, careful follow-up of symptomatic status and LV size and function is mandatory.
- The strongest indication for valve surgery is the presence of symptoms (spontaneous or on exercise testing) and/or the documentation of LVEF <50% and/or end-systolic diameter >50 mm.
- In patients with a dilated aorta, definition of the aortic pathology and accurate measurements of aortic diameters are crucial to guide the timing and type of surgery.
- Aortic valve repair and valve-sparing aortic surgery instead of aortic valve replacement should be considered in selected cases in experienced centres.

Gaps in evidence

- The impact of earlier markers of LV dysfunction on postoperative outcome requires further research.
- Criteria for the decision between valve replacement and valve repair must still be refined.

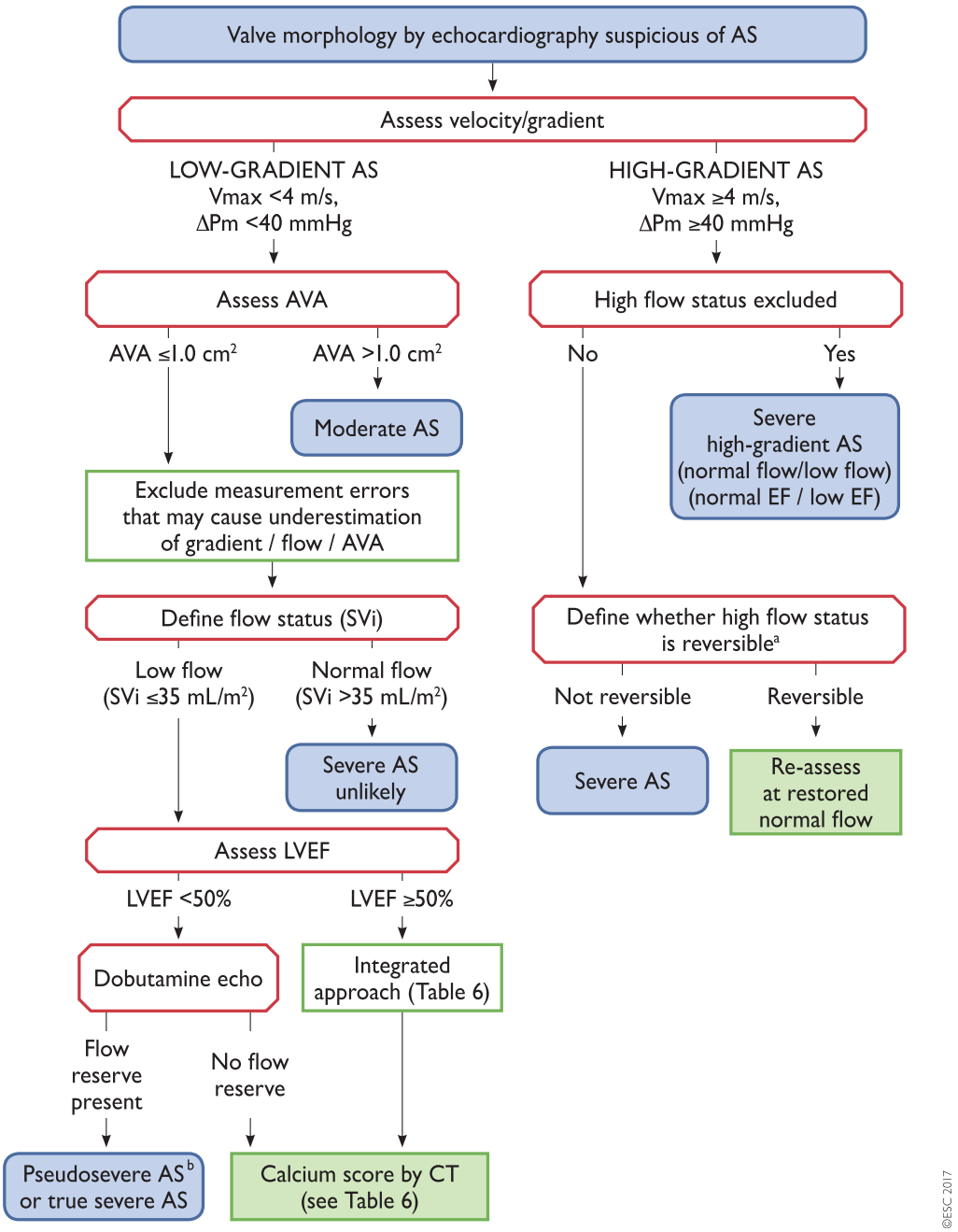

Figure 2: Stepwise integrated approach for the assessment of aortic stenosis severity (modified from Baumgartner *et al.* [4]). [a]High flow may be reversible in settings such as anaemia, hyperthyroidism, arteriovenous shunts. [b]Pseudosevere AS is defined by an increase to an AVA >1.0 cm^2 with flow normalization.
ΔPm: mean transvalvular pressure gradient; AS: aortic stenosis; AVA: aortic valve area; CT: computed tomography; EF: ejection fraction; LVEF: left ventricular ejection fraction; SVi: stroke volume index; Vmax: peak transvalvular velocity.

- Potential differences in the risk of aortic complications depending on subtypes of aortic aneurysms (site and morphology) should be studied.
- The effect of medical treatment on aortic enlargement in patients with bicuspid aortic valve needs to be studied.

5. AORTIC STENOSIS

Aortic stenosis is the most common primary valve disease leading to surgery or catheter intervention in Europe and North America, with a growing prevalence due to the ageing population.

5.1 Evaluation

5.1.1 Echocardiography. Echocardiography is the key diagnostic tool. It confirms the presence of aortic stenosis; assesses the degree of valve calcification, LV function and wall thickness; detects the presence of other associated valve disease or aortic pathology and provides prognostic information. Doppler echocardiography is the preferred technique for assessing the severity of aortic stenosis [4].

Figure 2 and Table 6 provide a practical stepwise approach for the assessment of aortic stenosis severity. Details can be found in a recent position paper from the European Association of Cardiovascular Imaging [4].

Table 6: Criteria that increase the likelihood of severe aortic stenosis in patients with AVA <1.0 cm^2 and mean gradient <40 mmHg in the presence of preserved ejection fraction (modified from Baumgartner *et al.* [4])

Criteria	
Clinical criteria	• Typical symptoms without other explanation • Elderly patient (>70 years)
Qualitative imaging data	• LV hypertrophy (additional history of hypertension to be considered) • Reduced LV longitudinal function without other explanation
Quantitative imaging data	• Mean gradient 30–40 mmHg[a]
	• AVA ≤0.8 cm^2
	• Low flow (SVi <35 mL/m^2) confirmed by techniques other than standard Doppler technique (LVOT measurement by 3D TOE or MSCT; CMR, invasive data)
	• Calcium score by MSCT[b] Severe aortic stenosis very likely: men ≥3000; women ≥1600 Severe aortic stenosis likely: men ≥2000; women ≥1200 Severe aortic stenosis unlikely: men <1600; women <800

3D: three-dimensional; AVA: aortic valve area; CMR: cardiovascular magnetic resonance; LV: left ventricular; LVOT: left ventricular outflow tract; MSCT: multi-slice computed tomography; SVi: stroke volume index; TOE: transoesophageal echocardiography.
[a]Haemodynamics measured when the patient is normotensive.
[b]Values are given in arbitrary units using Agatston method for quantification of valve calcification.

Although valve area represents, from a theoretical perspective, the ideal measurement for assessing the severity of aortic stenosis, it has technical limitations in clinical practice. It must, for clinical decision making, always be considered together with flow rate, mean pressure gradient (the most robust measurement), ventricular function, size and wall thickness, degree of valve calcification, blood pressure and functional status. Hypertensive patients should be reassessed when normotensive [4]. Four categories of aortic stenosis can be defined:

- High-gradient aortic stenosis (valve area <1 cm^2, mean gradient >40 mmHg). Severe aortic stenosis can be assumed irrespective of whether LVEF and flow are normal or reduced.
- Low-flow, low-gradient aortic stenosis with reduced ejection fraction [valve area <1 cm^2, mean gradient <40 mmHg, ejection fraction <50%, stroke volume index (SVi) ≤35 ml/m^2]. Low-dose dobutamine echocardiography is recommended in this setting to distinguish truly severe aortic stenosis from pseudosevere aortic stenosis, which is defined by an increase to an aortic valve area (AVA) of >1.0 cm^2 with flow normalization. In addition, the presence of flow reserve (also termed contractile reserve; increase of stroke volume >20%) has prognostic implications because it is associated with better outcome [10, 78].
- Low-flow, low-gradient aortic stenosis with preserved ejection fraction (valve area <1 cm^2, mean gradient <40 mmHg, ejection fraction ≥50%, SVi ≤35 ml/m^2). This is typically encountered in the elderly and is associated with small ventricular size, marked LV hypertrophy and frequently a history of hypertension [79,80]. The diagnosis of severe aortic stenosis in this setting remains challenging and requires careful exclusion of measurement errors and other reasons for such echocardiographic findings (Table 6). The degree of valve calcification by MSCT is related to aortic stenosis severity and outcome [13,14,81]. Its assessment has therefore gained increasing importance in this setting.
- Normal-flow, low-gradient aortic stenosis with preserved ejection fraction (valve area <1 cm^2, mean gradient <40 mmHg, ejection fraction ≥50%, SVi >35 m^2). These patients will in general have only moderate aortic stenosis [14, 82–84].

5.1.2 Additional diagnostic aspects, including assessment of prognostic parameters. Exercise testing is recommended in physically active patients for unmasking symptoms and for risk stratification of asymptomatic patients with severe aortic stenosis [85].

Exercise stress echocardiography may provide prognostic information in asymptomatic severe aortic stenosis by assessing the increase in mean pressure gradient and change in LV function during exercise [86].

TOE provides additional evaluation of concomitant mitral valve abnormalities. It has gained importance in the assessment before TAVI and after TAVI or surgical procedures [87].

MSCT and CMR provide additional information on the dimensions and geometry of the aortic root and ascending aorta and the extent of calcification. It has become particularly important for the quantification of valve calcification when assessing aortic stenosis severity in low-gradient aortic stenosis [13, 14, 81]. CMR may be useful for the detection and quantification of myocardial fibrosis, providing additional prognostic information regardless of the presence of CAD [88].

Natriuretic peptides have been shown to predict symptom-free survival and outcome in normal and low-flow severe aortic stenosis [89, 90] and may be useful in asymptomatic patients to determine optimal timing of intervention.

Retrograde LV catheterization to assess the severity of aortic stenosis is no longer routinely performed. Its use is restricted to patients with inconclusive non-invasive investigations.

5.1.3 Diagnostic workup before transcatheter aortic valve implantation. MSCT is the preferred imaging tool to assess the anatomy and dimensions of the aortic root, size and shape of the aortic valve annulus, its distance to the coronary ostia, the distribution of calcifications and the number of aortic valve cusps. It is essential to evaluate the feasibility of the various access routes, as this provides information on minimal luminal diameters, atherosclerotic plaque burden, the presence of aneurysms or thrombi, vessel tortuosity and thoracic and LV apex anatomy. CMR—as an alternative technique—is, in this context, inferior to MSCT with regards to assessment of inner vessel dimensions and calcifications. 3D TOE can be used to determine aortic annulus dimensions but remains more operator- and image quality–dependent than MSCT. However, TOE is an important tool for monitoring the procedure and evaluating the results, especially if complications occur.

5.2 Indications for intervention

The indications for aortic valve interventions are summarized on the next page (see table of indications for intervention in aortic stenosis and recommendations for the choice of intervention mode) and in Table 7 and are illustrated in Figure 3.

5.2.1 Indications for intervention in symptomatic aortic stenosis. Early therapy should be strongly recommended in all symptomatic patients with severe aortic stenosis because of their dismal spontaneous prognosis. The only exceptions are patients with severe comorbidities indicating a survival of < 1 year and patients in whom severe comorbidities or their general condition at an advanced age make it unlikely that the intervention will improve quality of life or survival.

As long as the mean gradient remains >40 mmHg, there is virtually no lower ejection fraction limit for intervention, whether surgery or TAVI. The management of patients with low-gradient aortic stenosis is more challenging:

- In patients with low-flow, low-gradient aortic stenosis and reduced ejection fraction in whom the depressed ejection fraction is predominantly caused by excessive afterload, LV function usually improves after intervention [10,104]. Conversely, improvement in LV function after intervention is uncertain if the primary cause is scarring due to extensive myocardial infarction or cardiomyopathy. Intervention is definitely advised when severe aortic stenosis is confirmed at increasing flow (true severe aortic stenosis) [10], while patients who are classified as having pseudosevere aortic stenosis at increasing flow should receive conventional treatment for heart failure [105]. Although the outcome of patients without flow reserve is compromised by a higher operative mortality, SAVR (as well as TAVI) has also been shown to improve ejection fraction and clinical status in such patients [10,78,104]. Decision making should take into account the clinical condition (in particular the comorbidities), the degree of valve calcification, the extent of coronary disease and the feasibility of concomitant or staged revascularization. The

Table 7: Aspects to be considered by the Heart Team for the decision between SAVR and TAVI in patients at increased surgical risk (see Table of Recommendations in section 5.2.)

	Favours TAVI	Favours SAVR
Clinical characteristics		
STS/EuroSCORE II <4% (logistic EuroSCORE I <10%)[a]		+
STS/EuroSCORE II ≥4% (logistic EuroSCORE I ≥10%)[a]	+	
Presence of severe comorbidity (not adequately reflected by scores)	+	
Age <75 years		+
Age ≥75 years	+	
Previous cardiac surgery	+	
Frailty[b]	+	
Restricted mobility and conditions that may affect the rehabilitation process after the procedure	+	
Suspicion of endocarditis		+
Anatomical and technical aspects		
Favourable access for transfemoral TAVI	+	
Unfavourable access (any) for TAVI		+
Sequelae of chest radiation	+	
Porcelain aorta	+	
Presence of intact coronary bypass grafts at risk when sternotomy is performed	+	
Expected patient–prosthesis mismatch	+	
Severe chest deformation or scoliosis	+	
Short distance between coronary ostia and aortic valve annulus		+
Size of aortic valve annulus out of range for TAVI		+
Aortic root morphology unfavourable for TAVI		+
Valve morphology (bicuspid, degree of calcification, calcification pattern) unfavourable for TAVI		+
Presence of thrombi in aorta or LV		+
Cardiac conditions in addition to aortic stenosis that require consideration for concomitant intervention		
Severe CAD requiring revascularization by CABG		+
Severe primary mitral valve disease, which could be treated surgically		+
Severe tricuspid valve disease		+
Aneurysm of the ascending aorta		+
Septal hypertrophy requiring myectomy		+

CABG: coronary artery bypass grafting; CAD: coronary artery disease; EuroSCORE: European System for Cardiac Operative Risk Evaluation; LV: left ventricle; SAVR: surgical aortic valve replacement; STS: Society of Thoracic Surgeons; TAVI: transcatheter aortic valve implantation.

[a]STS score (calculator: http://riskcalc.sts.org/stswebriskcalc/#/calculate); EuroSCORE II (calculator: http://www.euroscore.org/calc.html); logistic EuroSCORE I (calculator: http://www.euroscore.org/calcge.html); scores have major limitations for practical use in this setting by insufficiently considering disease severity and not including major risk factors such as frailty, porcelain aorta, chest radiation etc [103]. EuroSCORE I markedly overestimates 30-day mortality and should therefore be replaced by the better performing EuroSCORE II with this regard; it is nevertheless provided here for comparison as it has been used in many TAVI studies/registries and may still be useful to identify the subgroups of patients for decision between intervention modalities and to predict 1-year mortality.

[b]See section 3.3, general comments, for frailty assessment.

Indications for intervention in aortic stenosis and recommendations for the choice of intervention mode

A) Symptomatic aortic stenosis	Class[a]	Level[b]
Intervention is indicated in symptomatic patients with severe, high-gradient aortic stenosis (mean gradient ≥40 mmHg or peak velocity ≥4.0 m/s) [91–93].	I	B
Intervention is indicated in symptomatic patients with severe low-flow, low-gradient (<40 mmHg) aortic stenosis with reduced ejection fraction and evidence of flow (contractile) reserve excluding pseudosevere aortic stenosis.	I	C
Intervention should be considered in symptomatic patients with low-flow, low-gradient (<40 mmHg) aortic stenosis with normal ejection fraction after careful confirmation of severe aortic stenosis[c] (see Figure 2 and Table 6).	IIa	C
Intervention should be considered in symptomatic patients with low-flow, low-gradient aortic stenosis and reduced ejection fraction without flow (contractile) reserve, particularly when CT calcium scoring confirms severe aortic stenosis.	IIa	C
Intervention should not be performed in patients with severe comorbidities when the intervention is unlikely to improve quality of life or survival.	III	C
B) Choice of intervention in symptomatic aortic stenosis		
Aortic valve interventions should only be performed in centres with both departments of cardiology and cardiac surgery on site and with structured collaboration between the two, including a Heart Team (heart valve centres).	I	C
The choice for intervention must be based on careful individual evaluation of technical suitability and weighing of risks and benefits of each modality (aspects to be considered are listed in Table 7). In addition, the local expertise and outcomes data for the given intervention must be taken into account.	I	C
SAVR is recommended in patients at low surgical risk (STS or EuroSCORE II <4% or logistic EuroSCORE I <10%[d] and no other risk factors not included in these scores, such as frailty, porcelain aorta, sequelae of chest radiation) [93].	I	B
TAVI is recommended in patients who are not suitable for SAVR as assessed by the Heart Team [91, 94].	I	B
In patients who are at increased surgical risk (STS or EuroSCORE II ≥4% or logistic EuroSCORE I ≥10%[d] or other risk factors not included in these scores such as frailty, porcelain aorta, sequelae of chest radiation), the decision between SAVR and TAVI should be made by the Heart Team according to the individual patient characteristics (see Table 7), with TAVI being favoured in elderly patients suitable for transfemoral access [91, 94–102].	I	B
Balloon aortic valvotomy may be considered as a bridge to SAVR or TAVI in haemodynamically unstable patients or in patients with symptomatic severe aortic stenosis who require urgent major non-cardiac surgery.	IIb	C
Balloon aortic valvotomy may be considered as a diagnostic means in patients with severe aortic stenosis or other potential causes for symptoms (i.e. lung disease) and in patients with severe myocardial dysfunction, pre-renal insufficiency or other organ dysfunction that may be reversible with balloon aortic valvotomy when performed in centres that can escalate to TAVI.	IIb	C
C) Asymptomatic patients with severe aortic stenosis (refers only to patients eligible for surgical valve replacement)		
SAVR is indicated in asymptomatic patients with severe aortic stenosis and systolic LV dysfunction (LVEF <50%) not due to another cause.	I	C
SAVR is indicated in asymptomatic patients with severe aortic stenosis and an abnormal exercise test showing symptoms on exercise clearly related to aortic stenosis.	I	C
SAVR should be considered in asymptomatic patients with severe aortic stenosis and an abnormal exercise test showing a decrease in blood pressure below baseline.	IIa	C
SAVR should be considered in asymptomatic patients with normal ejection fraction 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 aortic stenosis 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 (>threefold age- and sex-corrected normal range) confirmed by repeated measurements without other explanations • Severe pulmonary hypertension (systolic pulmonary artery pressure at rest >60 mmHg confirmed by invasive measurement) without other explanation.	IIa	C

Continued

D) Concomitant aortic valve surgery at the time of other cardiac/ascending aorta surgery		
SAVR is indicated in patients with severe aortic stenosis undergoing CABG or surgery of the ascending aorta or of another valve.	I	C
SAVR should be considered in patients with moderate aortic stenosis[e] undergoing CABG or surgery of the ascending aorta or of another valve after Heart Team decision.	IIa	C

BNP: B-type natriuretic peptide; CABG, coronary artery bypass grafting; CT: computed tomography; EuroSCORE: European System for Cardiac Operative Risk Evaluation; LV: left ventricular; LVEF: left ventricular ejection fraction; SAVR: surgical aortic valve replacement; STS: Society of Thoracic Surgeons; TAVI: transcatheter aortic valve implantation; V_{max}: peak transvalvular velocity.

[a]Class of recommendation.

[b]Level of evidence.

[c]In patients with a small valve area but low gradient despite preserved LVEF, explanations for this finding other than the presence of severe aortic stenosis are frequent and must be carefully excluded. See Figure 2 and Table 6.

[d]STS score (calculator: http://riskcalc.sts.org/stswebriskcalc/#/calculate); EuroSCORE II (calculator: http://www.euroscore.org/calc.html); logistic EuroSCORE I (calculator: http://www.euroscore.org/calcge.html); scores have major limitations for practical use in this setting by insufficiently considering disease severity and not including major risk factors such as frailty, porcelain aorta, chest radiation, etc [103]. EuroSCORE I markedly overestimates 30-day mortality and should therefore be replaced by the better-performing EuroSCORE II with this regard; it is nevertheless provided here for comparison, as it has been used in many TAVI studies/registries and may still be useful to identify the subgroups of patients for decision between intervention modalities and to predict 1-year mortality.

[e]Moderate aortic stenosis is defined as a valve area of 1.0–1.5 cm^2 or a mean aortic gradient of 25–40 mmHg in the presence of normal flow conditions. However, clinical judgement is required.

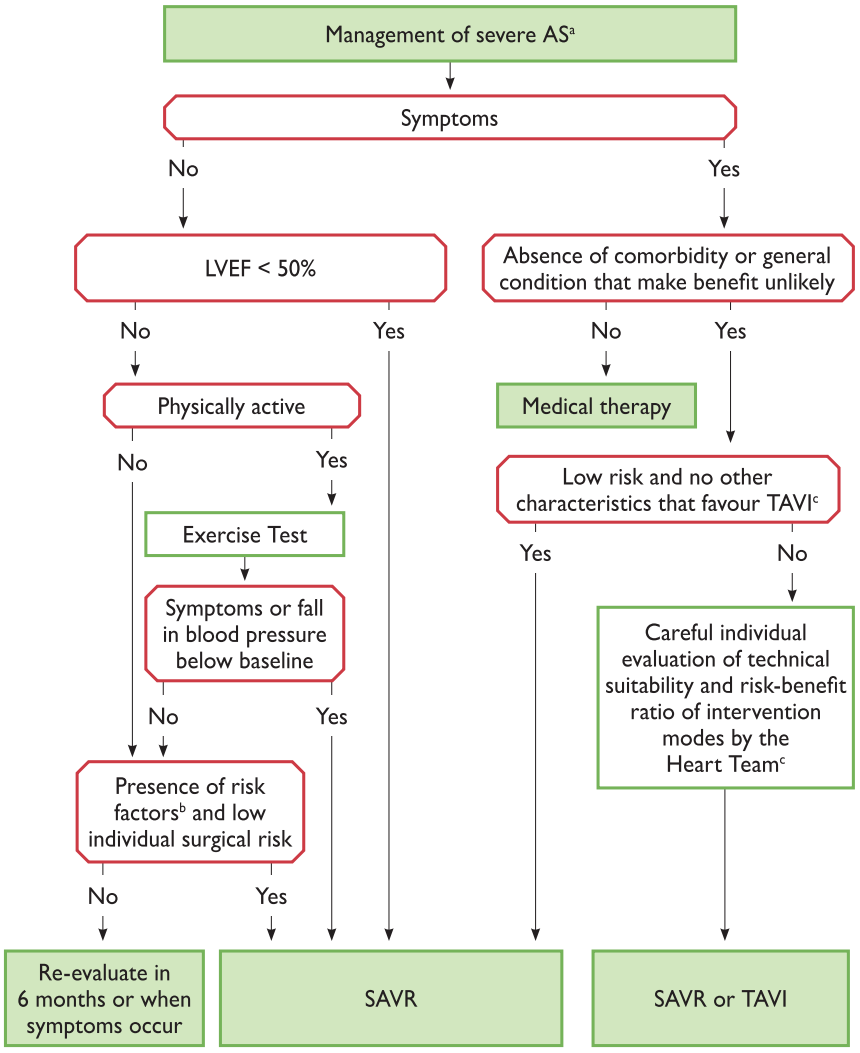

Figure 3: Management of severe aortic stenosis. AS: aortic stenosis; LVEF: left ventricular ejection fraction; SAVR: surgical aortic valve replacement; TAVI: transcatheter aortic valve implantation.

[a]See Figure 2 and Table 6 for the definition of severe AS. [b]Surgery should be considered (IIa C) if one of the following is present: peak velocity >5.5 m/s; severe valve calcification + peak velocity progression ≥0.3 m/s per year; markedly elevated neurohormones (>threefold age- and sex-corrected normal range) without other explanation; severe pulmonary hypertension (systolic pulmonary artery pressure >60 mmHg). [c]See Table 7 and Table of Recommendations in section 5.2 Indications for interventions in aortic stenosis.

ability to identify patients with severe aortic stenosis in this subgroup by CT calcium scoring and the availability of TAVI have lowered the threshold to intervene.

- Patients with low-flow, low-gradient aortic stenosis and preserved ejection fraction are the most challenging subgroup. Data on their natural history and outcome after surgical or catheter intervention remain controversial [80, 83, 84]. In such cases, intervention should only be performed when symptoms are present and if comprehensive evaluation suggests significant valve obstruction (see Figure 2 and Table 6).
- Patients with normal-flow, low-gradient aortic stenosis and preserved ejection fraction data should be re-evaluated. If normal flow and low gradient are confirmed, these patients will, in general, not have severe aortic stenosis and do not benefit from intervention [82, 83].

5.2.2 Choice of intervention mode in symptomatic aortic stenosis. The choice of the intervention mode should take into account the cardiac and extracardiac characteristics of the patient, the individual risk of surgery, which is assessed by the judgement of the Heart Team in addition to scores, the feasibility of TAVI and the local experience and outcome data.

Data on TAVI are still very limited for patients <75 years of age and for surgical low-risk patients, in whom SAVR remains the reference method. It has to be emphasized that younger patients differ with regard to anatomy (more bicuspid valves), which affects the results of TAVI (bicuspid valves were also in general excluded in clinical trials), and that long-term durability data for TAVI prosthetic valves are still lacking.

Available data from randomized controlled trials and large registries in elderly patients at increased surgical risk show that TAVI is superior in terms of mortality to medical therapy in extreme-risk patients [91], non-inferior or superior to surgery in high-risk patients [94–97] and non-inferior to surgery and even superior when transfemoral access is possible in intermediate-risk patients [98–102]. In the two large studies on intermediate risk, the mean ages of patients were 82 and 80 years [99, 102], mean STS scores were 5.8% and 4.5% [99, 102] and a high percentage were considered frail. Thus the results are valid only for comparable patient groups. Overall, rates of vascular complications, pacemaker implantation and paravalvular regurgitation were significantly higher for TAVI, while the degree of excess depended on the device used [101, 102]. On the other hand, severe bleeding, acute kidney injury and new-onset atrial fibrillation were significantly more frequent with surgery, whereas no difference was observed in the rate of cerebrovascular events [101, 102]. The favourable results of TAVI have been reproduced in multiple large-scale, nationwide registries supporting the generalizability of outcomes observed in randomized controlled trials. This favours the use of TAVI over surgery in elderly patients at increased surgical risk. However, the final decision between SAVR and TAVI (including the choice of access route) should be made by the Heart Team after careful individual evaluation. Table 7 provides aspects that should be considered for the individual decision. Balloon valvuloplasty may be considered as a bridge to surgery or TAVI, or diagnostically.

5.2.3 Asymptomatic aortic stenosis. Management of asymptomatic severe aortic stenosis remains controversial. The available studies do not provide convincing data to support the general recommendation of early SAVR, even in patients with asymptomatic very severe aortic stenosis [92, 106]. The decision to operate on asymptomatic patients requires careful weighing of the benefits against the risks. This section refers only to patients who are candidates for SAVR, as TAVI is not recommended in asymptomatic patients. Early elective surgery is indicated in asymptomatic patients with depressed LV function not due to other causes and in patients who develop symptoms during exercise testing [85, 107].

Predictors of symptom development and adverse outcomes in asymptomatic patients include clinical characteristics (older age, presence of atherosclerotic risk factors), echocardiographic parameters (valve calcification, peak aortic jet velocity [92, 108], LVEF, rate of haemodynamic progression [92], increase in mean gradient >20 mmHg with exercise [86], excessive LV hypertrophy [109], abnormal longitudinal LV function [110] and pulmonary hypertension [111]) and biomarkers (elevated plasma levels of natriuretic peptides, although the precise cut-off values have not yet been well defined [89, 90]). When early elective surgery is considered in patients with normal exercise performance because of the presence of such outcome predictors, the operative risk should be low (see table of recommendations in section 5.2 Indications for interventions in aortic stenosis). In patients without predictive factors, watchful waiting appears safe and early surgery is unlikely to be beneficial.

5.3 Medical therapy

No medical therapy for aortic stenosis can improve outcome compared with the natural history. Randomized trials have consistently shown that statins do not affect the progression of aortic stenosis [112]. Patients with symptoms of heart failure who are unsuitable candidates for surgery or TAVI or who are currently awaiting surgical or catheter intervention should be medically treated according to the heart failure guidelines [113]. Coexisting hypertension should be treated. Medical treatment should be carefully titrated to avoid hypotension and patients should be re-evaluated frequently. Maintenance of sinus rhythm is important.

5.4 Serial testing

In the asymptomatic patient, the wide variability in the rate of progression of aortic stenosis stresses the need for patients to be carefully educated about the importance of follow-up and reporting symptoms as soon as they develop. Stress tests should determine the recommended level of physical activity. Follow-up evaluation should focus on haemodynamic progression, LV function and hypertrophy and dimensions of the ascending aorta.

Asymptomatic severe aortic stenosis should be re-evaluated at least every 6 months for the occurrence of symptoms (change in exercise tolerance, ideally using exercise testing if symptoms are doubtful) and change in echocardiographic parameters. Measurement of natriuretic peptides should be considered.

In the presence of significant calcification, mild and moderate aortic stenosis should be re-evaluated yearly. In younger patients with mild aortic stenosis and no significant calcification, intervals may be extended to 2–3 years.

5.5 Special patient populations

Combined SAVR and CABG carry a higher risk than isolated SAVR. However, SAVR late after CABG is also associated with significantly

increased risk. Data from retrospective analyses indicate that patients in whom CABG is indicated and who have moderate aortic stenosis will in general benefit from concomitant SAVR. It has also been suggested that if age is <70 years and, more importantly, an average rate of aortic stenosis progression of 5 mmHg/year is documented, patients may benefit from valve replacement at the time of coronary surgery once the baseline peak gradient exceeds 30 mmHg [114]. Individual judgement is recommended, taking into consideration BSA, haemodynamic data, leaflet calcification, aortic stenosis progression rate, patient life expectancy and associated comorbidities, as well as the individual risk of either concomitant valve replacement or late reoperation [93]. Patients with severe symptomatic aortic stenosis and diffuse CAD that cannot be revascularized should not be denied SAVR or TAVI.

Combined PCI and TAVI has been shown to be feasible but requires more data before a firm recommendation can be made. The chronology of interventions should be the subject of individualized discussion based on the patient's clinical condition, extent of CAD and myocardium at risk.

When mitral regurgitation is associated with severe aortic stenosis, its severity may be overestimated in the presence of the high ventricular pressures and careful quantification is required. As long as there are no morphological leaflet abnormalities (flail or prolapse, post-rheumatic changes or signs of infective endocarditis), mitral annulus dilatation or marked abnormalities of LV geometry, surgical intervention on the mitral valve is in general not necessary. Non-severe secondary mitral regurgitation mostly improves after the aortic valve is treated. In patients with severe mitral regurgitation, combined or sequential TAVI and percutaneous mitral edge-to-edge repair have been demonstrated to be feasible, but there is not enough experience to make recommendations.

Concomitant aneurysm/dilatation of the ascending aorta requires the same treatment as in aortic regurgitation (see section 4).

For congenital aortic stenosis, see the ESC guidelines on grown-up congenital heart disease [115].

Key points

- The diagnosis of severe aortic stenosis requires consideration of AVA together with flow rate, pressure gradients (the most robust measurement), ventricular function, size and wall thickness, degree of valve calcification and blood pressure, as well as functional status.
- The assessment of the severity of aortic stenosis in patients with low gradient and preserved ejection fraction remains particularly challenging.
- The strongest indication for intervention remains symptoms of aortic stenosis (spontaneous or on exercise testing).
- The presence of predictors of rapid symptom development can justify early surgery in asymptomatic patients, particularly when surgical risk is low.
- Although current data favour TAVI in elderly patients who are at increased risk for surgery, particularly when a transfemoral access is possible, the decision between TAVI and SAVR should be made by the Heart Team after careful, comprehensive evaluation of the patient, weighing individually the risks and benefits.

Gaps in evidence

- The impact of earlier markers of LV dysfunction on postoperative outcome requires further research.
- The identification of patients with low-gradient aortic stenosis who have severe stenosis and would benefit from intervention requires improvement.
- The criteria for identification of patients who would benefit from early elective surgery in asymptomatic severe aortic stenosis requires further research.
- Long-term follow-up after TAVI is required; in particular, the long-term durability of the valves needs to be studied.
- Criteria for the decision between TAVI and SAVR in patients at increased operative risk who are eligible for both must be refined and must be studied in surgical low-risk patients.
- Criteria for when TAVI should no longer be performed since it would be futile need to be further defined.

6. MITRAL REGURGITATION

Mitral regurgitation is the second-most frequent indication for valve surgery in Europe [47]. It is essential to distinguish primary from secondary mitral regurgitation, particularly regarding surgical and transcatheter interventional management [116].

6.1 Primary mitral regurgitation

In primary mitral regurgitation, one or several components of the mitral valve apparatus are directly affected. The most frequent aetiology is degenerative (prolapse, flail leaflet). Endocarditis as one of the causes of primary mitral regurgitation is discussed in specific ESC guidelines [28].

6.1.1 Evaluation. Echocardiography is the principal investigation used to assess the severity and mechanism of mitral regurgitation, its consequences for the LV (function and remodelling), left atrium (LA) and pulmonary circulation, as well as the likelihood of repair.

Quantification should be performed in an integrative way, including qualitative, semi-quantitative and quantitative parameters. The criteria for defining severe primary mitral regurgitation are summarized in Table 4 [2, 7].

A precise anatomical description of the lesions, using the segmental and functional anatomy according to the Carpentier classification [2, 7] should be performed to assess the feasibility of repair. TTE also assesses mitral annular dimensions and the presence of calcification.

TTE is diagnostic in most cases, but TOE is recommended, particularly in the presence of suboptimal image quality [117]. Three-dimensional echocardiography provides additional information for selecting the appropriate repair strategy.

The consequences of mitral regurgitation on ventricular function are assessed by measuring LV size and ejection fraction. LA volume, systolic pulmonary artery pressure, tricuspid regurgitation and annular size and RV function are important additional parameters.

Determination of functional capacity and symptoms assessed by cardiopulmonary exercise testing may be useful in asymptomatic patients. Exercise echocardiography is useful to quantify exercise-induced changes in mitral regurgitation [118], in systolic pulmonary artery pressure and in LV function. It may be particularly helpful in patients with symptoms and uncertainty about the severity of mitral regurgitation based on measurements at rest. In asymptomatic patients, the significant increase of pulmonary artery pressure with exercise (>60 mmHg) has been reported to be of prognostic value [119]. The use of global

longitudinal strain could be of potential interest for the detection of subclinical LV dysfunction but is limited by inconsistent algorithms used by different echocardiographic systems.

Neurohormonal activation is observed in mitral regurgitation, with a potential value of elevated BNP levels and a change in BNP as predictors of outcome (particularly of symptom onset). In particular, low plasma BNP has a high negative predictive value and may be helpful in the follow-up of asymptomatic patients [120].

As echocardiographic measures of pulmonary pressure may show disagreement with invasive measures, the measurement should be invasively confirmed by right-heart catheterization if this is the only indication for surgery.

6.1.2 Indications for intervention. Urgent surgery is indicated in patients with acute severe mitral regurgitation. In the case of papillary muscle rupture as the underlying disease, valve replacement is in general required.

Indications for surgery in severe chronic primary mitral regurgitation are shown in the following table of recommendations (indications for intervention in severe primary mitral regurgitation) and in Figure 4. Surgery is obviously indicated in symptomatic patients with severe primary mitral regurgitation [121]. An LVEF ≤60% or LVESD ≥45 mm [122], atrial fibrillation [123] and a systolic pulmonary pressure ≥50 mmHg [124] predict a worse postoperative outcome independent of the symptomatic status and have therefore become triggers for surgery in asymptomatic patients. In patients with flail leaflet, an LVESD of 40–44 mm has been reported to predict a worse outcome compared with LVESD <40 mm [125]. Significant LA dilatation despite sinus rhythm has also been found to be a predictor of outcome [124]. In the presence of these two latter triggers, surgery should only be considered in heart valve centres and if surgical risk is low. An increase in systolic pulmonary artery pressure >60 mmHg on exercise echocardiography has also been proposed for risk stratification [119]. However, criteria that may indicate surgery have not been sufficiently well defined to be included in the current recommendations.

Watchful waiting is a safe strategy in asymptomatic patients with severe primary mitral regurgitation and none of the above indications for surgery [126], and ideally patients are followed in the setting of a heart valve centre [32].

Despite the absence of a randomized comparison between the results of valve replacement and repair, it is widely accepted that, when feasible, valve repair is the preferred treatment. Achieving a durable valve repair is essential. Degenerative mitral regurgitation due to segmental valve prolapse can be repaired with a low risk of mitral regurgitation recurrence and reoperation. The reparability of rheumatic lesions, extensive valve prolapse and—even more so—mitral regurgitation with leaflet calcification or extensive annular calcification is more challenging. Patients with a predictably complex repair should undergo surgery in experienced repair centres with high repair rates, low operative mortality and a record of durable results [127, 128]. When repair is not feasible, mitral valve replacement with preservation of the subvalvular apparatus is favoured. Additional tricuspid valve repair should be performed as indicated in section 8.2 (see table of recommendations on indications for tricuspid valve surgery).

Transcatheter mitral valve interventions have been developed to correct primary mitral regurgitation either through a transseptal or a transapical approach. Among the transcatheter procedures, currently only the edge-to-edge mitral repair is widely adopted [129]. Experience with transcatheter annuloplasty, transapical chordal implantation or valve replacement is still limited and general recommendations cannot yet be made. Transcatheter mitral valve treatment should be discussed by the Heart Team in symptomatic patients who are at high surgical risk or are inoperable. Percutaneous edge-to-edge repair is generally safe and can improve symptoms and provide reverse LV remodelling. However, the rate of residual mitral regurgitation up to 5 years is higher than with surgical repair [130].

Indications for intervention in severe primary mitral regurgitation

Recommendations	Class[a]	Level[b]
Mitral valve repair should be the preferred technique when the results are expected to be durable.	I	C
Surgery is indicated in symptomatic patients with LVEF >30% [121, 131, 132].	I	B
Surgery is indicated in asymptomatic patients with LV dysfunction (LVESD ≥45 mm[c] and/or LVEF ≤60%) [122, 131].	I	B
Surgery should be considered in asymptomatic patients with preserved LV function (LVESD <45 mm and LVEF >60%) and atrial fibrillation secondary to mitral regurgitation or pulmonary hypertension[d] (systolic pulmonary pressure at rest >50 mmHg) [123, 124].	IIa	B
Surgery should be considered in asymptomatic patients with preserved LVEF (>60%) and LVESD 40–44 mm[c] when a durable repair is likely, surgical risk is low, the repair is performed in a heart valve centre and at least one of the following findings is present: • flail leaflet or • presence of significant LA dilatation (volume index ≥60 ml/m^2 BSA) in sinus rhythm.	IIa	C
Mitral valve repair should be considered in symptomatic patients with severe LV dysfunction (LVEF <30% and/or LVESD >55 mm) refractory to medical therapy when the likelihood of successful repair is high and comorbidity low.	IIa	C
Mitral valve replacement may be considered in symptomatic patients with severe LV dysfunction (LVEF <30% and/or LVESD >55 mm) refractory to medical therapy when the likelihood of successful repair is low and comorbidity low.	IIb	C
Percutaneous edge-to-edge procedure may be considered in patients with symptomatic severe primary mitral regurgitation who fulfil the echocardiographic criteria of eligibility and are judged inoperable or at high surgical risk by the Heart Team, avoiding futility.	IIb	C

BSA: body surface area; LA: left atrial; LV: left ventricular; LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameter; SPAP: systolic pulmonary artery pressure.

[a]Class of recommendation.

[b]Level of evidence.

[c]Cut-offs refer to average-size adults and may require adaptations in patients with unusually small or large stature.

[d]If an elevated SPAP is the only indication for surgery, the value should be confirmed by invasive measurement.

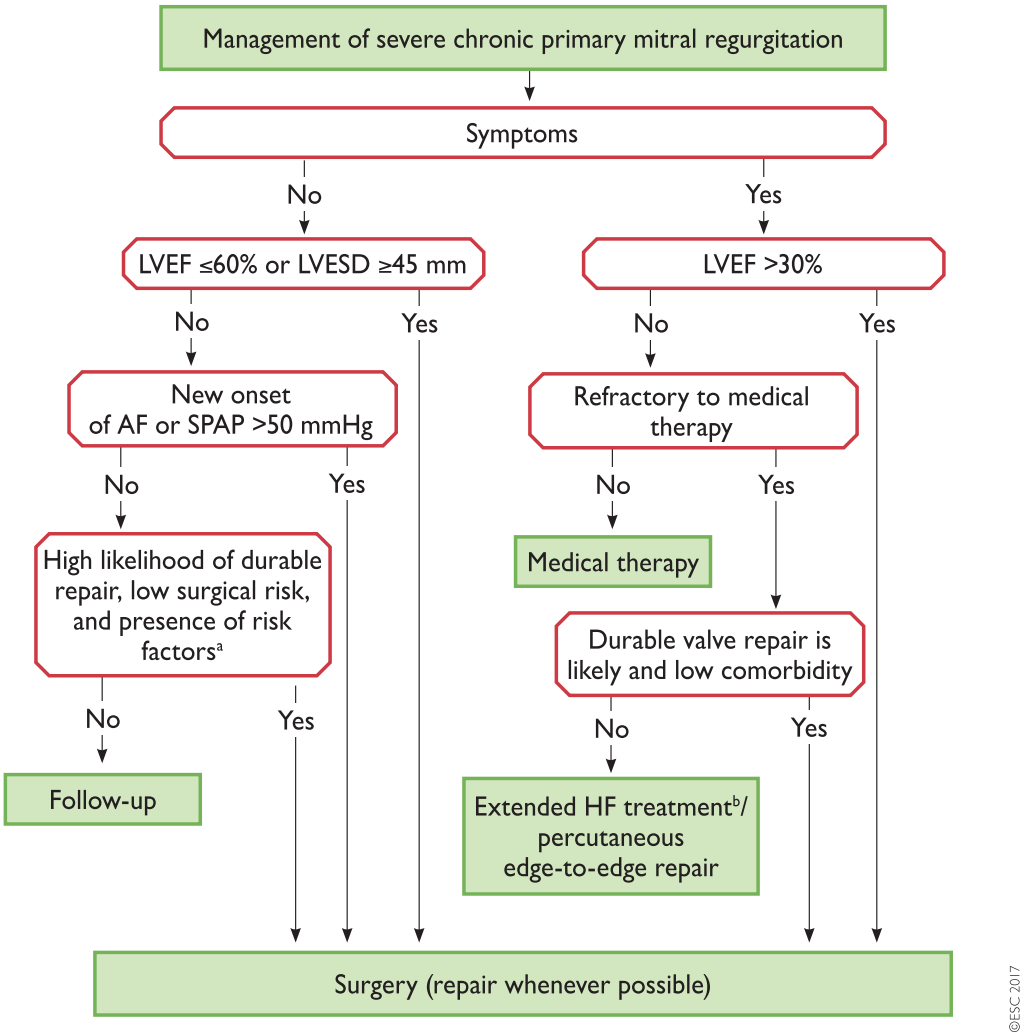

Figure 4: Management of severe chronic primary mitral regurgitation. AF: atrial fibrillation; BSA: body surface area; CRT: cardiac resynchronization therapy; HF: heart failure; LA: left atrial; LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameter; SPAP: systolic pulmonary arterial pressure.
[a]When there is a high likelihood of durable valve repair at a low-risk, valve repair should be considered (IIa C) in patients with LVESD ≥40 mm and one of the following is present: flail leaflet or LA volume ≥60 ml/m^2 BSA at sinus rhythm.
[b]Extended HF management includes the following: CRT; ventricular assist devices; cardiac restraint devices; heart transplantation.

6.1.3 Medical therapy. In acute mitral regurgitation, nitrates and diuretics are used to reduce filling pressures. Sodium nitroprusside reduces afterload and regurgitant fraction. Inotropic agents and an intra-aortic balloon pump are of use in hypotension and haemodynamic instability.

In chronic mitral regurgitation with good ventricular function, there is no evidence to support the prophylactic use of vasodilators, including ACE inhibitors. However, ACE inhibitors should be considered when heart failure has developed in patients who are not suitable for surgery or when symptoms persist after surgery. Beta-blockers and spironolactone (or eplerenone) should also be considered as appropriate.

6.1.4 Serial testing. Asymptomatic patients with severe mitral regurgitation and LVEF >60% should be followed clinically and echocardiographically every 6 months, ideally in the setting of a heart valve centre. Closer follow-up is indicated if no previous evaluation is available and when measured variables show significant dynamic changes or are close to the thresholds. When guideline indications for surgery are reached, early surgery—within 2 months—is associated with better outcomes [133]. Asymptomatic patients with moderate mitral regurgitation and preserved LV function can be followed on a yearly basis and echocardiography should be performed every 1–2 years.

6.2 Secondary mitral regurgitation

In secondary mitral regurgitation (previously also referred to as 'functional mitral regurgitation'), the valve leaflets and chordae are structurally normal and mitral regurgitation results from an imbalance between closing and tethering forces on the valve secondary to alterations in LV geometry [134]. It is most commonly seen in dilated or ischaemic cardiomyopathies. Annular dilatation in patients with chronic atrial fibrillation and LA enlargement can also be an underlying mechanism.

6.2.1 Evaluation. Echocardiography is essential to establish the diagnosis of secondary mitral regurgitation. In secondary mitral

regurgitation, lower thresholds have been proposed to define severe mitral regurgitation compared with primary mitral regurgitation [20 mm^2 for effective regurgitant orifice area (EROA) and 30 ml for regurgitant volume], owing to their association with prognosis [135]. However, it is unclear if prognosis is independently affected by mitral regurgitation compared with LV dysfunction. So far, no survival benefit has been confirmed for reduction of secondary mitral regurgitation.

For isolated mitral valve treatment (surgery or percutaneous edge-to-edge repair) in secondary mitral regurgitation, thresholds of severity of mitral regurgitation for intervention still need to be validated in clinical trials. The severity of secondary mitral regurgitation should be reassessed after optimized medical treatment. The severity of tricuspid regurgitation and RV size and function should also be evaluated.

Secondary mitral regurgitation is a dynamic condition; echocardiographic quantification of mitral regurgitation during exercise may provide prognostic information of dynamic characteristics. Myocardial viability testing may be useful in patients with ischaemic secondary mitral regurgitation who are candidates for revascularization.

6.2.2 Indications for intervention. The presence of chronic secondary mitral regurgitation is associated with impaired prognosis [135]. However, in contrast to primary mitral regurgitation, there is currently no evidence that a reduction of secondary mitral regurgitation improves survival. The limited data regarding secondary mitral regurgitation result in a lower level of evidence for treatment recommendations (see table of recommendations on indications for mitral valve intervention in chronic secondary mitral regurgitation) and highlight the importance of decision making by the Heart Team. Heart failure and electrophysiology specialists should be involved.

In patients with CAD undergoing revascularization, the evaluation and decision to treat (or not to treat) ischaemic mitral regurgitation should be made before surgery, as general anaesthesia may significantly reduce the severity of regurgitation. When mitral regurgitation severity is assessed intraoperatively, the use of acute volume challenge and an increase in afterload may be helpful.

The optimal surgical approach remains controversial [136]. While mitral valve repair with an undersized complete ring to restore leaflet coaptation and valve competence is the preferred technique, valve replacement should be considered in patients with echocardiographic risk factors for residual or recurrent mitral regurgitation [2].

Indications for surgery in secondary mitral regurgitation are particularly restrictive when concomitant revascularization is not an option, owing to significant operative mortality, high rates of recurrent mitral regurgitation and the absence of a proven survival benefit [137, 138].

Percutaneous edge-to-edge repair for secondary mitral regurgitation is a low-risk option, but its efficacy to reduce mitral regurgitation remains inferior to surgery [139]. It can improve symptoms, functional capacity and quality of life and may induce reverse LV remodelling [140]. Similar to surgery, a survival benefit compared with 'optimal' medical therapy according to current guidelines [113] has not yet been proven.

In patients with markedly reduced LV function (ejection fraction ≤30%) and no option for revascularization who remain symptomatic despite optimal heart-failure treatment [including cardiac resynchronization therapy (CRT) when indicated], the decision between palliative mitral regurgitation treatment—catheter-based or surgical, ventricular assist devices, heart transplantation—and continued conservative therapy should be made by the Heart Team after careful individual evaluation of the patient. Valve intervention is generally not an option when the ejection fraction is <15%.

There is continuing debate regarding the management of moderate ischaemic mitral regurgitation in patients undergoing CABG. A recent randomized controlled trial could not show a benefit of concomitant valve surgery [141]. Surgery is more likely to be considered if myocardial viability is present and if comorbidity is low. In patients capable of exercising, exercise-induced dyspnoea and a large increase in mitral regurgitation severity and systolic pulmonary artery pressure favour combined surgery.

Indications for mitral valve intervention in chronic secondary mitral regurgitation[a]

Recommendations	Class[b]	Level[c]
Surgery is indicated in patients with severe secondary mitral regurgitation undergoing CABG and LVEF >30%.	I	C
Surgery should be considered in symptomatic patients with severe secondary mitral regurgitation, LVEF <30% but with an option for revascularization and evidence of myocardial viability.	IIa	C
When revascularization is not indicated, surgery may be considered in patients with severe secondary mitral regurgitation and LVEF >30% who remain symptomatic despite optimal medical management (including CRT if indicated) and have a low surgical risk.	IIb	C
When revascularization is not indicated and surgical risk is not low, a percutaneous edge-to-edge procedure may be considered in patients with severe secondary mitral regurgitation and LVEF >30% who remain symptomatic despite optimal medical management (including CRT if indicated) and who have a suitable valve morphology by echocardiography, avoiding futility.	IIb	C
In patients with severe secondary mitral regurgitation and LVEF <30% who remain symptomatic despite optimal medical management (including CRT if indicated) and who have no option for revascularization, the Heart Team may consider a percutaneous edge-to-edge procedure or valve surgery after careful evaluation for a ventricular assist device or heart transplant according to individual patient characteristics.	IIb	C

CABG: coronary artery bypass grafting; CRT: cardiac resynchronization therapy; LVEF: left ventricular ejection fraction.
[a]See section 6.2.1 for quantification of secondary mitral regurgitation, which must always be performed under optimal treatment.
[b]Class of recommendation.
[c]Level of evidence.

6.2.3 Medical therapy. Optimal medical therapy in line with the guidelines for the management of heart failure [113] should be the first step in the management of all patients with secondary mitral regurgitation. Indications for CRT should be evaluated in accordance with related guidelines [113]. If symptoms persist after optimization of conventional heart failure therapy, options for mitral valve intervention should be evaluated.

Key points

- Echocardiography is essential to assess the aetiology of mitral regurgitation, as well as valve anatomy and function. An integrative approach is needed to assess the severity of mitral regurgitation.
- Indication for intervention in primary mitral regurgitation is guided by symptoms and risk stratification that includes the assessment of ventricular function and size, atrial fibrillation, systolic pulmonary pressure and LA size.
- In secondary mitral regurgitation, there is no conclusive evidence for a survival benefit after mitral valve intervention. Mitral surgery is recommended concomitantly in patients with an indication for CABG and may be considered in patients who are symptomatic despite optimal medical therapy (including CRT if indicated) or who have a low surgical risk when revascularization is not indicated.
- Mitral valve repair is the preferred method, but mitral valve replacement should be considered in patients with unfavourable morphological characteristics.
- Outcomes of mitral valve repair depend on surgeon experience and centre-related volume.
- Percutaneous edge-to-edge repair may be considered in patients at high surgical risk, avoiding futility.

Gaps in evidence

- The potential role of elective mitral valve surgery in asymptomatic patients with severe primary mitral regurgitation with preserved ventricular size and function who are in sinus rhythm and have not developed a high pulmonary artery pressure requires investigation in a randomized controlled trial.
- The impact of earlier markers of LV dysfunction on postoperative outcome requires further research.
- The thresholds to define severe secondary mitral regurgitation are controversial and need to be evaluated with regards to their impact on prognosis after mitral valve intervention.
- The potential impact of mitral valve intervention (surgery and catheter intervention) on survival in patients with secondary mitral regurgitation needs to be evaluated.
- The new percutaneous valve repair and valve implantation techniques require further evaluation.

7. MITRAL STENOSIS

The incidence of rheumatic mitral stenosis has greatly decreased in industrialized countries [142]. Degenerative calcific mitral valve disease is now encountered mainly in elderly patients [143]. Percutaneous mitral commissurotomy (PMC) has had a significant impact on the management of rheumatic mitral stenosis.

7.1 Evaluation

Echocardiography is the preferred method for diagnosing mitral stenosis and for assessing its severity and haemodynamic consequences. However, several specific issues should be considered. Valve area using planimetry is the reference measurement of mitral stenosis severity, whereas mean transvalvular gradient and pulmonary pressures reflect its consequences and have a prognostic value [3]. TTE usually provides sufficient information for routine management. Scoring systems have been developed to help assess suitability for PMC [144–146]. TOE should be performed to exclude LA thrombus before PMC or after an embolic episode. Echocardiography also plays an important role in monitoring the results of PMC during the procedure. Stress testing is indicated in patients with no symptoms or symptoms equivocal or discordant with the severity of mitral stenosis. Exercise echocardiography may provide additional objective information by assessing changes in mitral gradient and pulmonary artery pressure.

7.2 Indications for intervention

The type of treatment, as well as its timing, should be decided on the basis of clinical characteristics, valve anatomy and local expertise. In general, indication for intervention should be limited to patients with clinically significant (moderate to severe) mitral stenosis (valve area <1.5 cm^2). However, PMC may be considered in symptomatic patients with a valve area >1.5 cm^2 if symptoms cannot be explained by another cause and if the anatomy is favourable.

The management of clinically significant mitral stenosis is summarized in Figure 5 and the indications and contraindications for PMC are provided in the table of recommendations on indications for PMC and mitral valve surgery in clinically significant mitral stenosis and in Table 8. Intervention should be performed in symptomatic patients. Most patients with favourable valve anatomy currently undergo PMC, however, open commissurotomy may be preferred by experienced surgeons in young patients with mild to moderate mitral regurgitation.

In patients with unfavourable anatomy, decision making as to the type of intervention is still a matter of debate and must take into account the multifactorial nature of predicting the results of PMC [147–149]. PMC should be considered as an initial treatment for selected patients with mild to moderate calcification or impaired subvalvular apparatus who have otherwise favourable clinical characteristics. Surgery, which is mostly valve replacement, is indicated in the other patients.

Owing to the small but definite risk inherent to PMC, truly asymptomatic patients, as assessed using stress testing, are usually not candidates for the procedure, except in cases where there is increased risk of systemic embolism or haemodynamic decompensation. In such patients, PMC should only be performed if they have favourable characteristics and if it is undertaken by experienced operators.

In asymptomatic patients with mitral stenosis, surgery is limited to those rare patients at high risk of cardiac complications who have contraindications for PMC and are at low risk for surgery.

The most important contraindication to PMC is LA thrombus (Table 8). However, when the thrombus is located in the LA appendage, PMC may be considered in patients without urgent need for intervention, provided repeat TOE shows the thrombus has disappeared after 1–3 months of oral anticoagulation. Surgery is indicated if the thrombus persists.

Indications for PMC and mitral valve surgery in clinically significant (moderate or severe) mitral stenosis (valve area $\leq$1.5 cm^2)

Recommendations	Class[a]	Level[b]
PMC is indicated in symptomatic patients without unfavourable characteristics[c] for PMC [144, 146, 148].	I	B
PMC is indicated in any symptomatic patients with a contraindication or a high risk for surgery.	I	C
Mitral valve surgery is indicated in symptomatic patients who are not suitable for PMC.	I	C
PMC should be considered as initial treatment in symptomatic patients with suboptimal anatomy but no unfavourable clinical characteristics for PMC.[c]	IIa	C
PMC should be considered in asymptomatic patients without unfavourable clinical and anatomical characteristics[c] for PMC and: • high thromboembolic risk (history of systemic embolism, dense spontaneous contrast in the LA, new-onset or paroxysmal atrial fibrillation), and/or • high risk of haemodynamic decompensation (systolic pulmonary pressure >50 mmHg at rest, need for major non-cardiac surgery, desire for pregnancy).	IIa	C

LA: left atrium; PMC: percutaneous mitral commissurotomy.
[a]Class of recommendation.
[b]Level of evidence.
[c]Unfavourable characteristics for PMC can be defined by the presence of several of the following characteristics. Clinical characteristics: old age, history of commissurotomy, New York Heart Association class IV, permanent atrial fibrillation, severe pulmonary hypertension. Anatomical characteristics: echocardiographic score >8, Cormier score 3 (calcification of mitral valve of any extent as assessed by fluoroscopy), very small mitral valve area, severe tricuspid regurgitation. For the definition of scores see Table 9.

7.3 Medical therapy

Diuretics, beta-blockers, digoxin or heart rate–regulating calcium channel blockers can transiently improve symptoms. Anticoagulation with a target international normalized ratio (INR) between 2 and 3 is indicated in patients with either new-onset or paroxysmal atrial fibrillation.

In patients in sinus rhythm, oral anticoagulation is indicated when there has been a history of systemic embolism or a thrombus is present in the LA (recommendation class I, level of evidence C) and should also be considered when TOE shows dense spontaneous echocardiographic contrast or an enlarged LA (M-mode diameter >50 mm or LA volume >60 ml/m^2) (recommendation class IIa, level of evidence C). Patients with moderate to severe mitral stenosis and persistent atrial fibrillation should be kept on vitamin K antagonist (VKA) treatment and not receive NOACs.

Cardioversion is not indicated before intervention in patients with severe mitral stenosis, as it does not durably restore sinus rhythm. If atrial fibrillation is of recent onset and the LA is only moderately enlarged, cardioversion should be performed soon after successful intervention.

7.4 Serial testing

Asymptomatic patients with clinically significant mitral stenosis who have not undergone intervention should be followed up yearly by means of clinical and echocardiographic examinations and at longer intervals (2–3 years) in case of moderate stenosis.

Management of patients after successful PMC is similar to that of asymptomatic patients. Follow-up should be more frequent if asymptomatic restenosis occurs. When PMC is not successful, surgery should be considered early unless there are definite contraindications.

7.5 Special patient populations

When restenosis with symptoms occurs after surgical commissurotomy or PMC, reintervention in most cases requires valve replacement, but PMC can be proposed in selected candidates with favourable characteristics if the predominant mechanism is commissural refusion [151].

In the elderly population with rheumatic mitral stenosis when surgery is high risk, PMC is a useful option, even if only palliative. In other elderly patients, surgery is preferable [146,148,149]. However, in elderly patients with degenerative mitral stenosis with severely calcified mitral annulus, surgery is very high risk. As there is no commissural fusion in these cases, degenerative mitral stenosis is not amenable to PMC [143]. If degenerative mitral stenosis is severe, very preliminary experience has suggested that transcatheter valve implantation of a TAVI bioprosthesis in the mitral position is feasible in symptomatic elderly patients who are inoperable if the anatomy is suitable [152].

In patients with severe mitral stenosis combined with severe aortic valve disease, surgery is preferable when it is not contraindicated. The management of patients in whom surgery is contraindicated is difficult and requires a comprehensive and individualized evaluation by the Heart Team.

In cases with severe mitral stenosis with moderate aortic valve disease, PMC can be performed to postpone the surgical treatment of both valves.

In patients with severe tricuspid regurgitation, PMC may be considered in selected patients with sinus rhythm, moderate atrial enlargement and functional tricuspid regurgitation secondary to pulmonary hypertension. In other cases, surgery on both valves is preferred [153].

Valve replacement is the only option for the treatment of rare cases of severe mitral stenosis of non-rheumatic origin where commissural fusion is absent.

Key points

- Most patients with severe mitral stenosis and favourable valve anatomy currently undergo PMC.

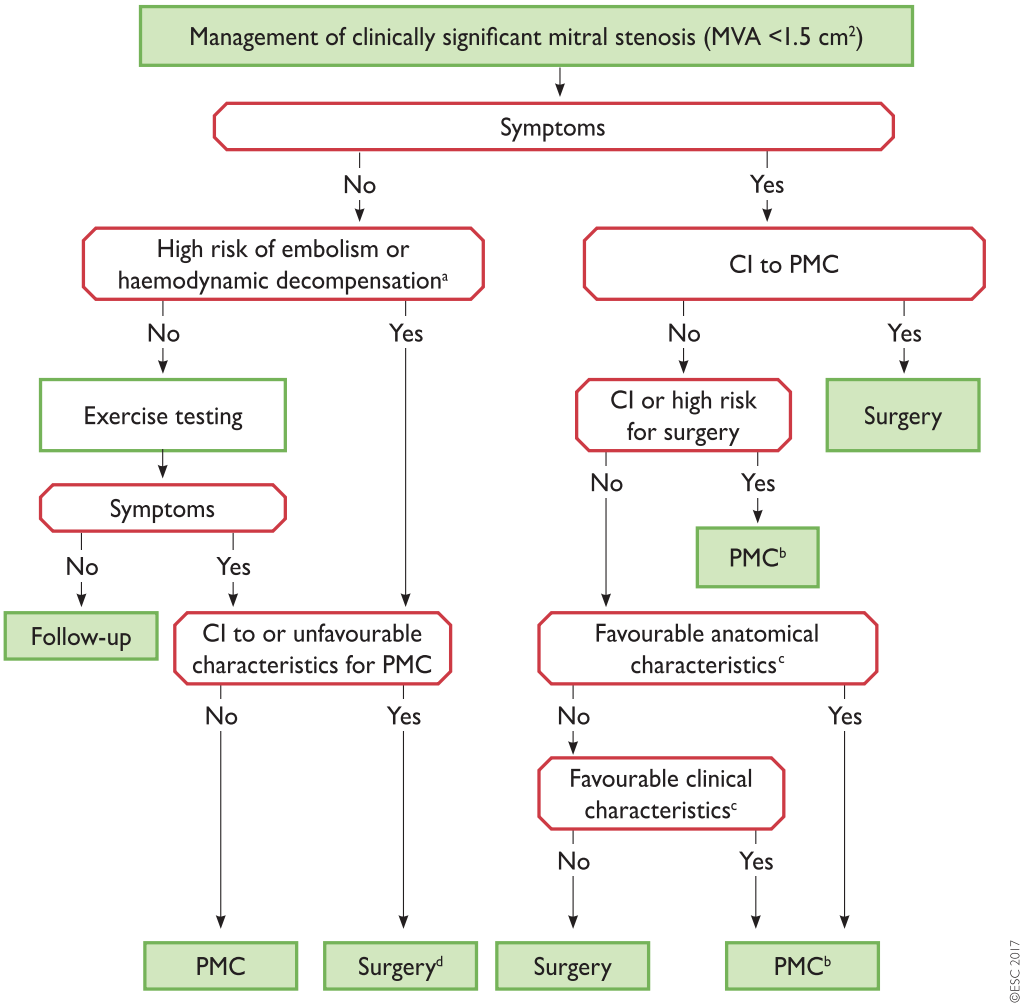

Figure 5: Management of clinically significant mitral stenosis. CI: contraindication; MS: mitral stenosis; PMC: percutaneous mitral commissurotomy.
[a]High thromboembolic risk: history of systemic embolism, dense spontaneous contrast in the left atrium, new-onset atrial fibrillation. High-risk of haemodynamic decompensation: systolic pulmonary pressure >50 mmHg at rest, need for major non-cardiac surgery, desire for pregnancy. [b]Surgical commissurotomy may be considered by experienced surgical teams or in patients with contraindications to PMC. [c]See table of recommendations on indications for PMC and mitral valve surgery in clinically significant mitral stenosis in section 7.2. [d]Surgery if symptoms occur for a low level of exercise and operative risk is low.

Table 8: Contraindications for percutaneous mitral commissurotomy (PMC)[a]

Contraindications
Mitral valve area >1.5 cm²[a]
Left atrial thrombus
More than mild mitral regurgitation
Severe or bi-commissural calcification
Absence of commissural fusion
Severe concomitant aortic valve disease, or severe combined tricuspid stenosis and regurgitation requiring surgery
Concomitant CAD requiring bypass surgery

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CAD: coronary artery disease.
[a]PMC may be considered in patients with valve area >1.5 cm² with symptoms that cannot be explained by another cause and if the anatomy is favourable.

- Decision making as to the type of intervention in patients with unfavourable anatomy is still a matter of debate and must take into account the multifactorial nature of predicting the results of PMC.

Gaps in evidence

- The scores predicting the results and complications of PMC, particularly those of severe mitral regurgitation, must be refined.
- The potential role of transcatheter mitral valve implantation in high-risk patients is to be determined, particularly those with severe degenerative mitral stenosis.

8. TRICUSPID REGURGITATION

Pathological tricuspid regurgitation is more often secondary, due to RV dysfunction following pressure and/or volume overload in the presence of structurally normal leaflets [2]. Possible causes of primary tricuspid regurgitation are infective endocarditis

Table 9: Echo scores: Wilkins score [145], Cormier score [150], and Echo Score "Revisited" for immediate outcome prediction [146]

Assessment of mitral valve anatomy according to the Wilkins score [145]				
Grade	**Mobility**	**Thickening**	**Calcification**	**Subvalvular thickening**
1	Highly mobile valve with only leaflet tips restricted	Leaflets near normal in thickness (4–5 mm)	A single area of increased echo brightness	Minimal thickening just below the mitral leaflets
2	Leaflet mid and base portions have normal mobility	Mid leaflets normal, considerable thickening of margins (5–8 mm)	Scattered areas of brightness confined to leaflet margins	Thickening of chordal structures extending to one third of the chordal length
3	Valve continues to move forward in diastole, mainly from the base	Thickening extending through the entire leaflet (5–8 mm)	Brightness extending into the mid portions of the leaflets	Thickening extended to distal third of the chords
4	No or minimal forward movement of the leaflets in diastole	Considerable thickening of all leaflet tissue (>8–10 mm)	Extensive brightness throughout much of the leaflet tissue	Extensive thickening and shortening of all chordal structures extending down to the papillary muscles
The total score is the sum of the four items and ranges between 4 and 16.				

Assessment of mitral valve anatomy according to the Cormier score [150]	
Echocardiographic group	**Mitral valve anatomy**
Group 1	Pliable non-calcified anterior mitral leaflet and mild subvalvular disease (i.e., thin chordae ≥10 mm long)
Group 2	Pliable non-calcified anterior mitral leaflet and severe subvalvular disease (i.e., thickened chordae <10 mm long)
Group 3	Calcification of mitral valve of any extent, as assessed by fluoroscopy, whatever the state of subvalvular apparatus

Echo Score "Revisited" for immediate outcome prediction [146]	
Echocardiographic variables	**Points for score (0 to 11)**
Mitral valve area ≤1cm²	2
Maximum leaflet displacement ≤12 mm	3
Commissural area ratio ≥1.25	3
Subvalvular involvement	3

Risk groups for Echo score "Revisited": low (score 0 - 3); intermediate (score 4 - 5); high (score 6 - 11).

(especially in intravenous drug addicts) [154], rheumatic heart disease, carcinoid syndrome, myxomatous disease, endomyocardial fibrosis, Ebstein's anomaly and congenitally dysplastic valves, drug-induced valve diseases, thoracic trauma and iatrogenic valve damage.

8.1. Evaluation

Echocardiography is the ideal technique to evaluate tricuspid regurgitation. In primary tricuspid regurgitation, the aetiology can usually be identified from specific abnormalities of the valve structure [28, 115]. In secondary tricuspid regurgitation, the degree of dilatation of the annulus, the RV dimension and function and the degree of tricuspid valve deformation should be measured [2]. Evaluation of tricuspid regurgitation severity (integration of multiple qualitative and quantitative parameters) and pulmonary systolic pressure should be carried out as currently recommended (Table 4) [2]. It has to be noted that the problem of elevated pulmonary vascular resistance may be disguised in the presence of severe tricuspid regurgitation since its velocity may be lower than expected in the case of pulmonary hypertension.

Evaluations of RV dimensions and function should be conducted despite the existing limitations of current indices of RV function [53]. The presence of associated lesions (looking carefully at the associated valve lesions, particularly on the left side) and LV function should be assessed.

In experienced laboratories, 3D measurements of RV volumes can be considered, which may be similar to those obtained by CMR [155]. However, when available, CMR is the preferred method for evaluating RV size and function and represents the gold standard for assessing RV volumes and function [155].

Cardiac catheterization is not needed to diagnose tricuspid regurgitation or estimate its severity but should be obtained in patients in whom isolated tricuspid valve surgery is contemplated for secondary tricuspid regurgitation to evaluate haemodynamics, in particular pulmonary vascular resistance.

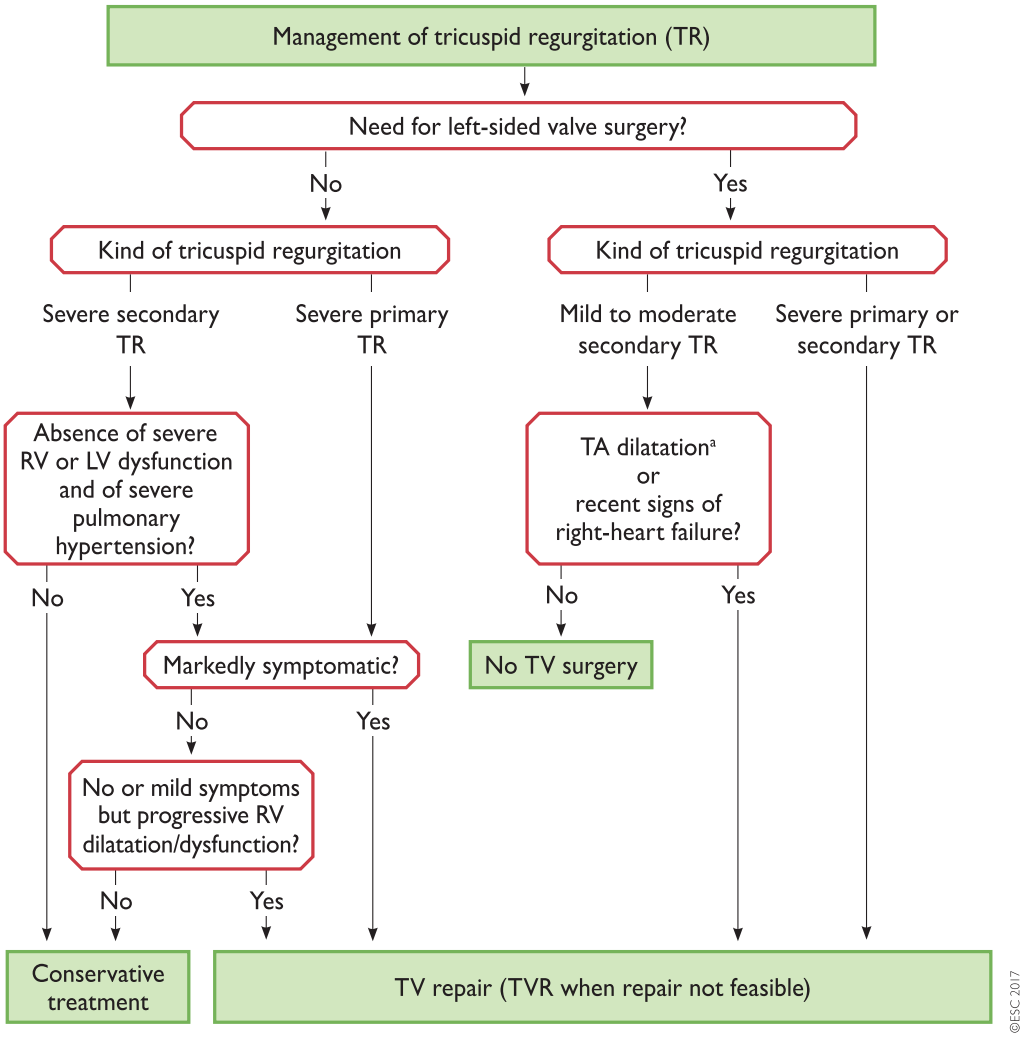

Figure 6: Indications for surgery in tricuspid regurgitation. LV: left ventricular; RV: right ventricular; TA: tricuspid annulus; TR: tricuspid regurgitation; TV: tricuspid valve; TVR: tricuspid valve replacement.
[a]TA ≥ 40 mm or > 21 mm/m^2.

8.2. Indications for intervention

The timing of surgical intervention remains controversial, mostly due to the limited data available and their heterogeneous nature (see table of recommendations for indications for tricuspid valve surgery and Figure 6) [156–160]. Surgery should be carried out sufficiently early to avoid irreversible RV dysfunction.

In severe primary tricuspid regurgitation, surgery is not only recommended in symptomatic patients but should also be considered in asymptomatic patients when progressive RV dilatation or decline of RV function is observed. Although these patients respond well to diuretic therapy, delaying surgery is likely to result in irreversible RV damage, organ failure and poor results of late surgical intervention.

In secondary tricuspid regurgitation, adding a tricuspid repair, if indicated, during left-sided surgery does not increase operative risk and has been demonstrated to provide reverse remodelling of the RV and improvement of functional status even in the absence of substantial tricuspid regurgitation when annulus dilatation is present [156, 157, 160]. It should therefore be performed liberally. Reoperation on the tricuspid valve in cases of persistent tricuspid regurgitation after mitral valve surgery carries a high risk, mostly due to the late referral and the consequently poor clinical condition of patients. To improve the prognosis of patients in this challenging scenario, the treatment of severe late tricuspid regurgitation following left-sided valve surgery should be considered earlier, even in asymptomatic patients, if there are signs of progressive RV dilatation or decline in RV function and in the absence of left-sided valve dysfunction, severe RV or LV dysfunction and severe pulmonary vascular disease/hypertension.

If possible, valve repair is preferable to valve replacement. Ring annuloplasty, preferably with prosthetic rings, is key to surgery for secondary tricuspid regurgitation [156, 161]. Valve replacement should be considered when the tricuspid valve leaflets are significantly tethered and the annulus is severely dilated. In the presence of transtricuspid pacemaker leads, the technique used should be adapted to the patient's condition and the surgeon's experience. Percutaneous repair techniques are in their infancy and must be further evaluated before any recommendations can be made.

Indications for tricuspid valve surgery

Recommendations	Class[a]	Level[b]
Recommendations on tricuspid stenosis		
Surgery is indicated in symptomatic patients with severe tricuspid stenosis.[c]	I	C
Surgery is indicated in patients with severe tricuspid stenosis undergoing left-sided valve intervention.[d]	I	C
Recommendations on primary tricuspid regurgitation		
Surgery is indicated in patients with severe primary tricuspid regurgitation undergoing left-sided valve surgery.	I	C
Surgery is indicated in symptomatic patients with severe isolated primary tricuspid regurgitation without severe RV dysfunction.	I	C
Surgery should be considered in patients with moderate primary tricuspid regurgitation undergoing left-sided valve surgery.	IIa	C
Surgery should be considered in asymptomatic or mildly symptomatic patients with severe isolated primary tricuspid regurgitation and progressive RV dilatation or deterioration of RV function.	IIa	C
Recommendations on secondary tricuspid regurgitation		
Surgery is indicated in patients with severe secondary tricuspid regurgitation undergoing left-sided valve surgery.	I	C
Surgery should be considered in patients with mild or moderate secondary tricuspid regurgitation with a dilated annulus (≥40 mm or >21 mm/m^2 by 2D echocardiography) undergoing left-sided valve surgery.	IIa	C
Surgery may be considered in patients undergoing left-sided valve surgery with mild or moderate secondary tricuspid regurgitation even in the absence of annular dilatation when previous recent right-heart failure has been documented.	IIb	C
After previous left-sided surgery and in absence of recurrent left-sided valve dysfunction, surgery should be considered in patients with severe tricuspid regurgitation who are symptomatic or have progressive RV dilatation/dysfunction, in the absence of severe RV or LV dysfunction and severe pulmonary vascular disease/hypertension.	IIa	C

2D: two-dimensional; LV: left ventricular; PMC: percutaneous mitral commissurotomy; RV: right ventricular.
[a]Class of recommendation.
[b]Level of evidence.
[c]Percutaneous balloon valvuloplasty can be attempted as a first approach if tricuspid stenosis is isolated.
[d]Percutaneous balloon valvuloplasty can be attempted if PMC can be performed on the mitral valve.

9. TRICUSPID STENOSIS

Tricuspid stenosis is often combined with tricuspid regurgitation, most frequently of rheumatic origin. It is therefore almost always associated with left-sided valve lesions, particularly mitral stenosis, that usually dominate the clinical presentation. Other causes are rare, including congenital, drug-induced valve diseases, Whipple's disease, endocarditis and large right atrial tumour.

9.1 Evaluation

Echocardiography provides the most useful information. Tricuspid stenosis is often overlooked and requires careful evaluation. Echocardiographic evaluation of the anatomy of the valve and its subvalvular apparatus is important to assess valve reparability. No generally accepted grading of tricuspid stenosis severity exists, but a mean gradient ≥5 mmHg at normal heart rate is considered indicative of clinically significant tricuspid stenosis [3]. Catheterization is no longer used for evaluating the severity of tricuspid stenosis.

9.2 Indications for intervention

The lack of pliable leaflet tissue is the main limitation for valve repair. Even though this is still a matter of debate, biological prostheses for valve replacement are usually preferred over mechanical ones because of the high risk of thrombosis carried by the latter and the satisfactory long-term durability of the former in the tricuspid position [162].

Percutaneous balloon tricuspid dilatation has been performed in a limited number of cases, either alone or alongside PMC, but frequently induces significant regurgitation. There is a lack of data on long-term results [163].

Intervention on the tricuspid valve is usually carried out at the time of intervention on the other valves in patients who are symptomatic despite medical therapy. The choice between repair or valve replacement depends on valve anatomy and surgical expertise. Balloon commissurotomy can be considered in the rare cases with anatomically suitable valves when tricuspid stenosis is isolated, or additional mitral stenosis can also be treated interventionally (see table of recommendations in section 7.2 listing indications for PMC and mitral valve surgery in clinically significant mitral stenosis).

9.3 Medical therapy

Diuretics are useful in the presence of heart failure but are of limited long-term efficacy.

Key points

- Tricuspid stenosis is a rare condition, whereas tricuspid regurgitation is more common, especially in its secondary form.
- For appropriate management, secondary tricuspid regurgitation has to be clearly distinguished from primary tricuspid regurgitation.

- Similar to mitral regurgitation, primary tricuspid regurgitation requires intervention sufficiently early to avoid secondary damage of the RV, which is associated with poor outcome.
- Secondary tricuspid regurgitation should be liberally treated at the time of left-sided valve surgery.
- Consideration of isolated surgery of secondary tricuspid regurgitation after previous left-sided valve surgery requires comprehensive assessment of the underlying disease, pulmonary haemodynamics and RV function.

Gaps in evidence

- Criteria for optimal timing of surgery in primary tricuspid regurgitation require refinement.
- Criteria for concomitant tricuspid valve surgery at the time of left-sided surgery in patients without severe tricuspid valve disease require refinement.
- The potential role of transcatheter tricuspid valve treatment in high-risk patients needs to be determined.

10. COMBINED AND MULTIPLE-VALVE DISEASES

Significant stenosis and regurgitation can be found on the same valve. Disease of multiple valves may be encountered in several conditions, particularly in rheumatic and congenital heart disease, but also less frequently in degenerative valve disease. There is a lack of data on combined or multiple-valve diseases. This does not allow for evidence-based recommendations [164]. The general principles for the management of combined or multiple-valve disease are as follows:

- When either stenosis or regurgitation is predominant, management follows the recommendations concerning the predominant VHD. When the severity of both stenosis and regurgitation is balanced, indications for interventions should be based on symptoms and objective consequences rather than on the indices of severity of stenosis or regurgitation. In this setting, consideration of the pressure gradient that reflects the haemodynamic burden of the valve lesion becomes more important than valve area and measures of the regurgitation for the assessment of disease severity.
- Besides the separate assessment of each valve lesion, it is necessary to take into account the interaction between the different valve lesions. As an illustration, associated mitral regurgitation may lead to underestimation of the severity of aortic stenosis, as decreased stroke volume due to mitral regurgitation lowers the flow across the aortic valve and hence the aortic gradient. This underlines the need to combine different measurements, including assessment of valve areas, if possible using methods that are less dependent on loading conditions, such as planimetry.
- Indications for intervention are based on global assessment of the consequences of the different valve lesions (i.e. symptoms or presence of LV dilatation or dysfunction). Intervention can be considered for non-severe multiple lesions associated with symptoms or leading to LV impairment.
- The decision to intervene on multiple valves should take into account the extra surgical risk of combined procedures.
- The choice of surgical technique should take into account the presence of the other VHD; repair remains the ideal option.

The management of specific associations of VHD is detailed in the individual sections of this document.

Key points

- In combined VHD, pathology is considered severe even if both stenosis and regurgitation are only of moderate severity and pressure gradients become of major importance for assessment.
- Management of multiple valve disease is dictated by the predominant VHD.

Gaps in evidence

- More data on the natural history and the impact of intervention on outcome are required to better define the indications for intervention.

11. PROSTHETIC VALVES

Every valve prosthesis introduces a new disease process. In practice, the choice is between a mechanical and a biological prosthesis. Randomized trials comparing both prostheses consistently found similar survival, no significant difference in rates of valve thrombosis and thromboembolism, higher rates of bleeding with mechanical prostheses and higher rates of reintervention with bioprostheses [165–167].

11.1 Choice of prosthetic valve

The choice between a mechanical and a biological valve in adults is determined mainly by estimating the risk of anticoagulation-related bleeding and thromboembolism with a mechanical valve versus the risk of structural valve deterioration with a bioprosthesis and by considering the patient's lifestyle and preferences. Rather than setting arbitrary age limits, prosthesis choice should be discussed in detail with the informed patient, cardiologists and surgeons, taking into account the factors detailed below (see tables of recommendations in section 11.1). Bioprostheses should be considered in patients whose life expectancy is lower than the presumed durability of the bioprosthesis, particularly if comorbidities may necessitate further surgical procedures, and in those with increased bleeding risk. In women who wish to become pregnant, the high risk of thromboembolic complications with a mechanical prosthesis during pregnancy and the low risk of elective reoperation are incentives to consider a bioprosthesis, despite the rapid occurrence of structural valve deterioration in this age group.

11.2 Management after valve intervention

Thromboembolism and anticoagulant-related bleeding present the majority of complications experienced by prosthetic valve recipients. Endocarditis prophylaxis and management of prosthetic valve endocarditis are detailed in a separate ESC guideline [28].

Choice of the aortic/mitral prosthesis in favour of a mechanical prosthesis; the decision is based on the integration of several of the following factors

Recommendations	Class[a]	Level[b]
A mechanical prosthesis is recommended according to the desire of the informed patient and if there are no contraindications to long-term anticoagulation.[c]	I	C
A mechanical prosthesis is recommended in patients at risk of accelerated structural valve deterioration.[d]	I	C
A mechanical prosthesis should be considered in patients already on anticoagulation because of a mechanical prosthesis in another valve position.	IIa	C
A mechanical prosthesis should be considered in patients <60 years of age for prostheses in the aortic position and <65 years of age for prostheses in the mitral position.[e]	IIa	C
A mechanical prosthesis should be considered in patients with a reasonable life expectancy[f] for whom future redo valve surgery would be at high risk.	IIa	C
A mechanical prosthesis may be considered in patients already on long-term anticoagulation due to the high risk for thromboembolism.[g]	IIb	C

LV: left ventricular.
[a]Class of recommendation.
[b]Level of evidence.
[c]Increased bleeding risk because of comorbidities, compliance concerns or geographic, lifestyle or occupational conditions.
[d]Young age (<40 years), hyperparathyroidism.
[e]In patients 60–65 years of age who should receive an aortic prosthesis and those between 65 and 70 years of age in the case of mitral prosthesis, both valves are acceptable and the choice requires careful analysis of factors other than age.
[f]Life expectancy should be estimated at >10 years according to age, sex, comorbidities and country-specific life expectancy.
[g]Risk factors for thromboembolism are atrial fibrillation, previous thromboembolism, hypercoagulable state and severe LV systolic dysfunction.

Choice of the aortic/mitral prosthesis in favour of a bioprosthesis; the decision is based on the integration of several of the following factors

Recommendations	Class[a]	Level[b]
A bioprosthesis is recommended according to the desire of the informed patient.	I	C
A bioprosthesis is recommended when good-quality anticoagulation is unlikely (compliance problems, not readily available) or contraindicated because of high bleeding risk (previous major bleed, comorbidities, unwillingness, compliance problems, lifestyle, occupation).	I	C
A bioprosthesis is recommended for reoperation for mechanical valve thrombosis despite good long-term anticoagulant control.	I	C
A bioprosthesis should be considered in patients for whom there is a low likelihood and/or a low operative risk of future redo valve surgery.	IIa	C
A bioprosthesis should be considered in young women contemplating pregnancy.	IIa	C
A bioprosthesis should be considered in patients >65 years of age for a prosthesis in the aortic position or >70 years of age in a mitral position or those with a life expectancy[c] lower than the presumed durability of the bioprosthesis.[d]	IIa	C

[a]Class of recommendation.
[b]Level of evidence.
[c]Life expectancy should be estimated according to age, sex, comorbidities and country-specific life expectancy.
[d]In patients 60–65 years of age who should receive an aortic prosthesis and those between 65 and 70 years of age in the case of mitral prosthesis, both valves are acceptable and the choice requires careful analysis of factors other than age.

11.2.1 Baseline assessment and modalities of follow-up.

All patients require lifelong follow-up by a cardiologist after valve surgery to detect early deterioration in prosthetic function or ventricular function or progressive disease of another heart valve. Clinical assessment should be performed yearly or as soon as possible if new cardiac symptoms occur. TTE should be performed if any new symptoms occur after valve replacement or if complications are suspected. After transcatheter as well as surgical implantation of a bioprosthetic valve, echocardiography, including the measurement of transprosthetic gradients, should be performed within 30 days (preferably ~30 days for surgery) after valve implantation (i.e. baseline imaging), at 1 year after implantation and annually thereafter [168]. TOE should be considered if TTE is of poor quality and in all cases of suspected prosthetic dysfunction or endocarditis [169,170]. Cinefluoroscopy for mechanical valves and MSCT scanning provide useful additional information if valve thrombus or pannus are suspected to impair valve function [170].

11.2.2 Antithrombotic management.

11.2.2.1 General management. Antithrombotic management should address effective control of modifiable risk factors for thromboembolism in addition to the prescription of antithrombotic drugs [171]. Indications for antithrombotic therapy after valve repair or replacement are summarized in the table of recommendations for indications for antithrombotic therapy after valvular surgery.

In patients with surgical aortic bioprostheses, the use of low-dose aspirin is now favoured as an alternative to postoperative anticoagulant therapy, although this relies on low-level evidence [42, 172, 173].

When postoperative anticoagulant therapy is indicated, oral anticoagulation should be started during the first postoperative days. Intravenous unfractionated heparin (UFH), monitored to an activated partial thromboplastin time of 1.5–2.0 times the control value, enables rapid anticoagulation to be obtained before the INR

Table 10: Target INR for mechanical prostheses

Prosthesis thrombogenicity	Patient-related risk factors[a]	
	None	≥1 risk factor
Low[b]	2.5	3.0
Medium[c]	3.0	3.5
High[d]	3.5	4.0

INR: international normalized ratio; LVEF: left ventricular ejection fraction.
[a]Mitral or tricuspid valve replacement; previous thromboembolism; atrial fibrillation; mitral stenosis of any degree; LVEF <35%.
[b]Carbomedics, Medtronic Hall, ATS, Medtronic Open-Pivot, St Jude Medical, On-X, Sorin Bicarbon.
[c]Other bileaflet valves with insufficient data.
[d]Lillehei-Kaster, Omniscience, Starr-Edwards (ball-cage), Bjork-Shiley and other tilting-disc valves.

rises [42]. Low-molecular-weight heparin (LMWH) seems to offer effective and stable anticoagulation and has been used in observational series mostly using enoxaparin [174, 175]. This is off-label use.

The first postoperative month is a high-risk period for thromboembolism. The addition of aspirin to anticoagulant therapy decreases postoperative thromboembolic risk but increases bleeding risk and cannot be recommended routinely [176].

VKAs should be favoured when long-term anticoagulant therapy is needed in patients with a bioprosthesis. Despite the absence of data from clinical trials, NOACs can be used in patients who have atrial fibrillation associated with a bioprosthesis after the third postoperative month [43]. There is no evidence to support the use of antiplatelet agents beyond 3 months in patients with surgical bioprostheses who do not have an indication other than the presence of the bioprosthesis itself.

A combination of low-dose aspirin and a thienopyridine is commonly used early after TAVI, followed by aspirin or a thienopyridine alone in patients who have no other indication for oral anticoagulation. Recent data suggest that single antiplatelet therapy may have a better safety profile than dual antiplatelet therapy after TAVI [177]. Observational findings suggest that anticoagulant therapy reduces the incidence of subclinical thrombosis compared with dual antiplatelet therapy [178]. The results of ongoing large-scale, dedicated trials are needed to improve evidence in this field.

11.2.2.2 Target international normalized ratio. Target INR should be adapted to patient risk factors and the thrombogenicity of the prosthesis (Table 10) [171]. Recent randomized trials supported lower target INRs for aortic prostheses [186–188]. However, limited statistical power, certain methodological concerns and the restriction to certain prostheses and/or to the use of INR self-management led the Task Force not to change recommendations for target INR.

We recommend a median INR value rather than a range to avoid considering extreme values in the target range as a valid target INR. High variability of the INR is a strong independent predictor of reduced survival after valve replacement. There is now evidence that INR self-management reduces INR variability and clinical events, including patients with heart valve prosthesis [181]; however, appropriate training and regular quality control are required. However, monitoring by an anticoagulant clinic should be considered for patients with unstable INR or anticoagulant-related complications. Systematic genotyping of patients on VKA treatment is not recommended in the absence of convincing clinical benefit and concerns regarding cost-effectiveness [189].

11.2.2.3 Management of vitamin K antagonist overdose and bleeding. The risk of major bleeding rises considerably when the INR exceeds 4.5 and increases exponentially above an INR of 6.0. An INR ≥6.0 therefore requires rapid reversal of anticoagulation because of the risk of subsequent bleeding.

In the absence of bleeding, management depends on the target INR, the actual INR and the half-life of the VKA used. It is possible to stop oral anticoagulation and to allow the INR to fall gradually or to give oral vitamin K in increments of 1 or 2 mg [190]. Immediate reversal of anticoagulation using intravenous prothrombin complex concentrate and vitamin K is required only for severe bleeding, defined as not amenable to local control, threatening life or important organ function (e.g. intracranial bleeding), causing haemodynamic instability or requiring an emergency surgical procedure or transfusion [190]. There are no data suggesting that the risk of thromboembolism due to transient reversal of anticoagulation outweighs the consequences of severe bleeding in patients with mechanical prostheses. The optimal time to restart anticoagulant therapy should be discussed in relation to the location of the bleeding event, its evolution and interventions performed to stop bleeding and/or to treat an underlying cause [191].

11.2.2.4 Combination of oral anticoagulants with antiplatelet drugs. The addition of aspirin with contemporary target INRs has not been studied in patients without vascular disease [42]. Underlying uncertainties on the risk–benefit ratio of the combination of VKA with aspirin account for discrepancies between different recommendations [192, 193]. When added to anticoagulation, antiplatelet agents decrease thromboembolic risk but increase the risk of major bleeding [194]. Therefore they should not be prescribed to all patients with prosthetic valves but should be reserved for specific indications according to the analysis of benefit and increased risk of major bleeding. If used, the lower recommended dose should be prescribed (e.g. aspirin 75–100 mg/day).

Indications for the addition of an antiplatelet agent to oral anticoagulants are detailed in section 11.2.2.1 (see table of recommendations for indications for antithrombotic therapy in patients with a prosthetic heart valve or valve repair) and in Figure 7. The use of prasugrel or ticagrelor as part of triple therapy should be avoided [37]. During triple antithrombotic therapy, close monitoring of INR is advised and INR should be kept in the low target range.

11.2.2.5 Interruption of anticoagulant therapy for planned invasive procedures. Anticoagulation during non-cardiac surgery requires careful management based on risk assessment [196]. It is recommended not to interrupt oral anticoagulation for most minor surgical procedures (including dental extraction, cataract removal) and those procedures where bleeding is easily controlled [197]. Major surgical procedures require an INR <1.5. In patients with a mechanical prosthesis, oral anticoagulant therapy should be stopped before surgery and bridging using heparin is recommended [196]. UFH remains the only approved heparin treatment in patients with mechanical prostheses; intravenous administration should be favoured over the subcutaneous route. The use of subcutaneous LMWH, although off-label, is an alternative to UFH for bridging. When LMWHs are used they should be administered twice a day using

Indications for antithrombotic therapy in patients with a prosthetic heart valve or valve repair

Recommendations	Class[a]	Level[b]
Mechanical prostheses		
Oral anticoagulation using a VKA is recommended lifelong for all patients [179, 180].	I	B
Bridging using therapeutic doses of UFH or LMWH is recommended when VKA treatment should be interrupted.	I	C
The addition of low-dose aspirin (75–100 mg/day) to VKA should be considered after thromboembolism despite an adequate INR.	IIa	C
The addition of low-dose aspirin (75–100 mg/day) to VKA may be considered in the case of concomitant atherosclerotic disease.	IIb	C
INR self-management is recommended provided appropriate training and quality control are performed [181].	I	B
In patients treated with coronary stent implantation, triple therapy with aspirin (75–100 mg/day), clopidogrel (75 mg/day) and VKA should be considered for 1 month, irrespective of the type of stent used and the clinical presentation (i.e. ACS or stable CAD) [182].	IIa	B
Triple therapy comprising aspirin (75–100 mg/day), clopidogrel (75 mg/day) and VKA for >1 month and up to 6 months should be considered in patients with high ischaemic risk due to ACS or other anatomical/procedural characteristics that outweighs the bleeding risk [182].	IIa	B
Dual therapy comprising VKA and clopidogrel (75 mg/day) should be considered as an alternative to 1-month triple antithrombotic therapy in patients in whom the bleeding risk outweighs the ischaemic risk [183, 184].	IIa	A
In patients who have undergone PCI, discontinuation of antiplatelet treatment should be considered at 12 months [185].	IIa	B
In patients requiring aspirin and/or clopidogrel in addition to VKA, the dose intensity of VKA should be carefully regulated with a target INR in the lower part of the recommended target range and a time in the therapeutic range >65–70% [182, 184].	IIa	B
The use of NOACs is contraindicated [45].	III	B
Bioprostheses		
Oral anticoagulation is recommended lifelong for patients with surgical or transcatheter implanted bioprostheses who have other indications for anticoagulation.[c]	I	C
Oral anticoagulation using a VKA should be considered for the first 3 months after surgical implantation of a mitral or tricuspid bioprosthesis.	IIa	C
Oral anticoagulation using a VKA should be considered for the first 3 months after surgical mitral or tricuspid valve repair.	IIa	C
Low-dose aspirin (75–100 mg/day) should be considered for the first 3 months after surgical implantation of an aortic bioprosthesis or valve-sparing aortic surgery.	IIa	C
Dual antiplatelet therapy should be considered for the first 3–6 months after TAVI, followed by lifelong single antiplatelet therapy in patients who do not need oral anticoagulation for other reasons.	IIa	C
Single antiplatelet therapy may be considered after TAVI in the case of high bleeding risk.	IIb	C
Oral anticoagulation may be considered for the first 3 months after surgical implantation of an aortic bioprosthesis.	IIb	C

ACS: acute coronary syndrome; CAD: coronary artery disease; INR: international normalized ratio; LMWH: low-molecular-weight heparin; LV: left ventricular; PCI: percutaneous coronary intervention; NOAC: non-vitamin K antagonist oral anticoagulant; TAVI: transcatheter aortic valve implantation; UFH: unfractionated heparin; VKA: vitamin K antagonist.

[a]Class of recommendation.

[b]Level of evidence.

[c]Atrial fibrillation, venous thromboembolism, hypercoagulable state or, with a lesser degree of evidence, severely impaired LV dysfunction (ejection fraction <35%).

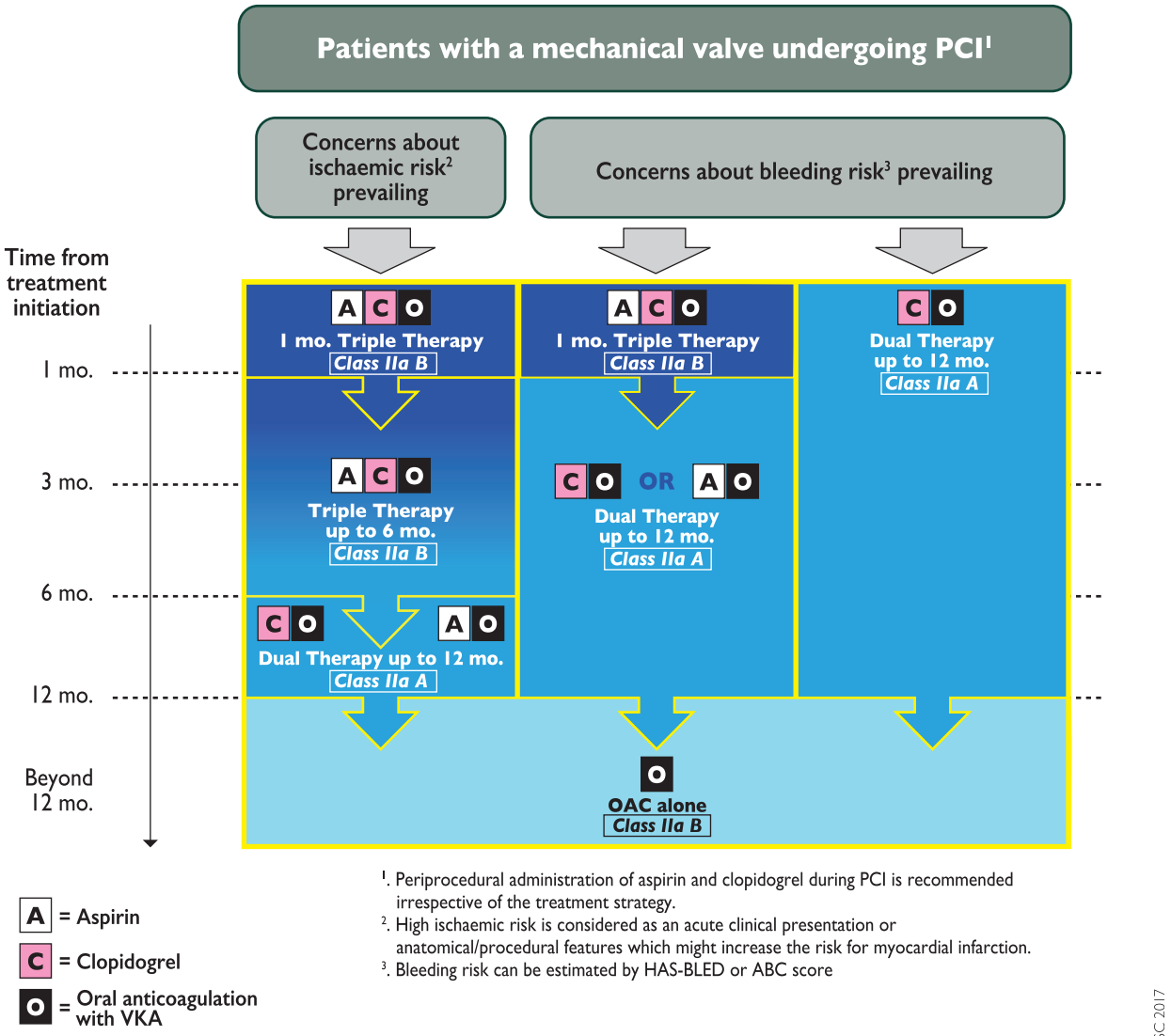

Figure 7: Antithrombotic therapy in patients with mechanical valve prosthesis undergoing PCI (adapted from the 2017 ESC Focused Update on Dual Antiplatelet Therapy [195]). A: aspirin; ABC: age, biomarkers, clinical history; ACS: acute coronary syndrome; C: clopidogrel; mo.: month(s); O: oral anticoagulation with a vitamin K antagonist; PCI: percutaneous coronary intervention. For more details regarding estimation of bleeding risk (HAS-BLED and ABC score) see the 2017 ESC Focused Update on Dual Antiplatelet Therapy [195].

therapeutic doses, adapted to body weight and renal function and, if possible, with monitoring of anti-Xa activity with a target of 0.5–1.0 U/ml. Fondaparinux should not be used for bridging in patients with mechanical prosthesis. Practical modalities of anticoagulation bridging are detailed in Figure 8.

If required, after a careful risk–benefit assessment, combined aspirin therapy should be discontinued 1 week before a non-cardiac procedure.

Oral anticoagulation can be continued at modified doses in the majority of patients who undergo cardiac catheterization, in particular using the radial approach. In patients who require transseptal catheterization for valvular interventions, direct LV puncture or pericardial drainage, oral anticoagulants should be stopped and bridging anticoagulation administered [171].

In patients who have a subtherapeutic INR during routine monitoring, bridging with UFH or preferably LMWH in an outpatient setting is indicated until a therapeutic INR value is reached.

11.2.3 Management of valve thrombosis. Obstructive valve thrombosis should be suspected promptly in any patient with any type of prosthetic valve who presents with recent dyspnoea or an embolic event. The diagnosis should be confirmed by TTE and TOE, cinefluoroscopy or CT scan if promptly available [169, 170].

The management of mechanical prosthetic valve thrombosis is high risk, whatever the option taken. Surgery is high risk because it is most often performed under emergency conditions and is a reintervention. On the other hand, fibrinolysis carries risks of bleeding, systemic embolism and recurrent thrombosis that are higher than after surgery [198].

Emergency valve replacement is recommended for obstructive prosthetic valve thrombosis in critically ill patients without a contraindication to surgery (see table of recommendations in section 11.2.3 for management of prosthetic dysfunction and Figure 9).

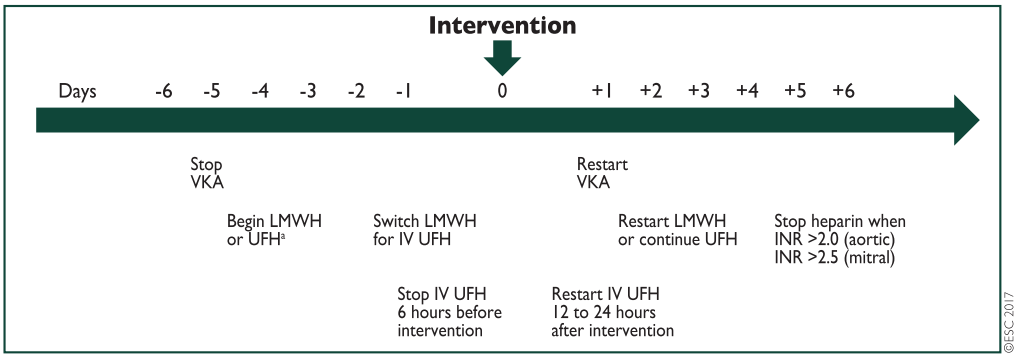

Figure 8: Main bridging steps for an intervention requiring interruption of oral anticoagulation in a patient with a mechanical prosthesis. Timing should be individualized according to patient characteristics, actual INR, and the type of intervention (reproduced with permission from Iung and Rodes-Cabau [42]). INR: international normalized ratio; IV: intravenous; LMWH: low-molecular-weight heparin; UFH: unfractionated heparin; VKA: vitamin K antagonist.
[a]IV UFH may be favoured in patients at high thrombotic risk.

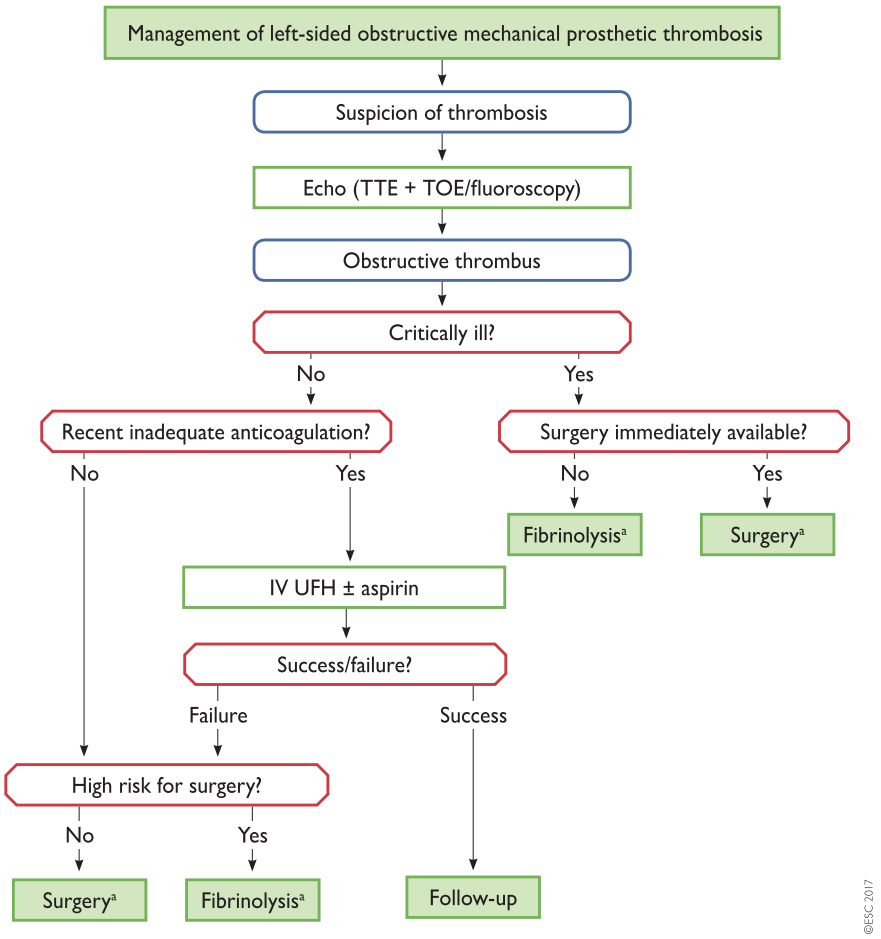

Figure 9: Management of left-sided obstructive mechanical prosthetic thrombosis. IV: intravenous; TOE: transoesophageal echocardiography; TTE: transthoracic echocardiography; UFH: unfractionated heparin.
[a]Risk and benefits of both treatments should be individualized. The presence of a first-generation prosthesis is an incentive to surgery.

Management of non-obstructive mechanical prosthetic valve thrombosis depends mainly on the occurrence of a thromboembolic event and the size of the thrombus (Figure 10). Surgery should be considered for a large (>10 mm) non-obstructive prosthetic valve thrombus complicated by embolism or which persists despite optimal anticoagulation [199]. Fibrinolysis may be considered if surgery is at high risk but carries a risk of bleeding and thromboembolism.

Valve thrombosis occurs mainly in mechanical prostheses. However, cases of thrombosis of bioprostheses have been reported after surgery or transcatheter valve implantation [200,201]. Subclinical thrombosis of bioprostheses may be more frequent when assessed by cardiac CT [202], and subclinical thrombosis of TAVI prostheses can be associated with a moderate increase in transprosthetic gradients, but the clinical consequences are unknown [203].

Anticoagulation using a VKA and/or UFH is the first-line treatment of bioprosthetic valve thrombosis.

Management of prosthetic valve dysfunction

Recommendations	Class[a]	Level[b]
Mechanical prosthetic thrombosis		
Urgent or emergency valve replacement is recommended for obstructive thrombosis in critically ill patients without serious comorbidity.	I	C
Fibrinolysis (using recombinant tissue plasminogen activator 10 mg bolus + 90 mg in 90 min with UFH or streptokinase 1 500 000 U in 60 min without UFH) should be considered when surgery is not available or is very high risk or for thrombosis of right-sided prostheses.	IIa	C
Surgery should be considered for large (>10 mm) non-obstructive prosthetic thrombus complicated by embolism.	IIa	C
Bioprosthetic thrombosis		
Anticoagulation using a VKA and/or UFH is recommended in bioprosthetic valve thrombosis before considering reintervention.	I	C
Haemolysis and paravalvular leak		
Reoperation is recommended if paravalvular leak is related to endocarditis or causes haemolysis requiring repeated blood transfusions or leading to severe symptoms.	I	C
Transcatheter closure may be considered for paravalvular leaks with clinically significant regurgitation in surgical high-risk patients (Heart Team decision).	IIb	C
Bioprosthetic failure		
Reoperation is recommended in symptomatic patients with a significant increase in transprosthetic gradient (after exclusion of valve thrombosis) or severe regurgitation.	I	C
Reoperation should be considered in asymptomatic patients with significant prosthetic dysfunction if reoperation is at low risk.	IIa	C
Transcatheter valve-in-valve implantation in the aortic position should be considered by the Heart Team depending on the risk of reoperation and the type and size of prosthesis.	IIa	C

UFH: unfractionated heparin; VKA: vitamin K antagonist.
[a]Class of recommendation.
[b]Level of evidence.

11.2.4 Management of thromboembolism. Thromboembolism after valve surgery is multifactorial in origin [171]. Thorough investigation of each episode of thromboembolism is therefore essential (including cardiac and non-cardiac imaging) (Figure 10) rather than simply increasing the target INR or adding an antiplatelet agent. Prevention of further thromboembolic events involves the treatment of risk factors, optimization of anticoagulation control and the addition of low-dose aspirin (≤100 mg daily) after careful analysis of the risk–benefit ratio.

11.2.5 Management of haemolysis and paravalvular leak. Blood tests for haemolysis should be part of routine follow-up after valve replacement. Lactate dehydrogenase, although non-specific, is related to the severity of haemolysis. The diagnosis of haemolytic anaemia requires TOE to detect a paravalvular leak if TTE is not contributory. Reoperation is recommended if the paravalvular leak is related to endocarditis or causes haemolysis requiring repeated blood transfusions or leading to severe symptoms (see table of recommendations in section 11.2.3 for management of prosthetic dysfunction). Medical therapy, including iron supplementation, beta-blockers and erythropoietin, is indicated in patients with severe haemolytic anaemia when contraindications to surgery are present. Transcatheter closure of a paravalvular leak is feasible, but experience is limited and there is presently no conclusive evidence to show a consistent efficiency [204].

11.2.6 Management of bioprosthetic valve failure. After transcatheter as well as surgical implantation of a bioprosthetic valve, echocardiography including the measurement of transprosthetic gradients should be performed within 30 days (preferably ~30 days for surgery) after valve implantation (i.e. baseline imaging), at 1 year after implantation and annually thereafter [168]. The definitions of structural valve deterioration and bioprosthetic valve failure have recently been standardized in a consensus publication [168].

Indications for reintervention are detailed in the table of recommendations for management of prosthetic dysfunction (section 11.2.3).

Percutaneous balloon interventions should be avoided in the treatment of stenotic left-sided bioprostheses.

Transcatheter valve-in-valve implantation is now an option for treating degenerated bioprostheses in patients with increased surgical risk. Experience is mostly for bioprostheses in the aortic position and remains limited in the mitral position and even more so in the tricuspid position [205,206]. Valve-in-valve and valve-in-ring procedures may be reasonable alternatives if the patient is at increased surgical risk, but it is necessary that the multidisciplinary Heart Team discusses every patient and chooses the best individualized approach.

11.2.7 Heart failure. Heart failure after valve surgery should lead to a search for prosthetic dysfunction or prosthesis-patient mismatch, deterioration of repair, LV dysfunction or progression of another valve disease. Non-valvular-related causes such as CAD, hypertension or sustained arrhythmias should also be considered. The management of patients with heart failure should follow the relevant guidelines [113].

Key points

- The choice between a mechanical prosthesis and a bioprosthesis should not overstress the role of age and should take into account the wishes of the informed patient.

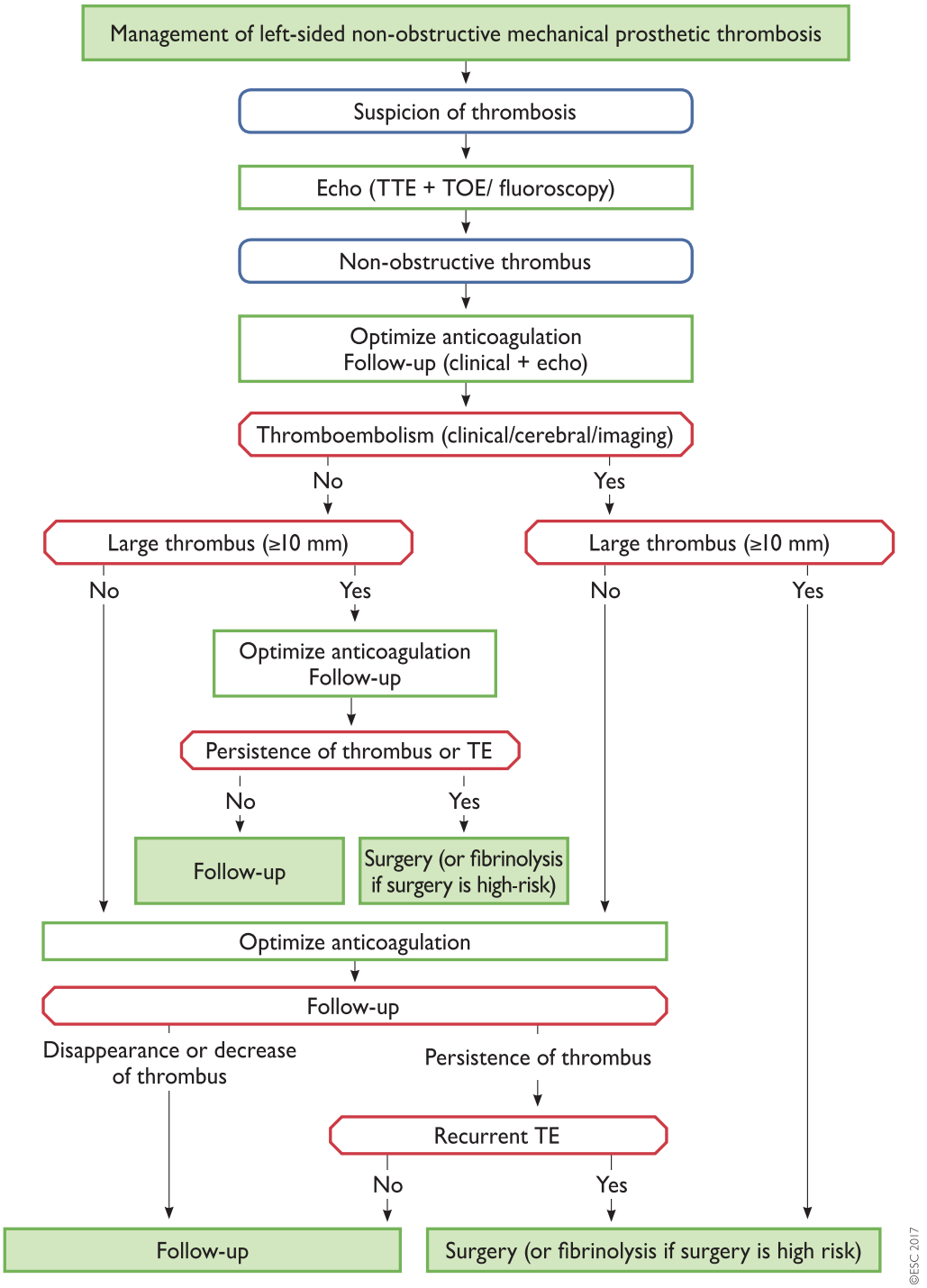

Figure 10: Management of left-sided non-obstructive mechanical prosthetic thrombosis. TE: thromboembolism; TOE: transoesophageal echocardiography; TTE: transthoracic echocardiography.

- Patients with a mechanical prosthesis require lifelong treatment using VKA with a target INR adapted to the prosthesis and patient characteristics.
- Low-dose aspirin should be added to VKA only in selected patients with a mechanical prosthesis who have atherosclerosis or recurrent embolism.
- The risk of thromboembolism and bleeding is higher during the postoperative period and requires increased awareness of the monitoring of anticoagulant therapy.
- The management of anticoagulant therapy during non-cardiac surgery should be adapted to the type of surgery. Minor surgical procedures generally do not require interruption of anticoagulation.

Gaps of evidence

- The safety and efficacy of very-low-target INRs (median <2.5) in patients with a mechanical prosthesis in the aortic position should be further studied.
- The safety and efficacy of NOACs in patients with a mechanical prosthesis require further research.
- The safety and efficacy of low-dose aspirin associated with contemporary target INRs in patients with a mechanical prosthesis, according to the presence or absence of atherosclerosis, require further evaluation.
- Optimal early antithrombotic therapy after implantation of surgical and transcatheter aortic bioprostheses needs to be better defined.
- Long-term outcome data of transcatheter valve-in-valve and valve-in-ring procedures are required.

12. MANAGEMENT DURING NON-CARDIAC SURGERY

Cardiovascular morbidity and mortality are increased in patients with VHD who undergo non-cardiac surgery. Symptomatic severe aortic stenosis or mitral stenosis may require valve replacement or percutaneous intervention before non-cardiac surgery. A detailed description of these recommendations is available [196].

12.1 Preoperative evaluation

Echocardiography should be performed in any patient with VHD. Determination of functional capacity is a pivotal step in preoperative risk assessment, measured either by exercise test or ability to perform activities in daily life. The decision for management should be taken after multidisciplinary discussion involving cardiologists, surgeons and anaesthesiologists.

12.2 Specific valve lesions

12.2.1 Aortic stenosis. In patients with severe aortic stenosis, urgent non-cardiac surgery should be performed under careful haemodynamic monitoring.

The management related to elective non-cardiac surgery depends on the presence of symptoms and the type of surgery [196, 207, 208]. In symptomatic patients, aortic valve replacement should be considered before non-cardiac surgery. In patients at increased surgical risk, TAVI is a therapeutic option. In asymptomatic patients, elective non-cardiac surgery can be performed safely, albeit with a risk of worsening heart failure [207, 208]. If non-cardiac surgery implies large volume shifts, aortic valve replacement should be considered first (Figure 11).

12.2.2 Mitral stenosis. Non-cardiac surgery can be performed safely in patients with non-significant mitral stenosis (valve area >1.5 cm^2) and in asymptomatic patients with significant mitral stenosis and a systolic pulmonary artery pressure <50 mmHg.

In symptomatic patients or in patients with systolic pulmonary artery pressure >50 mmHg, correction of mitral stenosis, by means of PMC whenever possible, should be attempted before non-cardiac surgery if it is high risk.

12.2.3 Aortic and mitral regurgitation. Non-cardiac surgery can be performed safely in asymptomatic patients with severe mitral regurgitation or aortic regurgitation and preserved LV function. The presence of symptoms or LV dysfunction should lead to consideration of valvular surgery, but this is seldom needed before non-cardiac surgery. If LV dysfunction is severe (ejection fraction <30%), non-cardiac surgery should be performed only if strictly necessary, after optimization of medical therapy for heart failure.

12.3 Perioperative monitoring

Heart rate control (particularly in mitral stenosis) and careful fluid management (particularly in aortic stenosis) are needed. TOE monitoring may be considered.

Key points

- In symptomatic patients with severe aortic stenosis, aortic valve replacement or TAVI should be considered before non-cardiac surgery.
- In patients with severe mitral stenosis and symptoms or pulmonary artery pressure >50 mmHg, PMC should be attempted before non-cardiac surgery.

13. MANAGEMENT DURING PREGNANCY

Detailed guidelines on the management of cardiovascular disease during pregnancy are available in another document [209].

The decision for management during pregnancy should be taken after multidisciplinary discussion involving cardiologists, obstetricians and anaesthesiologists [209]. Valve disease should be evaluated before pregnancy and treated if necessary. Pregnancy should be discouraged in severe mitral stenosis, severe symptomatic aortic stenosis and with an aortic diameter >45 mm in Marfan syndrome or > 27.5 mm/m^2 in Turner syndrome.

Caesarean section is recommended for patients with severe mitral or aortic stenosis, ascending aortic diameter >45 mm or severe pulmonary hypertension, as well as women on oral anticoagulants in preterm labour.

13.1 Native valve disease

Moderate or severe mitral stenosis with a valve area <1.5 cm^2 in pregnant women is usually poorly tolerated. PMC should be considered in severely symptomatic patients (NYHA class III-IV) and/or those with systolic pulmonary artery pressure >50 mmHg despite optimal therapy. PMC should be performed after the 20th week of pregnancy in experienced centres [209].

Complications of severe aortic stenosis occur mainly in patients who were symptomatic before pregnancy and among

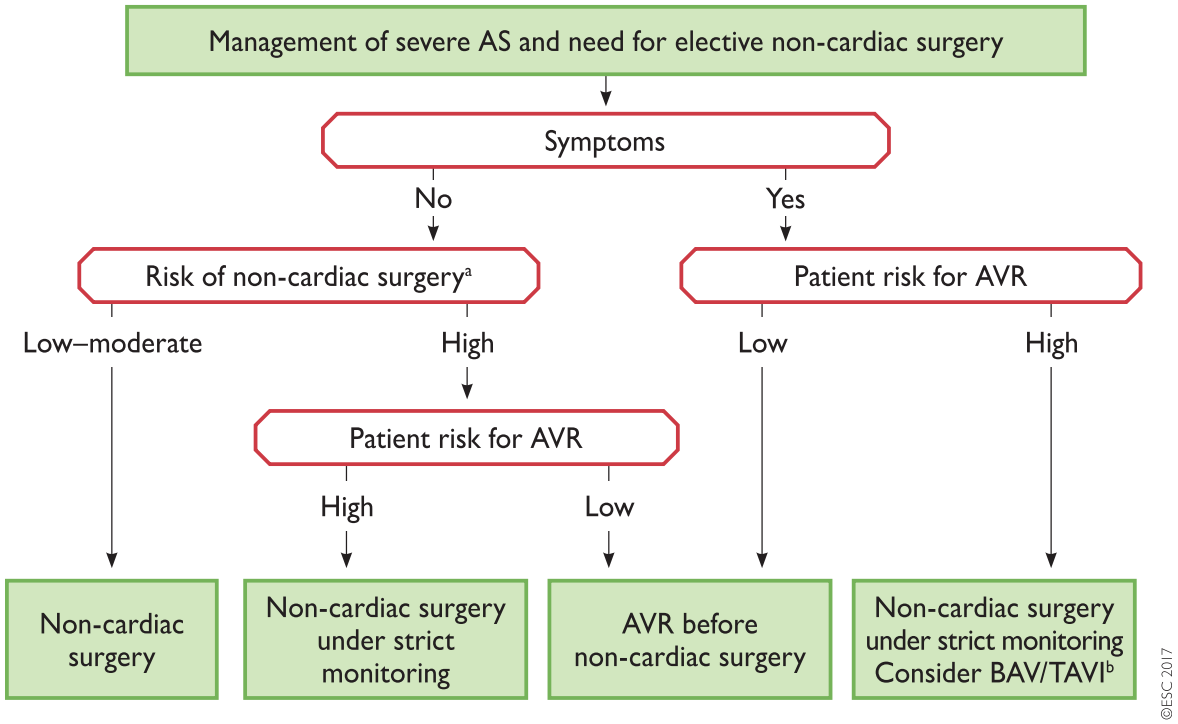

Figure 11: Management of severe aortic stenosis and elective non-cardiac surgery according to patient characteristics and type of surgery. AS: aortic stenosis; AVR: aortic valve replacement; BAV: balloon aortic valvuloplasty; TAVI: transcatheter aortic valve implantation.
[a]Classification into three groups according to the risk of cardiac complications (30-day death and myocardial infarction) for non-cardiac surgery (high-risk >5%; intermediate risk 1–5%; low risk <1%) [196].
[b]Non-cardiac surgery performed only if strictly needed. The choice between percutaneous aortic valvuloplasty and TAVI should take into account patient life expectancy.

those with impaired LV function. Evaluation with an exercise test is recommended before pregnancy.

Chronic mitral regurgitation and aortic regurgitation are well tolerated, even when severe, provided LV systolic function is preserved.

Surgery under cardiopulmonary bypass is associated with a foetal mortality rate of 15–30% [210] and should be restricted to the rare conditions that threaten the mother's life.

13.2 Prosthetic valves

Maternal mortality is estimated at 1–4% and serious events occur in up to 40% of women with mechanical valves [211].

Therapeutic anticoagulation is extremely important to avoid complications. In patients requiring ≤5 mg warfarin, oral anticoagulants throughout pregnancy and a change to UFH before delivery is favoured. In patients requiring higher doses, switching to LMWH during the first trimester with strict anti-Xa monitoring (therapeutic range 0.8–1.2 IU/ml) and the use of oral anticoagulants afterwards is favoured [209].

Key points

- Pregnancy should be discouraged in women with severe mitral stenosis and severe symptomatic aortic stenosis.
- Pregnancy in women with a mechanical valve, especially in the mitral position, is associated with a high risk for maternal and foetal complications. Therapeutic anticoagulation during pregnancy is of utmost importance in these patients.

Gaps in evidence

The optimal management of pregnant women with mechanical heart valves with regards to the antithrombotic regimen needs to be better defined.

14. TO DO AND NOT TO DO MESSAGES FROM THE GUIDELINES

Recommendations	Class[a]	Level[b]
Management of CAD in patients with VHD (adapted from Windecker *et al.* [16])		
Coronary angiography[c] is recommended before valve surgery in patients with severe VHD and any of the following: • history of cardiovascular disease • suspected myocardial ischaemia[d] • LV systolic dysfunction • in men aged over 40 years and postmenopausal women • one or more cardiovascular risk factors.	I	C
Coronary angiography is recommended in the evaluation of moderate to severe secondary mitral regurgitation.	I	C
CABG is recommended in patients with a primary indication for aortic/mitral valve surgery and coronary artery diameter stenosis ≥70%.	I	C
Management of atrial fibrillation in patients with VHD		
The use of NOACs is not recommended in patients with atrial fibrillation and moderate to severe mitral stenosis.	III	C
NOACs are contraindicated in patients with a mechanical valve [45].	III	B
Indications for surgery		
A) Severe aortic regurgitation		
Surgery is indicated in symptomatic patients [57,58,66,67].	I	B
Surgery is indicated in asymptomatic patients with resting LVEF ≤50% [57,58].	I	B
Surgery is indicated in patients undergoing CABG or surgery of the ascending aorta, or of another valve.	I	C
Heart Team discussion is recommended in selected patients[c] in whom aortic valve repair may be a feasible alternative to valve replacement.	I	C
B) Aortic root disease (irrespective of the severity of aortic regurgitation)		
Aortic valve repair, using the reimplantation or remodelling with aortic annuloplasty technique, is recommended in young patients 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 ascending aortic diameter ≥50 mm.	I	C
Indications for intervention in aortic stenosis and recommendations for the choice of intervention mode		
Intervention is indicated in symptomatic patients with severe, high-gradient aortic stenosis (mean gradient ≥40 mmHg or peak velocity ≥4.0 m/s) [91-93].	I	B
Intervention is indicated in symptomatic patients with severe low-flow, low-gradient (<40 mmHg) aortic stenosis with reduced ejection fraction, and evidence of flow (contractile) reserve excluding pseudosevere aortic stenosis.	I	C
Intervention should not be performed in patients with severe comorbidities when the intervention is unlikely to improve quality of life or survival.	III	C
Aortic valve interventions should only be performed in centres with both departments of cardiology and cardiac surgery on-site, and with structured collaboration between the two, including a Heart Team (heart valve centres).	I	C
The choice for intervention must be based on careful individual evaluation of technical suitability and weighing of risks and benefits of each modality (aspects to be considered are listed in Table 7). In addition, the local expertise and outcomes data for the given intervention must be taken into account.	I	C
SAVR is recommended in patients at low surgical risk (STS or EuroSCORE II <4% or logistic EuroSCORE I <10% and no other risk factors not included in these scores, such as frailty, porcelain aorta, sequelae of chest radiation) [93].	I	B
TAVI is recommended in patients who are not suitable for SAVR as assessed by the Heart Team [91,94].	I	B
In patients who are at increased surgical risk (STS or EuroSCORE II ≥4% or logistic EuroSCORE I ≥10%, or other risk factors not included in these scores such as frailty, porcelain aorta, sequelae of chest radiation), the decision between SAVR and TAVI should be made by the Heart Team according to the individual patient characteristics (see Table 7), with TAVI being favoured in elderly patients suitable for transfemoral access [91,94-102].	I	B
SAVR is indicated in asymptomatic patients with severe aortic stenosis and systolic LV dysfunction (LVEF <50%) not due to another cause.	I	C
SAVR is indicated in asymptomatic patients with severe aortic stenosis and abnormal exercise test showing symptoms on exercise clearly related to aortic stenosis.	I	C
SAVR is indicated in patients with severe aortic stenosis undergoing CABG, or surgery of the ascending aorta or of another valve.	I	C

Indications for intervention in severe primary mitral regurgitation		
Mitral valve repair should be the preferred technique when the results are expected to be durable.	I	C
Surgery is indicated in symptomatic patients with LVEF >30% [121,131,132].	I	B
Surgery is indicated in asymptomatic patients with LV dysfunction (LVESD ≥45 mm and/or LVEF ≤60%) [122,131].	I	B
Indications for mitral valve intervention in chronic secondary mitral regurgitation		
Surgery is indicated in patients with severe secondary mitral regurgitation undergoing CABG and LVEF >30%.	I	C
Indications for PMC and mitral valve surgery in clinically significant (moderate or severe) mitral stenosis (valve area ≤1.5 cm²)		
PMC is indicated in symptomatic patients without unfavourable characteristics for PMC [144,146,148].	I	B
PMC is indicated in any symptomatic patients with a contraindication or a high risk for surgery.	I	C
Mitral valve surgery is indicated in symptomatic patients who are not suitable for PMC.	I	C
Indications for tricuspid valve surgery		
Surgery is indicated in symptomatic patients with severe tricuspid stenosis.	I	C
Surgery is indicated in patients with severe tricuspid stenosis undergoing left-sided valve intervention.	I	C
Surgery is indicated in patients with severe primary tricuspid regurgitation undergoing left-sided valve surgery.	I	C
Surgery is indicated in symptomatic patients with severe isolated primary tricuspid regurgitation without severe right-ventricular dysfunction.	I	C
Surgery is indicated in patients with severe secondary tricuspid regurgitation undergoing left-sided valve surgery.	I	C
Choice of the aortic/mitral prosthesis – in favour of a mechanical prosthesis; the decision is based on the integration of several of the following factors		
A mechanical prosthesis is recommended according to the desire of the informed patient and if there are no contraindications to long-term anticoagulation.	I	C
A mechanical prosthesis is recommended in patients at risk of accelerated structural valve deterioration.	I	C
Choice of the aortic/mitral prosthesis – in favour of a bioprosthesis; the decision is based on the integration of several of the following factors		
A bioprosthesis is recommended according to the desire of the informed patient.	I	C
A bioprosthesis is recommended when good-quality anticoagulation is unlikely (compliance problems, not readily available) or contraindicated because of high bleeding risk (previous major bleed, comorbidities, unwillingness, compliance problems, lifestyle, occupation).	I	C
A bioprosthesis is recommended for reoperation for mechanical valve thrombosis despite good long-term anticoagulant control.	I	C
Indications for antithrombotic therapy in patients with mechanical prostheses and bioprostheses		
Mechanical prostheses		
Oral anticoagulation using a VKA is recommended lifelong for all patients [179,180].	I	B
Bridging using therapeutic doses of UFH or LMWH is recommended when VKA treatment should be interrupted.	I	C
INR self-management is recommended provided appropriate training and quality control are performed [181].	I	B
The use of NOACs is contraindicated [45].	III	B
Bioprostheses		
Oral anticoagulation is recommended lifelong for patients with surgical or transcatheter implanted bioprostheses who have other indications for anticoagulation.	I	C
Management of prosthetic valve dysfunction		
Urgent or emergency valve replacement is recommended for obstructive thrombosis in critically ill patients without serious comorbidity.	I	C
Anticoagulation using a VKA and/or UFH is recommended in bioprosthetic valve thrombosis before considering reintervention.	I	C
Reoperation is recommended if paravalvular leak is related to endocarditis or causes haemolysis requiring repeated blood transfusions or leading to severe symptoms.	I	C
Reoperation is recommended in symptomatic patients with a significant increase in transprosthetic gradient (after exclusion of valve thrombosis) or severe regurgitation.	I	C

15. WHAT IS NEW IN THE 2017 VALVULAR HEART DISEASE GUIDELINES?

What is new in the 2017 Valvular Heart Disease Guidelines?

Changes in recommendations	
2012	**2017**
Indications for intervention in symptomatic aortic stenosis	
IIb C Intervention may be considered in symptomatic patients with low-flow, low-gradient aortic stenosis and reduced ejection fraction without flow (contractile) reserve.	**IIa C** Intervention should be considered in symptomatic patients with low-flow, low-gradient aortic stenosis and reduced ejection fraction without flow (contractile) reserve, particularly when CT calcium scoring confirms severe aortic stenosis.
Choice of intervention in symptomatic aortic stenosis	
Recommendations for the use of TAVI (Tables on *"Contra-indications for TAVI"* and Table on *"Recommendations for the use of TAVI"*)	**Replaced by recommendations for the choice of intervention** See Section b in Table *"Indications for intervention in aortic stenosis and recommendations for the choice of intervention"* (Section 5.2), and Table 7 *"Aspects to be considered by the heart team for the decision between SAVR and TAVI in patients at increased surgical risk"*
Indications for surgery in asymptomatic aortic stenosis	
IIb C Markedly elevated BNP levels.	**IIa C** Markedly elevated BNP levels (>threefold age- and sex-corrected normal range) confirmed by repeated measurements without other explanations.
IIb C Increase of mean pressure gradient with exercise by >20 mmHg.	Taken out
IIb C Excessive LV hypertrophy in the absence of hypertension.	Taken out
Indications for intervention in asymptomatic severe primary mitral regurgitation	
IIb C Surgery may be considered in asymptomatic patients with preserved LV function, high likelihood of durable repair, low surgical risk, and: • Left atrial dilatation (volume index ≥60 mL/m² BSA) and sinus rhythm	**IIa C (modified!)** Surgery should be considered in asymptomatic patients with preserved LVEF (>60%) and LVESD 40–44 mm when a durable repair is likely, surgical risk is low, the repair is performed in heart valve centres, and the following finding is present: presence of significant LA dilatation (volume index ≥60 mL/m² BSA) in sinus rhythm.
Pulmonary hypertension on exercise (SPAP ≥ 60 mmHg at exercise)	Taken out
Indications for mitral valve intervention in secondary mitral regurgitation	
IIa C Surgery should be considered in patients with moderate secondary mitral regurgitation undergoing CABG	Taken out
IIb C When revascularization is not indicated, surgery may be considered in patients with severe secondary mitral regurgitation and LVEF >30%, who remain symptomatic despite optimal medical management (including CRT if indicated).	**IIb C (modified)** When revascularization is not indicated, surgery may be considered in patients with severe secondary mitral regurgitation and LVEF >30%, who remain symptomatic despite optimal medical management (including CRT if indicated) and have a low surgical risk. When revascularization is not indicated and surgical risk is not low, a percutaneous edge-to-edge procedure may be considered in patients with severe secondary mitral regurgitation and LVEF >30%, who remain symptomatic despite optimal medical management (including CRT if indicated) and who have a suitable valve morphology by echocardiography, avoiding futility. In patients with severe secondary mitral regurgitation and LVEF <30% who remain symptomatic despite optimal medical management (including CRT if indicated) and who have no option for revascularization, the Heart Team may consider percutaneous edge-to-edge procedure or valve surgery after careful evaluation for ventricular assist device or heart transplant according to individual patient characteristics. **Additional statement:** The lower thresholds defining severe MR compared to primary MR are based on their association with prognosis. However, it is unclear if prognosis is independently affected by MR compared to LV dysfunction. For isolated mitral valve treatment in secondary MR, thresholds of severity of MR for intervention still need to be validated in clinical trials. So far, no survival benefit has been confirmed for reduction of secondary MR.
Indications for antithrombotic therapy in patients with a prosthetic heart valve or valve repair	
IIa C The addition of low-dose aspirin (75–100 mg/day) to VKA should be considered in the case of concomitant atherosclerotic disease.	**IIb C** The addition of low-dose aspirin (75–100 mg/day) to VKA may be considered in the case of concomitant atherosclerotic disease.

What is new in the 2017 Valvular Heart Disease Guidelines? (continued)

2017 New recommendations

Management of CAD in patients with VHD

New IIa C recommendations:
- CT angiography should be considered as an alternative to coronary angiography before valve surgery in patients with severe VHD and low probability of CAD, or in whom conventional coronary angiography is technically not feasible or who are at high risk.
- PCI should be considered in patients with a primary indication to undergo TAVI and coronary artery diameter stenosis >70% in proximal segments.
- PCI should be considered in patients with a primary indication to undergo transcatheter mitral valve interventions and coronary artery diameter stenosis >70% in proximal segments.

Management of atrial fibrillation in VHD

New additional recommendations:
See new Table *"Management of atrial fibrillation in patients with VHD"* Section 3.7.2.

Indications for surgery in severe aortic regurgitation and aortic root disease

- **New I C recommendations:**
  Heart Team discussion is recommended in selected patientsc in whom aortic valve repair may be a feasible alternative to valve replacement.
- Aortic valve repair, using the reimplantation or remodelling with aortic annuloplasty technique, is recommended in young patients with aortic root dilation and tricuspid aortic valves, when performed by experienced surgeons.

- **New IIa C recommendation:**
  Surgery should be considered in patients who have aortic root disease with maximal ascending aortic diameter: ≥45 mm in patients with a *TGFBR1* or *TGFBR2* mutation (including Loeys-Dietz syndrome).

Diagnosis of severe aortic stenosis

See new recommendations for the diagnosis of severe aortic stenosis in Figure 2 and Table 6.

Indications for surgery in asymptomatic aortic stenosis

- **New IIa C recommendation:**
  Severe pulmonary hypertension (systolic pulmonary artery pressure at rest >60 mmHg confirmed by invasive measurement) without other explanation.

Indications for intervention in asymptomatic severe primary mitral regurgitation

New additional statement:
- If pulmonary hypertension (SPAP >50 mmHg at rest) is the only indication for surgery, the value should be confirmed by invasive measurement.

Management after valve intervention

New recommendation:
- After transcatheter as well as surgical implantation of a bioprosthetic valve, echocardiography − including the measurement of transprosthetic gradients − should be performed within 30 days (preferably around 30 days for surgery) after valve implantation (i.e. baseline imaging), at 1 year after implantation, and annually thereafter.

Indications for antithrombotic therapy in patients with a prosthetic heart valve or valve repair
New recommendations:

I B
- INR self-management is recommended provided appropriate training and quality control are performed.

IIa B
- In patients treated with coronary stent implantation, triple therapy with aspirin (75−100 mg/day), clopidogrel (75 mg/day), and VKA should be considered for 1 month, irrespective of the type of stent used and the clinical presentation (i.e. ACS or stable CAD).
- Triple therapy comprising aspirin (75–100 mg/day), clopidogrel (75 mg/day), and VKA for longer than 1 month and up to 6 months should be considered in patients with high ischaemic risk due to ACS or other anatomical/procedural characteristics that outweigh the bleeding risk.

IIa A
- Dual therapy comprising VKA and clopidogrel (75 mg/day) should be considered as an alternative to 1-month triple antithrombotic therapy in patients in whom the bleeding risk outweighs the ischaemic risk.

IIa B
- In patients who have undergone PCI, discontinuation of antiplatelet treatment should be considered at 12 months.
- In patients requiring aspirin and/or clopidogrel in addition to VKA, the dose intensity of VKA should be carefully regulated with a target INR in the lower part of the recommended target range and a time in therapeutic range >65−70%.

IIa C
- Dual antiplatelet therapy should be considered for the first 3–6 months after TAVI, followed by lifelong single antiplatelet therapy in patients who do not need oral anticoagulation for other reasons.

IIb C
- Single antiplatelet therapy may be considered after TAVI in the case of high bleeding risk.

III B
- The use of NOACs is contraindicated in mechanical valves

What is new in the 2017 Valvular Heart Disease Guidelines? (continued)

2017 New recommendations (continued)
Management of prosthetic valve dysfunction **New recommendations:**
I C Anticoagulation using a VKA and/or UFH is recommended in bioprosthetic valve thrombosis before considering reintervention.
I C Reoperation is recommended if paravalvular leak is related to endocarditis or causes haemolysis requiring repeated blood transfusions or leading to severe symptoms.
IIb C Transcatheter closure may be considered for paravalvular leaks with clinically significant regurgitation in surgical high-risk patients (Heart Team decision).
IIa C Transcatheter valve-in-valve implantation in aortic position should be considered by the Heart Team depending on the risk of reoperation and the type and size of prosthesis.
2017 NEW/REVISED CONCEPTS
New concept • Condense guideline document linked to ESC Textbook for more background information. • Key points and gaps in evidence after each section.
Heart valve centres and Heart Team **New concept!** • See new Table 5 *"Recommended requirements of a heart valve centre"*, see Section 3.6.

Class I	Class IIa	Class IIb	Class III

16. APPENDIX

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