

2021 ESC GUIDELINES

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ESC GUIDELINES

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

With the special contribution of the Heart Failure Association (HFA) of the ESC

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New concepts

A change of the term 'heart failure with mid-range ejection fraction' to 'heart failure with mildly reduced ejection fraction' (HFmrEF).

A new simplified treatment algorithm for HFrEF.

The addition of a treatment algorithm for HFrEF according to phenotypes.

Modified classification for acute HF.

Updated treatments for most non-cardiovascular comorbidities including diabetes, hyperkalaemia, iron deficiency, and cancer.

Updates on cardiomyopathies including the role of genetic testing and new treatments.

The addition of key quality indicators.

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KEY POINTS

- The nomenclature for HF with left ventricular ejection fraction (LVEF) of 41-49% has been revised to HF with mildly reduced EF (HFmEF). HF with LVEF $\leq 40\%$ remains HF with reduced EF (HFrEF), and HF with LVEF $\geq 50\%$ remains HF with preserved EF (HFpEF).
- All patients with suspected HF should have an electrocardiogram, transthoracic echocardiogram, chest X-ray, blood tests including cell count, urea and electrolytes, thyroid function, glycated hemoglobin (HbA1c), lipid, iron studies, and B-type natriuretic peptide (BNP/NT-proBNP). Cardiac magnetic resonance imaging is recommended in those with poor acoustic windows with an echo or in patients with suspected infiltrative cardiomyopathy, hemochromatosis, LV noncompaction, or myocarditis.
- Guideline-directed medical therapy (GDMT) for patients with HFrEF and New York Heart Association (NYHA) class II symptoms or worse now includes angiotensin receptor neprilysin inhibitor (ARNI) as a replacement for angiotensin-converting enzyme (ACE) inhibitors and addition of SGLT-2 inhibitors (dapagliflozin or empagliflozin) as Class I recommendations.

- Implantable cardioverter-defibrillators (ICDs) are recommended for primary prevention of sudden cardiac death for symptomatic ischemic or nonischemic cardiomyopathy with LVEF $\leq 35\%$ despite 3 months of GDMT if expected survival is >1 year. ICD is NOT recommended within 40 days of a myocardial infarction (MI) or for patients with NYHA class IV symptoms who are not candidates for advanced therapies.
- Cardiac resynchronization therapy is recommended for symptomatic HFrEF with EF $<35\%$ in sinus rhythm with a left bundle branch block (LBBB) over 150 msec duration despite GDMT. It is also recommended in HFrEF with EF $<35\%$ irrespective of symptoms or QRS duration if there is a high-grade atrioventricular (AV) block with need for a pacemaker.
- For HFmEF, diuretics are recommended to relieve congestion. ACE inhibitors/angiotensin-receptor blockers/ARNIs/beta-blockers/mineralocorticoid receptor antagonists may be considered as additional therapy to reduce mortality and hospitalization (Class IIa recommendation).

- For HFpEF patients, diagnosis and treatment of contributing factors (hypertension, kidney disease, etc.) and use of diuretics are recommended. No specific therapies have been proven to reduce mortality in HFpEF.
- For all HF patients, enrollment in a multidisciplinary HF program, home, or clinic-based program and use of self-management strategies are recommended. Exercise is recommended for all HF patients.
- For prevention of HF, appropriate treatment of hypertension, use of statins when indicated, SGLT2 inhibitors in diabetics at high risk for or with cardiovascular disease and counseling against smoking, alcohol, drug use, and obesity are all Class I recommendations.
- For acute decompensated HF, routine use of inotropes is NOT recommended in the absence of cardiogenic shock and routine use of opioids is NOT recommended. Routine use of intra-aortic balloon pump in post-MI cardiogenic shock is NOT recommended.

- Additional Class I recommendations for hospitalized acute HF patients include trial of oral GDMT and careful exclusion of volume overload prior to discharge with early follow-up within 1-2 weeks of discharge.
- For patients with atrial fibrillation (AF), routine use of anticoagulation for CHA₂DS₂-VASc ≥ 2 in men and ≥ 3 in women, preferably with direct-acting oral anticoagulants except in the presence of a prosthetic mechanical valve or moderate or severe mitral stenosis, is recommended. Urgent cardioversion for patients in AF with HF and hemodynamic compromise is recommended. Rhythm control including catheter ablation should be considered for AF patients with symptoms including HF.
- For patients with HF and severe aortic stenosis, transcatheter/surgical aortic valve replacement is recommended using a heart team approach.
- For HF patients with secondary mitral regurgitation, percutaneous edge-to-edge mitral valve repair should be considered if severe symptoms persist despite appropriate GDMT. For patients with secondary mitral regurgitation and coronary artery disease who need revascularization, coronary artery bypass grafting and mitral valve surgery should be considered.

- Cancer patients being considered for cardiotoxic chemotherapeutic agents who are at risk for cardiotoxicity, should be evaluated ideally by a cardio-oncologist prior to initiation of therapy.
- Tafamidis is a Class I recommendation in patients with TTR amyloidosis with NYHA class I-II symptoms.
- All HF patients should be periodically screened for iron deficiency anemia. Ferric carboxymaltose should be considered in symptomatic, ambulatory HF patients with iron deficiency anemia and EF \leq 45% or hospitalized HF patients with EF \leq 50%.

Management of HFrEF

To reduce mortality - for all patients

ACE-I/ARNI

BB

MRA

SGLT2i

To reduce HF hospitalization/mortality - for selected patients

Volume overload

Diuretics

SR with LBBB \geq 150 ms

CRT-P/D

SR with LBBB 130–149 ms or non LBBB \geq 150 ms

CRT-P/D

Ischaemic aetiology

ICD

Non-ischaemic aetiology

ICD

Atrial fibrillation

Anticoagulation

Atrial fibrillation

Digoxin

PVI

Coronary artery disease

CABG

Iron deficiency

Ferric carboxymaltose

Aortic stenosis

SAVR/TAVI

Mitral regurgitation

TEE MV Repair

Heart rate SR > 70 bpm

Ivabradine

Black Race

Hydralazine/ISDN

ACE-I/ARNI intolerance

ARB

For selected advanced HF patients

Heart transplantation

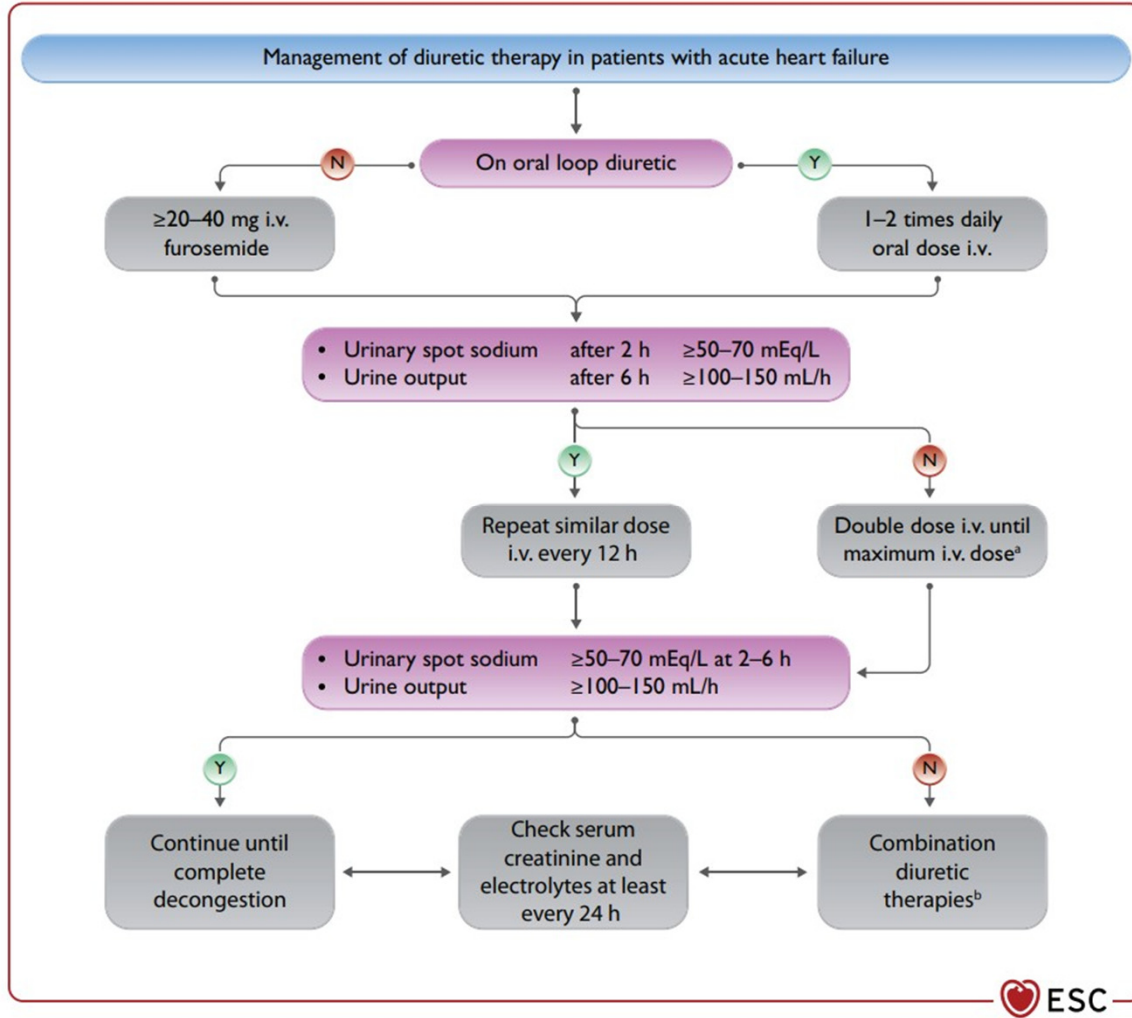
MCS as BTT/BTC

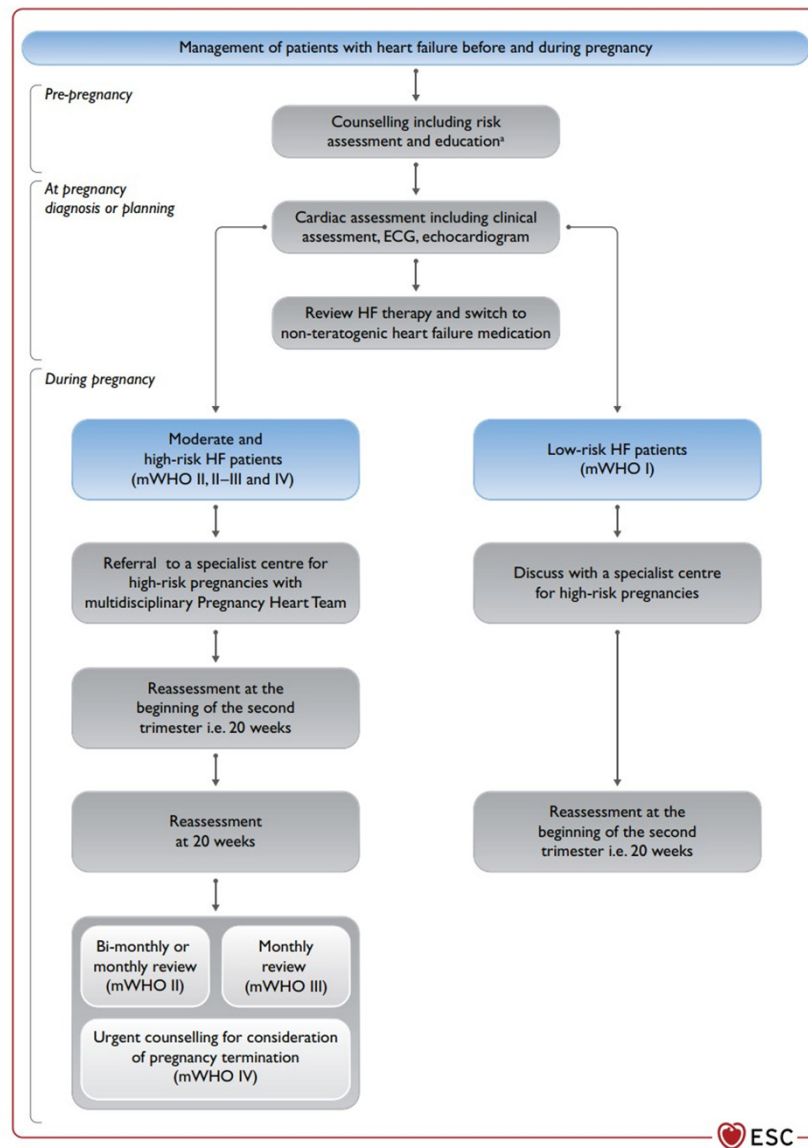
Long-term MCS as DT

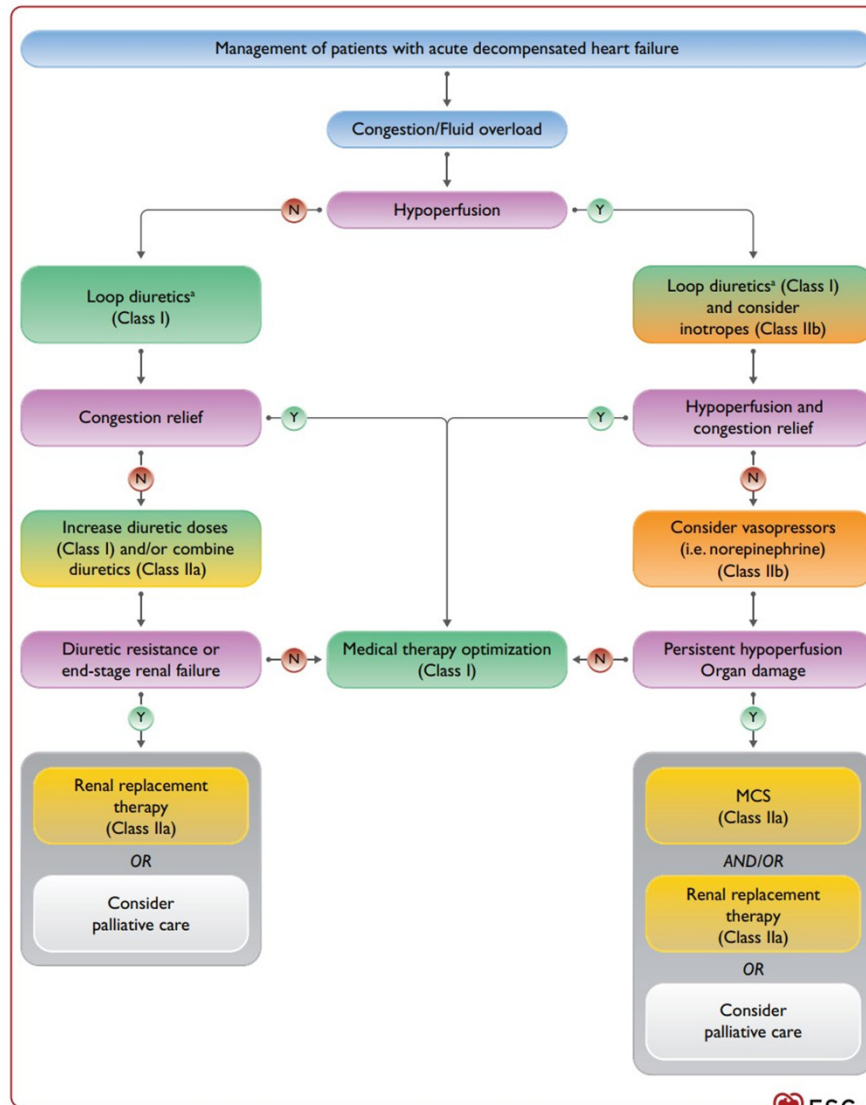
To reduce HF hospitalization and improve QOL - for all patients

Exercise rehabilitation

Multi-professional disease management









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ESC GUIDELINES

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice

Developed by the Task Force for cardiovascular disease prevention in clinical practice with representatives of the European Society of Cardiology and 12 medical societies

With the special contribution of the European Association of Preventive Cardiology (EAPC)

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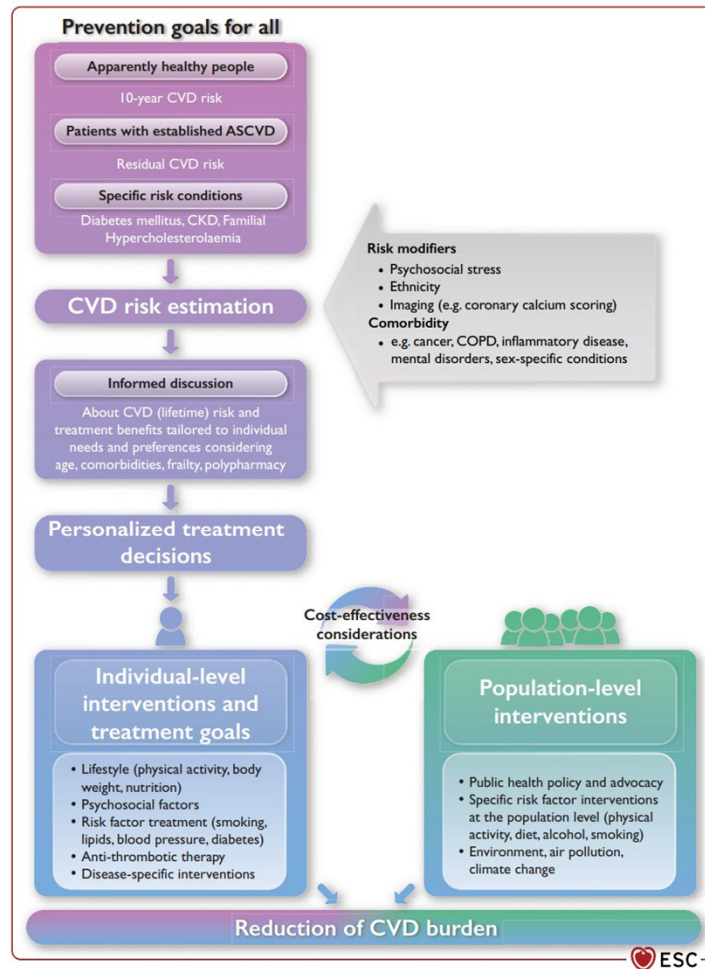


Figure 1 Central Illustration. ASCVD = atherosclerotic cardiovascular disease; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease

KEY POINTS

- The major risk factors for atherosclerotic cardiovascular disease (ASCVD) are high cholesterol, hypertension, cigarette smoking, diabetes mellitus, and adiposity. Risk factors are treated in a stepwise approach to reach the ultimate treatment goals in apparently healthy people, patients with established ASCVD, and patients with diabetes mellitus.
- Psychosocial stress is associated with risk of ASCVD. Frailty assessment is not a method to determine eligibility for any particular treatment, but rather serves to build an individualized care plan with predefined priorities.
- Air pollution is strongly associated with ASCVD. Air pollution contributes to mortality and morbidity, and specifically increases the risk of respiratory and CVDs. Environmental exposure has taken on new urgency, as air pollution, in addition to its health effects, has also been ascribed as a major contributor to climate changes, notably through the burning of fossil fuels leading to increasing emissions of carbon dioxide.

- Chronic kidney disease (CKD) is an independent risk factor for ASCVD, and ASCVD is the leading cause of death in CKD. Hypertension, dyslipidemia, and diabetes mellitus are prevalent among individuals with CKD and require a high-risk treatment strategy approach. Risk management includes lifestyle, smoking cessation, nutrition, sufficient renin-angiotensin-aldosterone system (RAAS) blockade, target blood pressure (BP) control, lipid management, and—in established CVD—aspirin.
- Mental disorders are common in the general population (12-month prevalence of 27%) and are associated with excess mortality. Excess mortality is mainly caused by behavior-dependent risk factors (e.g., smoking addiction) and an impaired capacity for self-care (e.g., treatment adherence).
- Regular physical activity is a mainstay of ASCVD prevention. Aerobic physical activity in combination with resistance exercise and the reduction of sedentary time are recommended for all adults. Achieving and maintaining a healthy weight through lifestyle changes has favorable effects on risk factors (BP, lipids, glucose metabolism) and lowers CVD risk.
- Stopping smoking rapidly reduces CVD risk and is the most cost-effective strategy for ASCVD prevention. There is strong evidence for medication-assisted interventions: nicotine-replacement therapy, bupropion, varenicline, and drugs in combination. The most effective are assistance using drug therapy and follow-up support. There should be restrictions on smokeless tobacco and e-cigarettes due to evidence of harm.

- **Lower is better:** The effect of low-density lipoprotein cholesterol (LDL-C) on the risk of CVD appears to be determined by both the baseline level and the total duration of exposure to LDL-C. Lowering LDL-C with statins, ezetimibe, and—if needed and cost-effective—PCSK9 inhibitors, decreases the risk of ASCVD proportionally to the absolute achieved reduction in LDL-C. When LDL-C goals according to level of risk cannot be attained, aim to reduce LDL-C by $\geq 50\%$ and then strive to reduce other risk factors as part of a shared decision-making process with the patient.
- Lifestyle interventions are indicated for all patients with hypertension and can delay the need for drug treatment or complement the BP-lowering effect of drug treatment. BP-lowering drug treatment is recommended in many adults when office BP is $\geq 140/90$ mm Hg and in all adults when BP is $\geq 160/100$ mm Hg. Wider use of single-pill combination therapy is recommended to reduce poor adherence to BP treatment. A simple drug treatment algorithm should be used to treat most patients, based on combinations of a RAS blocker with a calcium channel blocker or thiazide/thiazide-like diuretic, or all three. Beta-blockers may also be used where there is a guideline-directed indication.
- The number of patients with multiple CV and non-CV comorbidities is rapidly increasing. Therapeutic competition should be considered in multimorbid patients, as the treatment of one condition might worsen a coexisting condition. A paradigm shift from disease-focused to patient-centered care for multimorbid CVD patients is recommended.

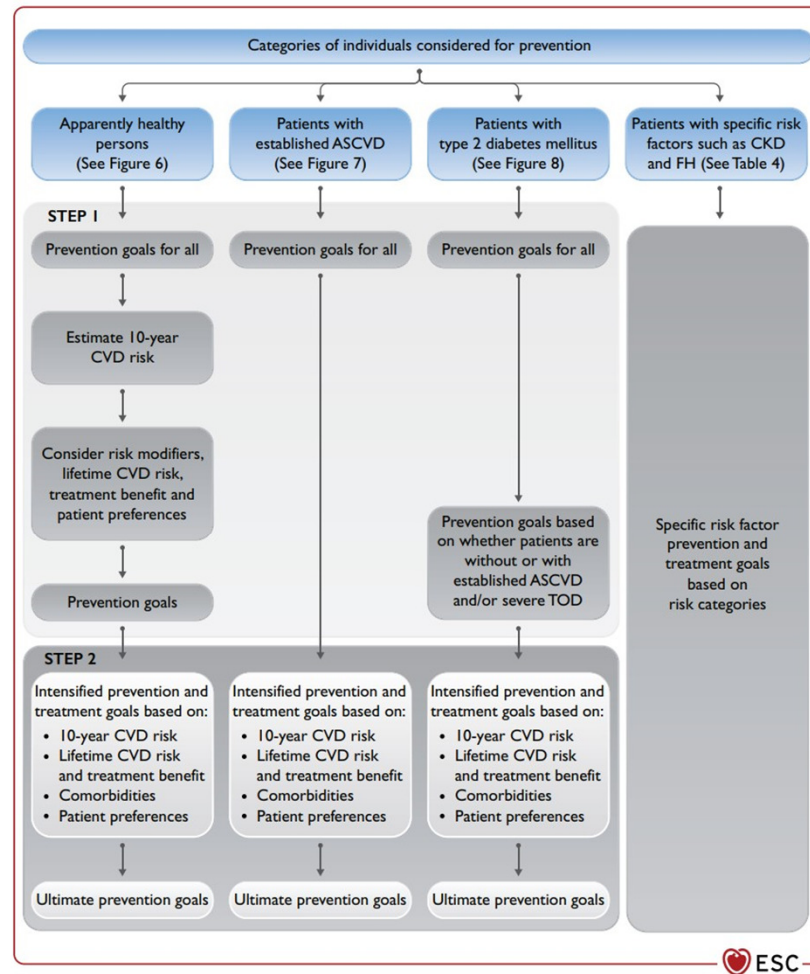
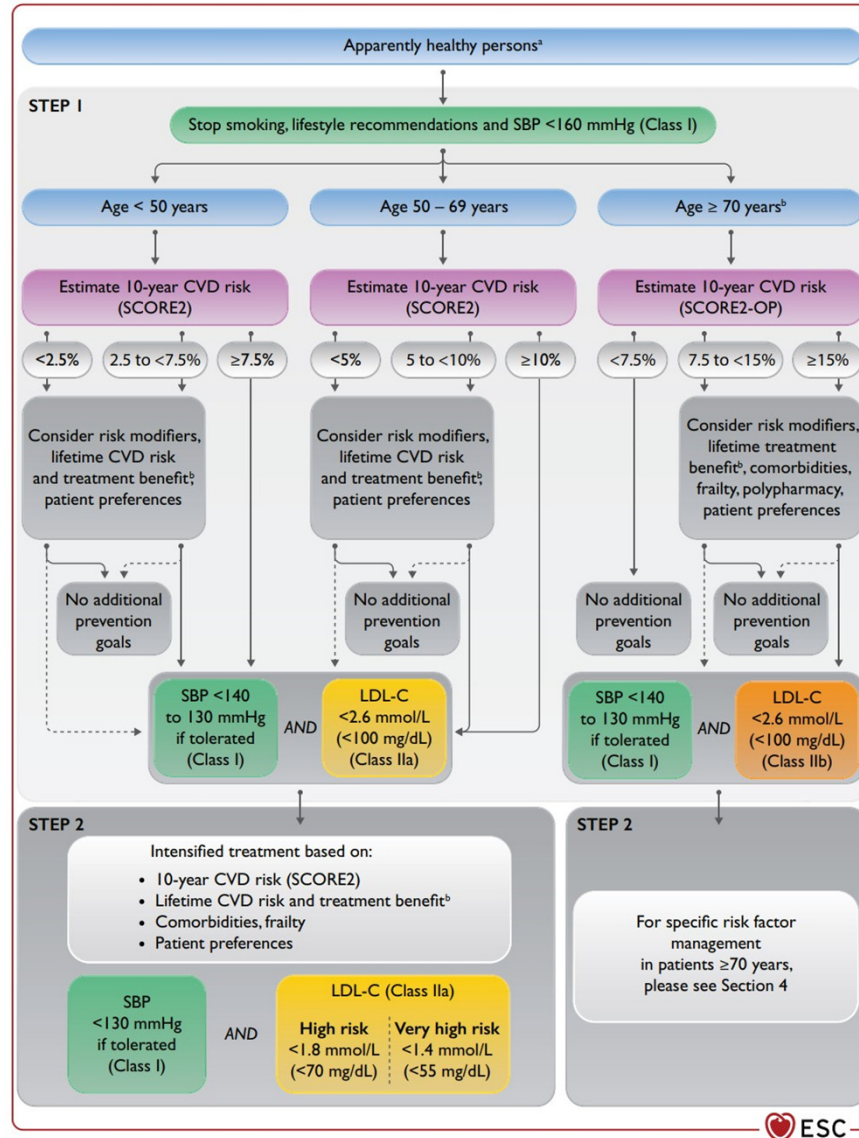


Figure 2 Examples of a stepwise approach to risk stratification and treatment options. ASCVD = atherosclerotic cardiovascular disease; CKD = chronic kidney disease; DM = diabetes mellitus; FH = familial hypercholesterolaemia; TOD = target organ damage.



2021 ESC/EACTS Guidelines for the management of valvular heart disease

Developed by 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)

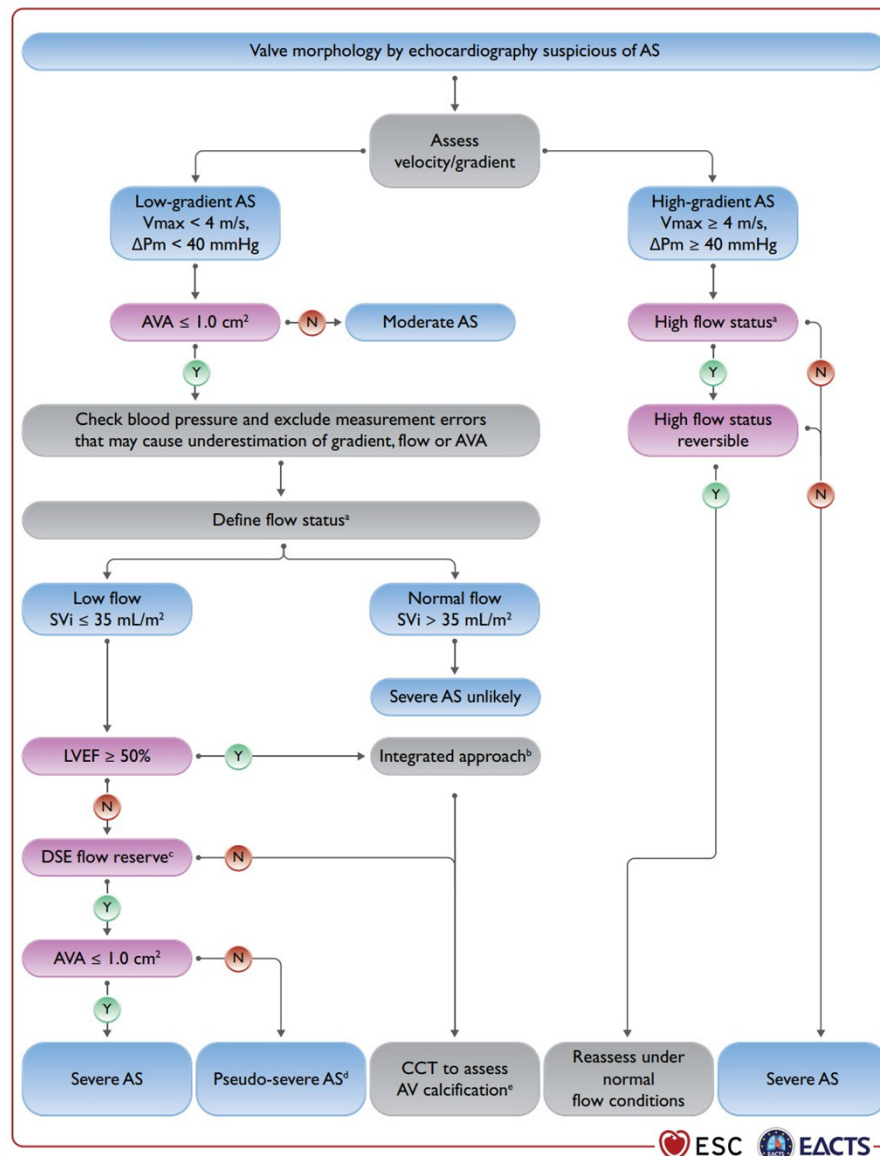
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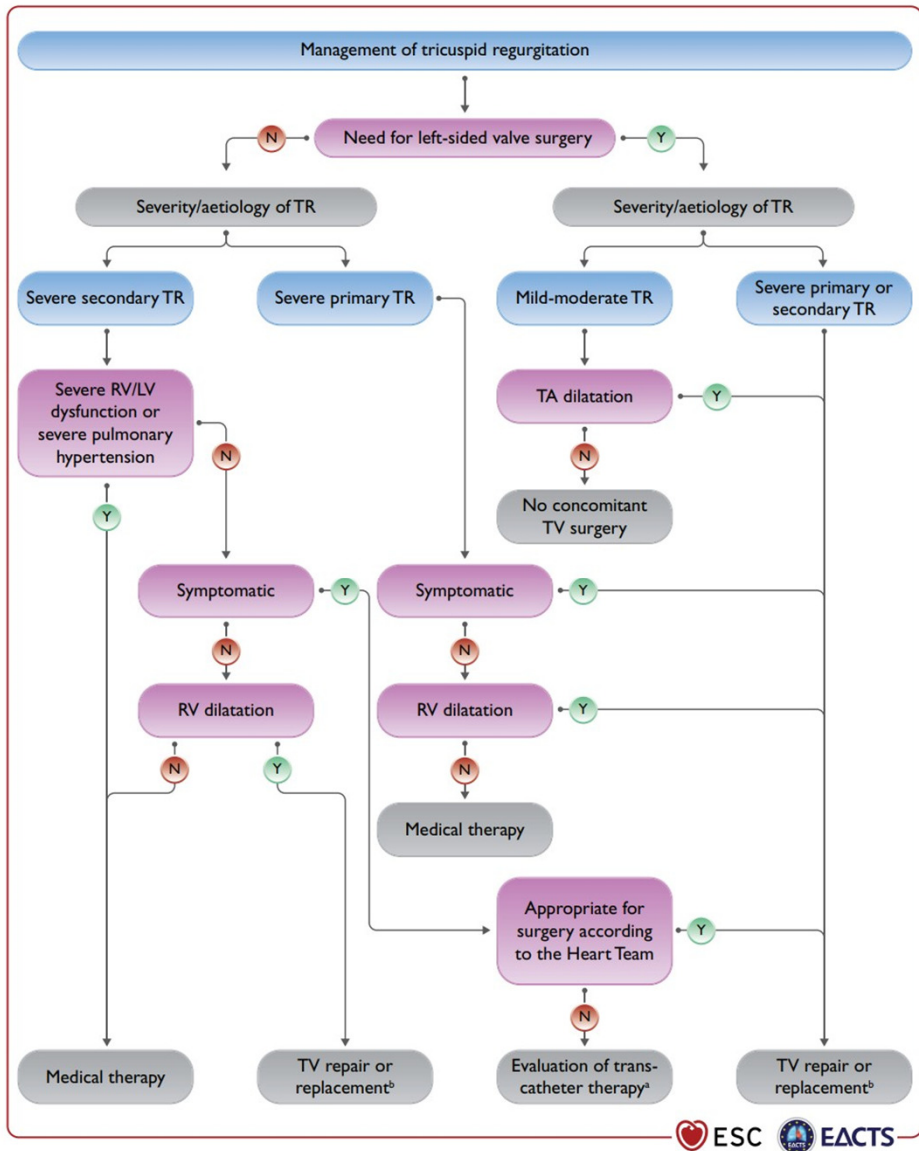
KEY POINTS

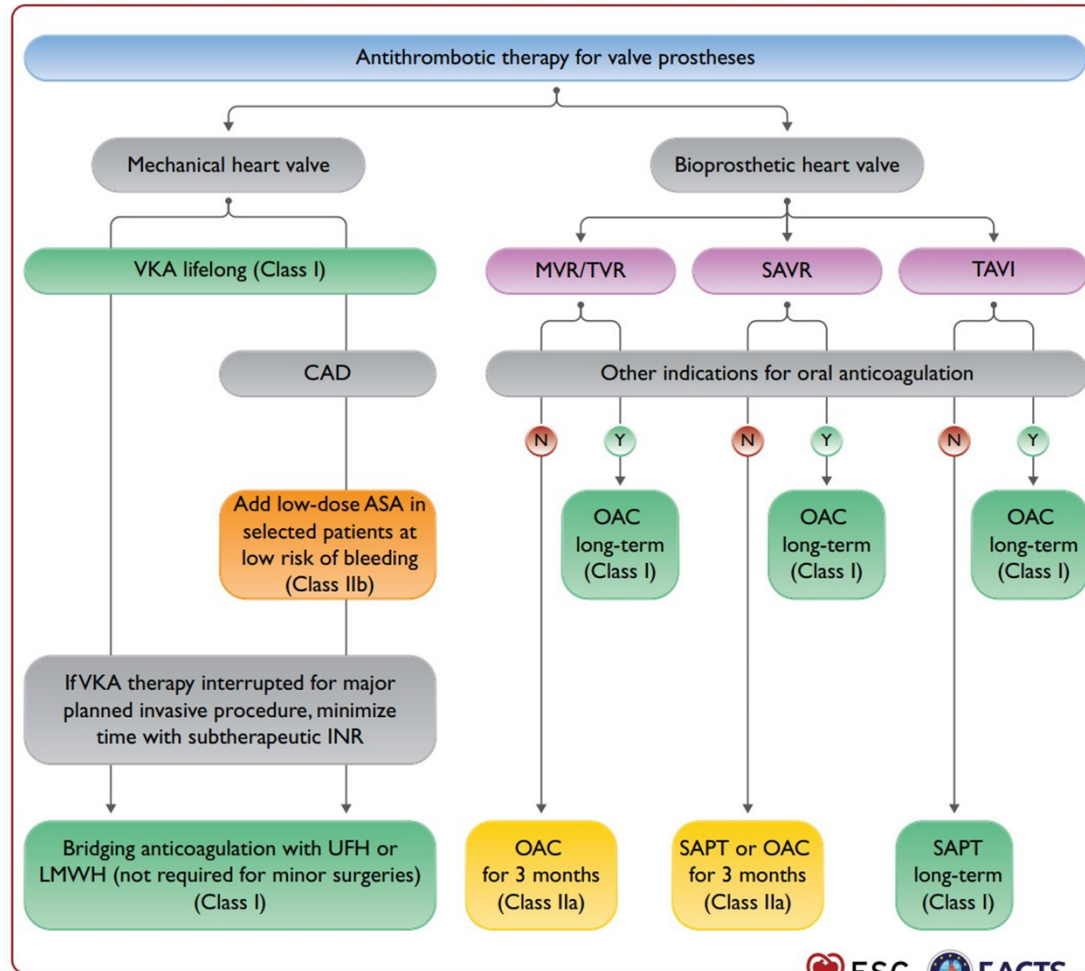
- Meticulous evaluation of the patient's history and symptomatic status, as well as proper physical examination, are crucial for the diagnosis and management of VHD.
- Echocardiography is the key technique to diagnose VHD and assess its severity and prognosis. Other noninvasive investigations such as cardiac magnetic resonance, cardiac computed tomography, fluoroscopy, and biomarkers provide important additional information in selected patients. Stress testing should be widely used in asymptomatic patients. Invasive investigation, beyond preoperative coronary angiography, is limited to situations where noninvasive evaluation is inconclusive.
- Decision making in elderly patients requires the integration of multiple parameters, including estimation of life expectancy and anticipated quality of life, evaluation of comorbidities, and general condition (including frailty). Informed patient expectations and values are an important part of the decision-making process.

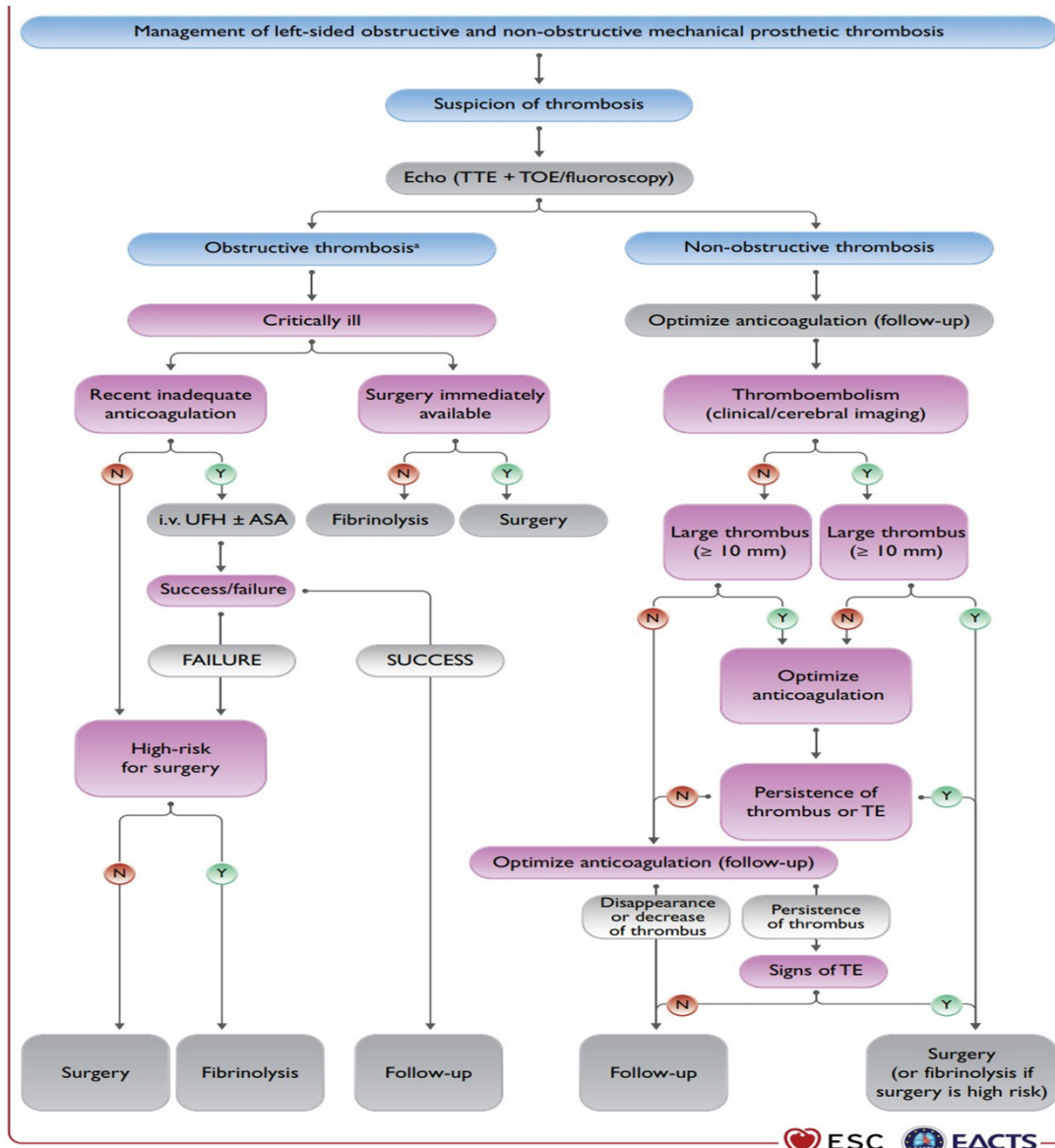
- Heart Valve Centers with multidisciplinary Heart Teams, Heart Valve Clinics, comprehensive equipment, and sufficient volumes of procedures are required to deliver high-quality care and provide adequate training.
- In patients with atrial fibrillation, nonvitamin K antagonist oral anticoagulants (NOACs) are contraindicated in patients with clinically significant mitral stenosis or mechanical valves. For stroke prevention in patients who are eligible for oral anticoagulation, NOACs are recommended in preference to VKAs in patients with aortic stenosis, aortic and mitral regurgitation, or aortic bioprostheses >3 months after implantation.
- Selection of the most appropriate mode of intervention for severe aortic stenosis by the Heart Team should take into account clinical characteristics (age and estimated life expectancy, general condition), anatomical characteristics, the relative risks of surgical aortic valve replacement (SAVR) and transcatheter aortic valve implantation (TAVI), the feasibility of transfemoral TAVI, local experience and outcome data, as well as informed patient preference.

- Surgical mitral valve repair is the preferred method of treatment in primary mitral regurgitation (MR) if a durable repair can be achieved. Transcatheter edge-to-edge repair (TEER) is a safe but less efficacious alternative that may be considered in patients with contraindications for surgery or high operative risk.
- On the other hand, in patients with severe secondary MR, guideline-directed medical therapy (including cardiac resynchronization therapy if indicated) should be the first step. If the patient remains symptomatic, mitral surgery is recommended concomitantly in patients with an indication for coronary artery bypass grafting or other cardiac surgery. Isolated valve surgery may be considered in selected patients. TEER should be considered in patients not eligible for surgery and fulfilling criteria indicating an increased chance of responding to the treatment. Circulatory support devices, cardiac transplantation, or palliative care should be considered as an alternative in patients with end-stage left ventricular and/or right ventricular (RV) failure.
- Tricuspid regurgitation should be liberally treated at the time of left-sided valve surgery. Isolated surgery of severe secondary tricuspid regurgitation (with or without previous left-sided valve surgery) requires comprehensive assessment of the underlying disease, pulmonary hemodynamics, and RV function.
- The choice between a mechanical prosthesis and a bioprosthesis should be patient-centered and multifactorial based on patient characteristics, the indication for lifelong anticoagulation, the potential and risks of a re-intervention, and the informed patient preference. Clinical assessment of prosthetic valves should be performed yearly and as soon as possible if new cardiac symptoms occur.









2021 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy

Developed by the Task Force on cardiac pacing and cardiac resynchronization therapy of the European Society of Cardiology (ESC)

With the special contribution of the European Heart Rhythm Association (EHRA)

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Table 3 New concepts and sections in current guidelines

Concept/section	Section
New section on types and modes of pacing, including conduction system pacing and leadless pacing	3.4
New section on sex differences in pacing	3.5
New section on evaluation of patients for pacing	4
Expanded and updated section on CRT	6
New section on alternative pacing strategies and sites	7
Expanded and updated section on pacing in specific conditions, including detailed new sections on post TAVI, postoperative and pacing in the presence of tricuspid valve diseases, and operations	8
A new section on implantation and perioperative management, including perioperative anticoagulation	9
An expanded revised section on CIED complications	10
A new section on various management considerations, including MRI, radiotherapy, temporary pacing, perioperative management, sport activity, and follow up	11
A new section on patient-centred care	12

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CIED = cardiovascular implantable electronic device; CRT = cardiac resynchronization therapy; MRI = magnetic resonance imaging; TAVI = transcatheter aortic valve implantation.

KEY POINTS

- A careful history and physical examination are essential for the evaluation of patients with suspected or documented bradycardia. In patients with suspected or documented symptomatic bradycardia, the use of cardiac imaging is recommended to evaluate the presence of structural heart disease, to determine left ventricular (LV) systolic function, and to diagnose potential reversible causes of conduction disturbances. Exercise testing is recommended in patients who experience symptoms suspicious of bradycardia during or immediately after exertion.
- Screening for sleep apnea syndrome is recommended in patients with symptoms of sleep apnea syndrome and in the presence of severe bradycardia or advanced atrioventricular (AV) block during sleep. In patients with infrequent unexplained syncope, in whom a comprehensive evaluation did not demonstrate a cause, long-term ambulatory monitoring with an implantable loop recorder is recommended. Multimodality imaging (cardiac magnetic resonance, computed tomography, or positron emission tomography) should be considered in search of the underlying myocardial disease, particularly in patients with conduction system disease who are <60 years. Genetic testing should be considered in patients with early-onset (age <50 years) of progressive cardiac conduction disease.

- In patients with syncope and bifascicular block, electrophysiologic study (EPS) should be considered when syncope remains unexplained after noninvasive evaluation. In such patients, a pacemaker is indicated in the presence of either a baseline His-ventricular interval of ≥ 70 ms, second- or third-degree intra- or infra-Hisian block during incremental atrial pacing, or an abnormal response to pharmacological challenge. Pacing is indicated in patients with alternating bundle branch block (BBB) with or without symptoms.
- Dual-chamber cardiac pacing is indicated to reduce recurrent syncope in patients aged >40 years, with severe, unpredictable, recurrent syncope who have: 1) spontaneous documented symptomatic asystolic pause(s) >3 seconds or asymptomatic pause(s) >6 seconds due to sinus arrest or AV block; or 2) cardioinhibitory carotid sinus syndrome; or 3) asystolic syncope during tilt testing.
- CRT is recommended for symptomatic patients with heart failure (HF) in sinus rhythm with LV ejection fraction (LVEF) $\leq 35\%$, QRS duration ≥ 150 ms, and left bundle branch block (LBBB) QRS morphology. CRT should be considered for symptomatic patients with HF in sinus rhythm with LVEF $\leq 35\%$, QRS duration 130-149 ms, and LBBB QRS morphology. CRT should be considered for patients with HF in sinus rhythm with LVEF $\leq 35\%$, QRS duration ≥ 150 ms, and non-LBBB QRS morphology. CRT should be considered for patients with HF and LVEF $\leq 35\%$ in NYHA class III or IV if they are in atrial fibrillation (AF) and have intrinsic QRS ≥ 130 ms, provided a strategy to ensure biventricular capture is in place. AV junction ablation should be added in the case of incomplete biventricular pacing ($<90-95\%$) due to conducted AF.

- In patients with sinus node dysfunction and a DDD pacemaker, minimization of unnecessary ventricular pacing through programming is recommended.
- Conduction system pacing (which includes His bundle and left bundle branch area pacing) is very likely to play a growing role in the future, pending randomized trials of safety and efficacy.
- Leadless pacemakers should be considered as an alternative to transvenous pacemakers when no upper extremity venous access exists or when risk of device pocket infection is particularly high, such as previous infection and patients on hemodialysis. The prevalence of leadless device infections is low as the principal sources of infection. There are no randomized controlled data available to compare clinical outcomes between leadless pacing and single-chamber transvenous pacing.
- Right bundle branch block (RBBB) is the most consistent and powerful predictor of the need for pacing after transcatheter aortic valve implantation (TAVI). Early permanent pacing should be considered in patients with pre-existing RBBB who develop any further conduction disturbance during or after TAVI. Permanent pacemaker implantation appears warranted in patients with intraprocedural AV block that persists for 24-48 hours after TAVI or appears later. Ambulatory electrocardiographic (ECG) monitoring or EPS should be considered for patients with new LBBB with QRS >150 ms or PR >240 ms with no further prolongation during >48 hours after TAVI. Ambulatory ECG monitoring or EPS may be considered for patients with a pre-existing conduction abnormality who develop prolongation of QRS or PR >20 ms.

- Not all patients with congenital heart block require pacing, especially if they are asymptomatic. Prophylactic pacing is indicated in asymptomatic patients with any of the following risk factors: 1) mean daytime heart rate <50 bpm, 2) pauses >3 times the cycle length of the ventricular escape rhythm, 3) a broad QRS escape rhythm, 4) prolonged QT interval, or 5) complex ventricular ectopy. Clinical symptoms, such as syncope, pre-syncope, HF, or chronotropic incompetence, are indications for pacemaker implantation.
- A clinically significant pocket hematoma increases the risk for subsequent device infection almost eightfold. In patients with low and intermediate thrombotic risk after PCI (>1 month after PCI, or >6 months after acute coronary syndrome at index PCI), the recommendation is to continue aspirin AND discontinue P2Y12 inhibitors. It is recommended that vitamin K anticoagulant is continued periprocedurally. Either stopping or continuing nonvitamin K antagonist oral anticoagulants might be reasonable at the time of device implantation.
- Infection rates are higher with device replacement or upgrade procedures, as well as CRT or implantable cardioverter-defibrillator implants compared with simple pacemaker implantation. Infections also occur more frequently with use of temporary pacing or other procedures before implantation (odds ratio [OR] 2.5 and 5.8, respectively), early reinterventions (OR 15), and lack of antibiotic prophylaxis (OR 2.5).
- In patients considered for pacemaker or CRT, the decision should be based on the best available evidence with consideration of individual risk-benefits, the patient's preferences, and goals of care, and it is recommended to follow an integrated care approach and use the principles of patient-centered care and shared decision making in the consultation.

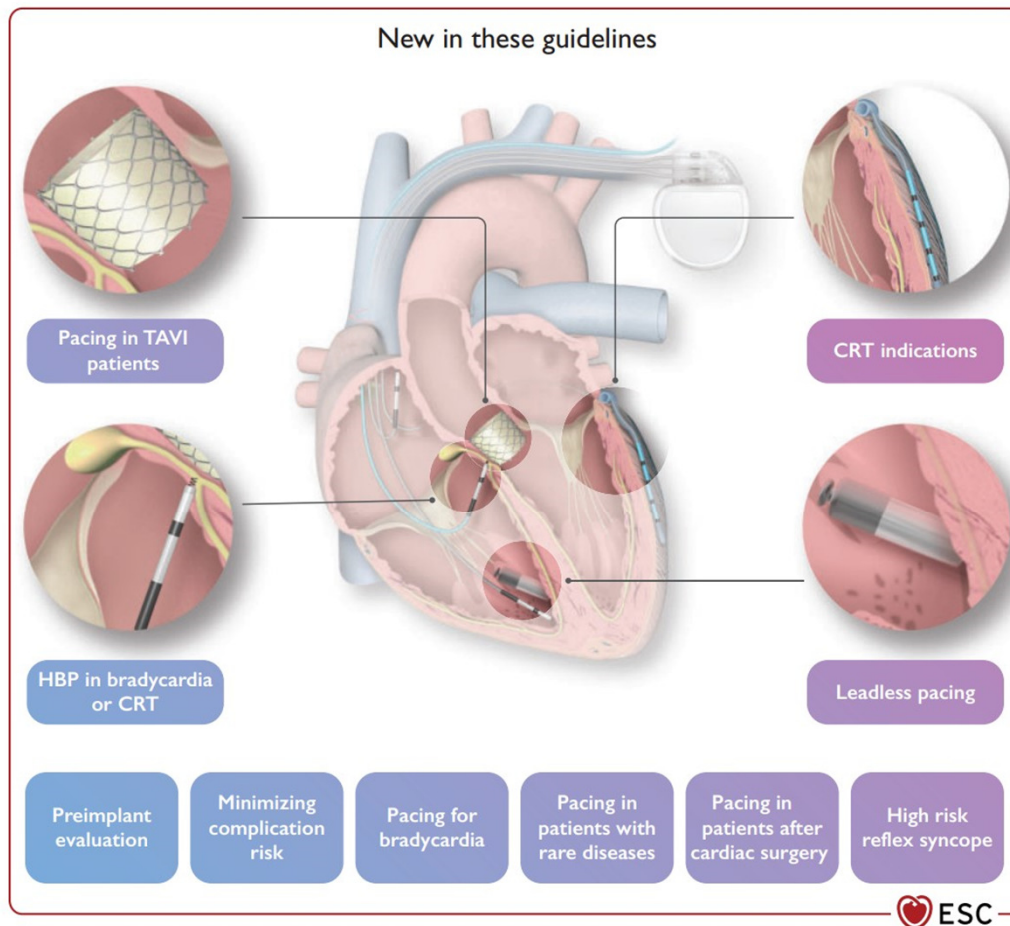


Figure 1 The 2021 ESC Guidelines on cardiac pacing and CRT present new and updated recommendations for these treatments in relevant patient populations.

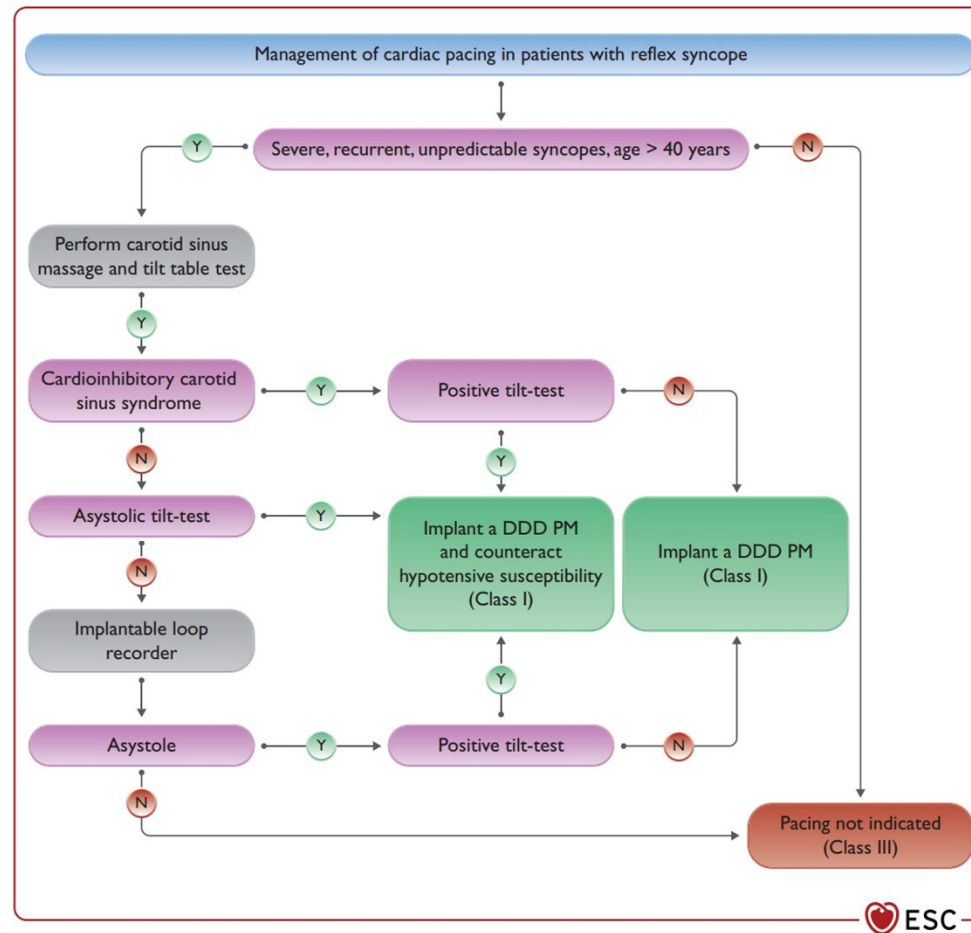


Figure 7 Decision pathway for cardiac pacing in patients with reflex syncope. DDD = dual-chamber, atrioventricular pacing. Note: cardioinhibitory carotid sinus syndrome is defined when the spontaneous syncope is reproduced by the carotid sinus massage in the presence of an asystolic pause >3 s; asystolic tilt positive test is defined when the spontaneous syncope is reproduced in the presence of an asystolic pause >3 s. A symptomatic asystolic pause(s) >3 s or asymptomatic pause(s) >6 s due to sinus arrest, atrioventricular block, or the combination of the two similarly define asystole detected by implantable loop recorder. Figure adapted from Brignole et al.⁶²

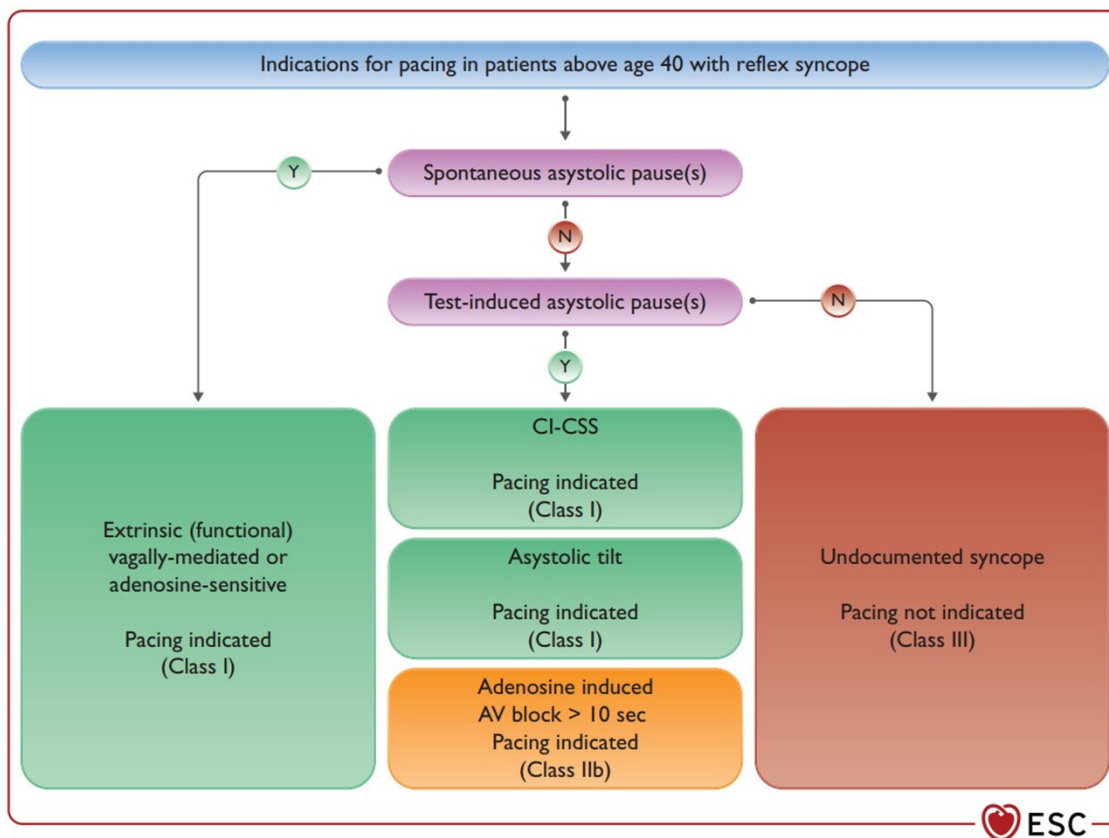
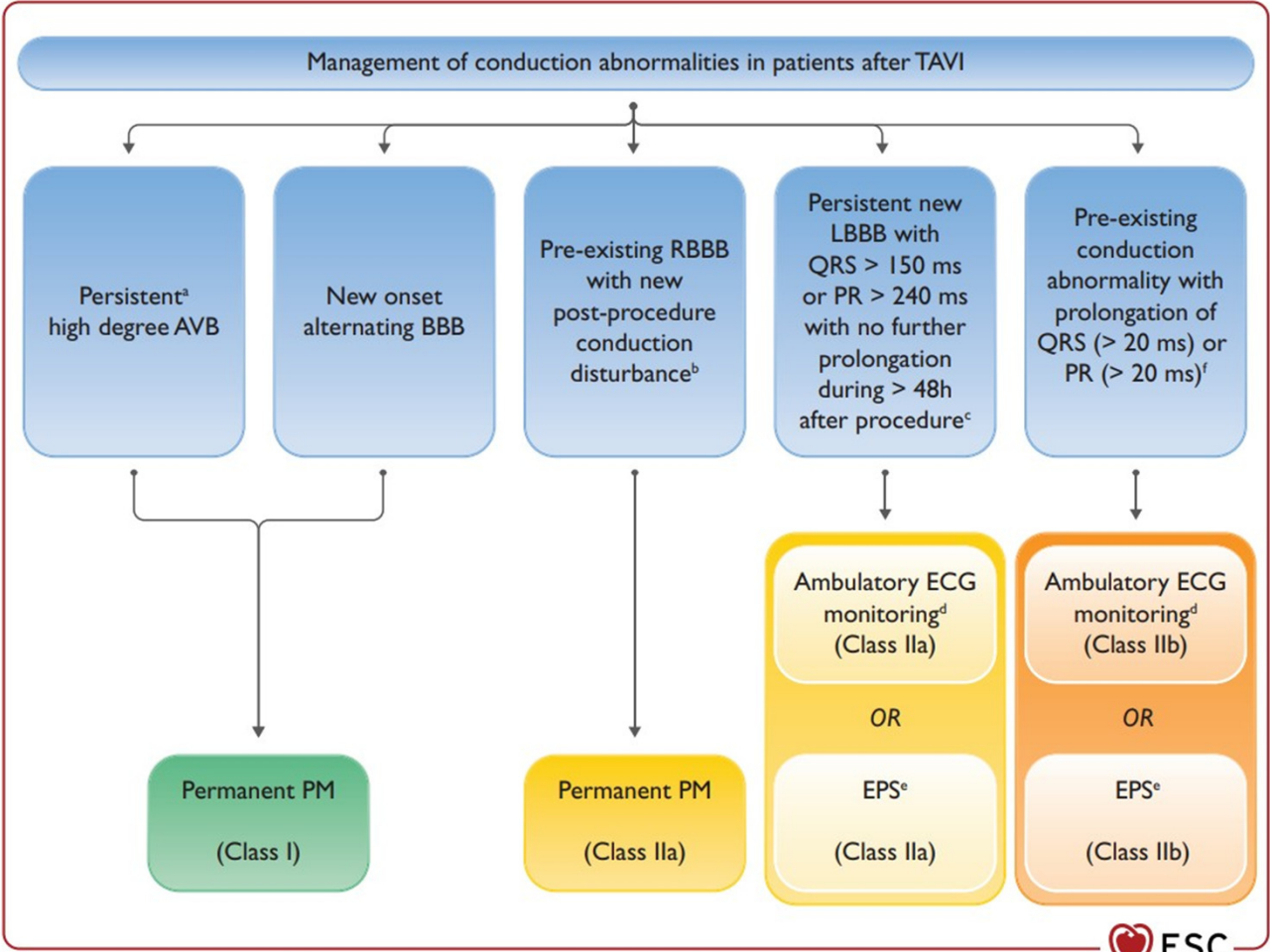



















Figure 8 Summary of indications for pacing in patients >40 years of age with reflex syncope. CI-CSS = cardioinhibitory carotid sinus syndrome. Note: spontaneous asystolic pause = 3 s symptomatic or 6 s asymptomatic. Adapted from Brignole et al.⁶²



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