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REVIEW ARTICLE



Summary of 2021 ESC Guidelines on cardiac pacing and cardiac resynchronisation therapy, on cardiovascular disease prevention, on the management of valvular heart disease and of heart failure

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ABSTRACT

During the ESC congress in September 2021, the new ESC guidelines were presented and are available on the ESC website. The new guidelines describes management recommendations on following cardiovascular domains : cardiac pacing and cardiac resynchronization therapy, cardiovascular prevention, valvular heart disease and heart failure. The present document gives a summary of these guidelines and highlights the most important recommendations and changes in the management of these diseases. It will help to increase awareness about the new guidelines and may stimulate to consult the full document for specific items. Ultimately, the authors hope that this document will enhance implementation of new ESC guidelines in daily clinical practice.

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Introduction

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The present document gives a summary of these guidelines and highlights the most important recommendations and changes in the management of these diseases.

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ESC guidelines on cardiac pacing and cardiac resynchronisation therapy

These new ESC guidelines [1] are issued 8 years after the late 2013 guidelines. New concepts and sections

have been added including conduction system pacing, leadless pacing, alternative pacing strategies, implantation and complications, and various management considerations such as MRI, radiotherapy, perioperative management, sport and follow up. Also highlighted is the concept of patient-centered care with shared decision making. Below are summarised the main novelties of these 2021 guidelines.

Pacing for bradycardia

Careful evaluation of the patient with suspected or documented bradycardia or conduction system disease is advocated, including long-term monitoring with an ILR when symptoms are infrequent, carotid sinus massage, tilt testing, exercise test, cardiac imaging, specific laboratory tests a (e.g. thyroid function tests, Lyme titre), screening for sleep apnoea syndrome, electrophysiological study or genetic testing when appropriate

Pacing is indicated in symptomatic patients with sinus node disease to correct bradyarrhythmias or enable pharmacological treatment of tachyarrhythmias and in patients with permanent or paroxysmal third- or high-degree AV block, irrespective of symptoms

Dual chamber cardiac pacing is also indicated to reduce recurrent syncope in patients aged >40 years with severe, unpredictable, recurrent syncope who have either symptomatic pauses > 3 sec or asymptomatic pauses > 6 sec, cardioinhibitory carotid sinus syndrome or asystolic syncope during tilt testing.

In patients with sinus node disease, minimisation of unnecessary ventricular pacing through programming is recommended.

Alternative pacing sites or modalities, such as his bundle pacing or leadless pacing only received a class IIb indication as an alternative to right ventricular pacing in specific conditions.

When AV block occurs after myocardial infarction, or after cardiac surgery, a waiting period of at least 5 days is recommended to assess whether the rhythm disturbance resolves or not. In these cases temporary transvenous pacing could be indicated. However, after TAVI, pacing is recommended sooner, if complete or high degree AV block persists for 24-48h or in presence of a new onset alternating BBB, or new conduction disturbances in patients with pre-existing RBBB, or of new LBBB with QRS > 150 ms or PR > 240 ms.

In specific syndromes, such as neuromuscular disease, LMNA gene mutation, Kearns-Sayre syndrome, sarcoidosis or congenital heart disease, specific recommendations have been updated.

Pacing for cardiac resynchronisation therapy (CRT)

Indications for CRT have been aligned with the guidelines for heart failure patients: CRT is recommended for symptomatic patients with heart failure despite optimal medical therapy, when in sinus rhythm with LVEF $\leq 35\%$, QRS duration ≥ 150 ms and LBBB, to improve symptoms and reduce morbidity and mortality. In patients who are candidates for an ICD, but also have CRT indication, implantation of a CRT-D is recommended. CRT is never indicated in patients with QRS < 130 ms without an indication for RV pacing.

In patients with symptomatic AF and an uncontrolled heart rate who are candidates for AV junction ablation, CRT should be considered in patients with HFrEF or HFmrEF but RV pacing alone should be considered in patients with HFpEF.

Quadrupolar leads should be considered as first choice to pace the coronary sinus. However, in CRT candidates in whom coronary sinus implantation is unsuccessful, His bundle pacing should be considered along with other techniques such as surgical epicardial lead.

Device management

Heparin bridging of anticoagulated patients is not recommended.

To reduce the risk of CIED infection, pacemaker implantation should be delayed until a patient with fever is afebrile for at least 24h, preoperative administration of antibiotic is recommended in all patients within 1h of skin incision, chlorhexidine alcohol instead of povidone-iodine alcohol should be considered for skin antisepsis, and rinsing the device pocket with normal saline solution should be considered before wound closure.

Remote monitoring is recommended in patients with difficulties to attend in-office visits (with at least one in-office visit every 24 months) or in case of device component recalled or on advisory.

In patients with MRI-conditional pacemakers, MRI can be performed safely following the manufacturer's instructions.

When pacing is no longer indicated, a decision on the management strategy should be based on an individual risk-benefit analysis in a shared decision-making process together with the patient.

Reference: Glikson M, Nielsen JC et al. 2021 ESC guidelines on cardiac pacing and cardiac resynchronisation therapy. Eur Heart J 2021 doi:10.1093/eurheartj/ehab364.

ESC guidelines on cardiovascular prevention

The updated guidelines on cardiovascular disease (CVD) prevention [2] were presented at the European Society of Cardiology (ESC) meeting in august 2021 and simultaneously published in the European Heart Journal (ref). A major change in this updated guideline is the focus on a more patient- personalised approach for CVD prevention with shared decision making, instead of a one-size fits all approach. Some of the major key messages for daily clinical practice can be summarised as follows:

1. Risk factors, risk assessment and risk modifiers

The estimation of an individual's risk of CVD (low – moderate – high and very high risk) is one of the cornerstones of the guidelines. To estimate the 10-year CVD risk in apparently healthy individuals 40-69 years the new SCORE2 algorithm is introduced; for those aged 70 years or older, the SCORE2-OP algorithm can now be used. These new algorithms estimate the 10 year global CVD risk (and thus not only CV mortality as previously in the SCORE model), based on European region specific tables that take into account age, gender, smoking status, blood pressure and total non-HDL cholesterol. Belgium is

considered as a low risk country. The thresholds to define an individual's risk are age dependent and are now also clearly defined according to different age categories.(see [Figure 1](#))

Coronary artery calcium scoring or carotid ultrasound for plaque determination may be used to improve CVD risk stratification. However, other imaging modalities or measurement of additional circulating and urine biomarkers or genetic risk scores are not advised. Frailty is considered as an important risk factor of CV and non-CV morbidity and mortality and can be used to create an individualised care plan with pre-defined priorities.

2. Treatment targets and how to get there

Regular physical activity, smoking cessation and a healthy diet remain the first 3 most important interventions for CVD prevention. Treatment targets for blood lipids, hypertension and glycaemia control remain in line with the most recent ESC guidelines on dyslipidemia, hypertension or diabetes. However, a new step-wise approach for treatment intensification to reach these targets is now introduced that takes not only into account CVD risk but also benefit of treatment, factors influencing risk, comorbidities and patient preferences. This step-wise approach is elaborated in more detail for patients with atherosclerotic cardiovascular disease, diabetes and apparently healthy individuals. New tables with life time CVD risk and benefit of treatment for smoking, blood pressure and lipids are additional tools to inform the patient and discuss potential treatment benefits.

3. New specific recommendations

Many new and revised recommendations are given and some of them are highlighted below

- Presence of migraine with aura should be considered in CVD risk assessment (new class IIa recommendation)
- Assessment of CVD risk should be considered in men with erectile dysfunction (new class IIa recommendation)
- Assessment of total cardiovascular risk may be considered in adults with chronic inflammatory conditions (new class IIb recommendation)
- Smoking cessation is recommended regardless of weight gain, as weight gain does not lessen the ASCVD benefits of cessation (new class I recommendation)
- Bariatric surgery for obese high-risk individuals should be considered when life-style changes

does not result in maintained weight loss (new class IIa recommendation)

- Patients with mental disorders need intensified attention and support to improve adherence to lifestyle changes and drug treatment (new class I recommendation)
- ASCVD patients with stress should be considered for referral to psychotherapeutic stress management to improve CVD outcomes and reduce stress symptoms (new class IIa recommendation)
- Participation in a medically supervised, structured, comprehensive, multidisciplinary cardiac rehabilitation and prevention program for patients after ASCVD events and/or revascularisation, and for patients with heart failure (mainly HFrEF) is recommended to improve patient outcomes (new class I recommendation)
- In persons with type 2 diabetes mellitus and ASCVD, the use of GLP-1RA or SGLT-2 inhibitor with proven outcome benefits is recommended to reduce CV and/or cardiorenal outcomes (revised class I recommendation)
- Putting in place measures to reduce air pollution, including reducing particulate matter emission and gaseous pollutants, reducing the use of fossil fuels, and limiting carbon dioxide emissions, are recommended to reduce CVD mortality and morbidity (new class I recommendation)

ESC/EACTS guidelines for the management of valvular heart disease

The latest European recommendations dealing with the management of Valvular Heart Disease (VHD) dated from 2017. The objective of this synthesis aims to highlight the novelties and modifications proposed by these new guidelines [3].

Emphasis has been put on the importance of a patient-centred evaluation for intervention within the heartteam considering the expectations and values of the patient as well as on the role of non-invasive multimodality cardiovascular imaging ([Figure 2](#)).

Aortic stenosis

Indication for intervention in a patient with asymptomatic severe aortic stenosis has been extended. Intervention should be considered, if the operative risk is low and ≥ 1 of the following parameters (class IIa):

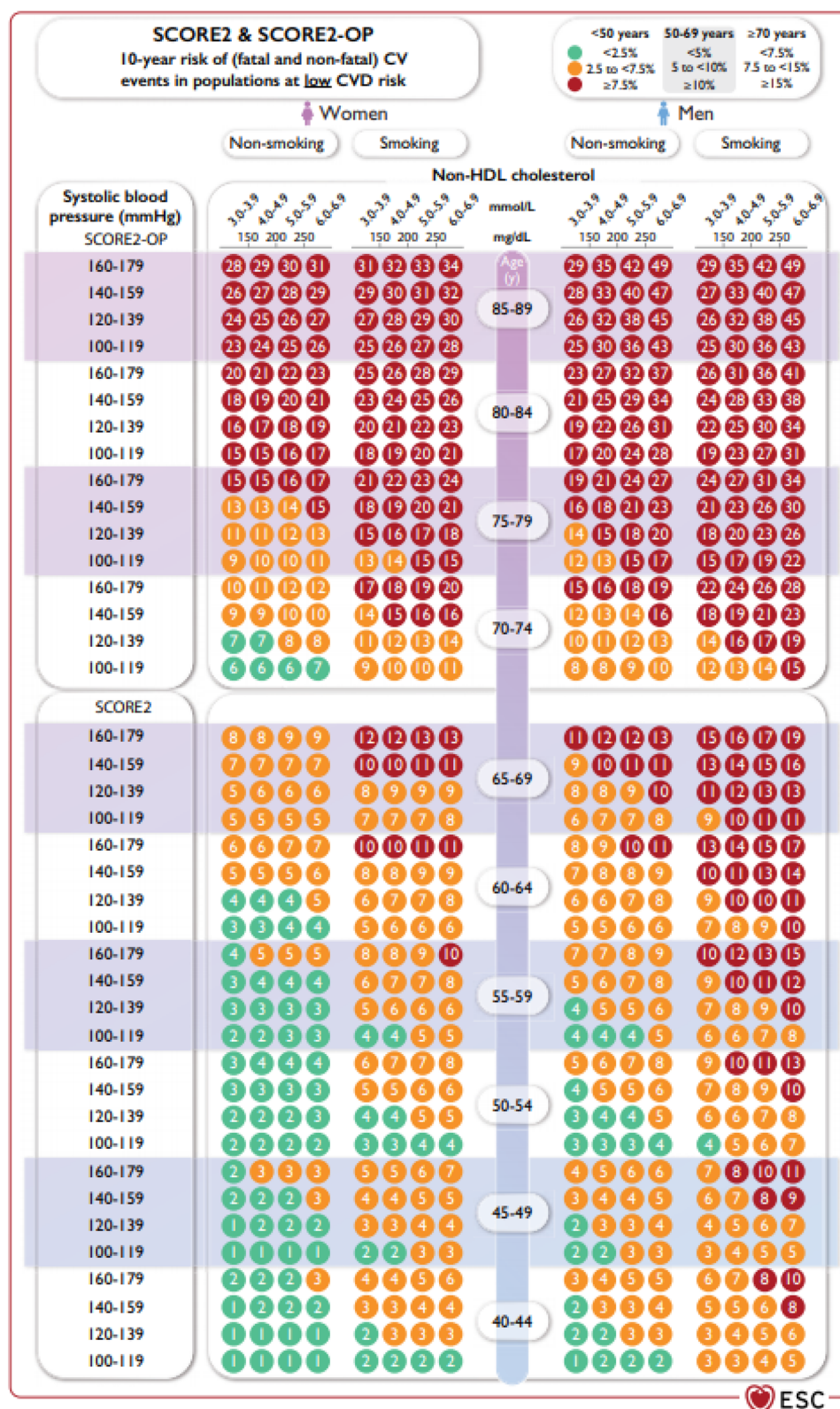


Figure 1. Systematic coronary risk estimation 2 and systematic coronary risk estimation 2-older persons risk charts for fatal and non-fatal (myocardial infarction, stroke) cardiovascular disease.

- Very tight stenosis with a $V_{max} > 5$ m/s (and no longer 5.5 m/s).
- Severe calcifications: ideally assessed by CT scan, and progression of $V_{max} \geq 0.3$ m/s/year.
- BNP elevation > 3 times normal, confirmed on repeated measurements and without further explanation.
- Systolic LV dysfunction ($LVEF < 55\%$)

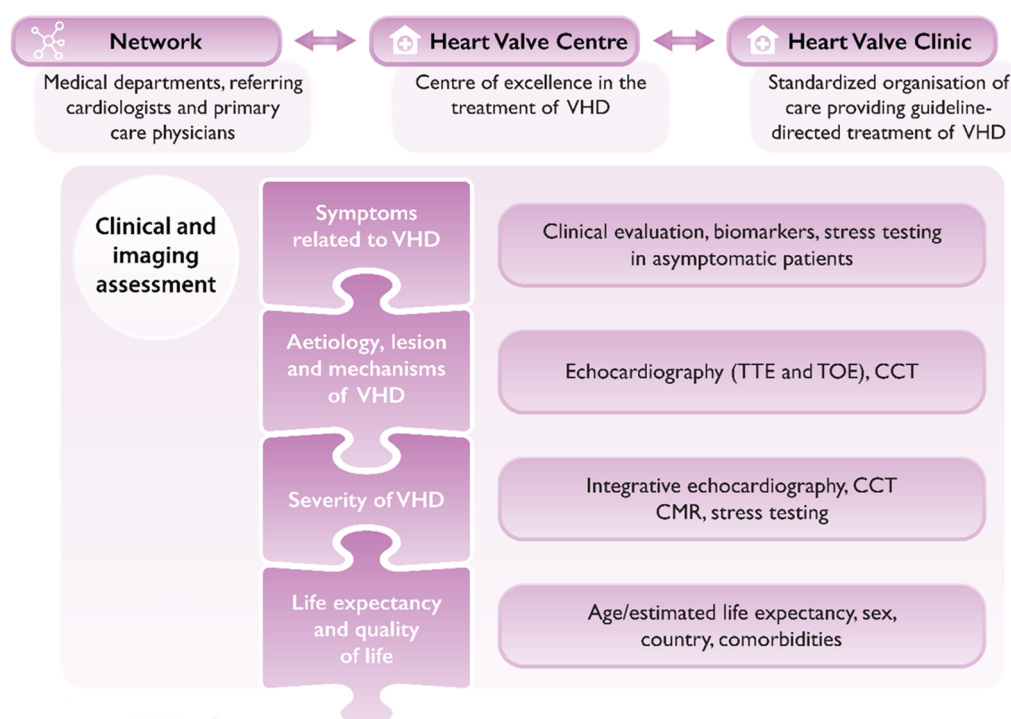


Figure 2. Patient-centred evaluation for intervention. VHD=valvular heart disease; CCT=cardiac computed tomography; CMR=cardiac magnetic resonance; TOE=transoesophageal echocardiography; TTE=transthoracic echocardiography.

Selection of the most appropriate mode of intervention (TAVI or surgery) by the Heart Team should consider the patient's age, surgical risk, clinical and anatomical characteristics (particularly feasibility of the transfemoral access), local experience and outcome data, and importantly, informed patient preference. Surgery is recommended in young patients at low risk (<75 years and STS PROM/Euroscore II < 4%) or operable and without a possible femoral access route for TAVI (class I). TAVI is recommended in older patients (> 75 years old) or in those at high risk (STS-PROM/EuroSCORE II > 8%) or unsuitable for surgery (class I). TAVI by non-femoral route may be considered in inoperable patients with non-suitable femoral approach (class IIb). With regard to antithrombotic therapy, single antiplatelet for life is recommended if there is no indication for an existing anticoagulation (class I).

Aortic regurgitation

Surgery is now recommended in an asymptomatic patient with severe aortic regurgitation (AR) and (class I):

- a LV end-systolic diameter (ESD) > 50 mm
- Or a LVESD index > 25 mm/m²
- Or a LVEF ≤ 50%.

Another novelty of these recommendations is to be able to consider surgery in an asymptomatic patient with an LVESDi > 20 mm/m² or a LVEF ≤ 55% in case of low-risk surgery (class IIb).

Mitral regurgitation (MR)

Surgery is recommended in asymptomatic patients with severe primary MR and LV dysfunction (a LV end-systolic diameter ≥ 40 mm (lowered from 45 to 40 mm from 2017 to 2021) and/or a LVEF ≤ 60% (class I).

Secondary MR is common in chronic heart failure (HF) with reduced LVEF, due to LV remodelling that prevents coaptation of the valve leaflets. Criteria for severe secondary MR have been revised and are now consistent with the American guidelines:

- An effective regurgitating orifice area (EROA) ≥ 40 mm², or ≥ 30 mm² if elliptical orifice or in case of low flow state (and no longer 20 mm² in the 2017 recommendations)
- A regurgitating volume: VR ≥ 60 ml, or ≥ 45 ml if low flow (and no longer 30 ml in the 2017 recommendations).

A TEER should be considered in selected patients who are not eligible for surgery fulfilling criteria

suggesting an increased chance of responding to TEER (change from class IIb to class IIa).

Tricuspid regurgitation

Introduction of the possibility of considering percutaneous treatment in inoperable symptomatic patients with severe tricuspid regurgitation (TR) in expert valve centres (class IIb).

Management of atrial fibrillation in a patient with valve disease

Surgical closure of the left atrial appendage should be considered for patients undergoing valve surgery and being in AF with a CHA₂DS₂-VASc score ≥ 2 (going from a class IIb to a class IIa).

Non-vitamin K antagonist oral anticoagulant (NOAC) are recommended in preference to VKA in patients with AF and aortic stenosis, aortic or mitral regurgitation (goes from class IIA to class I).

NOACs should be considered over VKA following surgical implantation of a bioprosthesis, in patients with AF (class IIa).

Complications of valve prostheses

Decision of surgical or percutaneous management of a significant paravalvular leaks should be considered based on patient risk status, leak morphology, and local expertise (class IIa).

Anticoagulation should be considered in patients with leaflet thickening or reduced mobility leading to an increase in trans-prosthetic gradients, at least until resolution (class IIa).

In the event of prosthesis dysfunction in the mitral or tricuspid position, percutaneous valve-in-valve can be considered in selected patients at high surgical risk (class IIb).

ESC guidelines for the diagnosis and treatment of acute and chronic heart failure

The new 2021 ESC HF guidelines [4] provide us with an extensive summary of the best current evidence for the management of patients with heart failure. A recent focus on the 10 commandments suggests these guidelines are not only suggestions, but standard quality of care, ranging from clear statements on drug therapy to fine tuning in the use of devices and treatment of comorbidities. The major treatment goals are clear: a reduction of mortality, a reduction of

hospitalisation and a focus on quality of life, functional status and symptoms.

First of all the medical treatment of heart failure patients evolved from an “add-on” scheme - as presented in previous guidelines - to an “all at once” implementations of 4 drug classes: 2 renin-angiotensin-aldosterone-system inhibitors (either an angiotensin converting enzyme inhibitor (ACEI) or sacubril-valsartan (ARNI)) and a mineralocorticoid receptor antagonist (MRA), a beta-blocker, and a sodium co-transporter-2 inhibitor (SGLT2i). A diuretic is added in the presence of congestion. The rationale is clear as data from recent randomised trials suggest that the treatment with all four drug classes is associated with an extra 3 years of life free of HF hospitalisation or death for an 80 year old and an extra 8 years for a 55 year old with HFREF compared to treatment with an ACEI or ARB and beta-blocker alone. Each class has additive prognostic benefit independent of the others. But still some questions are open, ranging from how to implement this in daily practice (a real “all at one”, a “fast consecutive” scheme and “which drug will come first”) to whether or not dose regimens could be individualised. Anyway all cardiologist should currently be aware scientific evidence provides us with 4 disease modifying drug classes for the treatment of heart failure.

In terms of terminology the formal and more abstract term of HF with mid range ejection fraction from the 2016 guidelines was exchanged for the term HF with mildly reduced ejection fraction, with adapts more to daily practice and emphasises the continuum of cardiac dysfunction. As no prospective randomised controlled trials were performed in this specific population, no strong recommendations can be formulated. The 2021 recommendations concerning HF with preserved ejection (LVEF $>50\%$) remain unchanged in the absence of additional evidence, but which might become available in the coming years.

A second change in the guidelines is a finetuning of the use of devices (CRT, ICD). CRT is indicated in selected patients with an LVEF $<35\%$, sinus rhythm and a QRS $>130\text{ms}$. Indeed a Ia status is still defined in patients with a LBBB and QRS $>150\text{ms}$, but as the prognostic benefit was less certain in 2 different patient-data meta-analysis from landmark trials, the strength of recommendation in patients with LBBB and QRS 130-149ms was downgraded to a IIa status, emphasising the uncertainty and illustrating the dilemma facing all guideline committees: should the recommendation be based on subgroup data or on the whole study population.

A similar change is observed in the recommendations concerning the use of an ICD. In secondary

prevention the guidelines are unchanged. On the contrary in primary prevention a split-up is made between patients with ischaemic versus a non ischaemic aetiology. Indeed none of the landmark trials that established the benefit of implantable cardioverter defibrillators (ICD) implantation specifically enrolled patients with non-ischaemic cardiomyopathy, while those who did were either neutral or were stopped early. In addition data from the more recent DANISH-trial, which only recruited patients with a non-ischaemic cardiomyopathy, found no reduction in all-cause mortality, although patients in the ICD group were less likely to die suddenly. In addition a reduction of 44% of sudden cardiac death in patients with heart failure, following the introduction of ACEI, beta-blocker, MRA, ARNI and SGLT2i, was observed. Thus the level of evidence for ICD implantation in primary prevention in patients with non-ischaemic heart failure was downgraded to a IIa status.

A selected group of patients with advanced heart failure is eligible for heart transplantation or the use of a mechanical circulatory support (MCS) device in the absence of other therapeutic options and after careful screening for contraindications.

A clear work-up is mandatory in patients with acute heart failure, resulting in detection and treatment of specific causes (i.e. acute coronary syndrome, hypertension emergency, arrhythmia, pulmonary embolism, mechanical cause (VSD, papillary or chorda rupture), infection, tamponade). Diuretics, vasodilators, inotropes, vasopressors and short term MCS are used according to the clinical presentation.

Most importantly before discharge a clear strategy should be implemented for the long term treatment and follow up of the patient. A predischarge visit is essential to assess the absence of congestion and the implementation of evidence-based drug therapies. A follow-up visit within 1 or 2 weeks should be scheduled as this appears critical to avoid early rehospitalization. In addition integration in a multidisciplinary heart failure management program, including exercise rehabilitation and self-management strategies are needed.

Finally attention should be given to comorbidities and red flags. It is recommended:

- To periodically screen for anaemia and iron deficiency in all HF patients, and intravenous iron supplementation with ferric carboxymaltose should be considered if the serum ferritin is <100ng/ml, or a serum ferritin 100-299ng/ml with TSAT <20%.
- To apply a long-term treatment with an oral anticoagulant in all patients with AF, HF, and a CHA2DS2-VASc score of >2 in men and >3 in women, DOACs being preferred to VKAs, and to consider pulmonary vein ablation for rhythm control when atrial fibrillation is associated with worsening symptoms of heart failure
- To apply aortic valve intervention (SAVR or TAVI) in patients with HF and a severe high-gradient aortic stenosis. The choice between SAVR or TAVI is made within the heart team.
- To consider edge-to-edge mitral valve repair in selected patients with secondary mitral regurgitation, not eligible for surgery and not needing coronary revascularization, who are symptomatic despite optimal medical treatment, and fulfil the COAPT-criteria (LVEF 20-50%, LVESD <70mm, PAPS <70mmHg, absence of moderate or severe RV dysfunction or severe TR and absence of hemodynamic instability).
- To use SGLT2i in patients with type 2 diabetes at risk for cardiovascular events to reduce hospitalisations for HF, major CV events, end-stage renal dysfunction and CV death.
- To organise a CV evaluation, preferably by a cardiologist with experience/interest in cardio-oncology, before scheduled anticancer therapy in cancer patients at increased risk for cardiotoxicity
- To screen for amyloidosis in heart failure patients >65j with an increased left ventricular wall thickness, as tafamidis is currently recommended as treatment in patients with transthyretin-mediated amyloidosis and NYHA class 1 or 2 symptoms.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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