

[Review article]

Summary 2015 ESC guidelines

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INTRODUCTION

During the ESC congress in September 2015 in London, the new ESC guidelines were presented and are now available on the ESC website (<http://www.escardio.org/guidelines>).

The new guidelines cover management recommendations on the following cardiovascular items: pericardial disease, non-ST-elevation ACS, infective endocarditis, pulmonary hypertension, ventricular arrhythmias and sudden cardiac death.

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 the new ESC guidelines in daily clinical practice.

GUIDELINES FOR THE DIAGNOSIS AND MANAGEMENT OF PERICARDIAL DISEASES

Summary by Guy Van Camp, MD, PhD, OLV Hospital Aalst, Belgium

Pericardial diseases affect the pericardial sac and may be an isolated disease or be part of a systemic disease. They can be divided into: pericarditis (acute, subacute, chronic and recurrent), pericardial effusion, cardiac tamponade, constrictive pericarditis, pericardial masses.

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Acute pericarditis

Acute pericarditis is an inflammatory pericardial syndrome with or without pericardial effusion and diagnosis can be made if at least 2 of the 4 following criteria are present: pericardial chest pain, pericardial rubs, new widespread ST-elevation or PR depression on ECG and pericardial effusion. Supporting findings are: elevation of markers of inflammation (CRP, ESR, WBC count), evidence of pericardial inflammation by an imaging technique (CT, MRI). Aetiology of pericarditis should only be searched for and patients should be hospitalized if predictors of poor prognosis are present. Major criteria of poor prognosis are: fever > 38°C, subacute onset, large pericardial effusion, cardiac tamponade, lack of response to aspirin or NSAIDs after at least 1 week of therapy and minor criteria are: myopericarditis (cfr. troponin rise), immunosuppression, trauma, oral anti-coagulation.

Aspirin (750-1,000 mg every 8 hours during 1-2 weeks and decreasing the dose by 250-500 mg every 1-2 weeks) or NSAIDs (ibuprofen 600 mg every 8 hours during 1-2 weeks and decreasing doses by 200-400 mg every 1-2 weeks) together with colchicine (0.5 mg once (< 70 kg) or b.i.d (≥ 70 kg) for 3 months) are the cornerstones of the treatment of acute pericarditis and gastro-protection should be provided. Serum CRP should be used to guide the treatment length and to assess the response to therapy. Low-dose corticosteroids (prednisone 0.25-0.50 mg/kg/day) with tapering depending on the total daily dose should be considered in case of contra-indication or failure of aspirin/NSAIDs and colchicine, only if an infectious cause has been excluded or when there is a specific indication (auto-immune disease). Exercise restriction is recommended until symptom resolution and normalization of CRP, ECG and echocardiogram for non-athletes and for at least 3 months in athletes.

In recurrent pericarditis (often inadequate treatment of the first episode and immune-mediated in most

immuno-competent patients), therapy should be targeted to the underlying aetiology if available. In case of incomplete response to aspirin/NSAIDs/ colchicine corticosteroids at low/moderate doses and immunosuppressive agents a can be added but they should be avoided in infections, particularly in bacterial pericarditis and tuberculosis. As a last resort pericardiectomy may be considered.

In cases of suspected associated myocarditis, coronary angiography is recommended in order to rule out acute coronary syndromes (according to the clinical presentation and risk factor assessment). CMR is recommended in these cases as is hospitalization and rest and avoidance of physical activity for 6 months. Empirical anti-inflammatory therapies should be used to control chest pain.

Pericardial effusion and tamponade

The diagnosis of pericardial effusion is generally performed by echocardiography. Chest X-ray is recommended in case of suspicion of pericardial effusion or pleuro-pulmonary involvement and CRP should be performed as a marker of inflammation. The first step should be to determine its size and to exclude tamponade. In case of elevated inflammatory markers anti-inflammatory therapy should be started empirically. If there is a known associated disease, this disease should be treated and in case of large effusions (> 20 mm) pericardiocentesis and drainage if chronic (> 3 months) should be considered. Pericardiocentesis should also be performed in case of symptomatic moderate to large effusions not responsive to medical therapy, and in case of suspicion of unknown bacterial or neoplastic aetiology.

In a patient with the clinical suspicion of cardiac tamponade, echocardiography is recommended as the first imaging technique to evaluate the size, location, and the degree of haemodynamic impact of the pericardial effusion and urgent pericardiocentesis under echocardiographic or fluoroscopic guidance or cardiac surgery (especially in purulent pericarditis and in urgent situations with bleeding into the pericardium) is recommended if tamponade is confirmed.

Constrictive pericarditis

Constrictive pericarditis can occur after any pericardial disease process, but only rarely follows recurrent pericarditis. The risk is related to the aetiology (low in viral and idiopathic, high in bacterial especially purulent pericarditis). The diagnosis is based on the association of clinical signs and symptoms of right heart failure and echocardiographic evidence of an impaired diastolic filling due to pericardial constriction and the main differential diagnosis is restrictive

cardiomyopathy. As second level imaging technique, CT and/or MRI can be used to assess calcifications (CT), pericardial thickness and the degree and extent of the pericardial involvement. If non-invasive diagnostic tools do not provide a definite diagnosis of constriction cardiac catheterization should be performed. Transient constriction associated with pericarditis should be recognized (CRP, pericardial inflammation on CT/MRI) since medical therapy may prevent the need for pericardiectomy. Chronic constriction is defined by persistent constriction after 3-6 months and pericardiectomy is the optimal treatment (medical therapy for advanced cases or high-risk of surgery or mixed forms with myocardial involvement).

Specific aetiologies of pericardial syndromes

Special and specific recommendations are defined in the new guidelines in several clinical conditions such as bacterial/tuberculous pericarditis, post-cardiac injury syndrome, pericardial involvement in neoplastic disease, radiation pericarditis, pericardial effusion in metabolic and endocrine disorders.

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Most important To Do and Not To Do messages: pericardial diseases	Recommendation level
Management of acute or recurrent pericarditis	
– Colchicine use as first-line therapy as an adjunct to aspirin/NSAID	I A NEW
– Corticosteroids are not recommended as first-line therapy	III C
Management of pericardial effusion	
– Pericardiocentesis or cardiac surgery is indicated for cardiac tamponade or for symptomatic moderate to large pericardial effusions not responsive to medical therapy and for suspicion of unknown bacterial or neoplastic aetiology	I C
Management of constrictive pericarditis	
– CT and/or CMR are indicated as second-level imaging techniques (after echocardiography and chest X-ray) and cardiac catheterization is indicated when non-invasive diagnostic methods are inconclusive	I C
– The mainstay of treatment of chronic permanent constriction is pericardiectomy	I C

GUIDELINES ON NSTEMI-ACS

Summary by Peter Sinnaeve, MD, PhD, FESC,
Leuven University Hospitals, Belgium.

The theory and practice of acute coronary syndromes (ACS) is a perpetually changing field. Here, a few of the most important highlights and changes are reviewed.

Risk assessment using high-sensitivity troponin

As in the previous guidelines, the new version elaborately addresses the timing and interpretation of serial high-sensitivity troponin (hs-cTn) measurements in the work-up of a patient presenting with acute chest pain suggestive for an NSTEMI-ACS. The existing classic 3-h triage scheme remains the recommended backbone of this assessment. As an alternative, a new, 1-h rule-in/rule-out algorithm is now introduced, with specific low and high cut-off values as well as absolute deltas between the initial and second sample suggested per available hs-cTn assay. In essence, two negative hs-cTn measurements within a 1-h interval effectively rules out an NSTEMI myocardial infarction, at least in patients not presenting very early (<1h) after onset of symptoms. Whatever troponin algorithm is used, it still does require careful integration with the ECG and clinical judgement.

The updated guidelines also spend considerable attention to risk assessment in general. In particular, the use of risk scores such as the GRACE score is highly recommended for outcome estimation; the CRUSADE bleeding score is only deemed useful for invasively managed patients.

Antithrombotic strategies

Not unexpected, the recommendations regarding dual antiplatelet therapy (DAPT) were also tweaked. Based on the results from ACCOAST, upfront preloading of prasugrel before an angiography and in the absence of a planned PCI is clearly contraindicated (i.e. a class III indication). In contrast, ticagrelor is now recommended for moderate-to-high risk NSTEMI-ACS patients, irrespective of an initially invasive or conservative strategy. While overall a one-year treatment remains the preferred and EBM-based length for DAPT in the new guidelines, more lenience is given towards *shorter* as well as *longer* DAPT durations for patients deemed at high *bleeding* versus high *ischaemic* risk (both receive a IIbA recommendation). The shortest listed duration after a DES in a NSTEMI-ACS patient at

high risk for bleeding now is 3 months. The Web-addenda to the 2015 guidelines present a very nice overview and rationale of the evidence behind shorter and longer DAPT durations. The new guidelines now offer guidance on how to combine DAPT (or not) with oral anticoagulant agents, based on common sense and opinion awaiting ongoing trials. The duration of triple therapy (ASA + clopidogrel + antico) is shortened to 1 to 6 months depending on the bleeding risk profile of the patient.

The recommendations on the use of parenteral anti-coagulation are in line with the previous guidelines and advocate fondaparinux as having the most favourable efficacy-safety profile.

Invasive management and transradial approach

Next, considerable attention is given to best practices in the invasive management of NSTEMI-ACS patients. The timing of angiography is depending on the risk profile of the patient with immediate invasive strategy (<2 h) for very high risk groups (e.g. haemodynamic instability, ongoing or severe ischaemia) and early invasive strategy (<24 h) for high-risk patients such as those with cardiac troponin rise or dynamic ST-T segment analysis or GRACE score >140. In addition, a transradial approach is now strongly recommended (class IA), at least in centres experienced in radial PCI.

Question & Answer and Web Addenda companion papers

New to the 2015 edition of the NSTEMI-ACS guidelines are the accompanying Questions & answers papers. There are actually three of them: one on revascularization, another on antithrombotics and a third one on diagnosis and risk assessment. These documents are wonderful gems and extremely useful as additional educational material. Finally, a Web Addenda paper gives additional insights and guidance in other important topics such as the management of bleeding complications and specific populations like the elderly, women, diabetic patients as well as patients with chronic kidney disease.

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Most important To Do and Not To Do messages: NSTE-ACS	Recommendation level
Diagnosis	
– Rapid rule out and rule in protocol at 0 h and 3 h is recommended if high-sensitivity cardiac troponin tests are available	I B
– Rapid rule-out and rule-in protocol at 0 h and 1 h is recommended if a high-sensitivity cardiac troponin test with a validated 0 h/1 h algorithm is available	I B NEW
Antiplatelet therapy	
– A P2Y12 inhibitor (ticagrelor, prasugrel) is recommended, in addition to aspirin, for 12 months unless there are contraindications such as excessive risk of bleeds	I B
– Clopidogrel is recommended in patients who cannot receive ticagrelor or prasugrel or who require oral anticoagulation	I B
– It is not recommended to administer prasugrel in patients in whom the coronary anatomy is not known	III B NEW
Invasive strategy	
– Invasive strategy is recommended with the timing depending on the risk profile of the patients	I A
– In centres experienced with radial access, a radial approach is recommended for coronary angiography and PCI	I A NEW
Secondary cardiovascular prevention	
– It is recommended to start high-intensity statin therapy as early as possible, unless contraindicated, and maintain it long-term	I A

GUIDELINES FOR THE MANAGEMENT OF INFECTIVE ENDOCARDITIS

Summary by Agnes Pasquet MD, PhD, FESC, Cliniques Universitaires Saint Luc, Brussels, Belgium.

Despite improvement in diagnosis and quality of care, endocarditis remains a deadly disease. For decades, large antibiotic prophylaxis was considered the cornerstone of endocarditis prevention. The 2009 guidelines restricted indications for antibiotic prophylaxis to high-risk patients undergoing a high-risk procedure (dental procedures requiring manipulation of the gingival or periapical region of the teeth or perforation of the oral mucosa care) and these guidelines were maintained in the current version.

Patients with the highest risk of endocarditis are: (class IIa, level c)

- Patients with a prosthetic valve or with prosthetic material used for cardiac valve repair. This also applies to transcatheter-implanted prostheses and homografts
- Patients with previous endocarditis
- Patients with uncorrected cyanotic congenital heart disease (CHD) and those with CHD having palliative shunts, conduits or other prostheses. After

surgical/endovascular repair with no residual defects, the Task Force recommends prophylaxis for the first 6 months after the procedure until endothelialization of the prosthetic material has occurred.

The guidelines emphasized the importance of dental and general hygiene to be applied both by patients and healthcare workers.

Non-specific prevention measures to be followed in high-risk and intermediate-risk patients are now clearly summarized in a table, including avoidance of piercings and tattoos and of self-medication with antibiotics.

Compared to the previous guidelines, a table with recommendations regarding antibiotic prophylaxis for the prevention of local and systemic infections before cardiac or vascular interventions is now added – new here is the recommendation to screen for nasal carriage of *S. aureus* in order to treat carriers (level IA)

Another new point in these revised guidelines is the advocacy for a multidisciplinary approach of the patient with the creation of an ‘endocarditis team’ imitating the heart valve clinic and the heart team. Clear recommendations including indications for referral, characteristics and role of the centre are provided in the guidelines.

Although echocardiography remains the technique of choice for the diagnosis of endocarditis, and plays a key role in the management and monitoring of these patients, the current guidelines recognize the emerging role of computed tomography to identify lesions related to endocarditis especially in patients with prosthesis as well as the role of nuclear techniques (SPECT/PET) to highlight infectious foci.

These new techniques were included in a revision of the Duke’s criteria and of the diagnostic algorithm for endocarditis proposed in the actual guidelines. The clinical diagnosis of endocarditis is retained in the presence of 2 major criteria; or 1 major criterion and 3 minor criteria; or 5 minor criteria. Endocarditis is considered as possible if 1 major criterion and 1 minor criterion, or 3 minor criteria are present.

Definitions of the terms used in the European Society of Cardiology 2015 modified criteria for the diagnosis of infective endocarditis

Major criteria

1. Blood cultures positive for IE

- a. Typical microorganisms consistent with IE from 2 separate blood cultures:
 - Viridans streptococci, *Streptococcus gallolyticus* (*Streptococcus bovis*), HACEK group, *Staphylococcus aureus*; or
 - Community-acquired enterococci, in the absence of a primary focus; or
- b. Microorganisms consistent with IE from persistently positive blood cultures:
 - ≥ 2 positive blood cultures of blood samples drawn > 12 h apart; or
 - All of 3 or a majority of ≥ 4 separate cultures of blood (with and last samples drawn ≥ 1 h apart); or
- c. Single positive blood culture for *Coxiella burnetii* or phase I IgG antibody titre > 1:800

2. Imaging positive for IE:

- a. Echocardiogram positive for IE:
 - Vegetation;
 - Abscess, pseudoaneurysm, intracardiac;
 - Valvular perforation or aneurysm;
 - New partial dehiscence of prosthetic valve.
- b. Abnormal activity around the site of prosthetic valve implantation detected by 18F-FDG PET/CT (only if the prosthesis was implanted for > 3 months) or radiolabelled leukocytes SPECT/CT. Paravalvular lesions by cardiac CT.

Minor criteria

1. Predisposition such as predisposing heart condition, or injection drug use.
2. Fever as temperature > 38°C.
3. Vascular phenomena (including those detected by imaging only): major arterial emboli, septic pulmonary infarcts, infectious (mycotic) aneurysm, intracranial haemorrhage, conjunctival haemorrhages, and Janeway's lesions.
4. Immunological phenomena: glomerulonephritis, Osler's nodes, Roth's spots, and rheumatoid factor.
5. Microbiological evidence: positive blood culture but does not meet a major criterion as noted above or serological evidence of active infection with organism consistent with IE.

The guidelines review the different antibiotic regimens according to the nature and sensitivity of the germs but acknowledge that they must be adapted according to bacteriological results and should be given 2 to 6 weeks depending on the strain susceptibility, the infected valve (native versus prosthesis) and clinical condition of the patient. In acutely severely ill patients empirical treatment can be initiated with ampicillin + cloxacillin + genta for community-acquired native valves or late prosthetic valves (> 12 months). For early prosthetic valve endocarditis (< 12 months post-surgery) or nosocomial and non-nosocomial healthcare-associated endocarditis a regimen of vancomycin + gentamicin is recommended.

More than one half of the patients require surgical treatment for endocarditis or complications. The indication for urgent (within a few days, < 7 days) or emergent (within 24 h) surgery are related to severe valve destruction with subsequent heart failure, uncontrolled infection or high risk of embolism.

Finally, a last part is dedicated to specific situations and sometimes challenging situations: prosthetic valve endocarditis, infective endocarditis in congenital heart disease, infective endocarditis affecting cardiac implantable electronic devices, right-sided infective endocarditis, infective endocarditis during pregnancy and the possible association between endocarditis and cancer.

Some additions to the previous recommendations clarify issues as antibiotic regimens for prophylaxis in case of device implantation, the recommendation to refer patients with CHD related endocarditis to specialized centres.

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Most important To Do and Not To Do messages: infective endocarditis	Recommendation level
Prophylaxis/prevention	
– Antibiotic prophylaxis should be considered only for patients at the highest risk for endocarditis (see text) and for dental procedures requiring manipulation of the gingival or periapical region of the teeth or perforation of the oral mucosa	Ila C
Diagnosis	
– TOE is recommended in all patients with clinical suspicion of IE and a negative or non-diagnostic TTE and when a prospective heart valve or an intracardiac device is present	I B
Treatment	
– Urgent surgery is recommended for uncontrolled infection (abscess, false aneurysms, fistula, enlarging vegetation), for persistent vegetation > 10 mm after ≥ 1 embolic episode despite appropriate antibiotic therapy and for severe valve destruction with poor haemodynamic tolerance	I B
– Infection caused by fungi or multidrug-resistant organisms must be treated by urgent surgery	I C
Cardiac device-related infective endocarditis (CDRIE)	
– Prolonged (i.e. before and after extraction) antibiotic therapy and complete hardware (device and leads) removal are recommended in definite CDRIE, as well as in presumably isolated pocket infection	I C NEW
– Percutaneous extraction is recommended in most patients with CDRIE, even those with vegetations > 10 mm.	I B NEW

GUIDELINES FOR THE MANAGEMENT OF PATIENTS WITH VENTRICULAR ARRHYTHMIAS (VA) AND THE PREVENTION OF SUDDEN CARDIAC DEATH (SCD)

Summary by Georges H. Mairesse, MD, FESC, Cliniques du Sud Luxembourg, Arlon, Belgium

Presented in September 2015, these guidelines enhance the fact that SCD is responsible for almost 25% of the 17 million annual deaths every year in the world caused by cardiovascular diseases. In the young, there is a predominance of channelopathies and cardiomyopathies, myocarditis and substance abuse, while in older populations chronic degenerative diseases, such as CAD, valvular heart diseases and heart failure, predominate. With a clinical perspective, specific sections are providing risk evaluation

schemes and treatments tailored in consideration of comorbidities, limitation of life expectancy and other circumstances.

With the exception of beta blockers, the guidelines emphasize that currently available anti-arrhythmic drugs have not been shown in randomized trials to be effective in the primary management of patients with life-threatening VA or in prevention of SCD, while each drug has a significant potential for causing adverse events, including pro-arrhythmia. Amiodarone should be considered to prevent VT recurrence in patients with or without an ICD, and may be considered for the relief of symptoms from VA in survivors of a myocardial infarction, but has no effect on mortality.

In addition to recommendations on ICDs, the current guidelines present, for the first time, recommendations on subcutaneous ICD and wearable cardioverter/defibrillators. Public access defibrillation is covered. Interventional therapy, through catheter ablation or anti-arrhythmic surgery, is also addressed.

In CAD, coronary revascularization has to be performed whenever possible and reevaluation of LVEF 6-12 weeks after an acute event is recommended to assess the potential need for primary prevention ICD implantation. ICD therapy is recommended to reduce SCD in patients with symptomatic heart failure (NYHA class II or III) and LVEF $\leq 35\%$ after ≥ 3 months of optimal medical therapy who are expected to survive at least 1 year in good functional status. Programmed ventricular stimulation should be considered in survivors of myocardial infarction with preserved LVEF and otherwise unexplained syncope.

Cardiac resynchronization therapy (CRT) in the primary prevention of SCD is recommended in patients with LVEF% $\leq 35\%$ and LBBB and in NYHA class III-IV despite at least 3 months of optimal pharmacological therapy. The level of evidence is stronger for QRS duration > 150 than for QRS duration of 120-150 ms and for sinus rhythm as compared to atrial fibrillation. For patients with NYHA class 2 CRT-D is recommended in patients with a LVEF $\leq 30\%$ and with QRS duration ≥ 130 msec.

Specific sections also provide recommendations for patients with hypertrophic cardiomyopathy (see also ESC guidelines 2014), arrhythmogenic right ventricular cardiomyopathy, other cardiomyopathies or inherited primary arrhythmia syndromes, including long QT, short QT, Brugada, catecholaminergic polymorphic ventricular tachycardia, and early repolarization syndromes. A subsequent chapter covers arrhythmias in paediatric and adult patients with congenital heart disease. Recommendations are also provided for selected populations, such as athletes, psychiatric, neurological, or pregnant patients, those with obstructive sleep apnoea, or patients with Wolff-Parkinson-White syndrome.

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Most important To Do and Not To Do messages: VA and SCD	Recommendation level
General population	
– It is recommended that public access defibrillation be established at sites where cardiac arrest is relatively common and suitable storage is available	I C NEW
– The analysis of blood and other adequately collected body fluids for toxicology and molecular pathology is recommended in all victims of unexplained sudden death	I C
Patients with heart failure	
– ICD therapy is recommended to reduce SCD in patients with symptomatic HF (NYHA class II or III) and LVEF $\leq 35\%$ after ≥ 3 months of optimal medical therapy who are expected to survive at least 1 year with good functional status	I A (ischaemic) I B (non-ischaemic)
– To reduce all-cause mortality, CRT-D is recommended in HF patients with LBBB, QRS duration ≥ 130 ms, with a LVEF $\leq 30\%$ and with NYHA class 2 despite at least 3 months of optimal pharmacological therapy who are expected to survive at least 1 year with good functional status	I A
– To reduce all-cause mortality, CRT is recommended in patients with a LVEF $\leq 35\%$ and LBBB and remain in NYHA class 3-4 despite at least 3 months of optimal pharmacological therapy who are expected to survive at least 1 year with good functional status	I A (QRS > 150 ms) I B (QRS 120-150) NEW
Sudden cardiac death in athletes	
– Physical examination and resting 12-lead ECG should be considered for pre-participation screening in younger athletes	Ila C

ESC/ERS GUIDELINES FOR THE DIAGNOSIS AND TREATMENT OF PULMONARY HYPERTENSION

Summary by Michel De Pauw, MD, FESC, University Hospital of Gent, Belgium

The 2015 ESC guidelines replacing the older version of 2009, are elaborated in cooperation with the European Respiratory Society (ERS) and are endorsed by the Association of European Paediatric and Congenital Cardiology (AEPC) and the International Society for Heart and Lung Transplantation (ISHLT) providing them a wide support.

The major findings and changes can be summarized as follows:

1. Definition and classification

Pulmonary hypertension (PH) definition is unchanged and is defined as an increase in invasively measured mean pulmonary arterial pressure at rest ≥ 25 mmHg. However, pulmonary vascular resistance (PVR) is reintroduced especially to define pulmonary arterial hypertension (PAH) and PH related to left heart disease. The term of out of proportion PH was dropped and replaced by the term combined post-capillary and pre-capillary PH. In a separate chapter on PH in left heart disease the rationale for this change is explained. The classification of PH was refined. Chronic haemolytic anaemia is reclassified from group 1 to group 5, pulmonary veno-occlusive disease has been more specified, and congenital heart diseases have been split up into group 1 and group 2, related to the underlying clinical picture.

2. Refinement of diagnostic algorithm

The diagnostic algorithm underwent no major changes, however, the diagnostic possibilities of echocardiography do not only include tricuspid regurgitation velocity (TRV) but underscore also the importance of echo signs of right ventricular failure and/or impaired systolic acceleration of the RV outflow Doppler signal. Secondly, the role of expert centres is put forward already starting with the diagnostic process. Vaso-reactivity testing is recommended in patients with idiopathic or heritable or drug-induced PAH to select patients who may have benefit from high doses of a calcium channel blocker. Finally, recommendations for pulmonary hypertension screening in systemic sclerosis, BMPR2-mutation carriers, first-degree family members of HPAH and PoPH are defined and published as a web addendum.

3. Prognostic evaluation and risk assessment

The need for a regular evaluation is stressed, using a multidimensional approach encompassing clinical assessment, exercise tests, biochemical markers (e.g. BNP), echocardiographic and invasive evaluation. The definition of satisfactory or unsatisfactory response is based on individual risk calculation. In addition the assessment of PAH patients should include evaluation of co-morbidities and disease complications.

4. Treatment algorithm

The treatment algorithm has been adapted with integration of information from a wide range of recent pharmacological trials testing various combinations of endothelin receptor antagonists, phosphor-diesterase

type-5 inhibitors, guanylate cyclase stimulators, prostanooids or IP-receptor agonists. For non-vasoreactive PH at low or intermediate risk (functional class 2-3) initial monotherapy or initial oral combination therapy is recommended with an additional oral drug class in case of inadequate clinical response. For class IV PH patients initial combination therapy including i.v. prostacyclin analogues is recommended. The chapter dedicated to chronic thromboembolic pulmonary hypertension (CTEPH) has been expanded including an elaborate view concerning the different treatment modalities such as surgical endarterectomy, medical and interventional treatment. For inoperable symptomatic CTEPH patients, treatment with guanylate cyclase stimulators (Riociguat) is recommended. Finally, criteria for lung transplantation and balloon atrial septostomy in end-stage PH disease are described.

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Most important To Do and Not To Do messages: pulmonary hypertension	Recommendation level
Diagnosis	
– Right heart catheterization is recommended to confirm the diagnosis of pulmonary arterial hypertension and to support treatment decisions	I C
– Vasoreactivity testing is recommended in patients with IPAH, HPAH and PAH induced by drugs use to detect patients who can be treated with high doses of a calcium channel blocker	I C
Management	
– Initial approved drugs monotherapy or combination therapy is recommended in treatment-naïve, low- or intermediate-risk patients with PAH	I A (mono) I B (combination)
– Sequential drugs combination therapy is recommended in patients with inadequate treatment response to initial monotherapy or to initial double combination therapy	I B NEW
– The use of PAH approved therapies is not recommended in patients with pulmonary hypertension due to left heart disease or lung diseases	III C
Chronic thromboembolic pulmonary hypertension	
– Surgical pulmonary endarterectomy in deep hypothermia circulatory arrest is recommended for patients with CTEPH and it is recommended that the assessment of operability and decisions regarding other treatment strategies (drug therapy or balloon pulmonary angioplasty) be made by a multidisciplinary team of experts	I C NEW