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Essential Messages from ESC Guidelines

**Clinical Practice
Guidelines Committee**

CARDIOMYOPATHIES

Guidelines for the management of
cardiomyopathies



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of Cardiology

Essential Messages

2023 ESC Guidelines for the management of cardiomyopathies

Developed by the task force on the management of cardiomyopathies of the European Society of Cardiology (ESC).

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Patient Forum

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ESSENTIAL MESSAGES FROM THE 2023 ESC GUIDELINES FOR THE MANAGEMENT OF CARDIOMYOPATHIES

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Key messages

1. Cardiomyopathies are more common than previously thought and they typically require nuanced management that may differ from conventional approach to patients with arrhythmia or heart failure.
2. Aetiology is fundamental to the management of patients with heart muscle disease and careful and systematic description of the morphological and functional phenotype is a crucial first step in the diagnostic pathway.
3. An approach to nomenclature and diagnosis of cardiomyopathies that is based on the predominant phenotype at presentation is recommended.
4. Patients with cardiomyopathy may seek medical attention due to symptoms onset (HF or arrhythmia-related), incidental abnormal findings or as a result of family screening following the diagnosis in a relative.
5. Multimodality imaging to characterize the cardiac phenotype (morphology and function) - including tissue characterization for non-ischaemic myocardial scar detection - is necessary, in combination with a detailed personal and family history, clinical examination, electrocardiography, and laboratory investigations.
6. Imaging results should always be interpreted in the overall clinical context, including genetic testing results, rather than in isolation.
7. Tissue characterization by CMR is of value in diagnosis, monitoring of disease progression and risk stratification in each of the main cardiomyopathy phenotypes.
8. DPD/PYP/HMDP bone-tracer scintigraphy or SPECT represent the gold standard for the diagnosis of ATTR-related cardiac amyloidosis.
9. The presence of non-ischaemic ventricular scar or fatty replacement on cardiac CMR and/or pathological examination, which can occur with or without ventricular dilatation and/or systolic dysfunction, can be the sole clue to the diagnosis of a cardiomyopathy and can have prognostic significance that varies with aetiology.
10. The aim of this multiparametric and systemic approach is to generate a phenotype-based aetiological diagnosis, interpreting available data with a cardiomyopathy-oriented mindset that combines cardiological assessment with non-cardiac parameters.
11. A multidisciplinary approach to patient care and appropriate transition of care from paediatric to adult cardiomyopathy services is needed.
12. Genetic testing should be performed in patients with cardiomyopathy, and may influence risk stratification and management.

Key messages

13. Genetic counselling, including pre- and post-test counselling, and psychological support are an essential aspect of the multidisciplinary care of patients with cardiomyopathy and their relatives.
14. Paediatric cardiomyopathies largely represent part of the same clinical spectrum as those seen in older adolescents and adults, but infant-onset (in the first year of life) cardiomyopathies are often associated with severe phenotypes and a high rate of heart failure-related morbidity and mortality.
15. Beyond the first year of life, genetic causes of childhood-onset cardiomyopathies are similar to those in adults.
16. Symptom management, identification and prevention of disease-related complications (including SCD, heart failure, and stroke) are the cornerstone of management of all cardiomyopathies.
17. Cardiac myosin inhibitors (Mavacamten) should be considered in patients with HCM and LVOTO who remain symptomatic despite optimal medical therapy.
18. Validated SCD risk-prediction tools (HCM Risk-SCD and HCM Risk-Kids) are the first step in sudden death prevention in patients with HCM.
19. Additional risk markers may be of use in patients with low or intermediate risk, but there is a lack of robust data on the impact of these parameters on the personalized risk estimates generated by the risk-prediction tools.
20. Pharmacological treatment of DCM patients does not differ from those recommended in chronic heart failure.
21. SCD risk of DCM and NDLVC patients varies depending on the underlying cause and genetic subtype.
22. CMR findings play an important role in guiding ICD implantation for patients with DCM and NDLVC.
23. In DCM and NDLVC patients, ICD should be considered for certain genetic forms even if LVEF is $\geq 35\%$.
24. It is of importance to define aetiology for a tailored management in patients with syndromic and metabolic cardiomyopathies (i.e. ERT/chaperone in lysosomal storage disease; tafamidis in ATTRwt, etc.).
25. Pregnancy and the postpartum period are associated with increased cardiovascular risk in women with known cardiomyopathy.

Key messages

26. A multidisciplinary team should evaluate the patient with cardiomyopathy to assess the risk associated with pregnancy.
27. Beta-blocker therapy on arrhythmic indication can safely be continued during pregnancy; safety data should be checked before initiation of new drugs in pregnancy.
28. Healthy adults of all ages and individuals with known cardiac disease should exercise with moderate intensity, totalling at least 150 min per week.
29. All patients with cardiomyopathy should have an individualized risk assessment for exercise prescription. Evaluation should be guided by three principles: (i) preventing life-threatening arrhythmias during exercise; (ii) symptom management to allow sports; and (iii) preventing sports-induced progression of the arrhythmogenic condition.
30. Individuals who are genotype-positive/phenotype-negative or have a mild cardiomyopathy phenotype and absence of symptoms or any risk factors, may be able to participate in competitive sports. In some high-risk patients with HCM, ARVC, and NDLVC, high-intensity exercise and competitive sports should be discouraged.
31. Patients with high-risk genotypes or associated factors for arrhythmic or heart failure complications or severe LVOTO should be referred for specialized investigations before undergoing elective NCS.
32. Identification and management of risk factors and concomitant diseases is recommended as an integral part of the management of cardiomyopathy patients.

Gaps in evidence

Although there have been major advances in the genetics, diagnosis, and treatments of patients with cardiomyopathy over the last few years, there are a number of areas where robust evidence is still lacking and deserve to be addressed in future clinical research.

1. Cardiomyopathy phenotypes
2. Epidemiology
 - a. Prevalence of NDLCV phenotype (children and adults)
 - b. Systematic assessment of prevalence of cardiomyopathy phenotypes in childhood
3. Integrated patient management
 - a. Embedding of telemedicine into cardiomyopathy networks
4. Patient pathway
 - a. Laboratory tests
 - i. Studies on novel 'omic' biomarkers (proteomics, metabolomics, and transcriptomics) are needed to assess their potential value for diagnostic and prognostic purposes in cardiomyopathies.
 - b. Multimodality imaging
 - i. Advanced echocardiographic techniques, including speckle tracking deformation imaging, are promising but lack robust validation in the setting of cardiomyopathies
 - ii. A universally accepted, standardized method for quantification of myocardial fibrosis by CMR is lacking
 - iii. CMR scans may be performed in patients with compatible implantable devices, but the quality is limited by artefacts
 - iv. Artificial intelligence enhanced electrocardiography and imaging for cardiomyopathy evaluation has been proving a novel tool to dramatically improve diagnosis and prognosis; further studies are needed for routine introduction in clinical practice
 - v. Impact of CMR on screening in genotype-positive relatives of individuals with cardiomyopathy and in gene elusive families

Gaps in evidence

c. Genetics

- i. Penetrance is poorly characterized for most pathogenic variants. This is true both for variants found through cascade screening of relatives of a patient with cardiomyopathy, and also for variants found in the wider population who may have clinical sequencing for another indication or may choose to have genome sequencing as a screening test
- ii. The benefits, harms, and costs of screening of cardiomyopathy-associated genes in individuals without a personal or family history of cardiomyopathy is not known

d. General principles in management

- i. Management of RV failure remains largely non-evidence-based
- ii. Large-scale studies are required to guide ventricular arrhythmia management in patients with genetic cardiomyopathies
- iii. Optimal rate control and AADs per subtype of cardiomyopathy
- iv. The role of ICDs in patients with well tolerated VT
- v. All risk calculators are developed using baseline data. Therefore, the utility of their application during follow-up visits of patients remains unclear and needs to be studied
- vi. Risk prediction in childhood cardiomyopathies other than HCM is still empirical - multicentre approach required to understand and develop SCD risk models in childhood
- vii. Lack of controlled studies on the effect of ablation in patients with AF and cardiomyopathy
- viii. Models to predict AF recurrence have not been validated in cardiomyopathy patients
- ix. Lack of randomized studies assessing the efficacy of cardiac sympathetic denervation for the prevention of VT/VF recurrences

e. Approach to paediatric cardiomyopathies

- i. Lack of randomized studies or large registries addressing the benefit and optimal dosing of drug therapy in paediatric population

Gaps in evidence

5. Hypertrophic cardiomyopathy

a. Epidemiology

- i. Imaging and genotype studies suggest a population prevalence of up to 1 in 200 of the population. However, HER based studies suggest a much lower number of 3-4/10 000. Further studies into the prevalence of clinically important disease are necessary

b. Aetiology

- i. Aetiology of gene elusive disease
- ii. The role of polygenic risk
- iii. Interaction between comorbidity and disease outcomes
- iv. Genetic and environmental determinants of disease expression in variant carriers

c. Symptom management

- i. Optimal timing of LVOTO management and its impact on disease progression
- ii. Prevention of AF and heart failure

d. Sudden death prevention

- i. Impact of genetics (Mendelian and complex) on risk of disease-related outcomes
- ii. Improved prediction models that reduce residual risk and prevent unnecessary ICD implantation
- iii. Refinement of risk-prediction models to include serial data.
- iv. Role of LVOTO in risk prediction in children (apparent discrepancy compared with adults)

e. New therapies

- i. Clinical utility of myosin inhibitors, other small molecules, and emerging genetic therapies.

Gaps in evidence

6. Dilated cardiomyopathy

- a. Genetic basis of familial DCM is still unknown in a high number of cases
- b. Detailed data about the specific clinical course in diverse genetic and non-genetic DCM forms are not available
- c. It is unknown if patients with DCM respond different to pharmacological treatment according to underlying aetiology
- d. Optimized SCD prevention strategy remains unsolved. There are not data from prospective clinical trials in modern cohorts with contemporary medical treatment. This gap in knowledge is particularly relevant for DCM patients with LVEF>35%
- e. Sport recommendations and utility of prophylactic pharmacological therapy to prevent DCM onset in genetic carriers

7. Non-dilated left ventricular cardiomyopathy

- a. Prevalence of disease
- b. Natural history and response to treatment
- c. SCD prevention
- d. Sports recommendations

8. Arrhythmogenic right ventricular cardiomyopathy

- a. RCTs for therapies for the management of arrhythmias and heart failure are lacking
- b. Studies on the effect of exercise remain largely retrospective
- c. Studies on the incidence and prognostication of heart failure remain limited
- d. Studies on the frequency and mode of clinical screening for asymptomatic family members are lacking

9. Restrictive cardiomyopathy

- a. SCD prevention

Gaps in evidence

10. Syndromic and metabolic cardiomyopathies

- a. Lack of randomized trials or large observational cohort studies assessing the role of new target therapies addressing RAS/MAPK pathway (i.e trametinib)
- b. There are few long-term outcome studies addressing ventricular remodelling in Ras-HCM
- c. HCM Risk-Kids has not been validated in paediatric patients with Ras-HCM. Data regarding SCD risk stratification are lacking, although candidate risk factors have been identified
- d. Lack of studies addressing the optimal timing to start ERT in adolescent and adults with late-onset Pompe disease
- e. Lack of standardized protocols to treat cross-reactive immunologic material-negative patients
- f. Lack of standardization of clinical endpoints in ERT/chaperone therapy trials
- g. Lack of head-to-head comparisons between agalsidase alpha and beta
- h. Optimal time to begin treatment in asymptomatic female patients with non-classic disease

11. Amyloid

- a. Further studies are needed to assess the efficacy and safety of tafamidis in NYHA class III patients
- b. SCD risk stratification and indications for ICD implantation should be carefully defined, taking into account the estimated life expectancy, competitive non-cardiovascular mortality and the high rate of pulseless electrical activity
- c. The need for drug therapy in patients with cardiac amyloidosis and subclinical cardiac involvement (i.e asymptomatic patients, positive scintigraphy with negative ECHO) has not been clearly defined.

12. Sports

- a. 'Return to play' for patients with low-risk cardiomyopathies (and how to define low risk in relation to exercise)
- b. SCD risk and exercise recommendations in phenotype-negative gene carriers
- c. Role of exercise in disease expression and progression
- d. Large, adequately powered randomized prospective studies are necessary to provide evidence-based recommendations for optimal exercise prescription without compromising safety

Gaps in evidence

13. Reproductive issues

- a. Several cardiomyopathies lack specific outcome data regarding pregnancy
- b. There is a lack of randomized trials on the use of AADs, heart failure drugs and interventions during pregnancy

14. Non-cardiac interventions

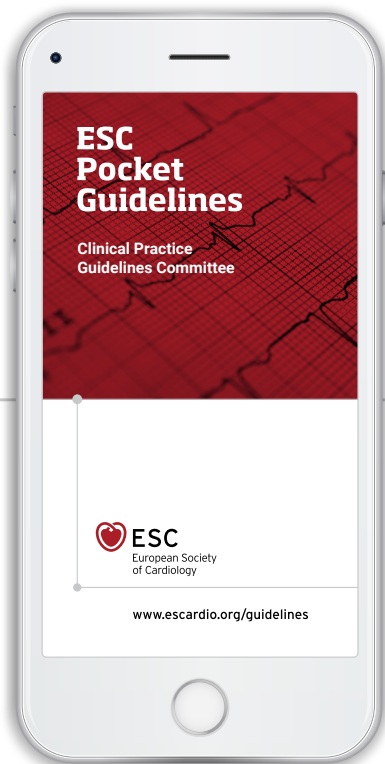
- a. There is a lack specific outcome data regarding risks of non-cardiac interventions

15. Management of cardiovascular risk factors in patients with cardiomyopathies

- a. There is a lack of data on the impact of comorbidities on penetrance, severity, and outcome of cardiomyopathies

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The following material was adapted from the 2023 ESC Guidelines for the management of cardiomyopathies (European Heart Journal; 2023 - doi: 10.1093/eurheartj/ehad194).

Post-publication corrections and updates are available at: www.escardio.org/guidelines

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