Dilated Cardiomyopathy: Clinical Assessment and Differential Diagnosis

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4.1 Introduction

Dilated cardiomyopathy (DCM) is a heart-muscle disorder characterized by systolic dysfunction and dilatation of the left ventricular (LV) cavity, with normal LV wall thickness. Sometimes, both ventricles are dilated and dysfunctional, but the involvement of the right ventricle (RV) is neither necessary nor sufficient for the diagnosis of DCM. This disease represents a relevant health problem in adult and pediatric populations, as it is associated with important morbidity and mortality rates and with frequent hospital admissions. Moreover, it is the third cause of heart failure (HF) and the first cause of heart transplant.

The estimated prevalence of DCM is about 1:2,500 of the general population, whereas the incidence is about 7:100,000 inhabitants per year [1]. However, due to the fact that many patients remain asymptomatic for a very long period until the onset of a marked ventricular dysfunction, the real incidence and prevalence of DCM could be significantly higher than the reported.

Males are more frequently affected than females, with an ~3:1 ratio [1], and symptoms tend to be age related, as they appear more frequently around the fourth to fifth decade of life, even though pediatric onset is not so rare. Familial/genetic forms are usually characterized by incomplete penetrance and variable age-related expression.

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4.2 Etiology

DCM can be familial or nonfamilial. Familial DCM accounts for only 30–48 % of cases of DCM, and the main pattern of inheritance is autosomal dominant (56 %). Autosomal recessive pattern accounts for 16 % of cases with genetic characterization, followed by X-linked forms (10 %), autosomal dominant forms associated with subclinical skeletal muscle disease (7.7 %), and nonclassifiable forms (7.7 %) [2].

The majority of nonfamilial forms have an acquired etiology, such as cardiotoxic drugs, alcohol abuse, heavy metals, autoimmune disorders, neuromuscular diseases, or infective agents, such as viral (coxsackievirus, adenovirus, parvovirus, HIV), bacterial (Borrelia, Rickettsia), mycobacterial, and fungal or parasitic (*Trypanosoma cruzi*). However, a genetic cause can be found in some apparently sporadic cases (new mutation, incomplete penetrance). Finally, a consistent group of DCM has no apparent cause and must be classified as idiopathic.

4.3 Clinical Phenotype

In DCM, the phenotype is widely heterogeneous: age of onset, clinical characteristics, and severity vary not only among different families, but also among members of the same family. Affected patients usually present signs and symptoms of HF associated with other cardiac manifestations, such as conduction disturbances [left bundle branch block (LBBB) or atrioventricular blocks], arrhythmias, and/or valvular diseases, such as functional mitral or tricuspid regurgitation. Complications, such as thromboembolism, and sudden death (SD) are not rare. A typical pattern of onset is characterized by a long clinically silent period of many years, and then the disease can become evident after a flu-like syndrome: during a prolonged recovery period, the patient suffers from dyspnea, extreme fatigue, and signs of HF-like edema. A study conducted in Trieste [3] reported the clinical/instrumental characteristics of DCM patients at first presentation according to the decade of enrolment (from 1978 to 2007) (Table 4.1). Progressive earlier diagnosis over time is clear: patients enrolled in the most recent decades had a progressively shorter history of HF, were less symptomatic for HF, and had less severe heart disease. Furthermore, patients with a previous history of HF episodes at enrolment progressively decreased in number, probably as an effect of systematic familial screening. Familial screening in DCM facilitates diagnosis in nonprobands at an early stage of disease, which is characterized by a less compromised LV and lower prevalence of LBBB, thus favorably impacting on the long-term prognosis [4].

4.4 Diagnostic Criteria

After clinical suspicion or screening, DCM is diagnosed by demonstration at imaging (typically 2D echocardiography) of LV dilatation and systolic dysfunction after excluding specific causes sufficient to determine the degree of myocardial

Table 4.1 Baseline clinical–instrumental characteristics of idiopathic dilated cardiomyopathy (DCM) patients according to decade of enrolment in the Heart Muscle Diseases Registry of Trieste

	First decade, 1978–1987; 110 (12.8 %)	Second decade, 1988–1997; 376 (44.1 %)	Third decade, 1998–2007; 367 (43.1 %)	*P* value
Age (years)	46 ± 17	44 ± 15	45 ± 14	0.425
Male gender (%)	74	73	71	0.856
Familial IDCM (%)	12	18	15	0.197
Duration of HF (months) [range]	2 [0–17][c]	3 [0–13][e]	0 [0–5]	**<0.001**[g]
SBP (mmHg)	126 ± 14	124 ± 16[e]	127 ± 19	**0.020**
NYHA III–IV (%)	36[c, d]	23	25	**0.029**
Patients with previous episodes of HF (%)	87	79	66	<0.001
Anemia[a] (%)	9	12	10	0.456
GFR ≤60 ml/min (%)	15	8	11	0.336
Sinus rhythm (%)	84	90	89	0.222
LBBB (%)	26	32	30	0.464
LVEF (%)	29 ± 9[c]	31 ± 11[e]	33 ± 11	**<0.001**
LVEDD-I (mm/m^2)	39 ± 7[c,d]	37 ± 6[e]	34 ± 5	**<0.001**
LVEDV-I (ml/m^2)	114 ± 60[c]	107 ± 41[e]	91 ± 34	**<0.001**
Restrictive filling pattern (%)		37[e]	17	**<0.001**[f]
Moderate–severe MR (%)[b]		39	34	0.157[f]
Beta-blockers after first evaluation (%)	11[c, d]	82	86	**<0.001**
ACE inhibitors or ARBs after first evaluation (%)	34[c, d]	93	93	**<0.001**
Digitalis after first evaluation (%)	66[c, d]	79[e]	38	**<0.001**
Aldosterone antagonists after first evaluation (%)	8	5[e]	18	**0.001**
ICD implantation during follow-up (%)	1[c, d]	14	13	**0.002**
Time from diagnosis to implantation (months) [range]	268	129 [99–165]	22 [2–47]	**<0.001**[g]
CRT implantation during follow-up (%)	0	6	6	0.301[f]
Time from diagnosis to implantation (months) [range]		151 [129–206]	23 [10–82]	**<0.001**[f, g]

Bold data *p* values <0.05

ARBs angiotensin receptor blockers, *BMI* body mass index, *CRT* cardiac resynchronization therapy, *GFR* glomerular filtration rate, *HF* heart failure, *ICD* implantable cardioverter defibrillator, *IDCM* idiopathic dilated cardiomyopathy, *LBBB* left bundle branch block, *LVEDD*-I indexed left ventricular end-diastolic diameter, *LVEDV-I* indexed left ventricular end-diastolic volume, *LVEF* left ventricular ejection fraction, *MR* mitral regurgitation, *SBP* systolic blood pressure

[a]Anemia: hemoglobin <13 g/dl for males, <12 g/dl for females

[b]MR with a jet area >4 cm^2 at color Doppler was classified as moderate or severe

[c]$P < 0.05$ between first and third decades

[d]$P < 0.05$ between first and second decades

[e]$P < 0.05$ between second and third decades

[f]*P* value computed only between second and third decades

[g]Kruskal–Wallis *p* value

Table 4.2 Major and minor criteria for diagnosing DCM

Major criteria
1 LVEF 45 % (>2 SD) and/or FS <25 % (>2 SD), as ascertained by echocardiography, radionuclide scanning or angiography
2 LVEDD >117 % of the predicted value corrected for age and body surface area, which corresponds to 2 SD of the predicted normal limit +5 %
Minor criteria
1 Unexplained supraventricular (atrial fibrillation or sustained arrhythmias) or ventricular arrhythmias, frequent (>1,000 . 24 h^{-1}) or repetitive (three or more beats with >120 beats/min^{-1}) before the age of 50
2 LVEDD >112 % of predicted value
3 Left ventricular dysfunction: LVEF <50 % or FS <28 %
4 Unexplained conduction disease: 2 or 3 atrioventricular conduction defects, complete LVBBB, sinus nodal dysfunction
5 Unexplained sudden death or stroke before 50 years of age
6 Segmental wall-motion abnormalities (<1 segment, or 1 if not previously present) in the absence of intraventricular conduction defect or ischemic heart disease

Adapted from Mestroni et al. [5]
DCM dilated cardiomyopathy, *SD* standard deviation, *LVEF* left ventricular ejection fraction, *LVEDD* left ventricular end diastolic diameter, *FS* fractional shortening, *LVBBB* left ventricular bundle branch block

dysfunction and dilatation, such as systemic arterial hypertension (>160/100 mmHg), coronary heart disease (stenosis >50 % of the luminal diameter in a major branch), chronic excessive alcohol consumption (>100 g/day), rapid and sustained supraventricular arrhythmias, systemic diseases, pericardial diseases, congenital heart diseases, and cor pulmonale. Clinical examination, electrocardiography (ECG) and chest X-ray radiography are not specific for DCM, whereas on echocardiography, it is possible to evaluate disease criteria.

In 1999 a collaborative European study proposed a standardization of diagnostic criteria and methods of enrollment in familial DCM. Inclusion criteria were a LV ejection fraction (EF) <45 % documented at 2D echocardiography or angiography and/or a fractional shortening <25 % at M-mode echocardiography and an LV end-diastolic diameter >117 % of the predicted value corrected for age and body surface area (BSA). Familial DCM was diagnosed in the presence of two or more affected individuals in a single family or in the presence of a first-degree relative of a DCM patient, with well-documented, unexplained SD at <35 years of age. Moreover, major and minor criteria were formulated to distinguish affected, possibly affected, and nonaffected family members (Table 4.2) [5].

4.5 Prognostic Stratification and Therapy

Prognosis of patients with DCM has significantly improved compared to the past, when ~50 % of affected patients died within 2 years of diagnosis [6]. In the last decade, in particular, an 8-year survival rate of >85 % was estimated in DCM, with an incidence

Table 4.3 Occurrence of major events in the study population according to decade of enrolment in the Heart Muscle Diseases Registry of Trieste

	First decade, 1978–1987; 110 patients	Second decade, 1988–1997; 376 patients	Third decade, 1998–2007; 367 patients	*P* value, first vs. second decade	*P* value, first vs. third decade	*P* value, second vs. third decade
Mean follow-up (months)	151 ± 29	153 ± 82	93 ± 41	0.389	**0.03**	**<0.001**
All-cause mortality/ heart transplant, *n* (%)	77 (70)	178 (47)	53 (14)	**<0.001**	**<0.001**	**<0.001**
Incidence (events/100 patients/years)	5.6	3.9	1.9			
Heart transplant, *n* (%)	6 (6)	51 (14)	17 (5)	**0.02**	0.724	**<0.001**
Incidence (events/100 patients/years)	0.4	1.1	0.6			
Cardiovascular death, *n* (%)	57 (52)	91 (24)	18 (5)	**<0.001**	**<0.001**	**<0.001**
Incidence (events/100 patients/years)	4.1	2.0	0.6			
Pump failure death, *n* (%)	38 (35)	32 (9)	6 (2)	**<0.001**	**<0.001**	**<0.001**
Incidence (events/100 patients/years)	2.8	0.7	0.2			
Unexpected sudden death, *n* (%)	16 (15)	51 (14)	9 (3)	0.793	**<0.001**	**<0.001**
Incidence (events/100 patients/years)	1.2	1.1	0.3			
Unknown cause death, *n* (%)	13 (12)	31 (9)	16 (4)	0.338	**0.004**	**0.014**
Incidence (events/100 patients/years)	1.0	0.7	0.6			
Appropriate intervention of ICD (% of implanted patients)	0	32	38	NC	NC	0.499
Incidence (events/100 implanted patients/ years)		2.4	4.8		NC	0.499

Bold data *p* values <0.05
ICD implantable cardioverter defibrillator, *NC p* value not calculated, only two patients implanted with ICD in the first decade

of fewer than two major events per 100 patients per year, significantly higher than in the previous two decades [3] (Table 4.3). Many factors contributed to the improvement during this time. First is earlier diagnosis, especially when the disease is diagnosed while still in the asymptomatic phase [7]. In this sense, familial screening is an important instrument for the early diagnosis of DCM in asymptomatic patients and can impact long-term survival [4]. Therefore, a systematic familial screening with clinical interview, physical examination, ECG, and echocardiography should be performed on all probands (even in sporadic cases) and their first-degree relatives from puberty to 50 years of age.

Another important factor that influences the better prognosis in DCM is evidence-based optimal medical treatment: many clinical trials demonstrated the beneficial role of angiotensin-converting enzyme (ACE) inhibitors (Enalapril) and beta-blockers (metoprolol, carvedilol, and bisoprolol) [8–11]. Also, nonpharmacological treatments, such as implantable cardioverter defibrillators (ICD) and cardiac resynchronization therapy (CRT) with a biventricular pacemaker impact favorably on DCM prognosis [12, 13].

Response to medical treatment can vary; it is estimated that cardiac function is normalized in one third of patients, one third remains stable, and one third worsens despite optimal medical treatment. Reasons for these differences are unknown, but probably, there is a genetic predisposition.

However, the role of follow-up over time should be considered essential, especially when considering LV reverse remodeling, which is associated with an impressively better outcome in terms of survival free from heart transplant and SD [14]. Therefore, an individualized, regular, long-term follow-up represents the cornerstone of good management of this disease due to the lack of prognostic models identifying precise subgroups of patients suitable for more aggressive and earlier therapies.

To date, the principal aims of therapy in DCM are to treat HF and prevent malignant arrhythmias and SD. Due to the fact that DCM is a rare disease, there are no specific randomized trials oriented specifically to treatment but only to HF in general.

Many studies demonstrated the efficacy of different drugs in alleviating symptoms and improving prognosis in patients with HF. ACE inhibitors [8], angiotensin receptor antagonists, beta-blockers [10], and antialdosterone agents (spironolactone and eplerenone) [15, 16] clearly impact survival, whereas diuretics such as furosemide relieve symptoms (they could also influence prognosis, but their role in this context has not yet been demonstrated). Anticoagulants can be used in select cases at higher risk of thromboembolism, especially in patients with LVEF <30 % and in those with atrial fibrillation. Not only drug type but also dosage optimization is fundamental in order to improve symptoms and positively impact on morbidity and mortality. Indeed, optimal medical therapy, defined as administration of evidence-based therapy at target dosages or maximum tolerated dosages, improves DCM prognosis, significantly increasing the survival-free from pump failure death. Moreover, CRT is useful in preventing HF death in patients with low LVEF (i.e., <35 %) and prolonged QRS mostly in advanced New York Heart Association (NYHA) classes, and lower functional classes [13, 17].

Concerning SD prevention, despite the proven effect of medical treatment with beta-blockers [18], ICD implantation proves to be the most valid therapeutic tool, as it dramatically decreased the incidence of SD in the past decade [3]. The device should be implanted at least 3 months after optimization of medical treatment [19], even though the related drawback could be loss of a nonnegligible proportion of patients in the meantime. The challenge is to identify which patients could benefit from an early ICD independent of optimized medical treatment [20].

New therapeutic options for HF are taking place. One is percutaneous mitral leaflet repair (MitraClip) in patients with severe functional mitral regurgitation (MR) at high risk of surgery. It is safe and effective in reducing MR, improving symptoms, and promoting reverse remodeling, with a reduction in LV volumes [21]. Another option in end-stage HF is implantation of a ventricular-assist device, which can support either LV or RV or both. It can be implanted as bridge to recovery or to heart transplantation or as destination therapy [22]. In case of refractory HF, when pharmacological and nonpharmacological treatment is no longer efficacious, the final option is heart transplant.

4.6 Problems in Differential Diagnosis

Ventricular dysfunction at imaging is not sufficient for the diagnosis of DCM as an exclusion diagnosis and represents a challenge for clinical cardiologists. In fact, many other conditions display the same abnormal pattern (Chaps. 5, 6 and 7).

Hypertensive heart disease in the dilated-hypokinetic stage [23] and ischemic heart disease with multivessel involvement are the most common examples encountered in clinical practice and should be excluded before establishing a diagnosis of idiopathic DCM. In the first case, LV dilatation and systolic dysfunction – frequently accompanied by overt HF – are present in patients with a long history of moderate to severe systemic hypertension. Previous documentation of LV hypertrophy with preserved LVEF can be present. LV hypertrophy usually remains evident, even if apparently reduced, in the overt HF hypokinetic phase, showing ECG and echocardiographic signs (i.e., LV eccentric hypertrophy with increased LV mass). On the other hand, chronic coronary artery disease may manifest as progressive HF without history of myocardial infarction or chest pain. This ischemic cardiomyopathy (CMP) is characterized by LV dilatation and systolic dysfunction and usually by segmental wall motion abnormalities (WMA) corresponding to ischemic ECG changes and coronary distribution. Also, some valvular diseases should be considered in the differential diagnosis of DCM. In fact, both severe MR and aortic stenosis (and, less frequently, aortic regurgitation or mitral stenosis) can lead to ventricular dysfunction due to severe volume or pressure overload, respectively. In this case, clinical and echocardiographic findings are fundamental in the differential diagnosis, and in selected cases, prompt surgical treatment could be decisive and can improve ventricular function.

When we excluded secondary causes of ventricular dysfunction, differential diagnosis of DCM remains necessary in the field of CMP. In fact, mild LV dilatation and ventricular WMA can be the result of active myocarditis that could mimic DCM, presenting frequently with HF or ventricular arrhythmias. Suggestive clinical history (i.e., new-onset HF in the absence of risk factors, recent flu-like syndrome), ECG (i.e., in some cases, low QRS voltage), echocardiography (i.e., ventricular dysfunction in the absence of severe dilatation, possible hypertrophic walls due to interstitial edema, WMA not corresponding to coronary distribution, intraventricular thrombi), and cardiac magnetic resonance (CMR) can orient treatment toward

endomyocardial biopsy, the gold standard for diagnosis of myocarditis, and may guide correct patient management.

Other CMP could manifest with the dilated pattern and should be considered in the differential diagnosis [24]. For instance, sometimes it is difficult to distinguish DCM and arrhythmogenic right ventricular cardiomyopathy (ARVC) with biventricular involvement [25]. However, the presence of RV dysfunction, WMA with multiple aneurysms in the right or both ventricles at echocardiography, and the presence of specific diagnostic ARVC criteria [26], can lead to a correct diagnostic classification. Even hypertrophic cardiomyopathy (HCM) could represent an issue in the differential diagnosis of DCM, as the echocardiographic pattern could be similar to DCM if the patient is evaluated for the first time in the advanced hypokinetic stage. Furthermore, it is noteworthy that amyloidosis and hemochromatosis with systolic dysfunction, dilatation, and normal wall thickness could be confused with DCM [27, 28].

A final issue in the differential diagnosis is the effect of alcohol on myocardial dilatation. The phenotype of alcoholic CMP is variable but usually manifests as DCM, even though LV hypertrophy is possible in initial stages of the disease [29]. Appropriate focused patient history is fundamental, and alcohol abstinence is frequently associated with marked functional improvement.

Conclusion

In conclusion, once differential diagnosis has been formulated through first-level exams [clinical, ECG, laboratory findings, echocardiography (*see* Chap. 5)], efforts should be directed toward more specific investigations, such as cardiac computed tomography, CMR, positron emission tomography, coronary angiography, right ventricle catheterization, and endomyocardial biopsy, to better and more precisely define the diagnosis and choose the correct treatment in selected cases. If DCM remains idiopathic, genetic screening should be performed, even though genetic DCM accounts for only 30–48 % of cases. It must be noted that, at present, the role of genetics in clinical management of DCM has not been clarified and must be considered a research tool.

References

1. Codd MB, Sugrue DD, Gersh BJ et al (1989) Epidemiology of idiopathic dilated and hypertrophic cardiomyopathy. A population-based study in Olmsted County, Minnesota, 1975-1984. Circulation 80:564–572
2. Mestroni L, Rocco C, Gregori D et al (1999) Familial dilated cardiomyopathy: evidence for genetic and phenotypic heterogeneity. Heart Muscle Disease Study Group. J Am Coll Cardiol 34:181–190
3. Merlo M, Pivetta A, Pinamonti B, Zecchin M et al (2013) Long-term prognostic impact of therapeutic strategies in patients with idiopathic dilated cardiomyopathy: changing mortality over the last 30 years. Eur J Heart Fail 16(3):317–24
4. Moretti M, Merlo M, Barbati G et al (2010) Prognostic impact of familial screening in dilated cardiomyopathy. Eur J Heart Fail 12:922–927

5. Mestroni L, Maisch B, McKenna WJ et al (1999) Guidelines for the study of familial dilated cardiomyopathies. Collaborative Research Group of the European Human and Capital Mobility Project on Familial Dilated Cardiomyopathy. Eur Heart J 20:93–102
6. Franciosa JA, Wilen M, Ziesche S et al (1983) Survival in men with severe chronic left ventricular failure due to either coronary heart disease or idiopathic dilated cardiomyopathy. Am J Cardiol 51:831–836
7. Aleksova A, Sabbadini G, Merlo M et al (2009) Natural history of dilated cardiomyopathy: from asymptomatic left ventricular dysfunction to heart failure–a subgroup analysis from the Trieste Cardiomyopathy Registry. J Cardiovasc Med (Hagerstown) 10:699–705
8. The SOLVD Investigators (1991) Effect of enalapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. N Engl J Med 325:293–302
9. Effect of metoprolol CR/XL in chronic heart failure: Metoprolol CR/XL Randomised Intervention Trial in Congestive Heart Failure (MERIT-HF) (1999). Lancet 353:2001–2007
10. Packer M, Bristow MR, Cohn JN et al (1996) The effect of carvedilol on morbidity and mortality in patients with chronic heart failure. U.S. Carvedilol Heart Failure Study Group. N Engl J Med 334:1349–1355
11. The Cardiac Insufficiency Bisoprolol Study II (CIBIS-II): a randomised trial (1999). Lancet 353:9–13
12. Bardy GH, Lee KL, Mark DB et al (2005) Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. N Engl J Med 352:225–237
13. Cleland JG, Daubert JC, Erdmann E et al (2005) The effect of cardiac resynchronization on morbidity and mortality in heart failure. N Engl J Med 352:1539–1549
14. Merlo M, Pyxaras SA, Pinamonti B et al (2011) Prevalence and prognostic significance of left ventricular reverse remodeling in dilated cardiomyopathy receiving tailored medical treatment. J Am Coll Cardiol 57:1468–1476
15. Pitt B, Zannad F, Remme WJ et al (1999) The effect of spironolactone on morbidity and mortality in patients with severe heart failure. Randomized Aldactone Evaluation Study Investigators. N Engl J Med 341:709–717
16. Zannad F, McMurray JJ, Krum H et al (2011) Eplerenone in patients with systolic heart failure and mild symptoms. N Engl J Med 364:11–21
17. Moss AJ, Hall WJ, Cannom DS et al (2009) Cardiac-resynchronization therapy for the prevention of heart-failure events. N Engl J Med 361:1329–1338
18. Grimm W, Christ M, Bach J et al (2003) Noninvasive arrhythmia risk stratification in idiopathic dilated cardiomyopathy: results of the Marburg Cardiomyopathy Study. Circulation 108:2883–2891
19. McMurray JJ, Adamopoulos S, Anker SD et al (2012) ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur Heart J 33:1787–1847
20. Zecchin M, Merlo M, Pivetta A et al (2012) How can optimization of medical treatment avoid unnecessary implantable cardioverter-defibrillator implantations in patients with idiopathic dilated cardiomyopathy presenting with "SCD-HeFT criteria?". Am J Cardiol 109:729–735
21. Whitlow PL, Feldman T, Pedersen WR et al (2012) Acute and 12-month results with catheter-based mitral valve leaflet repair: the EVEREST II (Endovascular Valve Edge-to-Edge Repair) High Risk Study. J Am Coll Cardiol 59:130–139
22. Osaki S, Edwards NM, Velez M et al (2008) Improved survival in patients with ventricular assist device therapy: the University of Wisconsin experience. Eur J Cardiothorac Surg 34:281–288
23. Iorio A, Pinamonti B, Bobbo M et al (2013) Characterization and long-term outcome of Hypertensive Dilated Cardiomyopathy. A distinct phenotype of hypertensive heart disease? J Am Coll Cardiol 61:10-S. doi:10.1016/S0735-1097(13)60595-1
24. Rapezzi C, Arbustini E, Caforio AL et al (2013) Diagnostic work-up in cardiomyopathies: bridging the gap between clinical phenotypes and final diagnosis. A position statement from the ESC Working Group on Myocardial and Pericardial Diseases. Eur Heart J 34:1448–1458

25. Pinamonti B, Sinagra G, Salvi A et al (1992) Left ventricular involvement in right ventricular dysplasia. Am Heart J 123:711–724
26. Marcus FI, McKenna WJ, Sherrill D et al (2010) Diagnosis of arrhythmogenic right ventricular cardiomyopathy/dysplasia: proposed modification of the task force criteria. Eur Heart J 31:806–814
27. Finocchiaro G, Pinamonti B, Merlo M et al (2013) Focus on cardiac amyloidosis: a single-center experience with a long-term follow-up. J Cardiovasc Med (Hagerstown) 14:281–288
28. Lj O (1987) Echocardiographic features of idiopathic emochromatosis. Am J Cardiol 60:885–889
29. Tobin JR Jr, Driscoll JF, Lim MT et al (1967) Primary myocardial disease and alcoholism. The clinical manifestations and course of the disease in a selected population of patients observed for three or more years. Circulation 35:754–764