CARDIOMYOPATHIES

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Abstract

Cardiomyopathies are heart muscle diseases and present a heterogeneous group of myocardial diseases with mechanical or electrical dysfunction, characterized by ventricular hypertrophy or dilatation. They can be strictly related to the heart muscle (primary), or as part of a systemic disease (secondary), and represent a factor that leads to a reduced quality of life, the occurrence of heart failure, and mortality. The primary ones are those that are genetically conditioned, the mixed ones include dilated and restrictive cardiomyopathy, whereas the acquired ones are caused by myocarditis, stress-induced, peripartum, tachycardia-induced and those caused by endocrine pathology (primarily in newborns of mothers with a diagnosis of diabetes mellitus). Etiologically, they can arise as a result of a genetic mutation, or an inflammatory process, and they are also divided into metabolic, toxic, and those due to some other cause. The article aimed to present the characteristics of cardiomyopathies themselves concerning the etiological factor, with a review of the diagnostic and therapeutic modality.

Keywords: cardiomyopathy, dilated cardiomyopathy, treatment

Introduction

Cardiomyopathies are heart muscle diseases in which the myocardium is structurally and functionally altered in the absence of coronary artery disease, valvular defects, or congenital heart anomalies[1]. They were first described in 1957 by V. Bridgen, as a "non-coronary heart muscle disease of unknown etiology"[2]. In the past, cardiomyopathies also included those caused by ischemia, valvular defects, or hypertensive diseases, but both the American and European Association of Cardiologists accepted the aforementioned definition. The distribution of cardiomyopathies is shown in table 1. Also, the MOGE(S) classification (M - morpho-functional phenotype, O - involved organs or organ systems, G - genetic or family mode of inheritance, E - etiological description, S - functional status) is used in practice[3].

Table 1. Classification of cardiomyopathies

Dilated cardiomyopathy (DCM)
Hypertrophic cardiomyopathy (HCM)
Restrictive cardiomyopathy (RCM)
Arrhythmogenic right ventricular cardiomyopathy (ARVC)
Unclassified cardiomyopathies (isolated left ventricular noncompaction, stress (*Takotsubo*) cardiomyopathy, cardiomyopathy due to liver cirrhosis)

Cardiomyopathies represent a heterogeneous group of myocardial diseases with mechanical or electrical dysfunction, characterized by ventricular hypertrophy or dilatation, and the cause is often genetic. They can be strictly related to the heart muscle (primary), or a part of the systemic disease (secondary) and represent a factor that leads to a decrease in the quality of life, the occurrence of heart failure, and mortality. Primary cardiomyopathies are genetically conditioned, the mixed ones include dilated (DCM) and restrictive cardiomyopathy (RCM), whereas the acquired ones are caused by myocarditis, stress-induced, peripartum, tachycardia-induced and those caused by endocrine pathology (primarily in newborns of mothers with a diagnosis of diabetes mellitus)[3]. Etiologically, they can arise as a result of a genetic mutation, or an inflammatory process, and they are also divided into metabolic, toxic, and those due to some other cause, which is shown in table 2.

The same etiological factor can be the cause of different forms of cardiomyopathy (table 3).

The diagnostic modality of patients with possible cardiomyopathy includes history, physical examination (with analysis of the characteristics of heart sounds and murmurs), electrocardiography (ECG), spirometry, ergospirometry, continuous 24-hour ECG Holter monitoring, radiological work-up, echocardiography, computerized tomography (CT), angiography, magnetic resonance imaging (MRI) of the heart, radionuclide ventriculography and

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Table 2. Etiological causes of cardiomyopathy[4-8]

Bacteria	*Corynebacterium diphtheriae, Mycobacterium tuberculosis, Salmonella Typhi, Streptococcus, Neisseria meningitidis, Neisseria gonorrhoeae, Brucella spp., Clostridium tetani, Burkholderia pseudomallei, Francisella tularensis, Bordetella pertussis, Chlamydia psittaci*
Spirochetes	*Treponema pallidum, Leptospira, Borelia*
Rickettsia	*Rickettsia typhi, Rickettsia prowazekii, Rickettsia tsutsugamushi, Coxiella burnetii*
Viruses	Parvovirus B19, Herpes virus 6, Poliovirus, *Haemophilus influenzae*, Morbile, *Rubella, Varicella, Epstein-Barr, Coxsackie, Echovirus, Citomegalovirus, Rabies virus*, Hepatitis, Herpes, Arbovirus
Fungi	*Actinomyces, Blastomyces, Candida, Aspergillus,* Histoplasma*, Cryptococcus, Coccidioides*
Protozoa	*Trypanosoma cruzi, Toxoplasma gondii, Plasmodium, Entamoeba histolytica, Leishmania, Sarcocystis, Balantidium coli*
Helminths	*Trichinella, Ehinococcus, Schistosoma, Ascaris lumbricoides, Heterophyidae, Taenia solium, Filarioidea*
Iatrogenic causes	doxorubicin, amphetamines, antimony, arsenic, carbon monoxide, catecholamines, cobalt, cocaine, cyclophosphamides, lithium, phosphorus, tricyclic antidepressants, zidovudine, radiation
Idiopathic	hypertrophic, dilatational
Endocrine causes	acromegaly, thyrotoxicosis, hypothyroidism, pheochromocytoma, *diabetes mellitus*
Storage diseases	Hand-Schuller-Christian disease, Niemann-Pick disease, Anderson-Fabry disease, Refsum disease, Gaucher disease, mucopolysaccharidosis, gangliosidosis, glycogen storage diseases
Nutritional cause	beri-beri, kwashiorkor, pellagra, selenium deficiency
Hematological caises	leukemia, myeloma, anemia, Henoch-Schonlein purpura, Sickle-cell anemia
Neoplastic	primary, metastatic
Deposit	amyloidosis, hemochromatosis, oxalosis, ochronosis
Neurological	Erb-Duchenn dystrophy, Landouzy-Dejereine dystrophy, humeroperoneal ataxia, Friedreich's ataxia, atrophic myotonia, *myasthenia gravis*, juvenile progressive spinal muscular atrophy, neurofibromatosis
Endomyocardial disease	fibrosis, fibroelastosis, hypereosinophilia
Connective tissue disease	rheumatoid heart disease, ankylosing spondylitis, systemic lupus erythematosus, scleroderma, dermatomyositis, periarteritis nodosa
Granulomatous	sarcoidosis, Wegener's granulomatosis, granulomatous myocarditis
Other inflammatory	hypersensitivity myocarditis, large cell myocarditis
Other	uremia, hypokalemia, carnitine deficiency

invasive diagnostics (catheterization, endomyocardial biopsy) with genetic analysis.

Dilated cardiomyopathy (DCM)

Dilated cardiomyopathy (DCM) is characterized by dilation and impaired contractility of one or both ventricles. Patients with impaired systolic function are candidates for the development of heart failure and supraventricular and/or ventricular arrhythmias. The diagnosis requires echocardiographically verified evidence of dilatation and reduced left ventricular ejection fraction (LVEF) (LVEF < 40% or fractional shortening < 25%). The diagnosis of idiopathic cardiomyopathy can be established if all possible causes of secondary dilated cardiomyopathy are excluded (myocarditis, ischemic disease, storage diseases, arterial hypertension, pregnancy, human immunodeficiency virus, connective tissue disease, opioid use, doxorubicin therapy)[9]. The incidence of DCM is 5-7 per 100,000 population, and the prevalence is 36 per 100,000 population. Echocardiography confirms ventricular dilatation (change in the shape of the chamber, which takes on a less ovoid and spherical appearance), normal or reduced thickness of the walls, and reduced systolic movement of the endocardium[9]. Also, enlargement of the left atrium can be verified (in addition to the measurement of the anteroposterior diameter, it is recommended to measure the volume of the left atrium), as well as the disturbance of the function of the right ventricle. The finding may further indicate globally weakened kinetics, i.e. dilation of all four ventricular cavities. Compensatory changes in the body are an increase in systemic vascular resistance, a decrease in arterial compliance and an increase in venous pressure, an increase in blood volume, as well as an increase in pre-load and after-load, which increases the stress on the chamber walls. It is recommended to measure the volume of the left ventricle - end-diastolic and end-systolic volume. Assessment of global longitudinal strain (GLS) is a more sensitive method for assessing left ventricular contractility[10]. In the case of involvement of the right heart, pulmonary hypertension also occurs, so an analysis of the dimensions of the right cavities, tricuspid valve, and GLS of the right ventricle is recommended[10-12].

Hypertrophic cardiomyopathy (HCM)

Hypertrophic cardiomyopathy (HCM) is a disease of the heart muscle caused in 60-70% of cases by mutation of genes responsible for the properties of the sarcomere and contractile apparatus of the heart. Genes that affect it are: cardiac troponin T - TNNT2 gene, cardiac troponin I - TNNI3 gene, regulatory myosin light chain - MYL2 gene, essential myosin light chain - MYL3 gene, cardiac myosin binding

Table 3. Type of cardiomyopathy correlated with genetic background[4-8]

	Genetically determined
DCM (dilated cardiomyopathy)	sarcomere-related protein mutations, Z line and cytoskeletal gene mutations (titin, dystrophin, desmin, metavinculin, sarcoglycan, epicardin, crystallin alpha B), nuclear membrane disorders, mitochondrial cytopathies, intercalated disk protein mutations
HCM (hypertrophic cardiomyopathy)	sarcomere-related protein mutations, glycogen storage diseases, lysosome diseases, lipid metabolism disorders, carnitine deficiency, phosphorylase B kinase deficiency, mitochondrial cytopathies, as part of syndromes (Noonan, LEOPARD, Friedrich's ataxia, Swyer syndrome, Beckwith-Wiedemann syndrome), familial amyloidosis, phospholamban induction
RCM (restrictive cardiomyopathy)	sarcomere-related protein mutations, amyloidosis, desminopathy, *pseudoxanthoma elasticum*, hemochromatosis, Anderson-Fabry disease, glycogen storage disease
ARVC (arrhythmogenic right ventricular cardiomyopathy)	mutations in intercalated disk protein (plakoglobin, desmoplakin, plakophilin 2, desmoglein 2, desmocholine 2), mutations in transmembrane protein 43 and growth factor β3
Other	isolated left ventricular noncompaction cardiomyopathy
Arrhythmia-induced	idiopathic, of unknown cause, SCN5A gene mutation, phospholamban mutation, mutations in intercalated disk protein and lamin
	Without the genetic component
DCM	myocarditis, Kawasaki disease, Churg-Strauss syndrome, iatrogenically induced, pregnancy, endocrine, effect of thiamine, carnitine, selenium values, hypophosphatemia, hypocalcemia, alcohol-induced, tachycardiomyopathy
HCM	obesity, newborns of mothers with *diabetes mellitus*, in professional athletes, in amyloidosis
RCM	in amyloidosis, scleroderma, endomyocardial fibrosis (hypereosinophilia, idiopathic, iatrogenically induced), carcinoid, cancer metastases, radiation, anti-tetracyclines
ARVC	The inflammatory process, systemic inflammatory process (unclear etiology)
Other	Takotsubo cardiomyopathy

protein - C- MYBPC3 gene, cardiac beta myosin heavy chain - MIH7 gene, alpha cardiac actin - ACTC1 gene, tropomyosin 1 - TPM1 gene, cardiac troponin C - TNNC1 gene, junctophilin 2 - JPH2 gene, cysteine-glycine-rich protein 3 - CSRP3 gene, alpha galactosidase gene - GLA gene (Anderson-Fabry disease), genes related to the RAS MAP kinase pathway (Noonan syndrome), muscle LIM protein gene - MLP gene, gene encoding gamma 2 - regulatory subunit adenosine monophosphate will activate protein kinase - PRKAG2 gene and gene for encoding protein membrane that binds to lysosome 2 - LAMP2 gene[12].

It occurs with an incidence of 1 in 500 adults. Left ventricular hypertrophy is the main feature of HCM. Analysis of the existence of hypertrophy or obstruction of the outflow tract of the left ventricle, diastolic function, the existence of ischemic heart disease, and the status of the mitral valve is essential[12]. The most common symptoms are rapid fatigue, dyspnea, anginal complaints, palpitations, presyncope, or syncope. They arise as a result of atrial fibrillation, the appearance of a block in atrioventricular conduction, obstruction of the left ventricular outflow tract (LVOT), ventricular baroreflex due to inadequate vasodilatation, and ischemia during physical exertion. The most common symptoms are rapid fatigue, dyspnea, anginal complaints, palpitations, presyncope, or syncope. They arise as a result of atrial fibrillation, the appearance of a block in atrioventricular conduction, obstruction of the left ventricular outflow tract (LVOT), ventricular baroreflex due to inadequate vasodilatation, and ischemia during physical exertion. The physical examination can confirm a systolic murmur due to LVOT obstruction or mitral regurgitation. LVOT obstruction occurs as a result of septal hypertrophy and systolic anterior motion of the mitral valve forward (systolic anterior motion - SAM). Significant LVOT obstruction is characterized by a crescendo-decrescendo type systolic murmur, which begins after the first heart sound, is best heard over the ictus and the left sternal border, and can spread towards the base or axilla.

The ECG often shows a Q wave in the inferior and lateral leads, changes in the P wave (due to enlargement of one or both atria; enlargement of the right atrium) and the presence of electrocardiographic signs of left ventricular hypertrophy, sinistrograms, and deep negative T waves from V2 to V4 which are highly suggestive of the diagnosis of HCM. Echocardiographic left ventricular wall thickening ≥ 15 mm is significant for HCM (≥ 13 mm for patients with a positive family history of HCM)[13]. A gradient over LVOT > 30 mmHg is associated with clinical symptoms, and > 50 mmHg is an indication for surgical treatment. In the presence of left ventricular systolic dysfunction, moderate to severe aortic regurgitation or ventricular septal defect with a gradient above LVOT below 50 mmHg, surgical treatment is indicated. It is necessary to check the systolic movement of the anterior mitral valve forward, i.e. its contact with the septum. It is imperative in patients with suspected LVOT obstruction, even if not proven at rest, to perform stress echocardiography to confirm an increase in the gradient > 50 mmHg in the LVOT, which is an indication for invasive (alcohol septal ablation) or operative treatment (septal myectomy). Systolic movement of the anterior mitral valve forward is graded: 0 - absent; 1+ present, with a minimum gap between the mitral valve and ventricular septum during systole > 10 mm; 2+ without mitral-septal contact, but with a gap < 10 mm between the mitral valve and the septum; 3+ short mitral-septal contact (< 30% during systole); 4+ prolonged placement of the mitral valve leaflets on the septum (> 30% during systole)[11]. Over 50% of patients with HCM, without significant LVOT obstruction, will show a gradient

of over 30 mmHg with exercise. Analysis of the left atrium (diameter, volume) is very important for the prediction and detection of atrial fibrillation. The use of 24-hour ECG Holter monitoring is essential in detecting both supraventricular and ventricular rhythm disorders. Magnetic resonance imaging (MRI) of the heart muscle is recommended for definitive diagnosis in patients with unclear features. Routine genetic testing is not recommended, although it is important in patients with a positive family history of sudden cardiac death or the existence of already verified HCM. In professional athletes, it is necessary to distinguish between the existence of an athletic heart. It should be noted that the cardiac chambers are larger in the athletic heart, while an end-diastolic left ventricular diameter < 54 mm is associated with HCM[13].

Restrictive cardiomyopathy (RCM)

RCM has distinct morphologic and hemodynamic features that separate it from DCM and HCM: nondilated ventricle with normal wall thickness, stiff ventricular walls resulting in severe diastolic dysfunction and a restrictive filling pattern with elevated filling pressures, dilated atrium, and normal left ventricular systolic function. Idiopathic or primary RCM is a disorder manifested by the characteristic, above-mentioned morphological and physiological changes without the existence of any identified cause[12]. The cause may be unknown, and may be sought in sarcoma protein mutations, troponin I and essential myosin light chain gene mutation, in the presence of familial amyloidosis, transthyretin and apolipoprotein mutation, desminopathies, hemochromatosis, Anderson-Fabry disease, glycogen storage disease, scleroderma, endomyocardial fibrosis, hypereosinophilic syndrome, radiation (radiation-induced heart disease), chemotherapy, carcinoid heart disease, and metastatic disease[14]. Coksackie virus B4 has recently been identified as a cause of neonatal restrictive cardiomyopathy. Clinical symptoms and signs are dyspnea, peripheral edema, palpitations, fatigue, weakness, and intolerance to physical exertion. RCM is associated with peripheral autonomic dysfunction with reduced baroreflex sensitivity, causing clinical deterioration and heart rhythm disturbances. In the later stages, there may be a significant increase in central venous pressure, leading to hepatosplenomegaly, ascites, and anasarca. Jugular venous pressure is generally elevated, and Kussmaul's sign may be seen. The first and second heart sounds are usually normal. A third heart sound (S3 gallop) is often present in restrictive cardiomyopathy (but not in constrictive pericarditis) because of the abrupt cessation of rapid ventricular filling. Soft systolic murmurs of functional mitral and tricuspid regurgitation are also common. Electrocardiographic changes are common and nonspecific and include atrial fibrillation, ST segment and T wave changes, and conduction disturbances. A chest X-ray usually shows cardiomegaly with increased pulmonary venous congestion and pleural effusions. The presence of pericardial calcification should raise the suspicion of constrictive pericarditis. RCMs are a heterogeneous group of heart muscle diseases that often appear similar on echocardiography. All have biatrial enlargement, normal or small left ventricular cavity size with generally preserved left ventricular systolic function, and abnormal diastolic function, often with a restrictive filling pattern. Although not pathognomonic, features of restrictive cardiomyopathy are reduced velocity, tissue Doppler analysis across the mitral valve (septal e' < 7 cm/sec, lateral e' < 10 cm/sec, E/e' > 14), and increased left atrial volume. In RCM, wall thickness is usually normal, although it can be increased by certain infiltrative processes (amyloidosis) or storage diseases (Anderson-Fabry disease)[5, 12]. The use of brain natriuretic peptide (BNP) is important because it can help distinguish RM from constrictive pericarditis and noncardiac causes of dyspnea. MRI of the heart enables the identification of myocardial fibrosis, scarring, necrosis, or infiltration. Endomyocardial biopsy (EMB) is recommended in selected patients with restrictive cardiomyopathy to evaluate the cause. There is no specific therapy for idiopathic restrictive cardiomyopathy, while therapy for some underlying diseases may be useful in patients with secondary restrictive cardiomyopathy[5, 14]. Heart failure is treated according to already established recommendations, and treatment is aimed at lowering venous pressure, controlling heart rate, increasing filling time, preventing heart rhythm disorders, and correcting anemia or electrolyte imbalance. Heart transplantation is a modality for patients whose symptoms cannot be controlled pharmacologically.

Arrthymogenic right ventricular cardiomyopathy (ARVC)

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is characterized by ventricular arrhythmia, which originates from the right ventricle and is characteristic of ventricular pathology (regional or global dilatation of the right ventricle and thinning of the wall, and the consequences may also apply to the left ventricle in the form of loss of myocyte fibrosis, especially the lateral and rear wall)[6]. ARVC was first described by Guy Fontaine in 1977. ARVC has a dominant autosomal-dominant type of inheritance, although forms with a recessive type (Naxos disease, Caravajal syndrome) have also been described. Macroscopically, there is the formation of a scar with a fibrous or fibro-lipidic change of myocytes. Pathological changes are found in the inlet and outlet tract, as well as on the top of the right ventricle, with the fact that the top of the right ventricle may be spared and changes on the side and back wall of the left ventricle. At the very beginning, the changes are in the form of regional outbursts in kinetics, which with the progression of the disease, leads to the expansion of all cavities and global hypokinesis[6]. Approximately 40 to 50% of ARVC patients have a mutation in the genes encoding the desmosome protein. It is estimated that the prevalence of ARVC in the adult population is 1 in 2.000-5.000 inhabitants and that it is an important

cause of sudden cardiac arrest in young adults, accounting for approximately 11% of cases. The most common clinical signs are palpitations, syncope, atypical anginal pains, and dyspnea, along with the clinical picture of right ventricular insufficiency. Palpitations and syncope are most often the results of ventricular tachycardia (most often monomorphic non-sustained episodes originating from the right ventricle according to the type of left bundle branch block). Sudden cardiac death may be the first presentation of the disease. The most common ECG abnormality observed in ARVC is T wave inversion in precordial leads from V1 to V3, and the epsilon wave is found in 50% of cases. The diagnosis is based on a combination of major and minor criteria. Major criteria are right ventricular dysfunction (severe dilatation and an accompanying reduction in right ventricular ejection fraction with minimal LV damage, localized right ventricular aneurysms, severe segmental dilatation of the right ventricle), myofibrillar changes of the myocardium on endomyocardial biopsy, conduction abnormalities, epsilon wave from V1 to V3, prolongation (more than 110 ms) of the QRS complex from V1 to V3, biopsy-confirmed disease in the family.

Minor criteria are right ventricular dysfunction (mild global right ventricular dilatation and/or reduced ejection fraction with normal left ventricular function), mild segmental right ventricular dilatation, regional right ventricular hypokinesia, negative T waves in V2 and V3 in patients older than 12 years in in the absence of right bundle branch block, ventricular tachycardia followed by the morphology of left bundle branch block, frequent ventricular extrasystoles (more than 1,000 during 24 hours), family history of sudden heart disease before the age of 35 and family history of ARVC[6]. Pharmacological treatment includes prevention of ventricular tachycardia and prevention of thrombus formation. Sotalol is the antiarrhythmic agent of choice. The use of warfarin is indicated to reduce the ejection fraction of the right ventricle in order to prevent the formation of thrombus and further complications. Radiofrequency ablation is indicated for the treatment of pharmacologically refractory ventricular tachycardia. It is successful in 60 to 90% of cases. The recurrence rate is 60% due to disease progression. The use of an implantable cardioverter defibrillator (ICD) is also indicated. Heart transplantation is the final therapeutic modality.

Unclassified cardiomyopathies

Isolated left ventricular noncompaction cardiomyopathy (ILVNC) is a rare cardiomyopathy classified as primary genetic cardiomyopathy, resulting from an intrauterine disorder in the development of the working muscles of the heart and the formation of deep trabecular depressions in the myocardial wall. ILVNC can be hereditary, but cases without a positive family history of the disease have also been described. Sporadic ILVNC can be acquired by professional athletes, patients with sickle cell anemia, and pregnant women[16]. In practice, most cases of ILVNC are diagnosed in patients with unexplained heart failure. Clinical symptoms are related to systolic or diastolic dysfunction. There are no clearly defined criteria for diagnosis. Electrocardiographic signs are uncharacteristic; there is a frequent occurrence of ventricular and supraventricular rhythm disorders that can lead to sudden cardiac death. Echocardiography verified the segmental thickening of the left ventricular myocardial wall, consisting of a thin compacted epicardial layer and a thickened endocardial layer with prominent trabeculations and deep depressions, and the ratio of noncompaction to compression was ≥ 2 at the end of systole. Cardiac MRI can be a useful method in establishing the diagnosis[16]. It is treated as heart failure, with prophylactic ICD therapy. Patients with severe heart failure are candidates for heart transplantation.

Stress cardiomyopathy (apical balloon syndrome, Takotsubo cardiomyopathy, broken heart syndrome, or stress-induced cardiomyopathy) is a syndrome characterized by transient regional left ventricular systolic dysfunction, with a clinical picture of acute myocardial infarction, but with a lack of angiographic evidence of obstructive coronary artery disease or acute plaque rupture[17]. The prevalence is estimated at 2-3% of all patients with acute coronary syndrome. In over 90% of cases, it affects women and is preceded by some stressful event. Analysis of the presence of LVOT obstruction is necessary. Mechanisms of occurrence include catecholamine activity, microvascular dysfunction, and coronary artery spasm. Electrocardiographically, ST-segment elevation in the precordial leads is a common finding, and depression of the ST segment is less common, while prolongation of the QT interval, inversion of the T wave, and other nonspecific changes can also be found[17]. It is characterized by temporary left ventricular systolic dysfunction, usually of a regional nature, absence of obstructive coronary disease or angiographic evidence of acute plaque rupture, new electrocardiographic abnormalities (either ST-segment elevation and/or T wave inversion), elevated cardiac troponin values, and absence of pheochromocytoma or myocarditis. It is most often of the apical type (systolic apical ballooning of the left ventricle, with frequent hypercontractility of the basal walls), less often midventricular (sparing the apex), basal, focal, or global. With concern to angiographic characteristics, the use of calcium channel blockers or selective beta-blockers is recommended in case of slow angiographic flow, and the therapy itself should be in accordance with echocardiographic findings[17].

Liver cirrhosis is associated with myocardial dysfunction independent of alcohol exposure. The causes and manifestations of cirrhotic cardiomyopathy are not well established. The condition is defined as unexplained left ventricular dysfunction in patients with liver cirrhosis. Electrocardiographically, QT interval prolongation, electrical desynchronization, and chronotropic incompatibility may occur. The left atrium may be dilated, but the dimensions of the left ventricle are normal, although they may be dilated.

Diagnostic criteria are: LVEF at rest < 55%, diastolic function altered by the type of prolonged relaxation or restriction, electrophysiological irregularities, abnormal chronotropic response, desynchronization of ventricular kinetics, prolonged QT interval, enlarged left atrium, increased myocardial mass, increased BNP and cardiac troponin values[18]. To date, there are no well-established guidelines regarding the diagnosis or treatment of cirrhotic cardiomyopathy. Since most patients remain asymptomatic at rest, treatment is initiated only when symptoms of heart failure become apparent[18]. Treatment of heart failure in patients with cirrhosis is similar to that of patients without cirrhosis, including salt and fluid restriction, diuretics, and reduced exercise. The use of a nonselective beta-blocker has been shown to reduce the prolonged QT interval to normal values in cirrhotic patients. Similar to other complications of cirrhosis, a liver transplant is a possible cure.

Specific cardiomyopathies

Peripartum cardiomyopathy (cardiomyopathy associated with pregnancy) is a rare cause of heart failure affecting women in late pregnancy or postpartum. The therapeutic modality is the same as in the treatment of heart failure, and additional therapy can be in the form of anticoagulant therapy or the use of bromocriptine. In patients diagnosed with peripartum cardiomyopathy, decisions about the time and method of delivery should be based on the decision of a multidisciplinary team (cardiologist, gynecologist, obstetrician, anesthesiologist, pediatric neonatologist)[19]. In patients with severely reduced LVEF, it makes sense to advise the patient not to breastfeed due to the potential adverse effects of prolactin and the high metabolic demands during breastfeeding. Patients with a diagnosis of peripartum cardiomyopathy or its existence in the anamnestic data should be advised to use contraception because every new pregnancy represents a risk for acute heart failure and mortality of the pregnant woman. Progesterone-containing contraception may increase volume loading, which may worsen heart failure. Contraceptive pills containing estrogen should be avoided in women with persistent left ventricular dysfunction due to their potential to increase the risk of thromboembolism. Patients with persistent left ventricular dysfunction with LVEF < 50% or LVEF ≤ 25% at diagnosis should be advised to avoid later pregnancy due to the risk of progression of heart failure and high mortality risk. Left ventricular function can be fully recovered (LVEF > 50%)[19]. After giving birth, the patient needs to be treated with therapy for heart failure. If the function of the left ventricle remains normal even after six months, the mineralocorticosteroid antagonist (spironolactone, eplerenone) can be excluded from therapy with the continuation of therapy with angiotensin-converting enzyme inhibitors (ACE inhibitors) or angiotensin receptor blockers (ARB), and a beta blocker. If left ventricular function remains normal six months after discontinuation of the mineralocorticosteroid antagonist, ACE inhibitors or ARB can be withdrawn from therapy, and treatment continued with a beta blocker. All this should be handled with echocardiographic controls, and the function of the chamber itself should be monitored with GLS - global longitudinal strain[19]. Diuretics can be discontinued at any time (even before full recovery of left ventricular function) if the patient has no congestive symptoms; appearance of congestive symptoms is an indication for the use of diuretic therapy.

Alcoholic cardiomyopathy is caused by long-term and excessive alcohol consumption, which is the leading cause of secondary DCM. However, heart function can recover if the disease is diagnosed early, and alcohol intake is reduced or stopped. The effect of acute alcohol intoxication on the heart is temporary, but chronic consumption can lead to permanent damage to myocardial contractility due to the effect of ethanol and its metabolites on the heart muscle[20]. When the diagnosis is suspected, it is necessary to exclude the existence of ischemic heart disease. Patients should have a balanced diet, and any nutritional deficiencies should be corrected.

Supplementation with vitamin B12, vitamin B6, and folates are important supplements, especially for people who regularly consume alcoholic beverages[20]. Electrolyte disturbances, including hypokalemia and hypomagnesemia, should be monitored and corrected. The generally accepted treatment for alcoholic cardiomyopathy would be total and permanent abstinence from alcohol consumption. The prognosis of alcoholic cardiomyopathy varies depending on the presence and extent of continuous alcohol use. Patients who abstain from alcohol use or drink moderately have a better or similar prognosis than those with idiopathic DCM, while continued heavy drinking of large amounts of alcohol is associated with a worse prognosis[20].

Diabetic cardiomyopathy is defined by the presence of abnormal myocardial structure and function in the absence of other causes, such as coronary artery disease, hypertension, and significant valvular disease in individuals diagnosed with diabetes mellitus. In its early phase, diabetic cardiomyopathy involves a latent subclinical period characterized by structural and functional abnormalities, including left ventricular hypertrophy, changes in wall stiffness and fibrosis, and diastolic dysfunction[21]. Hyperglycemia, systemic insulin resistance, and impaired metabolic signaling are involved in the pathogenesis of diabetic cardiomyopathy. There are no prospective clinical trials to confirm that hyperglycemia or hyperinsulinemia independently increase the risk of developing diabetic cardiomyopathy in the absence of other risk factors such as obesity, coronary heart disease, and hypertension. There is no clear consensus for screening and early detection of this pathology, and the use of cardio and nephroprotective drugs (sodium-glucose cotransporter 2 inhibitors or glucagon-like peptide-1 analogs in the treatment of diabetes, i.e. statin therapy in the treatment of lipid status disorders, as well as the use of pharmacological agents in the treatment of hypertension)[21]. Therapy should be followed by the individual characteristics of the patient.

Arrhythmia-induced cardiomyopathy is another modality of specific cardiomyopathy. Tachycardic cardiomyopathy is an important cause of heart failure leading to ventricular dilatation and systolic dysfunction[22]. Partial or complete reversibility of this condition is characteristic when control over the arrhythmia is established. It is necessary to differentiate whether the rhythm disorder is the main cause of cardiomyopathy[22]. It is associated with the presence of atrial tachycardia, atrial fibrillation or atrial flutter, circular supraventricular tachycardias, ventricular arrhythmias, and frequent ventricular or atrial ectopy. Supraventricular rhythm disturbances as causes of arrhythmia-induced cardiomyopathy include atrial tachycardia, atrial flutter, atrial fibrillation, atrioventricular nodal circular tachycardia, atrioventricular tachycardia, sustained nodal reciprocal tachycardia, and high-frequency atrial conduction. The most common causes of ventricular arrhythmias are: large ventricular ectopy, right ventricular outflow tract ventricular tachycardia, idiopathic ventricular tachycardia, circular ventricular tachycardia (with block), and high-frequency ventricular conduction[23-25]. The therapeutic modality includes the treatment of heart failure and optimal control of heart rate and rhythm[22, 24, 25].

The disease caused by the coronavirus (COVID-19) is characterized by Virchow's triad (endothelial dysfunction, stasis, hypercoagulable state), which lies at the very basis of COVID-19[26]. It is stated in the literature that 7.75% of patients with symptoms of acute coronary syndrome during the pandemic were diagnosed with cardiomyopathy caused by stress, primarily due to the fear of the pandemic itself and the psychosociological pressure caused by the pandemic[27].

Conclusion

Cardiomyopathies represent an entity in cardiology practice that must be clearly differentiated diagnostically because only this leads to an optimal therapeutic modality.

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