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A NARRATIVE REVIEW OF DILATED CARDIOMYOPATHY AMONG GENERAL POPULATION

Abdulaziz Sultan Abdullah Albaqami,Abdulaziz Mohammed Alotaibi,Amin Fouiz Alsobhi,Ahmed Ofan Aldadi,Salem Hammad Alotaibi,Eman Mohammed Allzez,Sittiy Salama Almalayou,Mushari Fahad Alharbi,Amal Saleh Allhiani,Abdul Rahim Dakhil Allah Al-Thubaiti

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Abstract:

This study focuses on some key issues in the medical diagnosis of DCM patients, such as etiology and pathophysiology. A correct diagnosis is critical for avoiding repercussions and receiving appropriate treatment. We searched major biological databases (CINAHL, EMBASE, MEDLINE) for publications on dilated cardiomyopathy management, employing thorough search algorithms for all relevant articles published up to 2018. Dilated cardiomyopathy (DCM) is characterized by ventricular dilatation and dysfunctional contraction. Patients who have been injured have altered systolic function and may or may not develop overt heart failure (HF). In the present, atrial and/or ventricular arrhythmias can exist, and sudden death can occur at any stage of the disease. Dilated cardiomyopathy requires evidence of left ventricle or both ventricular expansion and impaired contraction. If main and secondary causes of heart disease are ruled out by evaluation, which includes a history and physical examination, laboratory tests, and coronary angiography, the disease is called idiopathic.

Corresponding author:

Abdulaziz Sultan Abdullah Albaqami,

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INTRODUCTION:

Dilated cardiomyopathy (DCM) is a cardiac muscle mass condition characterized by left ventricular (LV) or biventricular dilatation and systolic dysfunction in the absence of stress, volume overload, or coronary artery disease [1]. Although DCM was once assumed to be an uncommon and orphan condition, contemporary estimates of its incidence range from 1/2500 to 1/250 people [2]. The condition often begins in the third or fourth decade of life, with a 3:1 male to female predominance. By the time a patient is diagnosed, he or she has a substantial contractile disorder and refurbishment of both ventricles, as well as an extended period of asymptomatic silent disorder advancement. Nonetheless, optimal pharmaceutical and non-pharmacological treatment has significantly increased the detection of DCM, with an estimated lifespan without death or heart transplantation of up to 85% at 10 years [4]. Furthermore, the lower prevalence of co-morbidities in DCM patients compared to the majority of patients with other kinds of LV systolic dysfunction suggests that people with DCM have less non-cardiovascular events [3]. These improved results are mirrored by higher rates of LV reverse remodelling (LVRR) with the best pharmacological and non-pharmacological therapies [3], [4].

Despite this treatment success, new evidence suggests that certain patients remain at risk of sudden cardiac death (SCD) and refractory heart failure (HF), necessitating a heart transplant or mechanical blood circulation support [4].

This review highlights some essential concepts of DCM patients, etiology and pathophysiology. The proper diagnosis is important in order to prevent consequences and for adequate treatment.

METHODOLOGY:

We conducted electronic search for papers on the management of dilated cardiomyopathy, employing major biomedical databases (CINAHL, EMBASE, MEDLINE) and thorough search algorithms for all relevant articles published up to 2021. Through biomedical databases, we used the following MeSH terms in our search strategy: "dilated cardiomyopathy, ventricular arrhythmias and hypertrophy, treatment, therapy." Furthermore, the references of the listed research were examined for additional relevant literature. Language restriction to English with human subject was applied.

DISCUSSION:

RISK THAT CONTRIBUTES IN DCM:

Individual features, attributes, or direct exposure to environmental factors such as harmful substances increase the likelihood of acquiring or worsening a disease condition as compared to the general population [5]. Continuous exposure to drugs that interfere with normal LV systolic function is a risk factor for DCM. Genetic mutations, cardiac diseases, and poisonous compounds are examples of these agents [6]. Offspring of parents with non-ischemic heart failure and other cardiac disorders are at a higher risk of developing DCM due to the possibility of inheriting the original mutant genes in hereditary mutations [6].

Myocardial abnormalities, such as myocardial ischemia, are also substantial risk factors, accounting for about 50% of DCM. Other conditions that cause global systolic issues, including as coronary artery disease, hypertension, and valvular disease, increase the probability of developing DCM [7]. Toxins like as excessive alcohol consumption and chronic exposure to chemotherapeutic drugs may predispose an individual to the development of DCM. Finally, in pediatric medicine, inborn metabolic rate error and malformation condition are substantial risk factors for developing DCM [8].

The hallmark of DCM is decreased LV systolic function caused by abnormal myocardial contractility [9]. The abnormal myocardium is unable to maintain normal systolic function and cardiac output. As a result, the LV and RV become overwhelmed with high cavitary blood volume, decreased ejection fraction, and elevated pressure, causing them to dilate—stretch, and thin [10]. Damaged LV systolic function may result in RV-ventricular (bi-ventricular) systolic dysfunction. While LV dysfunction has been well established in DCM patients, current investigations reveal that RV dysfunction is also prevalent in up to 65% of DCM patients [11]. When blood pressure rises, the arterial ventricular valves expand and lose synchronization, causing blood to vomit into the atria. As a result, increased atrial pressure causes the atria to widen, leading in increased pressure in the veins surrounding the heart, which eventually leads to heart failure, which is the final clinical goal of DCM [9].

ETIOLOGY:

Etiology is the study of the causes of sickness problems that can help with therapeutic management [12]. The etiology of DCM is extremely variable. Half of the cases (50%) are idiopathic, triggered primarily by inflammatory and immunological procedures,

while the other half are caused by a variety of underlying issues, including peripartum illness, heart disease, myocarditis, and hypertension [12]. Previously, DCM etiology was divided as genetic/familial, cytotoxic agents, starvation, myocarditis/viral, and autoimmune illnesses. However, due to genetic anomalies, familial DCM remains the most common etiology, accounting for 20-48% of all DCM cases [16]. A lot more just recently, the ESC functioning group on myocardial and pericardial diseases reclassified the etiology of DCM under 2 primary classes: hereditary and non-genetic. Non-genetic etiologies consist of drugs/toxins, infection and peripartum. Nonetheless, in some individuals, more than one etiologic agent may create DCM. In such people, genetic agents engage with environmental (non-genetic) agents to create DCM. Eliminating environmental agents is essential to avoid the stress of DCM. The ESC functioning group on myocardial and pericardial illness classifies sources of DCM right into genetic/familial, drugs/toxins, infection and peripartum [13]. (Table 1).

Table 1. Causes and Agents of DCM [13].

Group	Cause	Etiologic Agents
Genetic/Familial	Main Genes	Titin, lamin A/C, myosin heavy chain, troponin, myosin-binding protein C, RNA-binding Motif-20, Myopalladin, Na+ channel alpha unit and phospholamban
	Neuromuscular Disorders	Duchenne muscular dystrophy, Becker muscular dystrophy, myotonic dystrophy
	Syndromic Disease	Mitochondrial disease, Tafazin
Drugs/ Toxins	Drugs	Antineoplastic/psychiatric drugs
	Toxic Overload	Ethanol, cocaine, amphetamines, ecstasy or iron overload
	Nutritional Deficiency	Selenium, thiamine, zinc/copper and carnitine
	Electrolyte Disturbance	Hypocalcemia, hypophosphatemia
	Endocrinology	Hyper/hypo-thyroidism, Addison disease, phaeocromocytoma, acromegaly, diabetes mellitus
Infection	Auto-immune diseases (myocarditis)	Causes frequent AV-block and ventricular arrhythmias
	Inflammatory DCM	Caused by non-infectious myocarditis
Peripartum	Peripartum cardiomyopathy	Related to during or after pregnancy

DCM has a more noticable diversification in hereditary etiology than any other cardiomyopathy phenotypes. Hereditary etiologies consist of a selection of gene mutations in cytoskeleton, nucleoskeleton or mitochondrial proteins [15]. The primary pattern of genetic transmission is autosomal dominant. Inherited mutations in the sarcomere protein Titin (TTN) is the most regular hereditary cause of DCM, making up about 25% of familial DCM. Familial DCM refers to DCM inherited as solitary mutated genetics in a Mendelian pattern [16]. Various other common autosomal leading hereditary mutations are Lamin A/C, Myosin Heavy Chain, Troponin, Myosin-binding protein C, RNA-binding Motif-20, myopalladin, Na+ channel alpha system, and Phospholamban [14]. Although autosomal recessive anomalies are an unusual root cause of DCM accounting for about 1-2% of familial DCM, raising cases of X-linked recessive inheritance have been reported in tafazin genetics in pediatric populaces. Various other X-linked recessive hereditary causes are neuromuscular dystrophy and mitochondrial (syndromic) disorder [15].

Drugs/Toxins AS causes of DCM:

Medicines (also known as toxic chemicals), infection, and peripartum DCM are non-genetic causative causes of DCM. DCM can be caused by toxic drugs, notably chronic or severe alcohol consumption, or by repeated direct exposure to chemotherapeutic medicines. Alcohol-induced cardiomyopathy worsens LV systolic function and accounts for between 21% and 32% of DCM, but it improves with abstinence [17]. Chronic exposure to other chemotherapeutic drugs, such as anthracylines, can also impair LV function and develop DCM, but it either resolves on its own or persists in a subclinical form [13].

Infection

In genetically predisposed individuals, autoimmune viral infections such as myocarditis create swellings that lead to DMC. Infection-negative myocarditis in the absence or presence of DCM phenotype is an organ-specific autoimmune illness that is frequently

observed in genetically inclined patients. These patients have no symptoms yet have organ-specific anti-heart antibodies [18]. Anti-heart antibodies have been associated to mild LV issues, which predicts the development of DCM. If acute myocardial swelling stops and the etiology resolves, DCM caused by viral infection is typically easy to treat [18,19,20].

DIAGNOSIS

Diagnosis of DCM in patients with one influenced first-degree relative can be made with a full background, together with ECG and echocardiographic (two-dimensional) research studies. The analysis requirements for fDCM can be found in box 1. If there is no background symptomatic of fDCM or any type of second causes, iDCM might be considered a feasible diagnosis. The diagnostic requirements for idiopathic DCM (iDCM)can be discovered in box 2.

Box 1. Diagnostic criteria for a patient suspected of a familial dilated cardiomyopathy with one affected first-degree relative [21],[22].

Diagnosis of familial dilated cardiomyopathy (DCM) if one of the following criteria is met. Presence of two or more affected first-degree relatives in a single family (to diagnose first-degree relatives, one of the following criteria must be met)

- Diagnosis of DCM is already established
- Unexplained sudden death or stroke <30 years
- Two major two-dimensional echocardiographic (2DE) criteria:
  -Left ventricular end diastolic dimension (LVEDD) .117% of predicted value
  -Fractional shortening (FS) ,25%
- Three minor 2DE and/or ECG criteria:
  -LVEDD>112% of predicted value
  -FS<28%
  -Pericardial effusion
  -Unexplained conduction defects such as II ° or III ° atrioventricular block, bundle branch block or unexplained (supra-)ventricular arrhythmia <50 years)

OR

Presence of a first-degree relative of a DCM patient with a well-documented unexplained sudden cardiac death <35 years

Box 2. Diagnostic criteria for idiopathic dilated cardiomyopathy [23],[24].

Diagnosis if all of the following criteria are met

Criteria

- Ejection fraction < 0.45 and/or a fractional shortening of <25%
- Left ventricle end diastolic diameter of >117% (corrected for age and body surface area using the formula = (45.3× (body surface area)$^{1/32}$ -(0.03 × age)-27.2)±12%)

Exclusion criteria

- Absence of systemic hypertension (>160/100 mmHg)
- Coronary artery disease (50% in one or more branches)
- Chronic excess alcohol (>40 g/day female, >80 g/day for male)
- Systemic disease known to cause idiopathic dilated cardiomyopathy
- Pericardial disease
- Congenital heart disease
- Cor pulmonale

Endomyocardial biopsy

Endomyocardial biopsy may be used to rule out illnesses that have a similar clinical presentation to iDCM but require different treatment. Haemochromatosis, sarcoidosis, storage space disorders, and fatal illnesses are among these issues. Though biopsies may cause problems such as appropriate pneumothorax, air embolism, atrial arrhythmias, transient nerve palsies and paralysis, cardiac perforation and tamponade, they should still be performed if there is any clinical uncertainty of these other problems based on clinical history, physical examination, and preliminary non-invasive investigations [25,26]. A recent retrospective study from our institution compared the pathological diagnosis after transplantation to the clinical diagnosis, which was determined through a series of examinations that excluded endomyocardial biopsy.

After excluding patients with a pathological diagnosis of ischemic cardiomyopathy, the authors discovered that 46% (n = 152) were misdiagnosed prior to transplant. The majority of these patients were not given an endomyocardial biopsy as part of their pre-transplant care [27].

CONCLUSION:

Dilated cardiomyopathy (DCM) is characterized by dilation and damaged contraction of one or both ventricles. Damaged patients have impaired systolic function and may or may not establish overt heart failure (HF). Atrial and/or ventricular arrhythmias can be present in the present, and sudden death can occur at any stage of the disease. A diagnosis of dilated cardiomyopathy requires evidence of left ventricular extension and damaged contraction (eg, left ventricular ejection portion 40 percent or fractional shortening less than 25 percent). The disease is considered idiopathic if primary and secondary causes of heart disease (eg, myocarditis and coronary artery disease) are excluded by evaluation that includes history and physical examination, laboratory testing, coronary angiography. The illness is taken into consideration idiopathic if primary and secondary sources of cardiovascular disease (eg, myocarditis and coronary artery illness)are left out by evaluation consisting of background and checkup, laboratory testing, coronary angiography(to exclude > 50 percent obstruction of several coronary arteries), echocardiography, and endomyocardial biopsy when suggested. Most patients are between the ages of 20 and 60, but dilated cardiomyopathy can take place in youngsters and older adults. Affected patients can provide in a variety of various ways. Signs of heart failure (progressive dyspnea with exertion, damaged workout capacity, orthopnea, paroxysmal nocturnal dyspnea, and outer edema) are most common. Various other discussions include the subordinate detection of asymptomatic cardiomegaly and symptoms related to coexisting arrhythmia, transmission disturbance, thromboembolic complications, or sudden death.

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