DILATED CARDIOMYOPATHY

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ABSTRACT

Cardiomyopathy can be defined as a myocardial condition where the heart is structurally and functionally abnormal. DCM has a high risk of developing heart failure without any specific symptoms. The etiology both at the genetic and non-genetic level has been studied depending on their genetic linkage analysis and non- inflammatory or viral toxins. Patients of DCM may show thromboembolism or abrupt death when ignored early signs of fatigue, dyspnoea, dicrotic/ hypokinetic pulse or decreased blood supply to the brain which may lead to serious conditions. Genetic diagnosis can help predict prognosis, especially with regard to arrhythmia risk for certain subtypes. There are diagnostic criteria and imaging modalities which are used to diagnose the disease, including echocardiography, MRI, biopsy etc. Different types of pharmacological and non- pharmacological treatments have been discussed over here and these are considered for both the genetic and acquired factors.

KEYWORDS: Dilated cardiomyopathy, Idiopathic, Cardiac Disorder,Heart Failure

INTRODUCTION :

Dilated cardiomyopathy (DCM) is a myocardial disease that is identified by dilatation of the left ventricle along with impaired systolic function. Globally, dilated cardiomyopathy (DCM) is one of the most common reasons for a heart transplant in both adults and children and contributes majorly to heart failure (HF) and sudden cardiac death (SCD). The World Health Organization (WHO) defines DCM as a serious cardiac disorder in which structural or functional abnormalities of the heart muscle can lead to substantial morbidity and mortality owing to complications such as heart failure and arrhythmia [1] . Several pathogenic mechanisms have been identified, such as autoimmune reactions to acute viral myocarditis or genetic alterations in cytoskeletal components. Decades of research have revealed diverse aetiologies for DCM, including genetic mutations, infections, inflammation, autoimmune diseases, exposure to toxins, and endocrine or neuromuscular causes[2]. In the majority of cases, DCM is caused by idiopathic and familial illness. According to the definition of the WHO, primary cardiomyopathies are classified as dilated cardiomyopathy, hypertrophic cardiomyopathy, restrictive cardiomyopathy, and arrhythmogenic right ventricular cardiomyopathy [3].

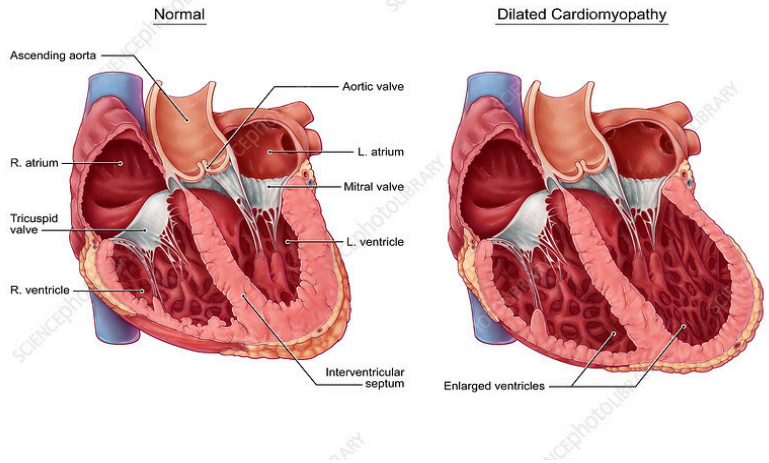


Fig 1.A

EPIDEMIOLOGY:

DCM is one of the most common causes of heart failure, with estimated prevalences of approximately 1:250–400 and up to 1:2500 in the general population[4,5]. 20%-50% of DCM cases are inherited, and more frequent abnormalities are visible in echocardiograms of asymptomatic relatives. In South Africa and Uganda, DCM accounts for 10% to 17% of all cardiac conditions encountered at autopsy[6,7,8] and in many parts of Africa, for 17% to 48% of patients who are hospitalized for heart failure. Whereas the incidence and prevalence of DCM in the United States and elsewhere are reported to be 4 to 8 per 100,000 person-years and 36.5 per 100,000 individuals, respectively[9]. In the western world, up to 36% of DCM cases are associated with alcohol abuse [12].If the 15 cases diagnosed only after death during the 12-year study period were included, the occurrence increased to 0.74 per 100,000 population per year. Fifty-six new cases of dilated cardiomyopathy and 40 new cases of hypertrophic cardiomyopathy were diagnosed during the study period, giving average annual occurrences of 0.34/100,000/year (95% CI 0.26–0.44) and 0.24/100,000/year (95% CI 0.17–0.33) for new cases of dilated and hypertrophic cardiomyopathies, respectively.

ETIOLOGY:

The cause of DCM can be classified into genetic DCM and non-genetic or acquired DCM.

Genetic DCM

More than 30 genes have been involved in the development of DCM through genome-wide linkage analyses, candidate gene sequencing, and genetic association studies. These genes can be grouped into four major categories depending on their development and functioning with its implication on DCM: proteins forming the myocyte cytoskeleton, sarcomeric proteins, nuclear envelope proteins, and calcium homeostasis and mitochondrial function regulators. Genetic alterations of an

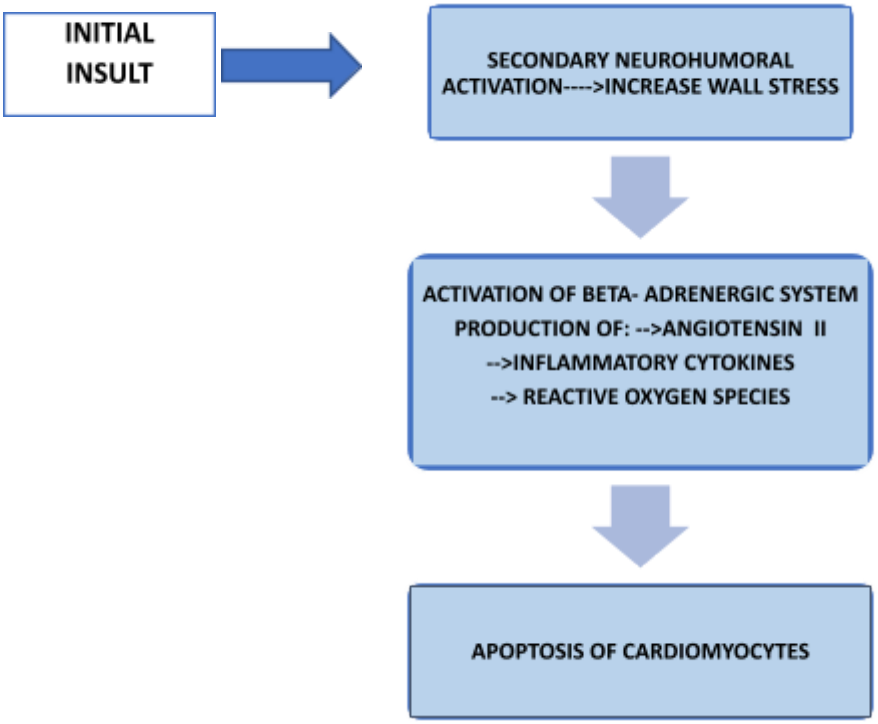
autosomal dominant trait are mostly inherited; inheritance in an X-linked, autosomal recessive, or mitochondrial pattern is rare. The most common gene in which is a variant associated with DCM is found to be the *TTN* (Titin) gene, the largest known human gene. Additional genes frequently linked to DCM include variations in BAG3, MYH7 (β-myosin heavy chain), MYH6 (α-myosin heavy chain), and LMNA (Lamin A/C).

Non-genetic DCM

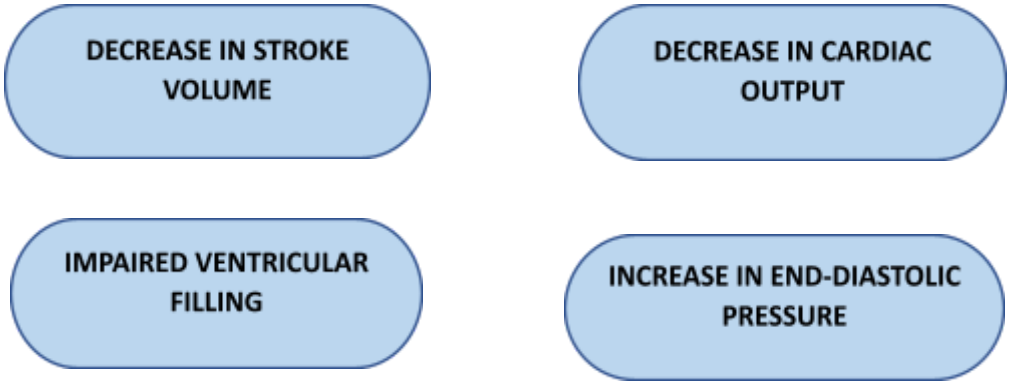
Idiopathic-inflammatory, viral, or autoimmune-mediated cardiomyocyte destructions are mediated directly via viropathic effects (acute phase) or indirectly via T-cell-mediated cytotoxicity (subacute phase)[10]. Fungi, parasites, and chemotoxins may lead to inflammation, which can be one of the causes of primary acute cardiomyopathy. In some families, a predisposition for autoimmune-mediated cardiomyocyte destruction has been observed. These patients' first-degree relatives had a higher frequency of autoimmune disorders, including juvenile diabetes, rheumatoid arthritis, thyroiditis, psoriasis, and asthma, pointing towards a possible role for MHC class II DQ polymorphisms in these familiar forms of autoimmune-mediated IDC[11].

PATHOPHYSIOLOGY:

Mutations in cytoskeletal components such as actin, desmin, and α-tropomyosin have been found[12]. The secondary causes include chemotherapy, excess alcohol consumption, and peripartum. Sometimes patients having DCM are unmasked due to myocardial insult or stress. Patient having DCM with no family history arises from acute myocarditis. An initial myocardial insult led by chronic inflammation, which leads to ventricular remodeling and dysfunction.



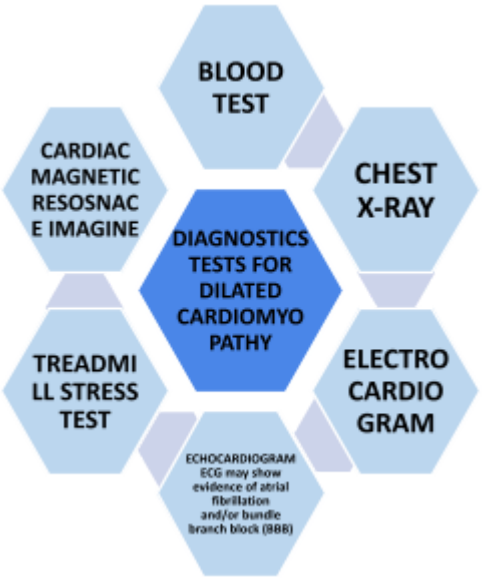
PATHOPHYSIOLOGICAL CHANGES INCLUDE:



SIGNS AND SYMPTOMS:

The signs and symptoms of DCM are similar to conventional CHF, even though patients are less symptomatic. Decreased cardiac output, which is one of the pathological changes, leads to fatigue, cachexia, narrow pulse pressure, dicrotic pulse/hypokinetic pulse, cool extremities, decreased blood supply to the brain (cognitive dysfunction), dyspnea, and reduced blood supply to the kidney (renal failure). DCM may show as thromboembolism, abrupt death, or heart failure. As an alternative, patients who have subclinical DCM discovered during family exams may receive a diagnosis. Even within the same family, clinical manifestations might differ significantly, as explained in the section above.

DIAGNOSIS:



In patients with DCM, the left ventricle will be dilated, with LVEDD >5cm [women] or 6 cm [men], though it should be connected to body surface area [BSA]. This will be associated with impaired systolic function. Cardiopulmonary exercise (CPEX) testing plays a role in measuring the adequacy of cardiac response to exertion and is a predictor of risk [13]. In individuals whose echocardiograms have less-than-ideal image quality, cardiac magnetic resonance imaging (MRI) may offer additional information and a more precise evaluation of chamber capacity and function. Electrocardiographic findings are nonspecific in most familial DCM; however, associated conduction disease should be considered. Prolongation of the PR interval is often the earliest manifestation of genetic DCM+E, and less common manifestations, such as atrial standstill, may develop with progressive disease[14]. Stress tests serve a dual role in the evaluation of a patient with presumed familial dilated cardiomyopathy: detection of coronary heart disease, along with quantification of exercise capacity.

TREATMENT:

The treatment of DCM aims to reduce the symptoms of heart failure and improve cardiac function. The standard drug therapy for heart failure in DCM patients includes beta-blockers and ACE inhibitors. Combined angiotensin receptor–neprilysin inhibitors reduce total mortality and hospital admissions compared with ACE inhibitors and could replace ACE inhibitors as one of the cornerstones of drug therapy in chronic heart failure [15].Diuretics and mineral corticoid receptor antagonists should be given to treat symptomatic heart failure NYHA II-IV. Digoxin is primarily used only in the treatment of NYHA III and IV and can be recommended in the event of atrial fibrillation. Patient with sinus rhythm and pulse rate of > 70/min are recommended Ivabradine. The two major surgical options for DCM patients with heart failure are heart transplantation and implantation of

long-term mechanical circulatory support, which would be a temporary measure while awaiting transplantation or permanently.

NON-PHARMACOLOGICAL TREATMENT:

Paying attention to nutrition, diet, and exercise can help patients with heart failure. Practice of aerobic exercise training, over the long term, can help reverse left ventricular remodeling. Importantly, exercise is contraindicated in the active phase of inflammatory cardiomyopathy, both in athletes and non-athletes, and in DCM due to lamin A/C mutations[16]. Dietary sodium restriction to 2-3 g/day is recommended, and fluid restriction to 2 L/day is recommended for patients with the condition of hyponatremia. Aim for a healthy weight by consuming no more calories than you require each day. When engaging in physical exercise, balance the calories you consume with the calories you expend. Obesity and excess weight can increase cardiac workload.

CONCLUSION:

In today's modern lifestyle, dilated cardiomyopathy (DCM) is a globally challenging disease that has a high risk of heart failure, sudden cardiac death, and the need for heart transplantation. DCM arises from comorbidities that include genetic and non-genetic factors, and sometimes it's idiopathic. Despite advancements in diagnostics, including imaging and genetic testing, a considerable number of cases remain undiagnosed until the disease progresses to severe stages.

Current treatment modalities, including pharmacological therapy with beta-blockers, ACE inhibitors, and emerging options like angiotensin receptor inhibitors, have shown promise in improving survival and reducing hospitalizations. However, for those with advanced disease, heart transplantation and mechanical circulatory support remain critical interventions. Heart devices are considered as a life-supporting treatment. Early diagnosis through improved screening tools, like MRI and ECHO, especially for at-risk populations, can help us prevent worsening of the condition.

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