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Review Spotlight on Cardiomyopathy

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ABSTRACT

Cardiomyopathy is a disease of the cardiac muscle in which heart loses its capacity to pump blood and, in some cases, heart rhythm also get disturbed, which leads to irregular heartbeats called arrhythmias. As disease worsens, heart becomes weaker and ultimately leads to heart failure. Future research advances in the causes, diagnosis and treatment of cardiomyopathy is based on a better understanding of it. The future research advances in the determining causes, diagnosis and treatment of cardiomyopathy and development of improved treatments need better understanding of the disease process.

INTRODUCTION

Cardiovascular diseases (CVD's) remain one of the major causes of deaths worldwide; although from last two decades cardiovascular mortality have decreased in many developed nations. Cardiomyopathy is a major reason of cardiac failure and it can be either acquired or inherited. There are two kinds of cardiomyopathy primary cardiomyopathy and secondary cardiomyopathy.

Primary Cardiomyopathy

In this type patient does not have other cardiac conditions congenital heart disease, coronary artery disease (CAD) or underlying diseases that can lead to cardiomyopathy. In some cases, cardiomyopathies are inherited from past generations and may be passed to next generations.

Secondary Cardiomyopathy

This type of cardiomyopathy is caused due to conditions (like high blood pressure, heart valve disease, congenital cardiac disease, CAD, or due to toxins/medications). The aim of treatment for people with these cardiomyopathies is to recognize and correct the underlying medical condition(s) that caused cardiomyopathy.

CAD is a prevalent and potentially reversible source of cardiomyopathy. Based on whether CAD is causing weakening of heart muscle, cardiomyopathy further divided into ischemic and non-ischemic cardiomyopathy.

Ischemic Cardiomyopathy

It is caused by CAD and cardiac attacks. The cardiac muscle becomes impaired because of coronary arteries blockages and it ultimately leads to cardiomyopathy ^[1,2].

Non-ischemic Cardiomyopathy

These cardiomyopathies are not due to CAD. They may be inherited or acquired [3]. There are four categories of non-ischemic cardiomyopathy:

- Dilated cardiomyopathy (DCM)
- Hypertrophic cardiomyopathy (HCM)
- Restrictive cardiomyopathy
- Arrhythmogenic Right Ventricular Dysplasia (ARVD)

There are other types of cardiomyopathy other than common classifications which include:

- Stress-induced (Takotsubo) cardiomyopathy
- Chemotherapy-induced cardiomyopathy
- Peripartum cardiomyopathy
- Diabetic Cardiomyopathy

Types of Cardiomyopathy

Dilated cardiomyopathy

DCM is the most prevalent type of the cardiomyopathy. This type predominantly occurs in adults of age group 20-60. Men are mostly affected than women. The cause of this cardiomyopathy is unknown sometimes. Approximately one-third of patients who have this cardiomyopathy inherit it from previous generation i.e. their parents. DCM may build up over many years and not cause notable problems [4-6].

DCM mainly affects the ventricles and atria. It often begins in the left ventricle and then cardiac muscle starts to dilate which causes the chamber inside to enlarge/expand. The problem may spread to the right ventricle and then also to the atria as the condition gets worse. Over a period of time, the heart gets weaker and leads to cardiac failure [7-10]. General symptoms of cardiac failure are apnoea, fatigue, tiredness and peripheral oedema. DCM can lead to cardiac valve complications, irregular heartbeats, and sometimes blood clots in the heart.

Alcoholic cardiomyopathy is a type of DCM caused because of direct toxic effects of alcohol on myocardium so the heart loses its capacity to pump blood efficiently, ultimately leading to cardiac failure [11].

Hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy (HCM) usually is inherited. Sometimes it's caused by some genes mutation (change) in cardiac muscle proteins. HCM also can develop over time due to hypertension or aging. Other conditions, like diabetes or thyroid gland disease, also contribute to HCM. Occasionally the root cause of the disease is unknown [12-15]. This cardiomyopathy occurs if cardiac muscle cells expand and cause ventricles walls (generally the left ventricle) to thicken but sometimes the right ventricle may also get affected [16-18].

Obstructive hypertrophic cardiomyopathy: In this the thickening/thickened cardiac muscle may interrupt the blood flow out of the left ventricle [19].

Non obstructive hypertrophic cardiomyopathy: Here thickened cardiac muscle doesn't obstruct blood passage out of the ventricle [20-22]. Some people show signs or symptoms of HCM others may not. Patients with no symptoms of the disease don't affect their lives. But others show severe symptoms and complications like shortness of breath, arrhythmias, or incapacity to exercise [23-28].

Restrictive cardiomyopathy

It mostly affects older adults. In this type both left and right ventricles become stiff and rigid due to replacing of abnormal tissue, like scar tissue with normal cardiac muscle so, over a period of time, blood flow in the heart is

decreased. Ultimately this leads to complications like cardiac failure or irregular heartbeats. Some diseases like hemochromatosis, connective tissue disorders, sarcoidosis, amyloidosis, some cancer therapies like radiation and chemotherapy can cause this cardiomyopathy.

Arrhythmogenic right ventricular dysplasia (ARVD/C)

ARVD/C generally affects teens or young adults. It can lead to sudden cardiac arrest (SCA) in athletes. This cardiomyopathy is distinguished by progressive fibro fatty replacement of the myocardium/heart muscle tissue that predisposes to ventricular tachycardia and sudden death. It mainly affects the right ventricle and with time it may involve left ventricle too. The disease presentation is highly variable even within families [29]. Symptoms are palpitations and fainting or fatigue after physical activities like walking, exercises etc. Researchers suppose that ARVD is inherited [30].

Stress-induced cardiomyopathy

This type of cardiomyopathy has many names such as Takotsubo cardiomyopathy (TCM) or transient/apical ballooning syndrome. TCM resembles an acute coronary syndrome, but that is typically characterized by coronary artery obstruction absence and immediate recovery of left ventricular function [31]. Symptoms are acute chest pain or dyspnea at rest, very wide range of EKG presentations, myocardial necrosis markers rise, and characteristic left ventricular apical akinesia with compensatory hyperkinesia of basal segments [apical ballooning] [32-36]. Hemodynamic involvement spectrum ranges from only mild to severe cardiogenic shock, but generally left ventricular function recovers spontaneously in a few hours or days [37,38].

TCM can be triggered by emotional or physical stress, but its pathophysiology yet to be completely established. Though hyper-catecholaminergic status seems to play a focal role in pathophysiology of Takotsubo cardiomyopathy, probable explanations of causes range from coronary vasospasm to microcirculatory dysfunction [39-43].

Chemotherapy-induced cardiomyopathy

Chemotherapy-induced cardiotoxicity (CIC) is poisonous or detrimental effect upon the heart that can delay cancer treatment, reduce survival, and rise morbidity. Acute and chronic cardiac failure is the 2nd most prevalent comorbidity for cancer survivors in children because of therapy with anthracyclines and chest radiation treatment, and it affects nearly up to 48% of cancer survivors in adults [44,45]. Researchers hypothesize that CIC can be because of increased oxidative stress on the cardiac muscle cells.

Anthracyclines (class of chemotherapy medications) include doxorubicin (Adriamycin), daunorubicin (Cerubidine), epirubicin and idarubicin (Idamycin). Cardiomyopathy that occurs from anthracyclines is related to the given dose. More anthracyclines medications leads to more likely cardiotoxicity. In cardiotoxicity heart muscle is damaged and blood isn't pumped efficiently [46,47]. Trastuzumab (Herceptin) also toxic to the heart but its effect is reversible, so stoppage of medication leads to relief from cardiomyopathy. Radiation taken near the chest puts more risk for cardiomyopathy [48].

Peripartum or postpartum cardiomyopathy (PPCM)

This cardiomyopathy is typically characterized by fast onset cardiac failure during the final weeks/last month of pregnancy or up to 6 months postpartum. The clinical profile of PPCM has the same appearance of a DCM, but differs from DCM other forms in its sudden development. Healthy women can show sufficiently serious cardiac failure to need even transplantation of heart [49-51]. Nearly 80% of symptomatic patients recover, although less than 30% attain full recovery with left ventricular function (LVF) normalization and chamber size. This cardiomyopathy is idiopathic cardiac failure which takes place in the lack of any specific definite cardiac disease in the last weeks of

pregnancy or the first five months following childbirth. The cause might be an amalgamation of both environmental and genetic factors [52-54].

Peripartum cardiomyopathy treatment involves both traditional cardiac failure therapies and also PPCM targeted therapies [55]. Therapeutic resolutions are invariably affected by drug-safety profiles during gestation, lactation. Sometimes mechanical support and heart transplantation might be required in serious cases. Despite up to 10% mortality rate and more risk of relapse in later pregnancies, many patients with PPCM recover within 3-6 months of cardiomyopathy onset [56-58].

Diabetic cardiomyopathy

Diabetes mellitus is one of the foremost causes of cardiac failure today in present clinical practice, independent of other conventional risk factors for cardiovascular diseases and cardiac failure like arterial sclerosis, coronary artery disease (CAD) or valvular cardiac disease. Diabetic cardiomyopathy is a disease which affects the cardiac muscle in diabetic patients causing a vast range of structural abnormalities slowly causing LVH [left ventricular (LV) hypertrophy] and diastolic and systolic dysfunction or a combination of both [59-64]. In many patients, especially those with Diabetes mellitus, diabetes associated changes likely increase the left ventricular hypertrophy development, raise the susceptibility of the heart to ischemic injury and augment the overall likelihood of developing cardiac failure [62-64].

Type 2 Diabetes reduces myocardial contractility and suppresses actomyosin ATPase function thereby causing changes in myocardial structure, calcium signalling and metabolism ultimately manifesting cardiac dysfunction. Diabetic cardiomyopathy was originally reported as a dilated phenotype with eccentric left ventricular remodelling and systolic left ventricular dysfunction [65]. Currently however, clinical studies on this disease mainly trace a restrictive phenotype with concentric left ventricular remodelling and diastolic left ventricular dysfunction [66-69]. Patients with high blood pressure and coronary artery disease may well have myocardial alterations related to these disease processes, but a specific cardiomyopathy may also affect the cardiac muscle secondary to diabetes mellitus responsible for synergistic adverse effect/events [70].

Miscellaneous cardiomyopathy

Uremic cardiomyopathy, cirrhosis-associated cardiomyopathy, chagasic cardiomyopathy and inflammatory cardiomyopathy are various types of cardiomyopathies caused because of chronic kidney disease, cirrhosis, protozoan parasite *Trypanosoma cruzi* infection and inflammation of the heart muscle respectively [71-74].

RISK FACTORS

People of all age groups and races can get affected with this cardiac disease. DCM is more prevalent in Afro-Americans than Whites and also it is more prevalent in men than women.

Following diseases, underlying conditions, and drugs also can contribute the cardiomyopathy:

- CAD, heart attack, hypertension, diabetes, disease to thyroid gland, viral hepatitis, AIDS, bronze diabetes (hemochromatosis), sarcoidosis, or amyloidosis
- Family history of cardiomyopathy [75], cardiac failure, or SCA
- Viral Infections (which inflame the heart muscle and increase load on the heart)
- Alcohol, especially with poor eating habits.
- Peripartum or postpartum complications
- Toxins (cobalt)

- Certain types of drugs such as cocaine and amphetamines
- Some chemotherapy medicines like doxorubicin, daunorubicin which are used to treat cancer

SIGNS AND SYMPTOMS

Few people with cardiomyopathy never show any signs or symptoms. Thus, it's crucial to identify persons who are at high risk for it. This can help averting future complications, such as severe arrhythmias or SCA.

As cardiomyopathy severe and heart further weakens, heart failure signs usually start appearing.

Symptoms of cardiac failure [76,77]:

- Fatigue, weakness
- Breath shortness/apnea
- Cough especially on lying down position
- Pulmonary edema/swelling of ankles, legs and feet due to fluid building
- Weight gain because of fluid retention
- Irregularity in heartbeats (arrhythmias)
- Other symptoms like dizziness; light-headedness; fainting, chest pain, particularly after physical strain or large meals; and cardiac murmurs/sounds

DIAGNOSIS

Diagnosis of cardiomyopathy depends on medical and family (past generation) histories, physical examination and from tests results.

- Physical exam using stethoscope help listen sounds of heart and also lungs, signs like swelling of the abdomen, ankles, feet, legs or veins help doctor diagnosing cardiomyopathy
- Diagnostic tests like blood tests, Chest x ray, EKG (electrocardiogram), holter and event monitors, echocardiography, stress test
- Diagnostic procedures like cardiac catheterization, coronary angiography, genetic testing or myocardial biopsy [78,79].

TREATMENT

People with cardiomyopathy but show zero symptoms may not require any treatment. For other people with symptoms, treatment is required. Treatment is based on the cardiomyopathy type, symptoms severity and complications seriousness, age and overall health of the patient. The main aim of cardiomyopathy treatment include managing underlying conditions that are responsible for this disease, controlling symptoms to live normally, stopping the condition from getting more worse, decreasing complications, preventing SCA risk [3,74].

Treatments include medication, surgery through implanted devices to treat arrhythmias, and/or a nonsurgical procedure like alcohol septal ablation, lifestyle changes.

Medicines

- ACE inhibitors, angiotensin II receptor blockers and beta blockers to decrease blood pressure, for slowing heart rate
- Antiarrhythmics, to prevent arrhythmias and for normal rhythm

- Balanced electrolytes
- Diuretics, or "water pills," to remove excessive fluid and sodium content from body
- Anticoagulants, or "blood thinners," to prevent clotting of blood and thin the blood
- Corticosteroids to decrease inflammation

Surgery and Surgically Implanted Devices

There are various types of surgeries like septal myectomy, devices, and lastly heart transplant for treating cardiomyopathy. Several devices like pacemaker, cardiac resynchronization therapy (CRT), left ventricular assist device (LVAD), an implantable cardioverter defibrillator (ICD) can be implanted in the heart to aid it work better. People with hypertrophic cardiomyopathy are offered surgery to remove thickened heart muscle parts.

Sudden cardiac arrest (SCA) can be prevented if persons at high risk are identified and treat with an ICD. When the cardiomyopathy symptoms aren't well controlled by treatment and patient's quality of life (QoL) is affected then as a last resort heart transplantation option may be examined [4,75].

Lifestyle Changes

Avoiding smoking, quitting alcohol and illicit drugs, having adequate sleep and proper rest, decreasing stress and treating underlying disease | maintaining blood pressure, blood cholesterol and blood glucose levels.

Healthy Diet with Moderate Physical Activity

Diet consisting of various fruits, different vegetables and whole-grain products need to be taken. Foods which are low saturated and trans fat content, and low cholesterol containing items like lean meats, poultry (skinless), beans, low fat milk products and also foods with little salt, low added sugar are to be included in diet. Maintaining healthy weight and balancing calories intake with moderate physical activity, like walking is good for health [74,75,80].

CONCLUSION

The burden of cardiac disease in the world is enormous and also increasing. By 2020 it is supposed that cardiovascular diseases will become the focal cause of the universal health burden, accounting for nearly 73% of total global mortality and approximately 56% of total morbidity. So it is best to diagnose and monitor this condition through proper understanding of the clinical and physiological characteristics of principal diseases like cardiomyopathy. There is need for more clinically relevant translational studies which may help to elucidate the mechanisms behind cardiomyopathies there by helping us to provide more precise therapeutics which, in conjunction with more advanced diagnostic tools, may allow potent and effective intervention at much beginning stages of the disease and reduce the risk of heart failure in individuals.

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