DIABETIC CARDIOMYPATHY

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DIMBETIC CARDIOMYPATHY

- **1-Definition of Diabetes**
- 2-Diagnosis of diabetes mellitus
- 3- Definition of cardiomyopathy
- 4- Definition of diabetic cardiomyopathy
- 5- Pathophysiology of diabetic cardiomyopathy
- 6- Histological picture in diabetic cardiomyopathy
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Definition of Diabetes

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both.

(Canadian diabetes association)

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Diagnosis of diabetes mellitus

The current WHO diagnostic criteria for diabetes should be maintained:-

fasting plasma glucose ≥ 7.0mmol/l (126mg/dl)

Or 2-h plasma glucose ≥ 11.1mmol/l (200mg/dl).

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Definition of cardiomyopathy

Cardiomyopathies are a heterogeneous group of diseases of the myocardium associated with mechanical and/or electrical dysfunction that usually (but not invariably) exhibit inappropriate ventricular hypertrophy or dilatation and are due to a variety of causes that frequently are genetic.

(American heart association)

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Definition of diabetic cardiomyopathy

structural and functional abnormalities of the myocardium in diabetic patients without coronary artery disease or hypertension.

Obviously, however, this type of cardiomyopathy should be present also in diabetics with coronary artery disease and/or hypertension, though it is difficult to separately assess the contribution of diabetic cardiomyopathy to overall ventricular dysfunction in such cases.

(Aneja et al; 2009)

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Pathophysiology of diabetic cardiomyopathy

DIABETES (hyperglycemia, hyperlipidemia, insulin deficiency or insulin resistance) **RAAS** Altered Ca2+ handling Glucotoxicity Cardiac Insulin Resistance Increased Lipid Uptake Ceramide 1 PPARα 1 Mitochondrial ROS PKC T Lipotoxicity 1 ROS 1 Glucose oxidation SERCA2A activity Mitochondrial Mitochondrial function AGE Ca2+ dynamics FA oxidation Mitochondrial uncoupling 1 SERCA2A/NCX/ RyR/PMCA Apoptosis I expression TCA cycle enzyme activity O-linked glycosylation Apoptosis 1 Fibrosis I Cardiac efficiency of mitochondrial proteins Hypertrophy **Energy depletion Energy depletion** EC coupling Mitochondrial function Diabetic Cardiomyopathy

DIABETIC CARDIOMYPATHY

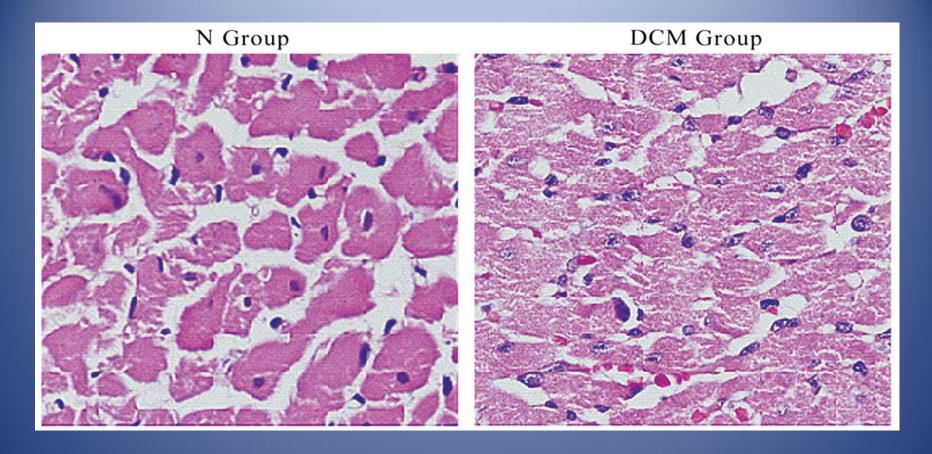
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Histological picture in diabetic cardiomyopathy

Interstitial and perivascular fibrosis is a histological hallmark of diabetic cardiomyopathy and the extent of fibrosis correlates with heart weight. In addition to the increase in collagen deposition, cross-linking of collagen fibers may be increased by diabetes, contributing to reduction in ventricular compliance.

Microangiopathy is also another hallmark in diabetic cardiomyopathy contributing to reduction in ventricular contractility.

(Miki et al; 2012)



Hematoxylin and eosin-stained heart sections from rats of the normal (N) and diabetic cardiomyopathy (DCM) groups (magnification, ×400).

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Clinical phenotypes of diabetic cardiomyopathy

Diabetes mellitus-related cardiomyopathy (DMCMP) has two main clinical phenotypes:-

- 1- Dilated phenotype with eccentric left ventricular (LV) remodeling and systolic LV dysfunction
- 2- Restrictive phenotype with concentric LV remodeling and diastolic LV dysfunction.

(European heart Journal)

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Clinical picture of diabetic cardiomyopathy

Clinical picture of:-

- 1- Coronary microangiopathy.
- 2- Systolic dysfunction and/or diastolic dysfunction.

Clinical picture of microangiopathy

>>> Typical ischemic chest pain

(Proved by exercise ECG and stress imaging. However; coronary angiography is usually normal or shows non significant lesions)

Clinical picture of systolic and diastolic dysfunction

>>> Heart failure manifestations:-

Dyspnea

Orthopnea

PND

LL oedema

Exercise intolerance

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Investigations of diabetic cardiomyopathy.

1- ECG >>>

- * High voltage and strain pattern:- in dilated type.
- * Ischemic changes due to microangiopathy
- * Tachycardia in case of heart failure

2- Chest X ray>>>

- * Cardiomeglay may be seen in dilated type (not in restrictive type)
- * Pulmonary venous congestion (in both types).

3- Echocardiography>>>

* In delated type: LV dilatation (with or without hypertrophy) + Impaired LV systolic function (EF < 40 %) +/- functional MR. (++ LV mass and mass index)

* In restrictive type:- Normal cavity diameters +/-LVH + Normal LV systolic function (EF > 50 %) + Restrictive pattern of LV diastolic dysfunction.

4- Novel echocardiography modalities>>>

They include tissue Doppler, strain, strain rate and speckle tracking echocardiography. These tests are very valuable in assessment of both systolic and diastolic cardiac functions with lesser subjective variations.



2D longitudinal strain speckle tracking echocardiography

5- Stress Echo >>> May show evidence of inducible RWMA (typically due to microangiopathy)

6- SPECT and PET >>> it shows areas of mixed scar and inducible ischemia due both ++ collagen deposition in the extracellular matrix and coronary microangiopathy.

7- Cardiac MRI >>> It's the golden test for evaluation of cardiac geometry and systolic function in patients with diabetic cardiomyopathy.

Combining cardiac MRI with dobutamine infusion is helpful for diagnosis of myocardial ischemia and microangiopathy.

8- Coronary CT angiography and invasive coronary angiography >>>

Based on definition of diabetic cardiomyopathy; coronary angiography is normal or shows non significant coronary lesions.

Laboratory investigations

BNP and NT Pro BNP >>>

Usually elevated if patients who developed heart failure (either systolic, diastolic or both).

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Treatment of diabetic cardiomyopathy

No specific treatment of diabetic cardiomyopathy.

Treatment is usually directed to:-

- 1- Control heart failure
- 2- and control ischemic chest pain

>> General measures and life style modification<<

- Weight reduction.
- Stop smoking.
- Salt restriction.
- Healthy diet rich in fibers and polyunsaturated fatty acids.
- Regular exercise.

>> Strict glycemic control <<

Most clinical studies support that target HbA1C between 6.5-7 mg/dl is associated with lower risk of cardiovascular complications.

Treatment of dilated type of diabetic cardiomyopathy

It is the same as ttt of heart failure due to any other cause. It includes:-

- B Blockers, ACEIs or ARBs, Diuretics +/- digoxin.
- <u>Ivabradine</u> was tried as and alternative or in combination with BB to control HR.
- <u>Trimetazidine</u> use is supported by some studies that shows significant increase in EF in those patients through its metabolic modulation effect.
- L Carnitine supplement:- it may have a role in mitochondrial activation in increase energy production by the cardiac myocytes leading in ++ contractility.

Treatment of restrictive type of diabetic cardiomyopathy

As all forms of heart failure with preserved EF % (HFpEF); no standard therapy for treatment of restrictive type of diabetic cardiomyopathy.

Diuretics is helpful to relieve dyspnea and congestive symptoms.

B blockers and or Ivabradine may improve symptoms through reduction of HR.

Control of ischemic chest pain and prevention of epicardial coronary lesions

Patients with diabetic cardiomyopathy and microangioapthy are very risky to develop coronary lesions in the large epicardial arteries.

Treatment includes:-

- I- Statings- essential not only in reduction of LDL levels and prevention of atherosclerosis but also in regression of atherosclerotic plaques through therir pleotropic effect.
- 2- Anti-platelet therapy:-
- * Low dose Aspirin (81 -162 mg/day).
- * Clopidogrel 75 mg:- an alternative to Aspirin or used in combination with aspirin.
- **3- Nitroley or Nicorandils-** useful in relief of chest pain through its coronary vasodilator effect. Nicorandil has a positive effect on cardiac preconditioning.
- 4- B Blockers: They relive chest pain through its —ve inotropic and chronotropic effect. Thus reducing myocardial demands of coronary blood flow. Ivabradine can be used as an alternative to BB or in combination with it to reach target HR (50-60 b/m)
- **5- Non-dihydropyridine** calcium channel blockers can be used as an alternative to BB in case of contraindications to BB or in combination with it to achieve target HR.
- **6- Amiophylline** use is suggested in some trials to relieve ischemic chest pain secondary to microangiopathy through its Adenosine receptors antagonist effect.

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Conclusion

- 1- Diabetic Cardiomyopathy remains not fully understood cardiac disorder.
- 2- Its diagnosis depends mainly on detection of cardiac dysfunction in diabetic patients without any other cause of cardiac dysfunction.
- 3- No specific treatment of diabetic cardiomyopathy until now. So; its management depends on conventional ttt of heart failure and ischemic chest

Thank you