“Diabetic Heart Disease”

Ram C Sharma, MD, DNB (Med), FRCP (Edin.), FACC, FSCAI
Associate Professor of Medicine
Div. Of cardiology, Quillen College of Medicine
East Tennessee State University
Johnson City, TN USA

Diabetes Heart Disease”

• Association between diabetes and heart diseases
• Prognosis
• Pathophysiology
• Clinical presentations and syndrome
• Treatment
• Guidelines: Update 2011

Disclosures: None

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Diabetes & CVD

- Framingham Heart Study showed that the frequency of heart failure is twice in diabetic men and five times in diabetic women compared with age-matched control subjects.

Diabetic Heart Disease

- Increased incidence of CV disease in diabetics.
- CVD in approx. 70% in diabetics.
- Though there is significant decline in CV disease in US but the increasing incidence of diabetes is threatening this trend.
- The direct economic cost of DMII has been estimated to be $172 billion in 2007 in US

Diabetes: Higher risk for

- CAD
- PVD
- Autonomic disturbances and arrhythmias
- Heart failure

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FHS: Diabetes is associated with 3 times risk of CV events and CV deaths
ACS: diabetes associated with worse prognosis
Diabetics are more likely to fail thrombolytic therapy.
Independent risk factor for stent thrombosis
SIRIUS trial were more likely than non-diabetics to require revascularization

Individuals with DM have higher absolute reductions in CVD outcomes than nondiabetic individuals when treated for hypertension and dyslipidemia
Coronary Equivalent

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Clinical Syndromes

- Macrovascular disease: Accelerated atherosclerosis
  - CAD
  - PVD
- Microvascular disease
- Myocardial dysfunction
  - Diastolic heart failure
  - Systolic heart failure

Pathogenesis

- Accelerated atherosclerosis
- Endothelial dysfunction
Pathogenesis

- Effect of insulin
- Effect of hyperglycemia
- Energy derangements
- Hypertension and dyslipidemia

Multifactorial

- Autonomic dysfunction
- Metabolic derangements
- Abnormalities in ion homeostasis
- Alteration in structural proteins
- Interstitial fibrosis

Endothelial Dysfunction

- Endothelial dysfunction is characterized by impaired endothelium-dependent vasodilation
- “Endothelial activation,” which is associated with a proinflammatory, proliferative, and procoagulatory milieu that promotes initiation and complications of atherogenesis.
- Insulin resistant

Macrovascular Disease

- Dyslipidemia is highly correlated with atherosclerosis, and up to 97% of pts with diabetes have dyslipidemia.
- DM: Mostly small dense LDL particles. Once oxidized, these particles act as “foreign” & attract leukocytes.
- Glycation of LDL lengthens its half-life, therefore make them more atherogenic.
- Glycation of HDL shortens its half-life and renders it less protective against atherosclerosis.
- Endothelial dysfunction

Microvascular Disease

- Small vessel disease in DM
- Diabetes contributes to defects in the autonomic NS, the endothelium, and local metabolism, all of which can result in microvascular disease.
- Patients with DAN have increased rates of SCD as well as a higher overall CV mortality rate.
- Endothelial dysfunction
- Capillary BM thickening: affect transport of metabolic products, permeability

Strong Heart Study

- “Non–insulin-dependent DM has independent adverse cardiac effects, including increased LV mass and wall thicknesses, reduced LV systolic chamber and myocardial function, and increased arterial stiffness.”

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Circulation. 2000;101:2271-2276.)
Morphologic Changes

- Histological studies of autopsy and biopsy specimens demonstrate a constellation of cardiac morphological abnormalities:
  - Myocyte hypertrophy
  - Perivascular fibrosis
  - Increased quantities of matrix collagen, cellular triglyceride, and cell membrane lipid.
- These findings are consistent with nonenzymatic glycation of vascular and membrane proteins, increased cellular fatty acid uptake, and hyperglycemia-induced oxidative stress.

Metabolic Adaptation

- Different Sustained Stimuli (e.g., Diabetes, Pressure Overload)
  - Metabolic Signals
  - Altered Metabolism (Pathological Accumulation of Glucose and Fatty Acid Metabolites)
  - Transcriptional Signals
  - Adaptation
    - i.e., Induction of Enzymes, Mitochondria Switching, Mitochondrial Cardiac Output

Metabolic Maladaptation

- Over-Intense or Multiple Sustained Stimuli (e.g., Diabetes plus Pressure Overload)
  - Metabolic Signals
  - Altered Metabolism (Pathological Accumulation of Glucose and Fatty Acid Metabolites)
  - Transcriptional Signals
  - Maladaptation
    - i.e., Induction of Apoptosis, Chronic Activation of PKCs, Mitochondrial Membrane Vesiculation, Reactive Oxygen Species Generation, Cardiac Membrane Dysfunction

Glucose transport in the heart
Effect of FFA on MVO2

- Multiple animal studies show 26-72% increase in MVO2
- This was reversed by GIK
- FAO requires 11% to 12% more oxygen for a given amount of ATP produced

Opie LH. J Am Coll Cardiol, 2009; 54:1637-1646
Diabetic Cardiomyopathy

- Common co-occurrence CHF & DM
- In ALLHAT, pts with diabetes had a nearly 2-fold risk for HF hospitalization or death after adjustment for other risk factors (RR, 1.95)
- FHS:
  - Increased risk of CHF in diabetics. X2 in men, X5 in women
  - The association was even stronger in younger pts (ages ≤ 65 yr), being 4-fold higher in male pts and 8-fold higher in female pts.
  - Mean survival after the onset of heart failure was 1.7 years in men and 3.2 years in women
  - 1-year and 5-year survival rates were 57% and 25% in men and 64% and 38% in women, respectively
- Leading cause of hospitalization in pts over 65 yr

ALLHAT 2006 Circulation 113: 2201–10

Patients with CHF have higher risk of developing diabetes.

Subgroup analysis of SOLVD showed that 5.9% of pts developed diabetes over mean f/u of 2.9 yrs.

Patients with diabetes that develop HF have a markedly increased mortality


Risk Factors for developing HF in Diabetics

- HbA1c
- BMI
- HTN
- CAD
- Increasing age
- Use of insulin
- End-stage renal disease, nephropathy
- Proteinuria and albuminuria
- Retinopathy
- Duration of DM
Diabetic Cardiomyopathy: Pathogenesis

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Management

- Tight control of glucose is associated with reduction in microvascular complications.
- The benefit is unclear for macrovascular disease.

Management: Exercise

- NHI survey: >62% responders no exercise
- Average Reduction
  - BMI 5%
  - Body fat 15%
  - BP 5.1mmHg
  - TG 26 mg/dl
  - HbA1c (intense exercise)
- Increase
  - HDL 5mg/dl
  - CV fitness
  - VO2 max

- Exercise improves insulin sensitivity
- Improves endothelial dysfunction
- Antiinflammatory effect
Exercise

- Clinical benefits are uncertain
- At least moderate intensity exercise
- Duration (per week)
  - Mod intensity >150 min
  - Vigorous-intensity >90 min
  - Minimum 10 min per session
- On non consecutive days
- Combined with other life style modifications.

Management

- The Diabetes Control and Complications Trial for type 1 diabetes mellitus and the United Kingdom Prospective Diabetes Study.
- Both trials demonstrated the efficacy of intensive glucose control in reducing the risk of microvascular complications such as retinopathy, neuropathy, and nephropathy
- UKPDS: For every 1% reduction in HbA1c in the risk of HF fell by 16%.