CARDIOVASCULAR PROPHYLAXIS IN DIABETES

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Diabetes and cardiovascular risk

- DM is a condition of premature cardiovascular complications in the setting of chronic hyperglycemia
Cardiovascular Risk

- So as soon as one is diagnosed as a case of diabetes, one should be considered to have a heart attack already.

A patient with diabetes = A patient with MI
Increased Risk of Heart Disease in Diabetes

- In patients with diabetes

- Risk of CHD increases by 3-4 fold
- 75-80% deaths are attributed to CHD
- High mortality rate in 1 year after first MI
  - 44% in Diabetic men
  - 37% in Diabetic women
MRFIT: Impact of Diabetes on Cardiovascular Disease Mortality

MRFIT=Multiple Risk Factor Intervention Trial.

Complications of acute myocardial infarction in diabetic and non-diabetic patients (n = 1929).
Diabetes Doubles Risk for MI Mortality Despite Advances in Cardiac Care

Factors Contributing to Cardiometabolic Risk

- Genetics
- Age
- Overweight/Obesity
- Insulin Resistance
- Insulin Resistance Syndrome
  - ↑Lipids
  - ↑BP
  - ↑Glucose
- Smoking, Physical Inactivity, Unhealthy Eating
- Hypertension
- Abnormal Lipid Metabolism
  - LDL ↑
  - ApoB ↑
  - HDL ↓
  - Triglycerides ↑

Cardiometabolic Risk
Global Diabetes/CVD Risk

Ages, Race, Gender, Family History

Inflammation, Hypercoagulation

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diabetes.org/CMR
Glycemic disorders

Dyslipidemia
- Low HDL
- Small, dense LDL
- Hypertriglyceridermia
- Postprandial lipemia

Hypertension

Impaired thrombolysis
- ↑ PAI-1, fibrinogen

Endothelial dysfunction/inflammation
- ↑ CRP, MMP-9,
  ↓ adiponectin

Microalbuminuria

Visceral Obesity

↑ Free Fatty Acids

Insulin Resistance

Atherosclerosis

Type 2 DM and cardiovascular risk

- Endothelial dysfunction
- Hypertension
- Advanced Glycation products
  - Prothrombosis - Fibrinogen/PAI 1 increased
  - Dyslipedemia - Total C/TG/LDL/Apo B HDL-C
Cardiovascular Risk factors specific for Diabetes

- Serum Insulin
- Microalbuminuria
- Massive proteinuria
- PAI-1
- Abnormal Platelet function
- Fibrinogen level
Cardiovascular Risk Factors In Diabetes

- Fasting/postprandial hyperglycemia
- Overweight/obesity
- Elevated systolic and diastolic blood pressure,
- Dyslipidemia.
- Smoking
Risk factors - Hypertension, Obesity, Diabetes, Cholesterol, Smoking

Preclinical disease -
- Hypertrophy: LVH, Vascular
- Atherosclerosis: Carotid, Cardiac

Morbid Events -
- MI, Stroke, Arrhythmia, SCD
So, how to keep the CV risk at bay in diabetics?
First step is to keep a good glycemic control.
Studies have shown that control of diabetes can reduce the CV complications

- DCCT 1984-1992
- UKPDS 1978-1998
- KUMAMOTO 1992-2000
- EDIC 1996
- ACCORD 2002-2007
- ADVANCE
Improved Glycemic Control Reduces Risk of Complications

According to the United Kingdom Prospective Diabetes Study (UKPDS) 35, every 1% decrease in A1C resulted in:

- Decrease in risk of microvascular complications ($P < .0001$)
- Decrease in risk of any diabetes-related end point ($P < .0001$)
- Decrease in risk of MI ($P = .04$)
- Decrease in risk of stroke ($P = .04$)
- Decrease in risk of microvascular complications ($P < .0001$)

UKPDS Follow-up

- UKPDS 66 Patients with fatal MI had higher HbA(1c) than those with nonfatal MI (odds ratio 1.17 per 1% HbA(1c), P = 0.014).

- Patients with fatal stroke had higher HbA(1c) than those with nonfatal stroke (odds ratio 1.37 per 1% HbA(1c), P = 0.007).
Glycemic Control and Risk of Development of HF in Diabetes

\[ P=0.001 \]

HF and/or death rate/1,000 person-years

A1C (%)

- <7: 4.5
- 7 to <8: 5.8
- 8 to <9: 6.3
- 9 to <10: 8.3
- ≥10: 9.2

HF=heart failure.

ADA Standards of Care 2011

- ADA recommends a general A1C target of <7%
- The goal of therapy for the individual patient is to achieve an A1C as close to normal as possible without hypoglycemia
- More stringent glycemic goals may reduce the risk of serious diabetes-related complications
- Less stringent treatment goals may be appropriate for certain patient populations and patients with severe or more frequent hypoglycemia
Life style modification

- Diet
- Weight loss
- Physical activity/Exercise
- Cessation of smoking
Diet and diabetes

- Individualised
- Realistic
- Flexible
- Suitable to patient’s life style
What not eat

Sweets
Chocolates
Beef fry
Pastry
Mutton
Cola
Chips
Sugar
Weight Loss
Benefits of 10% weight loss

- 20% fall in mortality
- 30% fall in diabetes related death
- 40% fall in obesity related death
- 20% fall in SBP
- 10% fall in DBP
- 15% fall in LDL-C
- 30% fall in TG
- 8% increase in HDL-C
Exercise
Exercise

- Benefits
  - Good glycemic control
  - Improves insulin sensitivity
  - Optimizes body weight
  - Gives psychological well being
  - Decreases cardiovascular mortality
Exercise

- Disadvantages of unplanned exercise
  - Strain the compromised CVS
  - Predisposes hypoglycemia
  - Injures musculoskeletal system
Calorie expenditure

- Lying down/sleeping/sitting: 1
- Standing/ desk work/ driving: 2
- Level walking level bi cycling: 3
- Social double badminton: 4
- Social singles badminton: 5
- Gardening, swimming: 6
- Competitive badminton: 7
- Jogging: 8
- Basketball: 9
- Running 1 km/hour: 10
Calories spent in various activities

- Walking 3 miles/hour     275/hr
- Walking 5 miles/hour     420/hr
- Cycling 8 miles/hour     325/hr
- Mopping/vacuuming       240/hr
- Scrubbing floors         300/hr
- Gardening               220/hr
- Vigorous dancing         400/hr
Exercise guidelines

- Medical evaluation for CVD, PVD and PN
- Choose enjoyable activities
- Walking at least 20 min/day
- 5 min warm up
- 5 min cool down
- Education on hypoglycemia
- Proper foot care and footwear
- Pre and post RBS monitoring
- Insulin and carbohydrate adjustments
- Should carry snacks along with
Smoking
Cessation of smoking reduces 50% risk of MI in first year after quitting
Control of Hypertension
Treatment of hypertension

- Target blood pressure
- How to treat?
- What is the preferred one?
HOT: Cardiovascular Events by Target DBP in Diabetes Subgroup

Events per 1,000 patient-years

- Major CV events
- MI
- Stroke
- CV mortality

- ≤90 mm Hg (n=6,264)
- ≤85 mm Hg (n=6,264)
- ≤80 mm Hg (n=6,262)

\[ P \text{ for trend } = \text{ *0.005; } \dagger0.11; \ddagger0.34; \text{ } \S0.016. \]

DBP=diastolic blood pressure.

Syst-Eur: Reduction in Event Rate in Adults (≥60 Years) With Diabetes

*P<0.01 compared with no diabetes.
Syst-Eur=Systolic Hypertension in Europe.

Target blood pressure

- Systolic less than 130 mm Hg
- Diastolic less than 80 mm Hg
- ACEi/ARB - Decrease IR, LDL, Increase HDL slightly
- HCTZ – Increase IR, LDL, Decrease HDL slightly
- B Blockers - Increase IR, LDL, Decrease HDL slightly
- Alpha Blockers - Decrease IR, LDL, Increase HDL slightly
- Ca channel blocker - neutral
Cholesterol
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<th>Name</th>
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<th>Baseline LDL-C</th>
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<th>Reduction in cardiovascular events %</th>
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Target level of Cholesterol ADA 2011

- **LDL -C**
  - Less than 100 mg/dl (2.6mmol/L) if patient has no overt CVD
  - Less than 70 mg/dl (1.8 mmol/L) in diabetic patients with CVD
  - 30-40 % reduction from baseline

- **HDL –C**
  - More than 40 mg/dl (1 mmol/L) in male
  - More than 50 mg/dl (1.3 mmol/L)

- **Triglyceride**
  - Less than 150 mg/dl (1.7 mmol/L)
What to do reduce Cholesterol?

- Lifestyle modification
- Statin therapy
- Fibrates
When to start statin in diabetes?

- All diabetic patients
  - With a history of overt CVD
  - Over 40 years of age with one or more risk factors
  - If LDL-C is more than 100 mg/dl in absence of risk other factor
Modifications of lipoprotein levels:

Glucose lowering medications

- Improved control of hyperglycemia can reduce some degree of dyslipidemia
- Glucose lowering medication can decrease triglyceride level
- Thiazolidinediones increase HDL-C level but can also decrease LDL-C level
- Optimal glycemic control may result in less atherogenic LDL particle
- Complete reversal of dyslipidemia by improved glycemic control is usually unacheivable
Role of Aspirin
Effect of Aspirin Use on Survival in Patients With CAD

Patients with diabetes

Patients without diabetes

Survival (%)

Time (y)

Aspirin
No aspirin

CAD=coronary artery disease.

Use of aspirin

- HOT trial: 36% risk reduction of MI & 15% reduction in major CV events
- Physicians Health study: 44% risk reduction of MI & 18% reduction in major CV events
- APT trial: 33% reduction in MI/Stroke
- ETDRS: 18% risk reduction of fatal/non fatal MI
Aspirin: When to use?

- **For primary prevention this should be used**
  - 10 year cardiovascular risk > 10%
  - In male > 50 years and in female > 60 years with at least one additional risk factor eg. HTN, Smoking, F/H of CVD, Dyslipidemia, Albuminuria

- **For secondary prevention**
  - All diabetic patients with a history of CVD
HOPE: Outcomes in Patients With Diabetes

Event rate (%)

- Combined: Placebo 19.8, Ramipril 15.3 (25% RR, P=0.0004)
- MI: Placebo 12.9, Ramipril 10.2 (22% RR, P=0.01)
- Stroke: Placebo 6.1, Ramipril 4.2 (33% RR, P=0.0074)
- CV death: Placebo 9.7, Ramipril 6.2 (37% RR, P=0.0001)
- Overt nephropathy: Placebo 8.4, Ramipril 6.5 (24% RR, P=0.027)

RR = risk reduction.

Microalbuminuria is a significant risk factor for cardiovascular events.

ACE-I inhibits the progression from microalbuminuria to macroalbuminuria.

ACE-I is recommended to all patients of diabetes with hypertension.

Patients with Type 2 Diabetes and hypertension treated with ACE-I have a significantly lower risk of major vascular events than those treated with B blockers or calcium channel blockers.
Take Home Messages

- Having Diabetes is as bad as having an AMI
- Death in DM patients is majority from acute coronary events
- IR plays major role in atherosclerosis
- Coronary events are more extensive and more fatal in DM patients
- Dietary and life style modification are vital
- Anti hypertensives should be judiciously selected
- Lipid lowering therapy should be aggressive
- Aspirin is also an important tool for CV prophylaxis
THANK YOU