Cardiovascular Complications in Diabetes

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The Challenge of Diabetes

- 2013 IDF estimates diabetes mellitus prevalence of:
  - 8.3% of population (382 million people)¹
- People with Type 2 Diabetes have a 2-4 times higher risk of CHD vs. non-diabetics²
- Diabetes is an established CAD equivalent

Major public health problem !!

Global Burden

- The number of people with type 2 diabetes is increasing in every country
- 383 million people have diabetes by 2035 this will rise to 592 MILLION
- 80% of people with diabetes live in low- and middle-income countries

Global Burden

The greatest number of people with diabetes are between 40 and 59 years of age

Cost of the disease

- Diabetes consumes 10% of total healthcare costs²
- CV disease consumes the greatest proportion of direct costs²

Diabetes caused at least USD 548 billion dollars in health expenditure in 2013 – 11% of total health spending on adults
Cardiovascular Diseases in Diabetes

Cardiovascular diseases that accompany diabetes are:
- Angina
- Heart attack
- Stroke
- Peripheral artery Disease
- Congestive heart disease

Aggravate the cardiovascular condition
- High Blood pressure
- High Cholesterol

Cardiovascular disease is the most common cause of death and disability among the people with Diabetes.

Diabetes Nepal 15th February, 2014

The Cardiovascular Disease Triad

Diabetes Nepal 15th February, 2014

Diabetes and Lifetime Risk for CHD

Diabetes Nepal 15th February, 2014

Cardiometabolic Risk

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Clinical Consequence

- People with diabetes have the same risk of heart attack as people without diabetes who have already had a heart attack.
- Women with diabetes are subject to sudden death 300% more often and men with diabetes 50% more often than their counterparts without diabetes of the same age.
- A person with diabetes has a two to three-fold greater risk of heart failure compared to a person without diabetes.
- Diabetes kills more people than AIDS and breast cancer combined.
Blood Pressure Screening and Management

- Patients with blood pressure 120/80 mmHg should be advised on lifestyle changes to reduce blood pressure.
- Patients with confirmed blood pressure >140/80 mmHg should, in addition to lifestyle therapy, have prompt initiation and timely titration of pharmacological therapy to achieve blood pressure goals.
- Blood pressure to 140mmHg systolic and 80 mmHg diastolic in individuals with diabetes.

CVD Risk factors and Risk reduction

- Adapted from Turnbull et al. Diabetologia. 2009;52(11):2288-98

Benefit of different interventions in Diabetics

- Per 4 mmHg lower SBP
- Per 1 mmol/L lower LDL-C

Stroke

- A leading cause of death in the United States
- Strokes occur twice as often in people with diabetes and hypertension as in those with hypertension alone.
- On average, someone suffers a stroke every 40 seconds in America
- A leading cause of adult disability
- Up to 80% of all strokes are preventable through risk factor management

Definition of Stroke

- Lack of blood flow to the brain caused by a clot or rupture of a blood vessel
- Ischemic = Clot (makes up approximately 87% of all strokes)
- Hemorrhagic = Bleed
  - Bleeding around brain
  - Bleeding into brain

Stroke Facts

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- On average, someone suffers a stroke every 40 seconds in America
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**TIA**

- Symptoms of TIAs are the same as stroke
- TIA symptoms can resolve within minutes or hours
- Transient ischemic attack (TIA) is a warning sign of a future stroke – up to 40% of TIA patients will have a future stroke
- It is important to seek immediate medical attention if you suspect that you are having or have had a TIA

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**Stroke Recovery**

- 10% of stroke survivors recover almost completely
- 25% recover with minor impairments
- 40% experience moderate to severe impairments requiring special care
- 10% require care within either a skilled-care or other long-term care facility
- 15% die shortly after the stroke

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**Peripheral Vascular Disease**

- Diabetes is the most common cause of amputation which is not the result of an accident.
- Diabetic are 15 to 40 times more likely to require a lower-limb amputation compared to the general population
- Every 30 seconds a foot is lost to Diabetes.
- The combination of nerve damage and insufficient blood supply leads to painful ulcers, infection and gangrene.
- Initial screening for PAD should include a history for claudication and an assessment of the pedal pulses

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**Major Metabolic Defects in Type 2 Diabetes**

- Decreased pancreatic insulin secretion
- Peripheral insulin resistance in muscle and fat tissue
- Deficient incretin hormones response
- Increased hepatic glucose output

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**Beyond glucose: Multiple risk factor intervention**

- Steno-2 Study (5yr follow up)
- Multiple drug combinations and behavior modification
**Risk Factors**

**Modifiable**
- Overweight
- Abnormal lipid metabolism
- Inflammation, hypercoagulation
- Hypertension
- Smoking
- Physical inactivity
- Unhealthy diet
- Insulin resistance

**Non-modifiable**
- Age
- Race/ethnicity
- Gender
- Family history

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**Obesity and Overweight**

- Measure BMI routinely at each regular check-up.
- Classifications:
  - BMI 18.5-24.9 = normal
  - BMI 25-29.9 = overweight
  - BMI 30-39.9 = obesity
  - BMI ≥40 = extreme obesity

- Large waist circumference can identify some at increased risk over BMI alone
- Measure WC in addition to BMI

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**The relationship BMI and the risk type 2 Diabetes**

- The graph shows the relationship between Body mass index (kg/m²) and the risk of type 2 diabetes.
- Women and men data are plotted separately.

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**Factors Associated with Obesity and CVD**

- Overnutrition
- Metabolic Disturbance
- Intermediate Vascular Disease Risk Factor
- Intravascular Pathology
- Clinical Event

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**Country/ethnic specific values for waist circumference**

<table>
<thead>
<tr>
<th>Country/Ethnic group</th>
<th>Waist circumference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Europids</td>
<td>Male 84 cm</td>
</tr>
<tr>
<td></td>
<td>Female 80 cm</td>
</tr>
<tr>
<td>Americans/Caucasians</td>
<td>Male 102 cm</td>
</tr>
<tr>
<td></td>
<td>Female 88 cm</td>
</tr>
<tr>
<td>South Asians</td>
<td>Male 90 cm</td>
</tr>
<tr>
<td></td>
<td>Female 80 cm</td>
</tr>
<tr>
<td>Japanese/Chinese</td>
<td>Male 90 cm</td>
</tr>
<tr>
<td></td>
<td>Female 80 cm</td>
</tr>
<tr>
<td>Ethnic South and Central Africans</td>
<td>Use South Asian recommendations</td>
</tr>
<tr>
<td></td>
<td>until more specific data are available</td>
</tr>
<tr>
<td>Sub-Saharan Africans</td>
<td>Use European data until more specific data are available</td>
</tr>
<tr>
<td>Eastern Mediterranean and Middle East (Arab) populations</td>
<td>Use European data until more specific data are available</td>
</tr>
</tbody>
</table>
**Landmark Statin Trials: LDL-C Levels vs. Events**

- **WOSCOPS-S**
- **WOSCOPS-P**
- **AFCAPS-S**
- **AFCAPS-P**
- **ASCOT-S**
- **ASCOT-P**

### Percentage with CHD Event

- **Primary prevention**
- **Pravastatin**
- **Lovastatin**
- **Atorvastatin**

### LDL-C, mmol/L (mg/dL) vs. Events

- **2.3 (90)**
- **2.8 (110)**
- **3.4 (130)**
- **4.0 (170)**
- **4.9 (190)**

### Comparison
- **ASCOT**
- **WOSCOPS**
- **AFCAPS**

**S = statin treated; P = placebo treated**

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**What do the guidelines recommend?**

- **ADA 2014 guidelines¹**
  - In most adult patients with diabetes, measure fasting lipid profile at least annually.
  - Meta-analyses from over 18,000 patients with diabetes from 14 randomized trials of statin therapy (mean follow-up 4.3 years), demonstrate a 9% reduction in all-cause mortality, and 23% reduction in vascular mortality, for each mmol/L reduction in LDL cholesterol.

- **ATP 4 guidelines²**
  - Use a risk calculator, and if > over 7.5% then use a high-intensity statin. Otherwise, diabetics should get a moderate-intensity statin.
  - For primary prevention in patients age 40-75 years, use a moderate- or high-intensity statin if they’re greater than 7.5%.

- **Meta-analyses from over 18,000 patients with diabetes from 14 randomized trials of statin therapy (mean follow-up 4.3 years), demonstrate a 9% reduction in all-cause mortality, and 13% reduction in vascular mortality, for each mmol/L reduction in LDL cholesterol.**

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**Statins and Diabetes**

**Are Asian Indians different?**

- Diabetic or atherogenic dyslipidaemia characteristically seen in Indians.
  - Indians have lower HDL-C compared with other South Asians.
  - South Asians: Insulin resistance is associated with raised TG and low HDL-C.

- **HeartSCORE and IndiaSCORE studies³**
  - 9% of Indians had HDL-C >50 mg/dL, while >70% of blacks and whites had HDL-C >50 mg/dL.
  - Higher serum triglycerides: compared with white or black.

- **Pattern of dyslipidaemia among Asian Indians relative to American whites**

<table>
<thead>
<tr>
<th>Lipid</th>
<th>Relative serum concentrations</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC</td>
<td>Similar</td>
</tr>
<tr>
<td>LDL</td>
<td>Similar</td>
</tr>
<tr>
<td>Small dense LDL</td>
<td>Similar</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>Higher</td>
</tr>
<tr>
<td>HDL</td>
<td>Lower</td>
</tr>
<tr>
<td>Lp (A)</td>
<td>Higher</td>
</tr>
</tbody>
</table>

- Triglycerides:
  - Age-adjusted CHD mortality rates increased from baseline 9.2 to 16.9 with increasing triglyceride quintile values.
  - Meta-analysis found a 7-fold increase in the risk as triglyceride concentrations increased from 131 to 299 mg/dL.

- **Non-HDL-C:**
  - Increase in non-HDL-C level by 1 mg/dl increases the risk of death due to cardiovascular disease by 5%.

- **LDL-C:**
  - 1% decrease in HDL-C is associated with a 2% to 3% increase in CHD risk.

- **Atherogenic dyslipidaemia:**
  - Each subfactor markedly increases the risk of mortality.

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**Beyond LDL-C**

CHD risk is predicted by lipid factors other than LDL:

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  - Age-adjusted CHD mortality rates increased from baseline 9.2 to 16.9 with increasing triglyceride quintile values.
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- Non-HDL-C:
  - Increase in non-HDL-C level by 1 mg/dl increases the risk of death due to cardiovascular disease by 5%.

- HDL-C:
  - 1% decrease in HDL-C is associated with a 2% to 3% increase in CHD risk.

- Atherogenic dyslipidaemia:
  - Each subfactor markedly increases the risk of mortality.
**Glycemic Control**

**The benefits of early tight control: UKPDS**

![Diagram showing the benefits of early tight control with UKPDS data](image1)

**Post-prandial Hyperglycemia**

- Elevated PPG levels, even in the absence of fasting hyperglycemia, increase the risk of cardiovascular disease and is an independent risk factor.
- Woerle et al., on post-meal glucose—PPG accounted for approximately 40% of HbA1c when HbA1c was >9.0
- Monnier et al.—PPG contributes to 30%–40% of the total daytime hyperglycemia; 40% contribution when HbA1c levels were above 9.3%.

**Smoking**

- Compared to non-smokers with diabetes, people with diabetes who smoke have twice the risk of premature death.
- The risk of complications is nearly 14 times higher than the risk of either smoking or diabetes alone.
- Risk of heart disease, which is further elevated if they smoke.
- Smoking-related risk of diabetes increases with the number of cigarettes smoked.
- Advise all patients not to smoke or use tobacco products.
- Include smoking cessation counseling and other forms of treatment as a routine component of diabetes care.
**Lifestyle**

- 3 new cases of diabetes is diagnosed every 10 secs or almost 10 million per year. Increase is mainly due to obesity and sedentary lifestyles.

**Lifestyle interventions**

- Modest weight loss (5%–10%) helps in reduction of glucose values.
- Foods high in fiber such as vegetables, fruits, whole grains and legumes, low-fat dairy products and fresh fish should be consumed.
- High-energy foods, including those rich in saturated fats, and sweet desserts and snacks should be eaten less frequently and in lower amounts.

**Hypoglycaemia**

- Increased risk among –
  - Elderly
  - African Americans
  - Less well educated
  - Longer duration of diabetes
  - Insulin therapy
  - Peripheral neuropathy
  - Renal dysfunction

**Who’s at risk?**

Risk factor profile for people at risk

- Increased risk among –
- Elderly
- African Americans
- Less well educated
- Longer duration of diabetes
- Insulin therapy
- Peripheral neuropathy
- Renal dysfunction

**Hypoglycaemia susceptibility**
Hypoglycemia – clinical consequences

- Hypoglycaemia has proarrhythmic effects
  - Q-T interval prolongation
  - Ca\(^{++}\) Channel overload
  - Suppression of K\(^{+}\) channel activation during repolarisation

- Autonomic nervous system over activation
  - Hypoglycemia associated with cognitive dysfunction and delayed recovery in the elderly
  - Hypoglycemia associated with increased anxiety
  - Hypoglycemia linked to pro-thrombotic and pro-inflammatory effects

Hypoglycaemia and mortality: the ACCORD experience

- **Overall mortality (%)**
  - **Never experienced severe hypoglycaemia**: 1.2%
  - **Experienced severe hypoglycaemia**: 3.3%

Treatment

- Consider ACE inhibitor therapy and use aspirin and statin therapy (if not contraindicated) to reduce the risk of cardiovascular events.
- In patients with a prior MI, b-blockers should be continued for at least 2 years after the event.
- In patients with symptomatic heart failure, avoid thiazolidinedione treatment.
- In patients with stable CHF, metformin may be used if renal function is normal but should be avoided in unstable or hospitalized patients with CHF.

Conclusion

- Consider aspirin therapy (75–162 mg/day) as a primary prevention at increased cardiovascular risk (10-year risk 10%).
- This includes most men aged 50 years or women aged 60 years who have at least one additional major risk factor
- Family history of CVD
- Hypertension
- Smoking
- Dyslipidemia
- Albuminuria
Conclusions

- Early tight glycaemic control is associated with a significant reduction in:
  - Total mortality, CV mortality, Vascular events
- In longstanding, high risk patients "too tight" or "too rapid tightening of" glycaemic control may increase the chance of arrhythmias/CV events and death, possibly due to increased risk of hypoglycemia
- Individualization of targets and therapies is vital
- Some drugs have the potential to improve glycaemic control with low risk of hypoglycemia and weight gain.

Thank you