Case Study: Hypertension and Diabetes
Case

Mr. MK, a 55-year-old man.

T2DM and hypertension for 10 years. Medications:
    Metformin 1 g bd
    Gliclazide 160 mg bd
    Amlodipine 10 mg daily

Referred for further management of poorly controlled diabetes and hypertension.
What are the possible causes for his poorly controlled diabetes and hypertension?

• Non-compliant to diet

• Non-compliant to treatment

• Hypoglycaemia?

• Underlying infections?

• Silent ischaemia?
• Social history:  Salesman
   Frequent travelling
   On and off missed his medications
   Diet not controlled

• Family history:  Mother – diabetic, on dialysis
    Father – stroke (residual left hemiparesis)
On examination:

- Obese
- Weight 98 kg, BMI 35 kg/m$^2$
- BP 160/90 mmHg
- PR 88 beats/minute
- Bilateral proliferative retinopathy
- Minimal bilateral leg oedema
- Other systemic examination: unremarkable
Investigation results:

- A1c: 9.2%
- FBS: 11.8 mmol/L
- Creatinine: 106 μmol/L
- e-GFR: 88 ml/min/1.73 m²
- 24h urinary protein: 200 mg/24h
- ECG: LVH
What are the issues that need to be addressed?

1. Poorly controlled diabetes with presence of microvascular complications

2. BP level not to target

3. Obesity could contribute to the poorly control diabetes and HPT

4. Need to explore any morbidities associated with the obesity (sleep apnoea, fungal infections etc)
Questions

What would be the A1c and BP target?

How would you manage him?

What would be the choices of anti-hypertensives or anti-diabetic agents?
Glycaemic Control

- Target A1c: $\leq 6.5\%$
- Add GLP1-receptor agonist or SGLT2-inhibitor
- Continue Metformin

Blood Pressure Control

- Target BP $\leq 135/75$ mmHg (based on ADVANCE ON trial)
- Pharmacological approach:
  - add ARB: Irbesartan 150 mg daily (renoprotection)
- Non-pharmacological approach
  - sodium restriction
  - exercise
  - weight loss
ADVANCE -
post trial ObservatioNal Study

BP Arm Results
11,140 underwent randomisation into the blood pressure control arm

5,569 assigned to Active
  - 408 patients died
  - 5,161 eligible for ADVANCE-ON
    - 883 non-participating patients and sites
    - 4,278 participated in ADVANCE-ON
      - 592 died
      - 1,048 no final visit
      - 2,638 at final visit, 2013

5,571 assigned to Placebo
  - 471 patients died
  - 5,100 eligible for ADVANCE-ON
    - 884 non-participating patients and sites
    - 4,216 participated in ADVANCE-ON
      - 623 died
      - 1,100 no final visit
      - 2,493 at final visit, 2013

N=11,140 (100%)
N=10,261 (92%)
N=8,494 (83% of those still alive)
N=5,131 (70% of those still alive in 2013)
## BP levels: in-trial and post trial
*(before and after stopping randomised treatment)*

<table>
<thead>
<tr>
<th>BP arm</th>
<th>BP level (mmHg) Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Active</td>
</tr>
<tr>
<td>Pre-randomization</td>
<td>145/81</td>
</tr>
<tr>
<td>Last randomized visit (after median of 4.4 years)</td>
<td>136/74</td>
</tr>
<tr>
<td>First ADVANCE-ON visit (a further 2.9 years later)</td>
<td>137/75</td>
</tr>
<tr>
<td>Final ADVANCE-ON visit (a further 3 years later)</td>
<td>137/74</td>
</tr>
</tbody>
</table>
Effects on Mortality

All cause mortality

Cardiovascular death

Relative risk reduction 14%; p=0.025

Relative risk reduction 18%; p=0.027

IRMA 2  Study Design

- 590 patients with hypertension, type 2 diabetes, microalbuminuria (albumin excretion rate 20–200 µg/min), and normal renal function

* Adjunctive antihypertensive therapies (excluding ACE inhibitors, angiotensin II receptor antagonists, and dihydropyridine calcium channel blockers) could be added to all groups to help achieve equal blood pressure levels.

IRMA 2 Primary Endpoint
Time to Overt Proteinuria

IRMA 2 Primary Endpoint
Development of Overt Proteinuria

IRMA 2
Normalisation of UAE Rate

Table 8 (A): Choice of antihypertensive drugs in diabetes patients with concomitant conditions (Adapted from Malaysian CPG for Hypertension 2008)

<table>
<thead>
<tr>
<th>Concomitant Disease</th>
<th>Diuretics</th>
<th>β-blockers</th>
<th>ACEIs</th>
<th>CCBs</th>
<th>Peripheral α-blockers</th>
<th>ARBs</th>
</tr>
</thead>
<tbody>
<tr>
<td>DM (without nephropathy)</td>
<td>+</td>
<td>+/-</td>
<td>+++</td>
<td>+</td>
<td>+/-</td>
<td>+++</td>
</tr>
<tr>
<td>DM (with nephropathy)</td>
<td>++</td>
<td>+/-</td>
<td>+++</td>
<td>+++*</td>
<td>+/-</td>
<td>+++</td>
</tr>
<tr>
<td>Gout</td>
<td>+/-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Dyslipidaemia</td>
<td>+/-</td>
<td>+/-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>+</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Heart failure</td>
<td>+++</td>
<td>+++#</td>
<td>+++</td>
<td>+@</td>
<td>+</td>
<td>+++</td>
</tr>
</tbody>
</table>

Grading of recommendation (+) to (+++) is based on increasing levels of evidence + current widely accepted practice

- +/- Use with care
- Contraindicated
- * Only non-dihydropyridine CCBs
- # Metoprolol, bisoprolol, carvedilol – dose needs to be gradually titrated
- @ Current evidence available for amlodipine and felodipine only
Take Home Messages

• Target A1c ≤ 6.5%

• Target BP ≤ 135/75 mmHg

• Most patients with hypertension will require two or more antihypertensive agents to achieve their BP goals

• Pharmacological treatment should comprise a regimen that includes either an ACEI or an ARB as first line.