Chronic Ischemic Cardiopathy & Acute Coronary Syndrome in Chronic Kidney Disease patients

Debasish Banerjee, Nephrologist
St Georges University Hospital NHS Foundation Trust and St Georges University of London UK
ACS & Chronic Ischaemia in CKD

• Epidemiology
• Mechanism and Risk Factors
• Clinical features
• Prognosis
• Investigations and Management
Case Study

SS, 54 y/F

- IgA nephropathy - 2007
- On haemodialysis, (wt 57 Kg, BP 128/50, Chol 4.1) - 2011
- Treated for skeletal tuberculosis - 2012
- Exercise stress test for transplant : 5 min, + test - 2014
- Dobutamine Stress test: + test 3/5/14

- Admitted with shortness of breath 26/6/2014
- Troponin 450: Angiogram 3 VD with calcification: 2 drug eluting stents, discharged, aspirin & clopidogrel for 6 mo
Cardiovascular event rates in CKD

Adjusted hazard ratio for cardiovascular events with decreasing eGFR in 1.1 mill patients over 2.8 y

Go et al NEJM 2004 351 1296
Mortality and CV deaths in CKD

105,872 participants 14 studies 730,577 person years

CKDPC Lancet 2010 375 2073
CVD mortality is very high on Dialysis

CVD mortality in dialysis patients (USRDS) compared to the general population (NCHS)

Foley et. al., 1998 Am J Kid Disease 32
Prevalence of CAD in CKD

Asymptomatic patients on HD (67) and CKD 5 (31)

- HD
  - No CAD: 39
  - 1 vessel: 7
  - 2 vessel: 10
  - 3 vessel: 11

- CKD 5
  - No CAD: 15
  - 1 vessel: 10
  - 2 vessel: 4
  - 3 vessel: 2

deFilippi JAMA 2003 290 353
Ohtake JASN 2005 16 1141
Coronary atherosclerosis; outcome

50 patients (78% diabetes) 40% +DSE; 6/27 had events over $22 \pm 10$ m 12%/year

Sensitivity /specificity of CAD diagnosis = 75/76%
Case Study: Atherosclerosis in CKD

SS, 54 y/F

- IgA nephropathy - 2007
- On haemodialysis, (wt 57 Kg, BP 128/50, Chol 4.1) - 2010
- Treated for skeletal tuberculosis - 2012

Patients radial artery in 2010 (b) showing intimal hyperplasia compared to (a)
Mechanism and Risk Factors

CVD Risk factors in CKD

Endothelial dysfunction

Inflammation and repair

Intimal hyperplasia

Atherosclerosis MI/CVA/PVD

Age, Gender
Hypertension
Diabetes
Smoking
Lipids

Inflammation
Oxidative stress
Anaemia
Insulin resistance
Calcification
PTH, Ca, FGF 23
Vitamin D Deficiency
Endothelial dysfunction in CKD

Flow Mediated Dilation, %

Controls: 5.4
Predialysis: 3.3
Dialysis: 0.7
Transplant: 3.1

FMD decreases with dialysis and improves with transplantation

Recio-Mayoral & Banerjee et al Atherosclerosis 2011 216(2) 446
Mechanism of Endothelial Dysfunction

FMD decreases with increasing HOMA-IR n=70
CRP can inhibit insulin mediated NO release via PI3K by inhibiting Akt

FMD decreases with decreasing Vitamin D=50

FMD decreases with increasing CRP n=78
Clinical features of ACS in CKD

NSTEMI is commoner in CKD patients and increases with decreasing eGFR

49,491 ACS patients from US

Fox Circulation 2010 121 357
Clinical features of ACS on admission

<table>
<thead>
<tr>
<th>Characteristics (%)</th>
<th>Dialysis N=2390</th>
<th>CKD 29 319</th>
<th>No CKD 274 717</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>STEMI</td>
<td>18</td>
<td>16</td>
<td>32</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Chest pain</td>
<td>41</td>
<td>40</td>
<td>62</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MI diagnosis</td>
<td>20</td>
<td>23</td>
<td>40</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>52</td>
<td>52</td>
<td>27</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

USRDS and Third National Registry of MI US 1998-2000

Shroff and Herzog AHJ 2012
Clinical features of ACS on admission

Renal function and its relation to symptoms, ECG in ACS

SWEDEHEART Registry

Szummer J Int Med 2010 268 40
In hospital events of ACS 1998-2000

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<thead>
<tr>
<th>Characteristics (%)</th>
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<th>P value</th>
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</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>21</td>
<td>23</td>
<td>12</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Length of Stay</td>
<td>8.4 days</td>
<td>8.3 days</td>
<td>6.4 days</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bleeding</td>
<td>4.4</td>
<td>4.9</td>
<td>3.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypotension</td>
<td>25</td>
<td>20</td>
<td>15</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VT/VF</td>
<td>9</td>
<td>6</td>
<td>6</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

USRDS and Third National Registry of MI US 1998-2000

Shroff and Herzog AHJ 2012
In-hospital mortality in CKD

High in-hospital mortality with deceasing kidney function
49,491 ACS patients from US

Fox Circulation 2010 121 357
## Treatment of ACS 1998-2000

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<thead>
<tr>
<th>Characteristics (%)</th>
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<th>No CKD 274 717</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiogram</td>
<td>26</td>
<td>17</td>
<td>33</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Aspirin</td>
<td>66</td>
<td>66</td>
<td>78</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Beta Blockers</td>
<td>56</td>
<td>53</td>
<td>63</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ACEi/ARB</td>
<td>40</td>
<td>43</td>
<td>62</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

USRDS and Third National Registry of MI US 1998-2000

Shroff and Herzog AHJ 2012
Mortality after MI in Dialysis

High mortality 73% at 2 years after MI | 34,189 US patients

Herzog NEJM 1998 339 799
Mortality, management MI+HF in CKD

Post ACS survival in CKD in 14,527 patients with MI and CHF
Lowest use of aspirin, statin, BB, revascularisation in CKD

Anavekar NEJM 2004 351 1285
Mortality post MI - comparison

2y mortality (%) post MI in CKD

- HD: 73%
- CKD 4: 40%
- Tx: 33.6%
- General Population: 16%

Gottlieb NEJM 1998; 339: 489
Herzog AJKD 2000; 36 145
Herzog NEJM 1998; 339 799
Management of Risk Factors for CAD

17% reduction in major atherosclerotic events in 9270 patients over 4.9 y with 0.85 mmol/L reduction in LDL cholesterol

Baigent Lancet 2011 377 2181
Management of risk factors for CAD

- Salt restriction
- Blood pressure control
- Control of diabetes (not <7%)
- Exercise
- Weight loss
- Stop smoking
Revascularisation for CAD

657 patients, 181 predialysis, 103/184 significant CAD most asymptomatic
Patients who declined intervention 16/184 had HR 6.7 for CV event 6.0 mortality

Kumar CJASN 2011 6 1912
## Revascularisation - comparison

<table>
<thead>
<tr>
<th>Study</th>
<th>Strategies</th>
<th>Number</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shroff 2013</td>
<td>CABG, BMS, DES</td>
<td>23033 HD</td>
<td>CABG (IMG+) better</td>
</tr>
<tr>
<td>Chang 2012</td>
<td>CABG, PCI</td>
<td>21981 HD</td>
<td>CABG better</td>
</tr>
<tr>
<td>Sunagawa 2010</td>
<td>CABG, DES</td>
<td>94 HD</td>
<td>CABG better</td>
</tr>
<tr>
<td>Ashriworth 2010</td>
<td>CABG, DES</td>
<td>812 CKD/HD</td>
<td>No significant difference</td>
</tr>
<tr>
<td>Manabe 2009</td>
<td>CABG, DES</td>
<td>46</td>
<td>CABG lower events</td>
</tr>
<tr>
<td>Aoki 2005</td>
<td>CABG Stent</td>
<td>142 CKD</td>
<td>No difference</td>
</tr>
<tr>
<td>Himmelgran 2004</td>
<td>CABG, PCI, None</td>
<td>1421</td>
<td>CABG better in CKD</td>
</tr>
<tr>
<td>Herzog 2002</td>
<td>CABG Stent PTCA</td>
<td>15000 HD</td>
<td>CABG better</td>
</tr>
</tbody>
</table>

*Observational studies comparing strategies of revascularisation; CABG particularly with IMG is better*
Revascularisation trends in US

USRDS 23033 dialysis patients 6178 CABG 5011 BMS 11,844 DES

Shroff Circulation 2013 127 1861
Survival after revascularisation

USRDS 23033 dialysis patients 6178 CABG, 5011 BMS, 11844 DES

Long term survival is poor in all groups, slightly improved with CABG (IMG)

Shroff Circulation 2013 127 1861
# Pharmacotherapy in CKD with ACS

<table>
<thead>
<tr>
<th>Medication Class</th>
<th>Summary of available evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>Should be used</td>
</tr>
<tr>
<td>Fibrinolytic</td>
<td>Can be used if no PCI (more bleeding than non CKD)</td>
</tr>
<tr>
<td>Clopidogrel (P2Y$_{12}$i)</td>
<td>Should be used, newer agents in non dialysis CKD only</td>
</tr>
<tr>
<td>Glycoprotein IIb/IIIa</td>
<td>Can be used with dose adjustment in CKD (more bleeding)</td>
</tr>
<tr>
<td>Anticoagulant</td>
<td>Should be used with dose adjustment (less bleeding with fondaparinux and bivalirudin in CKD 3)</td>
</tr>
<tr>
<td>Beta blocker</td>
<td>Should be used</td>
</tr>
<tr>
<td>ACEi/ARB</td>
<td>Should be used with LVF (monitor K)</td>
</tr>
<tr>
<td>Aldosterone blocker</td>
<td>Should be considered with LVF, limited data (monitor K)</td>
</tr>
<tr>
<td>Statin</td>
<td>Should be considered</td>
</tr>
</tbody>
</table>

**AHA Scientific Statement**

Limited evidence no RCT

Washam Circulation 131 1123
ACS & Chronic Ischaemia in CKD

- Incidence is high; prognosis is poor
- Multiple risk factors, mainly non-traditional
- Endothelial dysfunction is common (reversible)
- Coronary disease is diffuse
- Clinical features, asymptomatic, more NSTEMI
- Less revascularisation, antiplatelets, BB, ACEi
- High mortality even with revascularisation (CABG better)
- We need better understanding, better treatment
Thank you

Questions?
Management of ACS and CAD in CKD

Two first patients with implanted pacemakers in UK – St Georges Hospital

Courtsey Science Museum London
Acknowledgements

Juan Carlos Kaski
Marek Malik
David Goldsmith
Geeta Hampson
Dimitrios Poulakakos
Alejandro R Mayoral
Nihil Chitalia
Azhar Ali

All CKD and dialysis patients from St Georges
Survival after diagnosis

Survival of patients with cardiovascular diagnoses & procedures, by modality, 2009–2011

- CHF
- CVA/TIA
- PAD
- Cardiac arrest
- AMI
- Coronary revascularization: PCI
- Coronary revascularization: Surgical
- ICD/CRT-D

Survival probability vs. Months

Hemodialysis
Peritoneal dialysis
Transplant