Cardiovascular Risk Factors in Chronic Renal Patients

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The Heart & The Kidney: Fatal Twins?

Chronic Kidney Disease
- ESRD
- CRI (↓ GFR)
- Albuminuria, Proteinuria
- Elderly, DM, HTN

Cardiovascular Disease
- CHF
- ASCVD Events
- CAD, LVH
- Elderly, DM, HTN

Initiation
- "At-risk"

Progression
- End-stage

Chronic Kidney Disease
- Cardiovascular Disease
### Chronic kidney disease and CV risks

<table>
<thead>
<tr>
<th>Traditional risk factors</th>
<th>Non-traditional risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Age</td>
<td>• Microalbuminuria / Proteinuria</td>
</tr>
<tr>
<td>• Sex</td>
<td>• Renal dysfunction</td>
</tr>
<tr>
<td>• Hypertension</td>
<td>• Ca/phosphate metabolism</td>
</tr>
<tr>
<td>• Dyslipedemia</td>
<td>• Anaemia</td>
</tr>
<tr>
<td>• Diabetes</td>
<td>• Hyperuriceamia</td>
</tr>
<tr>
<td>• Smoking</td>
<td>• Inflammation</td>
</tr>
<tr>
<td>• Physical activity</td>
<td>• Salt and water overload</td>
</tr>
<tr>
<td>• Family history of CVD</td>
<td>• Oxidative stress</td>
</tr>
<tr>
<td>• LVH</td>
<td>• Malnutrition</td>
</tr>
<tr>
<td></td>
<td>• Risks of therapiotic intervention</td>
</tr>
</tbody>
</table>
Multiple risk factors: Additive risk

The total severity of multiple low-level risk factors often exceeds that of a single severely elevated risk factor.

Prevalence of hypertension in chronic renal diseases

MCN=minimal change nephropathy  CIN=chronic interstitial nephritis  IgA=IgA nephropathy  MGN=membranous glomerulonephritis  APKD=adult-onset polycystic kidney disease  DN=diabetic nephropathy  MPGN=membranoproliferative glomerulonephritis  FSGN=focal segmental glomerulonephritis

Risk factors for progressive hypertensive nephrosclerosis

1. Genetic:
   - Polymorphism of ACE gene (DD genotype):
   - Over-expression of sodium-hydrogen exchange (NHE) system (increases Na absorption).
   - Increased sodium-lithium counter transport.

2. Biochemical:
   - Lipid pattern.
   - Hyperuricemia
   - Endothelial dysfunction
   - Microalbuminuria.

3. Clinical:
   - Blacks.
   - Salt sensitivity.
   - Low birth weight.
   - Obesity.
   - Smokers.
Meta Analysis: Lower Mean BP Results in Slower Rates of Decline in GFR in Diabetics and Non-Diabetics

- **GFR (mL/min/year)**
- **MAP (mmHg)**


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Meta Analysis: Lower Systolic BP Results in Slower Rates of Decline in GFR in Diabetics and Non-Diabetics

![Graph showing the relationship between systolic blood pressure (SBP) and glomerular filtration rate (GFR). The graph displays a linear regression line with data points indicating a negative correlation. The equation for the line is $r = 0.69; P < .05$.]


Hypertensive Patients with New-onset Diabetes Have Similar CV Risk as Patients with Existing Diabetes

Patients with new or prior diabetes were ≈3-times more likely to have a CV event than those without diabetes

## Estimated prevalence (%) of lipoprotein abnormalities

<table>
<thead>
<tr>
<th>Category</th>
<th>TC &gt; 240 mg%</th>
<th>LDL-C &gt; 130 mg%</th>
<th>HDL-C &lt; 35 mg%</th>
<th>TG &gt; 200 mg%</th>
</tr>
</thead>
<tbody>
<tr>
<td>General population</td>
<td>20</td>
<td>40</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>20</td>
<td>30</td>
<td>50</td>
<td>45</td>
</tr>
<tr>
<td>Peritoneal dialyses</td>
<td>25</td>
<td>45</td>
<td>20</td>
<td>50</td>
</tr>
<tr>
<td>Renal transplant</td>
<td>60</td>
<td>60</td>
<td>15</td>
<td>35</td>
</tr>
</tbody>
</table>

Potential ameliorative effects of VDR activation on arterial disease

<table>
<thead>
<tr>
<th>Arterial disease</th>
<th>VDR activation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Atheroma formation</strong></td>
<td></td>
</tr>
<tr>
<td>Inducers</td>
<td></td>
</tr>
<tr>
<td>Th1 cells</td>
<td>↓ (by ↓ IFNγ)</td>
</tr>
<tr>
<td>IL-1β, IL-6</td>
<td>↓</td>
</tr>
<tr>
<td>Inhibitors</td>
<td></td>
</tr>
<tr>
<td>Th2 cells</td>
<td>↑ (by ↑ IL-10)</td>
</tr>
<tr>
<td>IL-4</td>
<td>↑</td>
</tr>
<tr>
<td><strong>Thrombogenesis</strong></td>
<td>↓</td>
</tr>
</tbody>
</table>
Hyper homocystinaemia

**Mechanism of vascular injury:**
- Impairment of nitric oxide production.
- Direct injury by free radicals (oxidation of reduced Hcy).
- Pro-aggrigatory effect on platelets.
- Formation of aggregates with LDL cholesterol taken by foam cells.
- Prothrombolic effects.
## Definition of microalbuminuria

<table>
<thead>
<tr>
<th>Category</th>
<th>24-hour urines</th>
<th>Urine spot</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mg/24 hours</td>
<td>µg/min</td>
</tr>
<tr>
<td>Normal</td>
<td>&lt;30</td>
<td>&lt;20</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td>30–300</td>
<td>20–200</td>
</tr>
<tr>
<td>Macroalbuminuria</td>
<td>&gt;300</td>
<td>&gt;200</td>
</tr>
</tbody>
</table>
Cardiovascular risk factors that cluster with microalbuminuria

- General obesity.
- Insulin resistance.
- Low HDL cholesterol.
- High triglyceride levels.
- Systolic HTN.
- Absent nocturnal drop in BP.
- Salt sensitivity.
- Male sex.
- Increased CV oxidative stress.
- Impaired endothelial function.
- Abnormal coagulation/fibrinolytic profiles.
- Left ventricular hypertrophy.
- Smoking.
# Predictive Value of Microalbuminuria 20-199 mcg/min

<table>
<thead>
<tr>
<th>Disease</th>
<th>Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cardiovascular</td>
</tr>
<tr>
<td>Hypertension</td>
<td>++</td>
</tr>
<tr>
<td>Type 2 DM</td>
<td>++</td>
</tr>
<tr>
<td>Type 1 DM</td>
<td>+</td>
</tr>
</tbody>
</table>
S. creat >124 µmol/L

Microalbuminuria

Both

Systolic and diastolic BP NOT significant risk factors

HR for primary outcome (CV death, MI, stroke)

Renal dysfunction and cardiovascular disease
Kidney disease is an independent risk factor

- **Framingham heart study:**
  - Patients with SCr 1.4 - 3.0:
    - Prevalence of CVD was 18-20% vs 8-14% in controls.

- **HOPE study:**
  - 980 pts with 1.4 < SCr < 2.3:
    - Higher incidence of CV death, MI, stroke.

- **RR for CVS events in CRD stages:**
  - Greater than general population (G. Bakris, 2003; NephSAP):
    - 16% in stage II.
    - 38% in stage III & IV.

Even mild renal insufficiency ⇒ increased CV mortality

50-75 years
n=631, age, sex and glucose tolerance stratified
follow up 10 years
RR CV death
1.11 per 5 µmol/l increase S-creatinine
1.26 per 5 ml/min/1.73m² decrease GFR

Increased mortality of acute MI even at low normal eGFR
Cardiovascular Death by Scr at One Year Post Transplant

% Cardiovascular death free survival

Months post-transplant

Scr mg/dl @1 year

<1.3
1.3-1.4
1.5-1.6
1.7-1.8
1.9-2.1
2.2-2.5
2.6-4.0