Pre-Op Assessment of The Patient With Renal Disease

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What Do We Mean By Kidney Disease?
Do We Mean the ESRD Patient....
The Dialysis Patient

- High Mortality Risk
  - (8 studies: 4% ranging from 0-47% in emergency cases)

- High Morbidity rate
  - 54% (12-64%)

- Cardiac surgery greatest risk
  - Mortality risk 10% Morbidity rates 46%
  - Mortality associated with valvular repair twice that of CABG
Why So High?

- High incidence of coronary artery disease & myocardial dysfunction
- Difficulty adjusting fluid/electrolytes in the perioperative period in anephric patients
- Hyperkalemia is the most common complication possibly requiring immediate postoperative dialysis
Why So High?

- Failure to normally excrete and/or metabolise anaesthetics and analgesics
- Increased bleeding complications
- Poor blood pressure control
Pre Op Assessment

- Anaemia status
- Boost the Hb
  - Use of additional erythropoiesis-stimulating agents (ESAs)
  - Transfusions are frequently necessary
  - Postop is characterized by ESA resistance
Pre Op Assessment

- **Nutrition**
  - Maximise healing by ensuring that the dialysis patient is well-nourished
  - Related to the delivery of appropriate amounts of dialysis
Pre Op Assessment

- Intensive dialysis
- ? improves outcomes

Recommendations:
- Daily dialysis for a few days prior to cardiac surgery
- Intraoperative hemodialysis during cardiac surgery
Do We Really Mean This?

Probably Not...
We Mean This...

**Diabetic chronic kidney disease**
- Diabetic nephropathy (type 1 or 2 diabetes mellitus)

**Non-diabetic chronic kidney disease**

**Vascular**
- With or without haematuria or proteinuria
  - Large-vessel disease (renal artery stenosis)
  - Small-vessel disease (hypertension, vasculitis, microangiopathy)

**Glomerular**
- Haematuria or albuminuria
  - Primary nephritis (IgA nephropathy)
  - Autoimmune disorders (connective tissue disease)
  - Systemic infection (bacteria, virus, parasite)
  - Malignant disease (solid organ, haematological)
  - Drugs
  - Hyperfiltration (reduced renal mass, obesity)

**Tubulointerstitial**
- With or without mild proteinuria or pyuria
  - Autoimmune disorders (connective tissue disease, granulomatous disease)
  - Drug toxic effects (analgesics, metals)
  - Chronic infection (bacteria, virus, parasite)
  - Obstructive nephropathy (chronic urinary-tract obstruction)
  - Post-acute kidney injury (ischaemic/toxic injury)

**Cystic**
- Evident on renal imaging
  - Polycystic kidney disease (autosomal dominant polycystic kidney disease)
<table>
<thead>
<tr>
<th>Stage</th>
<th>GFR</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>90+</td>
<td>Urine Abnormality, Structural Abnormality, Genetic Trait</td>
</tr>
<tr>
<td>2</td>
<td>60-89</td>
<td>As above, Mildly Reduced Function</td>
</tr>
<tr>
<td>3a(p)</td>
<td>45-59</td>
<td>Moderate Reduced Function</td>
</tr>
<tr>
<td>3b(p)</td>
<td>30-44</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>15-29</td>
<td>Severely Reduced Function</td>
</tr>
<tr>
<td>5</td>
<td>&lt;15</td>
<td>Endstage</td>
</tr>
<tr>
<td>Stage</td>
<td>GFR</td>
<td>Description</td>
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<tr>
<td>3</td>
<td>&lt;15</td>
<td>Endstage</td>
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<tr>
<td>Stage</td>
<td>Findings</td>
<td></td>
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<td>-------</td>
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</tr>
<tr>
<td>1</td>
<td>HT More Frequent</td>
<td></td>
</tr>
</tbody>
</table>
| 2     | HT More Frequent  
Mild Elevation PTH |
| 3     | HT Common  
Decreased Calcium absorption  
Decreased Phosphate excretion  
Increased PTH  
Renal Anaemia  
LVH |
| 4     | Metabolic Acidosis  
Hyperkalaemia |
| 5     | Salt & Water Retention  
Anorexia  
Vomiting Pruritus |
How Common?

- 43.8% Diabetes
- 26.8% High blood pressure
- 7.6% Glomerulonephritis
- 2.3% Cystic diseases
- 2.0% Urologic diseases
- 17.5% Other
Quite Common...
More CKD Patients Admitted...
And it’s an Expensive Business…
Increases With Age
Chronic Kidney Disease

- Increasingly Common
- More In-Hospital Episodes
- Increases With Age

So many of the patients you will see will be old with CKD.....
The Ageing Kidney

Let's consider what happens to our kidneys as we get older.

By the end of this lecture I don't expect to tell you anything you don't already know.
RENAL FUNCTION DETERIORATES WITH AGE
Thanks for your Attention
The Ageing Kidney

- Renal function declines substantially with age

- Usually sufficient for:
  - Removing bodily wastes
  - Regulating ECF
  - Regulating Acid-Base
Old kidneys have decreased physiological reserve and thus increased clinical sequelae to renal insult
The Ageing Kidney: Blood Flow

- Renal blood flow 1200ml/min in our 30's
- By age 80 it has fallen to about 600mls
The Ageing Kidney: Blood Flow

Kidney size decreases from 250g to 180g from age 30 to age 70. The loss is primarily cortical (Ultrafiltration) and the Medulla is relatively spared (Salt & Water balance).

<table>
<thead>
<tr>
<th>JM Region: Formation of direct channels between AA and EA</th>
<th>agglomerular arterioles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortex: Atrophy of both AA and EA → global sclerosis</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Forms of Efferent Arterioles</th>
<th>Juxtamedullary Type</th>
<th>Cortical Type</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tr>
</tbody>
</table>

[Diagram showing forms of efferent arterioles with Juxtamedullary and Cortical types illustrated]
Ageing Kidney: Vascular Changes

Results in decreased blood flow per g of remaining tissue.

- Changes more pronounced in the cortical vasculature than the medullary.
- Consistent with histology changes which show selective loss of cortical vasculature with age.

The percentage of sclerosed glomeruli increases with age, but with wide variability.
Ageing Kidney: Vascular Changes

The ageing kidney is also highly susceptible to smaller changes in renal perfusion pressure than in youth...
Ageing Kidney: Vascular Changes

CKD (and normal aging): Dilated afferent arteriole allows transmission of high systemic pressure, resulting in glomerular capillary hypertension.

More Susceptible to Hypoperfusion
Ageing Kidney: GFR Changes

- The number of actual glomeruli decreases
- The number of sclerosed glomeruli increases
  - 1% at age 4
  - 12% by age 70
Ageing Kidney: GFR Changes

Declines by about 8ml/decade from age 40
Is this explosion real?

Or a reflection of the aging population…?
Ageing Kidney: Tubular Changes

- Deteriorates with Age
- Concentrating ability decreases
- Impaired ability to conserve salt and water
Ageing Kidney: RAS System

- Vulnerable to volume depletion
- Thirst response to increased osmolality or volume depletion is reduced in the elderly
Ageing Kidney: RAS System

- GFR affects $K^+$ excretion
- Ageing kidney is slower at dealing with acidosis
- Therefore an increased tendency to hyperkalaemia
CKD: Patients At Risk!!

Less Physiological Reserve

Lower GFR & RBF

Reduced Ability to Preserve Volume

Greater Tendency to Acidosis

Greater Tendency to Hyperkalaemia
In The Patient With CKD?

What Strategies Can We Employ to Improve Outcome?
Strategies For Improvement

- Depends on time scale
- Depends on ‘urgency’ of surgery

- Depends on your relationship with a friendly nephrologist
We Do Know CKD is Bad

- Increased mortality risk
- Even small changes in creatinine are significant
Strategies For ‘Improvement’: Examples

- In diabetes we know intervention can ‘protect’ the kidneys...
- Protects does not improve 18 Week Pathway??

ACE inhibitor slows progression of nephropathy

18 Week Pathway??
Protein restriction slows progression of diabetic nephropathy

Dietary restriction of protein to 0.6 to 0.8 g/kg/day and tight glycemic control of patients with type 2 diabetes and diabetic nephropathy led to a 75 percent reduction in the rate of loss of glomerular filtration rate (GFR) at 18 to 36 months.

Strategies For ‘Improvement’:

Examples

In Hypertension we know intervention can ‘protect’ the kidneys…

Protects does not improve

Mean fall in glomerular filtration rate (GFR) according to the degree of proteinuria in patients treated with usual blood pressure control (mean BP about 130/80) or with more aggressive antihypertensive therapy in which the mean BP was 4.7 mmHg lower over a three year period. The rate of fall in GFR varied directly with protein excretion and the benefit of aggressive BP control was absent in the 420 patients excreting less than 1 g/day, modest in the 104 patients excreting between 1 and 3 g/day, and substantial (3.5 mL/min per year slower) and statistically significant in the 54 patients excreting at least 3 g/day.

ACE inhibitor and calcium blocker therapy protect against progressive glomerulosclerosis in rats by different mechanisms.

At eight weeks, both drugs lowered the blood pressure to an equivalent degree and were associated with better maintenance of the glomerular filtration rate (GFR) and a lesser degree of glomerulosclerosis than untreated rats. However, the mechanism of protection appeared to be different: enalapril lowered the glomerular capillary pressure (PGC), while nifedipine minimized glomerular hypertrophy as manifested by a reduction in glomerular volume.

What do we do with our CKD patient who needs Emergency Surgery?

- Limited Time
- Potentially at high risk
- AKI & Mortality
Factors Increasing Susceptibility to Renal Hypoperfusion

- Failure to Decrease Arteriolar Resistance

- Structural Changes
  - Old Age
  - Atherosclerosis
  - Chronic HT
  - CKD(!!)
  - Malignant / Accelerated HT
Factors Increasing Susceptibility to Renal Hypoperfusion

- Failure to Decrease Arteriolar Resistance
- Reduction in vasodilatory PGE’s
  - Cox-2 Inhibitors
  - Devil’s Medicines
Factors Increasing Susceptibility to Renal Hypoperfusion

- Failure to Increase Efferent Arteriolar Resistance
- ACE Inhibitors
- ARB’s
- RAS
Strategies For Treatment

How Do We Prevent AKI?
Post Operative AKI

- Often (always) multifactorial
- Can we expect to find a ‘cure-all’??
- No
- What has been tried
Vasoactive Drugs

Diuretics

NAc, Statins, Ascorbate

EPO, IgF-1, Insulin

Renal Vasodilators

five criminals. one line up. no coincidence
No Evidence In Patients of Any Benefit

MESNA
Retinoic Acid
Carvedilol
Statins
Spironolactone
Pentoxifyline
AND MANY OTHERS

No Evidence In Patients of Any Benefit
High-dose Furosemide in patients with Established AKI

Table 2. Study End Points in the Population Assessable for Efficacy With Stratification According to SAPS

<table>
<thead>
<tr>
<th></th>
<th>Furosemide (n = 166)</th>
<th>Placebo (n = 164)</th>
<th>Significance (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients alive at the end of the study (n = 221)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAPS ≤15</td>
<td>60</td>
<td>67</td>
<td>0.36*</td>
</tr>
<tr>
<td>SAPS &gt;15</td>
<td>47</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>107</td>
<td>114</td>
<td></td>
</tr>
<tr>
<td>Deaths (n = 109)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAPS ≤15</td>
<td>16</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>SAPS &gt;15</td>
<td>43</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>59</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>No. of RRT sessions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAPS ≤15</td>
<td>5.6 ± 5.5</td>
<td>5.7 ± 4.5</td>
<td>0.37†</td>
</tr>
<tr>
<td>SAPS &gt;15</td>
<td>7.3 ± 5.3</td>
<td>7.9 ± 5.6</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>6.5 ± 5.4</td>
<td>6.9 ± 5.3</td>
<td></td>
</tr>
<tr>
<td>Time on RRT (d)</td>
<td>11.4 ± 8.6</td>
<td>12.4 ± 8.7</td>
<td>0.21†</td>
</tr>
<tr>
<td>Time to achieve a serum creatinine level &lt;2.26 mg/dL without RRT (d)</td>
<td>19.7 ± 40.6</td>
<td>21.4 ± 65.1</td>
<td>0.99†</td>
</tr>
<tr>
<td>Time to achieve a 2-L/d diuresis (d)</td>
<td>5.7 ± 5.8</td>
<td>7.8 ± 6.8</td>
<td>0.004†</td>
</tr>
</tbody>
</table>

Cantarovic F, Am J Kidney Dis 2004
Results. Renal recovery, the need for dialysis, and death were no different in the three groups. Patients given a loop diuretic had a significant rise in urine flow rate in the first 24 h compared to placebo ($P = 0.02$). Based on the urine flow rate during the first post-medication day patients were divided into two groups - oliguric ($< 50 \text{ ml/h}$) and non-oliguric ($\geq 50 \text{ ml/h}$). Non-oliguric patients had a significantly lower mortality than oliguric patients ($43\% \text{ vs } 69\%, P = 0.01$). However, they were less ill (APACHE II score $17.2 \text{ vs } 20.6, P = 0.008$) and had less severe renal failure at entry (creatinine clearance $14 \text{ ml/min} \text{ vs } 4 \text{ ml/min}, P < 0.0001$).

Conclusion. The use of loop diuretics in oliguric patients with ARF can result in a diuresis. There is no evidence that these drugs can alter outcome.
Furosemide for Prevention/ Treatment of AKI

No Difference In: Need for RRT Mortality

HO KM, BMJ 2006
Diuretics and AKI

- Despite Repeated Trials...

- We cannot believe it... They must work...
Dopamine

• Rationale
• ? Preferential Renal Vasodilatation
• ? Evidence
Effect of ‘low-dose’ dopamine on Renal Resistive Index

norepinephrine \((n = 20)\). In conclusion ‘low-dose’ dopamine can worsen renal perfusion in patients with ARF, which adds to the rationale for abandoning the routine use of ‘low-dose’ dopamine in critically ill patients.


Figure 5 | Effect of dopamine on RI values in patients with and without norepinephrine (NE) infusion.
DOPAMINE DOES NOT PREVENT AKI

RCT - dopamine 2μg/kg/min throughout ITU stay

...And No Effect on the development of AKI

Lancet 2000;356:2139
Mechanisms AKI

- Inadequate Renal Perfusion
- SEPSIS
- Nephrotoxins

Often Multifactorial...

Acute Kidney Injury
Preoperative tests
The use of routine preoperative tests for elective surgery
ASA Grade 2: adults with comorbidity from renal disease

<table>
<thead>
<tr>
<th>Test</th>
<th>16 to &lt;40</th>
<th>40 to &lt;60</th>
<th>60 to &lt;80</th>
<th>80</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest X-ray</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ECG†</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Full blood count</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Haemostasis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal function</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Random glucose</td>
<td></td>
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<tr>
<td>Urine analysis</td>
<td></td>
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<tr>
<td>Blood gases</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung function</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

†Depending on the cause of renal disease (e.g., diabetes and hypertension)
PreOperative Tests

- Nephrologists love urinanalysis…
- Should it be ‘considered’ or recommended?
- I think it should be mandatory…
Remember This?

Primary Causes of Kidney Failure (2005)

- 26.8% High blood pressure
- 7.6% Glomerulonephritis
- 2.3% Cystic diseases
- 2.0% Urologic diseases
- 17.5% Other
- 43.8% Diabetes
Diabetic Renal Disease

Insulin dependent diabetes

- Risk 4% if diabetic for 35+ years
- Risk higher in men
- ESRD more likely if diagnosed 11-20yr
- Time from proteinuria to dialysis is 7-14 years
- 80% develop ESRD if persistently microalbuminuric
Diabetic Renal Disease

Non Insulin dependent diabetes

- Less well studied

- Prevalence nephropathy increases steadily with duration of diabetes
  - 10% at 5 years
  - 30% at 20 years
Diabetes & the Kidney
Non Insulin dependent diabetes

- Once they develop proteinuria..
- 32% die within 4 years of microalbuminuria
- 50% die within 4 years of macroalbuminuria

Just think about that.....
What do they die From?

**Probability of MI**

**Probability of CCF**

In all cases having diabetes increases your risk
So, diabetes is really bad for you...and your kidneys

So it must be really really bad after an operation if you end up in the ICU.
Who Agrees with that Statement?
So….Diabetes is bad for you: Right?

Insulin-treated diabetes is not associated with increased mortality in critically ill patients

Jean-Louis Vincent¹*, Jean-Charles Preiser², Charles L Sprung³, Rui Moreno⁴, Yasser Sakr⁵

Vincent et al. Critical Care 2010, 14:R12
Figure 1 Cumulative hazard of death during the first 28 days in the intensive care unit in patients with and without a history of insulin-treated diabetes.
Over 1000 Surgical Patients
AKI as defined by AKIN
Major determinants of AKI?

Critical Care 2009 13:R79
BUT NOT DIABETES
Diabetes & ICU Outcomes

■ Is this a surprise??

■ In fact conflicting results in the literature......

What We Need Is A Meta-Analysis!!!
And What A meta-Analysis…

The effect of diabetes meta-analysis: systematic review
Results: We included 141 studies containing 12,489,574 patients, including 2,705,624 deaths (21.7%). Of these patients at least 2,327,178 (18.6%) had diabetes. Overall no association between the presence of diabetes and mortality risk was found. Analysis for ICU type showed a significant disadvantage for patients with diabetes for all mortality definitions when admitted at the surgical ICU (ICU mortality: OR [CI] 1.48 [1.04-2.11]; hospital mortality: 1.59 [1.28-1.97]; 30-day mortality: 1.62 [1.13-2.34]). In medical and mixed ICU’s no effect of diabetes was seen for all outcomes. Sensitivity analysis showed that the disadvantage in the diabetic surgical population was attributable to cardiac surgery (1.77 [1.45-2.16], P<0.00001) and not to general surgery patients (1.21 [0.96-1.53], P=0.11).
Conclusions: This meta-analysis showed that diabetes was not associated with increased mortality risk in any ICU population except for those who underwent cardiac surgery.
Evidence For Diabetic Kidneys Being Different?
No obvious problem with DM here....
Table 4. Multivariable Logistic Regression Analysis for Hospital Mortality in Critically Ill Patients With Acute Renal Failure*

<table>
<thead>
<tr>
<th>Independent Variables</th>
<th>OR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age in 1-year increments</td>
<td>1.02 (1.01-1.03)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Duration between hospital admission and inclusion to study in 1-day increments</td>
<td>1.02 (1.01-1.03)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>SAPS II in 1-point increments</td>
<td>1.02 (1.01-1.03)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>2.11 (1.58-2.82)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Vasopressors/inotropes</td>
<td>1.95 (1.50-2.55)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Diagnostic medical groupings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Metabolic</td>
<td>0.37 (0.18-0.76)</td>
<td>.007</td>
</tr>
<tr>
<td>Hematologic</td>
<td>2.70 (1.32-5.50)</td>
<td>.006</td>
</tr>
<tr>
<td>Contributing factors to ARF</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sepsis/septic shock</td>
<td>1.36 (1.03-1.79)</td>
<td>.03</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>1.41 (1.05-1.90)</td>
<td>.02</td>
</tr>
<tr>
<td>Hepatorenal syndrome</td>
<td>1.87 (1.07-3.28)</td>
<td>.03</td>
</tr>
<tr>
<td>Features of intensive care unit</td>
<td></td>
<td></td>
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<tr>
<td>Tlve</td>
<td></td>
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</tr>
</tbody>
</table>

Score
*Model fit was good (Hosmer-Lemeshow c test, 20.01; P = .33).

No obvious problem with DM here either....
Meta Analysis Did Tell Us That Cardiac Surgery & DM Was Bad…

Table 4. Factors associated with postoperative acute kidney injury defined by the Acute Kidney Injury Network Criteria (n = 1052)

<table>
<thead>
<tr>
<th>Covariate</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>1.03 (1.01 to 1.05)</td>
<td>0.0001</td>
</tr>
<tr>
<td>DM</td>
<td>1.66 (1.14 to 2.44)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Recent MI</td>
<td>1.78 (1.16 to 2.72)</td>
<td>0.009</td>
</tr>
<tr>
<td>IABP</td>
<td>3.56 (1.83 to 6.96)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nonelective surgery</td>
<td>3.66 (2.15 to 6.25)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Proteinuria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>no proteinuria</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>mild proteinuria</td>
<td>1.66 (1.09 to 2.52)</td>
<td>0.018</td>
</tr>
<tr>
<td>heavy proteinuria</td>
<td>2.30 (1.35 to 3.90)</td>
<td>0.002</td>
</tr>
<tr>
<td>CKD stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>preserved eGFR</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>stage 3</td>
<td>1.68 (1.12 to 2.52)</td>
<td>0.012</td>
</tr>
<tr>
<td>stage 4</td>
<td>3.01 (1.57 to 6.03)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Tao-Min Huang J Am Soc Nephrol 2010 22:
But is it Diabetes or Proteinuria??
But is it Diabetes or Proteinuria??

Table 5. Factors associated with postoperative AKI needing RRT (n = 1052)

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Odds Ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>1.06 (1.02 to 1.10)</td>
<td>0.003</td>
</tr>
<tr>
<td>Low LVEF</td>
<td>3.31 (1.36 to 8.79)</td>
<td>0.009</td>
</tr>
<tr>
<td>ECMO</td>
<td>15.75 (6.01 to 41.26)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nonelective surgery</td>
<td>6.49 (2.84 to 14.86)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cardiopulmonary bypass</td>
<td>3.90 (1.86 to 8.20)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Heavy proteinuria</td>
<td>7.29 (3.00 to 17.73)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Huge Study : 920,985 Patients

All hospital admissions between 2002-2007

Median FU 35 months

0.7% Admitted to hospital with AKI

James et al Lancet 2010 376 2096-103
In those with normal eGFR (>60) the adjusted risk of AKI was 4.4 higher in those with proteinuria.

In those with heavy proteinuria the risk of AKI and AKI requiring RRT was raised regardless of GFR.

James et al. Lancet 2010 376 2096-103
So: Should we Measure Proteinuria in patients with CKD?

- My Personal View

- It is. We know that from studies on CKD

- BUT: Is it all to do with Proteinuria??

- I think so.....
Your Proteinuric Kidney

- Normal kidney
- Fibrotic kidney
- Chronic inflammation
- Glomerulosclerosis
- Extracellular matrix
- Tubulointerstitial fibrosis
- Ang II
- TGF-β1
- CTGF
Tubular epithelial cell proteolysis, complement activation, oxidative stress

Activation of MAC, NF-κB, STAT

MCP-1, CCL5, fractalkine, IL-8, TNF-α, osteopontin, ICAM₁, VCAM₁, angiotensin II

Inflammatory cell infiltration

TGF-β

Myofibroblasts, collagen deposition, reduced matrix degradation

Tubulointerstitial fibrosis

Antigenic peptides?
All Patients But Especially Those With Renal disease Should have Urinalysis!!

<table>
<thead>
<tr>
<th>Test</th>
<th>55</th>
<th>60 to 80</th>
<th>80</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest X-ray</td>
<td>NA</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>ECG†</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Full blood count</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Haemostasis</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Renal function</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Random glucose</td>
<td>NA</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Urine analysis</td>
<td>NA</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Blood gases</td>
<td>NA</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Lung function</td>
<td>NA</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

†Depending on the cause of renal disease (e.g. diabetes and hypertension)
And Finally…

If we don’t want our patients to end up looking like this…..
We May Want Them To Look More Like This...
And Finally…. A Different Approach?

- Exercise therapy correlates with improving renal function through modifying lipid metabolism in patients with cvs disease and ckd

- Toyama et al

- J Cardiol 56 142-146(2010)
And Finally... A Different Approach?

- Patients with CVD and CKD ($n = 19$)
- Exercise ($n = 10$) and non-exercise ($n = 9$) therapy groups for 12 weeks
- Exercise therapy significantly improved
  - anaerobic metabolic threshold
  - HDL-C levels
  - reduced triglyceride levels
A Different Approach?

Exercise therapy also improved eGFR

Change in eGFR correlated significantly and positively with change in AT- and HDL-C, and negatively with change in triglyceride levels
Conclusions

- CKD = High Risk
- CKD + Proteinuria = Highest Risk

? Exercise for all?
Thank You For Listening
Devil’s Medicine

- Huerta et al. AJKD 2005
- Nested case-control study using the GP Research Database
- 386,916 patients aged 50-84 years
- Free of known cancer, renal disorder, cirrhosis, or systemic CTD
Devil’s Medicine

- RR for ARF of 3.2 (95% CI 1.8 to 5.8)
- Risk declined after treatment was discontinued
Devil’s Medicine

- Increased risk was present with both short- and long-term therapy

- Slightly greater among users of high doses
Devil’s Medicine

- History of
  - Heart failure
  - HT
  - DM
  - Hospitalizations & consultant visits in the previous year

- All associated with a greater risk for AKI
Devil’s Medicine

- Risk increased with concomitant use of:
  - NSAIDs and diuretics (RR: 11.6)
  - NSAIDs and CCB’s (RR: 7.8)
Devil’s Medicine

- NSAID users 3-fold greater risk for developing clinical ARF compared with non-NSAID users
- NSAIDs should be used with special caution in patients with HT and/or HF