Chronic Kidney Disease (CKD)

Getting it right from the start
Increased demand for ESRF Treatment

2007

No of patients on dialysis - 2064

New Patients 461

41% - Type II Diabetes

20% were late referrals to nephrology
i.e. seen < 3 months before commencing dialysis
Improving patient outcomes

Mortality Rates on Dialysis 2007

N Z  -  14.5% (295)

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>Aust</th>
<th>N Z</th>
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<tbody>
<tr>
<td>Cardiac</td>
<td>40%</td>
<td>41%</td>
</tr>
<tr>
<td>Vascular</td>
<td>11%</td>
<td>7%</td>
</tr>
<tr>
<td>Withdrawal from treatment</td>
<td>23%</td>
<td>23%</td>
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Early v Late Referral

Dialysis outcomes are associated with conditions present at the start of dialysis:–

- anaemia
- malnutrition
- residual renal function
- exposure to a nephrologist
- presence of permanent access
- cardiac risk factors
Echocardiographic findings in patients at starting dialysis therapy

- Systolic dysfunction: 16%
- Normal: 16%
- Left ventricular dilatation: 28%
- Concentric left ventricular hypertrophy: 41%

Referral patterns

Early

- Halt progression
  - ACEI and BP control
  - Anemia therapy
  - Nutrition
  - Mineral metabolism

- Delay progression
  - Prepare for RRT
  - Access creation
  - Modality choice/Tx
  - Timely initiation

Late

- Start dialysis
  - Temporary access
  - Anemia
  - LVH, CAD
  - Hypoalbuminemia
  - HPTH
# Stages of Chronic Kidney Disease
from NKF – K/DOQI

<table>
<thead>
<tr>
<th>Stage</th>
<th>GFR  ml/min</th>
<th>Consequences</th>
</tr>
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<tbody>
<tr>
<td>1 - normal</td>
<td>&gt;90</td>
<td></td>
</tr>
<tr>
<td>2 – early</td>
<td>60 – 89*</td>
<td>increased PTH</td>
</tr>
<tr>
<td>3 – moderate</td>
<td>30 – 59</td>
<td>decreased Ca absorption</td>
</tr>
<tr>
<td></td>
<td></td>
<td>malnutrition</td>
</tr>
<tr>
<td></td>
<td></td>
<td>anaemia - low EPO</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Left Ventricular hypertrophy</td>
</tr>
<tr>
<td>4 – severe</td>
<td>15 – 29</td>
<td>High phosphates</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Acidosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Potassium may rise</td>
</tr>
<tr>
<td>5 – ESRF</td>
<td>&lt;15</td>
<td>Uraemia</td>
</tr>
</tbody>
</table>

* With proteinuria
Stages of Chronic Kidney Disease
from NKF – K/DOQI

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<tr>
<th>Stage</th>
<th>GFR  ml/min</th>
<th>Prevalence</th>
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<tr>
<td></td>
<td></td>
<td>USA</td>
</tr>
<tr>
<td>1 - normal</td>
<td>&gt;90</td>
<td>3%</td>
</tr>
<tr>
<td>2 – early</td>
<td>60 – 89*</td>
<td>3%</td>
</tr>
<tr>
<td>3 – moderate</td>
<td>30 – 59</td>
<td>4.3%</td>
</tr>
<tr>
<td>4 – pre –ESRF</td>
<td>15 – 29</td>
<td>0.2%</td>
</tr>
<tr>
<td>5 – ESRF</td>
<td>&lt;15</td>
<td>0.1%</td>
</tr>
</tbody>
</table>
Risk factor management in CKD

Hypertension
Lipids
Blood sugars
Lifestyle
Anaemia
BP target - <130 / 80

if U alb:creat ratio > 100 < 120 / 75
i.e. >1gm proteinuria / 24 hours

Treatment of choice - ACE I or ARBs
Effect of Blood Pressure Control on CKD Progression

Summary of studies on nephropathy progression used in figure
- Viberti GC et al. JAMA, 1993
- Bakris GL. Hypertension, 1997
- GISEN Group, Lancet, 1997*

MAP (mm Hg)

GFR (mL/min/year)

r = 0.69; P < 0.05

Untreated HTN

130/85 140/90
Common Reasons for Poor Hypertension Control in CKD

Failure to restrict dietary salt
Insufficient antihypertensive meds
Inadequate doses of diuretics
Fear of side effects
Inappropriate withdrawal of RAAS blockade
  (with rising creatinine and potassium)
Initial management of hyperkalaemia < 6 is with dietary potassium restriction
Use of Diuretics:

- **eGFR > 30 ml/min** - use thiazide diuretics
  - doubling the dose is effective in improving BP control

- **eGFR < 30 ml/min** – use loop diuretics

**Nephrotic syndrome**
- approximately half the dose of frusemide is lost bound to albumin via the urine
Average number of agents needed to achieve BP goals is 2 to 4

- ALLHAT (<140/90 mm Hg BP)
- UKPDS (<85 mm Hg DBP)
- ABCD (<75 mm Hg DBP)
- MDRD (<92 mm Hg MAP)
- HOT (<80 mm Hg DBP)
- AASK (<92 mm Hg MAP)

Number of antihypertensive agents

MAP, mean arterial pressure.

Fig 6 Reduction in incidence of coronary heart disease (CHD) events and stroke in relation to reduction in diastolic blood pressure according to drug dose, number of drugs, pretreatment diastolic blood pressure, and age. *Blood pressure reductions are more uncertain and hence also reductions in disease incidence.
Lipid lowering agents in CKD

all CKD 1-4 patients should have an annual lipid profile

Prospective clinical trials support the protective effect of statins for patients with CKD not yet on dialysis
- improved eGFR
- reduction in risk of Cardiovascular event

Awaiting results of SHARP 2010

TNT – efficacy of lowering LDL to low levels in high risk patients
No contraindication to use of statins and ezetamibe

Fibrates - increased risk of myopathy (rhabdomyolosis) unexplained increase in serum Creatinine
reverses on stopping the fibrate
Diabetes and CKD

Target HbA1c - < 7%

Drugs - 2nd generation sulfonylureas
Avoid metformin if eGFR < 60ml / min
Insulin with CHO counting

Lifestyle

CKD – 5 half life of insulin is prolonged - risk of hypoglycaemia

reduce doses of insulin and oral sulphonylureas
Metformin

Not recommended if s Creatinine > 125umol/l

Risk of lactic acidosis
  0.06 cases per 1000 pt years
  fatal in 50% of cases

At risk – increasing creatinine
  liver disease
  sepsis
  CCF
  use of iodine based contrast
    stop metformin 48 hours prior to study and
    restart 24 hours later
HbA$_{1c}$ Concentration by Group at the End of the DCCT and in the EDIC Study: Type 1 Diabetes

Nathan DM et al. JAMA 2003;290:2159-2167
Prevalence and Cumulative Incidence of Microalbuminuria in DCCT/EDIC

A. Annual Prevalence

- Intensive
- Conventional

B. Cumulative Incidence

Nathan DM et al. JAMA 2003;290:2159-2167
To what extent does prevention of nephropathy account for CVD risk reduction?

- Microalbuminuria and macroalbuminuria were each strongly associated with increased CVD risk (HRs 2.93 and 2.57, p<0.001 and p=0.009, respectively).
- Effect of intensive therapy on outcomes was partly mediated by reduction in incidence of diabetic nephropathy.
Can Type 2 Diabetes Be Prevented?
Diabetes Prevention Program (DPP):

- Placebo: 29%
- Metformin: 22%
- Intensive Lifestyle Intervention*: 14%

Risk Reduction:
- 31%
- 58%

Percentages show cumulative incidence at 3 y. *Exercising 150 minutes per week.
Haemoglobin targets

Range and action thresholds for haemoglobin

In people with anaemia of CKD, treatment should maintain stable Hb levels between 105gm / l and 125 mg/l for adults and children older than 2 years of age.

This should be achieved by:
– adjusting treatment, typically when Hb rises above 120 or falls below 110 gm / l.
Iron Supplements

People receiving Epo maintenance therapy should be given iron supplements to keep their:

– serum ferritin levels between 200 and 500 μg/l

and either

transferrin saturation level above 20% (unless ferritin is greater than 800 μg/l) or

percentage hypochromic red cells (%HRC) less than 6% (unless ferritin is greater than 800 μg/l).

In practice it is likely this will require intravenous iron.
Steno-2 Study: Changes in Risk Factors at 7.8 Years

![Graph showing changes in risk factors over 7.8 years with Intensive Therapy and Conventional Therapy.](image)

**Intensive Therapy (n=67)**  
- FPG: -52%*  
- TRG: -41%†  
- TC: -50%*  
- LDL: -41%*  
- SBP: -13%  
- DBP: -12%‡

**Conventional Therapy (n=63)**  
- FPG: -18%  
- TRG: 9%  
- TC: -3%  
- LDL: -3%  
- SBP: -3%  
- DBP: -8%

*P<.001. †P=.015. ‡P=.006. Intensive therapy=strict treatment goals and stepwise implementation of behavior modification and targeted pharmacologic therapy overseen by project team. Conventional therapy=treatment from general practitioner according to Danish Medical Association guidelines.

STENO-2: Estimates of the Composite End Point of Death

- Conventional therapy
- Intensive therapy

50% Risk Reduction

% Death due to CV causes, nonfatal MI, coronary artery bypass grafting, percutaneous coronary intervention, nonfatal stroke, amputation, or surgery for peripheral atherosclerotic artery disease in the conventional-therapy group and the intensive-therapy group.

To do good is noble.

To tell others to do good is even more noble and much less trouble.

Mark Twain
Management of Chronic Kidney Disease (CKD)
Identification of CKD

Early detection of CKD is important to prevent further injury and progressive loss of renal function.

High risk populations, i.e. those with
- Diabetes
- Hypertension
- Vascular disease
- Multisystem diseases – SLE, Rh Arthritis, myeloma, vasculitis
- Family History of above
should have annual screening with

- serum creatinine - and estimated GFR
- urine dipstick for blood and protein
if positive for protein, then MSU / urinary alb:creat ratio
Stage 1 & 2 CKD
eGFR >60ml/min

Identify those at risk for disease progression
- proteinuria > 1gm / 24 hours
- proteinuria and haematuria
- Adult Polycystic Kidney Disease

Refer if diagnosis unclear

Assessment and management of risk factors

Monitor Creatinine and Potassium
Stage 3 CKD  eGFR 30 – 59 ml/min

Monitor  FBC, U&E, Calcium, Phosphate, PTH, cholesterol, BP  -
minum of 3 monthly if eGRF<45
Request Renal Ultrasound
Refer if progressive rise in serum creatinine

BP control  - treat if > 140 / 90
               target  130 / 80
               if u alb:creat >100  120 / 75
First line treatment  - ACE I / ARB
               check creatinine and K within two weeks
               stop ACE I / ARB and refer if > 20 % rise in creatinine

Treat hypercholesterolaemia
Advise on weight loss / smoking cessation
Stage 3 CKD  eGFR 30 – 59 ml/min

Anaemia - exclude other causes refer if Hb <100gm / l

Calcium / Phosphate range (PTH)
- refer if outside normal
- dietary Phos restriction
- Phosphate binders
- Vit D

Review drug doses
Avoid nephrotoxins - NSAIDs
Stage 4  (15 – 29 ml/min)

Refer for Nephrology opinion
probable outcome:
Treatment of anaemia - Erythropoietin and i.v. Iron
Treatment of Ca, Phos, PTH
Manage CVS risk factors
Dietary advice - Na, K, Phos, Protein (BS, cholesterol)
Pre – dialysis education
  - preparation for dialysis / transplantation
  - or conservative treatment
Stage 5 (< 15ml/min)

Immediate referral-

Patients not suitable for renal replacement therapy
  - Uncooperative / refusing treatment
  - significant co-morbidities with no prospect of improvement in QoL / life expectancy
  e.g. - moderate to severe dementia
References

Parmar MS. Chronic Renal Disease. BMJ 2002;325:85
Mendelssohn DC et al. Elevated levels of serum creatinine: recommendations for management and referral. CMAJ.1999:161;413
www.cari.kidney.org.au.. Caring for Australasians with Renal Impairment
www . Kidney Health New Zealand