Diagnosis and Management of Metabolic Problems in Kidney Transplant Recipients
(CKD-CMBD-Tx)
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associate professor

McGill University Health Centre, Montreal, Quebec, Canada

Semmelweis University
Budapest, Hungary
- CKD in Tx
- DM
- Lipids
- Obesity
- Malnutrition/inflammation
  - Bone
- How to manage this...
The ESRD cycle

GFR ml/min/1.73 m²

transplantation

dialysis
Majority of transplant recipients have kidney function equivalent to stage 3 CKD or worse (UK data)

19,074 adult patients with a functioning kidney transplant at the end of 2005
Figure 1: The mean number of complications per patient according to chronic kidney disease stage. The following complications were counted: hypertension (blood pressure ≥ 140/90 mmHg), serum calcium < 8.5 mg/dL, serum phosphorous > 4.5 mg/dL, hemoglobin < 11 g/dL, serum albumin < 3.5 g/dL, LDL > 100 mg/dL and total CO₂ < 22 mEq/L.
Kidney Disease: Improving Global Outcomes (KDIGO) Guidelines

Levey As, et al. Kidney Int 67: 2089, 2005

- Consider all kidney transplants recipients to have CKD, irrespective of GFR level or presence or absence of markers of kidney damage.

- The rationale for this is based on damage to native kidneys, presumed damage to the kidney transplant based on studies of "protocol biopsies," and need for life-long care caused by complications of prior CKD and chronic allograft nephropathy.
Figure 2. Cardiovascular mortality in kidney transplant recipients

cardiovascular disease management after renal transplantation

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Metabolic effects of common immuno-suppressive agents

<table>
<thead>
<tr>
<th>Condition</th>
<th>CSA</th>
<th>TAC</th>
<th>SRL</th>
<th>MMF</th>
<th>AZA</th>
<th>Steroid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyslipidaemia</td>
<td>++</td>
<td>+</td>
<td>+++</td>
<td>-</td>
<td>-</td>
<td>++</td>
</tr>
<tr>
<td>Hypertension</td>
<td>++</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>++</td>
</tr>
<tr>
<td>NODAT</td>
<td>+</td>
<td>+ (+)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>++</td>
</tr>
</tbody>
</table>

How to improve outcome in kidney transplanted patients?

An important issue for long term patient outcomes is to reduce ISU toxicity and to manage CV disease.

• Before Tx:
  – Dialysis vintage
  – CV management
  – CV interventions

• After Tx: medical management
  – DM
  – Dyslipidaemia
  – Obesity
  – Smoking
  – Inflammation
  – Anemia
  – Bone
  – ...

• After Tx: medical management
  – DM
  – Dyslipidaemia
  – Obesity
  – Smoking
  – Inflammation
  – Anemia
  – Bone
  – ...
Diabetes mellitus (new and old)
Patient Survival and Cardiovascular Risk After Kidney Transplantation: The Challenge of Diabetes

Figure 1: Left: Kaplan–Meier plots of patient survival after transplantation in recipients without DM (—) and those with DM (…….) (log-rank, p < 0.0001). Right: Kaplan–Meier plots of the incidence of fatal and nonfatal posttransplant CV events in recipients without DM (—) and those with DM (…….) (log-rank, p < 0.0001).
Table 5. Risk factors for NODAT\(^a\)

<table>
<thead>
<tr>
<th>Recipient characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>older age (&gt;45 yr)</td>
</tr>
<tr>
<td>higher body mass index (≥30)</td>
</tr>
<tr>
<td>black race</td>
</tr>
<tr>
<td>family history of diabetes</td>
</tr>
<tr>
<td>Hispanic ethnicity</td>
</tr>
<tr>
<td>education (no college degree)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Donor</th>
</tr>
</thead>
<tbody>
<tr>
<td>deceased donor</td>
</tr>
<tr>
<td>male gender</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Transplant era (after 1995)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tacrolimus use</td>
</tr>
<tr>
<td>HLA mismatch</td>
</tr>
<tr>
<td>Acute rejection</td>
</tr>
<tr>
<td>HCV infection</td>
</tr>
</tbody>
</table>

\(^a\)HCV, hepatitis C virus; NODAT, new-onset diabetes after transplantation.

Figure 1. Distribution of various glucose metabolism alterations in stable renal transplant patients. IFG, impaired fasting glucose; IGT, impaired glucose tolerance; pDM, provisional diabetes.
KDIGO clinical practice guideline for the care of kidney transplant recipients

15.1: SCREENING FOR NEW-ONSET DIABETES AFTER TRANSPLANTATION

15.1.1: We recommend screening all nondiabetic KTRs with fasting plasma glucose, oral glucose tolerance testing, and/or HbA$_{1c}$ (1C) at least:
- weekly for 4 weeks (2D);
- every 3 months for 1 year (2D); and
- annually, thereafter. (2D)

15.1.2: We suggest screening for NODAT with fasting glucose, oral glucose tolerance testing, and/or HbA$_{1c}$ after starting, or substantially increasing the dose, of CNIs, mTORi, or corticosteroids. (2D)
Diabetes management after the first posttransplant year

<table>
<thead>
<tr>
<th>Oral Agent</th>
<th>Target Population</th>
<th>Advantage</th>
<th>Disadvantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfonylurea</td>
<td>DM2 &lt; 5 year duration</td>
<td>↓ cost</td>
<td>↑ Weight, ↑ hypoglycemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rapid effect</td>
<td></td>
</tr>
<tr>
<td>Meglitinides</td>
<td>Recent DM2 ↑ PPG</td>
<td>↓ hypoglycemia short acting</td>
<td>↑ cost</td>
</tr>
<tr>
<td>Biguanides</td>
<td>Overweight/Obese Insulin resistance</td>
<td>No ↑ weight ↓ hypoglycemia</td>
<td>GI side-effects, Lactic acidosis (rare)</td>
</tr>
<tr>
<td>Thiazolidinediones</td>
<td>Overweight/Obese Insulin resistance</td>
<td>↓ Insulin requirement ↓ hypoglycemia</td>
<td>↑ Cost, weight, ↑ Liver toxicity, Slow onset of action</td>
</tr>
<tr>
<td>α-glucosidase inhibitor</td>
<td>↑ PPG</td>
<td>↓ hypoglycemia</td>
<td>GI side-effects, ↑ cost</td>
</tr>
</tbody>
</table>


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Dyslipidemia
# Table 2. Effect of immunosuppressive drugs on lipid parameters

<table>
<thead>
<tr>
<th>Drug</th>
<th>TC</th>
<th>LDL-C</th>
<th>HDL-C</th>
<th>TG</th>
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</thead>
<tbody>
<tr>
<td>Cyclosporine</td>
<td>↑↑</td>
<td>↑↑</td>
<td>↓</td>
<td>↑↑</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>↑</td>
<td></td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td>Sirolimus</td>
<td>↑↑</td>
<td>↑↑</td>
<td>↓</td>
<td>↑↑↑</td>
</tr>
<tr>
<td>Everolimus</td>
<td>↑↑</td>
<td>↑↑</td>
<td>↓</td>
<td>↑↑↑</td>
</tr>
<tr>
<td>Mycophenolate mofetil</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Prednisone</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Deflazacort</td>
<td>↑</td>
<td>↑</td>
<td>↑↑</td>
<td>↑</td>
</tr>
</tbody>
</table>

HDL-C—high-density lipoprotein cholesterol; LDL-C—low-density lipoprotein cholesterol; TC—total cholesterol; TG—triglyceride.
Prevalence of Hyperlipidemia in Renal Transplant Patients Based on CKD Stage

Karthikeyan V, Am J Transplant 4:262-269, 2004

- Cholesterol > 200 mg/dl
- Triglycerides > 150 mg/dl
- Lipid Lowering Therapy

Graph showing prevalence percentages for different stages of CKD.
Hypercholesterolemia: Relative Risk for Ischemic Heart Disease in Patients More Than One Year After Renal Transplantation

Relative Risk of IHD in Males From the Framingham Heart Study (FHS) or Transplant Patients

- Cholesterol (mg/dL)
  - ≥280
  - 240-279
  - 200-239
  - 160-199
  - <160

- Transplant patients
- FHS

ALERT: Assessment of Lescol in Renal Transplantation

• Randomized, double blind, placebo controlled multicentric study, 2102 Tx patients

• Fluvastatin (40 mg/d - 80 mg/d) or placebo

• Outcome: cardiac mortality, AMI, coronary intervention
Effect of fluvastatin on cardiac outcomes in renal transplant recipients: a multicentre, randomised, placebo-controlled trial


ITT, intent-to-treat population.

SHARP: Major Atherosclerotic Events

Risk ratio 0.83 (0.74 – 0.94)
Logrank 2P=0.0022
Endorsement of the Kidney Disease Improving Global Outcomes (KDIGO) guidelines on kidney transplantation: a European Renal Best Practice (ERBP) position statement

Uwe Heemann\textsuperscript{1}, Daniel Abramowicz\textsuperscript{2}, Goce Spasovski\textsuperscript{3} and Raymond Vanholder\textsuperscript{4} for the European Renal Best Practice (ERBP) Work Group on kidney transplantation

16.2.1: Measure a complete lipid profile in all adult (≥18 years old) and adolescent (puberty to 18 years old) KTRs (based on KDOQI Dyslipidemia Recommendation 1):

- 2–3 months after transplantation;
- 2–3 months after a change in treatment or other conditions known to cause dyslipidaemias;
- at least annually, thereafter.

doi: 10.1093/ndt/gfr169
Advance Access publication 9 May 2011
Endorsement of the Kidney Disease Improving Global Outcomes (KDIGO) guidelines on kidney transplantation: a European Renal Best Practice (ERBP) position statement

Uwe Heemann¹, Daniel Abramowicz², Goce Spasovski³ and Raymond Vanholder⁴ for the European Renal Best Practice (ERBP) Work Group on kidney transplantation

16.2.2.1: For KTRs with fasting triglycerides ≥500 mg/dL (≥5.65 mmol/L) that cannot be corrected by removing an underlying cause, treat with:

- Adults: therapeutic lifestyle changes and a triglyceride-lowering agent (based on KDOQI Recommendation 4.1);
- Adolescents: therapeutic lifestyle changes (based on KDOQI Recommendation 5.1).

doi: 10.1093/ndt/gfr169
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Uwe Heemann\textsuperscript{1}, Daniel Abramowicz\textsuperscript{2}, Goce Spavoski\textsuperscript{3} and Raymond Vanholder\textsuperscript{4} for the European Renal Best Practice (ERBP) Work Group on kidney transplantation

- Adults: If low density lipoprotein cholesterol (LDL)-C $\geq 100$ mg/dL ($\geq 2.59$ mmol/L), treat to reduce LDL-C to $<100$ mg/dL ($<2.59$ mmol/L) (based on KDOQI Guideline 4.2);
- Adolescents: If LDL-C $\geq 130$ mg/dL ($\geq 3.36$ mmol/L), treat to reduce LDL-C to $<130$ mg/dL ($<3.36$ mmol/L) (based on KDOQI Guideline 5.2).

doi: 10.1093/ndt/gfr169
Advance Access publication 9 May 2011
Obesity
Obesity is BAD!

1. Obesity is associated with increased morbidity and mortality, esp. Metabolic Syndrome and Diabetes mellitus, in the general population.

2. Obesity is a risk factor for the development of CKD and ESRD.

3. Obesity is a risk factor for CVD, CAD and CHF.

4. Obesity is associated with increased pro-inflammatory cytokines & oxidative stress.

\[
\text{BMI} = \frac{\text{Weight (kg)}}{\text{height (m)}^2}
\]

- <20: Lean (<18.5: Malnourished?)
- 20-25: Healthy ?
- 25-30: Overweight
- 30-35: Obese
- >35: Morbidly obese (>40 if no other risk)
Who will survive longer on dialysis?

Female: 28 y/o
weight 123 lbs
BMI 21 kg/m²
BP 110/65
Cholesterol 141 mg/dL

Female: 26 y/o
weight 241 lbs
BMI 43 kg/m²
BP 165/105
Cholesterol 220 mg/dL
BMI and Death Risk: General Population vs. Hemodialysis Patients

Relative Risk of Death

BMI categories (kg/m²)
Why is there a reverse epidemiology in the dialysis population?

Are there other populations with similar epidemiology?
Aging → Risk Factor Reversal

> 65 years  
![Graph for > 65 years](image)

65-75 years  
![Graph for 65-75 years](image)

>75 years  
![Graph for >75 years](image)

Obesity-related excess mortality declines with age at all levels of obesity!

Stevens et al, NEJM, 1998  
Bender et al. JAMA, 1999  
Landi et al, Arch Int Med, 2000
Risk-adjusted five year survival in CHF patients for the BMI categories

Horwich et al, J Am Coll Cardiol 2001;38:789-795
## Arnold’s BMI: 37 kg/m² (1995)

<table>
<thead>
<tr>
<th>Actor or Athlete</th>
<th>Height</th>
<th>Weight in lbs. (in 2003)</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sylvester Stallone</td>
<td>5'9&quot;</td>
<td>228</td>
<td>34</td>
</tr>
<tr>
<td>Arnold Schwarzenegger</td>
<td>6'2&quot;</td>
<td>257</td>
<td>33</td>
</tr>
<tr>
<td>Sammy Sosa</td>
<td>6'0&quot;</td>
<td>220</td>
<td>30</td>
</tr>
<tr>
<td>Harrison Ford</td>
<td>6'1&quot;</td>
<td>218</td>
<td>29</td>
</tr>
<tr>
<td>George Clooney</td>
<td>5'11&quot;</td>
<td>211</td>
<td>29</td>
</tr>
<tr>
<td>Bruce Willis</td>
<td>6'0&quot;</td>
<td>211</td>
<td>29</td>
</tr>
<tr>
<td>Mike Piazza</td>
<td>6'3&quot;</td>
<td>215</td>
<td>27</td>
</tr>
<tr>
<td>Brad Pitt</td>
<td>6'0&quot;</td>
<td>203</td>
<td>27</td>
</tr>
<tr>
<td>Michael Jordan</td>
<td>6'6&quot;</td>
<td>216</td>
<td>25</td>
</tr>
</tbody>
</table>

From: “Celebrity Height Weight Chart”
Associations of Pretransplant Weight and Muscle Mass with Mortality in Renal Transplant Recipients

Elani Streja,† Miklos Z. Molnar,‡ Csaba P. Kovesdy§§ Suphamai Bunnapradist† Jennie Jing,‡ Allen R. Nissenson,† ‡† Istvan Mucsi, ‡‡ Gabriel M. Danovitch, ‡ and Kamyar Kalantar-Zadeh† ‡‡

CJASN ePress. Published on March 17, 2011
Associations of Pretransplant Weight and Muscle Mass with Mortality in Renal Transplant Recipients

Elani Streja,* ‡ Miklos Z. Molnar,∗ ‡ Csaba P. Kovesdy§‖ Suphaimai Bunnapradist‡ Jennie Jing,* Allen R. Nissenson,∗ ‡‡ Istvan Mucsi, ‡ Gabriel M. Danovitch,† and Kamyar Kalantar-Zadeh* ‡§

![Graph showing associations of pretransplant weight and muscle mass with mortality in renal transplant recipients.](image)

*CJASN ePress. Published on March 17, 2011*
Adipocytokines → modulation of inflammation

Bad Cytokines
- TNF-α
- IL-6
- Leptin
- Resistin

Inflammation

Good Cytokines
- Adiponectin
- IL-10

?
2.5 year survival follow-up in 535 MHD Patients

Lowest Body Fat → Worse Survival

Body Mass Index, Waist Circumference and Mortality in Kidney Transplant Recipients

Figure 1: Kaplan–Meier curves of unadjusted (A) and waist circumference-adjusted (B) cumulative incidence of all-cause mortality in kidney transplant recipients grouped according to their body mass index.

C. P. Kovesdy\textsuperscript{a,b,*}, M. E. Czira\textsuperscript{c}, A. Rudas\textsuperscript{c}, A. Ujszaszi\textsuperscript{c}, L. Rosivall\textsuperscript{d}, M. Novak\textsuperscript{c,e}, K. Kalantar-Zadeh\textsuperscript{f}, M. Z. Molnar\textsuperscript{c,d,f} and I. Micsi\textsuperscript{c,d,g}

American Journal of Transplantation 2010; 10: 2644–2651
Body Mass Index, Waist Circumference and Mortality in Kidney Transplant Recipients

Figure 2: Kaplan–Meier curves of unadjusted (A) and body mass index-adjusted (B) cumulative incidence of all-cause mortality in kidney transplant recipients grouped according to their waist circumference. Median waist circumference was 103 cm in males and 93 cm in females.

C. P. Kovesdy\textsuperscript{a,b,*}, M. E. Czira\textsuperscript{c}, A. Rudas\textsuperscript{c}, A. Ujszaszi\textsuperscript{c}, L. Rosivalld, M. Novak\textsuperscript{c,e}, K. Kalantar-Zadehf, M. Z. Molnar\textsuperscript{c,d,f} and I. Mucsi\textsuperscript{c,d,g}

American Journal of Transplantation 2010; 10: 2644–2651
### Why is there an Obesity Paradox?

<table>
<thead>
<tr>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney Disease Wasting (Malnutrition-inflammation-complex syndrome)</td>
</tr>
<tr>
<td>Time discrepancy between competitive risk factors: overnutrition vs. undernutrition</td>
</tr>
<tr>
<td>Unusual genetic constellation due to survival selection during CKD progression</td>
</tr>
<tr>
<td>Sequestration/storage of uremic toxins in fat tissue</td>
</tr>
<tr>
<td>Anti-inflammatory cytokines related to body mass, including adiponectins</td>
</tr>
<tr>
<td>Tumor necrosis factor alpha receptors</td>
</tr>
<tr>
<td>Endotoxin-lipoprotein hypothesis</td>
</tr>
<tr>
<td>Stability of hemodynamic status in obese patients</td>
</tr>
<tr>
<td>Neurohormonal alterations in obesity</td>
</tr>
<tr>
<td>Alteration of conventional risk factors in uremic milieu (“beyond Framingham”)</td>
</tr>
<tr>
<td>Reverse causation</td>
</tr>
<tr>
<td>Survival bias</td>
</tr>
<tr>
<td>Advantages of obesity in the history of man kind (the Ultimate Hypothesis)</td>
</tr>
</tbody>
</table>

*Kalantar-Zadeh & Kopple, Contrib Nephrol 2006*
Reverse Epidemiology of ESRD: Competitive Risk Factors with Time Discrepancy

*Over Nutrition*

10 year risk

*Under Nutrition*

"One" year risk

When play together: one-year undernutrition wins!
16.4: OBESITY

16.4.1: Assess obesity at each visit. *(Not Graded)*

- Measure height and weight at each visit, in adults and children.
- Calculate BMI at each visit.
- Measure waist circumference when weight and physical appearance suggest obesity, but BMI is <35 kg/m².

16.4.2: Offer a weight-reduction program to all obese KTRs. *(Not Graded)*
Malnutrition-inflammation/
Protein-energy wasting
Malnutrition Inflammation Complex Syndrome (MICS)
Protein-Energy Wasting
Kidney Disease Wasting
Cachexia-in-Slow-Motion

1. Evidence of Protein-Energy Malnutrition (PEM):
   – Wasting syndrome (cachexia), ↓ BMI
   – ↓ lean body mass
   – ↓ appetite, ↓ food intake, ↓ nPNA (nPCR)
   – ↓ cholesterol, ↓ albumin, ↓ transferrin

2. Evidence of Inflammation:
   – ↑ CRP
   – ↑ pro-inflammatory cytokines (IL-6, TNF-α, IL-1β)
   – ↑ EPO resistance

3. High cardiovascular disease, high mortality
Malnutrition-inflammation complex syndrome (MICS)

Fig 2. Schematic representation of the causes and consequences of MICS. Abbreviation: DM, diabetes mellitus.

Kalantar-Zadeh; AJKD; 2003
MICS in kidney transplanted patients

Bone disorders-CKD-MBD

Depression

Post-transplant anemia

Quality of Life

MICS
Malnutrition-inflammation

Other?

Mortality and Chronic Allograft Injury
Malnutrition and Inflammation Score (MIS)  
(Kalantar-Zadeh et al.)

A. **Medical history**
   A. Change in weight over past 3-6 months
   B. Dietary intake
   C. Gastrointestinal symptoms
   D. Functional capacity
   E. Comorbidity

B. **Physical exam** (according to SGA criteria)
   A. Decreased fat stores or loss of subcutaneous fat
   B. Signs of muscle wasting

C. **Body mass index** (BMI)

D. **Laboratory results**
   A. Serum albumin
   B. Serum transferrin

- MICS was assessed by the MIS score developed by Kalantar-Zadeh.
Distribution of MIS in our KTx patients
Association between the malnutrition-inflammation score and post-transplant anaemia

![Bar Chart]

**Fig. 2.** Predicted Hb levels from the final, fully adjusted multivariate linear regression model (Model 2) in subgroups defined by MIS and eGFR.

Association of the Malnutrition-Inflammation Score With Clinical Outcomes in Kidney Transplant Recipients
Red Cell Distribution Width?

- RDW = the variation in red blood cell volume (anisocytosis)
- Elevated in variety of diseases
  - Iron deficiency
  - Malnutrition
  - Chronic kidney disease
- Calculated automatically on every CBC
Red cell distribution width in heart failure: Prediction of clinical events and relationship with markers of ineffective erythropoiesis, inflammation, renal function, and nutritional state

Table IV. Baseline characteristics of the cohort stratified by RDW values

<table>
<thead>
<tr>
<th></th>
<th>RDW ≤13.9%</th>
<th></th>
<th>RDW 13.9%-15.2%</th>
<th></th>
<th>RDW ≥15.2%</th>
<th></th>
<th>P*</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Median</td>
<td>Interquartile range</td>
<td>Median</td>
<td>Interquartile range</td>
<td>Median</td>
<td>Interquartile range</td>
<td></td>
</tr>
<tr>
<td>Markers of ineffective erythropoiesis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iron (μmol/L)</td>
<td>15.4</td>
<td>10.9-19.4</td>
<td>13</td>
<td>9-16.9</td>
<td>10</td>
<td>6.64-13.7</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Ferritin (μg/L)</td>
<td>140.7</td>
<td>94.6-259.4</td>
<td>135.8</td>
<td>66.5-220.7</td>
<td>98.8</td>
<td>57.6-157.9</td>
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<tr>
<td>Transferrin (g/L)</td>
<td>2.7</td>
<td>2.4-3.0</td>
<td>2.7</td>
<td>2.4-3.1</td>
<td>2.8</td>
<td>2.4-3.2</td>
<td>.53</td>
</tr>
<tr>
<td>Transferrin sat. (%)</td>
<td>23</td>
<td>18-28</td>
<td>18.5</td>
<td>13.5-24</td>
<td>16</td>
<td>10-20</td>
<td>&lt;.0001</td>
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<tr>
<td>Soluble transferrin receptor (nmol/L)</td>
<td>2.3</td>
<td>2.7-4.3</td>
<td>4.8</td>
<td>5.9-7.8</td>
<td>5.9</td>
<td>4.7-7.2</td>
<td>&lt;.0001</td>
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<tr>
<td>EPO (U/mL)</td>
<td>8.9</td>
<td>4.9-15.2</td>
<td>12.6</td>
<td>7.4-18.9</td>
<td>14.1</td>
<td>7.9-25.7</td>
<td>.002</td>
</tr>
<tr>
<td>Markers of inflammation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>IL-6 (pg/mL)</td>
<td>6.62</td>
<td>3.88-12.35</td>
<td>10.89</td>
<td>6.89-14.18</td>
<td>14.59</td>
<td>8.52-25.32</td>
<td>.0001</td>
</tr>
<tr>
<td>TNF-α (pg/mL)</td>
<td>2.03</td>
<td>1.07-3.62</td>
<td>2.37</td>
<td>1.68-3.47</td>
<td>2.78</td>
<td>1.73-4.75</td>
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<td>TNF-RII (ng/mL)</td>
<td>4.61</td>
<td>3.42-6.69</td>
<td>6.64</td>
<td>3.81-10.37</td>
<td>6.93</td>
<td>4.22-10.68</td>
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<td>TNF-RII (ng/mL)</td>
<td>3.40</td>
<td>2.34-4.57</td>
<td>4.42</td>
<td>3.40-5.78</td>
<td>5.07</td>
<td>3.75-6.68</td>
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<td>Preactin (g/L)</td>
<td>0.26</td>
<td>0.21-0.30</td>
<td>0.21</td>
<td>0.17-0.27</td>
<td>0.18</td>
<td>0.14-0.24</td>
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<td>CRP (mg/L)</td>
<td>4.2</td>
<td>1.7-10.7</td>
<td>8.36</td>
<td>3.6-15.3</td>
<td>6.7</td>
<td>3.9-15.9</td>
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<td>Markers of damaged renal function</td>
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<td>GFR (mL/1.73 m² per min)</td>
<td>75</td>
<td>59-95</td>
<td>65.5</td>
<td>45-81</td>
<td>55</td>
<td>38-77.5</td>
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<td>Creatinine (μmol/L)</td>
<td>91</td>
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<td>97.5</td>
<td>78-142</td>
<td>111.5</td>
<td>84.5-165.5</td>
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<td>Markers of nutritional deficiency</td>
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<td>Albumin (g/L)</td>
<td>43</td>
<td>40.5-45</td>
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<td>39-44</td>
<td>39</td>
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<td>Total protein (g/L)</td>
<td>72</td>
<td>67-76</td>
<td>73</td>
<td>69-78</td>
<td>70</td>
<td>62.76</td>
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<tr>
<td>Total cholesterol (mmol/L)</td>
<td>4.21</td>
<td>3.81-5.31</td>
<td>4.48</td>
<td>3.89-5.11</td>
<td>3.62</td>
<td>2.95-4.14</td>
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CHARM Adjusted HR by quintile of RDW for CV Death or HF Hospitalization

Events = 952
Survival of KTx patients with RDW below vs above median

Log Rank test: p=0.002

<table>
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<th>Follow-up time (days)</th>
<th>Number of remaining cases</th>
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<tr>
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<td>RDW &gt;=13.7</td>
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</table>
Hazard ratio (95% confidence intervals) of mortality versus RDW using adjusted Cox regression analyses
Multidisciplinary care
CAD treatment gap in the community

Provider awareness does not equal successful implementation

NCEP = National Cholesterol Education Program

Steno 2: Intensive Therapy
NB: combined cardio/renal protection

- Multidisciplinary team (MD, nurse, dietician)
- Diet
- Exercise 30 minutes 3 – 5x/wk
- Smoking cessation courses
- ACEI/ARB independent of BP
- Vitamin – mineral supplement
- ASA
- Glycemic control
- BP control
- Lipid control

Gaede P et al. NEJM 2003; 348: 383-393
Steno 2: Outcomes

- Hazard ratio = 0.47 in favor of intensive group (.24 - .73, p=0.008)
- Absolute RR = 20%
- NNT 5 patients to prevent one CV event in 7.8 years

Gaede P et al. NEJM 2003; 348: 383-393
The short- and long-term impact of multi-disciplinary clinics in addition to standard nephrology care on patient outcomes
Role of Remission Clinics in the Longitudinal Treatment of CKD

Piero Ruggenenti,∗† Elena Perticucci,† Paolo Cravedi,∗† Vincenzo Gambara,† Marco Costantini,∗ Sanjib Kumar Sharma,∗‡ Annalisa Perna,* and Giuseppe Remuzzi∗†
Multidisciplinary care

- Education program
- Protocollized clinic f/u
- Protocollized lab
- Regular audits/CQI
- Nephrologist
- Nurse practitioner
- Social worker/psychologist
- Dietician
- Pharmacist
- Physiotherapist
Summary and conclusion

- Multiple metabolic derangements are prevalent in KTx patients and they are associated with increased mortality/CV events
- Screening for impaired glucose metabolism using OGT is necessary
- Treatment of impaired glucose metabolism by implementing life style modifications and using appropriate pharmacotherapy is indicated
- Regular screening for dyslipidemia is recommended
- Lifestyle modifications and statins are likely to improve outcomes
- Protein-energy wasting/inflammation is prevalent in KTx patients and is associated with worse clinical outcomes
- Multidisciplinary “risk management clinics” may be necessary to target all these metabolic problems among kidney transplant recipients to improve patient outcomes