Cardio Renal Disease

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PREVALENCE OF CVD IS HIGH

<table>
<thead>
<tr>
<th>Condition</th>
<th>CAD (CLINICAL)</th>
<th>LVH (ECHO)</th>
<th>CHF (CLINICAL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GENERAL POPULATION</td>
<td>5-12%</td>
<td>20%</td>
<td>5%</td>
</tr>
<tr>
<td>CKD</td>
<td>NA</td>
<td>25-50%</td>
<td>NA</td>
</tr>
<tr>
<td>HEMODIALYSIS</td>
<td>40%</td>
<td>75%</td>
<td>40%</td>
</tr>
<tr>
<td>PERITONIAL DIALYSIS</td>
<td>40%</td>
<td>75%</td>
<td>40%</td>
</tr>
<tr>
<td>RENAL TRANSPLANT</td>
<td>15%</td>
<td>50%</td>
<td>NA</td>
</tr>
</tbody>
</table>

SARNAK AND LEVEY AJKD 2000, 35: 9117 - 131
Def:

Cardio renal syndrome - a relatively normal kidney is dysfunctional because of a diseased heart, with the assumption that in the presence of a healthy heart same kidney performs normally.
DEF:

Cardiorenal syndrome, general definition: a pathophysiological disorder of the heart and kidneys in which acute or chronic dysfunction in one organ may induce acute or chronic dysfunction in the other organ.
CRS type 1 (acute CRS).

- Type 1 CRS is characterized by a rapid worsening of cardiac function, leading to acute kidney injury (AKI).
Acute heart failure (HF) may be divided into 4 subtypes:

- hypertensive pulmonary edema with preserved left ventricular (LV) systolic function
- acutely decompensated chronic HF
- cardiogenic shock, and
- predominant right ventricular failure
**Figure 1** CRS Type 1

**Acute heart disease or procedures**
- Acute decompensation
- Ischemic insult
- Coronary angiography
- Cardiac surgery

**Humorally mediated damage**
- RAA activation
- Na + H₂O retention
- Vasoconstriction

**Hormonal factors**
- BNP
- Natriuresis

**Immune mediated damage**
- Monocyte activation
- Endothelial activation

**Exogenous factors**
- Contrast media
- ACE inhibitors
- Diuretics

**Decreased CO**
- Decreased perfusion
- Increased venous pressure
- Toxicity
- Vasoconstriction

**Sympathetic activation**

**Humorally mediated damage**

**Endothelial activation**

**Acute renal injury**
- Acute hypoperfusion
- Reduced oxygen delivery
- Necrosis/apoptosis
- Decreased GFR
- Resistance to ANP/BNP

**Biomarkers**
- KIM-1
- Cystatin-C
- NGAL
- Creatinine
Type II: chronic cardiorenal syndrome.

Chronic abnormalities in cardiac function (e.g. chronic congestive heart failure) causing progressive and potentially permanent chronic kidney disease
Chronic heart disease

- Anemia
- Na + H2O retention
- Uremic solute retention
- Ca and Phos abnormalities
- Hypertension

Genetic risk factors
Acquired risk factors
Low cardiac output (CO)
Subclinical inflammation
Endothelial dysfunction
Accelerated atherosclerosis
Chronic hypoperfusion
Increased renal vascular resistance
Increased venous pressure
Embolism

Increased susceptibility to insults

Chronic hypoperfusion
Apoptosis

Insult and initiation of kidney damage

Sclerosis - Fibrosis

Progression of CKD

Anemia, hypoxia
RAA and sympathetic activation
Na + H2O retention
Ca and Phos abnormalities
Hypertension, LVH

Anemia
Na + H2O retention
Uremic solute retention
Ca and Phos abnormalities
Hypertension
Type III: acute renocardiac syndrome

. Abrupt worsening of renal function (e.g. acute kidney ischaemia or glomerulonephritis) causing acute cardiac disorder (e.g. heart failure, arrhythmia, ischaemia)
Type IV: chronic renocardiac syndrome

. Chronic kidney disease (e.g. chronic glomerular or interstitial disease) contributing to decreased cardiac function, cardiac hypertrophy and/or increased risk of adverse cardiovascular events
Figure 4  CRS Type 4
Type V: Secondary cardiorenal syndrome

- Systemic condition (e.g. diabetes mellitus, sepsis) causing both cardiac and renal dysfunction
Systemic diseases
Diabetes
Amyloidosis
Vasculitis
Sepsis

Heart failure
- Sympathetic system activation
- Neurohormonal stress
- Inflammation
- Hemodynamic changes
- Hypoperfusion
- ↓Perfusion pressure
- ↑RVR
- Ischemia/reperfusion
- Hypoxia
- Oxidative stress
- Toxemia
- Exogenous toxins
- Heme proteins, antibiotics
- Contrast media
- LPS/endotoxin
- Monocyte activation
- Cytokines

Organ damage/dysfunction

Renal insufficiency
Current Approaches to managing Cardiorenal Dysfunction

- Neurohormonal antagonists
- Other vasoactive therapies
  - Positive ionotropes
  - Natriuretic peptides
- Agents that target the kidney
  - Vasopressin
  - Adenosine antagonists
- Renal replacement therapy (Ultrafiltration)
- Mechanical circulatory support
Current Options May Have Undesirable Clinical Impacts

_ Favorable aspects of diuretic therapy
  – Increases urine output; reduces total body volume in majority of patients

_ Adverse aspects of diuretic therapy
  – Direct activation of renin-angiotensin-aldosterone system
  – Enhanced myocardial aldosterone uptake
  – Loss of K, Mg, Ca, secondary myocyte Ca loading
  – Indirect reduction of cardiac output
  – Increased total systemic vascular resistance
  – Reduced natriuresis and GFR
  – Associated with increased morbidity and mortality
Furosemide Monotherapy Causes Significant Decline in Renal Function (GFR)

Change in GFR after IV furosemide 80 mg in CHF

GFR (% Change)

-25 -20 -15 -10 -5 0 5 10 15

0 500 1000 1500 2000 2500

Urine Output (mL) 0–8 h

Placebo

IV furosemide

Relief for Acutely Fluid Overloaded Patients With Decompensated Congestive Heart Failure

The RAPID-CHF Trial

Early Ultrafiltration in Patients With Decompensated HF and Observed Resistance to Intervention With Diuretic Agents

The EUPHORIA Trial
Ultrafiltration versus IV Diuretics for Patients Hospitalized for Acute Decompensated Congestive HF: A Prospective Randomized Clinical Trial

UNLOAD Trial

Conclusions

- Early ultrafiltration produces greater weight loss than IV diuretics, without changes in renal function

- An early ultrafiltration strategy reduces 90-day

  - Percentage of patients requiring rehospitalization for HF
  - Number of HF rehospitalizations
  - Days of rehospitalization for HF
  - Emergency department and unscheduled office visits

WHY ULTRAFILTRATION?

PATIENT—effective control of symptoms
- early control of symptoms
- short hospital stay
- no requirement for ICU
- diuretic side effects

HOSPITAL—faster turnaround time
- less requirement ICU bed
- day heart failure clinic (like CRF)
Pathophysiology

IL₁
IL₆
ANP

MDF

(Myocardial depressant factors)

Removed by UF
Renal function and survival in CHF

- Most powerful predictor mortality in CHF
- 1906 pts Crcl. < 44 ml/min (CG equation) mortality risk 2.85 (P= <0.001)
- RF stronger predictor factor than Na, K, Mg, EF or NYHA Class
- N terminal ANP

Evolution of CRRT

- IHD 1960
- SCUF 1977
- CAVH 1978
- CAVHD 1984
- CAVHDF 1984
- CVVHDF 1988
- CVVHD 1986
- CVVH 1985
- SLOW IHD 1993
- CHF Control
  - SCUF 1982
  - CAVH 1986
  - CVVH 1992

Cytokine control

Paganini et al – Seminars in dialysis vol9, No.2 (Mar-Apr)1996; 200-203
AIM OF THE STUDY

Role of CAPD in refractory congestive heart failure at our centre during the period 2008-2009

Prospective study continued till date
Inclusion Criteria

- Refractory heart failure
- Severe systolic dysfunction (EF<35%)
- No possibility of surgical treatment
- No response to the best medical therapy available (fluid decongestive therapy)
- Adequate socio – financial support
21 patients with severe congestive heart failure refractory to optimal pharmacological therapy

All patients had NYHA class IV with varying stages of CKD III-IV

CAPD prescription is based on the amount of UF needs to be achieved

The total follow up ranged between 6 months to 2 years

Statistical analysis: paired student ‘t’ test
# Clinical and technical Data

<table>
<thead>
<tr>
<th>Pt.</th>
<th>Gender</th>
<th>Age</th>
<th>Diagnosis</th>
<th>PD Prescription</th>
<th>Ultra-filtration</th>
<th>PD Follow-up (months)</th>
<th>Peritonitis episodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>63</td>
<td>Ischaemic CMP</td>
<td>One Icodextrin nocturnal exchange</td>
<td>900 ± 300</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>54</td>
<td>RHD+MVR</td>
<td>One Icodextrin nocturnal exchange + 1.5% one exchange</td>
<td>1500 ± 400</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>60</td>
<td>Ischaemic CMP</td>
<td>One Icodextrin nocturnal exchange + 1.5% one exchange</td>
<td>1100 ± 200</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>57</td>
<td>Ischaemic CMP</td>
<td>One Icodextrin nocturnal exchange + 2.5% one exchange</td>
<td>800 ± 300</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>63</td>
<td>Ischaemic CMP</td>
<td>One Icodextrin nocturnal exchange</td>
<td>800 ± 400</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>58</td>
<td>Ischaemic CMP</td>
<td>One 2.5% exchange per day</td>
<td>1200 ± 200</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>57</td>
<td>Ischemic CMP</td>
<td>Three 2.5% exchange per day</td>
<td>1500 ± 300</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>59</td>
<td>Ischemic CMP</td>
<td>One 2.5% exchange per day</td>
<td>800 ± 300</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>70</td>
<td>Ischemic CMP</td>
<td>Two 2.5% exchange per day</td>
<td>1100 ± 200</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>63</td>
<td>Ischemic CMP</td>
<td>Three 2.5% exchange</td>
<td>1500 ± 400</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>
RESULTS

- Of the 21 patients studied 17 were males and 4 were females
- The mean age was 59.6 yrs
- There was a significant improvement in NYHA class IV to II in 4 patients and NYHA class IV to III in 1 patient NYHA class IV to I in 1 patient (p=0.0006)
- We have observed significant improvement in quality of life, reduction in morbidity and decreased hospitalization rates (p=0.0010)
- Only one patient had an episode of peritonitis during the follow up
<table>
<thead>
<tr>
<th>Pt.</th>
<th>Gender</th>
<th>Age</th>
<th>Diagnosis</th>
<th>Ejection Fraction % Before→After</th>
<th>Renal functions @ eGFR CKDstages</th>
<th>Hospitalisation days (before)</th>
<th>Hospitalisation days (after)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>63</td>
<td>Ischaemic CMP</td>
<td>25 → 40</td>
<td>4</td>
<td>83</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>54</td>
<td>RHD+MVR</td>
<td>25 → 55</td>
<td>3</td>
<td>59</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>60</td>
<td>Ischaemic CMP</td>
<td>20 → 30</td>
<td>4</td>
<td>52</td>
<td>17</td>
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<tr>
<td>4</td>
<td>F</td>
<td>57</td>
<td>Ischaemic CMP</td>
<td>25 → 35</td>
<td>3</td>
<td>109</td>
<td>40</td>
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<tr>
<td>5</td>
<td>M</td>
<td>63</td>
<td>Ischaemic CMP</td>
<td>25 → 55</td>
<td>4</td>
<td>120</td>
<td>8</td>
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<tr>
<td>6</td>
<td>M</td>
<td>58</td>
<td>Ischaemic CMP</td>
<td>25 → 35</td>
<td>4</td>
<td>90</td>
<td>12</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>57</td>
<td>Dilated cardiomyopathy</td>
<td>18 → 30</td>
<td>4</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>59</td>
<td>RHD</td>
<td>22 → 28</td>
<td>2</td>
<td>36</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>70</td>
<td>Dilated cardiomyopathy</td>
<td>33 → 46</td>
<td>2</td>
<td>33</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>63</td>
<td>Dilated cardiomyopathy</td>
<td>26 → 40</td>
<td>4</td>
<td>40</td>
<td>0</td>
</tr>
</tbody>
</table>
Change in the functional class

NYHA Grade

NYHA(before)

NYHA(after)

p=0.0006
Improvement in LV Ejection fraction

Ejection fraction (before)
Ejection fraction (after)

Patients

Ejection Fraction %

Ejectiuon fraction(before)
Ejection fraction(after)
CONCLUSION

- Independent of the renal functions peritoneal dialysis appears to be a promising therapeutic option for patients with refractory CHF.
- Peritoneal Dialysis offers significant improvement in quality of life, reduction in morbidity and decreased hospitalization rates in patients with refractory CHF.
- One exchange (Dextrose/ Icodextrin) is sufficient enough for achieving fluid balance.
**Definition of CIN**

- CIN is most commonly defined as: an acute impairment of renal function following the use of CM with an increase in serum creatinine (SCr) of
  - ♣ ≥ 44.2 µmol/l (0.5 mg/dl),
    - or as an increase of ≥ 25% from baseline
- within 72 h after Intravascular CM administration
- In the absence of an alternative etiology

ESUR, European Society of Urogenital Radiology
Thomsen HS. *Curr Opin Urol.* 2007;17:70-76.
CIN adversely affects survival for many years after the episode

Adjusted 8-year survival by creatinine elevation 35

Proportion survived

0 0.5 1.0

0 1 2 3 4 5 6 7 8 9 10

Years

No ↑ in Scr
Transient ↑ in Scr
Persistent ↑ in Scr
Are We Failing to Identify Patients With Renal Impairment Because of How We Screen for Them?

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Normal SCr</th>
<th>Patients with Abnormal eGFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-59</td>
<td>Yes</td>
<td>1.2%</td>
</tr>
<tr>
<td>60-69</td>
<td>Yes</td>
<td>12.6%</td>
</tr>
<tr>
<td>≥70</td>
<td>Yes</td>
<td>47.3%</td>
</tr>
</tbody>
</table>

Creatinine filtration

$N = 171$

Serum creatinine (mg/dl)

$C_{\text{inulin}}$ (ml/min 1.73 m$^2$)
Estimating Kidney Function

Cockcroft Gault: estimates creatinine clearance (mL/min)

\[
\frac{(140 - \text{age}) \times \text{weight (kg)}}{72 \times \text{SCr (mg/dL)}} \times 0.85 \text{ (if female)}
\]

4-variable MDRD: estimates GFR (mL/min/1.73 m^2)

\[
186.3 \times \text{SCr}^{-1.154} \times \text{age}^{-0.203} \times \left(0.742 \text{ if female}\right) \times \left(1.21 \text{ if black}\right)
\]

6-variable MDRD: estimates GFR (mL/min/1.73 m^2)

\[
170 \times \left(\text{SCr} \times 0.011\right)^{-0.999} \times \left(\text{age}\right)^{-0.176} \times \left(\text{SUN} \times 2.801\right)^{-0.170} \times \\
\left(\text{SAlb} \times 0.1\right)^{0.318} \times 1.180 \text{ (if African-American)} \times 0.762 \text{ (if female)}
\]

Coritsidis GN. Available at: http://www.uhmc.sunysb.edu/internalmed/nephro/webpages/Part_A.htm.
Stages of CKD
Adapted from the National Kidney Foundation K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease; Evaluation, Classification, and Stratification.

Figure 1. Expected outcomes ↑risk of radiocontrast-induced nephropathy (RCN), dialysis, and death.

- **Expected Outcomes**
  - **Stage I**: CKD risk factors/damage with preserved GFR
  - **Stage II**: Mild ↓kidney function

- **Risk of RCN, Dialysis, and Death**
  - **Stage III**: Moderate ↓kidney function
  - **Stage IV**: Severe ↓kidney function
  - **Stage V**: Kidney failure ↑end-stage renal disease (ESRD)

**Kidney Function (GFR) mL/min/1.73 m²**

130 120 110 100 90 80 70 60 50 40 30 20 15 10 0
# The CIN Risk Index

## CIN Risk Factors and Scores

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Integer Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension</td>
<td>5</td>
</tr>
<tr>
<td>Presence of an intra-aortic balloon pump</td>
<td>5</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>5</td>
</tr>
<tr>
<td>Age &gt;75 years</td>
<td>4</td>
</tr>
<tr>
<td>Anemia</td>
<td>3</td>
</tr>
<tr>
<td>Diabetes</td>
<td>3</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>4 (Scr &gt;1.5 mg/dL)</td>
</tr>
<tr>
<td></td>
<td>2 (GFR 40–60)</td>
</tr>
<tr>
<td></td>
<td>4 (GFR 20–40)</td>
</tr>
<tr>
<td></td>
<td>6 (GFR &lt;20)</td>
</tr>
<tr>
<td>Volume of contrast agent used</td>
<td>1 per each 100 cc³</td>
</tr>
</tbody>
</table>

The time-course of CIN

Change in SCr over time in patients undergoing uro-radiology procedures who developed CIN

Adapted from Detrenis 2007
Algorithm for Management of Patients Receiving Iodinated CM

Calculate eGFR
Assess CIN risk

eGFR <30 mL/min
- Hospital admission
- Nephrology consultation
- Dialysis planning*
- Other strategies as for eGFR 30–59 mL
  - Serial SCr and electrolytes

eGFR 30–59 mL/min
- Discontinue NSAIDs, other nephrotoxic drugs, metformin
- Intravenous volume expansion†
- Consider choice of contrast medium
- Limit contrast volume (<100 mL)
- Consider pharmacological treatment‡
- SCr before discharge or within 24–72 h

eGFR ≥60 mL/min
- Discontinue metformin
- Good clinical practice

Plans should be made in case CIN occurs and dialysis is required
† IV isotonic crystalloid 1–1.5 mL/kg/h for 3–12 h before and 6–24 h after the procedure
‡ Consider potentially beneficial agents (theophylline, statins, ascorbic acid, PGE₃); none approved for this indication

Adapted from McCullough PA, et al. Am J Cardiol. 2006;98[Suppl]:2K-4K.
Fluids – What?

- 0.9% saline significantly reduced contrast nephropathy compared to 0.45% saline (0.7% vs. 2%; P = 0.04)
- Hydration with isotonic sodium bicarbonate decreased the incidence of contrast nephropathy compared to 0.9% saline (1.7% vs. 13.6%; P = 0.02)

USE ISOTONIC CRYSTALLOIDS


Check e GFR
Stop ACEI /ARB’s /DRI’s
Stop Metformin
Stop diuretics
No NSAID’S
IV hydration
NS – 1 ml /kg/hr/12-24 hrs (pre & post)
If HF _ ml/kg/hr/12-24 hrs (pre & post)
- Maintain I/O check
- IV Na HCo₃ ?
- NAC -1200 mg 3 doses (Vol of contrast, type of contrast)
- Check S. Creatinine 48 hrs
# Society Recommendations: Type of CM for High-risk Patients

<table>
<thead>
<tr>
<th>Society</th>
<th>Isosmolar</th>
<th>Low-osmolar</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACC/AHA/SCAI 2007 (PCI)</td>
<td>✓</td>
<td>–</td>
</tr>
<tr>
<td>ACC/AHA 2007 (UA/NSTEMI)</td>
<td>✓</td>
<td>–</td>
</tr>
<tr>
<td>Hungarian Society of Nephrology 2007</td>
<td>✓</td>
<td>–</td>
</tr>
<tr>
<td>National Kidney Foundation (K/DOQI) 2005</td>
<td>✓</td>
<td>–</td>
</tr>
<tr>
<td>Norwegian Society of Nephrology 2004</td>
<td>✓</td>
<td>–</td>
</tr>
<tr>
<td>German Cardiac Society 2004</td>
<td>✓</td>
<td>–</td>
</tr>
<tr>
<td>ESUR 2005</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>French Radiologic Society 2004</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Head-to-head studies</td>
<td>NEPHRIC¹</td>
<td>RECOVER²</td>
</tr>
<tr>
<td>---------------------------</td>
<td>----------</td>
<td>----------</td>
</tr>
<tr>
<td>Type of injection/examination</td>
<td>IA - coronary/aortofemoral angiography</td>
<td>IA - coronary angiography ± PCI</td>
</tr>
<tr>
<td>Number of patients</td>
<td>129</td>
<td>275</td>
</tr>
<tr>
<td>Contrast agents used</td>
<td>a. VISIPAQUE b. iohexol</td>
<td>a. VISIPAQUE b. ioxaglate</td>
</tr>
<tr>
<td>% renally impaired</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>% diabetes - VISIPAQUE - LOCM</td>
<td>100</td>
<td>34.3</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>36.2</td>
</tr>
<tr>
<td>Baseline SCr μmol/l</td>
<td>132 ± 46.9</td>
<td>122 ± 49.5</td>
</tr>
<tr>
<td>- VISIPAQUE - LOCM</td>
<td>141 ± 46.0</td>
<td>115 ± 44.2</td>
</tr>
<tr>
<td>Baseline CrCl/GFR ml/min</td>
<td>CrCl</td>
<td>CrCl</td>
</tr>
<tr>
<td>- VISIPAQUE - LOCM</td>
<td>50.1 ± 12.8</td>
<td>45.2 ± 11.4</td>
</tr>
<tr>
<td></td>
<td>47.3 ± 16.6</td>
<td>44.9 ± 10.3</td>
</tr>
<tr>
<td>Head-to-head studies</td>
<td>NEPHRIC&lt;sup&gt;1&lt;/sup&gt;</td>
<td>RECOVER&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>--------------------------------------</td>
<td>----------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>Number of follow-up SCr measures</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Timing of follow-up SCr measures</td>
<td>day 2, 3, 7</td>
<td>day 1, 2</td>
</tr>
<tr>
<td>Volume (ml) - VISIPAQ - LOCM</td>
<td>163 ± 88</td>
<td>204.6 ± 159.2</td>
</tr>
<tr>
<td></td>
<td>162 ± 82</td>
<td>194.8 ± 123.9</td>
</tr>
<tr>
<td>Definition of CIN - SCr ↑</td>
<td>≥ 44.2 μmol/l</td>
<td>≥ 25% or ≥ 44.2 μmol/l</td>
</tr>
<tr>
<td>Overall CIN rate (%)</td>
<td>14.7</td>
<td>12.4</td>
</tr>
<tr>
<td>CIN rate VISIPAQ (%)</td>
<td>3.1</td>
<td>7.9**</td>
</tr>
<tr>
<td>CIN rate LOCM (%)</td>
<td>26.2</td>
<td>17.0**</td>
</tr>
<tr>
<td>p value</td>
<td>p=0.002</td>
<td>p=0.021</td>
</tr>
</tbody>
</table>

<sup>1</sup> NEPHRIC (2011)  
<sup>2</sup> RECOVER (2013)  
<sup>3</sup> NGUYEN (2014)  
<sup>4</sup> CARE (2015)  
<sup>5</sup> IMPACT (2016)  
<sup>6</sup> ACTIVE (2017)
“As medicine is practised in the 1990s the pt with heart disease and renal disease are frequently managed by physicians who are interested in only one of the two organ systems. In circumstances when the pt is visited by both, the physicians frequently take opposite points of view and make therapeutic recommendations that are principally designed to preserve a single organ system”.

Packer M

Cardio Renal Disease (II Ed) 1992 PP III - VI
Anemia Begins Early in CKD

Kazmi, AJKD, in press
Greater Boston Area Chart Audit
ANEMIA MANAGEMENT IN CKD

- Critical links: CKD – CVD – Anemia
- Adverse consequences of anemia
- Anemia and clinical outcomes
  1) observational studies
  2) Interventional trials
- Challenges of targeting higher hb
- Trends in anemia management
- Epoetin vs. Darbepoetin
Heart Failure after MI - Benefit beyond Hemoglobin from Erythropoetin

- Erythropoetin Induces Neovascularization and Improves Cardiac Function in Rats with Heart Failure after Myocardial Infarction.
  - Van der Meer et al. J Am Coll Cardiol 46: 125-133, 2005


- High dose Epo - A Limitation
Increased diastolic pressure
Increased diastolic stress
Series addition of new sarcomeres
Chamber enlargement
Eccentric hypertrophy

Increased systolic pressure
Increased systolic stress
Parallel addition of new myofibrils
Wall thickening
Concentric hypertrophy

Primary stimulus

Volume overload
Pressure overload

Increment
 decrement

Series addition of new sarcomeres
Parallel addition of new myofibrils
Initial insult

- Hypoxia
- Oxidative stress

**GLOMERULAR INJURY**
- Proteinuria
- Tubular dysfunction

**INTERSTITIAL FIBROSIS**
- Destruction of capillaries
- Hypoxia
- Oxidative stress
- Epoetin?

**GLOMERULO-SCLEROSIS**
- Hypoxia
- Oxidative stress

**REDUCED NEPHRON NUMBER**
- Glomerular hypertension/hypertrophy
CKD-MBD

Ca X P > 55
PTH

Phosphate binders
- Ca containing
- Non Ca containing
  - Sevelamer
  - Lanthanum

Calcinimetics
Vit D analogues