Developing, Implementing and Maintaining a CRRT Program

Jorge Cerdá, MD, FACP, FASN
Clinical Professor of Medicine
Albany Medical College
# Indications for Specific Renal Replacement Therapies

<table>
<thead>
<tr>
<th>THERAPEUTIC GOAL</th>
<th>HEMODYNAMICS</th>
<th>PREFERRED THERAPY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluid Removal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IUF</td>
<td>Stable</td>
<td>Intermittent isolated ultrafiltration</td>
</tr>
<tr>
<td></td>
<td>Unstable</td>
<td>Slow Continuous Ultrafiltration</td>
</tr>
<tr>
<td>SCUF</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urea Clearance</td>
<td>Stable</td>
<td>Intermittent Hemodialysis</td>
</tr>
<tr>
<td></td>
<td>Unstable CRRT</td>
<td>Convection: CAVH, CVVH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Diffusion: CAVHD, CVVHD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Both: CAVHDF, CVVHDF</td>
</tr>
<tr>
<td>Severe Hyperkalemia</td>
<td>Stable/Unstable</td>
<td>Intermittent Hemodialysis</td>
</tr>
<tr>
<td>Severe Metabolic Acidosis</td>
<td>Stable</td>
<td>Intermittent Hemodialysis</td>
</tr>
<tr>
<td></td>
<td>Unstable</td>
<td>CRRT</td>
</tr>
<tr>
<td>Severe Hyperphosphoremia</td>
<td>Stable/Unstable</td>
<td>CRRT</td>
</tr>
<tr>
<td>Brain edema</td>
<td>Unstable</td>
<td>CRRT</td>
</tr>
</tbody>
</table>

Table 1

Considerations in Renal Replacement Therapy for Acute Renal Failure

**DIALYSIS MODALITY**
- Intermittent hemodialysis: Daily, Every Other Day, SLED
- Continuous renal replacement therapies: AV, VV
- Peritoneal dialysis

**DIALYSIS BIOCOMPATIBILITY: MEMBRANES**

**DIALYZER PERFORMANCE**
- Efficiency
- Flux

**DIALYSIS DELIVERY**
- Timing of Initiation
- Intensity of Dialysis: Prescription vs. Delivery
- Adequacy of Dialysis: Dose of Dialysis
MODALITIES OF CRRT

1. **SCUF**
   - Blood In
   - UFC \(\rightarrow\) Uf
   - \(Q_b = 100\ \text{ml/min} \quad Q_f = 2-8\ \text{ml/min}\)

2. **CVVH**
   - Blood In
   - Uf \(\rightarrow\) V
   - \(Q_b = 100-200\ \text{ml/min} \quad Q_f = 10-30\ \text{ml/min}\)
   - \(K = 15-45\ \text{L/24 h}\)

3. **CVVHD**
   - Blood In
   - V \(\rightarrow\) D
   - \(Q_b = 100-200\ \text{ml/min} \quad Q_f = 2-4\ \text{ml/min}\)
   - \(K = 15-45\ \text{L/24 h}\)

4. **CVVHDF**
   - Blood In
   - UF+D \(\rightarrow\) V
   - \(Q_b = 100-200\ \text{ml/min} \quad Q_f = 10-30\ \text{ml/min}\)
   - \(Q_d = 10-30\ \text{ml/min} \quad K = 20-50\ \text{L/24 h}\)

5. **CVVHDF-SLED**
   - Blood In
   - Uf \(\rightarrow\) D
   - \(Q_b = 100-200\ \text{ml/min} \quad Q_f = 2-8\ \text{ml/min}\)
   - \(Q_d = 50-200\ \text{ml/min} \quad K = 40-60\ \text{L/24 h}\)
   - Diffusion+Convection (Back Filtration)

6. **CPF-PE**
   - Blood In
   - Plasmafilter \(\rightarrow\) V
   - \(Q_b = 100-200\ \text{ml/min} \quad Pf = 20-30\ \text{ml/min}\)
   - Can be coupled with CVVH or CVVHDF

7. **CHP**
   - Blood In
   - Adsorbent \(\rightarrow\) V
   - \(Q_b = 100-200\ \text{ml/min}\)
   - Can be coupled with CVVH or CVVHDF

8. **CPFA**
   - Blood In
   - Plasmafilter \(\rightarrow\) Adsorbent \(\rightarrow\) Uf
   - \(Q_b = 100-200\ \text{ml/min} \quad Pf = 20-30\ \text{ml/min}\)
   - Can be coupled with CVVH or CVVHDF

9. **HVHF**
   - Blood In
   - V \(\rightarrow\) Uf
   - \(Q_b = 200-300\ \text{ml/min} \quad Q_f = 50-100\ \text{ml/min}\)
   - \(K = 60-120\ \text{L/24 h}\)

*Source: Cerda & Ronco, Handbook of CRRT, 2008*
Factors Affecting Implementation and Performance of a CRRT Program

• FACTORS AFFECTING IMPLEMENTATION
  • Number of ICU beds, Number of ARF patients/yr, Number of patients dialyzed ICU/yr
  • Dialysis services: Nephrological MD and RN support
  • ICU staffing support: Intensivist staff, intensivist nurses part and full-time
  • Level of Intensive Care Unit

• FACTORS AFFECTING PERFORMANCE
  • Clear delineation of nursing responsibilities
    – Setup, initiation, monitoring, troubleshooting
  • Clear delineation of physician responsibilities and interaction
  • Formal and continuous instruction (lectures, hands-on, skill assessments and patient care experience
  • Standardized and updated protocols
  • Continuous identification of areas of improvement
Initiating a New CRRT Program: When Administration Says "Let's Look at the Evidence"

- **Timing of Initiation**
  - No RCT demonstrates benefit of early vs. late initiation: Next most important study

- **Modality**
  - No RCT demonstrates differences
    - Design problems: sample size, randomization
    - Study will never be done again

- **Dose**
  - Ronco: Yes
  - ATN: No
  - RENAL: No
  - Are studies really comparable: convection vs diffusion
  - Can you realistically DELIVER the minimum dose in your critically ill patient?

- **Hemodynamic Stability**
  - Brain edema
  - Other non-renal apps
  - Renal functional recovery

- **Renal Functional Recovery**

- **Cost**
Treatment of ARF in the Critically Ill Patient

- Intermittent Hemodialysis is used in more than two-thirds of cases in recent US surveys
  - Lewis et al, JASN 1997;8:A0673
  - Mehta-Lettieri AJN 1999;19:377

- Continuous Renal Replacement Therapies are used increasingly in Europe and almost exclusively in Australia
Utilization of Dialysis Modalities for the Treatment of ARF

70% Respondents

Management of AKI: International Survey of Nephrologists
Lapsiwala et al ASN 2009

• Most common initial RRT: IHD 63%
  – >4 X/WK (59%)

• 69% considered CRRT better tolerated but only 22% used it as initial modality

• CRRT:
  – Weight based RX important 40%
  – UFH 50%
  – Teaching hospital: OR pre-emptive CRRT
INDIVIDUALIZED DOSE PRESCRIPTION ON THE BASIS OF BODY WEIGHT HAS INCREASED FROM 28 TO 52.4%

PERCENT RESPONDERS WHO ARE "NOT SURE" WHAT IS AN ADEQUATE DOSE OF RRT HAS DECREASED FROM 37% TO 25%

THE COMMONEST RESPONSE WAS 25 ml/Kg/hr
Utilization of Renal Replacement Therapy for Critically Ill Patients
Factors Influencing the Choice of Intermittent Hemodialysis in the Treatment of ARF

Factors Influencing the Choice of Intermittent Hemodialysis

Utilization of Renal Replacement Therapy for Critically Ill Patients

Although 89% agree that CRRT is an acceptable alternative to IHD in the ICU, the major barrier for adopting CRRT is the lack of evidence on outcome.

DIALYSIS MODALITY

% Patients

N=398 (64%)
Matthew Pesacreta, Pamela Overberger, Paul M. Palevsky, VA/NIH Acute Renal Failure Trial Network. Renal-Electrolyte Division, University of Pittsburgh, Pittsburgh, PA; VA Pittsburgh Healthcare System, Pittsburgh, PA 
ASN 2004

DOSING
TARGET URR >65% 31% RESPONDENTS
TARGET Kt/V >1.2 7% RESPONDENTS
NO TARGET 56% RESPONDENTS
CRRT DOSE TARGET 14%, 81%>35 ml/kg/hr

IHD: DIALYSIS FREQUENCY/WK

<table>
<thead>
<tr>
<th>3XWK</th>
<th>4XWK</th>
<th>5XWK</th>
<th>6XWK</th>
<th>7XWK</th>
</tr>
</thead>
<tbody>
<tr>
<td>51%</td>
<td>31%</td>
<td>9%</td>
<td>3%</td>
<td>4%</td>
</tr>
</tbody>
</table>
Practical Aspects of Running a CRRT Program

• Who should run the CRRT Program?
  – Nephrologists or Intensivists?
    • Credentialing process
  – Renal Nurses or Critical Care Nurses?
  – Joint ventures: the best of all worlds
WHO DOES IT? [1]
HEALTH CARE PERSONNEL RESPONSIBLE FOR THE CARE OF ARF PATIENTS IN THE ICU

WHO DOES IT? [2]
HEALTH CARE PERSONNEL RESPONSIBLE
FOR THE CARE OF ARF PATIENTS ON CRRT

ARF in the world

- Regional differences in choice of RRT modality
# ARF in the world

## Table 2 Who manages renal replacement therapy in the intensive care unit?

<table>
<thead>
<tr>
<th></th>
<th>IRRT</th>
<th>CRRT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Who prescribes RRT?</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nephrologists</td>
<td>22 (40.7%)</td>
<td>11 (20.4%)</td>
</tr>
<tr>
<td>Intensivists</td>
<td>12 (22.2%)</td>
<td>32 (59.3%)</td>
</tr>
<tr>
<td>Both</td>
<td>14 (25.9%)</td>
<td>11 (20.4%)</td>
</tr>
<tr>
<td>Not available</td>
<td>6 (11.1%)</td>
<td></td>
</tr>
<tr>
<td><strong>Who primes circuit?</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dialysis nurses</td>
<td>36 (66.7%)</td>
<td>9 (16.7%)</td>
</tr>
<tr>
<td>ICU nurses</td>
<td>7 (13.0%)</td>
<td>32 (59.3%)</td>
</tr>
<tr>
<td>Nephrologists</td>
<td>–</td>
<td>2 (3.7%)</td>
</tr>
<tr>
<td>Intensivists</td>
<td>1 (1.9%)</td>
<td>6 (11.1%)</td>
</tr>
<tr>
<td>Any of above</td>
<td>1 (1.9%)</td>
<td>1 (1.9%)</td>
</tr>
<tr>
<td>ICU nurses or doctors</td>
<td>–</td>
<td>2 (3.7%)</td>
</tr>
<tr>
<td>Medical engineers</td>
<td>3 (5.6%)</td>
<td>2 (3.7%)</td>
</tr>
<tr>
<td>Not available</td>
<td>6 (11.1%)</td>
<td>–</td>
</tr>
</tbody>
</table>

IRRT, intermittent renal replacement therapy; CRRT, continuous renal replacement therapy; ICU, intensive care unit.
Figure 2 Difference of practice for renal replacement therapy in the world


Curr Opin Crit Care 12:538–543.
Who Should Manage CRRT in the ICU? The Intensivist’s Viewpoint

• The obvious answer to this controversy is that the person most competent to manage this technique in a given institution should be the one directing its use.

Who Should Manage CRRT in the ICU?
The Intensivist’s Viewpoint

- Such patients cannot safely be left in the hands of physicians who see them for a limited period of time during a morning ward round, who are not immediately available if an emergency arises and who have no experience in mechanical ventilation and organ support.

Nephrology Curriculum. ASN, 1996
Program Content for ARF and ICU Nephrology

• 1. Normal regulation of renal and glomerular hemodynamics
• 2. Differential diagnosis of ARF:
  – Pathophysiology of prerenal azotemia
  – Pathophysiology of intrinsic renal failure including acute GN, ATN and ATIN
  – Pathophysiology of obstructive renal failure
• 3. Mechanisms of postoperative ARF
• 4. Mechanisms of ARF in hepatobiliary disease
• 5. Causes of ARF in patients with cancer and immunosuppression
• 6. Causes of ARF in patients with AIDS
• 7. Metabolic consequences of ARF
  – Hormonal, nutritional, electrolyte, acid-base, volume
• 8. Evaluation and management of ARF
  – Radiological techniques in ARF
  – Nondialytic therapy
  – Dialytic therapies
    • Hemodialysis
    • Peritoneal dialysis
    • Continuous therapies
• 9. Hemodynamic monitoring of critically ill patients
• 10. Management of electrolyte and acid base disturbances in patients with ARF
• 11. Management of fluid in critically ill patients
• 12. Use of vasoactive drugs in critically ill patients
• 13. Role of extracorporeal therapy in the management of drug overdoses
  – Ethylene glycol, methanol, lithium, theophylline, salicylate, barbiturate
Potential Advantages of and Intensivist-Based Management of ICU Patients with ARF Requiring Renal Replacement Therapy

- Decreased fragmentation of care
- Immediate availability of service
- Continuous and immediate availability for troubleshooting
- CRRT seen within the context of overall management
- Elimination of costs of double specialist consult
- Direct involvement and control of therapy by ICU nurses
- Elimination of costs of dialysis nurse involvement
- Frequent readjustment of goals of therapy
- Greater attention to hemodynamic effects of therapy

The Problem of Specialization

They're everything!

<table>
<thead>
<tr>
<th>SPECIALISTS</th>
<th>INTENSIVISTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Internists, Surgeons</td>
<td>1987</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SUB SPEC</th>
<th>INTENSIVISTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nephrol</td>
<td>Cardiol</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ADMINISTRATIVE ROLE</th>
<th>INTENSIVISTS</th>
</tr>
</thead>
</table>

1995-1997 Boarded in Critical Care
6,875 physicians: 1,600 surgeons, 4,620 pulmonologists
604 anesthesiologists, 486 cardiologists, 190 nephrologists (2.7%)
Which one is it?

- **THE NEPHROLOGIST:**
  - Intensivists don’t let Nephrologists work in the ICU.
  - Intensivists don’t understand Nephrology.

- **THE INTENSIVIST:**
  - Nephrologists are worthless in the ICU.
  - Nephrologists don’t want to come to work in the ICU.
Why don’t Nephrologists want to go to the ICU?

• They don’t want to be bothered
  – Number of hospital visits
  – Number of phone calls, pages day and night
• They are not paid or not paid extra or have other jobs that are better paid
• They no longer have the necessary expertise
  – Critical care medicine
  – ICU nephrology, acute dialysis, CRRT
• They find the ICU a hostile environment that makes them irrelevant
  – Closed vs. Open ICU
What good are the Nephrologists in the ICU?

- Deeper understanding of the pathophysiology of ARF
- Profound understanding of:
  - Hemodialysis
  - Peritoneal dialysis
  - Hemoperfusion, Hemofiltration
  - Apheresis
- Is dialysis a "renal or non renal" application?
  - Dialysis in ARDS
  - Dialysis in sepsis
- Continuity of care: post-ICU care for survivors

But if you don’t use it, You lose it
The Future

• “…this important field of medicine, where critical care and nephrology overlap, is now so significant in size of practice and so wide in scope of knowledge that the evolution of a new subspecialty, Critical Care Nephrology, is justified.”

# The Nursing Collaborative Model

## ADVANTAGES

- Neph nurse dedicated to start and maintain CRRT
- CC and Neph nurses assess and use CRRT to meet goals
- Brings high level of expertise from both areas
- Probably cost-effective

## DISADVANTAGES

- Possibly delays initiation of therapy
- Roles and responsibilities can become ambiguous
- Differences in philosophies and standards can hamper efforts
- Possibly not cost-effective

---

R K Martin, AJKD 1997;30(5)Suppl 4:S105-8
A peek into Judy’s job

Hunger, Thirst
Bathroom
Call home
Check kids

2 Disagreeing Card Surgeons
Endo, Cardio Nephro, Nutr Pulm-CC
FAMILY!!!
If there is a commonality I’ve observed among most non-renal hospital consultants and senior decision-makers, it is a tendency to underestimate the complexity of hemodialysis and related processes. This is not surprising since highly proficient nephrology nurses who work in acute care can create the illusion of making it look relatively simple.

- Kathy Ellis, BSN, CNN, MHS. Acute Dialysis Unit Director, Ochsner Medical Center, New Orleans, LA
As our medical care and the accompanying skills and technologies grow in complexity, nurses have become more specialized. Safe and optimal use of CRRT requires concurrent advanced hemodynamic and oxygenation assessment, manipulation of fluids and vasoactive infusion, and early recognition of the patient’s intolerance of acute abnormalities. Identification and integration of this information for the critically ill patient is the hallmark of the experienced critical care nurse.

- Kathleen M. Burns, MNEd, BSN, RN, CCRN, Clinical Nurse Specialist, Cardiovascular Intensive Care Unit, Vanderbilt University Medical Center, Nashville TN
• Although adding CRRT machine set-up to the ever expanding responsibilities of the critical care nurse initially causes a few whimpers, one of the worst scenarios for a diehard critical care nurse is to have something attached to a patient that the nurse doesn’t know how to troubleshoot. To be responsible for a patient, but not to be able to do anything except silence an alarm and call for help causes frustration not only to the nurse, but also to the patient and his family. They need to know that someone is ALWAYS there to fix things.

Kathleen M. Burns, MNEd, BSN, RN, CCRN, Clinical Nurse Specialist, Cardiovascular Intensive Care Unit, Vanderbilt University Medical Center, Nashville TN
Implementing CRRT: Requirements for a successful program

- Motivation and involvement of Nephrologist
- Educated nursing staff
- Standardized protocols and orders
- Periodic in-services
Implementing a CRRT program

• **Staff Education:**
  – Nurses (Critical Care and Nephrology)
  – Physicians:
    • Ongoing education
    • Grand Rounds, small groups
    • BECOME AN ACCEPTED PART OF THE TEAM
  – Pharmacists
  – Nutritionists
Factors affecting the development of a CRRT program

- **Resources Available**
  - ICU staff support
  - Nephrology staff support
  - Dedicated budget
  - ICU staff education, training and support
Factors Affecting Performance of CRRT

• Clear delineation of nursing responsibilities (setup, initiation, monitoring, troubleshooting)
• Clear delineation of physician responsibilities and interaction
• Formal and continuous education
• Standardized and updated protocols
• Continuous quality improvement and innovation
When you start rounds at 0700, and the CRRT machine is parked outside the room with a sign across its face...
CRRT and Nursing Frustration

- Treatment stopped due to excess pt fluid loss 7130ml × 2. Second setup only lasted 50 min.
  This machine caused more problems than it was worth.

Micheele

10/26/08
2100
Implementing a CRRT program

- Equipment Decisions:
  - Ease of use
  - Accuracy of measures
  - Affordability
  - Clinical support vs. technical support
    - Who answers the phone on Christmas Eve at 0230 hours when the screen of the machine goes suddenly black and the reset button doesn’t do it?
      - A Tech?
      - A Nurse?
Delivery of Prescribed CRRT Dose
Major RCT

- Ronco (heparin)
  - % delivery $\approx 95\%$ (compensatory UF increases)
  - Filter changed every 24 hrs

- Saudan (heparin)
  - Delivered dose during first 24 hrs = $83\%$
  - Filter changed every 24 hrs for first two days

- Tolwani (citrate RCA in 91% of patients)
  - Patients achieving $>80\%$ of prescribed dose = $79\%$

- ATN (no anticoagulation in 60% of patients)
  - Average daily CRRT duration = $21$ hrs ($88\%$)

- RENAL (heparin): $85\%$ delivery of prescribed dose
CRRT Prescription vs Delivery
Venkataraman et al, J Crit Care, 2002

- Prescribed Dose (ml/kg/hr): 24.5 ± 6.7
- Delivered Dose (ml/kg/hr): 16.6 ± 5.4
- Time/Day (hours): 16.1 ± 3.5

68% of prescribed dose
67% of total hours in day
DoReMi Database (N=865)

Median delivered = 27 mL/kg/h
Median prescribed = 34 mL/kg/h
• In fact, the delivered dose of dialysis for acute kidney injury is frequently not even assessed, highlighting a need to apply the tools of quality assurance and performance improvement that are routine in outpatient dialysis to the practice of renal replacement therapy for acute kidney injury. Adopting such tools will ensure that we provide treatment that is at least as intensive as that provided in the lower-intensity groups in these two studies.
Practical Aspects of Running a CRRT Program

Financial Considerations
Characteristics of the “Ideal” Treatment Modality of ARF in the ICU

- Preserves homeostasis
- Does not increase co-morbidity
- Does not worsen patient’s underlying condition
- Is inexpensive
- Is simple to manage
- Is not burdensome to the ICU staff

Main determinants of outcome

Lameire et al, NDT 1999;14:2570
Mr. R.N.

• Admitted with acute abdomen, underwent colostomy, abdominal sepsis, developed subsequent acute respiratory failure requiring mechanically assisted ventilation and acute renal failure.

• Treated initially with CRRT and permanent IHD thereafter.

• Discharged home alive on IHD.
Mr. R.N.

TIME ON CRRT 336 hrs=14 days
Avge filter life 56±28 hrs; total 6 filters

**Costs:** 
\[\text{[(}385 \text{ fluids} \times 14) + (160 \text{ filter sets} \times 6)\text{]=}6350\]

**Average cost of one day ICU stay:** $5,278+1707

12 subsequent HD treatments: $12,780

Total Patient cost: $180,430.69: CRRT=3.5%

---

**DAILY COSTS**

<table>
<thead>
<tr>
<th>Item</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Repl Fluid</td>
<td>$18</td>
</tr>
<tr>
<td>Dialysate</td>
<td>$113</td>
</tr>
<tr>
<td>CaCl2</td>
<td>$34</td>
</tr>
<tr>
<td>Citrate</td>
<td>$220</td>
</tr>
<tr>
<td>TOTAL</td>
<td>$385</td>
</tr>
<tr>
<td>Filter set</td>
<td>$160</td>
</tr>
</tbody>
</table>

---

* Chest and Abdomen CT Scans ($5725 total)

Avge. cost room=$800/day ($400 RN salary) 14 days=$5600

---

* Chest and Abdomen CT Scans ($5725 total)
Mr. R.E.

- Admitted with Staph Aureus Sepsis and multiple organ failure due to septic iatrogenic arthritis. Transferred to St Peter’s Hospital for CRRT and critical care. Prolonged ARDS, ARF requiring CRRT, subsequent IHD.
- Discharged home after a Rehab stay, with normal renal function and residual pulmonary interstitial fibrosis.
Mr. R.E.

TIME ON CRRT 263 hrs = 11 days
Avge filter life 33 ± 25 hrs; total 8 filters

Costs: [($385 fluids \times 11) + ($160 filter sets \times 8)] = $5515

Average cost of one day ICU stay: $4289 ± 1099
19 subsequent HD treatments: $20,235
Total Patient cost: $139,989.83 CRRT = 3.9%

Avge. Cost room = $800/day ($400 RN salary) 11 days = $4400
Mr. B.D.

- 35 y.o.w.m, history of sleep-apnea, moderate obesity
- 1/28/02 Uvulopalatopharyngoplasty/septoplasty
- Respiratory failure post-extubation, emergent tracheostomy
- 1/28-1/2/02 Progressive pulmonary edema, bloody resp. secretions, worsening respiratory acidosis and hypoxemia, fever, hypotension, tachycardia. APACHE II APDR: 39%
- Progressive oliguria not responsive to furosemide gtt, worsening acidemia, BUN/Cr 110/4.7
- 2/3/02 CRRT started
- APACHE II APDR: 83%, Liaño score: 0.899
Mr. B.D.

- Prolonged ICU hospitalization: ARF requiring CRRT, severe ARDS, pulmonary hypertension, critical hypoxemia, resp acidosis.
- **CRRT** allowed compensation of permissive hypercarbia, fluid management and nutrition.
- Received inhalational **Nitric Oxide** which allowed decrease in pulmonary resistance and oxygenation.
- Eventually recovered normal renal and pulmonary function, was transiently transferred to Sunnyview Hospital and eventually went back home.
DAILY COSTS
Repl Fluid $18
Dialysate $113
CaCl2 $34
Citrate $220
TOTAL $385
Filter set $160

TIME ON CRRT 284 hrs = 12 days
Avge filter life 70.75+13 hrs; total 4 filters

Costs: [($385 fluids X 12) + ($160 filter sets X 4)] = $5645
Average cost of one day ICU stay: $3279 + 2399
Nitric Oxide cost: $12,000
Total Patient cost: $155,231
CRRT = 3.6% NO = 7.7%

 MAV = $236 x 32 = $7552 = 4.8%
Treatment of ARF in the ICU: Financial Considerations

• Is dialysis is very costly?
  – The overall picture
  – Analysis of costs
  – Financial strategies
  – Physician reimbursement
  – Facility reimbursement
Expenditures Associated with ARF in Medicare Beneficiaries

JL Xue, J Liu, PW Eggers, J Himmelfarb, AJ Collins
ASN Meeting October 2004

- Cost and LOS related to ARF MC pts
- N=5,403,015 admissions 1992-01
- Adjusted Incidence is up 10%/year:
  - 14/1000 in 1993
  - 36/1000 in 2001

<table>
<thead>
<tr>
<th></th>
<th>ARF PRIMARY</th>
<th>ARF SECONDARY</th>
<th>NO ARF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>INCIDENCE (%)</strong></td>
<td>30,910 (0.6%)</td>
<td>96,704 (1.8%)</td>
<td>5,275,401 (97.6%)</td>
</tr>
<tr>
<td><strong>LOS (DAYS)</strong></td>
<td>9.1</td>
<td>13.5</td>
<td>6.7</td>
</tr>
<tr>
<td><strong>ICU ADMISSIONS (%)</strong></td>
<td>27.4</td>
<td>46.8</td>
<td>19.3</td>
</tr>
<tr>
<td><strong>COST ADMISSION (US$)</strong></td>
<td>7,532</td>
<td>15,571</td>
<td>6,367</td>
</tr>
<tr>
<td><strong>INPT DIALYSIS (%)</strong></td>
<td>21.9</td>
<td>14.0</td>
<td>-</td>
</tr>
</tbody>
</table>
# CVVHDF Cost Analysis: Pharmacy

<table>
<thead>
<tr>
<th>ITEM</th>
<th>COST PER UNIT</th>
<th>QUANTITY</th>
<th>TOTAL ITEM COST</th>
</tr>
</thead>
<tbody>
<tr>
<td>D 21/2% in 1/2 NS 1 L bag</td>
<td></td>
<td>1</td>
<td>$2.22</td>
</tr>
<tr>
<td>3 L Sterile Empty bag</td>
<td></td>
<td>1</td>
<td>$5.55</td>
</tr>
<tr>
<td>Sodium Chloride</td>
<td></td>
<td>120 mEq</td>
<td>$1.30</td>
</tr>
<tr>
<td>Potassium Chloride</td>
<td></td>
<td>12 mEq</td>
<td>$0.083</td>
</tr>
<tr>
<td>Magnesium Sulfate</td>
<td></td>
<td>4.5 mEq</td>
<td>$0.062</td>
</tr>
<tr>
<td>Ancillary Supplies*</td>
<td>N/A</td>
<td>N/A</td>
<td>$3.00</td>
</tr>
<tr>
<td>Labor (assume 15 min/bag)</td>
<td>N/A</td>
<td>N/A</td>
<td>$4.00</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td></td>
<td></td>
<td><strong>$16.22 / 3 L bag</strong></td>
</tr>
</tbody>
</table>

| Sodium Bicarbonate^                 |               | 120 mEq | $5.42           |
| **TOTAL**                           |               |          | **$20.34/3 L bag** |

| Sodium Bicarbonate^^                |               | 120 mEq | $0.84           |
| **TOTAL**                           |               |          | **$15.76 / 3 L bag** |

*Compounder tubing, needles, syringes
** Approx $27.03 per 5 L bag
^Made using 8.4% 50 ml vials
^^Made using 5% 500 bottles
#Approx $33.9 per 5 L bag
##Approx $26.26 per 5 L bag
CVVHDF Cost Analysis: Pharmacy

Patients typically use 8X3L bags/day

- **Total cost for SPH-prepared dialysate:**
  - $126.08 to $162.72 per day

- **Prismasate B22GK4/0 5 L bag=$44.00**

- **Total cost for Prismasate dialysate:**
  - $211.20 per day

- **Savings $211.2-126.08=$85.12 per day**
  - *(67.5% increase in costs but disposables and labor approaches zero)*
COST OF CRRT AS A FRACTION OF TOTAL ICU ADMISSION
St. Peter’s Hospital data year 2001, n=29 patients

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVGE COST ICU ADMISSION</td>
<td>$55,155</td>
</tr>
<tr>
<td>ICU LENGTH OF STAY (DAYS)</td>
<td>22.43</td>
</tr>
<tr>
<td>COST/DAY</td>
<td>$2,955</td>
</tr>
<tr>
<td>AVGE COST CRRT</td>
<td>$1,819</td>
</tr>
<tr>
<td>AVGE DURATION CRRT (DAYS)</td>
<td>4</td>
</tr>
<tr>
<td>COST/DAY</td>
<td>$600</td>
</tr>
<tr>
<td>COST CRRT AS % ICU ADMISSION</td>
<td>4.9</td>
</tr>
<tr>
<td>FRACTIONAL COST CRRT/DAY ICU</td>
<td>0.9</td>
</tr>
</tbody>
</table>
COST OF CRRT AS A FRACTION OF TOTAL ICU ADMISSION
St. Peter's Hospital data year 2001, n=29 patients

<table>
<thead>
<tr>
<th>COST CRRT AS % ICU ADMISSION</th>
<th>4.9</th>
</tr>
</thead>
<tbody>
<tr>
<td>FRACTIONAL COST CRRT/DAY ICU</td>
<td>0.9</td>
</tr>
</tbody>
</table>

THEREFORE, IF CRRT TREATMENT HELPS REDUCE ICU L.O.S. BY ONE DAY, IT HAS ALREADY PAID FOR ITSELF!
Cost

• Is CRRT more expensive than IHD?
  – Depends on what you count:
    • Use of personnel
      – 1:1 vs. 1:2 nursing; dialysis nurses involved?
    • Equipment:
      – Initial expense: type of machine
      – Filter life
      – Replacement and dialysis fluids: pharmacy costs
    • Lab costs
    • Respirator days, ICU length of stay

\[ \sim \text{ } 200 \text{ a day} \]
Be careful how you attribute costs
Rauf et al JICM 2008;23(3)

Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>CRRT (N = 84)</th>
<th>IHD (N = 77)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>58.2 ± 15.6</td>
<td>65.7 ± 14.0</td>
<td>.002</td>
</tr>
<tr>
<td>Male gender, N (%)</td>
<td>49 (58)</td>
<td>59 (77)</td>
<td>.014</td>
</tr>
<tr>
<td>Mean arterial blood pressure</td>
<td>70.3 ± 26.8</td>
<td>80.6 ± 31.1</td>
<td>.027</td>
</tr>
<tr>
<td>CRF(^a)</td>
<td>27 (32)</td>
<td>38 (49)</td>
<td>.026</td>
</tr>
<tr>
<td>History of hypertension(^b)</td>
<td>38 (45)</td>
<td>55 (71)</td>
<td>.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>18 (21)</td>
<td>21 (27)</td>
<td>.387</td>
</tr>
<tr>
<td>CHF(^c)</td>
<td>34 (41)</td>
<td>36 (47)</td>
<td>.422</td>
</tr>
<tr>
<td>Cancer</td>
<td>33 (39)</td>
<td>27 (35)</td>
<td>.580</td>
</tr>
<tr>
<td>Sepsis</td>
<td>39 (46)</td>
<td>23 (30)</td>
<td>.031</td>
</tr>
<tr>
<td>Respiratory disease</td>
<td>45 (56)</td>
<td>28 (39)</td>
<td>.039</td>
</tr>
<tr>
<td>Liver disease</td>
<td>13 (17)</td>
<td>11 (15)</td>
<td></td>
</tr>
<tr>
<td>HIV negative</td>
<td>84 (100)</td>
<td>77 (100)</td>
<td>.708</td>
</tr>
<tr>
<td>MI in last 30 days</td>
<td>9 (11)</td>
<td>11 (14)</td>
<td>.493</td>
</tr>
<tr>
<td>Immunosuppression(^d)</td>
<td>23 (27)</td>
<td>19 (25)</td>
<td>.696</td>
</tr>
<tr>
<td>Oliguric(^e)</td>
<td>54 (64)</td>
<td>36 (47)</td>
<td>.025</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>73 (87)</td>
<td>45 (58)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Inotropic support(^f)</td>
<td>60 (71)</td>
<td>33 (43)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>DNR/DNI status</td>
<td>19 (24)</td>
<td>8 (11)</td>
<td>.050</td>
</tr>
<tr>
<td>Nonsurgical ICU</td>
<td>40 (48)</td>
<td>31 (40)</td>
<td>.348</td>
</tr>
<tr>
<td>APACHE II score</td>
<td>32.3 ± 7.1</td>
<td>27.9 ± 7.0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Resource Demand Scale</td>
<td>485.7 ± 519.0</td>
<td>469.2 ± 413.9</td>
<td>.824</td>
</tr>
</tbody>
</table>
Be careful how you attribute costs
Rauf et al JICM 2008;23(3)

Table 2. Observed Economic Outcomes by Method of Renal Replacement*

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>CRRT (N = 84), Mean ± SD</th>
<th>IHD (N = 77), Mean ± SD</th>
<th>Difference (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total costs</td>
<td>$106 377 ± 122 327</td>
<td>$54 821 ± 64 091</td>
<td>$51 556 ($20 749, $82 363)</td>
<td>.001</td>
</tr>
<tr>
<td>Hospital costs</td>
<td>$97 116 ± 113 813</td>
<td>$49 711 ± 58 983</td>
<td>$47 404 ($18 803, $76 005)</td>
<td>.001</td>
</tr>
<tr>
<td>Room and board</td>
<td>$35 995 ± 52 180</td>
<td>$23 645 ± 28 563</td>
<td>$12 350 (~$1087, $25 787)</td>
<td>.071</td>
</tr>
<tr>
<td>Dialysis b</td>
<td>$8052 ± 8691</td>
<td>$3254 ± 4036</td>
<td>$4799 ($2657, $6940)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Pharmacy</td>
<td>$18 486 ± 21 617</td>
<td>$6768 ± 10 964</td>
<td>$11 718 ($6309, $17 128)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Laboratory</td>
<td>$13 087 ± 12 941</td>
<td>$5879 ± 7658</td>
<td>$7208 ($3860, $10 556)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Physician costs</td>
<td>$9262 ± 9462</td>
<td>$5110 ± 6016</td>
<td>$4152 ($1658, $6645)</td>
<td>.001</td>
</tr>
<tr>
<td>Length of stay</td>
<td>17.2 ± 28.24</td>
<td>10.8 ± 13.22</td>
<td>6.48 (~0.48, 13.45)</td>
<td>.068</td>
</tr>
</tbody>
</table>

NOTE: CI = confidence interval; CRRT = continuous renal replacement therapy; IHD = intermittent hemodialysis; SD = standard deviation.

*aUnadjusted direct medical costs and length of stay from initiation of renal replacement therapy to intensive care unit discharge. All costs reflect 2004 constant dollars.
bDialysis-related hospital costs included costs categorized by revenue codes 801 (inpatient hemodialysis) and 881 (ultrafiltration).

Table 3. Observed Economic Outcomes Among Hospital Survivors by Method of Renal Replacement*

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>CRRT (N = 44), Mean ± SD</th>
<th>IHD (N = 54), Mean ± SD</th>
<th>Difference (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total costs</td>
<td>$183 188 ± 167 622</td>
<td>$94 997 ± 91 371</td>
<td>$88 191 ($35 329, $141 054)</td>
<td>.001</td>
</tr>
<tr>
<td>Hospital costs</td>
<td>$166 694 ± 155 019</td>
<td>$85 365 ± 82 905</td>
<td>$81 329 ($32 687, $129 971)</td>
<td>.001</td>
</tr>
<tr>
<td>Physician costs</td>
<td>$16 494 ± 14 191</td>
<td>$9631 ± 8985</td>
<td>$6863 ($2183, $11 543)</td>
<td>.005</td>
</tr>
<tr>
<td>Length of stay</td>
<td>49.1 ± 49.8</td>
<td>29.9 ± 25.7</td>
<td>19.3 (3.8, 34.8)</td>
<td>.015</td>
</tr>
</tbody>
</table>

NOTE: CI = confidence interval; CRRT = continuous renal replacement therapy; IHD = intermittent hemodialysis; SD = standard deviation.

*aUnadjusted direct medical costs and length of stay from initiation of renal replacement therapy to hospital discharge. All costs reflect 2004 constant dollars.
Be careful how you attribute costs
Rauf et al JICM 2008;23(3)

Table 4. Adjusted Costs Per Patient Associated With Continuous Renal Replacement Therapy and Intermittent Hemodialysis for Patients With Acute Renal Failure

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>CRRT (N = 84), Mean ± SD</th>
<th>IHD (N = 77), Mean ± SD</th>
<th>Difference (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total costs in ICU (^b)</td>
<td>$118 569 ± 107 735</td>
<td>$57 742 ± 52 466</td>
<td>$60 827 ($42 246, $79 407)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hospital costs</td>
<td>$109 134 ± 103 246</td>
<td>$52 570 ± 49 734</td>
<td>$56 564 ($38 794, $74 333)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Physician costs</td>
<td>$9739 ± 6211</td>
<td>$5279 ± 3366</td>
<td>$4461 ($3366, $5556)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Length of stay</td>
<td>20.4 ± 20.4</td>
<td>11.0 ± 10.9</td>
<td>9.5 (5.9, 13.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Total hospitalization costs (^c)</td>
<td>$140 733 ± 55 227</td>
<td>$93 611 ± 36 736</td>
<td>$47 122 ($36 837, $57 406)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hospital costs</td>
<td>$128 261 ± 51 058</td>
<td>$84 365 ± 33 584</td>
<td>$43 896 ($34 420, $53 372)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Physician costs</td>
<td>$12 779 ± 6490</td>
<td>$9593 ± 4872</td>
<td>$3186 ($1928, $4445)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Length of stay</td>
<td>35.7 ± 23.9</td>
<td>26.0 ± 17.4</td>
<td>9.7 (5.1, 14.3)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

NOTE: CI = confidence interval; CRRT = continuous renal replacement therapy; ICU = intensive care unit; IHD = intermittent hemodialysis; SD = standard deviation.

\(^a\)All costs reflect 2004 constant dollars.

\(^b\)Costs assessed from initiation of renal replacement therapy to death or ICU discharge.

\(^c\)Costs assessed from initiation of renal replacement therapy to death or hospital discharge.
Costs of CRRT
Forni, NEJM 1997 - United Kingdom

• Assumptions:
  – CRRT
    • Average 9.3 days treatment duration
    • Filter life 2.5 days
  – IHD
    • 10 daily treatments

• Costs
  – Consumables (HF, lines, RF)
  – $1,614 total (RF=$880)
  – Equivalent cost IHD $672
  – (no labor included in the calculations!)
Costs of Treatment: IHD vs. CRRT
Mehta et al, KI 2001;60:1154-1163
Southern California UCSD, UC Irvine, USNMC, VAMC

• Cost calculated prospectively (materials and labor)
• MATERIALS:
  – CRRT $338 - IHD $66
    • Dialysate 33% cost
    • Filters 20% cost
    • Rental of pumps 20%
• LABOR
  – CRRT $205 - IHD $216
• TOTAL DIRECT COSTS: Dependent on cost/Rx and # Rx
  – CRRT $543 - IHD $282

• TOTAL COST PER PATIENT TREATED
  – CRRT $3946 - IHD $3077
Outcome in Children Receiving CVVH
Goldstein SL et al Pediatrics 2001;107:1309-1312
Baylor College of Medicine, Houston Texas

• COST ANALYSIS
  – Data on 16 patients (8 survivors)
  – Mean total PICU cost $124,496 $24,149 to $405,199
    – Mean cost of CRRT $884 per patient
      $148 to $2215

Mean percentage cost of CRRT accounted for only 0.9% ± 0.5 (0.1 to 1.5%) of total PICU cost per patient PICU stay.

No difference between survivors and non survivors
CRRT: Cost

• Other modifiers of cost:
  – **Pre-determined changes of extracorporeal circuit**
    • Scheduled changes
    • Minimal FUN/BUN ratio (generally 0.8)
  – **Anticoagulation**
    • Filter survival
    • Replacement solutions
    • Labs
Cost and Intensity of Treatment

- Cost increases when higher amounts of therapy are delivered:
  - IHD: personnel costs increase
  - CRRT: replacement solutions and dialysate
Areas of Potential Cost Reduction in CRRT

• Dialyzers
  – Type of membrane
  – Access (MAJOR)
  – Anticoagulation (MAJOR)

• Personnel
  – ICU alone vs. Nephrology/ICU collaboration

• Dialysate and replacement fluids

• Service, support

• Appropriateness of treatment/patient selection
St Peter's Hospital CRRT Program

FILTER DURATION

PATIENT NUMBER

HOURS

0  10  20  30  40  50  60  70  80

St. Peter's HEALTH CARE SERVICES
FILTER SURVIVAL ANALYSIS

OVERALL

BEFORE FUN/BUN

AFTER FUN/BUN
Cost and Intensity of Treatment

• Cost increases when higher amounts of therapy are delivered:
  – IHD: personnel costs increase
  – CRRT: replacement solutions and dialysate
Daily Cost (US Dollars) of Maintaining CRRT Providing a Urea Clearance of 33 ml/min

<table>
<thead>
<tr>
<th>ITEM</th>
<th>TYPE</th>
<th>COST/UNIT (US$)</th>
<th>COST/DAY (US$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>REPLACEMENT FLUID</td>
<td>0.9% NS</td>
<td>0.75</td>
<td>18</td>
</tr>
<tr>
<td>DIALYSATE</td>
<td>Pharmacy Prepared</td>
<td>4.70</td>
<td>113</td>
</tr>
<tr>
<td>CaCl₂</td>
<td>Pharmacy Prepared</td>
<td>1.42</td>
<td>34</td>
</tr>
<tr>
<td>Trisodium Citrate</td>
<td>Baxter</td>
<td>9.16</td>
<td>220</td>
</tr>
<tr>
<td>Filter Set</td>
<td>Gambro M60</td>
<td>160</td>
<td>53</td>
</tr>
<tr>
<td><strong>SUBTOTAL</strong></td>
<td></td>
<td><strong>438</strong></td>
<td></td>
</tr>
<tr>
<td>Nursing Cost</td>
<td>50% daily wages US$25/hr</td>
<td><strong>300</strong></td>
<td></td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td></td>
<td><strong>738</strong></td>
<td></td>
</tr>
</tbody>
</table>
Weekly Cost (US Dollars) of Maintaining CRRT Providing a Urea Clearance of 10 and 15 Ml/min

<table>
<thead>
<tr>
<th>UREA CLEARANCE</th>
<th>CVVH, CAVH</th>
<th>CVVHD, CAVHD</th>
<th>IHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 ml/min</td>
<td>1,050-4,000</td>
<td>500-1,200</td>
<td>450-540</td>
</tr>
<tr>
<td>15 ml/min</td>
<td>1,100-5,500</td>
<td>600-1,300 +12%</td>
<td>600-800 +41%</td>
</tr>
</tbody>
</table>

Cost of Acute Renal Replacement Therapy

• US SUPPORT Trial (Hamel et al, Ann Int Med 1997)
  – Hospitalization cost after initiation of dialysis in the ICU: ~31,000 USD (1994 dollars)
  – Total hospitalization cost for patient receiving dialysis in the ICU: ~63,000 USD (1994 dollars) => ~108,000 USD in 2005 dollars (5% inflation rate)
  – Therefore, approximately 50% of total costs are incurred prior to initiation of dialysis

• Canadian trial (Manns et al, Critical Care Med 2003)
  – Hospitalization cost after initiation of dialysis in the ICU: ~37,000 CAD (1999 dollars)
  – Based on cost breakdown from SUPPORT Trial, total hospitalization cost for patient receiving dialysis in the ICU: ~75,000 CAD (1999 dollars) => 100,000 CAD in 2005 dollars (5% inflation rate)
Cost of Acute Renal Replacement Therapy

• Canadian SLED Study (Berbece et al, Kidney Int 2006): assuming average treatment duration of 6 days
  – SLED cost: 1431 CAD
  – CRRT heparin cost: 2235 CAD
  – CRRT citrate cost: 2648 CAD

• Expressed as a percentage of total hospitalization cost:
  – SLED: 1.4%
  – CRRT heparin: 2.2%
  – CRRT citrate: 2.7%

• When viewed in the context of the overall cost of managing a critically ill ARF patient, the cost difference between SLED and CRRT is very small
Economic Evaluation of CRRT
Klarenbach et al, U Alberta, Canada

• CRRT associated with similar health outcomes but higher costs ($3,679 more than IHD per patient)

• Alternate sources and more intense IHD (duration, frequency) CRRT remained more costly

• Sensitivity analysis indicated that even small differences in mortality risk or need for long term dialysis led to dramatic changes in cost-effectiveness between modalities
Natural History of AKI
AKIN, Vancouver 2006

Cerda et al, CJASN 2008
AKI Increases Risk of ESRD Among the Elderly

Ishani, Xue, Himmelfarb, Eggers, Kimmel, Molitoris, Collins
JASN Jan, 2009

Log-rank test: P<0.0001 DF=1

No AKI or CKD
AKI only
CKD only
AKI and CKD

PROBABILITY OF ESRD

DAYS FROM HOSPITAL DISCHARGE

Log-rank test: P<0.0001 DF=3

0.9%  2.69%  4.08%  6.96%

0.00  0.03  0.06

0.00  0.10  0.16

AKI
AKI + CKD

1.61%  4.76%  7.91%  14.29%
AKI Increases Risk of ESRD Among the Elderly

Ishani, Xue, Himmelfarb, Eggers, Kimmel, Molitoris, Collins
JASN Jan, 2009
One-Year Outcomes of Critically Ill Patients with AKI
Palevsky et al, SA-FC414, ASN 2008

<table>
<thead>
<tr>
<th></th>
<th>ALL PATIENTS (N=1124)</th>
<th>Intensive Rx (N=563)</th>
<th>Low-Intensity Rx (N=561)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alive at day 60</td>
<td>528/1119 47.2%</td>
<td>259/561 46.2%</td>
<td>269/558 48.2%</td>
<td>0.49</td>
</tr>
<tr>
<td>Alive at 1 year</td>
<td>371/1092 34%</td>
<td>183/546 33.5%</td>
<td>188/546 34.4%</td>
<td>0.75</td>
</tr>
<tr>
<td>Survived to day 60 and alive 1 yr</td>
<td>371/501 74.1%</td>
<td>183/244 75%</td>
<td>188/257 73.2%</td>
<td>0.64</td>
</tr>
<tr>
<td>Alive 1 yr. and dialysis independent between 60 d-1 yr</td>
<td>281/315 89.2%</td>
<td>139/156 89.1%</td>
<td>142/159 89.3%</td>
<td>0.95</td>
</tr>
</tbody>
</table>

Late mortality (>60 d) in patients post AKI was high: >25% 60-d survivors die within 1 yr.
ESRD After ARF: Effect on Survival
Bhandari and Turney, QJM 1996

The graph demonstrates the survival rates of patients with ESRF and ARF over time. The survival rates are shown for individuals aged 50-64 years. The graph indicates a statistically significant difference in survival rates between the two groups, with a p-value of 0.03.
Why is avoiding CKD and optimizing the care of advanced CKD patients important?

The number of patients with kidney failure is rising.

[Graph showing the increase in the number of patients with CKD from 1984 to 2010, with labels indicating the number of patients in thousands at various years.]
But if I start dialysis early, will that not *finish off the kidneys*?
CRRT vs. IHD in Renal Recovery

• Several recent articles suggest CRRT is superior to IHD with respect to renal recovery.

• Implications go far beyond just hard endpoint of renal recovery:
  • Need for chronic dialysis impairs quality of life
  • If LOS in ICU can be reduced this will have major impact on hospital budget
  • Patient dependent on chronic dialysis will consume significant health care resources and have an impact on community health care budget
Effect of Dialysis Modality on Recovery of Renal Function in ARF
# CRRT vs. IHD for Renal Recovery

Manns et al, Crit Care Med 2003

<table>
<thead>
<tr>
<th>Initial Dialysis Modality</th>
<th>Overall (n = 261)</th>
<th>CRRT (n = 178)</th>
<th>Intermittent Hemodialysis (n = 83)</th>
<th>p Value for Comparison of CRRT with IHD$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital death (%)</td>
<td>163 (62.5)</td>
<td>128 (71.9)</td>
<td>35 (42.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>In-hospital renal recovery, as a proportion of total patients, n = 261 (%)</td>
<td>84 (32.2)</td>
<td>51 (28.6)</td>
<td>33 (39.8)</td>
<td>.07</td>
</tr>
<tr>
<td>In-hospital renal recovery, as a proportion of patients alive at hospital discharge, n = 98 (%)</td>
<td>70 (71.4)</td>
<td>40 (80.0)</td>
<td>30 (62.5)</td>
<td>.06</td>
</tr>
<tr>
<td>Mean duration of dialysis in patients who recovered renal function in days, n = 84 (SD)</td>
<td>14.7 (16.5)</td>
<td>14.7 (14.8)</td>
<td>14.5 (19.1)</td>
<td>.91</td>
</tr>
</tbody>
</table>

Leading the way...
CRRT vs. IHD for Renal Recovery
Manns et al, Crit Care Med 2003

<table>
<thead>
<tr>
<th>Status at Hospital Discharge</th>
<th>Alive with Renal Recovery (n = 70)</th>
<th>Alive on Dialysis (n = 28)</th>
<th>Dead (n = 163)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (SD)</td>
<td>58.2 (17.1)</td>
<td>56.1 (16.8)</td>
<td>60.3 (16.5)</td>
</tr>
<tr>
<td>Initial APACHE II score (SD)</td>
<td>22.5 (7.5)</td>
<td>20.4 (5.4)</td>
<td>28.7 (8.6)</td>
</tr>
<tr>
<td>Baseline creatinine in µmol/L, n = 181 (SD)</td>
<td>142 (63)</td>
<td>198 (145)</td>
<td>143 (89)</td>
</tr>
<tr>
<td>Mean (median, 25–75th percentile) number of days in the ICU after first dialysis</td>
<td>10.3 (7, 3–15)</td>
<td>11.1 (5, 2–17)</td>
<td>8.9 (5, 2–13)</td>
</tr>
<tr>
<td>Mean (median, 25–75th percentile) number of days in the hospital after first dialysis</td>
<td>38.2 (32, 16–53)</td>
<td>47.7 (33, 17.5–62)</td>
<td>12.2 (5, 2–16)</td>
</tr>
<tr>
<td>Mean in-hospital costs after first dialysis</td>
<td>$47,694</td>
<td>$56,035</td>
<td>$29,425</td>
</tr>
</tbody>
</table>
### CRRT vs. IHD for Renal Recovery

Manns et al, Crit Care Med 2003

<table>
<thead>
<tr>
<th></th>
<th>Patients with In-Hospital Renal Recovery (n = 46)</th>
<th>Patients WhoWere on Dialysis at Hospital Discharge (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (SD)</td>
<td>59.4 (19.0)</td>
<td>54.9 (18.8)</td>
</tr>
<tr>
<td>Initial APACHE II score (SD)</td>
<td>22.9 (5.6)</td>
<td>20.2 (4.7)</td>
</tr>
<tr>
<td>Charlson comorbidity index (SD)</td>
<td>4.6 (1.9)</td>
<td>4.4 (1.8)</td>
</tr>
<tr>
<td>Baseline creatinine in μmol/L, n = 58 (sd)</td>
<td>145 (6)</td>
<td>221 (149)c</td>
</tr>
<tr>
<td>Renal recovery in subsequent year (%)</td>
<td>NA</td>
<td>2 (10)</td>
</tr>
<tr>
<td>Death in subsequent year (%)</td>
<td>7 (15.2)</td>
<td>3 (15)</td>
</tr>
<tr>
<td>Mean (median, 25–75th percentile) hospital days in subsequent year</td>
<td>11.3 (0, 0–11)</td>
<td>22.5 (16, 0–32)d</td>
</tr>
<tr>
<td>Mean hospital costs in subsequent year (excludes physician claims)</td>
<td>$8,199</td>
<td>$17,596d</td>
</tr>
<tr>
<td>Mean physician billing (for inpatient and outpatient care) in subsequent year</td>
<td>$2,710</td>
<td>$8,791d</td>
</tr>
<tr>
<td>Mean cost of outpatient hemodialysis in subsequent year</td>
<td>0</td>
<td>$36,013</td>
</tr>
<tr>
<td>Mean cost of day surgery/emergency room visits in subsequent year</td>
<td>$283</td>
<td>$961d</td>
</tr>
<tr>
<td>Mean cost of high-cost drugs (erythropoietin, intravenous iron) in subsequent year</td>
<td>0</td>
<td>$9,912</td>
</tr>
<tr>
<td><strong>Total direct healthcare costs in subsequent year</strong></td>
<td><strong>$11,192</strong></td>
<td><strong>$73,273d</strong></td>
</tr>
</tbody>
</table>
CRRT Improves Survival from ARF
Jacka et al, 2005

<table>
<thead>
<tr>
<th>TABLE V</th>
</tr>
</thead>
<tbody>
<tr>
<td>A) ICU survival vs RRT mode</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>CRRT</td>
</tr>
<tr>
<td>IHD</td>
</tr>
<tr>
<td>B) Hospital survival vs RRT mode</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>CRRT</td>
</tr>
<tr>
<td>IHD</td>
</tr>
<tr>
<td>C) Renal recovery vs RRT mode</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>CRRT</td>
</tr>
<tr>
<td>IHD</td>
</tr>
</tbody>
</table>

RRT = renal replacement therapy; CRRT = continuous renal replacement therapy; IHD = intermittent hemodialysis.
## BEST Kidney: Baseline Patient Characteristics


<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>CRRT</th>
<th>IRRT</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (bpm)</td>
<td>98 (85 - 114)</td>
<td>99 (85 - 115)</td>
<td>96 (82 - 110)</td>
<td>0.039</td>
</tr>
<tr>
<td>Respiratory rate (bpm)</td>
<td>18 (15 - 22)</td>
<td>18 (15 - 22)</td>
<td>20 (15 - 24)</td>
<td>0.010</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>75 (66 - 86)</td>
<td>74 (65 - 84)</td>
<td>80 (72 - 98)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CVP (mmHg)</td>
<td>14 (10 - 18)</td>
<td>14 (10 - 18)</td>
<td>13 (10 - 18)</td>
<td>0.42</td>
</tr>
<tr>
<td>PA catheter usage (%)</td>
<td>25.8%</td>
<td>29.5%</td>
<td>8.5%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PAOP (mmHg)</td>
<td>18 (15 - 22)</td>
<td>18 (15 - 22)</td>
<td>18 (12 - 23)</td>
<td>0.45</td>
</tr>
<tr>
<td>Glasgow Coma Score</td>
<td>14 (10 - 15)</td>
<td>14 (10 - 15)</td>
<td>14 (10 - 15)</td>
<td>0.97</td>
</tr>
<tr>
<td>Mechanical ventilation (%)</td>
<td>80.2%</td>
<td>84.4%</td>
<td>61.8%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Vasopressors / inotropes</td>
<td>74.0%</td>
<td>78.8%</td>
<td>50.7%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Factor</td>
<td>Odds ratio (95% CI)</td>
<td>P value</td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------------------------------------</td>
<td>-----------------------------------</td>
<td>---------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>0.975 (0.966 - 0.985)</td>
<td>p&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>From hospital to ICU (days)</td>
<td>0.951 (0.932 - 0.97)</td>
<td>p&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Platelet count (*10^9/μL)</td>
<td>1.003 (1.002 - 1.004)</td>
<td>p&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine (μmol/L)</td>
<td>1.003 (1.002 - 1.004)</td>
<td>p&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>pH</td>
<td>30.92 (6.675 - 143.0)</td>
<td>p&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CF: sepsis / septic shock</td>
<td>0.534 (0.390 - 0.731)</td>
<td>p&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>0.461 (0.304 - 0.699)</td>
<td>p=0.0003</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CF: Hepato-renal syndrome</td>
<td>0.330 (0.173 - 0.629)</td>
<td>p=0.0008</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAPS-II (points)</td>
<td>0.986 (0.977 - 0.994)</td>
<td>p=0.0013</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>1.014 (1.004 - 1.025)</td>
<td>p=0.0074</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CF: low cardiac output</td>
<td>0.623 (0.440 - 0.882)</td>
<td>p=0.0077</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reason: High urea / creatinine</td>
<td>0.652 (0.473 - 0.900)</td>
<td>p=0.0092</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vasopressors / inotropes</td>
<td>0.635 (0.441 - 0.916)</td>
<td>p=0.015</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other diuretics</td>
<td>0.495 (0.278 - 0.882)</td>
<td>p=0.017</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Furosemide (mg/6hrs)</td>
<td>0.998 (0.997 - 1.000)</td>
<td>p=0.018</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urine output (ml/6hrs)</td>
<td>1.001 (1.000 - 1.001)</td>
<td>p=0.032</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Propensity score</td>
<td>1.721 (1.345 - 2.202)</td>
<td>p=0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRRT</td>
<td>0.970 (0.644 - 1.461)</td>
<td>p=0.88</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

From hospital to ICU = duration between hospital admission and ICU admission; CF = contributing factor; MAP = mean arterial pressure
BEST Kidney: Effect of Modality on Survival and Renal Recovery
Recovery from Dialysis Dependence: BEST Kidney


Leading the way…
Recovery from Dialysis Dependence: BEST Kidney
Clark et al, Blood Purif 2006

P<0.001

% of patients
Recovery from Dialysis Dependence: CRRT vs IHD

_Bell et al, Intensive Care Med 2007_

- Characteristics of study
  - 2,022 patients across 32 Swedish hospitals
  - Modality breakdown: CRRT - 86%; IHD - 14%

- Dependence on chronic dialysis at 90 days differed significantly between the two modalities
  - CRRT – 8%; IHD – 17%

- For those patients who developed ESRD, long-term risk of death also differed significantly
  - IHD:CRRT odds ratio for death was 2.29
Odds ratios of renal failure for patients treated with IHD vs CRRT among the 1,102 patients surviving 90 days after inclusion in the cohort

<table>
<thead>
<tr>
<th></th>
<th>CRRT (n=944)</th>
<th>IHD (n=158)</th>
<th>OR</th>
<th>n (%)</th>
<th>OR^a (95% CI)</th>
<th>OR^b (95% CI)</th>
<th>OR^c (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESRD</td>
<td>78 (8.3)</td>
<td>26 (16.5)</td>
<td>1.0</td>
<td>2.19 (1.4–3.5)</td>
<td>2.13 (1.3–3.5)</td>
<td>2.60 (1.5–4.3)</td>
<td></td>
</tr>
</tbody>
</table>

A OR, crude
B OR, adjusted for age, sex, diabetes or heart failure before admission and calendar year
C OR, adjusted for age, sex, diabetes or heart failure before admission, calendar year, hospital type and main diagnosis at ICU
Survival Comparison After ARF Treated with CRRT or IHD

Bell et al, Intensive Care Med 2007
Effect of Modality on Recovery of Renal Function

  - 17% of IHD patients vs 4% of CRRT patients had CKD at hospital discharge or death (intent-to-treat; P=0.01)
  - 92% vs 59% of patients receiving adequate trial of monotherapy (CRRT vs IHD, respectively; P<0.01) had complete recovery of renal function
  - Patients crossing over from IHD to CRRT had significantly higher rate of complete recovery of renal function vs opposite direction (45% vs 7%, P<0.01)

- BEST Study (2007)
- SWING Study (2007)
Several recent articles suggest CRRT is superior to IHD with respect to "renal recovery".

Implications go far beyond just "hard" endpoint of renal recovery:

- Need for chronic dialysis impairs quality of life
- If LOS in ICU can be reduced this will have major impact on hospital budget
- Patient dependent on chronic dialysis will consume significant health care resources and have an impact on community health care budget
How often does AKI lead to CKD?

<table>
<thead>
<tr>
<th>ARF etiology</th>
<th>Number of survivors (%)</th>
<th>Maximum follow-up in months</th>
<th>Long-term survival (%)</th>
<th>Functional outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obstetric causes</td>
<td>112 (21%)</td>
<td>372</td>
<td>91%</td>
<td>1 year, 79%&lt;sup&gt;h&lt;/sup&gt;, 5 years: 75%&lt;sup&gt;h&lt;/sup&gt;, 10 years: 72%&lt;sup&gt;h&lt;/sup&gt;</td>
</tr>
<tr>
<td>ATN</td>
<td>226 (46%)</td>
<td>144</td>
<td>100%</td>
<td>67% (5 years)&lt;sup&gt;h&lt;/sup&gt;</td>
</tr>
<tr>
<td>ATN</td>
<td>40 (70%)</td>
<td>12</td>
<td>97%</td>
<td>81%&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>Most ATN</td>
<td>79 (66%)</td>
<td>18</td>
<td>79&lt;sup&gt;e&lt;/sup&gt;</td>
<td>NA</td>
</tr>
<tr>
<td>ATN</td>
<td>150 (58%)</td>
<td>6</td>
<td>57%</td>
<td>87% (6 months)&lt;sup&gt;h&lt;/sup&gt;</td>
</tr>
<tr>
<td>ATN and ATN</td>
<td>23 (68%)</td>
<td>12</td>
<td>100%</td>
<td>Period 77-79: 21%&lt;sup&gt;g&lt;/sup&gt;</td>
</tr>
<tr>
<td>ATN</td>
<td>37 (48%)</td>
<td>12</td>
<td>100%</td>
<td>Period 91-92: 30%&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>NR(?)</td>
<td>24</td>
<td>NA</td>
<td>31% (2 years)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>ATN</td>
<td>34 (45%)</td>
<td>60</td>
<td>35% (5 years)&lt;sup&gt;q&lt;/sup&gt;</td>
<td>Chronic dialysis 8%&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>161 (56%)</td>
<td>36</td>
<td>100%</td>
<td>Chronic dialysis 10%&lt;sup&gt;g&lt;/sup&gt;</td>
</tr>
<tr>
<td>Probably mainly ATN</td>
<td>301 (69%)</td>
<td>88</td>
<td>89%</td>
<td>Chronic dialysis 2%&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>ATN</td>
<td>187 (55%)</td>
<td>264</td>
<td>95%</td>
<td>50% (10 years)&lt;sup&gt;h&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>Liano F et al Kidney Int 2007
Increase in ESRD incidence

• 1. Increase in CKD prevalence
• 2. More liberal dialysis entry criteria
  – Increased GFR 7.5 → 10, decreased SCr 10 → 7
• 3. Better survival to competing causes
  – MI, CVA
• 4. Role of AKI
  – Not demonstrated
  – Unquantified
  – Approximately 5% increase
  – Increased incidence
  – Better survival
  – Increased non-recovery of function
Increase in ESRD incidence: Role of AKI

• 1. Increased incidence
  ➢ Waikar et al (1988-2002 sample): Incidence increased from 4 to 27 per 100,000 pop.

• 2. Survival
  ➢ Waikar et al (1988-02 sample: survival increased 59 to 72%
    ➢ Thus new ESRD from AKI increased from 2.4 to 19.4 per 100,000

• 3. Non-recovery of function
    ➢ MAJOR CAUSE

THUS, PERHAPS UP TO 1/4 OF NEW ESRD IS DUE TO AKI
Incidence of new ESRD cases - USA

Figure 1 Number of new treated end-stage renal disease (ESRD) cases among black and white subjects aged 25–79 years in the USA from 1985 to 1996 (modified from [5]).

Bars show the number of new cases of ESRD among black and white subjects aged 25–79 years in the USA from 1985 to 1996. Model A is observed (unadjusted) rate of increase in incidence (8.0% per year). Model B is adjusted for population growth and demographic characteristics (6.9% per year). Model C is adjusted for population growth, demographic characteristics, and prevalence of stage 3–4 chronic kidney disease (6.1% per year).
After adjusting for increase in CDK incidence or risk factors for ESRD including age, sex, race, DM, BP, BMI, education, cholesterol, proteinuria, hematuria, serum Cr, there remained an unexplained 8% increase in incidence (RR 1.08 (1.06-1.11 95% CI) associated with year of cohort entry.
Prevalence of CKD by Stage and Non-recovery of AKI

Table 1: Stability in the prevalence of chronic kidney disease in the USA from 1988–1994 to 1999–2000 (modified from [6])

<table>
<thead>
<tr>
<th>CKD (GFR in ml/min/1.73 m²)</th>
<th>Prevalence (%)</th>
<th>Prevalence ratio (95% CI)</th>
<th>No. in USA in 2000, thousands (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1 (GFR ≥90 and persistent albuminuria)</td>
<td>2.2</td>
<td>2.8</td>
<td>1.26 (1.00–1.59)</td>
</tr>
<tr>
<td>Stage 2 (GFR 60–89 and persistent albuminuria)</td>
<td>2.2</td>
<td>2.8</td>
<td>1.27 (1.00–1.61)</td>
</tr>
<tr>
<td>Stage 3 (GFR 30–59)</td>
<td>4.2</td>
<td>3.7</td>
<td>0.88 (0.67–1.10)</td>
</tr>
<tr>
<td>Stage 4 (GFR 15–29)</td>
<td>0.19</td>
<td>0.13</td>
<td>0.68 (0.07–1.44)</td>
</tr>
<tr>
<td>All stages</td>
<td>8.8</td>
<td>9.4</td>
<td>1.07 (0.93–1.22)</td>
</tr>
</tbody>
</table>

CKD, chronic kidney disease; GFR, glomerular filtration rate.

Table 2: Change in incidence of nonrecovery from acute renal failure vs. change in overall incidence of end-stage renal disease in the USA from 1988 to 2002

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Observed incidence of dialysis requiring ARF (per 100,000 population), from [14]</td>
<td>4</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Observed rate of survival among ARF patients, from[14]</td>
<td>59%</td>
<td>72%</td>
<td></td>
</tr>
<tr>
<td>Estimated proportion of ARF survivors requiring permanent dialysis, extrapolated from [15]</td>
<td>15%</td>
<td>25%</td>
<td></td>
</tr>
<tr>
<td>Calculated incidence of ESRD generated among ARF survivors (per 100,000 population)</td>
<td>0.4</td>
<td>4.9</td>
<td>4.5</td>
</tr>
<tr>
<td>Observed incidence of ESRD (per 100,000 population), from USRDS [16]</td>
<td>16</td>
<td>34</td>
<td>18</td>
</tr>
</tbody>
</table>

ARF, acute renal failure; ESRD, end-stage renal disease; USRDS, United States Renal Data System.