



 <p>AHFMR ALBERTA HERITAGE FOUNDATION FOR MEDICAL RESEARCH</p> 
 <p>Critical Care Medicine</p>	<p>TIMING OF INITIATION OF RENAL SUPPORT IN AKI</p> <p><small>Dean M. Waghans, MD, MSc, FRCPC Division of Critical Care Medicine, University of Alberta, Edmonton, Canada</small></p>

 <p>Critical Care Medicine</p>	<p>DISCLOSURES/CONFLICTS</p>
	<ul style="list-style-type: none"> ⊙ Inverness Medical Innovations ⊙ Baxter Inc

 <p>Critical Care Medicine</p>	<p>OUTLINE</p>
	<ul style="list-style-type: none"> ⊙ Epidemiology ⊙ Definition of "Timing" ⊙ Current Practice ⊙ Available Evidence ⊙ Fluid Accumulation ⊙ Summary

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ACUTE KIDNEY INJURY: THEN AND NOW

Then	Now
<ul style="list-style-type: none"> ● No ICU support ● Not ventilated ● No vasopressors ● Isolated kidney failure ● Limited study design ● Limited statistical analysis 	<ul style="list-style-type: none"> ● Older ● Co-morbid disease ● CKD prevalence ● Complex procedures ● Advanced technology ● Illness severity ● Multi-organ support

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CONTRIBUTING FACTORS FOR AKI

...however, AKI is increasingly multi-factorial and multi-insult

Uchino et al JAMA 2005

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OUTCOME IN SEVERE AKI

Cause	Mortality (%)	Incidence (%)
Shock	84	~4
Septic	71	~4
Myocardial	63	~5
Obstructive	62	~4
Respiratory	60	~4
ESRF	62	~4
CNS	50	~3
Subarachnoid	52	~10

JAMA Chronic Dialysis and Death Among Survivors of Acute Kidney Injury Requiring Dialysis
 Ron Wald, Robert R. Quinn, Jin Luo, et al
 JAMA. 2009;302(11):1179-1185. doi:10.1001/jama.2009.1322
 http://jama.ama-assn.org/cgi/content/full/302/11/1179

A Chronic dialysis risk

Follow-up (y)	Acute kidney injury and dialysis (%)	No acute kidney injury (%)
0	0	0
1	~5	~2
2	~8	~3
3	~10	~4
4	~12	~4.5
5	~13	~5
6	~14	~5.5
7	~15	~5.8
8	~16	~6
9	~17	~6.2
10	~18	~6.5

Wald et al JAMA 2009

HOW DO WE DEFINE "TIMING" OF RRT INITIATION?

Symptom onset

Serum/urine biochemistry

Novel biomarkers (i.e. NGAL)

Relative to onset of AKI

Relative to hospital/ICU admission

WHAT IS CURRENT PRACTICE?

Original Articles

Management of Renal Replacement Therapy in Acute Kidney Injury: A Survey of Practitioner Prescribing Practices

Pamela Overberger,¹ Matthew Pesacreta,² and Paul M. Palevsky,^{3*}
 for the VA/NIH Acute Renal Failure Trial Network

¹Research Service and ²Renal Section, Medical Specialty Service Line, VA Pittsburgh Healthcare System, and ³Renal-Electrolyte Division, Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania

Nephrol Dial Transplant (2006) 21: 499-506
 doi:10.1093/ndt/gfi296
 Advance Access publication 2 December 2005

Original Article

Practice patterns in the management of acute renal failure in the critically ill patient: an international survey

Zaccaria Ricci^{1,2}, Claudio Ronco², Giuseppe D'amico¹, Riccardo De Felice¹, Stefano Rossi¹, Irene Bolgan³, Monica Bonello², Nergo Zamperetti³, Dimitris Petras⁴, Gabriella Salvatori^{4,5}, Maurizio Dan⁶ and Pasquale Piccini⁷



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WHAT IS CURRENT PRACTICE?

Trials	Criteria for RRT Initiation
Ronco (2000)	AKI defined as elevated urea/SCr and oliguria (200mL/12hr), despite fluid resuscitation and furosemide
Mehta (2001)	AKI defined as sustained rise in baseline SCr >88.4, absolute >177 or urea>40
Schiffli (2002)	Attending nephrology decided when to initiate RRT
Saudan (2006)	AKI, not otherwise defined
Vinsonneau (2006)	AKI defined as urea>36, SCr>310
ATN Study (2008)	AKI defined as SCr>177 in men, >133 in women, within 4 days, oliguria (<20mL/hr), despite fluid resuscitation
RENAL Study (2009)	AKI defined by oliguria (<100mL/6hr) despite fluid resuscitation, K>6.5, pH<7.20, urea>25, SCr>300 or significant organ edema



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WHAT IS CURRENT PRACTICE?

Study	ICU (days)	Hospital (days)
BEST Kidney Study	1.0 (0-5)	5.0 (1-12)
CANA KI Study	1.0 (0-4)	3.0 (1-10)
ATN Trial	6.4 (±7.8)	10.3 (±14.7)
Tolwani et al Trial	8.0 (±11)	-
RENAL Trial	2.1 (±4.2)	-





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CLASSIC "RESCUE" INDICATIONS FOR RRT

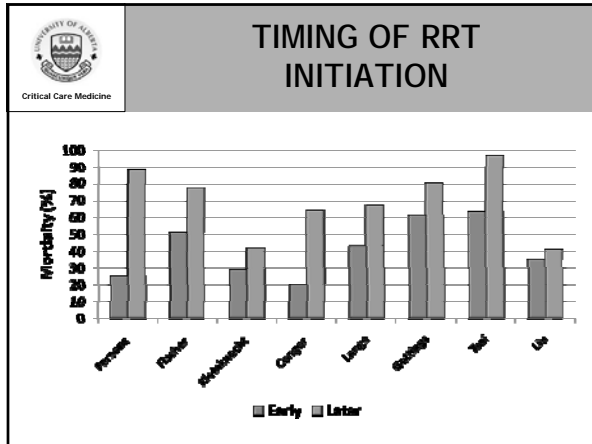
"Absolute" Indications for RRT initiation	
Oligo-anuria	Urine output <200mL/12 hr or anuria
Azotemia	Urea>36 mmol/L or uremic organ complications
Hyperkalemia	K+ >6.5 and/or rapidly rising and/or ECG abnormalities
Metabolic acidosis	pH <7.15
Sodium disorders	Progressive and/or uncontrolled hypo/hyponatremia
Thermoregulation	Uncontrolled hyperthermia and/or hypothermia (>39.5 C)
Volume overload	Clinically significant, diuretic-unresponsive organ edema
Overdose	Drug overdose with dialyzable toxin

Any Critical Care or Nephrology Textbook

 <small>Critical Care Medicine</small>	PATIENT-SPECIFIC FACTORS
	Pre-morbid kidney function
	Current kidney function/anticipated demand
	Co-morbid disease/physiologic reserve
	AKI/illness severity/trajjectory
	Prevention of uremic/organ toxicity

 <small>Critical Care Medicine</small>	CLINICIAN-SPECIFIC FACTORS
	Goals of therapy
	Relative indications
	Individual thresholds for initiation
	Local practice patterns/standard of care
	Prescribing service

 <small>Critical Care Medicine</small>	ORGANIZATIONAL FACTORS
	Country
	Institution type
	ICU type
	Machine/nurse resource availability
	Health resources/costs

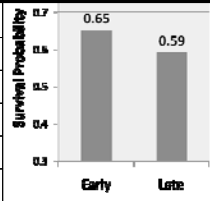


Timing of Initiation of Dialysis in Critically Ill Patients with Acute Kidney Injury

Kathleen D. Liu,^{*} Jonathan Himmelfarb,[†] Emil Paganini,[‡] T. Alp Ikizler,[§] Sharon H. Soroko,[¶] Ravindra L. Mehta,^{||} and Glenn M. Chertow^{**}
^{*}Division of Nephrology, Department of Medicine, University of California San Francisco, San Francisco, California; [†]Division of Nephrology, Department of Medicine, Maine Medical Center, Portland, Maine; [‡]Division of Nephrology, Department of Medicine, Cleveland Clinic Foundation, Cleveland, Ohio; [§]Division of Nephrology, Department of

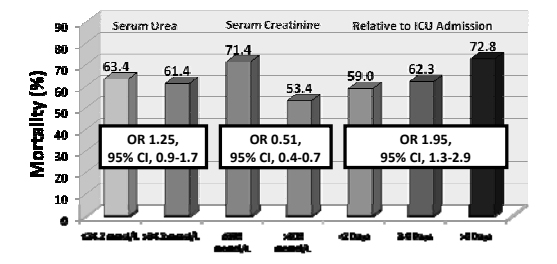
University of California San Francisco
Death at 60-days:
HR 1.85 (95% CI, 1.16-2.96)

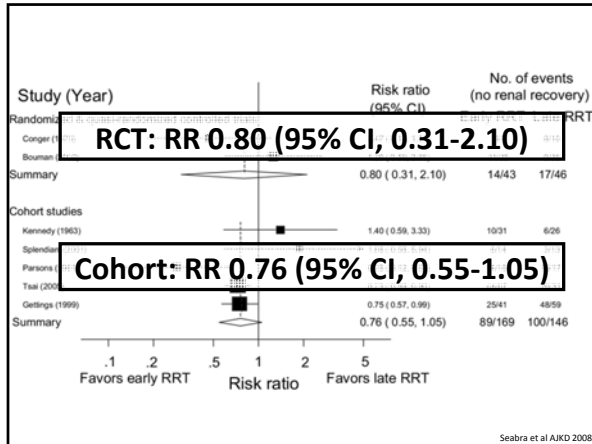
	(N=122)	(N=121)	
Urea (mmol/L)	17	41	<0.001
Creatinine (umol/L)	301	415	<0.001
No. Organ Failures	4	3	0.008
Sepsis (%)	37	46	0.14
Initial RRT (CRRT) (%)	69	43	0.001

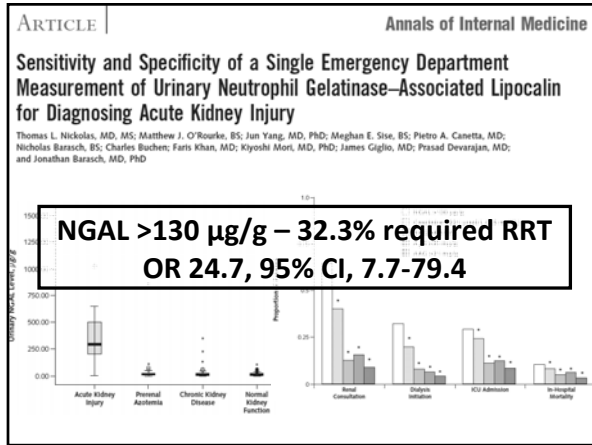


Timing of renal replacement therapy and clinical outcomes in critically ill patients with severe acute kidney injury

Journal of Critical Care
 Sean M. Bagshaw MD, MSc^{a,b,*}, Shigehiko Uchino MD^c, Rinaldo Bellomo MD^d, Hiroshi Morimatsu MD^e, Stanislaw Morgera MD^f, Miet Schetz MD^g, Ian Tan MD^h, Catherine Bouman MDⁱ, Ettiene Macedo MD^j, Noel Gibney MD^k, Ashita Tolwani MD^l, Heleen M. Oudemans-van Straaten MD^m, Claudio Ronco MDⁿ, John A. Kellum MD^o, for the Beginning and Ending Supportive Therapy for the Kidney (BEST Kidney) Investigators







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FLUID ACCUMULATION

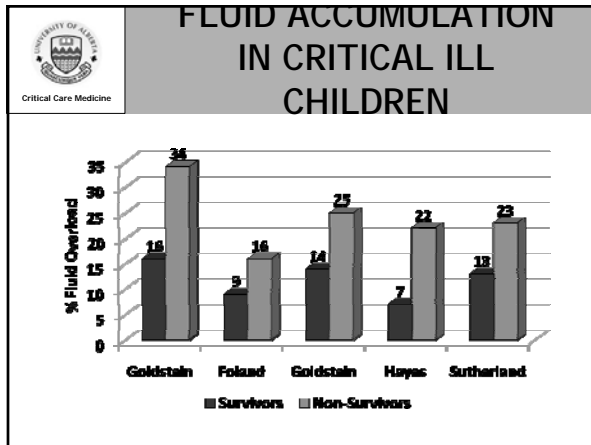
EARLY GOAL-DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

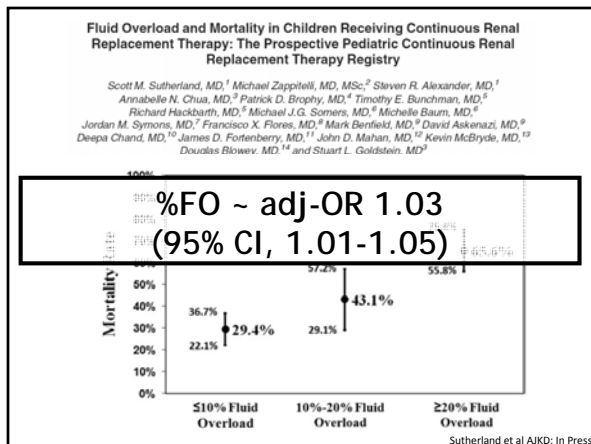
EMANUEL RIVERS, M.D., M.P.H., BRYANT NGUYEN, M.D., SUZANNE HAUSTAD, M.A., JULIE RESSLER, B.S., ALEXANDRIA MUZZIN, B.S., BERNHARD KNOBlich, M.D., EDWARD PETERSON, Ph.D., AND MICHAEL TOMLANOVICH, M.D. FOR THE EARLY GOAL-DIRECTED THERAPY COLLABORATIVE GROUP*

Total Fluids (mL)	0-6 hrs	7-72 hrs	0-72 hrs
Standard	3499	10602	13358
EGDT	4981	8625	13443

Rivers et al NEJM 2001

Study	Year	N	Population	Exposure	Outcome
Simmons	1987	113	ARDS	(+) daily and cumulative fluid balance, weight gain	↑ Mortality
Schuller	1991	89	ALI/ARDS	(+) fluid balance >1L over 36 hr	↑ duration MV, ↑ ICU, hospital stay
Mitchell	1992	101	Critically ill (EVLW ~ 7mL/kg)	RCT: restrictive vs. standard of care (PAC)	Restrictive: ↓ duration MV, ↓ ICU stay
Alsous	2000	36	Septic shock	Failure to achieve (-) >500 mL in 1 of 3 days	↑ Mortality
Brandstrup	2003	172	Colorectal surgery	RCT: restrictive vs. standard of care	Restrictive: ↓ complications
Sakr	2005	393	ALI/ARDS	(+) cumulative fluid balance	↑ Mortality
Uchino	2006	331	Critically ill	(+) daily fluid balance	↑ Mortality

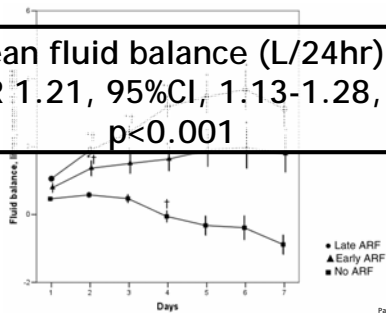




A positive fluid balance is associated with a worse outcome in patients with acute renal failure

Didier Payen¹, Anne Cornélie de Pont², Yasser Sakr³, Claudia Spies⁴, Konrad Reinhart³, Jean Louis Vincent⁵ for the Sepsis Occurrence in Acutely Ill Patients (SOAP) Investigators

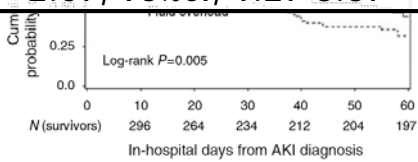
Mean fluid balance (L/24hr)
HR 1.21, 95%CI 1.13-1.28,
p<0.001




Fluid accumulation, survival and recovery of kidney function in critically ill patients with acute kidney injury

Josée Bouchard¹, Sharon B. Soroko¹, Glenn M. Chertow², Jonathan Himmelfarb³, T. Alp Ikizler⁴, Emil P. Paganini⁵ and Ravindra L. Mehta¹, Program to Improve Care in Acute Renal Disease (PICARD) Study Group


Adj-OR death for fluid overload at RRT initiation
2.07, 95%CI 1.27-3.37





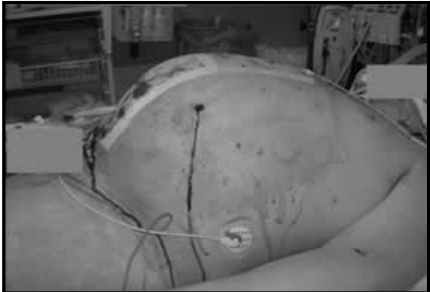
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THE AKI THERAPY REFLEX



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ABDOMINAL COMPARTMENT SYNDROME



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AKI DESPITE FLUID THERAPY

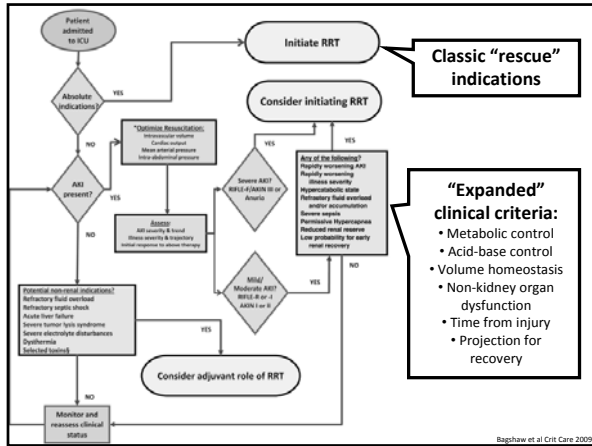
Characteristic	AKI (n=29)	No AKI (n=228)	P
APACHE II score	19.2	17.2	0.10
MAP (mmHg)	66	72	0.004
CVP (mmHg)	10	5	0.008
Vasopressors (%)	57	36	0.04
Ventilated (%)	80	73	0.42
Fluid balance (L/d)	2.1	1.0	<0.001
Furosemide (%)	72	19	0.001
PaO₂/FiO₂	121	208	0.003


Van Biesen et al / Nephrol 2005

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FLUID THERAPY IS NOT BANAL AND CAN CAUSE HARM!





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	<ul style="list-style-type: none"> ● Unnecessarily exposed to risks of RRT <ul style="list-style-type: none"> ○ Extracorporeal circulation ○ Central venous catheter ● In trial by Bouman et al (2002): <ul style="list-style-type: none"> ○ 4 patients in late group ~ spontaneous recovery ○ 2 patients in late group ~ died before RRT ○ No complications in early group

Bouman et al 2002

 Critical Care Medicine	<h2>OPTIMAL TIMING FOR RRT INITIATION IN ICU</h2>
	<ul style="list-style-type: none"> ● Decision to initiate RRT ~ complex <ul style="list-style-type: none"> ○ Context-specific – needs individualization ● "Classic" indications alone not optimal ● "Expanded" indications in critical illness: <ul style="list-style-type: none"> ○ Illness severity/organ dysfunction ○ Maintaining homeostasis ○ "Prevention" of complications ● Needs evaluation in clinical trials



**THANK YOU FOR
YOUR ATTENTION!**