Updates in Acute Kidney Injury

Brian Cronin, MD

March 10, 2023

BCNephro

- Definition
- Differential Diagnosis
- IVF
- Contrast Nephropathy
- Dialysis Initiation
- Dialysis Modalities

Acute Kidney Injury

- Definition
  - An Abrupt Decrease in Kidney Function
  - Increase in Creatinine by 0.3 g/% within 48 hrs
  - Increase in Creatinine of 1.5 x baseline within 7 days
  - UOP < 0.5 ml/kg/hr x 6 hours
- Stage
- Cause

KDIGO Clinical Practice Guideline for Acute Kidney Injury March 2012

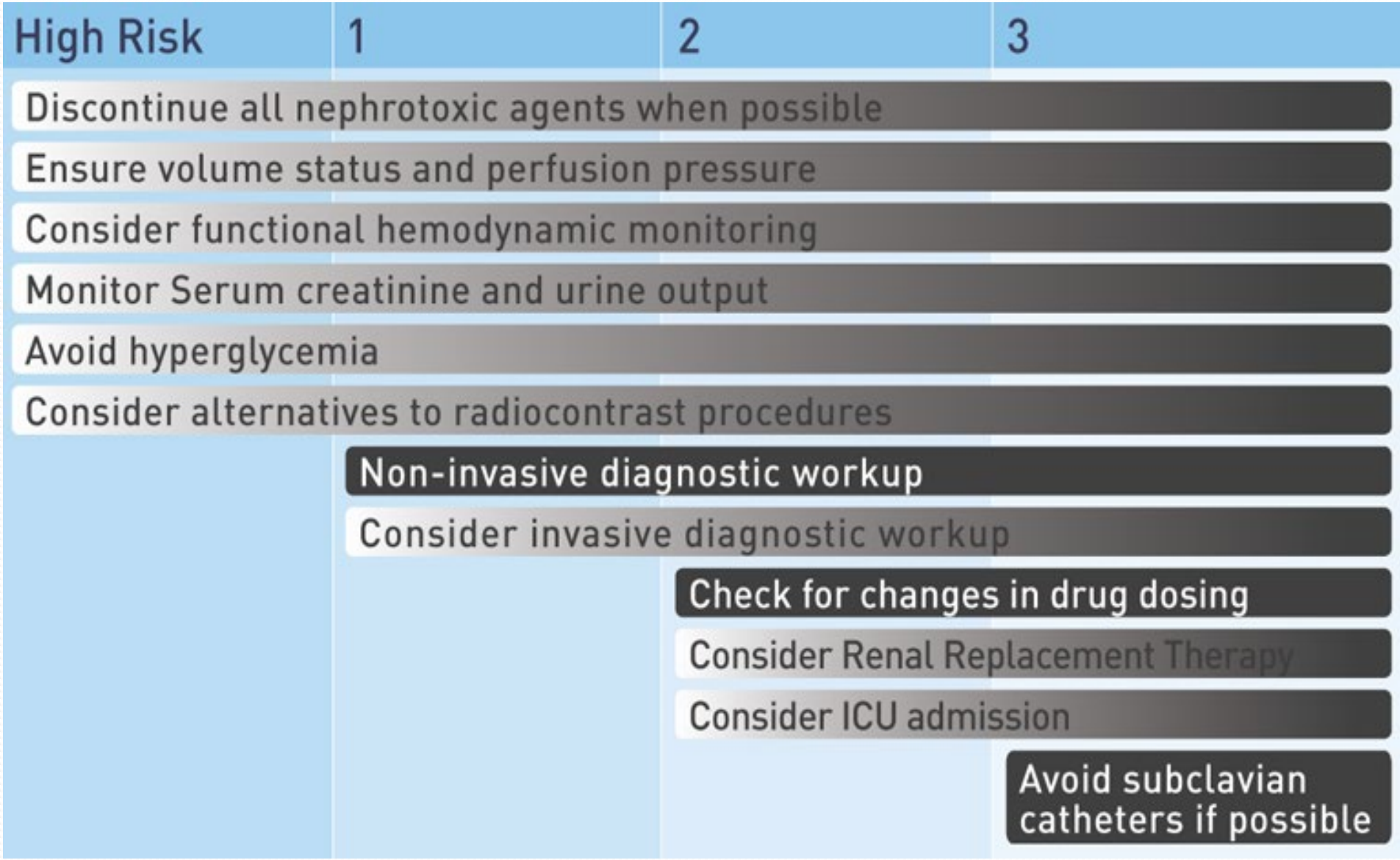
Criteria for acute kidney injury

	Serum creatinine criteria			Urine output criteria
	RIFLE	AKIN	KDIGO	
Definition	Increase in serum creatinine of >50 percent developing over <7 days	Increase in serum creatinine of 0.3 mg/dL or >50 percent developing over <48 hours	Increase in serum creatinine of 0.3 mg/dL developing over 48 hours or >50 percent developing over 7 days	Urine output of <0.5 mL/kg/hr for >6 hours
Staging				
RIFLE-Risk AKIN/KDIGO stage 1	Increase in serum creatinine of >50 percent	Increase in serum creatinine of 0.3 mg/dL or >50 percent	Increase in serum creatinine of 0.3 mg/dL or >50 percent	Urine output of <0.5 mL/kg/hr for >6 hours
RIFLE-Injury AKIN/KDIGO stage 2	Increase in serum creatinine of >100 percent	Increase in serum creatinine of >100 percent	Increase in serum creatinine of >100 percent	Urine output of <0.5 mL/kg/hr for >12 hours
RIFLE-Failure AKIN/KDIGO stage 3	Increase in serum creatinine of >200 percent	Increase in serum creatinine of >200 percent	Increase in serum creatinine of >200 percent	Urine output of <0.3 mL/kg/hr for >12 hours or anuria for >12 hours
RIFLE-Loss	Need for renal replacement therapy for >4 weeks			
RIFLE-End-stage	Need for renal replacement therapy for >3 months			

AKIN: Acute Kidney Injury Network; KDIGO: Kidney Disease/Improving Global Outcomes.

References:

1. *Bellomo R, Ronco C, Kellum JA, et al. Acute renal failure-definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care 2004; 8:B204. Copyright © 2004 BioMed Central Ltd.*
2. *Mehta RL, Kellum JA, Shah SV, et al. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. Crit Care 2007; 11:R31. Copyright © 2007 BioMed Central Ltd.*
3. *Kidney Disease: Improving Global Outcomes (KDIGO). Acute Kidney Injury Work Group. KDIGO clinical practice guidelines for acute kidney injury. Kidney Int Suppl 2012; 2:1.*


High Risk
1
2
3
Discontinue all nephrotoxic agents when possible
Ensure volume status and perfusion pressure
Consider functional hemodynamic monitoring
Monitor Serum creatinine and urine output
Avoid hyperglycemia
Consider alternatives to radiocontrast procedures
Non-invasive diagnostic workup
Consider invasive diagnostic workup
Check for changes in drug dosing
Consider Renal Replacement Therapy
Consider ICU admission
Avoid subclavian catheters if possible

Drug Dosing

- eGFR only accurate if creatinine in steady state
  - If creatinine rising eGFR overestimates true GFR – If rising briskly eGFR should be presumed 0 ml/min
  - If creatinine falling eGFR underestimates true GFR
- Renally cleared meds:
  - Metformin
  - Gabapentin
  - Cefepime
  - Morphine

https://www.uptodate.com/contents/overview-of-the-management-of-acute-kidney-injury-aki-in-adults

Cause – Differential Diagnosis

- Prerenal
- Intrinsic Renal
  - Glomerular
  - Tubulointerstitial
  - Vascular
- Post Renal

Intrinsic Renal

- Glomerular
  - Nephritic urine sediment
  - ANCA – pauci immune
  - Immune Complex (lupus; cryoglobulinemia; IgA)
  - Anti GBM

Intrinsic Renal

- Tubulointerstitial
  - Bland or variable UA
  - ATN
  - AIN
  - Crystalline nephropathy

ATN	AIN	Crystalline
Ischemic	Medications:	Medications:
Myoglobin/Hemoglobin	Antibiotics	Methotrexate
Medications:	PPI	Acyclovir
Contrast	Checkpoint Inhibitors	Light Chain
Aminoglycoside	Autoimmune:	Calcium Oxalate
Vancomycin	Sjogren/ Sarcoid	Calcium Phosphate
Cisplatin	TINU/IgG4	Uric Acid

Intrinsic Renal

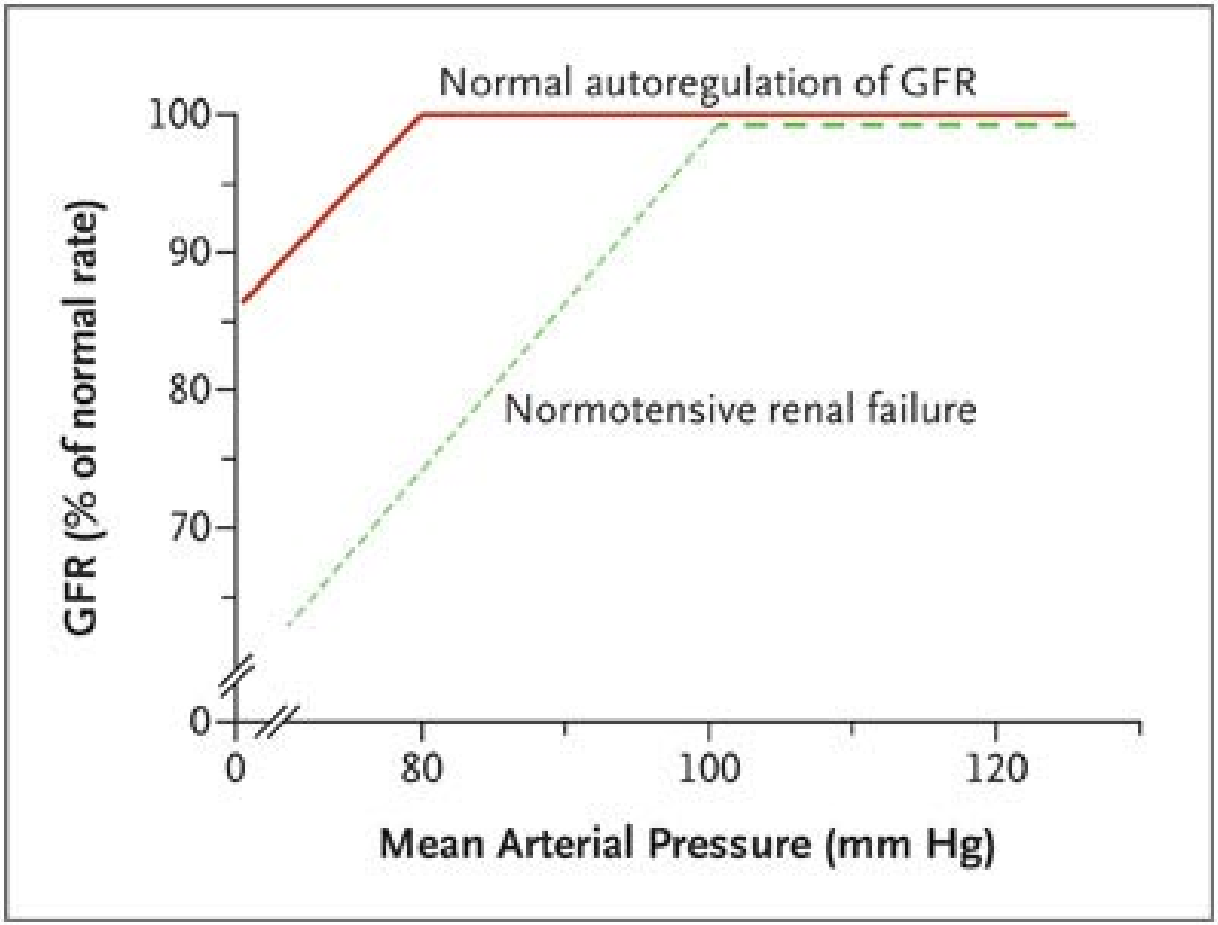
- Vascular
  - Microvascular
  - TTP
  - HUS

Normotensive Ischemic AKI

- Increased Renal Susceptibility to modest reductions in perfusion pressure
- Impaired autoregulation
  - GFR maintained throughout range of perfusion pressures via autoregulation
  - Below autoregulatory range endogenous vasoconstrictors lead to increased afferent arteriolar pressure leading to decreased GFR
  - If increased severity and/or duration can lead to ATN

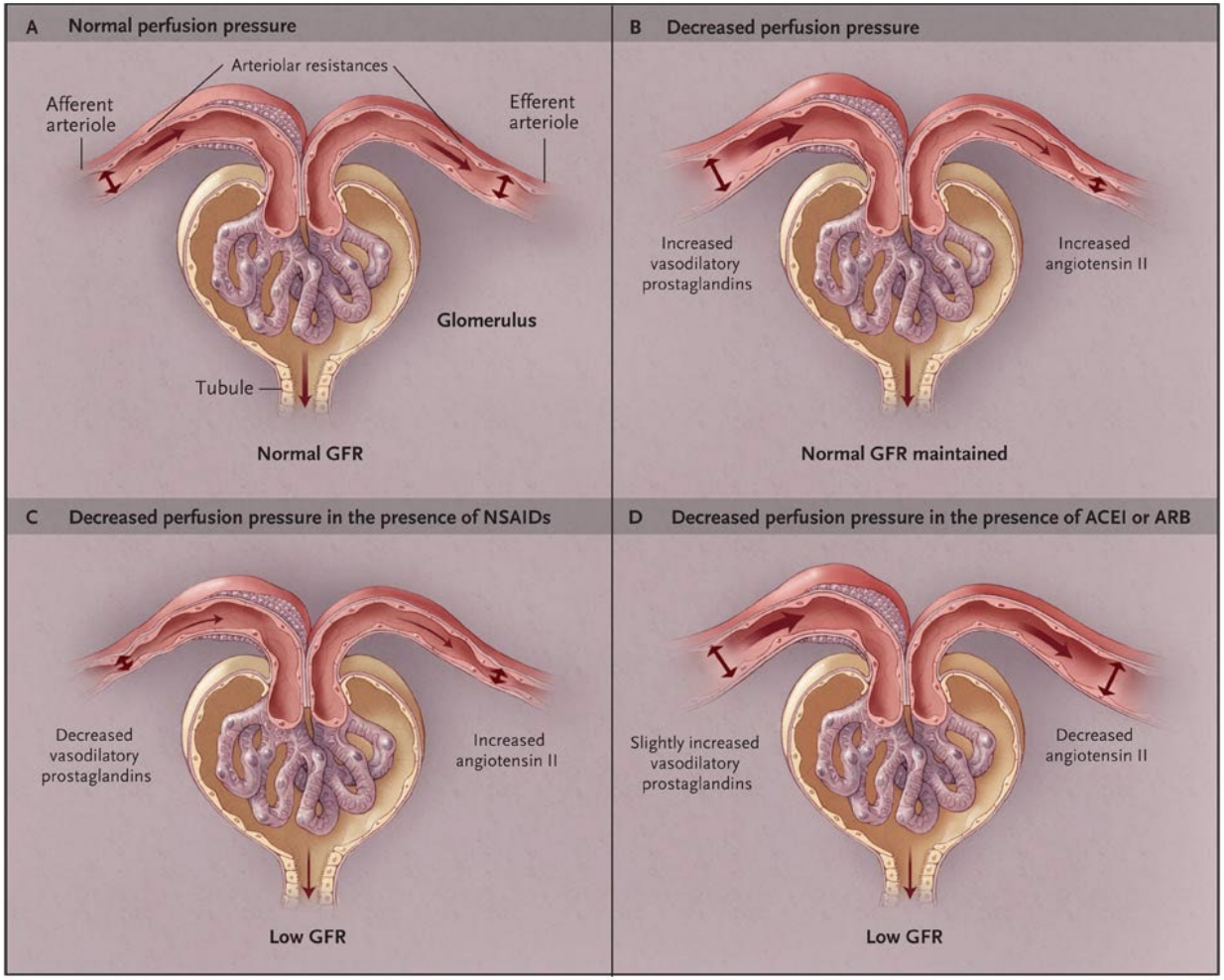
Abuelo, N Engl J Med 2007; 357: 789-805

Normal and Impaired Autoregulation of the Glomerular Filtration Rate during Reduction of Mean Arterial Pressure



Abuelo J. N Engl J Med 2007;357:797-805

Intrarenal Mechanisms for Autoregulation of the Glomerular Filtration Rate under Decreased Perfusion Pressure and Reduction of the Glomerular Filtration Rate by Drugs



Abuelo J. N Engl J Med 2007;357:797-805

The NEW ENGLAND JOURNAL of MEDICINE

- When creatinine 1st rises
  - BP usually below typical BP although may be still in "normal range"
  - May be signs of early sepsis (hypothermia; confusion; leukocytosis; cool extremities) but no fever or localizing infectious symptoms
  - Diuretics continued in a patient with decreased intake

IVF - Normal Saline vs Physiologic Solutions

Association Between a Chloride-Liberal vs. Chloride-Restrictive Intravenous Fluid Administration Strategy and Kidney Injury in Critically Ill Adults

Yunus et al. JAMA 2012: 308 1566-1572

Balanced Crystalloids versus Saline in Non-critically ill Adults

SALT ED: Self W.H et al. N Engl J Med 2018; 378:819-828

Balanced Crystalloids versus Saline in Critically ill Adults

SMART: Semler M.W. et al. N Engl J Med 2018; 378:829-839

Balanced Multielectrolyte Solution versus Saline in Critically Ill Adults

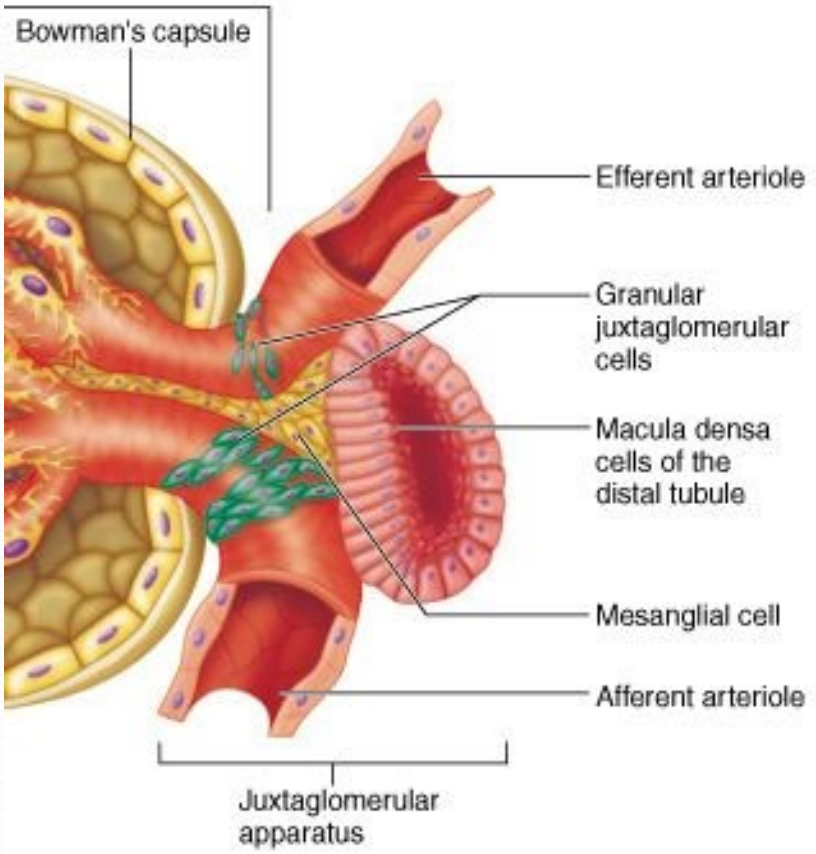
PLUS: Simon Finfer et al. N Engl J Med 2022;386:815-826

Is Chloride Bad?

- Normal saline – 154 meq chloride
- Lactated Ringers – 109 meq chloride
- Plasma-lyte A – 98 meq chloride
- NS associated with
  - Hyperchloremic metabolic acidosis
  - May increase renal inflammation
  - May impair renal perfusion via vasoconstriction

Renal Physiology

- Juxtaglomerular Apparatus
  - Juxtaglomerular Cells (Afferent Arteriole)
  - Macula Densa (Thick Ascending Limb)
    - Increased Chloride delivery to Macula Densa
      - Afferent Arteriole constriction (TGF) – Decreased GFR
      - Decreased Renin release



Association Between a Chloride-Liberal vs. Chloride-Restrictive Intravenous Fluid Administration Strategy and Kidney Injury in Critically Ill Adults

- Sequential Observational Study
  - 6 months standard fluids
  - 6 months low chloride fluids ie. Balanced electrolyte solution (Plasma-Lyte)

Yunus et al. JAMA 2012: 308 1566-1572

From: **Association Between a Chloride-Liberal vs Chloride-Restrictive Intravenous Fluid Administration Strategy and Kidney Injury in Critically Ill Adults**

JAMA. 2012;308(15):1566-1572. doi:10.1001/jama.2012.13356

Table 3. Incidence of Acute Kidney Injury Stratified by Risk, Injury, Failure, Loss, and End-Stage (RIFLE) Serum Creatinine Criteria

	No. (%) [95% CI] of Patients[a]		
	Control Period (n = 760)	Intervention Period (n = 773)	*P* Value
RIFLE class			
Risk	71 (9.0) [7.2-11.0]	57 (7.4) [5.5-9.0]	.16
Injury	48 (6.3) [4.5-8.1]	23 (3.0) [1.8-4.2]	.002
Failure	57 (7.5) [5.6-9.0]	42 (5.4) [3.8-7.1]	.10
Injury and failure	105 (14) [11-16]	65 (8.4) [6.4-10.0]	<.001

[a] The control period was from February 18 through August 17, 2008, and the intervention period was from February 18 through August 17, 2009.

Figure Legend:

From: **Association Between a Chloride-Liberal vs Chloride-Restrictive Intravenous Fluid Administration Strategy and Kidney Injury in Critically Ill Adults**

JAMA. 2012;308(15):1566-1572. doi:10.1001/jama.2012.13356

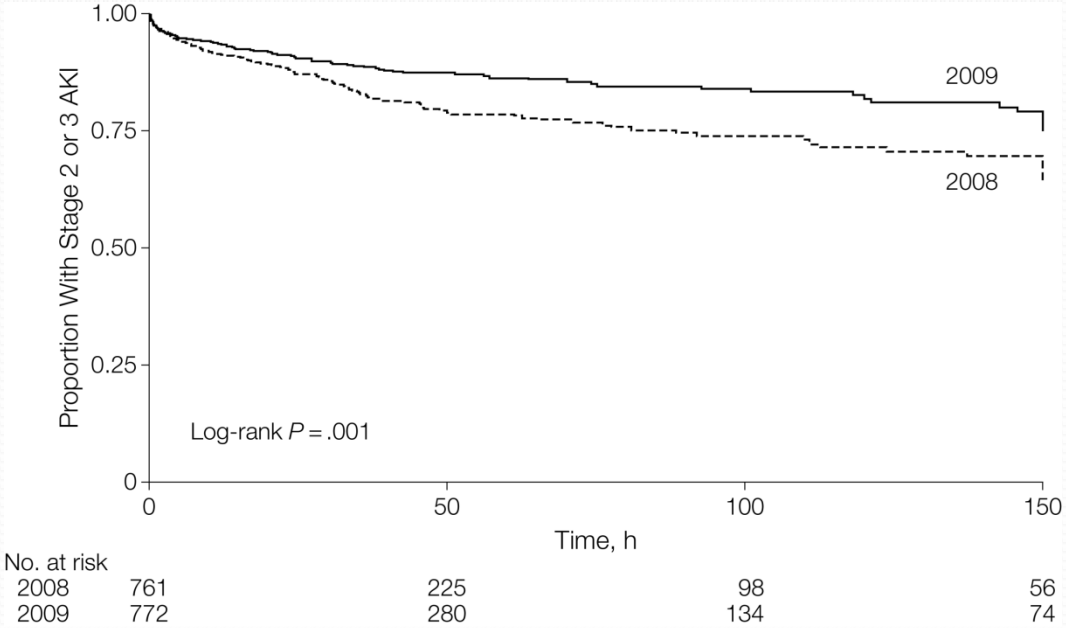


Figure Legend:

Stage 2 or 3 defined according to the Kidney Disease: Improving Global Outcomes clinical practice guideline.

From: **Association Between a Chloride-Liberal vs Chloride-Restrictive Intravenous Fluid Administration Strategy and Kidney Injury in Critically Ill Adults**

JAMA. 2012;308(15):1566-1572. doi:10.1001/jama.2012.13356

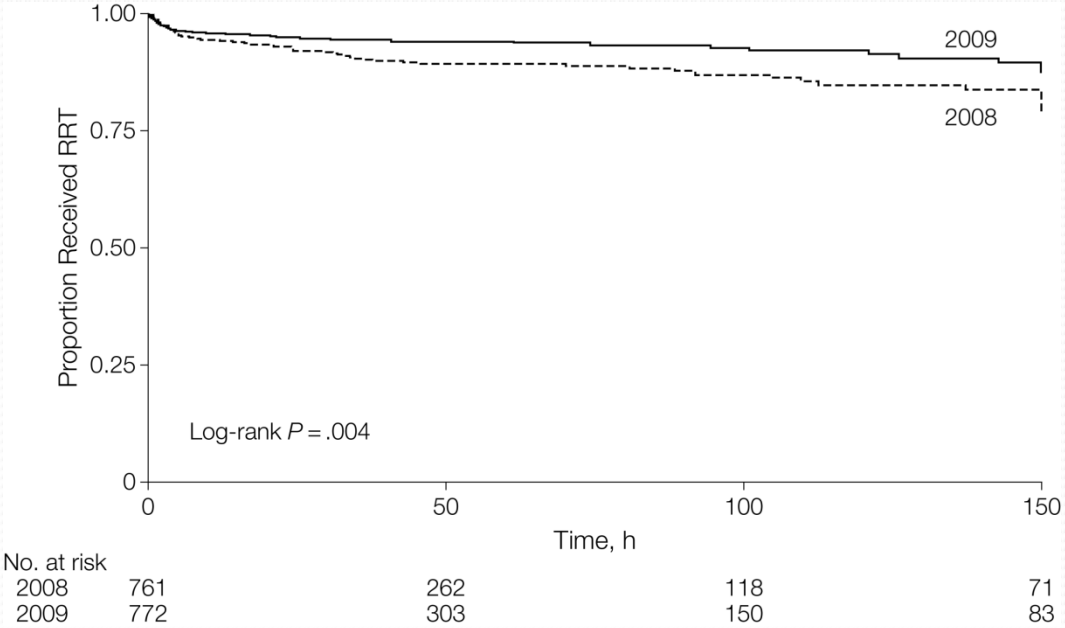


Figure Legend:

Balanced Crystalloids versus Saline in Noncritically ill Adults (SALT-ED)

ED patients hospitalized (non ICU) and received > 500 ml IVF in ER Type of IVF varied by month	
Normal Saline	**Balanced Crystalloid (LR or plasmalyte)**
Primary Outcome – Hospital free days at day 28 No difference (median 25 days) p=0.41	
Secondary Outcomes Major adverse kidney events – Composite of death, new RRT, Creatinine ≥ 200% baseline at discharge or 30 days Favored balanced crystalloids (4.7% vs. 5.6% p=0.01) Largest benefit in patients with renal dysfunction at presentation – Stage 2 or greater AKI (28.0% vs. 37.6% p <0.001)	
Stage 2 or greater AKI No difference (8.0% vs. 8.6% p=0.19)	

Self W.H et al. N Engl J Med 2018; 378:819-828

Balanced Crystalloids versus Saline in Critically ill Adults (SMART)

ICU patients	
Normal Saline	**Balanced Crystalloid**
Primary Outcome – Major adverse kidney events – Composite of death, new RRT, Creatinine ≥ 200% baseline at discharge or 30 days Favored balanced crystalloids (10.7% vs. 11.5% p=0.04)	
Stage 2 or greater AKI No difference (10.7% vs. 11.5% p=0.09)	

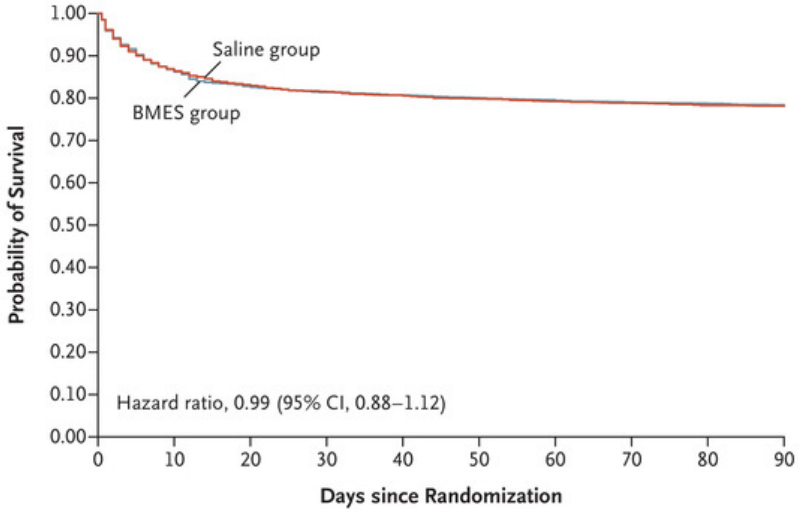
Semler M.W. et al. N Engl J Med 2018; 378:829-839

Balanced Multielectrolyte Solution versus Saline in Critically Ill Adults

Double – Blind Randomized Controlled Trial Critically Ill Patients	
Plasma-Lyte 148	NS
Primary Outcome – Death at 90 days	
21.8%	22.0%
Secondary Outcome – New RRT	
12.7%	12.9%
Secondary Outcome – Maximum Creatinine increase (mean)	
0.41 ± 1.06	0.41 ± 1.02
Higher blood pH, Lower Chloride in Balanced IVF Group	

PLUS: Simon Finfer et al. N Engl J Med 2022;386:815-826

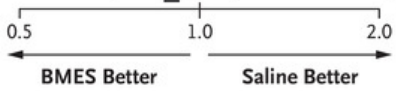
A Kaplan–Meier Estimates of the Probability of Survival



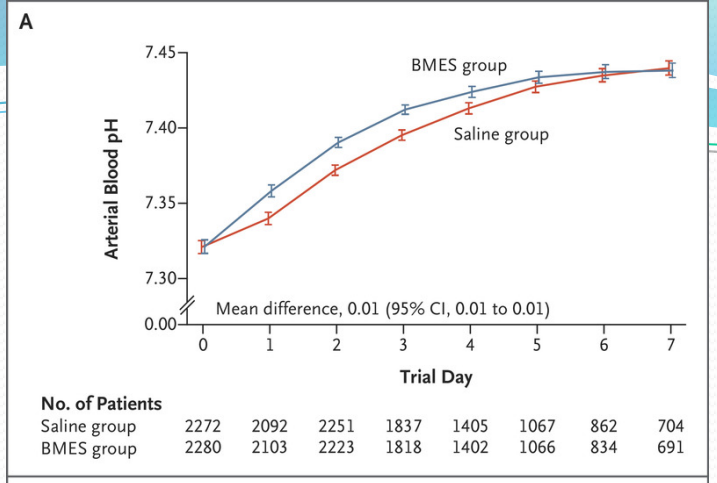
No. of Patients										
BMES group	2446	2119	2019	1983	1964	1949	1937	1922	1916	1906
Saline group	2430	2109	2015	1973	1952	1929	1913	1904	1890	1884

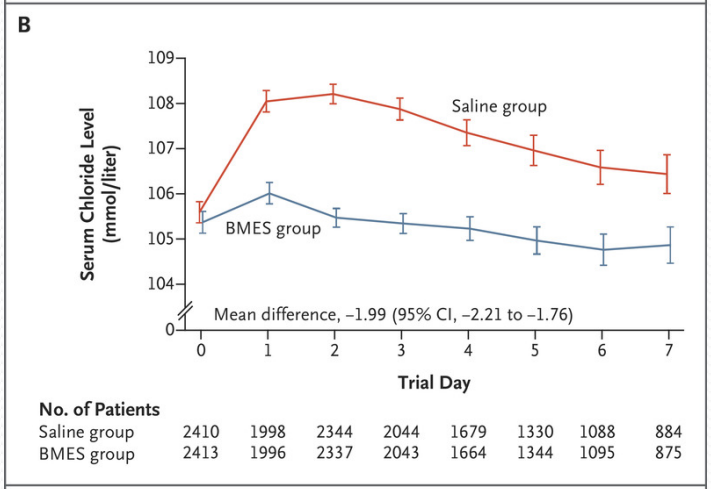
B Subgroup Analysis of Death from Any Cause

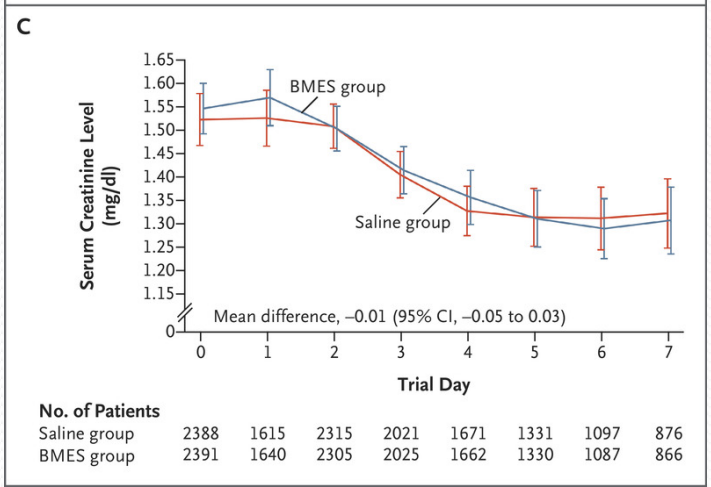
Subgroup	BMES Group	Saline Group	Odds Ratio (95% CI)
	no. of events/total no. (%)		
Age			
<65 yr	184/1250 (14.7)	188/1207 (15.6)	0.93 (0.74–1.16)
≥65 yr	346/1183 (29.2)	342/1206 (28.4)	1.06 (0.88–1.26)
Sex			
Male	328/1531 (21.4)	323/1437 (22.5)	0.94 (0.79–1.12)
Female	202/902 (22.4)	207/976 (21.2)	1.09 (0.87–1.35)
Kidney injury			
Yes	160/468 (34.2)	155/451 (34.4)	0.98 (0.74–1.29)
No	361/1934 (18.7)	370/1931 (19.2)	0.97 (0.83–1.15)
Sepsis			
Yes	276/1068 (25.8)	265/1026 (25.8)	1.01 (0.83–1.23)
No	254/1362 (18.6)	265/1386 (19.1)	0.97 (0.80–1.17)
Admitted from surgery			
Yes	171/1087 (15.7)	179/1109 (16.1)	0.97 (0.77–1.22)
No	359/1344 (26.7)	351/1304 (26.9)	0.99 (0.84–1.18)
APACHE II score			
<25	287/1753 (16.4)	275/1739 (15.8)	1.05 (0.88–1.26)
≥25	243/678 (35.8)	255/673 (37.9)	0.90 (0.72–1.12)



PLUS: Simon Finfer et al. N Engl J Med 2022;386:815-826







PLUS: Simon Finfer et al. N Engl J Med 2022;386:815-826

IVF - Summary

- Meta analysis – (% relative reduction – 1% relative increase in mortality with balanced crystalloid
- Balanced solutions may be preferred in DKA
- Balanced solutions may be harmful (NS) improved in TBI

Contrast Nephropathy

Contrast Associated AKI	Contrast Induced AKI
AKI within 48 hours of contrast	AKI caused by contrast administration
Higher with coronary angiography than with IV contrast	Stable baseline eGFR > 45 – not nephrotoxic Stable baseline eGFR 30-44 – not or rarely nephrotoxic
Higher incidence in cardiac angiography then with IV contrast	

Contrast Nephropathy - Prevention

- Assess Risk for CI-AKI
- Type of Contrast
- Prophylaxis
- Hemodialysis/ Hemofiltration

KDIGO Clinical Practice Guideline for Acute Kidney Injury March 2012

Contrast Nephropathy - Risk

CKD	CA - AKI	CI - AKI
eGFR > 60	5%	Near 0%
eGFR 45-59	10%	Near 0%
eGFR 30-44	15%	0-2%
eGFR < 30	30%	0-17%

Use of Intravenous Iodinated Contrast Media in Patients with Kidney Disease: Consensus Statements from the ACR and NKF Radiology 2020; 294:660-668

Assess Risk

- ACR Manual on Contrast Media 2023
  - "In fact, since each contrast medium administration always implies a risk-benefit analysis for the patient, contrast medium administration for all patients should always be taken in the clinical context, considering all risks, benefits and alternatives"
  - "…there are now two large propensity score-adjusted studies that stratify CI-AKI risk by eGFR. One showed no risk of CI-AKI from IV iodinated contrast material, regardless of baseline eGFR, while another identified patients with an eGFR < 30 mL / min/1.73m2 to be at significant risk (patients with eGFR 30-44 mL / min/1.73m2 were at borderline but not statistically significant risk)"

- ACR Manual on Contrast Media 2023
  - “no serum creatinine or eGFR threshold is adequate to stratify risk for patients with AKI because serum creatinine in this setting is unreliable. However, in patients with AKI, the administration of iodinated contrast medium should only be undertaken with appropriate caution, and only if the benefit to the patient outweighs the risk”
  - “patients with AKI are particularly susceptible to nephrotoxin exposure and therefore it is probably prudent to avoid intravascular iodinated contrast medium in these patients when possible.”

Type of Contrast

High Osmolar	Low Osmolar	Iso-osmolar
> 1400	@ 600	@ 290
Not used	Difference in CA-AKI risk	not clinically meaningful

Prophylaxis

Volume Expansion	
Isotonic Normal Saline: 1 hour before; 3-12 hours post	
LVEDP guided strategy: Poseidon trial Lancet 383: 1814-1823 2014	
NS – Pre-contrast: 3ml/kg over 1 hour	Post-contrast: 4 hours
	LVEDP - low (<13) 5 ml/kg/hr
CI – AKI 6.7 vs 16.3%	LVEDP - medium (13-18) 3 ml/kg/hr
	LVEDP - high(>18) 1.5 ml/kg/hr
	Control - 1.5 ml/kg/hr
AKI or CKD with eGFR < 30	
Consider with eGFR 30-44	

Use of Intravenous Iodinated Contrast Media in Patients with Kidney Disease: Consensus Statements from the ACR and NKF Radiology 2020; 294:660-668

Prophylaxis

- Sodium Bicarbonate
- N acetylcysteine

PRESERVE Trial NEJM 2018 378: 603-614	
Primary Endpoint: Death; Dialysis; Creatinine increase 50% at 90 days	Secondary Endpoint: CA-AKI
$NaHCO_3$ vs. NS 4.4 % vs. 4.7% - p = 0.62	$NaHCO_3$ vs. NS 9.5 % vs. 8.3% - p = 0.13
Acetylcysteine vs. Placebo 4.6% vs 4.5% - p = 0.88	Acetylcysteine vs. Placebo 9.1% vs. 8.7% - p = 0.58

Hemodialysis/ Hemofiltration

- No
- Should not be initiated or have schedule changed solely based on contrast administration
- Demonstrated lack of benefit

Use of Intravenous Iodinated Contrast Media in Patients with Kidney Disease: Consensus Statements from the ACR and NKF Radiology 2020; 294:660-668

An Aside

- What About Dialysis After Contrast in a Patient with ESRD?
  - "Patients should not have acute dialysis nor continuous renal replacement therapy initiated or alter their schedule solely based on iodinated contrast media regardless of renal function due to risks, costs, and lack of benefit"
- Consider residual kidney function
  - "…there is a theoretical risk of converting an oliguric patient on dialysis to an anuric patient"

Gadolinium

Nephrogenic Systemic Fibrosis
Associated with Group I Gadolinium Based Contrast Agents (GBCA)
Risk: ESRD, CKD 5, CKD4 – risk 1-7% AKI
Group II agents recommended: Gadobenate (MultiHance) Gadobutrol (Gadovist) Gadoteric Acid (Dotarem) Gadoteridol (ProHance)
Coordinate prior to regularly scheduled dialysis (in ESRD) if feasible
Dialysis initiation or alteration of schedule not recommended

Timing of RRT in AKI

Initiation Strategies for Renal-Replacement Therapy in the Intensive Care Unit (AKIKI – Artificial Kidney Initiation in Kidney Injury) **Gaudry S. et al. N Eng J Med 2016; 375: 122-133**
Timing of Renal-Replacement Therapy in Patients with Acute Kidney Injury and Sepsis (IDEAL-ICU) Barber S.D. et al: N Eng J Med 2018; 379: 1431-1442
Timing of Initiation of Renal-Replacement Therapy in Acute Kidney Injury The STARRT-AKI Investigators. N Eng J Med 2020; 383: 240-251
Comparison of Two Delayed Strategies for Renal Replacement Therapy Initiation for Severe Acute Kidney Injury (AKIKI 2) Gaudry S. et al: Lancet 2021; 397 – 1293-1300

AKIKI

AKI stage 3 with VDRF and/or pressor requirement	
Early Initiation	Delayed initiation
Within 6 hours of AKI 3 diagnosis	Severe hyperkalemia (K > 6 or > 5.5 despite medical Rx)
	Metabolic acidosis (pH < 7.15 with pCO_2 < 35 or > 50 and inability to increase mechanical ventilation)
	Pulmonary edema (O_2 > 5 L/min or Fio_2 > 50% to maintain SaO_2 > 95% despite diuretics)
	BUN > 112
	Oliguria > 72 hrs

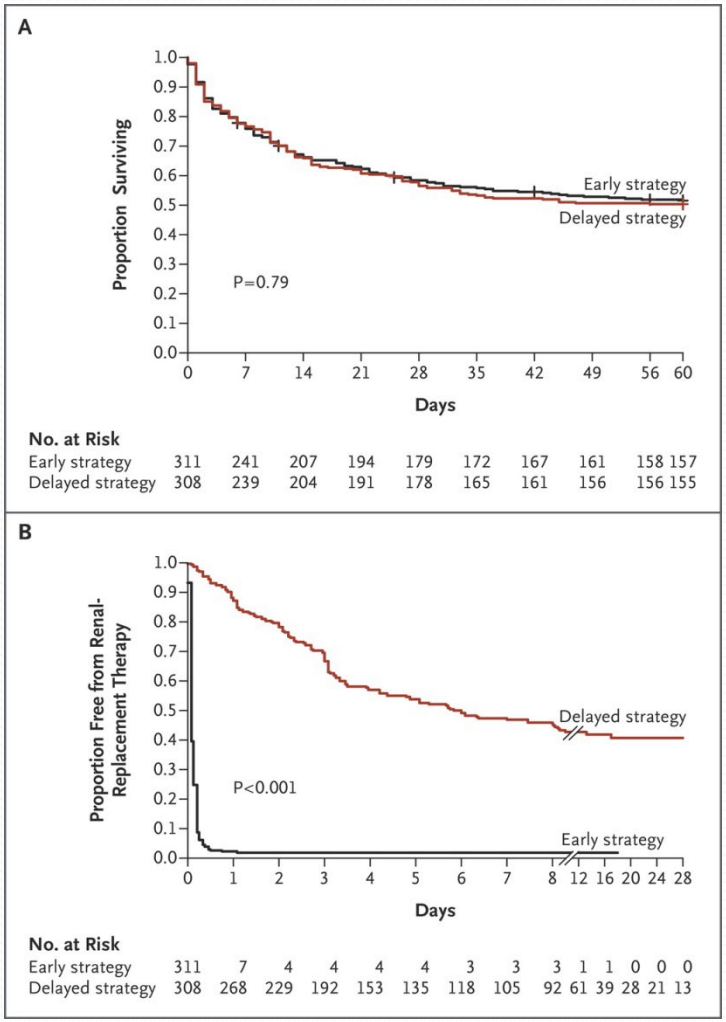
Gaudry S. et al. N Eng J Med 2016; 375: 122-133

AKIKI- Outcomes

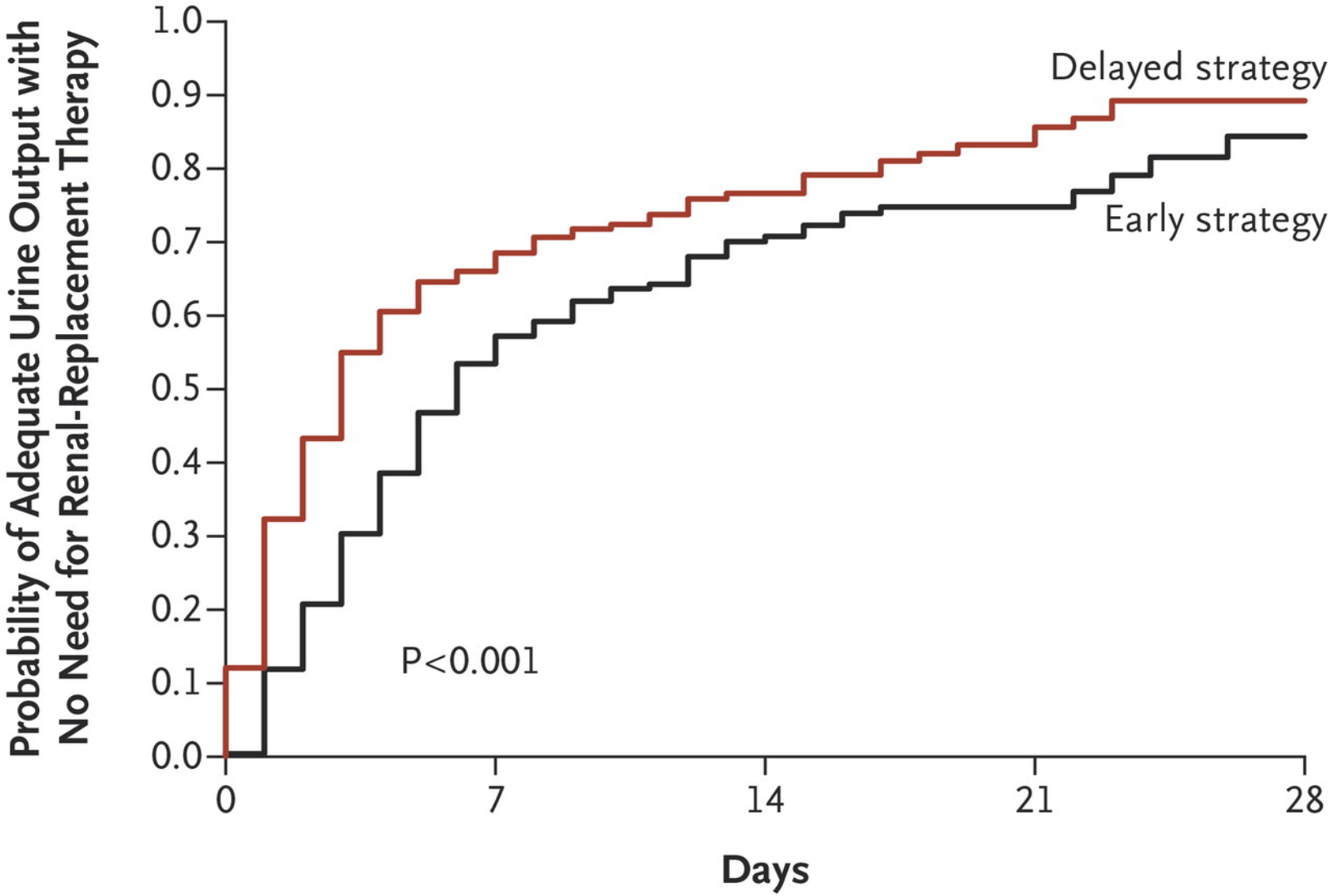
No difference in 60-day mortality (48.5 vs 49.7%)
Delayed Dialysis group
49% did not require RRT
Diuresis returned earlier
Less catheter blood stream infections (5 vs 10%)
Less hypophosphatemia

Gaudry S. et al. N Eng J Med 2016; 375: 122-133

Pro[illegible]ing of Renal-Replacement Therapy.



Gaudry S et al. N Engl J Med 2016;375:122-133.



No. at Risk

Early strategy	311	99	42	27	10
Delayed strategy	308	68	29	14	7

Gaudry S. et al. N Eng J Med 2016; 375: 122-133

Timing of Renal-Replacement Therapy in Patients with Acute Kidney Injury and Sepsis (IDEAL-ICU)

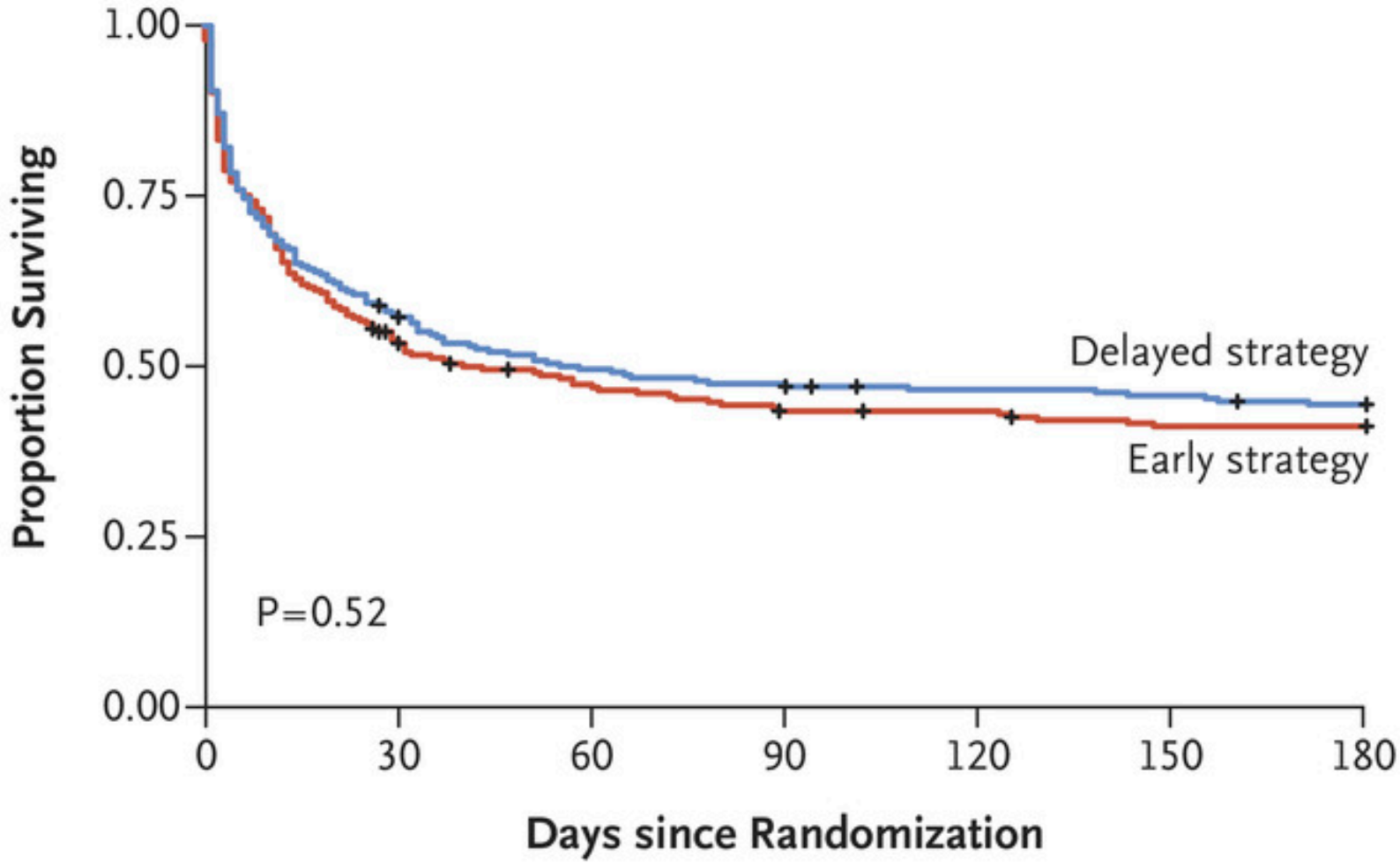
Early-stage Septic Shock (within 48 hrs of vasopressors) and Severe AKI (RIFLE – Failure stage)	
Early RRT	Delayed RRT
Within 12 hrs	Emergent Indication: Hyperkalemia (K > 6.5) Metabolic acidosis (pH < 7.15) Fluid overload/pulmonary edema refractory to diuretics
	No recovery after 48 hrs

Barber S.D. et al: N Eng J Med 2018; 379: 1431-1442

Timing of Renal-Replacement Therapy in Patients with Acute Kidney Injury and Sepsis (IDEAL-ICU)

Early RRT	Delayed RRT
Primary Outcome – Death at 90 days	
58%	54%
	38% did not require RR 29% recovery 8% death 2% other
	17% required emergent HD prior to 48 hrs

Barber S.D. et al: N Eng J Med 2018; 379: 1431-1442



No. at Risk

Delayed strategy	242	137	117	112	107	105	101
Early strategy	246	127	109	99	98	92	92

Barber S.D. et al: N Eng J Med 2018; 379: 1431-1442

Table 3. Complications and Adverse Events.

Complication or Adverse Event	Early Strategy (N=246)	Delayed Strategy (N=242)	P Value
Complications potentially related to acute kidney injury or renal-replacement therapy in the first 7 days after enrollment			
Metabolic acidosis*			
No. of patients (%)	22 (9)	40 (17)	0.07
Median pH (IQR)	7.1 (7.1–7.1)	7.1 (7.0–7.1)	0.36
Hyperkalemia†			
No. of patients (%)	0	10 (4)	0.03
Median potassium level (IQR) — mmol/liter	—	7.0 (6.7–7.3)	—
Fluid overload — no. of patients (%)‡	1 (<1)	9 (4)	0.16
Severe cardiac-rhythm disorder — no. of patients (%)§	23 (10)	13 (5)	0.77
Symptomatic bradycardia	15 (6)	11 (4)	0.67
Ventricular tachycardia or ventricular fibrillation	10 (4)	3 (1)	0.25
Severe bleeding event¶			
No. of patients (%)	12 (5)	15 (6)	0.52
Median volume of packed red cells transfused per patient (IQR) — units	4.0 (3.5–7.0)	5.0 (3.0–7.0)	0.98
Hypotensive episode during renal-replacement therapy‖			
No. of patients/total no. (%)	86/239 (36)	57/149 (38)	0.62
Median mean arterial pressure of the most severe episode (IQR)	47 (40–52)	44 (36–52)	0.40
Other adverse events that occurred during the trial — no. of patients (%)			
Other cardiovascular complication	94 (38)	95 (39)	0.81
New infection	55 (22)	44 (18)	0.25
Respiratory complication	25 (10)	36 (15)	0.11
Gastrointestinal complication	32 (13)	25 (10)	0.36
Neurologic complication	29 (12)	20 (8)	0.19
Thrombotic or embolic complication	13 (5)	14 (6)	0.81
Minor bleeding event¶	52 (21)	53 (22)	0.84
Other hematologic complication	22 (9)	23 (10)	0.83
Other metabolic complication**	9 (4)	8 (3)	0.83

* Metabolic acidosis was defined as a pH of less than 7.15 and a base deficit of more than 5 mmol per liter or a bicarbonate level of 18 mmol or less per liter.
† Hyperkalemia was defined as a potassium level of more than 6.5 mmol per liter with characteristic electrocardiographic changes.
‡ Fluid overload was defined as extravascular fluid overload that was refractory to diuretics with pulmonary edema.
§ Severe cardiac-rhythm disorders were defined as ventricular tachycardia, ventricular fibrillation, torsades de pointes, third-degree atrioventricular block, or extreme bradycardia requiring medical treatment.
¶ Severe bleeding events were defined as the need for transfusion of 3 or more consecutive units of packed red cells in the same day. Minor bleeding events were defined as the need for transfusion of less than 3 units of packed red cells in the same day.
‖ Hypotensive episodes during renal-replacement therapy were defined as a mean arterial pressure of 55 mm Hg or less and an increase in vasopressor dose or a reintroduction of vasopressors. The frequency of this adverse event was calculated only in patients who underwent renal-replacement therapy.
** Other metabolic complications were defined as severe hypophosphatemia (serum phosphate <0.5 mmol per liter [<1.5 mg per deciliter]) or severe hypoglycemia (glucose <2.8 mmol per liter [<50 mg per deciliter]).

Timing of Initiation of Renal-Replacement Therapy in Acute Kidney Injury (STARRT-AKI)

Accelerated RRT	Standard RRT
Within 12 hrs	Conventional Indications: clinical equipoise (dialysis discouraged unless) $K > 6.0$ $pH < 7.20$/ $HCO_3 < 12$ $PaO_2/FiO_2 \leq 200$
	AKI > 72 hours

The STARRT-AKI Investigators. N Eng J Med 2020; 383: 240-251

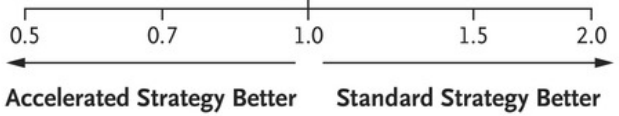
Timing of Initiation of Renal-Replacement Therapy in Acute Kidney Injury (STARRT-AKI)

Accelerated RRT	Standard RRT
Primary Outcome – Death at 90 days	
43.9%	43.7%
Secondary Outcome – Dependence on RRT	
10.4%	6.0%
No Meaningful Difference in Other Secondary Outcomes	
Adverse Events	
23% (hypotension; hypophosphatemia)	
Serious Adverse Events No Significant Difference	

The STARRT-AKI Investigators. N Eng J Med 2020; 383: 240-251

Subgroup Analyses.

Subgroup	Accelerated Strategy	Standard Strategy	Odds Ratio (95% CI)
	no. of events/total no.		
Sex			
Female	191/470	207/467	0.91 (0.69–1.20)
Male	452/995	432/995	1.12 (0.93–1.36)
Estimated GFR			
<45	184/401	150/365	1.26 (0.93–1.71)
≥45	459/1064	488/1097	0.99 (0.82–1.18)
SAPS II			
>58	387/701	403/751	1.08 (0.87–1.34)
≤58	256/764	236/711	1.02 (0.81–1.28)
Sepsis			
Yes	392/855	402/834	0.95 (0.78–1.18)
No	251/610	237/628	1.21 (0.95–1.54)
Type of ICU admission			
Surgical	185/492	156/473	1.20 (0.91–1.59)
Medical	458/973	483/989	0.99 (0.82–1.19)
Geographic region			
North America	231/497	225/497	1.08 (0.83–1.42)
Europe	254/574	260/572	1.00 (0.78–1.29)
Australia or New Zealand	91/275	86/278	1.12 (0.77–1.64)
Asia or South America	67/119	68/115	0.94 (0.53–1.67)



The STARRT-AKI Investigators. N Engl J Med 2020;383:240-251.

Adverse Events.*

Table 3. Adverse Events.*

Adverse Events	Accelerated Strategy (N=1503)		Standard Strategy (N=1489)		P Value†
	Patients	Events	Patients	Events	
	no. (%)	*no. (per 1000 patient-mo)*	*no. (%)*	*no. (per 1000 patient-mo)*	
Any adverse event	346 (23.0)	556 (195.7)	245 (16.5)	364 (128.1)	<0.001
Associated with renal-replacement therapy					
Hypotension	131 (8.7)	188 (66.2)	83 (5.6)	112 (39.4)	0.001
Arrhythmia	37 (2.5)	45 (15.8)	23 (1.5)	29 (10.2)	0.07
Seizure	1 (0.1)	1 (0.4)	0	0	1.00
Bleeding	4 (0.3)	4 (1.4)	1 (0.1)	1 (0.4)	0.37
Allergic reaction	1 (0.1)	1 (0.4)	1 (0.1)	1 (0.4)	1.00
Decreased phosphate (<0.5 mmol/liter)	112 (7.5)	124 (43.7)	62 (4.2)	68 (23.9)	<0.001
Decreased potassium (<3.0 mmol/liter)	34 (2.3)	43 (15.1)	34 (2.3)	40 (14.1)	0.97
Decreased ionized calcium (<0.90 mmol/liter)	80 (5.3)	102 (35.9)	66 (4.4)	80 (28.1)	0.26
Associated with use of a dialysis catheter					
Pneumothorax or hemothorax	4 (0.3)	5 (1.8)	2 (0.1)	2 (0.7)	0.69
Bleeding	6 (0.4)	6 (2.1)	4 (0.3)	4 (1.4)	0.75
Thrombus (as confirmed on ultrasonography)	3 (0.2)	3 (1.1)	5 (0.3)	5 (1.8)	0.51
Arterial puncture	3 (0.2)	3 (1.1)	2 (0.1)	2 (0.7)	1.00
Bloodstream infection	7 (0.5)	7 (2.5)	1 (0.1)	1 (0.4)	0.07
Other	21 (1.4)	24 (8.4)	20 (1.3)	19 (6.7)	0.90
Serious adverse events — no. (%)	15 (1.0)	17 (6.0)	8 (0.5)	8 (2.8)	0.15

* Listed are data through 14 days for 2992 of 3019 patients (99.1%) who had undergone randomization and remained in the ICU; not included are 27 patients for whom consent had been withdrawn. Individual investigators made the determination of whether the adverse event was related to renal-replacement therapy or the use of a dialysis catheter. To convert the values for phosphate to milligrams per deciliter, divide by 0.3229. To convert the values for potassium to milligrams per deciliter, divide by 0.2558. To convert the values for ionized calcium to milligrams per deciliter, divide by 0.250.

† P values are for the between-group difference in the percentage of patients with a specific adverse event and have not been adjusted for multiple comparisons.

The STARRT-AKI Investigators. N Engl J Med 2020;383:240-251.

Comparison of Two Delayed Strategies for Renal Replacement Therapy Initiation for Severe Acute Kidney Injury (AKIKI 2)

Critically ill patients with AKI stage 3 and oliguria > 72 hours or BUN > 112	
Delayed Strategy	More Delayed Strategy
Initiate Dialysis	Initiate HD if Mandatory Indication (Hyperkalemia; metabolic acidosis; pulmonary edema) Or BUN > 140
Primary Outcome # days alive without RRT at day 28 98% vs 78% required HD (p < 0.0001)	
12 days	10 days
60 day mortality 44% - delayed vs 55% - more delayed (p = 0.071)	
Hazard ratio for death (multivariable analysis) – more delayed 1.65 (1.09-2.50) p = 0.018	

Gaudry S. et al: Lancet 2021; 397 – 1293-1300

Modality of RRT in AKI

Intermittent Hemodialysis (IHD)	BFR: 300 – 500 ml/ min	DFR: 500 – 800 Ml/ min
Continuous Renal Replacement Therapy (CRRT) CVVH CVVHD CVVHDF	BFR: 100 – 250 ml/min	2-6 liters/ hr
Slow Low Efficiency Dialysis (SLED)	BFR: 100-300 ml/ min	DFR: 100-300 ml/ min
Prolonged Intermittent Renal Replacement Therapy (PIRRT)	BFR: 100-300 ml/ min	DFR: 100-300 ml/ min
Acute Peritoneal Dialysis (PD)		

- **5.6.1: Use continuous and intermittent RRT as complementary therapies in AKI patients.**

- No difference in outcome (mortality or renal recovery)
  - Rabindranath K et al. Cochrane Database Sys Rev 2007: CD003773

- **5.6.2: We suggest using CRRT, rather than standard intermittent RRT, for hemodynamically unstable patients.**

- **5.6.3: We suggest using CRRT, rather than intermittent RRT, for AKI patients with acute brain injury or other causes of increased intracranial pressure or generalized brain edema.**

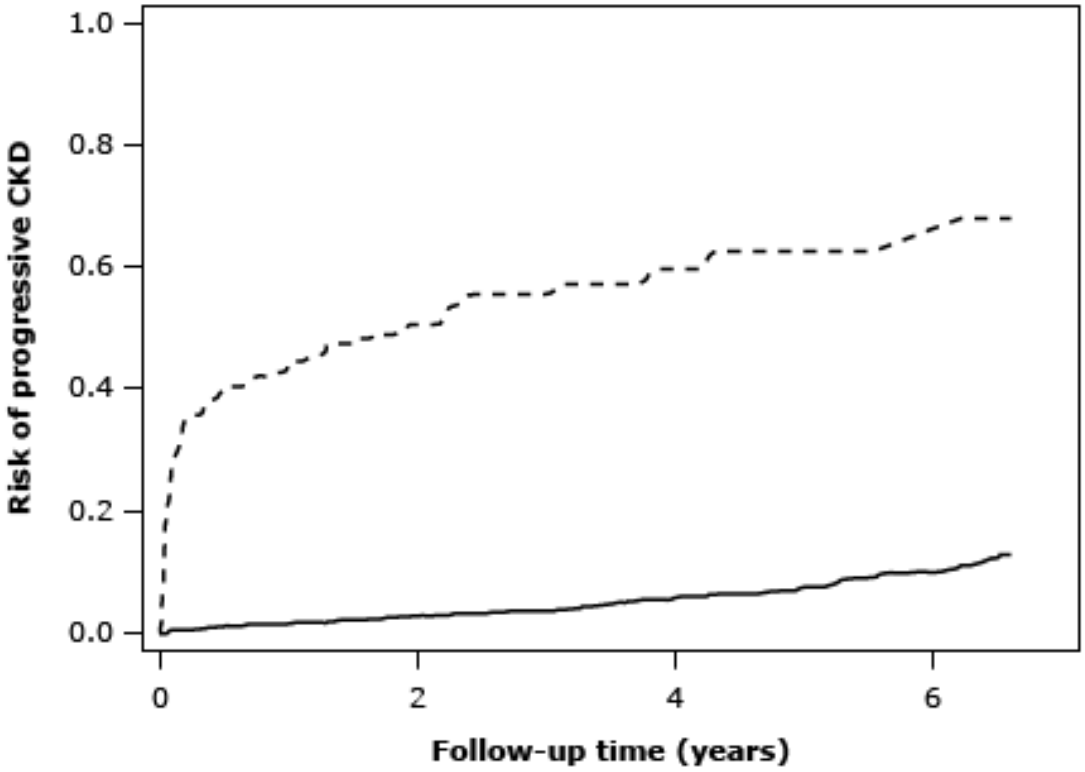
Dose of RRT in AKI

- IHD: 6 vs 3 days a week
  - VA/NIH ATN study: No difference (if each treatment dose adequate Kt/V > 1.2)

    Pavlesky PM et al N Eng J Med 2008: 359; 7-20

- CRRT: effluent volume
  - Target 20-25 ml/kg/hr

Risk of progressive CKD



Kaplan-Meier curves showing long-term risk of progressive chronic kidney disease (CKD) (stage 4 or higher) among patients who did (dashed line) or did not (solid line) suffer acute renal failure.

Follow Up

- **2.3.4: Evaluate patients 3 months after AKI for resolution, new onset, or worsening of pre-existing CKD.**
  - **If patients have CKD, manage these patients as detailed in the KDOQI CKD Guideline**
  - **If patients do not have CKD, consider them to be at increased risk for CKD and care for them as detailed in the KDOQI CKD Guideline for patients at increased risk for CKD.**

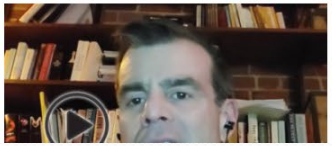
bcnephro.com

BCNephro

Home About Categories Blog Dreams And Passions Contact

Welcome To BCNephro

This blog was created to share experiences as a physician, as a nephrologist, and in life. It will highlight how I approach and think about the diagnosis and treatment of nephrologic conditions as well as life experiences I have enjoyed and look forward to. It is intended for medical residents, students, practitioners and anyone with a passion for learning and enjoying life.



bcnephro.com/contact-dr-cronin/

BCNephro

Home About Categories Blog Dreams And Passions Contact

Contact Dr. Cronin

Brian Cronin

brian@bcnephro.com

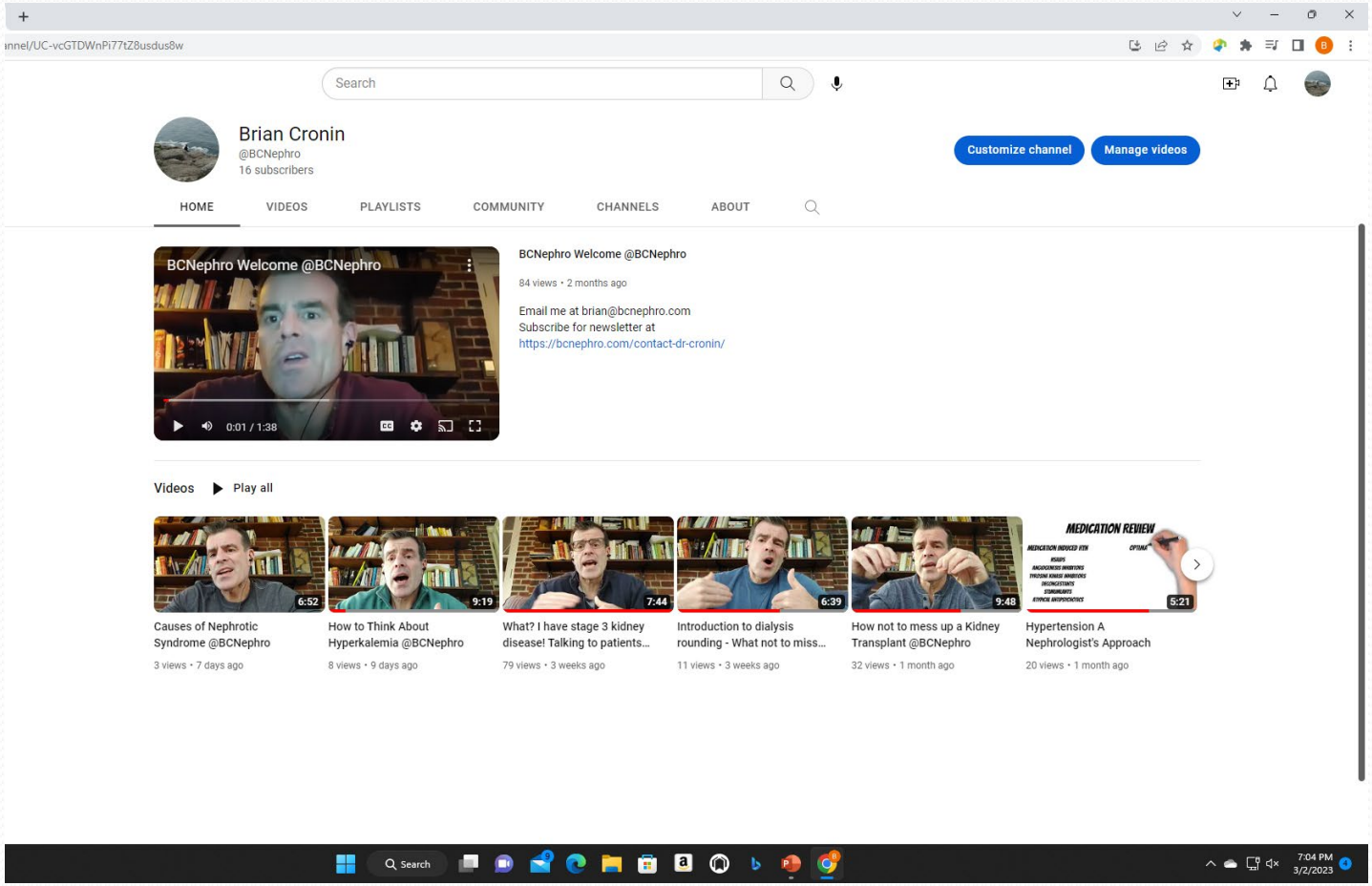
Join Our Mailing List

Fields marked with an * are required

Name *

Email *

Submit


nnel/UC-vcGTDWnPi77tZ8usdus8w
Search
Brian Cronin
@BCNephro
16 subscribers
Customize channel
Manage videos
HOME
VIDEOS
PLAYLISTS
COMMUNITY
CHANNELS
ABOUT
BCNephro Welcome @BCNephro
0:01 / 1:38
BCNephro Welcome @BCNephro
84 views • 2 months ago
Email me at brian@bcnephro.com
Subscribe for newsletter at
https://bcnephro.com/contact-dr-cronin/
Videos
Play all
6:52
Causes of Nephrotic Syndrome @BCNephro
3 views • 7 days ago
9:19
How to Think About Hyperkalemia @BCNephro
8 views • 9 days ago
7:44
What? I have stage 3 kidney disease! Talking to patients...
79 views • 3 weeks ago
6:39
Introduction to dialysis rounding - What not to miss...
11 views • 3 weeks ago
9:48
How not to mess up a Kidney Transplant @BCNephro
32 views • 1 month ago
MEDICATION REVIEW
5:21
Hypertension A Nephrologist's Approach
20 views • 1 month ago
Search
7:04 PM
3/2/2023