급성 신손상의 내과적 치료:
투석 이전에 시행하는 치료를 중심으로

고신대학교 복음병원 신장내과
신호식

증례

- **52세/남자**
- **주소** : 하루 동안의 흉부불편감과 호흡곤란
- **현병력** :

내원13년전 지방간 진단

최근 한달사이 식사는 거의하지 않고 매일 소주2병을 먹음

3일전 속이 갑갑하고 매스껍고 물만 마셔도 구역질 발생함

금일 가슴답답함과 호흡곤란으로 내원함

- **과거력 :** 내원3-4년전 당뇨,고혈압 진단
- **사회력 :** 담배 1갑/하루, 술 소주2명/하루
- **가족력** : 특이 소견없음
- **생체징후** : 혈압 100/50 mmHg, 호흡수 20회/분, 체온 35.8도, 맥박수 104회/분

HEMATOLOGY	WBC Count	13.43	H	x10.e3/uL
	WBC Diff			
	%Neutro	81.3	H	%
	%Lymph	13.1	L	%
	%MONO	5.2		%
	%EOS	0.1	L	%
	%BASO	0.3		%
	ANC(Neutro+BAND)	81.3		%
	Hb	10.6	L	g/dL
	HT	35.3	L	%
	RBC Count	3.35	L	x10.e6/uL
	MCV	105.4	H	fL
	MCH	31.7		pg
	MCHC	30.1	L	g/dL
	RDW	16.1	H	%
	PLT Count	93	L	x10.e3/uL
	PCT	0.08	L	%
	MPV	8.4		fL
	PDW	18.7	H	%
혈액화학검사(1)	BUN	35	H	mg/dl
	Creatinine(CR)	3.7	H	mg/dl
	[eGFR, MDRD]	18		mls/min
	Sodium(Na)	123	L	meq/L
	Potassium(K)	5.7	H	meq/L
	Chloride(CL)	68	L	meq/L
	Total CO2	5.0	L	meq/L
	[Anion Gap]	55.70		(단, pCO_2
	Calcium(Ca)	7.7	L	mg/dL
	Phosphorus(P)	15.7	H	mg/dL
	[Ca*P]	120.89		mg/dL
	Magnesium(Mg)	2.5		mg/dL
	Protein Total	6.3		gm/dL
	Albumin	3.7		g/dl
	[Corrected Calcium]	8		mg/dL
	Bilirubin Total	4.1	H	mg/dl
	Direct Bilirubin	3.0	H	mg/dl

	r-GTP	219	H	U/L
	S-GOT	691	H	IU/L
	S-GPT	120	H	IU/L
	L.D.H	2867	H	IU/L
	Amylase Total	119	H	U/L
	Lipase	268	H	U/L
혈액응고및특수	Prothrombin Time	20.0	H	sec
	PT INR	1.73	H	(pt)
	PT %	45	L	%
	PTT	47.7	H	sec
HEMATOLOGY	ESR	36	H	mm/hr
Miscellaneous	HS-CRP	18.62	H	mg/dL
혈액화학검사(2)	CK-MB	>305.00	H	U/L
	Troponin-i	0.34	H	ng/ml
	Pro-BNP(Brain Natriure	1514	H	pg/mL
심전도검사	E K G(병동용)			
혈청검사(1)	ABO Type			
	Front Type	B		
	Back Type	B		
	Interpretation	B		
	Rho	+		
	Chest PA Lat			
	Abdomen Erect,Supine			
혈액화학검사(1)	Cholesterol Total	204.0		mg/dl
	HDL-Cholesterol	76	H	mg/dl
	Triglyceride	1049	H	mg/dl
	LDL-Cholesterol	64		mg/dl

혈액화학검사(2)	Blood gas analysis			
	Blood PH	6.96	L	Irteria
	Po_2 arterial	122	H	mmHg
	Pco_2 arterial	16	L	mmHg
	Hco_3	3.6	L	mmol/L
	Base excess	-26.6	L	
	O_2 Saturation	96		%

Blood PH

단위 | 참고치

	의뢰일	NO	결과	F	
5	13/06/17	209	7.434		13/06/17(ABG)
6	13/06/17	206	7.407		13/06/17(ABG)
7	13/06/17	196	7.343	L	13/06/17(ABG)
8	13/06/16	182	7.343	L	13/06/16(ABG)
9	13/06/16	175	7.362		13/06/16(ABG)
10	13/06/16	174	7.376		13/06/16(ABG)
11	13/06/16	138	7.406		13/06/16(ABG)
12	13/06/15	132	7.412		13/06/15(ABG)
13	13/06/15	116	7.382		13/06/15(ABG)
14	13/06/15	115	7.403		13/06/15(ABG)
15	13/06/15	106	7.458	H	13/06/15(ABG)
16	13/06/14	73	7.429		13/06/15(ABG)
17	13/06/14	71	7.197	L	13/06/14(ABG)
18	13/06/14	53	7.03	L	13/06/14(ABG)
19	13/06/14	40	7.079	L	13/06/14(ABG)
20	13/06/14	27	6.94	L	13/06/14(ABG)
21	13/06/14	11	6.88	L	13/06/14(ABG)
22	13/06/14	7	6.96	L	13/06/14(ABG)

분류	종목	결과	F
소변검사	TO 10		
	Color-APP	st-cl	
	SG	1.004	
	pH	5.0	
	Leucocyte	Neg	
	Protein	Neg	
	Glucose	Neg	
	Ketone	Neg	
	Urobilinogen	Neg	
	Bilirubin	Neg	
	Nitrite	Neg	
	Erythrocyte	250/ul +4	H
	Urine Microscopy		
	WBC	1-4	/
	RBC	5-10	H /
	Epi.cell	21-30	H /
	Bacteria	+	
	Fungus	-	
	Urine RBC Morphology	Old:90%,fresh:10%	
	Myoglobin	Neg	
혈액화학검사(1)	C.P.K(CK)	3000↑	H
혈액화학검사(2)	Myoglobin	3775.40	H
Miscellaneous	Aldolase		
혈액화학검사(1)	Cystatin C	2.03	H

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급성 신손상의 정의 및 분류

Table 2. KDIGO AKI stage [1]

Stage	혈청 크레아티닌	요량
1	기저치로부터 48시간 내 혈청 크레아티닌의 0.3 mg/dL 이상 상승 또는 7일 내 1.5-1.9배 상승	6시간 이상 요량 < 0.5 mL/kg/h
2	기저치로부터 7일 내 혈청 크레아티닌의 2-2.9배 상승	12시간 이상 요량 < 0.5 mL/kg/h
3	기저치로부터 7일 내 혈청 크레아티닌의 3배 이상 상승, 또는 혈청 크레아티닌이 4.0 mg/dL 이상(동시에 기저치로부터 48시간 내 혈청 크레아티닌의 0.3 mg/dL 이상 상승 또는 7일 내 1.5배 이상 상승한 경우로 한함) 또는 신대체 요법의 개시	24시간 동안 요량 < 0.3 mL/kg/h 또는 12시간 동안 무뇨

KDIGO, international kidney disease improving global outcomes; AKI, acute kidney injury.

대한내과학회지: 제 88 권 제 4 호 2015

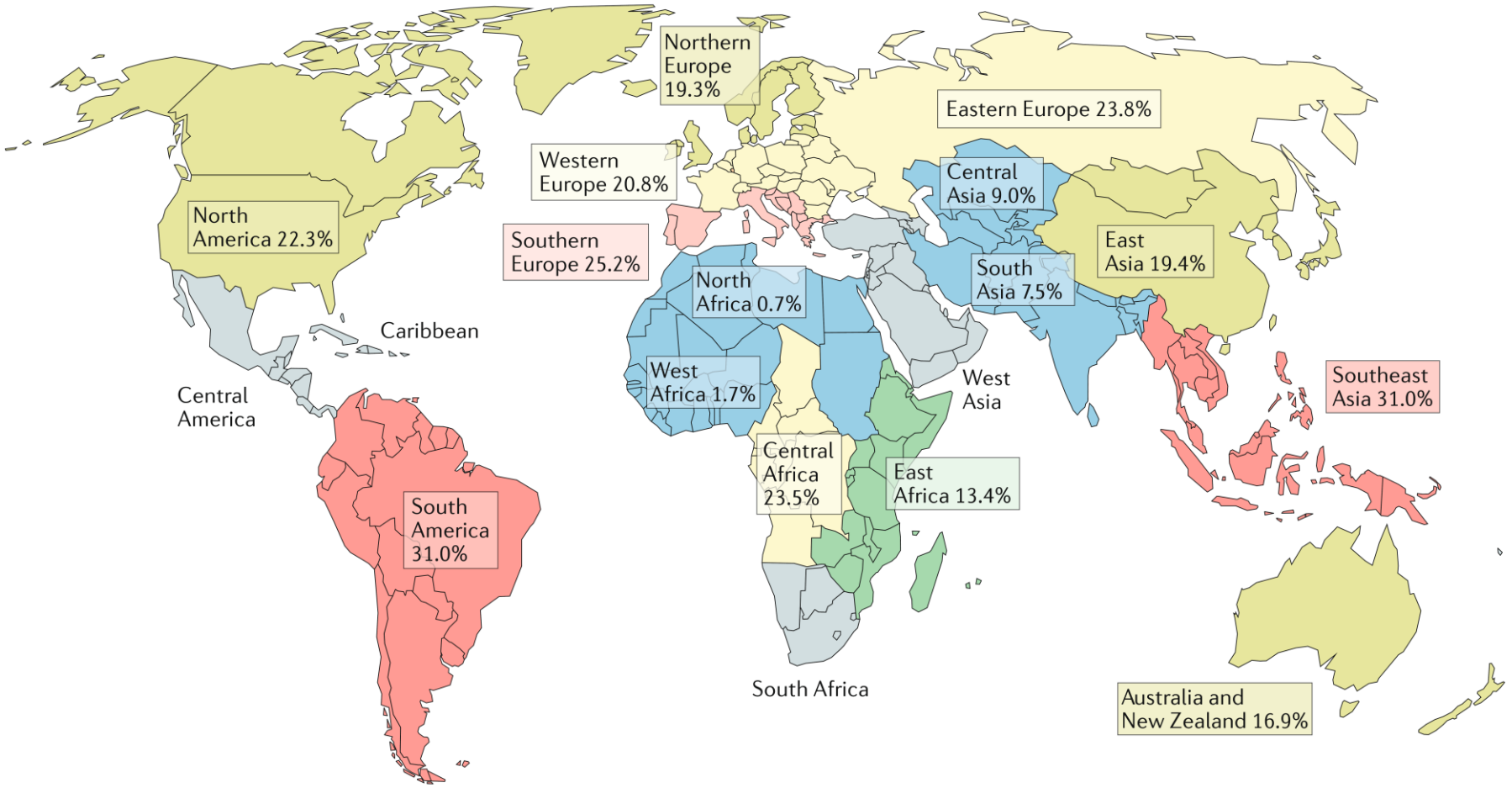
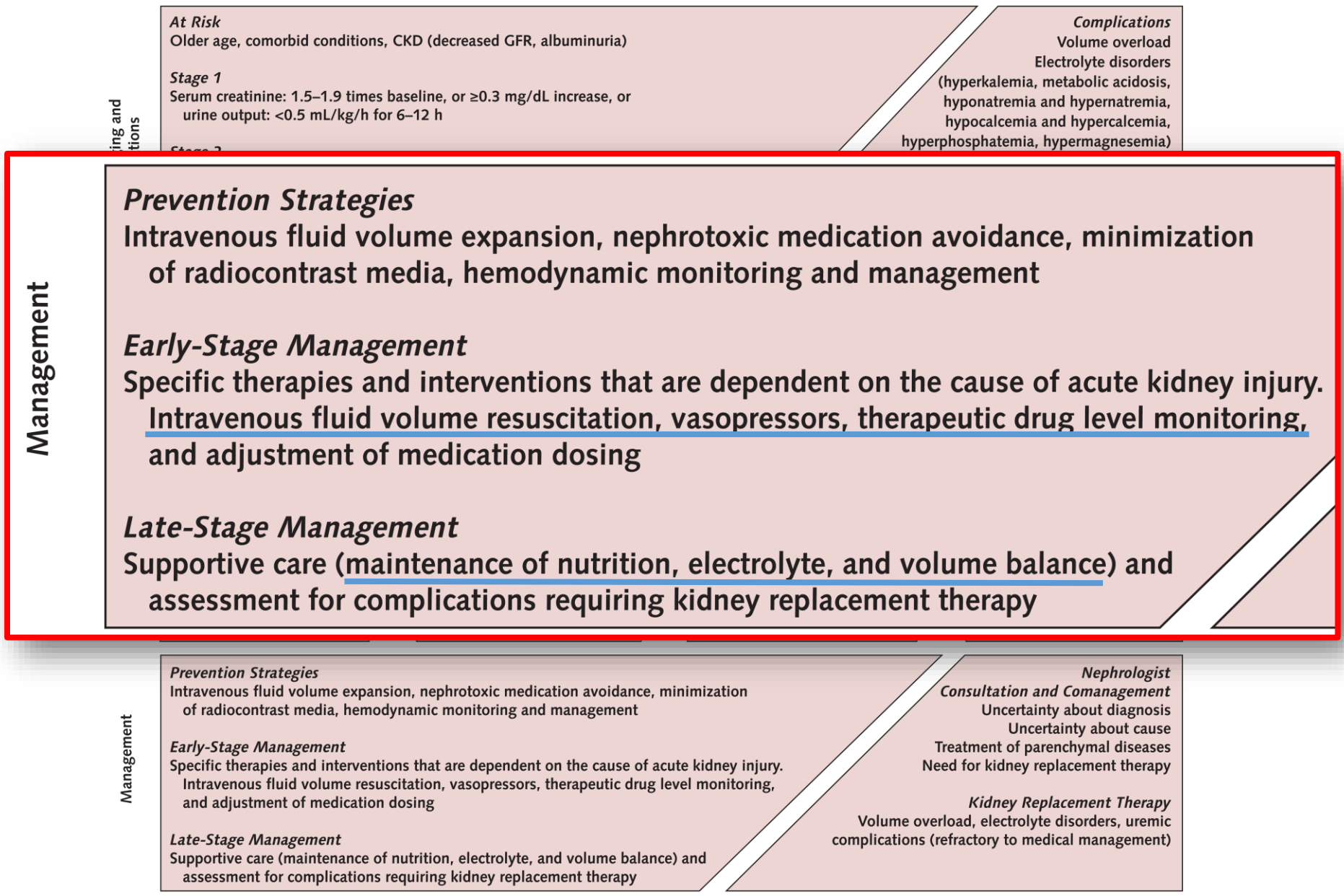
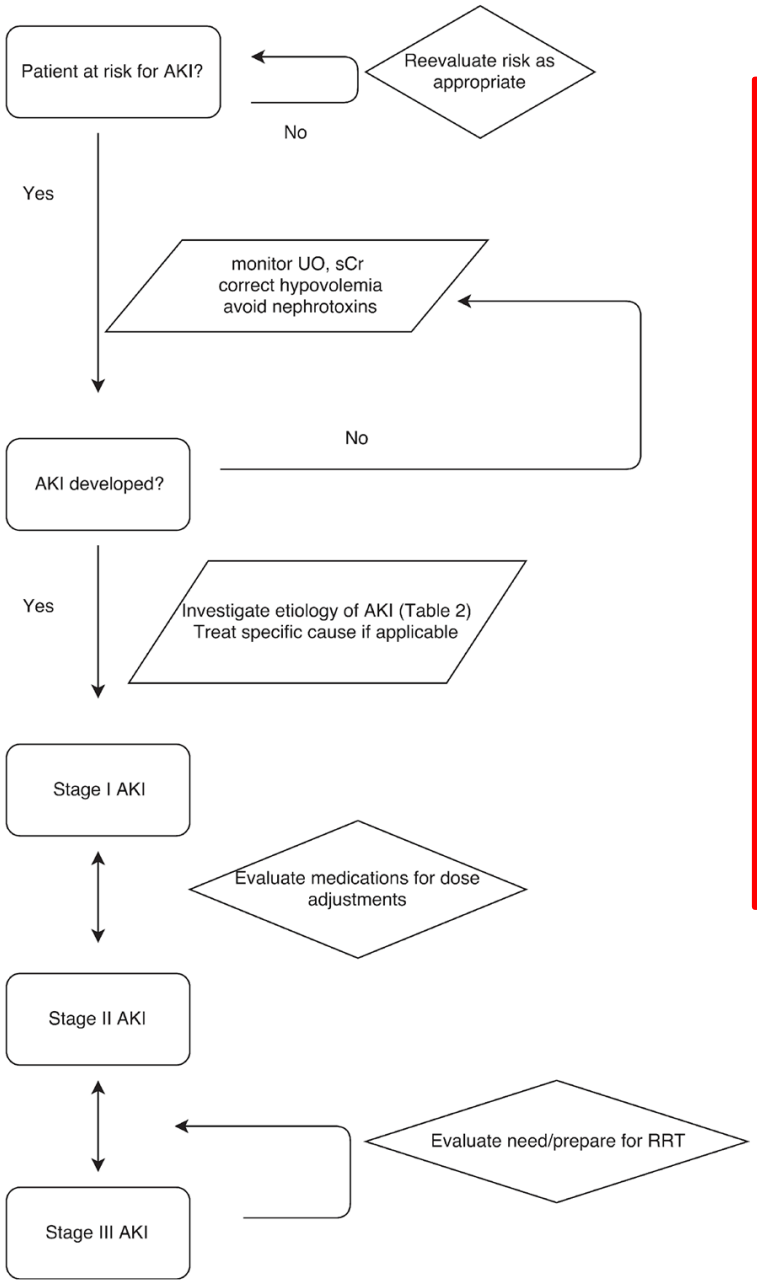


Fig. 3 | **Global variation in the incidence of AKI.** Published estimates of the incidence of acute kidney injury (AKI) as defined using Kidney Disease: Improving Global Outcomes (KDIGO) criteria vary widely across countries and regions. The percentages shown represent the proportion of the hospitalized population with AKI. Data from REFS[3,20].

Figure 2. **Overview of acute kidney injury.**



1.1. Scr, U/O, Volume status & Hemodynamics



Conceptual model for the diagnosis and treatment of AKI

1. Renal function monitored closely by Scr & U/O

2.Careful assessment of vol status & hemodynamics

1.2. Medication

Box 1. Medications Commonly Associated With Acute Tubular Necrosis

- Aminoglycosides (tobramycin, gentamycin)
- NSAIDs (ibuprofen, naproxen, ketorolac, celecoxib)
- ACEi (captopril, lisinopril, benazepril, ramipril)
- ARB (losartan, valsartan, candesartan, irbesartan)
- Amphotericin
- Cisplatin
- Foscarnet
- Iodinated contrast
- Pentamidine
- Tenofovir
- Zolendronic acid

Note: Although not a classic cause of acute tubular necrosis, volume depletion caused by diuretics can exacerbate the effects of some of these other medications. This table does not include common causes of pigment or crystal nephropathy (which are described in Table 2) or medications associated with osmotic injury.
Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; NSAIDs, nonsteroidal anti-inflammatory drugs.

Box 2. Key Medications Requiring Dose Adjustment (or Cessation) in AKI

- Analgesics (morphine, meperidine, gabapentin, pregabalin)
- Antiepileptics (lamotrigine)
- Antivirals (acyclovir, gancyclovir, valgancyclovir)
- Antifungals (fluconazole)
- Antimicrobials (almost all antimicrobials need dose adjustment in AKI, with important exceptions of azithromycin, ceftriaxone, doxycycline, linezolid, moxifloxacin, nafcillin, rifampin)
- Diabetic agents (sulfonylureas, metformin)
- Allopurinol
- Baclofen
- Colchicine
- Digoxin
- Lithium
- Low-molecular-weight heparin
- NOACs

Note: Medications that are associated with acute tubular necrosis (Box 1) should be withheld, if possible.
Abbreviations: AKI, acute kidney injury; NOAC, novel anticoagulants.

1. Very high level of VM (> 50 ug/mL) → Nephrotoxic
2. If creatinine is rising acutely, assume GFR < 10.
3. Pay close attention to narcotics and anti-coagulants, which may accumulate in renal failure.

Am J Kidney Dis. 2018 Jul;72(1):136-148
MGH Nephrology guide

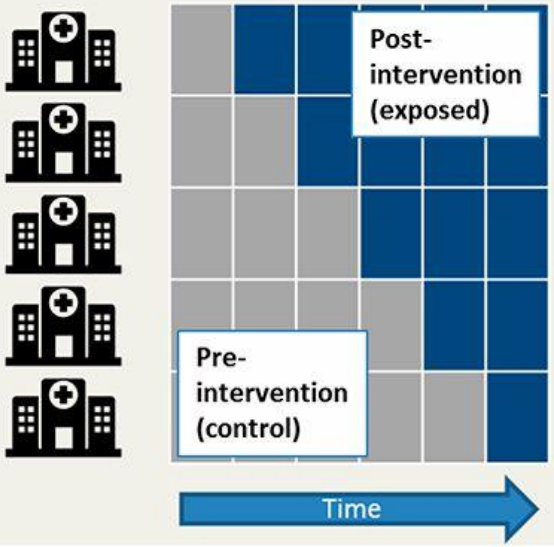
Tackling AKI Study: Organisational Level Interventions for Acute Kidney Injury

METHODS:

Multicentre stepped-wedge cluster randomised trial.

Intervention: hospital-wide AKI e-alerts, care bundle and education.

24,059 AKI episodes
5 hospitals

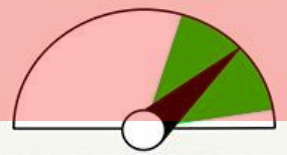


OUTCOMES:

- **30-day mortality**
  (Primary outcome)
- **AKI progression**

- **Hospital length of stay**
  (in those with longer LoS)

- **AKI incidence**
  (improved detection)



- **Delivery of AKI care**

CONCLUSION: **A complex, hospital-wide intervention for AKI did not alter mortality but reduced hospital length of stay, whilst improving quality of care and AKI recognition.**

doi: 10.1681/ASN.2018090886

JASN March 2019, 30 (3) 505-515;

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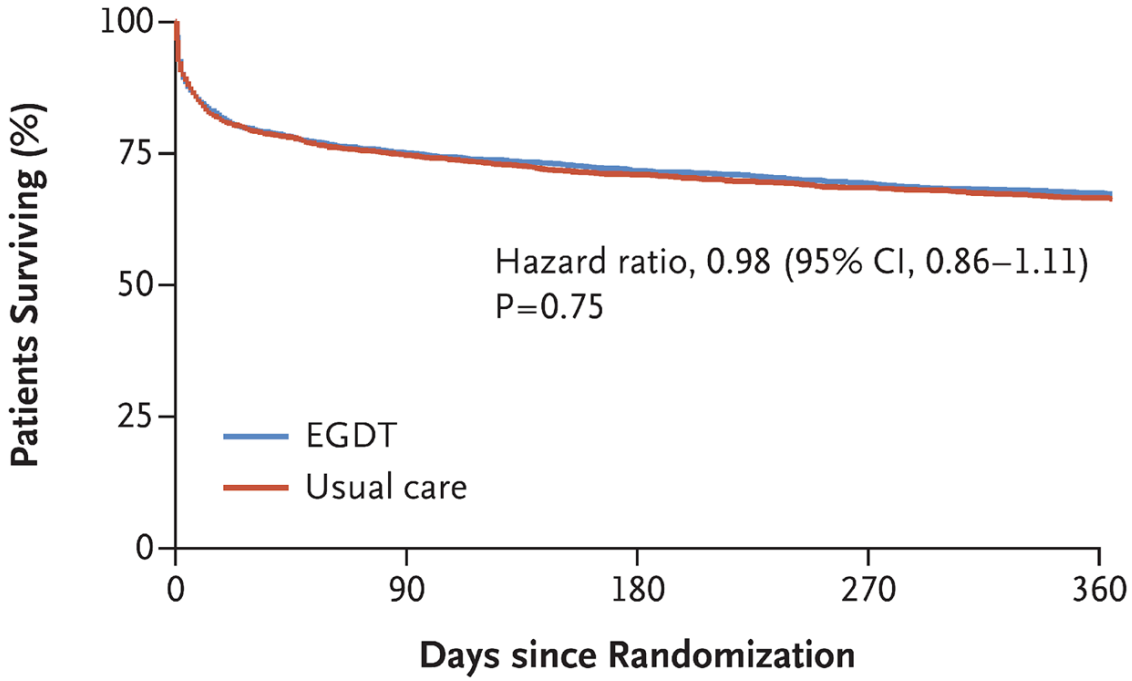
2.1.Intravenous Fluid Resuscitation

- **No** randomized trials comparing **intravenous fluids** to placebo for **AKI prevention**
- **Early goal-directed therapy**, in which septic patients received intravenous crystalloids, inotropes, and transfusions according to predefined protocols,

had **no effect on mortality or need for RRT** in 3 subsequent large trials



No. at Risk					
EGDT	1857	1391	1287	1209	1119
Usual care	1880	1395	1295	1206	1110

Figure 1. Patient Survival over a Period of 1 Year.

N Engl J Med 2017;376:2223-34.

Assessment of fluid responsiveness

- **Multiple clinical assessments and repeated measures** to assess fluid responsiveness.
- Intravenous fluids should be used judiciously in patients with AKI who are not “volume responsive.”
- After significant volume resuscitation, even if patients remain volume responsive, vasopressor support should be considered to avoid markedly positive fluid balance.

2.1.Intravenous Fluid Resuscitation

Method	Threshold
Pulse pressure/stroke volume variations [22]	12%
Inferior vena cava diameter variations [44]	12%
Superior vena caval diameter variations [44]	36%*
Passive leg raising [55]	10%
End-expiratory occlusion test [75]	5%
"Mini"-fluid challenge (100 mL) [84]	6%**
"Conventional" fluid challenge (500 mL) [81]	15%

2.2. Colloid Versus Crystalloid

SAFE trial

Patients	Albumin Group	Saline Group	Relative Risk (95% CI)
	no. of deaths/total no.		
Overall	726/3473	729/3460	0.99 (0.91–1.09)
Trauma			
Yes	81/596	59/590	1.36 (0.99–1.86)
No	641/2831	666/2830	0.96 (0.88–1.06)
Severe sepsis			
Yes	185/603	217/615	0.87 (0.74–1.02)
No	518/2734	492/2720	1.05 (0.94–1.17)
ARDS			
Yes	24/61	28/66	0.93 (0.61–1.41)
No	697/3365	697/3354	1.00 (0.91–1.09)

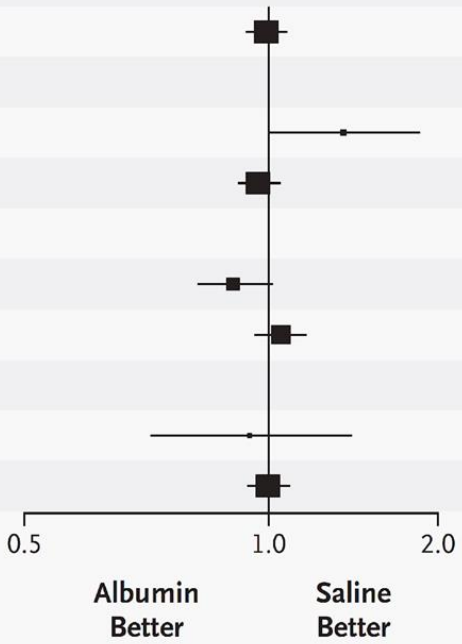
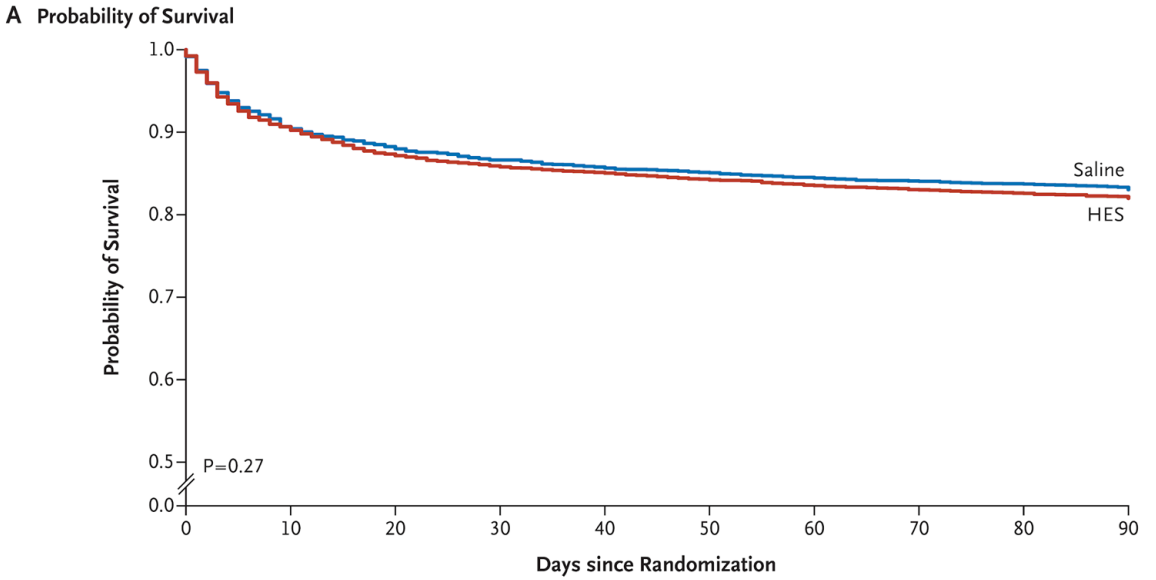


Figure 2. Relative Risk of Death from Any Cause among All the Patients and among the Patients in the Six Predefined Subgroups.

1. use of either 4 percent albumin or normal saline for fluid resuscitation results in similar outcomes at 28 days.
2. **Ix for albumin**: large-vol paracentesis for patients with ESLD
3. **Cix for albumin**: patients with traumatic brain injury

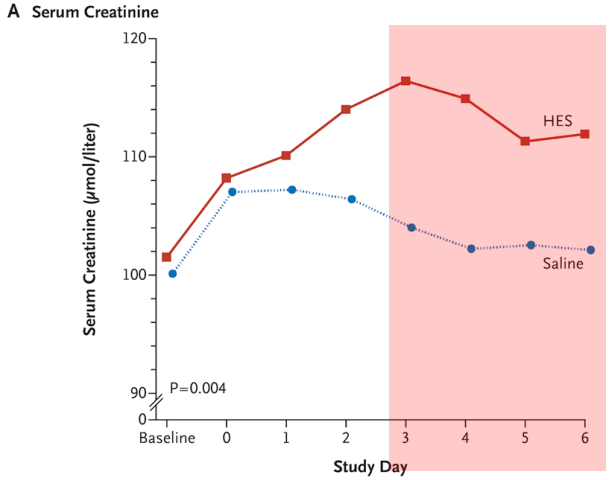
N Engl J Med 2004;350:2247-56.

2.2. Colloid Versus Crystalloid



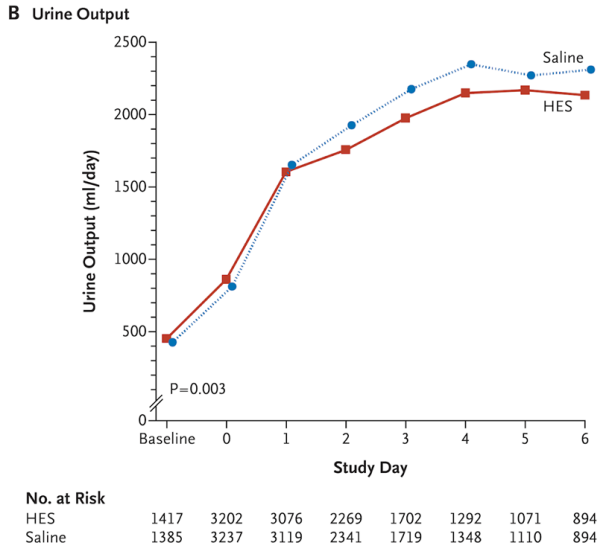
No. at Risk

Saline	3336	3024	2943	2889	2860	2837	2816	2801	2788	2752
HES	3315	3004	2895	2846	2819	2791	2766	2747	2731	2695



No. at Risk

HES	3260	2197	2899	2111	1576	1238	998	851
Saline	3283	2253	2916	2196	1614	1291	1026	857



No. at Risk

HES	1417	3202	3076	2269	1702	1292	1071	894
Saline	1385	3237	3119	2341	1719	1348	1110	894

CHEST study:

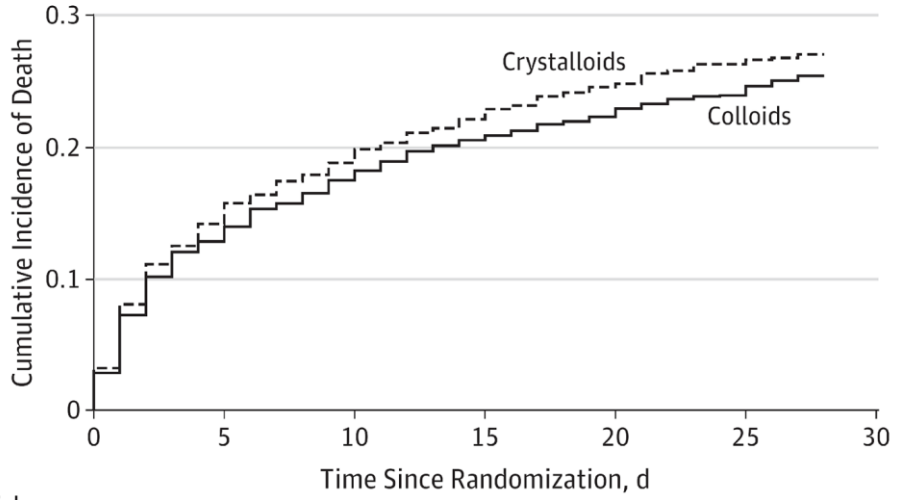
1. In patients in the ICU, there was no significant difference in 90-day mortality between patients resuscitated with 6% HES (130/0.4) or saline. However, more patients who received resuscitation with HES were treated with renal-replacement therapy.
2. Following the publication of this study, the FDA added additional warnings to the packaging for HES.

N Engl J Med 2012;367:1901-11.

Effects of Fluid Resuscitation With Colloids vs Crystalloids on Mortality in Critically Ill Patients Presenting With Hypovolemic Shock

The CRISTAL Randomized Trial

Figure 2. Cumulative Incidence of Death Within First 28 Days After Randomization



JAMA. 2013;310(17):1809-1817.

Table 2. Study Outcomes by Treatment Group

	No. (%) of Patients			
	Colloids (n = 1414)	Crystalloids (n = 1443)	RR (95% CI)	*P* Value[a]
Death				
Within 28 d	359 (25.4)	390 (27.0)	0.96 (0.88 to 1.04)	.26
Within 90 d	434 (30.7)	493 (34.2)	0.92 (0.86 to 0.99)	.03
In ICU	355 (25.1)	405 (28.1)	0.92 (0.85 to 1.00)	.06
In hospital	426 (30.1)	471 (32.6)	0.94 (0.87 to 1.02)	.07

Table 1. Properties of 0.9% Saline, Lactated Ringer's, and Plasma-Lyte Solutions

	0.9% Saline	Lactated Ringer's	Plasma-Lyte
Sodium, mEq/L	154	130	140
Potassium, mEq/L	0	4	5
Calcium, mEq/L	0	2.7	0
Magnesium, mEq/L	0	0	3
Chloride, mEq/L	154	109	98
Lactate, mEq/L	0	28	0
Acetate, mEq/L	0	0	27
Gluconate, mEq/L	0	0	23
Osmolarity, mOsm/L	308	273	294
pH	5.5	6.5	7.4

Am J Kidney Dis. 2018 Dec;72(6):900-902

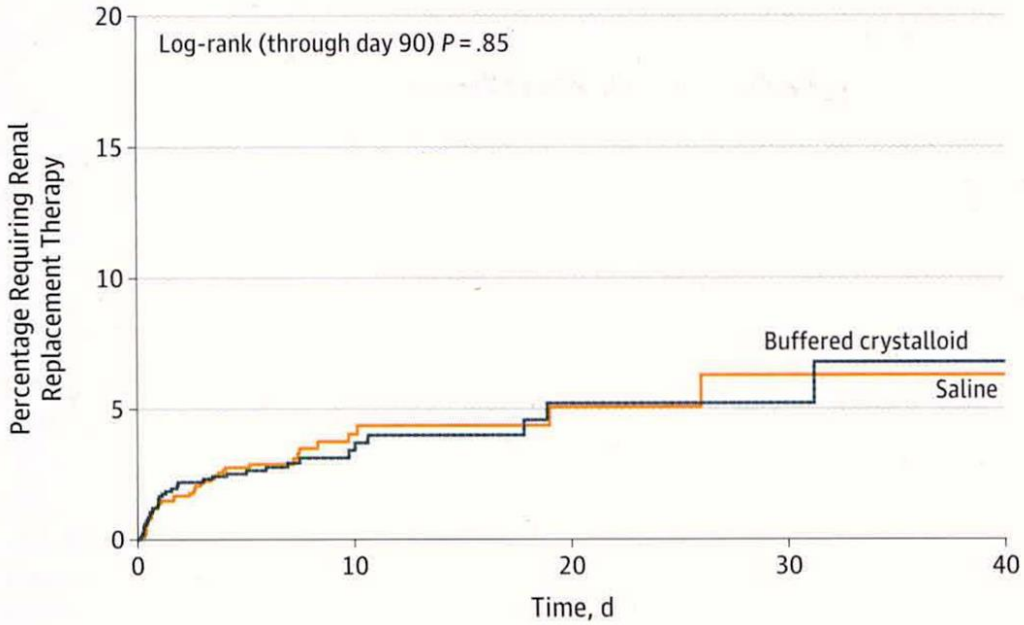
Isotonic 0.9% saline solution

- Higher chloride content than the extracellular space in humans (154 vs w110 mmol/L)
- risk for hyperchloremic metabolic acidosis.
- Hyperchloremia associated with ↑renal vascular resistance, ↑renin activity, and ↓GFR in animal studies
- associated with ↑extravascular volume and ↓renal cortical tissue perfusion compared to a balanced salt solution in healthy volunteers,

2.3. Physiologic Balanced Salt Solution Versus Normal Saline Solution

Effect of a Buffered Crystalloid Solution vs Saline on Acute Kidney Injury Among Patients in the Intensive Care Unit
The SPLIT Randomized Clinical Trial

Figure 2. Cumulative Incidence of Patients Requiring Renal Replacement Therapy Until Day 90 After Enrollment in the SPLIT Trial



No. at risk					
Buffered crystalloid	1152	341	134	62	36
Saline	1110	310	124	64	28

JAMA. 2015;314(16):1701-1710.

2.3. Physiologic Balanced Salt Solution Versus Normal Saline Solution

SMART study

" We'd be lucky to improve mortality by 1 percent with an expensive drug, much less a fluid that costs $2."

Table 2. Selected Results of the SMART[6] and SALT-ED[7] Trials

Components of Primary Outcome	SMART (ICU) Balanced Crystalloid, %	SMART (ICU) Saline, %	SMART (ICU) Difference	SALT-ED (Non ICU) Balanced Crystalloid, %	SALT-ED (Non ICU) Saline, %	SALT-ED (Non ICU) Difference
In-hospital death before 30 d	10.3%	11.1%	0.8%	1.4%	1.5%	0.1%
New RRT	2.5%	2.9%	0.4%	0.3%	0.5%	0.2%
Final serum creatinine ≥ 200% of baseline	6.4%	6.6%	0.2%	3.8%	4.5%	0.8%
Major adverse kidney events within 30 d	14.3%	15.4%	1.1%	4.7%	5.6%	0.9%

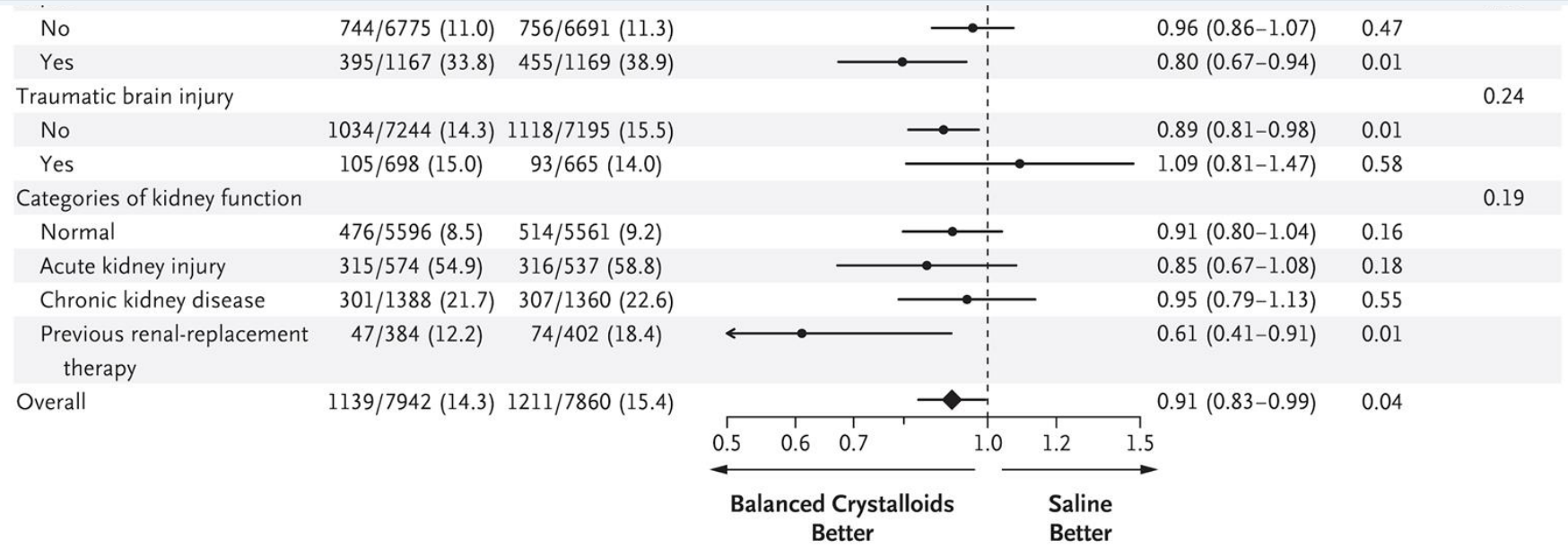


Figure 3. Subgroup Analysis of Rates for the Composite Outcome of Death, New Receipt of Renal-Replacement Therapy, or Persistent Renal Dysfunction.

N Engl J Med 2018;378:829-39.

Prevention of acute kidney injury and protection of renal function in the intensive care unit: update 2017

Expert opinion of the Working Group on Prevention, AKI section, European Society of Intensive Care Medicine

- We recommend controlled fluid resuscitation in volume depletion, while, however, avoiding volume overload (Grade 1C).
- We recommend against the use of starches (Grade1A) as harm has been shown and suggest not using gelatine or dextrans for fluid resuscitation (Grade2C).
- We recommend correction of hypovolaemia/dehydration using isotonic crystalloids in patients receiving intravascular contrast media (Grade 1B).
- We recommend regular monitoring of chloride levels and acid–base status in situations where chloride rich solutions are used (BPS).
- We suggest the use of balanced crystalloids for large volume resuscitation (Grade 2C).
- We suggest using human serum albumin if a colloid is deemed necessary for the treatment of patients with septic shock (Grade 2C)

Intensive Care Med (2017) 43:730–749

High versus Low Blood-Pressure Target in Patients with Septic Shock

SEPSISPAM study

Table 2. Clinical Results, Primary and Secondary Outcomes, and Serious Adverse Events.

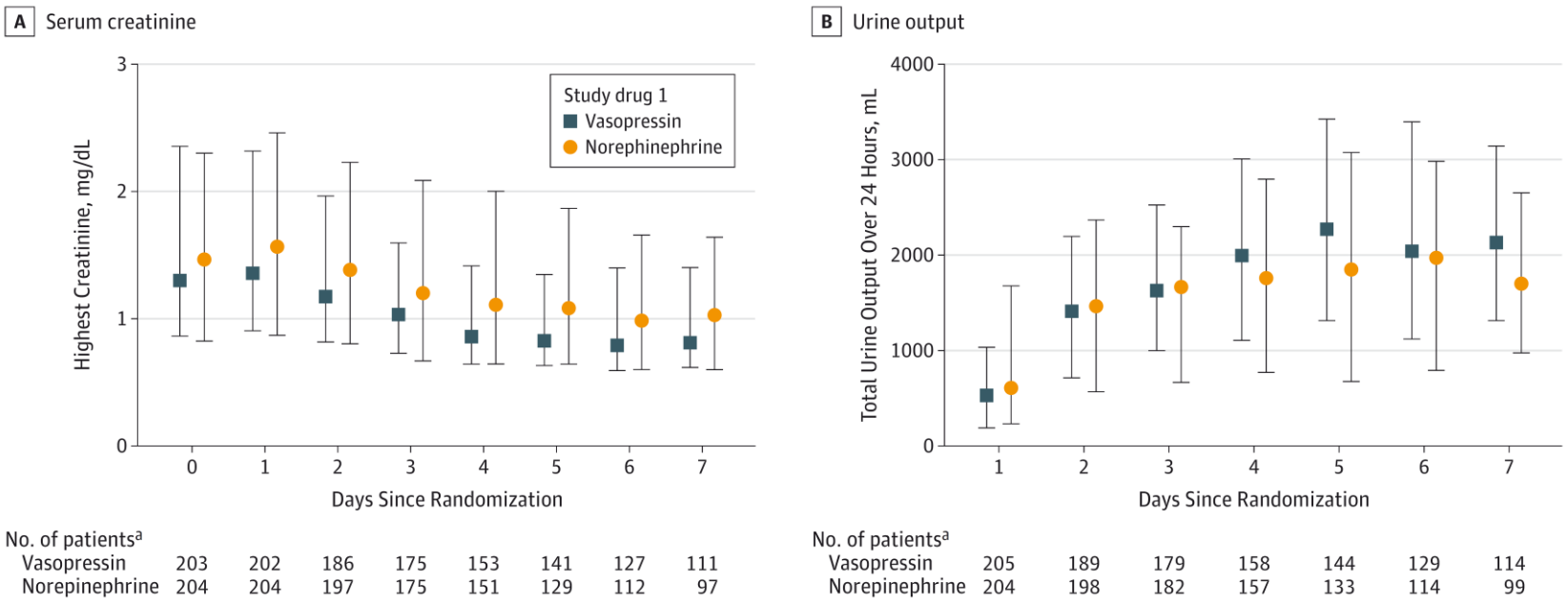
Variable	Low-Target Group (N = 388)	High-Target Group (N = 388)	P Value
Cumulative fluid intake from day 1 to day 5 — liters	10.0 (5.8–14.0)	10.5 (5.5–14.0)	0.89
Cumulative urine output from day 1 to day 5 — liters	6.7 (2.9–10.7)	6.9 (2.4–10.7)	0.87
Cumulative fluid balance from day 1 to day 5 — liters	2.8 (0.0–6.2)	2.4 (0.0–6.0)	0.74
Median dose of norepinephrine (IQR) — μg/kg/min			
Day 1	0.45 (0.17–1.21)	0.58 (0.26–1.80)	<0.001
Day 2	0.16 (0.03–0.48)	0.38 (0.14–0.90)	<0.001
Day 3	0.02 (0.00–0.16)	0.14 (0.01–0.50)	<0.001
Day 4	0.00 (0.00–0.05)	0.03 (0.00–0.22)	<0.001
Day 5	0.00 (0.00–0.03)	0.01 (0.00–0.15)	<0.001
Duration of catecholamine infusion — days	3.7±3.2	4.7±3.7	<0.001
Primary outcome: death at day 28 — no. (%)*	132 (34.0)	142 (36.6)	0.57
Secondary outcomes — no./total no. (%)			
Death at day 90†	164 (42.3)	170 (43.8)	0.74
Survival at day 28 without organ support‡	241 (62.1)	235 (60.6)	0.66
Doubling of plasma creatinine	161 (41.5)	150 (38.7)	0.42
No chronic hypertension	71/215 (33.0)	85/221 (38.5)	0.32
Chronic hypertension	90/173 (52.0)	65/167 (38.9)	0.02
Renal-replacement therapy from day 1 to day 7	139 (35.8)	130 (33.5)	0.50
No chronic hypertension	66/215 (30.7)	77/221 (34.8)	0.36
Chronic hypertension	73/173 (42.2)	53/167 (31.7)	0.046

N Engl J Med 2014;370:1583-93.

Vasoactive Medications in AKI

The VANISH Randomized Clinical Trial

Figure 4. Serum Creatinine and Urine Output Over the First 7 Days by Study Drug 1



- Recent evidence continues to show no benefit of dopamine and its agonists for the prevention or treatment of AKI.
- **Angiotensin II** shows promise as a vasoactive agent for the treatment of distributive shock

Crit Care 18: 534, 2014
JAMA 316: 509–518, 2016

Prevention of acute kidney injury and protection of renal function in the intensive care unit: update 2017

Expert opinion of the Working Group on Prevention, AKI section, European Society of Intensive Care Medicine

- We *recommend* titrating vasopressors to a **MAP of 65–70 mmHg** (Grade 1B) rather than a higher MAP target (80–85 mmHg) in patients with septic shock. However, for patients with chronic hypertension we *recommend* aiming for a higher target (80–85 mmHg) for renal protection in septic shock (Grade 1C).
- We *recommend* lowering systolic pressure to 140–190 mmHg rather than to 110–139 mmHg in patients with acute cerebral haemorrhage with severe admission hypertension (Grade 1C).
- If vasopressors are needed for treatment of hypotension, we *recommend* norepinephrine (along with correction of hypovolaemia) as the first-choice vasopressor vasopressor to protect kidney function (Grade 1B) and *suggest* vasopressin in patients with vasoplegic shock after cardiac surgery (Grade 2C).
- We *suggest* individualizing target pressure when premorbid blood pressure is available (BPS).

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Prevention of acute kidney injury and protection of renal function in the intensive care unit: update 2017

Expert opinion of the Working Group on Prevention, AKI section, European Society of Intensive Care Medicine

- We recommend against loop diuretics given solely for the prevention of acute kidney injury (Grade 1B).
- We suggest using diuretics to control or avoid fluid overload in patients that are diuretic-responsive (Grade 2D).

Intensive Care Med (2017) 43:730–749

Development and Standardization of a Furosemide Stress Test to Predict the Severity of Acute Kidney Injury

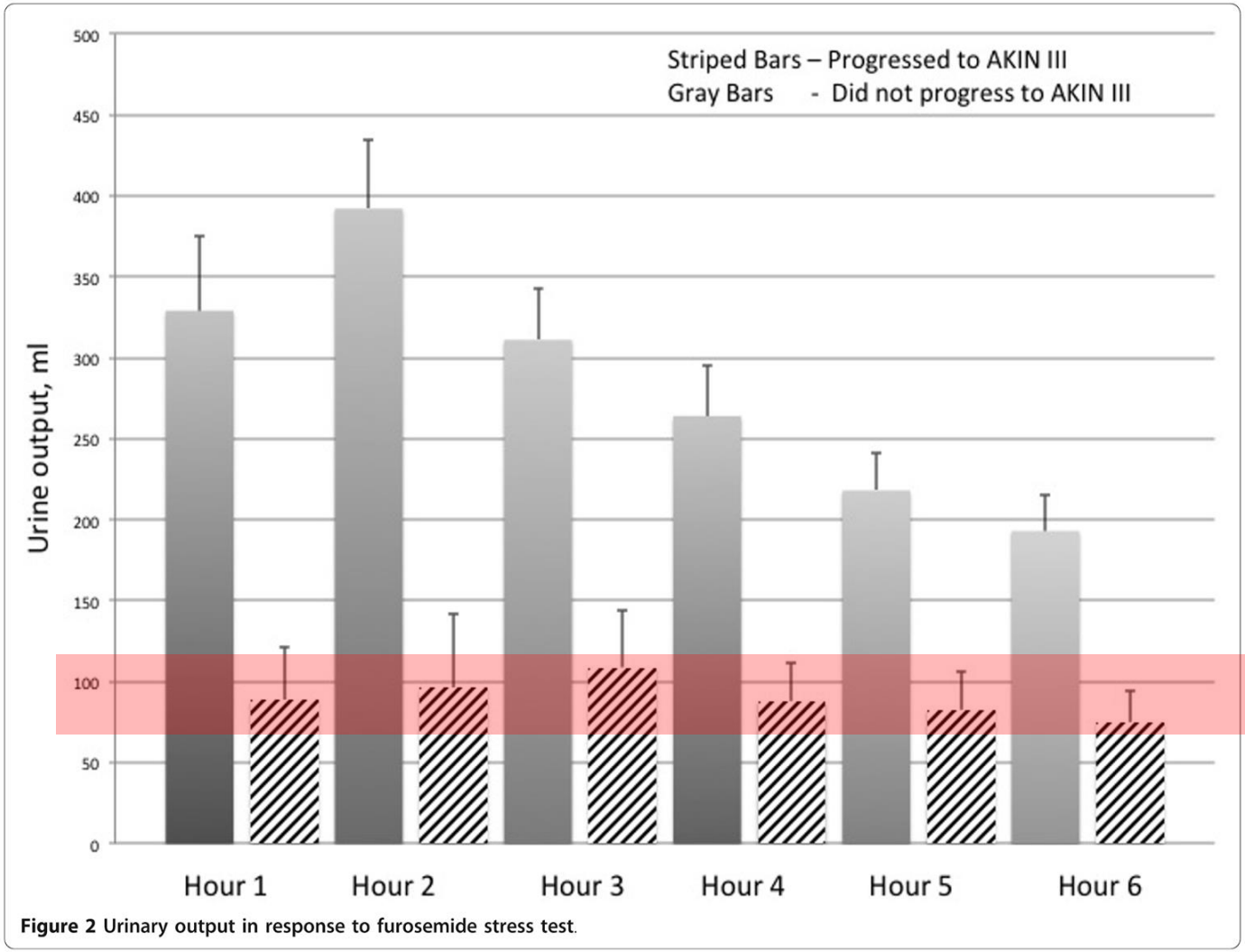
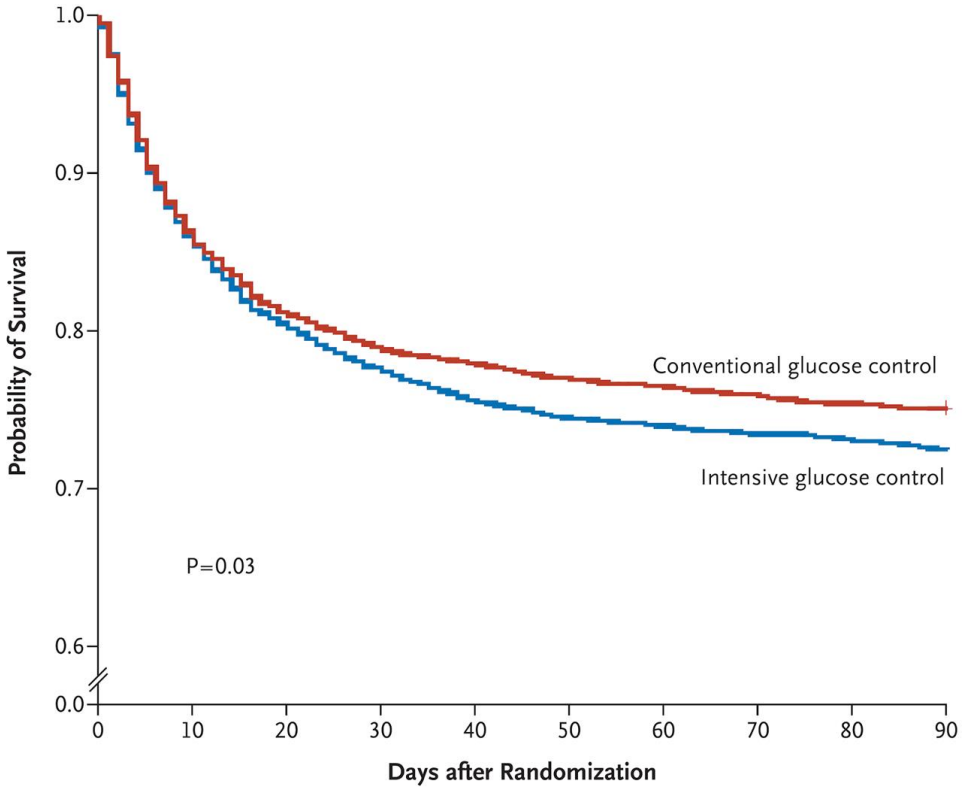


Figure 2 Urinary output in response to furosemide stress test.

Critical Care 2013, 17:R207
J Am Soc Nephrol 26: 2023–2031, 2015

Intensive versus Conventional Glucose Control in Critically Ill Patients

The NICE-SUGAR Study

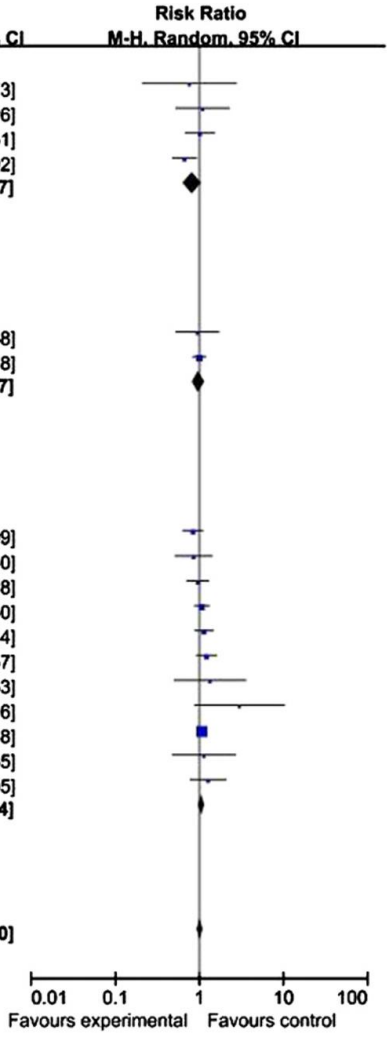


No. at Risk				
Conventional control	3014	2379	2304	2261
Intensive control	3016	2337	2227	2182

N Engl J Med 2009;360:1283-97.

Intensive versus conventional glucose control in critically ill patients: A meta-analysis of randomized controlled trials

Study or Subgroup	intensive Events	Total	conventional Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
5.1.1 Surgical ICU						
Cao et al, 2011	4	92	5	87	0.3%	0.76 [0.21, 2.73]
Coester et al, 2010	11	42	11	46	1.0%	1.10 [0.53, 2.26]
Meng et al, 2009	35	121	34	119	3.1%	1.01 [0.68, 1.51]
Van den Berghe et al,2001	55	765	85	783	4.6%	0.66 [0.48, 0.92]
Subtotal (95% CI)		**1020**		**1035**	**8.9%**	**0.82 [0.63, 1.07]**
Total events	105		135			
Heterogeneity: Tau² = 0.01; Chi² = 3.42, df = 3 (P = 0.33); I² = 12%						
Test for overall effect: Z = 1.46 (P = 0.15)						
5.1.2 Medical ICU						
Oksanen et al, 2007	13	39	18	51	1.5%	0.94 [0.53, 1.68]
Van den Berghe et al,2006	178	595	182	605	14.0%	0.99 [0.84, 1.18]
Subtotal (95% CI)		**634**		**656**	**15.4%**	**0.99 [0.84, 1.17]**
Total events	191		200			
Heterogeneity: Tau² = 0.00; Chi² = 0.03, df = 1 (P = 0.87); I² = 0%						
Test for overall effect: Z = 0.12 (P = 0.91)						
5.1.3 Mixed ICU						
Arabi et al, 2008	72	266	83	257	6.6%	0.84 [0.64, 1.09]
Arabi et al, 2011	23	120	27	120	2.0%	0.85 [0.52, 1.40]
Brunkhorst et al, 2008	61	247	75	290	5.5%	0.95 [0.71, 1.28]
COIITSS study, 2010	117	255	109	254	11.4%	1.07 [0.88, 1.30]
De La Rosa et al, 2008	93	254	81	250	7.9%	1.13 [0.89, 1.44]
Glucontrol study, 2009	100	550	83	551	6.6%	1.21 [0.93, 1.57]
Iapichino et al, 2008	8	45	6	45	0.5%	1.33 [0.50, 3.53]
Mitchell et al, 2006	9	35	3	35	0.3%	3.00 [0.89, 10.16]
NICE-SUGAR study, 2009	670	3054	627	3050	31.8%	1.07 [0.97, 1.18]
Savioli et al, 2009	9	45	8	45	0.7%	1.13 [0.48, 2.65]
Taslimi et al, 2009	26	67	19	62	2.1%	1.27 [0.78, 2.05]
Subtotal (95% CI)		**4938**		**4959**	**75.6%**	**1.06 [0.99, 1.14]**
Total events	1188		1121			
Heterogeneity: Tau² = 0.00; Chi² = 9.02, df = 10 (P = 0.53); I² = 0%						
Test for overall effect: Z = 1.65 (P = 0.10)						
Total (95% CI)		**6592**		**6650**	**100.0%**	**1.02 [0.95, 1.10]**
Total events	1484		1456			
Heterogeneity: Tau² = 0.00; Chi² = 17.34, df = 16 (P = 0.36); I² = 8%						
Test for overall effect: Z = 0.66 (P = 0.51)						
Test for subgroup differences: Not applicable						



European Journal of Internal Medicine 23 (2012) 564–574

Goals of Nutrient Intakes in AKI

- 칼로리: 20-30 kal/kg/day
- Preferably provided via the enteral route
- Timing of nutritional support: enteral nutrition is the preferential modality in the first 24 to 48 hours of intensive care unit stay
- Protein goal: 0.8-1.0 g/kg/day in non-catabolic pts, 1.1-1.5 g/kg/day in RRT, max 1.7 g/kg/day in hypercatabolic or CRRT
- Insulin therapy targeting plasma glucose: 110 to149mg/dL
- Vit C: 50 to 100 mg/day.

Journal of Renal Nutrition, Vol 23, No 3 (May), 2013: pp 255-258
KDIGO guideline 2012

NE, ANP, multipotent stem, ALP

TABLE 70.3 Summary of Drugs Used in Treatment of Acute Kidney Injury

Drug	Level of Evidence	Results	Comments
Dopamine	RCTs	No effect on mortality or kidney function	
Fenoldopam	Small RCTs One meta-analysis	No effect on mortality or kidney function Beneficial effect on mortality and need for dialysis	Further studies required
Norepinephrine	Prospective observational studies	Possible beneficial effect on kidney function	Further studies required
Loop diuretics	RCTs and meta-analyses	No effect on kidney function	Further studies required
Atrial natriuretic peptide	RCTs	Possible beneficial effect on survival and kidney function	Further studies required
B-type natriuretic peptide	RCT in acute heart failure	No effect on kidney function	
Multipotent stem	Animal models and human studies	Beneficial effect on kidney function in animal models but no effect in one human study	Further studies required; ongoing study in cisplatin-induced AKI
Erythropoietin	Animal models and human studies	Controversial effect on kidney function	Further studies required
Alkaline phosphatase	Small RCT	Beneficial effect on kidney function in sepsis	Further studies required; ongoing phase 2 trial

3.3. Pharmacotherapies for AKI

Box 3. Agents Tested in Selected Trials for Treatment of AKI

Trials ongoing

- Alkaline phosphatase (sepsis-associated AKI)
- L-Carnitine (sepsis-associated AKI)
- Remote ischemic preconditioning (post operative AKI)
- p53-targeted siRNA (post–cardiac surgery AKI)
- Extracorporeal devices (dialysis-requiring AKI)
- Vitamin D (hospitalized AKI)
- Uremic toxin absorption/pentoxifylline (hospital-acquired AKI)

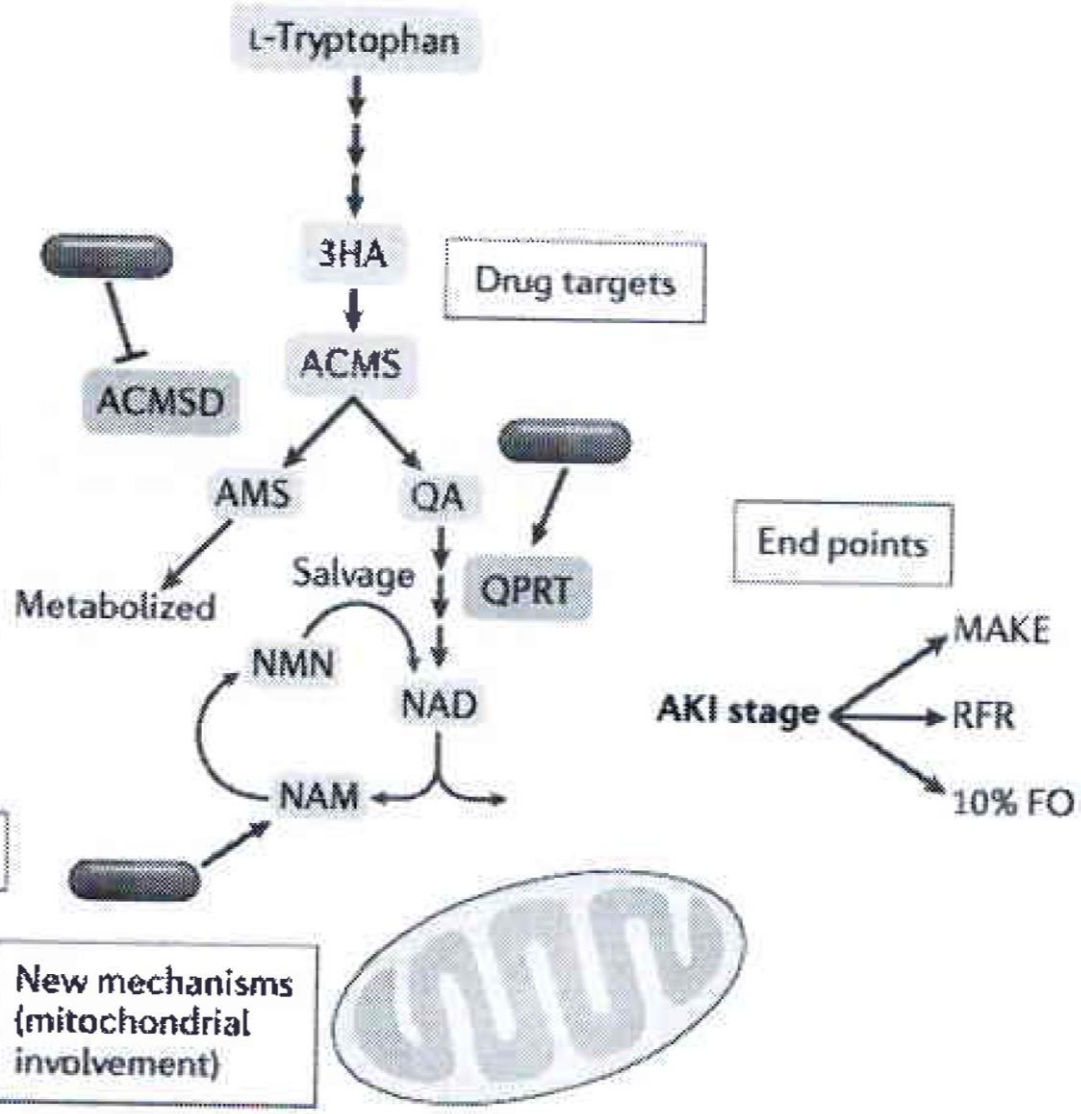
No clear evidence of benefit

- α-Melanocyte-stimulating hormone
- Atrial natriuretic peptide
- Calcium channel blockers
- Diuretics[a]
- Dopamine
- Erythropoietin
- Fenoldopam
- Insulin growth factor
- *N*-Acetylcysteine
- Statins
- Aminophylline/theophylline[b]

Abbreviations: AKI, acute kidney injury; siRNA, short interfering RNA.
[a]Potentially useful for volume management, but not for treatment of AKI.
[b]Some interest remains for AKI prevention in neonates.

Am J Kidney Dis. 2018 Jul;72(1):136-148.

The handwriting is on the wall: There will soon be a drug for AKI



1. The new drugs for mitochondrial dysfunction in AKI

1) ACMSD (Alpha-amino-beta-carboxymuconate-e-semialdehyde decarboxylase)

2) QPRT (Qinolinate Phosphoribosyltransferase)

3) NAM (Nicotinamide)

2. Trial end points including AKI stage

1) MAKE (Major Adverse Kidney Events)

2) RFR (Renal Functional Reserve):

3) FO (10% Fluid Overload)

J Med Syst (2016) 40:167

Nat Rev Nephrol. 2019 Feb;15(2):65-66

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Tx of Volume depletion

- judicious administration, beginning with 1 to 3 liters of fluid, with careful and repeated clinical assessment to assess the patient's response to this therapy
- Fluids should be targeted to physiologic endpoints such as mean arterial pressure or urine output or, among patients in whom invasive monitoring is utilized, to dynamic changes in cardiac output
- Although no consensus exists to guide therapy, among hemodynamically stable patients who do not have overt evidence of volume depletion, we administer 75 to 100 mL per hour for a total of 1 to 3 liters.

4.1. Volume Depletion

Table 10. The FACTT Lite fluid management protocol

Central Venous Pressure (Recommended)	Pulmonary Artery Occlusion Pressure (Optional)	Mean Arterial Pressure ≥60 mmHg and Off Vasopressors for ≥12 h	
		Urine Output <0.5 ml/kg per hour	Urine Output ≥0.5 ml/kg per hour
>8	>12	Furosemide[a] and reassess in 1 h	Furosemide[a] and reassess in 4 h
4–8	8–12	Give fluid and reassess in 1 h	Furosemide[a] and reassess in 4 h
<4	<8	Give fluid and reassess in 1 h	No intervention and reassess in 4 h

Modified with permission from Grissom CK, Hirshberg EL, Dickerson JB, Brown SM, Lanspa MJ, Liu KD, Schoenfeld D, Tidswell M, Hite RD, Rock P, Miller RR 3rd, Morris AH; National Heart Lung and Blood Institute Acute Respiratory Distress Syndrome Clinical Trials Network: Fluid management with a simplified conservative protocol for the acute respiratory distress syndrome. *Crit Care Med* 43: 288–295, 2015

[a]Furosemide dosing is recommended to begin with a 20-mg bolus, a 3-mg/h infusion, or the last known effective dose. Double each subsequent dose until the goal is achieved (oliguria reversal or intravascular pressure target) or a maximum infusion rate of 24 mg/h or a 160-mg bolus is reached. Do not exceed 620 mg/d.

Tx of Fluid overload

- **Diuretics**: continuous infusion can be tried because it is less ototoxic
- currently no evidence to support the use of natriuretic peptides as an adjunctive treatment in AKI.
- **Morphine and nitrates** can be used to alleviate the respiratory symptoms of pulmonary edema in urgent situations.

1) Morphine can be administered intravenously at an initial dose of 2 to 4 mg over a 3-minute period and repeated at 5- to 15-minute intervals as needed.

2) Nitrates are also commonly used. Nitroglycerin reduces left ventricular filling pressure through venodilation; an initial dose of 5 mcg of intravenous nitroglycerin per minute can be used

Comprehensive Clinical Nephrology 8th p,834

Tx of K disorders

- severe hyperkalemia (serum K > 6.5 mmol/L or with ECG changes)
- Calcium gluconate to reduce the risk of arrhythmia
- Next step: to enhance the shift of K to ICF (insulin plus dextrose, beta agonists, or sodium bicarbonate)
- K excretion: sorbitol with sodium polystyrene sulfonate or calcium polystyrene sulfonate resins
- **New agent**: not studied to treat acute hyperK

1) Patiromer (approved by FDA)

2) ZS-9 (Na zirconium cyclosilicate)

Ann Intern Med. 2017 Nov 7;167(9):ITC66-ITC80

Tx of Na disorders

- **HypoNa**:

1) 체액량 부족: 생리식염수 투여

2) 체액량 과다: 수분제한 및 furosemide, 소금 섭취 제한,

- **HyperNa**:

1) 원인: in AKI with dehydration, NS투여후, 수분제한

2) Tx: providing water via enteral routes or IV hyponatric solutions.

Ann Intern Med. 2017 Nov 7;167(9):ITC66-ITC80

Tx of Ca, P & Mg

- **HyperP**

1) **원인:** 신장에서 제거 감소, 횡문근 융해증시 세포외 누출 증가

2) No RCT about the benefits of treating HyperP

3) Tx: dietary P restriction & oral phosphate binders

- **HyperCa**

1) 원인: 다발성 골수종에 동반된 AKI

2) Tx: volume expansion & furosemide 투여

- **HypoCa**:

1) 원인: HyperP, PTH에 저항성, calcitriol 생산 감소, bicarbonate투여로 인해서 hypoCa 심해짐

2) Tx: Ca gluconate (혈관외 누출시 조직괴사를 덜 일으킴)

- **HyperMg**

1) 원인: Mg infusion

2) Tx: Mg 주입 중지, furosemide 투여

Ann Intern Med. 2017 Nov 7;167(9):ITC66-ITC80

Tx of Acid-Base disorders

- **Metabolic acidosis(M/C)** by reduced regeneration of bicarbonate & failure to excrete ammonium ions
- **Na-bicarbonate** if serum HCO3 < 15-18
- most physicians **restrict the administration of sodium bicarbonate** to patients with severe metabolic acidosis (arterial pH <7.10 to 7.15)
- Alternative forms of base treatment such as tris(hydroxymethyl)aminomethane **(THAM) are not recommended** in patients with AKI because THAM can cause hyperkalemia.
- **protein restriction is not recommended** in AKI.

질 문

1. 신대체요법의 적응증은 무엇인가요?
2. 신대체요법을 언제 시작하고 언제 중지할까요?
3. 간헐적 HD를 할까요, CRRT를 할까요?
4. 가장 안전하고 가장 효과적인 항응고제는 무엇인가요?
5. 시행해야 할 투석량은 어느 정도인가요?
6. CRRT가 신기능 회복에 미치는 영향은 어떤가요?
7. 신대체요법시 항생제 등의 약제 적정투여용량이 있나요?

N Engl J Med 2012;367:2505-14.

Advances in Chronic Kidney Disease, Vol 20, No 1 (January), 2013: pp 76-84

TABLE 4. **Comparison of Randomized Trials of Early Versus Late Dialysis in Patients with AKI**

	ELAIN	AKIKI	IDEAL-ICU	STARRT-AKI
Study design	Randomized controlled trial	Randomized controlled trial	Randomized controlled trial	Randomized controlled trial
Country/Setting	Germany Single center ICU	France 31 ICUs	France 27 ICUs	15 countries, 111 ICUs
Patient population	231 patients with critical illness and at least stage 2 AKI Mostly surgical ICU (47% cardiac surgery)	620 patients with critical illness and stage 3 AKI Mostly medical ICU	864 patients with septic shock and AKI (RIFLE stage failure)	2,866 patients with severe AKI
Intervention (early dialysis initiation)	Within 8 hours of stage 2 AKI	Within 6 hours of stage 3 AKI	Within 12 hours after diagnosis of AKI	Within 12 hours of study eligibility
Control (delayed dialysis initiation)	Within 12 hours of stage 3 AKI	Standard indications for RRT	At least 48 hours after diagnosis of AKI	>12 hours of study eligibility
Dialysis modality	Continuous venovenous hemodiafiltration	Provider discretion (47% intermittent RRT only)	Provider discretion	Provider discretion
Primary outcome	Mortality at 90 days	Mortality at 60 days	Mortality at 90 days	Mortality at 90 days
Results	20-hour difference between groups Lower mortality in early dialysis group (HR 0.66, 95% CI 0.45-0.97) Greater renal recovery at 90 days, shorter duration of RRT, and shorter hospital length of stay with early dialysis	55-hour difference between groups No difference in mortality between groups (P = .79) 49% of the delayed dialysis group did not get dialysis A higher rate of catheter-related bloodstream infections in the early dialysis group (10% vs 5%, P =.03)	To be determined	To be determined

Indication of CRRT in Gospel Hospital

1. 절대 적응증

1) 혈역학적으로 불안정할 때
2) Fulminant hepatic failure
3) Generalized brain edema
4) 대사성 산증이 동반된 심한 패혈증

2. 상대 적응증

1) 저혈압의 위험인자가 있을 경우 (간부전, 간경변증 등)
2) 횡문근 융해증
3) 종양 융해 증후군
4) 심한 체액량 과다
5) **진료과의 강력한 요청** 등

지속적신대체요법의 renal indication은 ( )이다

1. 과다한 체액량을 내과적 치료로 조절하지 못하고 혈압이 낮은 경우
2. 고칼륨혈증을 내과적 치료로 조절하지 못하고 혈압이 낮은 경우
3. 대사성산증을 내과적 치료로 조절하지 못하고 혈압이 낮은 경우
4. 요독증을 내과적 치료로 조절하지 못하고 혈압이 낮은 경우
5. 급성신손상이 동반된 외상성 뇌손상이 있는 경우
6. 급성신손상이 동반된 간부전이 있는 경우

지속적신대체요법의 nonrenal indication은 ( )이다

- 간부전
- 췌장염
- 체액량 과다 (>10%)
- 횡문근 융해증
- 조영제 신손상
- 난치성 고열상태
- 급성 신경계 손상
- 저혈압이 동반된 중독
- 급성 비보상성 심부전
- 심한 패혈증과 패혈성 쇼크

지속적신대체요법을 마치는 시기는?

- 일반병실 이동
- 환자의 전신상태
- Ccr > 12-20 mL/min
- 혈청 크레아티닌 < 3.0 mg/dL
- 승압제 없이 혈압 및 맥박수 유지
- 소변량 최소 하루 1000-1500 mL이상 (최소 500-600 cc이상)

STOP

Criteria for consideration of RRT Cessation

Clinical STATUS

- Need for volume removal does not exceed daily urine output
- No hyperkalemia refractory to medical management
- No acidemia refractory to medical management

TIMED urine creatinine clearance

- >15ml/min on 24 hour collection

Urine OUTPUT

- Urine output >400ml/24 hours
- Urine output>2000ml/24 hours with diuretics

Seminars in Dialysis. 2019;1–5.

순서

1. 급성신손상에서 일반치료
2. 급성신손상에서 혈역학적 유지
3. 급성신손상에서 이뇨제, 영양요법
4. 급성신손상에서 합병증 치료
5. 마무리

A Euvolemic Kidney is a Happy Kidney, Fluids are NOT always the answer

1. **Optimize hemodynamics**: Stop NSAIDs, ACEi/ARBs. Correct volume status.

1) Administer fluids if hypovolemic, diuretics if volume overloaded w/ physiologic targets (e.g. MAP, UOP).

2) No evidence of benefit for dopamine (Ann Int Med 2005;142:510), empiric diuretics in oliguria (JAMA 2002;288:2547), or mannitol

2. **Manage complications**: hyperK treatment, phos binders, DDAVP 0.3 mcg/kg IV prn uremic bleeding

3. **Avoid nephrotoxins**: iodinated contrast, NSAIDs, ACEi/ARB, calcineurin inhibitors, aminoglycosides, fleets enemas

4. **Renally dose meds**: antibiotics, narcotics, LMWH→ UFH, Keppra (remember Cr much overestimates GFR in AKI)

Harvard Board Review 2018 (Joseph V. Bonventre MD PhD)
MGH Nephrology Guide 2018

마무리

1. 일반치료

1) 콩팥기능 (Serum Cr & 소변량) 모니터링 및 체액량과 혈역학적 상태 확인

2) 약제 중지/조절

3) KDIGO bundle: 체액량/혈역학적 유지, 신독성 약제 피하기. 고혈당 피하기

2. 혈역학적 유지

1) 수액투여 반응 평가: 맥압/심박출량, IVC 지름, SCV 지름 등

2) Colloid (in liver failure or burns)? Vs Crystalloid **!**

3) HES: no longer recommended(European Medicines Agency & FDA)

4) Cl Crystalloid (염소와 산염기 평가)? Vs Balanced Crystalloid **!** (다량 주입시)

5) 혈압: MAP 65-70, 80-85 in HBP, NE **!**, VP in vasoplegic shock

마무리

3. 이뇨제, 영양요법

1) 이뇨제: 체액량 조절, Furosemide stress test (UO < 100cc/hr → poor Px)
2) 혈당: BST 110-149 유지,
3) 영양요법: 칼로리, enteral route, protein goal
4) AKI약제: NE, ANP, multipotent stem, ALP 등

4. 합병증 치료

1) Fluid Mx protocol: CVP(4<,4-8,8-12,>12), MAP(>60), Off Vasopressor, UO (>0.5)
2) 체액 결핍(1-3리터/day, MAP/UO), 체액 과다(이뇨제, morphine/nitrates)
3) HyperK (> 6.5 or ECG변화): Ca gluconate, shift of K to ICF, excretion, new drug?
4) HypoNa/HyperNa
5) HyperP, HypoCa/HyperCa, HyperMg
6) 대사성 산증: NaHCO3?, 단백 섭취제한??

마무리

5. The new drugs for mitochondrial dysfunction in AKI

1) ACMSD (Alpha-amino-beta-carboxymuconate-e-semialdehyde decarboxylase)

2) QPRT (Qinolinate Phosphoribosyltransferase)

3) NAM (Nicotinamide)

6. Trial end points including AKI stage

1) MAKE (Major Adverse Kidney Events): death, new RRT, 지속적 신기능 이상

2) RFR (Renal Functional Reserve): furosemide stress test

3) FO (10% Fluid Overload)

A Euvolemic Kidney is a Happy Kidney,

Fluids are NOT always the answer

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