Universitätsklinikum Münster

Cardiac-surgery associated AKI

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- German Resaerch Foundation
- Else-Kröner Fresenius Stiftung
- Astute Medical
- Braun
- Baxter
- Fresenius
- Astellas
- Quarks Pharmaceuticals

Cardiac-surgery associated AKI

Outline

- Epidemiology and Characteristics of CSA-AKI
- Pathophysiology and prediction of AKI
- Biomarkers in CSA-AKI
- Prevention

Cardiac-surgery associated AKI

Outline

- Epidemiology and Characteristics of CSA-AKI

Acute Kidney Injury: A Common Complication of Cardiac Surgery

Table 6 | Causes of AKI: exposures and susceptibilities for non-specific AKI

Exposures	Susceptibilities
Sepsis	Dehydration or volume depletion
Critical illness	Advanced age
Circulatory shock	Female gender
Burns	Black race
Trauma	CKD
Cardiac surgery (especially with CPB)	Chronic diseases (heart, lung, liver)
Major noncardiac surgery	Diabetes mellitus
Nephrotoxic drugs	Cancer
Radiocontrast agents	Anemia
Poisonous plants and animals	

CKD, chronic kidney disease; C

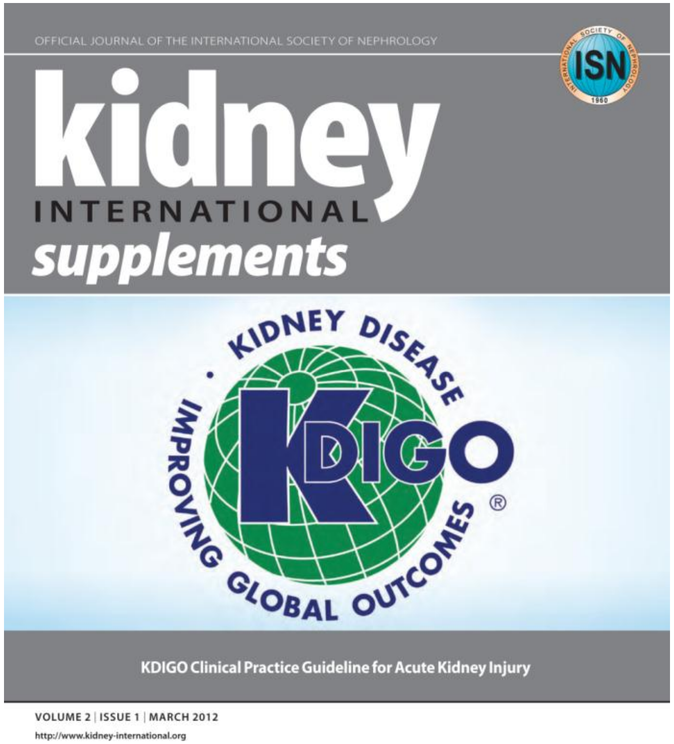
Author	Year	*N*	Reported incidence of AKI (%)
RIFLE			
Kim *et al.* [19]	2015	783	3.1
Scrascia *et al.* [18]	2015	41	36.6
Hu *et al.* [16▪▪]	2016	320086	18.8
Yi *et al.* [34▪]	2016	51934	4.2
AKIN			
Hertzberg *et al.* [17]	2015	36106	14.4
Kim *et al.* [19]	2015	783	2.5
Koyner *et al.* [25]	2015	1219	34.8
Lee *et al.* [24]	2015	2185	36.0
Schley *et al.* [20]	2015	110	34.0
Sim *et al.* [22]	2015	1386	29.9
Takaki *et al.* [26]	2015	1137	15.0
Hu *et al.* [16▪▪]	2016	320086	28.0
Omar *et al.* [40]	2016	201	20.4
DIGO			
m *et al.* [19]	2015	783	3.1
t *al.* [23]	2015	166	28.1
et al. [31▪]	2016	8,024	14.7
al. [16▪▪]	2016	320086	24.2
lhammer *et al.* [30]	2016	4022	25.6
u *et al.* [21]	2016	3245	39.9

AKI occurs after 2–40% of cardiac surgical procedures with variability in reported rates because of differences in study populations and AKI definitions

KDIGO Clinical Practice Guideline for Acute Kidney Injury. *Kidney Int Suppl*. 2012;2:1-128
Fuhrmann et al. *Curr Opin Anesthesiol*, 2017:30

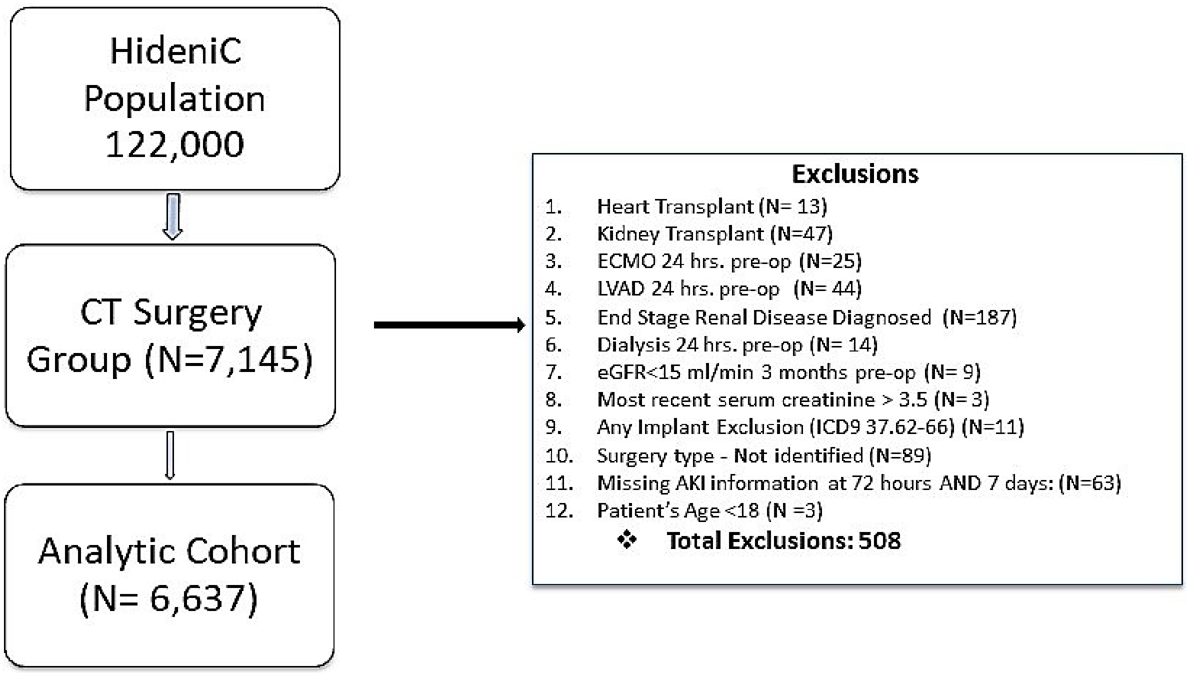
Definitions of AKI

	Serum creatinine	Urine output
STAGE 1	1.5–1.9 times baseline in 7d *or* increase ≥0.3 mg/dl (≥26.5µmol/l) in 48h	<0.5 ml/kg/h for 6-12 hours
STAGE 2	2.0–2.9 times baseline	<0.5 ml/kg/h for ≥12 hours
STAGE 3	≥3.0 times baseline *or* creatinine ≥4.0 mg/dl *or* initiation of RRT *or* in patients <18 years, eGFR <35 ml/min/1.73m^2	<0.3 ml/kg/h for ≥24 hrs *or* anuria for ≥12 hours



Cardiac-surgery associated AKI

Participant Flow Diagram



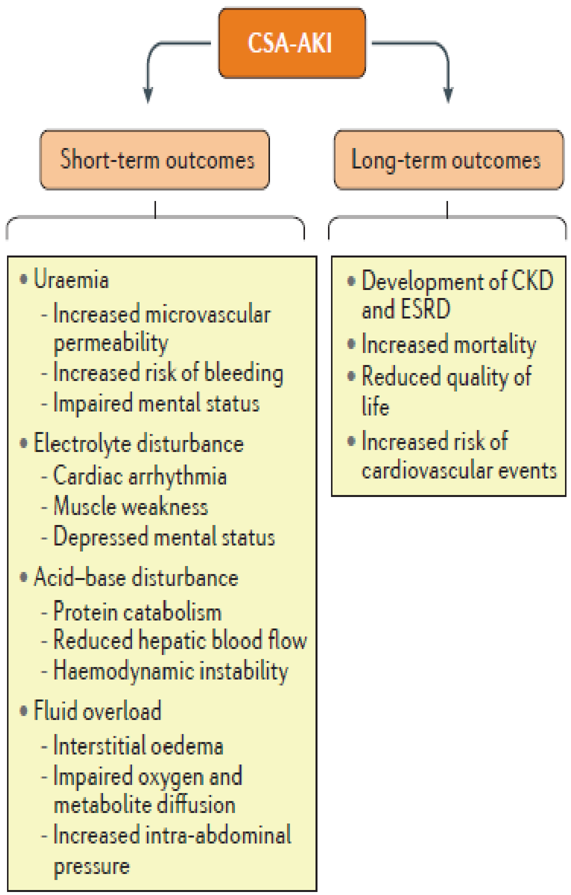
Cardiac-surgery associated AKI

SCR_72hrs	UO_72hrs							
	No AKI (N, %)		Stage 1 (N, %)		Stage 2 (N, %)		Stage 3 (N, %)	
No AKI	1,248	18.80%	748	11.27%	1,873	28.22%	206	3.10%
180 day mortality	27	2.16%	20	2.67%	64	3.42%	8	3.88%
180 day RRT	2	0.16%	1	0.13%	4	0.21%	0	0.00%
180 day Death or Dialysis	29	2.32%	21	2.81%	68	3.63%	8	3.88%
MAKE180	56	4.49%	57	7.62%	138	7.37%	20	9.71%
Stage 1	370	5.57%	242	3.65%	1,134	17.09%	349	5.26%
180 day mortality	20	5.41%	16	6.61%	101	8.91%	53	15.19%
180 day RRT	6	1.62%	5	2.07%	28	2.47%	20	5.73%
180 day Death or Dialysis	26	7.03%	21	8.68%	126	11.11%	70	20.06%
MAKE180	45	12.16%	36	14.88%	185	16.31%	99	28.37%
Stage 2	30	0.45%	19	0.29%	174	2.62%	121	1.82%
180 day mortality	3	10.00%	1	5.26%	28	16.09%	23	19.01%
180 day RRT	1	3.33%	0	0.00%	0	0.00%	8	6.61%
180 day Death or Dialysis	4	13.33%	1	5.26%	28	16.09%	30	24.79%
MAKE180	6	20.00%	2	10.53%	44	25.29%	40	33.06%
Stage 3	6	0.09%	4	0.06%	38	0.57%	75	1.13%
180 day mortality	2	33.33%	1	25.00%	13	34.21%	25	33.33%
180 day RRT	0	0.00%	0	0.00%	3	7.89%	10	13.33%
180 day Death or Dialysis	2	33.33%	1	25.00%	15	39.47%	35	46.67%
MAKE180	4	66.67%	1	25.00%	16	42.11%	46	61.33%

Unpublished

Presence of CSA-AKI is associated with increased in-hospital morbidity, death, LOS, and treatment costs

Patient impact



Financial impact

Table 3. An Adjusted Generalized Linear Model for Total Hospitalization Cost With Gamma Distribution

Variable	Change in Cost in USD Average (95% CI)	*p*
Status		
Discharged alive	Reference	
Died	21,259 (18,741–23,777)	<0.001
AKI status		
No AKI	Reference	
AKI without RRT	25,914 (24,105–27,723)	<0.001
AKI with RRT	69,241 (62,750–75,732)	<0.001

Alshaikh H et al Ann Thorac Surg 2018;105:469–76
Wang, et al *Nature Rev Nephrol*. 2017;13:697-711

Cardiac-surgery associated AKI

Cardiovascular Surgery

Acute Kidney Injury Is Associated With Increased Long-Term Mortality After Cardiothoracic Surgery

Charles E. Hobson, MD; Sinan Yavas, MD; Mark S. Segal, MD, PhD; Jesse D. Schold, PhD; Curtis G. Tribble, MD; A. Joseph Layon, MD; Azra Bihorac, MD

Hobson CE, Circulation 2009;119:2444

- Retrospective study of 2973 patients undergoing cardiac surgery (1992-2002)
- AKI was diagnosed by using the RIFLE classification

Cardiac-surgery associated AKI

		AKI					
	No AKI (n=1708; 57%)	All AKI (n=1265; 43%)	$RIFLE_{max}$-R (n=637; 22%)	$RIFLE_{max}$-I (n=386; 13%)	$RIFLE_{max}$-F (n=242; 8%)	*P**	*P*†
Demographics							
Age, y	60 (13)	64 (13)	64 (12)	64 (13)	64 (13)	<0.001	0.84
Female sex (n=1019, 34%)	552 (32%)	467 (37%)	205 (32%)	162 (42%)	100 (41%)	0.009	0.002
Black ethnicity (n=174, 6%)	105 (6%)	69 (5%)	19 (3%)	33 (9%)	17 (7%)	0.46	0.006
Baseline renal function							
Baseline sCr level, mg/dL	0.90 (0.16)	0.89 (0.16)	0.91 (0.15)	0.89 (0.18)	0.90 (0.17)	0.45	0.001
Baseline GFR, $mL \cdot min^{-1} \cdot 1.73\ m^{-2}$	89 (20)	85 (20)	83 (17)	87 (24)	85 (22)	0.09	0.001
Highest sCr level, mg/dL	0.93 (0.26)	2.27 (1.62)	1.40 (0.38)	1.98 (0.55)	4.11 (2.18)	<0.001	<0.001
Comorbidities							
Hypertension (n=1410, 47%)	762 (45%)	648 (51%)	314 (49%)	207 (54%)	127 (52%)	<0.001	0.47
Diabetes mellitus (n=602, 20%)	309 (18%)	293 (23%)	150 (24%)	97 (25%)	50 (21%)	<0.001	0.42
Atrial fibrillation (n	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	.001	0.02
Congestive heart f (n=699, 24%)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	.001	<0.001
Chronic pulmonary disease (n=504, 17%)	268 (16%)	236 (19%)	103 (16%)	78 (20%)	55 (23%)	0.02	0.07
Chronic liver disease (n=41, 1%)	15 (1%)	26 (2%)	9 (1%)	4 (1%)	13 (5%)	0.006	0.001
IABP (n=143, 5%)	58 (3%)	85 (7%)	43 (7%)	18 (5%)	24 (10%)	<0.001	0.04
CPB (n=2122, 71%)	1217 (71%)	905 (72%)	485 (76%)	271 (70%)	149 (62%)	0.86	0.001

- Only 6% of the patients with AKI required RRT

Cardiac-surgery associated AKI

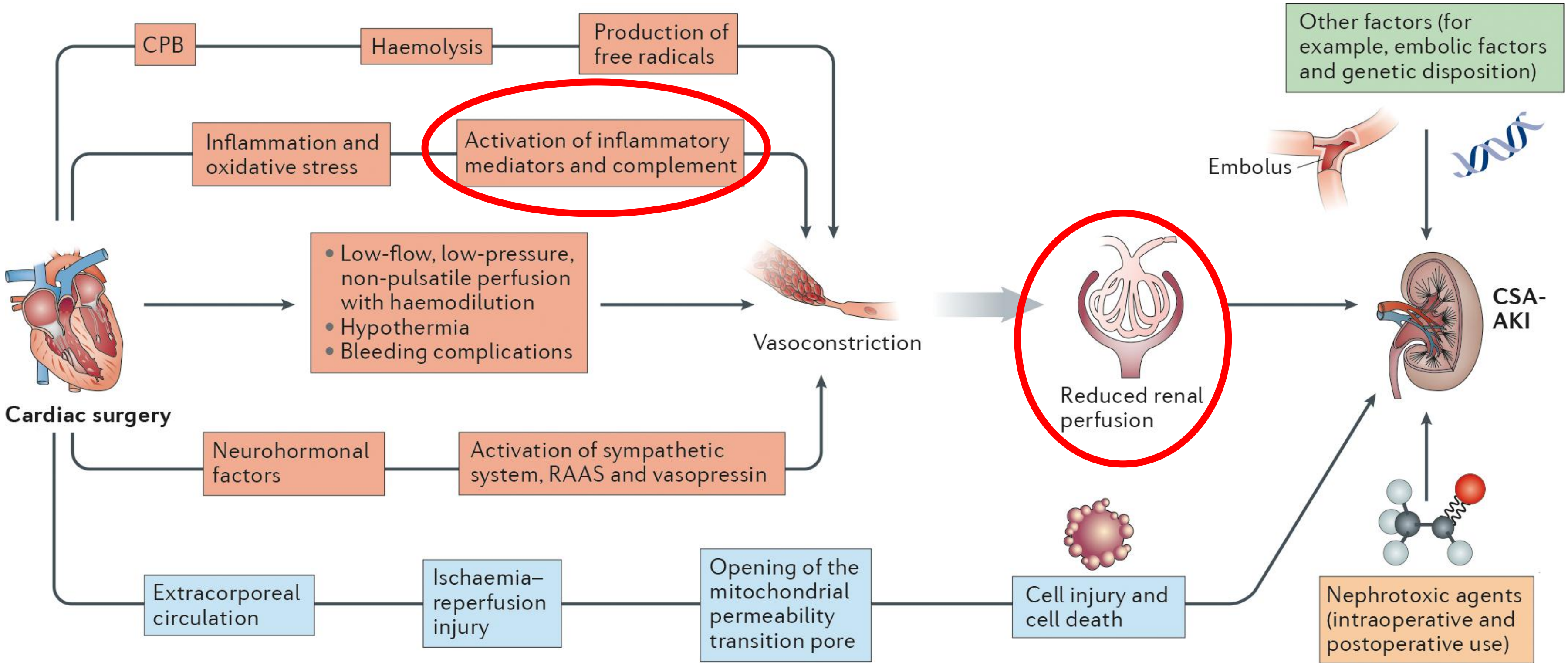
		AKI					
	No AKI (n=1708; 57%)	All AKI (n=1265; 43%)	$RIFLE_{max}$-R (n=637; 22%)	$RIFLE_{max}$-I (n=386; 13%)	$RIFLE_{max}$-F (n=242; 8%)	*P**	*P*†
Complications							
Stroke (n=227, 7%)	96 (6%)	131 (10%)	70 (11%)	32 (8%)	29 (12%)	<0.001	0.19
Mechanical ventilation (n=394, 13%)	89 (5%)	305 (24%)	84 (13%)	89 (23%)	132 (55%)	<0.001	<0.001
Tracheostomy (n=118, 4%)	16 (1%)	102 (8%)	17 (3%)	24 (6%)	61 (25%)	<0.001	<0.001
Sepsis (n=103, 3%)	11 (1%)	92 (7%)	16 (3%)	27 (7%)	49 (20%)	<0.001	<0.001
Renal outcomes							
Highest sCr level, mg/dL	0.93 (0.26)	2.27 (1.62)	1.40 (0.38)	1.98 (0.55)	4.11 (2.18)	<0.001	<0.001
RRT		75 (6%)	0 (0%)	0 (0%)	75 (31%)		<0.001
Renal recovery at discharge							<0.001
Complete recovery		754 (60%)	469 (74%)	199 (52%)	86 (36%)		
Partial recovery		476 (37%)	168 (26%)	187 (48%)	121 (50%)		
No recovery		35 (3%)	0 (0%)	0 (0%)	35 (14%)		
Days in hospital	9 (7–12)	15 (10–26)	12 (9–18)	16 (11–27)	29 (19–51)	<0.001	<0.001
Days in ICU	3 (2–4)	6 (3–12)	4 (2–7)	7 (4–13)	17 (7–33)	<0.001	<0.001
Discharge to home (n=2392, 80%)	1531 (90%)	861 (68%)	513 (81%)	260 (67%)	93 (38%)	<0.001	<0.001
Billing code for acute renal failure‡		159 (13%)	5 (1%)	32 (8%)	122 (50%)		<0.001

Cardiac-surgery associated AKI

Outline

- Pathophysiology and prediction of AKI

Cardiac-surgery associated AKI



Cardiac-surgery associated AKI

A Clinical Score to Predict Acute Renal Failure after Cardiac Surgery

Charuhas V. Thakar,*§ Susana Arrigain,† Sarah Worley,† Jean-Pierre Yared,‡ and Emil P. Paganini*

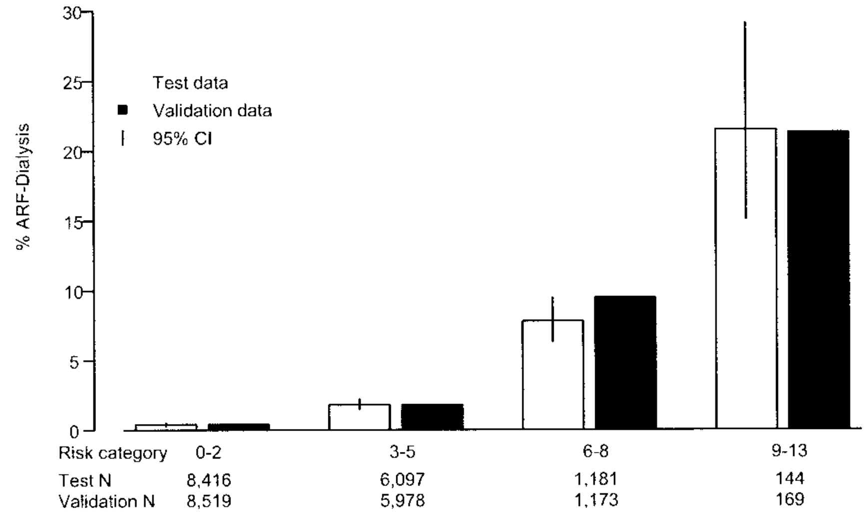
*Departments of *Nephrology and Hypertension, †Biostatistics and Epidemiology, and ‡Cardiothoracic Anesthesiology, Cleveland Clinic Foundation; and §Division of Nephrology and Hypertension, University of Cincinnati Medical Center, Cincinnati, Ohio*

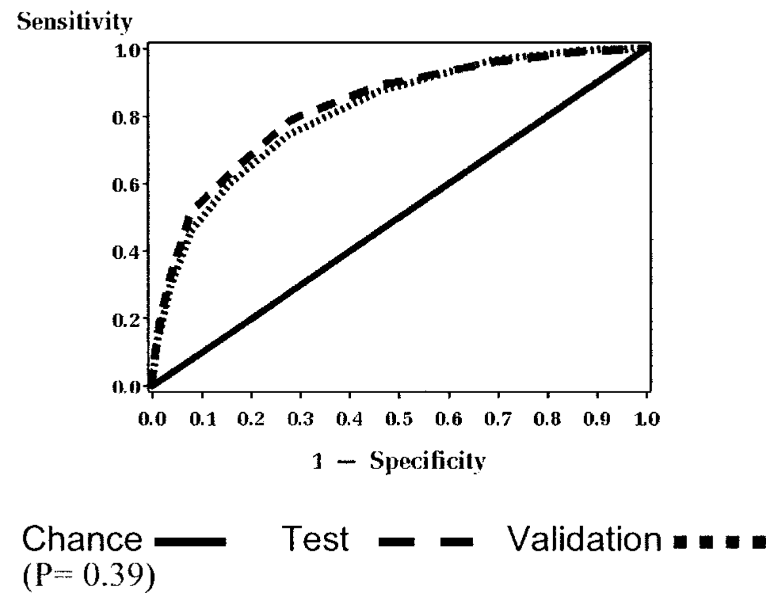
- 33,217 patients underwent open-heart surgery at the Cleveland Clinic Foundation (1993 to 2002)
- Primary outcome: AKI that required dialysis
- The scoring model was developed in a randomly selected test set (15,838)
- Model was evaluated in 17,000 patients

Cardiac-surgery associated AKI

Table 4. ARF score[a]

Risk Factor	Points
Female gender	1
Congestive heart failure	1
Left ventricular ejection fraction <35%	1
Preoperative use of IABP	2
COPD	1
Insulin-requiring diabetes	1
Previous cardiac surgery	1
Emergency surgery	2
Valve surgery only (reference to CABG)	1
CABG + valve (reference to CABG)	2
Other cardiac surgeries	2
Preoperative creatinine 1.2 to <2.1 mg/dl (reference to 1.2)	2
Preoperative creatinine ≥2.1 (reference to 1.2)	5





The AUC for the score in the test data set was 0.81 (95% CI 0.78 to 0.83), whereas it was 0.82 (95% CI 0.80 to 0.85) evaluation cohort

Cardiac-surgery associated AKI

RESEARCH Open Access

Predictive models for kidney disease: improving global outcomes (KDIGO) defined acute kidney injury in UK cardiac surgery

Kate Birnie[1], Veerle Verheyden[2], Domenico Pagano[3], Moninder Bhabra[4], Kate Tilling[1], Jonathan A Sterne[1], Gavin J Murphy[2*] and on behalf of the UK AKI in Cardiac Surgery Collaborators

- Prospective routinely collected clinical data (n=30,854)
- UK cardiac surgical centres (Bristol, Birmingham and Wolverhampton)
- AKI was defined by using the KDIGO criteria
- The model was developed using the Bristol and Birmingham datasets, and externally validated using the Wolverhampton data.

Cardiac-surgery associated AKI

- Any stage of AKI affected 23.7% patients in the Bristol dataset, 20.9% patients in Birmingham and 24.6% patients in Wolverhampton.

- 23 factors were investigated for their association with AKI

- 20 factors were strongly associated with any stage of AKI
  - Age
  - Sex (male)
  - Body mass index
  - Smoking status
  - Angina
  - Dyspnoea
  - Previous operation
  - Preoperative diabetes
  - Peripheral vascular disease
  - Operative priority
  - Neurological disease
  - Hypertension
  - Haemoglobin
  - GFR
  - Heparin or nitrates
  - Critical preoperative event
  - Catheter to surgery
  - Triple vessel disease
  - EF
  - Cardiac procedures

Cardiac-surgery associated AKI

Table 8 Discrimination: area under ROC curves for the different scores and for different procedures (complete case data)

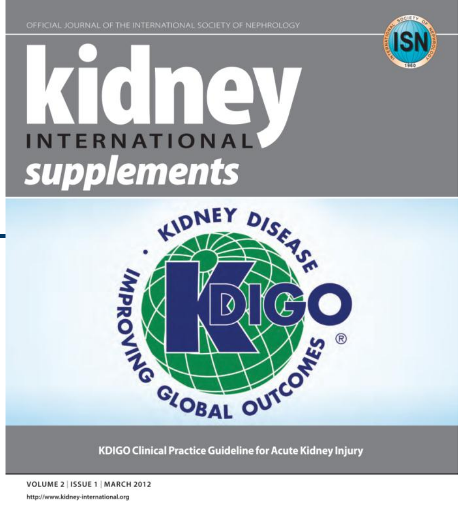
	Area under the curve (95% CI)			
	Development sample Bristol and Birmingham n = 16,527		Validation sample Wolverhampton n = 4,468	
	Any-stage AKI	Stage-3 AKI	Any-stage AKI	Stage-3 AKI
Initial model (*P* <0.001)	0.73 (0.72, 0.74)	0.79 (0.77, 0.80)	0.74 (0.72, 0.76)	0.78 (0.75, 0.80)
More inclusive model (*P* <0.05)	0.74 (0.73, 0.75)	0.79 (0.78, 0.81)	0.74 (0.72, 0.76)	0.79 (0.76, 0.81)
Comparison Scores				
Euroscore	0.66 (0.65, 0.67)	0.71 (0.69, 0.73)	0.68 (0.66, 0.70)	0.73 (0.70, 0.76)
Cleveland clinic	0.65 (0.64, 0.66)	0.74 (0.72, 0.76)	0.70 (0.69, 0.72)	0.78 (0.75 0.81)
Metha score	0.71 (0.70, 0.72)	0.79 (0.77, 0.80)	0.74 (0.72, 0.76)	0.79 (0.77, 0.82)
Ng score	0.70 (0.69, 0.71)	0.77 (0.75, 0.79)	0.73 (0.71, 0.75)	0.79 (0.76, 0.82)
Procedure type				
Coronary artery bypass graft only	0.73 (0.72, 0.74)	0.78 (0.75, 0.81)	0.72 (0.70, 0.74)	0.78 (0.73, 0.82)
Valve only	0.72 (0.70, 0.74)	0.75 (0.70, 0.80)	0.73 (0.69, 0.77)	0.78 (0.72, 0.84)
Coronary artery bypass graft + valve	0.70 (0.66, 0.72)	0.74 (0.70, 0.79)	0.71 (0.67, 0.75)	0.70 (0.62, 0.76)
Other/multiple	0.70 (0.67, 0.73)	0.69 (0.64, 0.74)	0.70 (0.64, 0.76)	0.72 (0.62, 0.81)

Cardiac-surgery associated AKI

Outline

- Biomarkers in CSA-AKI

Cardiac-surgery associated AKI



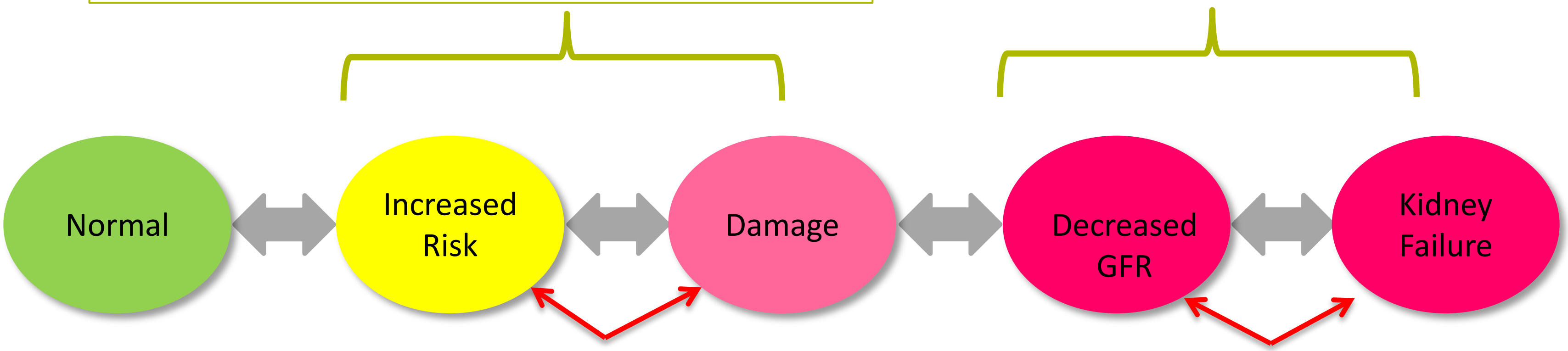
The Golden hour of AKI

Biomarkers

Risk assessment, may identify the "golden hours" prior to diagnosis in which early treatment may change course of disease

KDIGO

Diagnosis and staging, typically over several days



Clinically silent

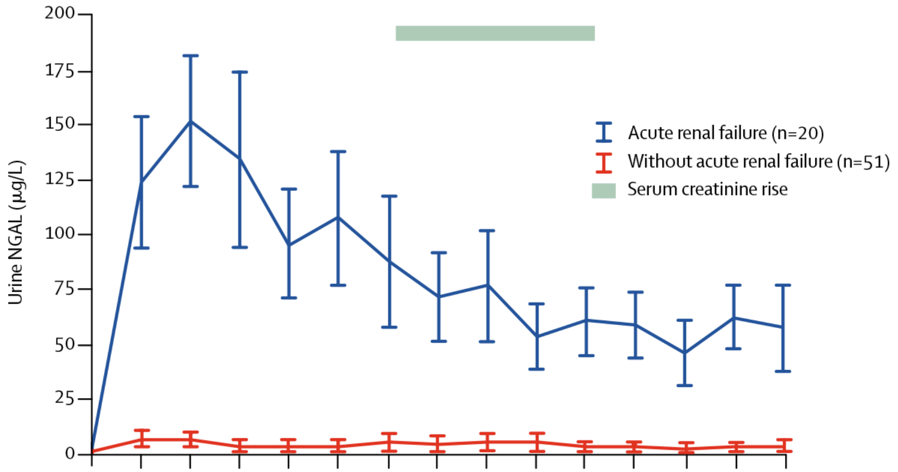
Clinically manifests as AKI stage 1-3*

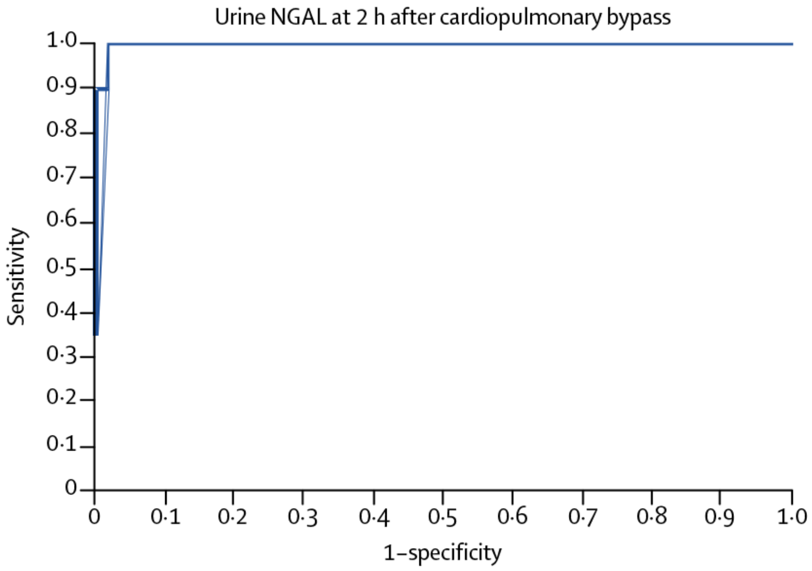
KDIGO Guidelines

Cardiac-surgery associated AKI

Neutrophil gelatinase-associated lipocalin (NGAL) as a biomarker for acute renal injury after cardiac surgery

Jaya Mishra, Catherine Dent*, Ridwan Tarabishi*, Mark M Mitsnefes, Qing Ma, Caitlin Kelly, Stacey M Ruff, Kamyar Zahedi, Mingyuan Shao, Judy Bean, Kiyoshi Mori, Jonathan Barasch, Prasad Devarajan*





Cardiac-surgery associated AKI

Original Articles

Urinary Biomarkers in the Clinical Prognosis and Early Detection of Acute Kidney Injury

Jay L. Koyner,* Vishal S. Vaidya,† Michael R. Bennett,‡ Qing Ma,‡ Elaine Worcester,* Shahab A. Akhter,§ Jai Raman,§ Valluvan Jeevanandam,§ Micheal F. O'Connor,‖ Prasad Devarajan,‡ Joseph V. Bonventre,† and Patrick T. Murray¶

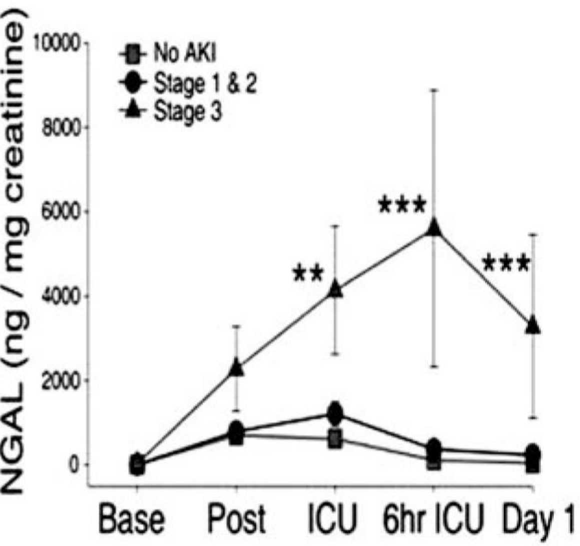


Table 2. Biomarker performance for stage 1 AKI—entire cohort and stratified by eGFR

Stage 1 AKI	Entire Cohort (n = 123)	eGFR <60 ml/min (n = 49)	eGFR >60 ml/min (n = 74)
NGAL (pg/ml)			
baseline	0.44 (0.32 to 0.57)	0.52 (0.30 to 0.73)	0.44 (0.28 to 0.60)
ICU arrival	0.69 (0.57 to 0.80)[a]	0.62 (0.44 to 0.81)	0.71 (0.57 to 0.85)[a]
6-hour ICU	0.72 (0.61 to 0.83)[b]	0.58 (0.37 to 0.79)	0.81 (0.70 to 0.92)[a]
early max	0.68 (0.57 to 0.79)[a]	0.61 (0.42 to 0.80)	0.71 (0.57 to 0.85)[a]

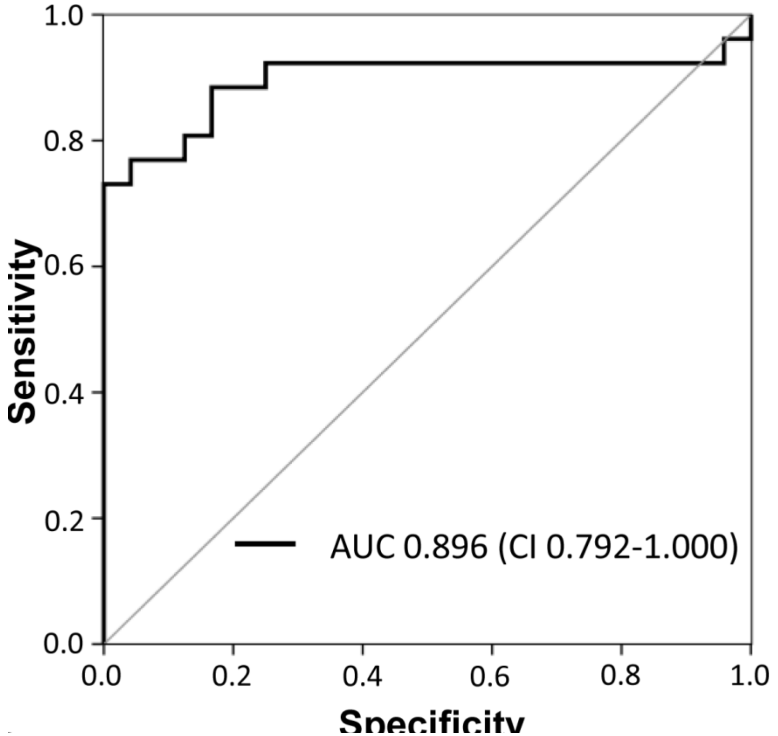
Table 3. Biomarker performance for stage 3 AKI—entire cohort and stratified by eGFR

Stage 3 AKI	Entire Cohort (n = 123)	eGFR <60 ml/min (n = 49)	eGFR >60 ml/min (n = 74)
NGAL (pg/ml)			
baseline	0.73 (0.56 to 0.89)[a]	0.81 (0.59 to 0.98)[a]	0.59 (0.42 to 0.75)
ICU arrival	0.79 (0.65 to 0.94)[a]	0.68 (0.41 to 0.94)	0.92 (0.78 to 0.98)[a]
6-hour ICU	0.88 (0.73 to 0.99)[b]	0.73 (0.34 to 0.97)	0.97 (0.90 to 0.99)[a]
early max	0.82 (0.66 to 0.97)[a]	0.73 (0.44 to 0.97)	0.92 (0.75 to 0.98)[a]

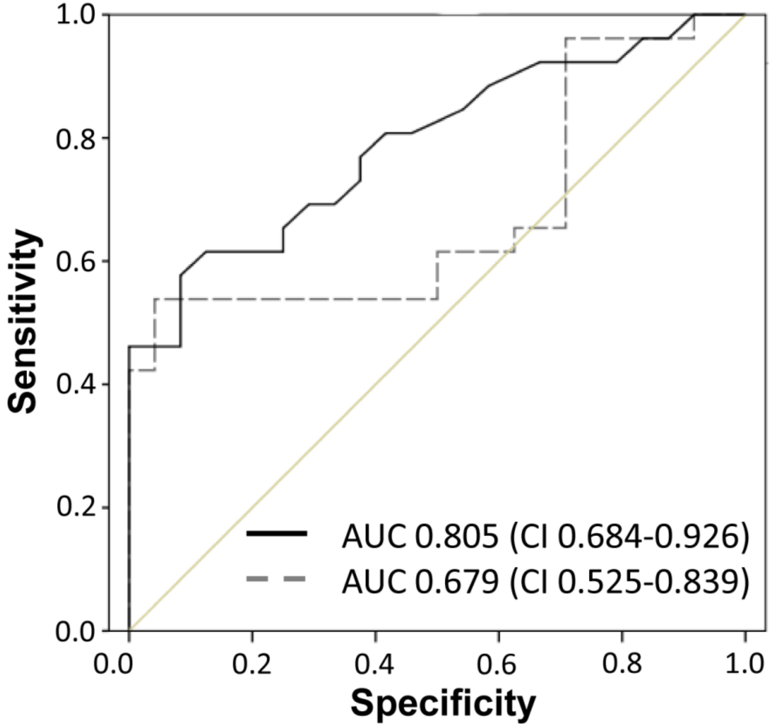
Koyner JL, CJASN, 2010, 2154

Cardiac-surgery associated AKI

Composite value (highest value within the first 24h)



4h value



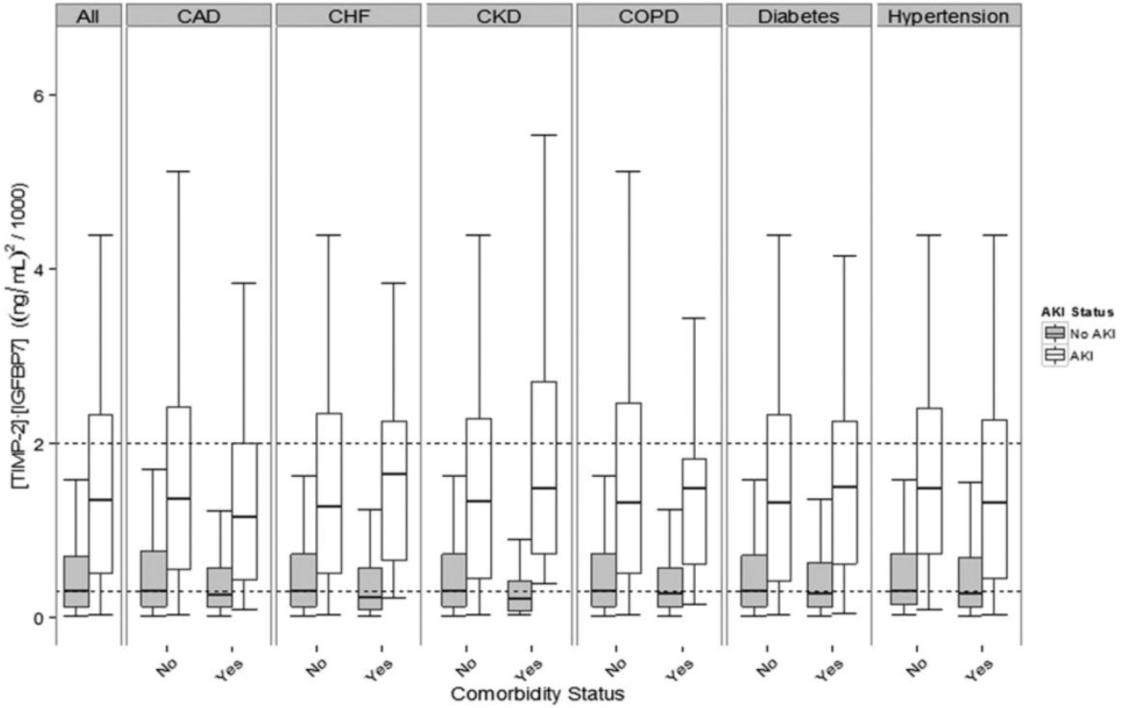
—— TIMP2/IGFB7

- - - NGAL

Cardiac-surgery associated AKI

Common chronic conditions do not affect performance of cell cycle arrest biomarkers for risk stratification of acute kidney injury

Michael Heung[1], Luis M. Ortega[2], Lakhmir S. Chawla[3], Richard G. Wunderink[4], Wesley H. Self[5], Jay L. Koyner[6], Jing Shi[7] and John A. Kellum[8] for the Sapphire and Topaz Investigators[*]



	All	CAD No	CAD Yes	CHF No	CHF Yes	CKD No	CKD Yes	COPD No	COPD Yes	Diabetes No	Diabetes Yes	Hypertension No	Hypertension Yes
No AKI	992	681	296	798	174	908	84	779	213	718	274	393	599
AKI	139	96	40	104	32	126	13	116	23	87	52	38	101

Cardiac-surgery associated AKI

Urinary Biomarkers of AKI and Mortality 3 Years after Cardiac Surgery

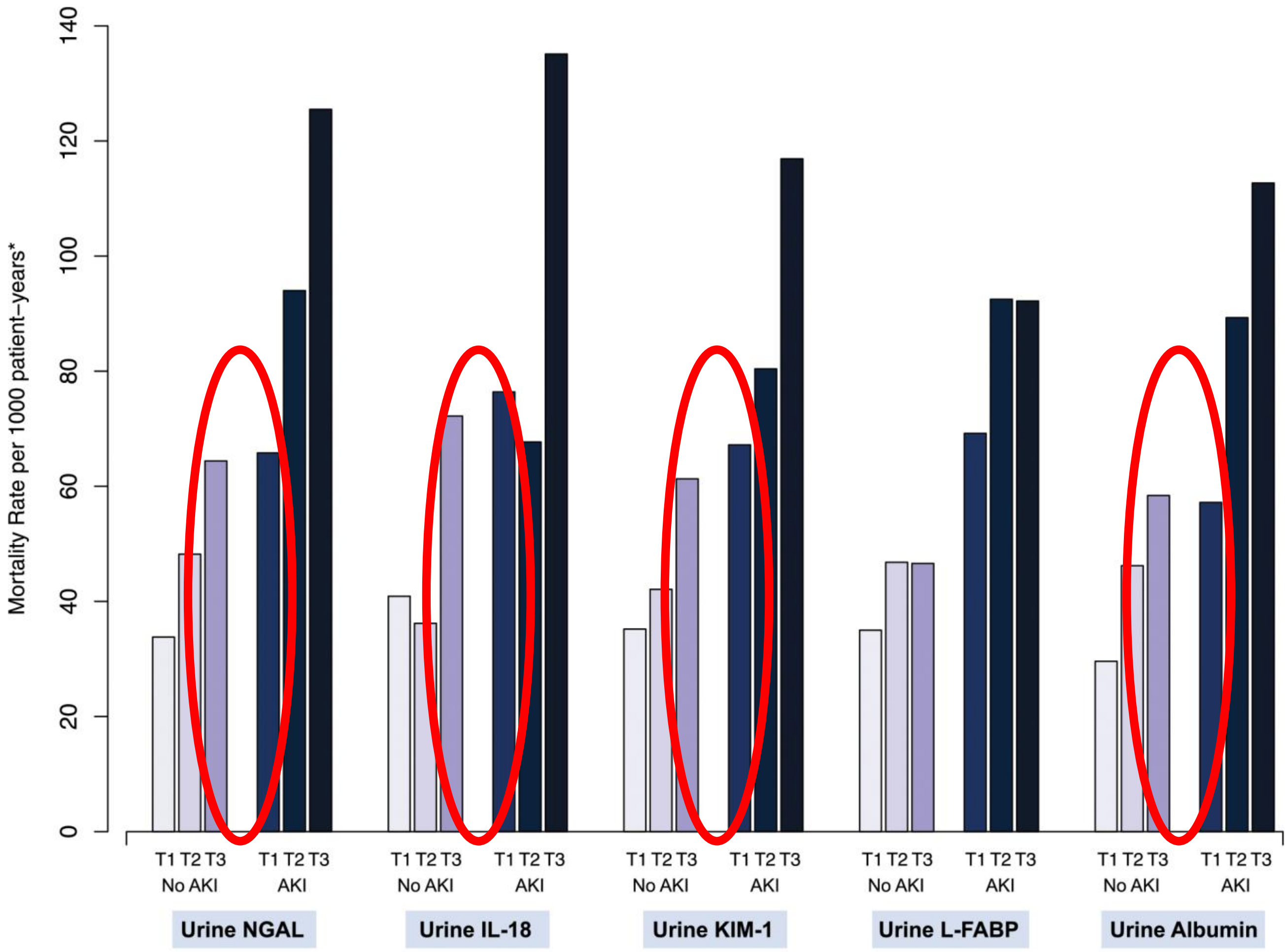
Steven G. Coca,* Amit X. Garg,[†] Heather Thiessen-Philbrook,[†] Jay L. Koyner,[‡] Uptal D. Patel,[§] Harlan M. Krumholz,[‖] Michael G. Shlipak,[¶] and Chirag R. Parikh* for the TRIBE-AKI Consortium

*Section of Nephrology, Yale University School of Medicine, Program of Applied Translational Research, Veterans Affairs Connecticut Healthcare System, New Haven, Connecticut; [†]Division of Nephrology, Department of Medicine, Western University, London, Ontario, Canada; [‡]Section of Nephrology, Department of Medicine, University of Chicago, Chicago, Illinois; [§]Duke Clinical Research Institute, Duke University School of Medicine, Durham, North Carolina; [‖]Section of Cardiovascular Medicine, Department of Internal Medicine, Yale University School of Medicine, Center for Outcomes Research and Evaluation, Yale-New Haven Hospital, New Haven, Connecticut; and [¶]Division of General Internal Medicine, San Francisco Veterans Affairs Medical Center, University of California, San Francisco

Coca SG et al., JASN 2014, 25: 1063

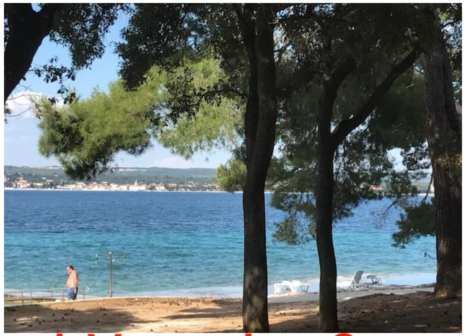
- International, multicenter, prospective study (6 centers)
- 1199 patients undergoing cardiac surgery (2007-2009)
- Aim: Investigation of the association between kidney damage biomarkers and all-cause mortality

Cardiac-surgery associated AKI



Cardiac-surgery associated AKI

ADQI XX:
Cardiac surgery-associated AKI



Cardiac and Vascular Surgery–Associated Acute Kidney Injury: The 20th International Consensus Conference of the ADQI (Acute Disease Quality Initiative) Group

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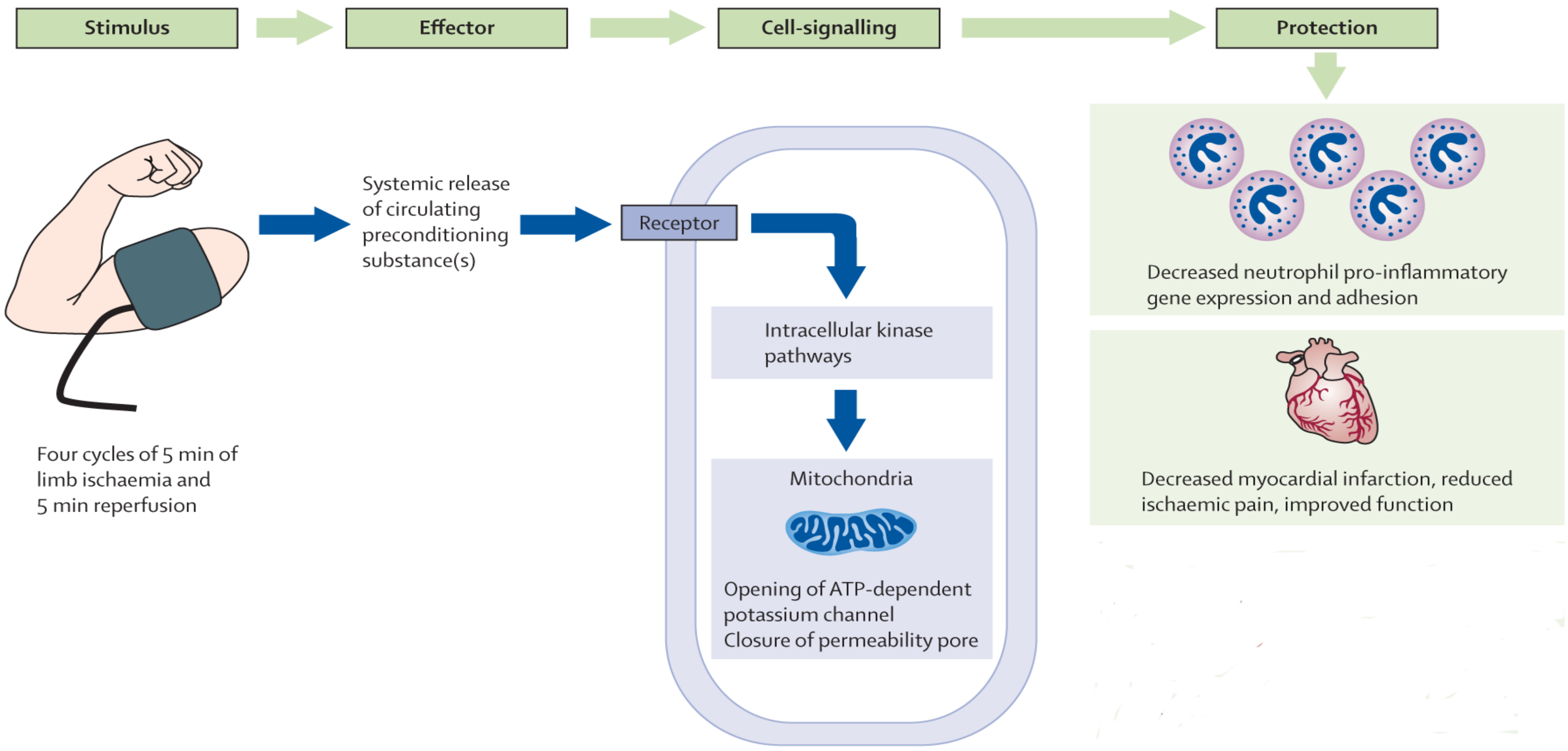
Cardiac-surgery associated AKI

Preoperative strategies to prevent AKI

Recommendations	Class
ACEi/ARBs: • Discontinuation 48h preop and after surgery • Preop use associated with functional but not structural (increased biomarkers) AKI	1C
Aldosterone inhibitors: • Discontinuation 48h preop and after surgery	Not rated
Statins: • Continuation	1A
Contrast media: • When possible delay surgery 48 to 72h, ideally give contrast media prior to admission, mixed evidence, retrospective studies	2C

Cardiac-surgery associated AKI



Cardiac-surgery associated AKI

Research

Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Remote Ischemic Preconditioning on Kidney Injury Among High-Risk Patients Undergoing Cardiac Surgery
A Randomized Clinical Trial

Alexander Zarbock, MD; Christoph Schmidt, MD; Hugo Van Aken, MD; Carola Wempe, PhD; Sven Martens, MD; Peter K. Zahn, MD; Britta Wolf, MD; Ulrich Goebel, MD; Christian I. Schwer, MD; Peter Rosenberger, MD; Helene Haeberle, MD; Dennis Görlich, PhD; John A. Kellum, MD; Melanie Meersch, MD; for the RenalRIPC Investigators

IMPORTANCE No interventions have yet been identified to reduce the risk of acute kidney injury in the setting of cardiac surgery.

OBJECTIVE To determine whether remote ischemic preconditioning reduces the rate and severity of acute kidney injury in patients undergoing cardiac surgery.

DESIGN, SETTING, AND PARTICIPANTS In this multicenter trial, we enrolled 240 patients at high risk for acute kidney injury, as identified by a Cleveland Clinic Foundation score of 6 or higher, between August 2013 and June 2014 at 4 hospitals in Germany. We randomized them to receive remote ischemic preconditioning or sham remote ischemic preconditioning (control). All patients completed follow-up 30 days after surgery and were analyzed according to the intention-to-treat principle.

INTERVENTIONS Patients received either remote ischemic preconditioning (3 cycles of 5-minute ischemia and 5-minute reperfusion in one upper arm after induction of anesthesia) or sham remote ischemic preconditioning (control), both via blood pressure cuff inflation.

MAIN OUTCOMES AND MEASURES The primary end point was the rate of acute kidney injury defined by Kidney Disease: Improving Global Outcomes criteria within the first 72 hours after cardiac surgery. Secondary end points included use of renal replacement therapy, duration of intensive care unit stay, occurrence of myocardial infarction and stroke, in-hospital and 30-day mortality, and change in acute kidney injury biomarkers.

RESULTS Acute kidney injury was significantly reduced with remote ischemic preconditioning (45 of 120 patients [37.5%]) compared with control (63 of 120 patients [52.5%]; absolute risk reduction, 15%; 95% CI, 2.56%-27.44%; $P = .02$). Fewer patients receiving remote ischemic preconditioning received renal replacement therapy (7 [5.8%] vs 19 [15.8%]; absolute risk reduction, 10%; 95% CI, 2.25%-17.75%; $P = .01$), and remote ischemic preconditioning reduced intensive care unit stay (3 days [interquartile range, 2-5]) vs 4 days (interquartile range, 2-7) ($P = .04$). There was no significant effect of remote ischemic preconditioning on myocardial infarction, stroke, or mortality. Remote ischemic preconditioning significantly attenuated the release of urinary insulinlike growth factor–binding protein 7 and tissue inhibitor of metalloproteinases 2 after surgery (remote ischemic preconditioning, 0.36 vs control, 0.97 $ng/mL^2/1000$; difference, 0.61; 95% CI, 0.27-0.86; $P < .001$). No adverse events were reported with remote ischemic preconditioning.

CONCLUSIONS AND RELEVANCE Among high-risk patients undergoing cardiac surgery, remote ischemic preconditioning compared with no ischemic preconditioning significantly reduced the rate of acute kidney injury and use of renal replacement therapy. The observed reduction in the rate of acute kidney injury and the need for renal replacement warrants further investigation.

TRIAL REGISTRATION German Clinical Trials Register Identifier: DRKS00005333

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Editorial

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A Zarbock and coauthors

Effect of Remote Ischemic Preconditioning on Kidney Injury Among High-Risk Patients Undergoing Cardiac Surgery: A Randomized Clinical Trial

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Cardiac-surgery associated AKI

	Control (n=120)	RIPC (n=120)	value
Primary outcome			
AKI within 72 hrs [%]	63 (52.5)	(37.5)	0.02
Stage 1 [%]	32 (26.7)	30 (25)	
Stage 2 [%]	14 (11.7)	8 (6.7)	
Stage 3 [%]	17 (14.2)	7 (5.8)	
Secondary outcomes			
RRT [%]	19 (15.8)	7 (5.8)	0.01
Time on mechanical ventilation [h]	15 (12-21)	14 (11-21)	0.16
Intensive Care Unit stay [days]	4 (2-7)	3 (2-5)	0.04
Hospital stay [days]	13 (10-19)	12 (9-19)	0.45
In-hospital death [%]	4 (3.3)	6 (5.0)	0.54
30-day mortality [%]	5 (4.2)	7 (5.8)	0.77
Myocardial infarction [%]	5 (4.2)	6 (5.0)	0.76
Stroke [%]	3 (2.5)	2 (1.7)	0.65

OR 0.71

Stage 2-3
25.9%

OR 0.48

Zarbock et al. JAMA 2015

Cardiac-surgery associated AKI

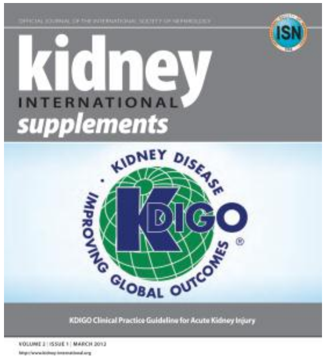
- No benefit of RIPC in studies of unselected patients with non-standardized intraoperative technique

Hausenloy DJ et al. NEJM 2015
Meybohm P et al. NEJM 2015

- More than 95% of the patients were treated with propofol, which may attenuate the protective effect of RIPC

Recommendations	**Class**
RIPC in high-risk patients	2B

Biomarkers to Identify High-risk Patients for Medical Intervention: PrevAKI RCT



KDIGO Consensus Guideline for AKI

KIDNEY DISEASE · IMPROVING GLOBAL OUTCOMES KDIGO

	AKI Stage		
High Risk	**Stage 1**	**Stage 2**	**Stage 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

Prevention of cardiac surgery-associated AKI by implementing the KDIGO guidelines in high risk patients identified by biomarkers: the PrevAKI randomized controlled trial

Melanie Meersch[1], Christoph Schmidt[1], Andreas Hoffmeier[2], Hugo Van Aken[1], Carola Wempe[1], Joachim Gerss[3] and Alexander Zarbock[1*]

Patients undergoing cardiac surgery

Measuring [TIMP2]*[IGFBP7] 4h after cardiac surgery: if [TIMP2]*[IGFBP7] is ≥ 0.3

Enrollment and informed consent

Randomization

Control group | Intervention group

Control group

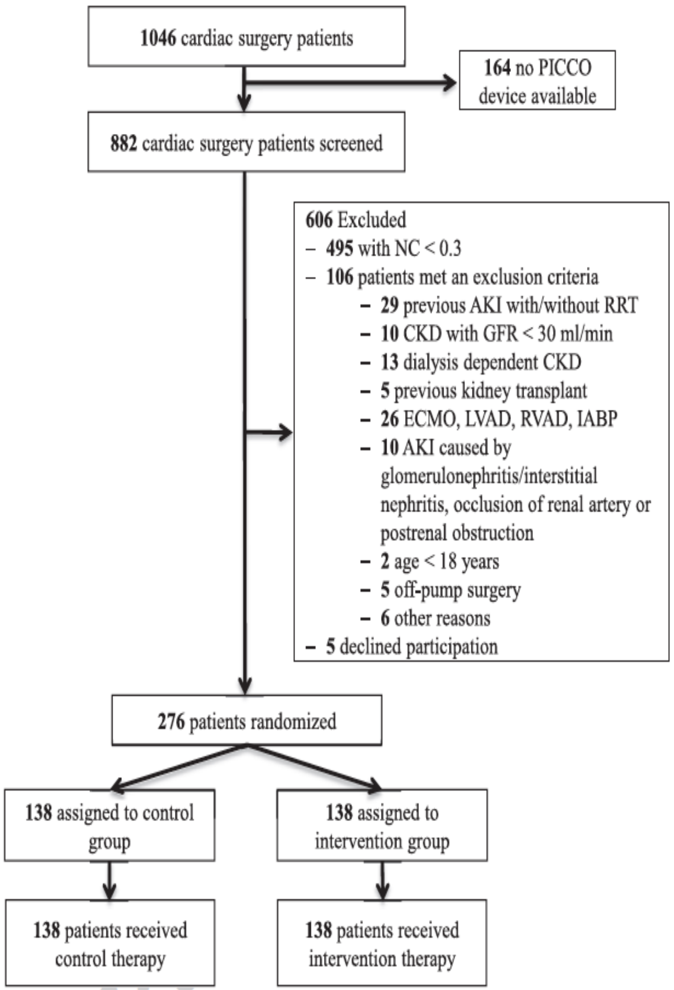
- Standard of care

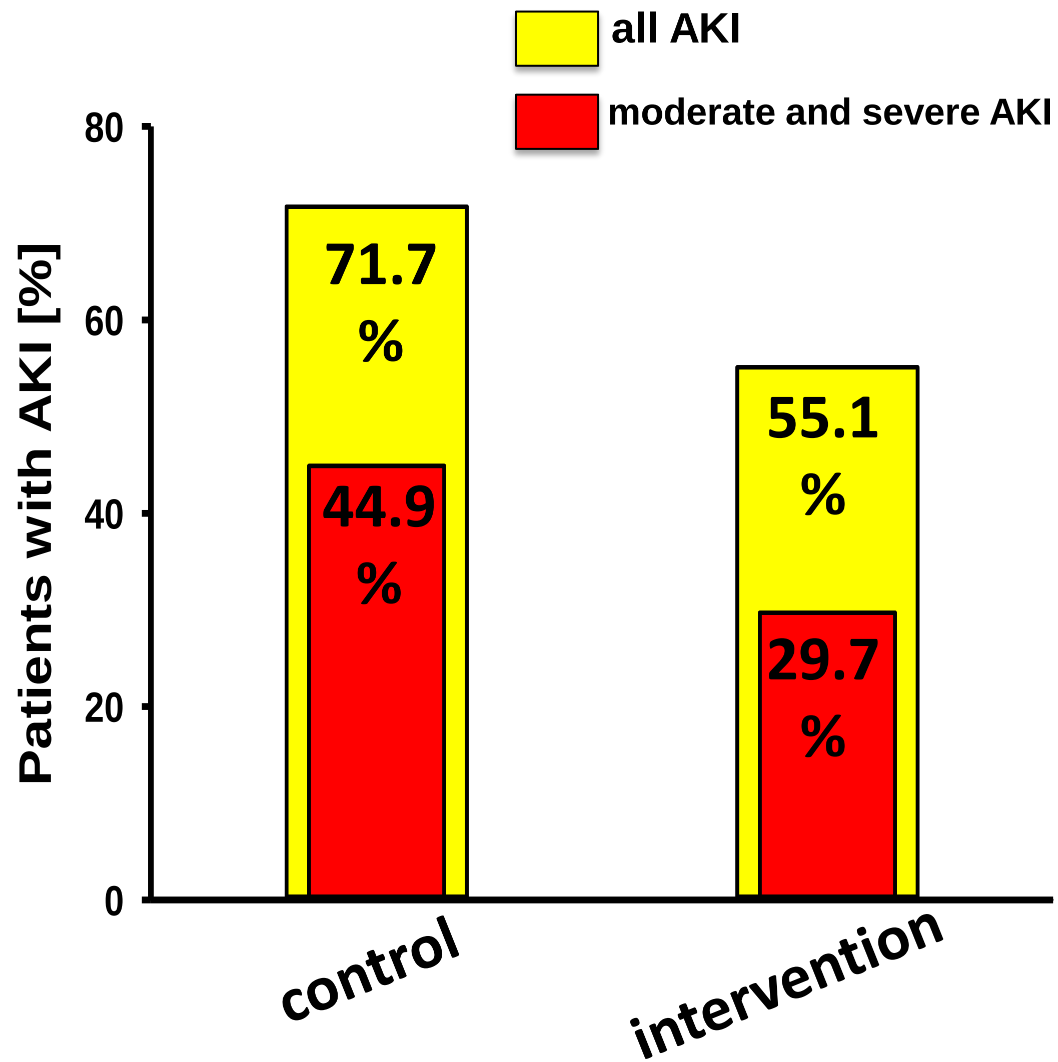
(MAP > 65 mmHg, CVP 8-10 mmHg

Intervention group (* see next slide)

- Discontinue all nephrotoxic agents when possible (no ACE inhibitors for the first 2 days)
- Hemodynamic monitoring and parameters: next slide
- Monitor serum creatinine and urine output
- Avoid hyperglycemia
- Consider alternatives to radiocontrast procedures

Biomarkers to Identify High-risk Patients for Medical Intervention: PrevAKI RCT





Meersch M et al. Intensive Care Med (2017) 43:1551–1561

Early biomarker-triggered implementation of KDIGO care bundle to prevent AKI After Major Surgery

TABLE 3. Clinical Outcomes for Intervention Group Versus Standard Care Group

	Intervention n = 60	Standard Care n = 61	Effect Estimate (95% CI)	*P*
Primary outcome				
Overall AKI (%)	19 (31.7)	29 (47.5)	1.96 (0.93, 4.10)*	0.076
Secondary outcomes				
AKI stage II and III (%)	4 (6.7)	12 (19.7)	3.43 (1.04, 11.32)*	**0.035**
Relevant Cr increase (ΔCr >25%) (%)	24 (40.0)	38 (62.3)	2.48 (1.19, 5.15)*	**0.015**
ICU length of stay, median (IQR) days	3 (2–5)	3 (2–7)	1 (0,2)†	**0.035**
Hospital length of stay, median (IQR) days	16 (12–22)	21 (15–39)	5 (0, 8)†	**0.036**
Requirement of RRT during hospital stay no (%)	2 (3.3)	4 (6.6)	2.04 (0.36, 11.55)*	0.663
In-hospital mortality (%)	4 (6.7)	5 (8.2)	1.25 (0.32, 4.90)*	0.981
MAKE by discharge (%)	5 (8.3)	8 (13.1)	1.66 (0.51, 5.40)*	0.399
Relative change urine (TIMP-2) × (IGFBP7) 12 h vs baseline, $(ng/mL)^2/1000$, median (IQR)	2.66 (1.41–7.04)	1.84 (0.78–3.19)	−0.825 (−1.7, 0.08)†	**0.028**

*Odds ratio (95% CI).
†Hodges-Lehmann estimate (95% CI).

Optimising volume status in combination with maintenance of adequate perfusion pressure and discontinuation of nephrotoxic agents through nephrology consultation significantly reduced the incidence of moderate and severe AKI.

Go¨cze et al. Annals of Surgery Volume 267, Number 6, June 2018

Recommendations	**Class**
KDIGO bundle	1B

Cardiac-surgery associated AKI

Summary

- CSA-AKI is a common complication and is associated with an increased morbidity and mortality
- Urine output and serum creatinine should be used to diagnose and stage an AKI after cardiac surgery
- A kidney damage without a loss of function is associated with an increased mortality
- Different measures exist that might prevent the development of CSA-AKI