KDIGO Clinical Practice Guideline for Acute Kidney Injury

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Interdisciplinary Representation

Experts from:

- Nephrology (Adult & Pediatric)
- Critical Care
- Radiology
- Cardiology
- Infectious Diseases
- Epidemiology

KDIGO Guideline Development

- KDIGO Board: selection of topic
- Executive Committee: selection of WG Co-Chairs
- Meeting of WG Co-Chairs, ERT and KDIGO Co-Chairs
- WG and ERT meet for 4 face to face meetings
- KDIGO Board review and revision
- Public review and revision
- WG final review and approval
- Submission for publication
- Translation and implementation tools

Abbeviations: WG-Work Group; ERT-Evidence Review Team

WG Financial Disclosures & Sponsorship

Work Group members are required to complete, sign and submit a disclosure & attestation form showing all financial relationships that might be perceived or actual conflicts of interest. All reported information is published in the Guideline section: *Biographical and Disclosure Information*

<u>KDIGO is supported by a consortium of sponsors and no funding is accepted for the development of specific guidelines.</u>

Rationale for an AKI Guideline

- AKI is prevalent
- AKI is amenable to early detection and potential prevention
- AKI imposes a heavy burden of illness (morbidity and mortality)
- Cost per person of managing AKI is high
- There is considerable clinical practice variability in preventing, diagnosing, treating, and achieving outcomes
- Clinical practice guidelines have the potential to reduce variations, improve outcomes, and reduce costs

Guideline Outline

- AKI Diagnosis, Staging and Risk Assessment
- Prevention and Treatment of AKI
- Contrast-Induced AKI
- Dialysis Interventions for Treatment of AKI

Guideline Outline

Prevention and Treatment of AKI

1. Advises general prevention and treatment measures (e.g., volume status and hemodynamic monitoring; glycemic control)
2. Assesses various pharmacologic interventions and their efficiacy (e.g., diuretics; vasodilators; growth factors; adenosine receptor antagonists, etc.)
3. Provides guidance on prevention of aminoglycoside- and amphotericin-related AKI
4. Reviews other methods of AKI prevention: On-pump vs. Off-pump coronary artery bypass

Chapter 2.2: Risk Assessment

2.2.1: We recommend that patients be stratified for risk of AKI according to their susceptibilities and exposures. (*1B*)

Risk Prediction

Overview table of observational studies of prediction equations for AKI

Author Year Country	Population	Outcome	Study design
Prediction equations for predicting AKI			
Candela-Toha[130] 2008 Spain	External validation of Thakar and Wijeysundera in 1780 patients with cardiac surgeries at a University Hospital in Madrid, Spain from 2002-2006	AKI	Retrospective cohort Single-center
Thakar[89] 2005 US	33,217 patients with open-heart surgery at the Cleveland Clinic Foundation from 1993-2002	AKI requiring dialysis	Retrospective cohort Single-center
Wijeysundera[129] 2007 Canada	20,131 cardiac surgery under cardiopulmonary bypass patients at two hospitals in Ontario, Canada from May 1999-July 2004	RRT	Retrospective cohort Multicenter
McCullough[139] 2007 US	1,826 consecutive patients undergoing coronary intervention at William-Beaumont Hospital, Michigan from December 1993-August1994.	RRT	Retrospective cohort Single-center
Mehran[86] 2004 US	8,357 patients who underwent PCI possibly at Columbia Medical Center, New York, New York, over a period of 6 years(dates unspecified).	CI-AKI	Retrospective cohort Presumed single-center
Skelding[107] 2007 US	External validation of William Beaumount score in 3,213 patients from the Mayo Clinic PCI Registry who underwent PCI at the from July 1, 2000 to June 30, 2003	CI-AKI	Retrospective cohort
Ghani[140] 2009 Kuwait	247 patients undergoing PCI in Kuwait from March to May 2005	CI-AKI	Prospective cohort Single-center
Drawz[87] 2008 US	540 hospitalized patients in three hospitals in Cleveland, Ohio since January 1, 2003	Hospital-acquired AKI	Case-controlled

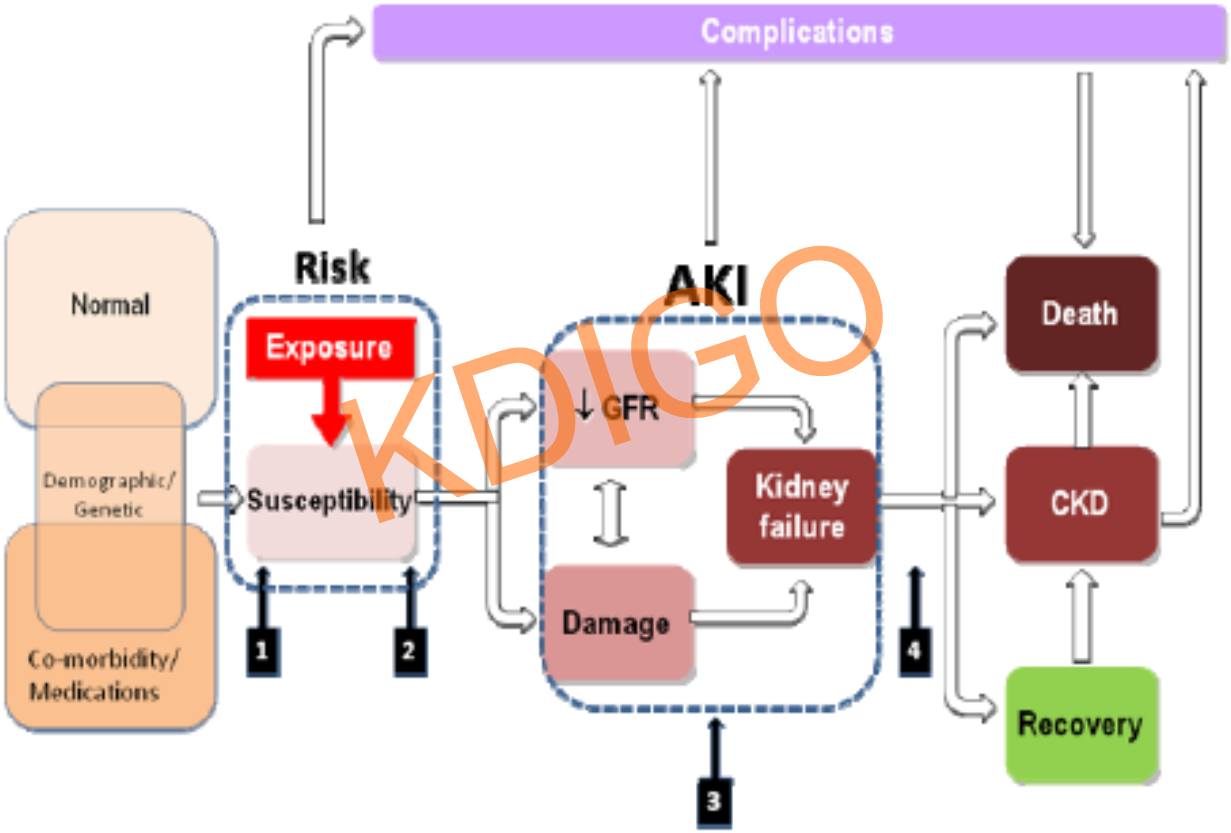
Chapter 2.2: Risk Assessment

2.2.2: Manage patients according to their susceptibilities and exposures to reduce the risk of AKI. (*Not Graded*)

2.2.3: Test patients at increased risk for AKI with measurements of SCr and urine output to detect AKI. (*Not Graded*)

Individualize frequency and duration of monitoring based on patient risk and clinical course. (*Not Graded*)

Conceptual framework for risk



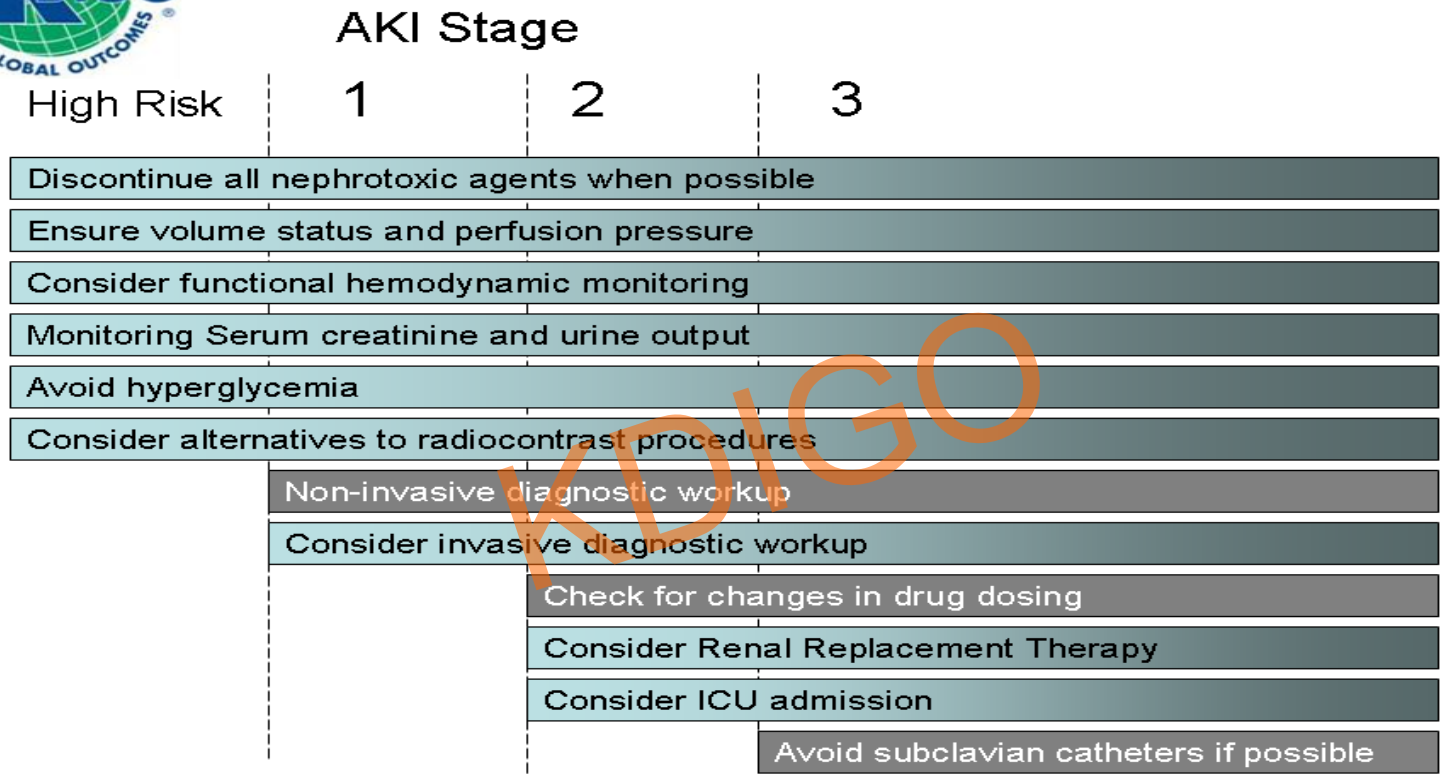
Chapter 2.3: Evaluation and general management of patients with and at risk for AKI

2.3.1: Evaluate patients with AKI promptly to determine the cause, with special attention to reversible causes. (*Not Graded*)

2.3.2: Monitor patients with AKI with measurements of SCr and urine output to stage the severity, according to Recommendation 2.1.2. (*Not Graded*)

2.3.3: Manage patients with AKI according to the stage and cause [see next slide]. (*Not Graded*)

Stage-Based Management



Stage-based management of AKI: Shading of boxes indicates priority of action—solid shading indicates actions that are equally appropriate at all stages whereas graded shading indicates increasing priority as intensity increases.

Kidney Disease: Improving Global Outcomes

Risk-Guided Decision Tree: Cardiothoracic Surgery

Action	Low Risk	Moderate Risk	High Risk
Monitor sCr	Standard Care (daily)	Every 12 hrs until decrease	Every 12hrs until decrease
Monitor Urine Output	(I/0s reviewed every 12 hours)	Strict I/0s keep Foley	Strict I/0s keep Foley
Ensure volume status	Standard Care Lasix as needed	For Oliguria, may use balanced fluid IF CVP < 8; Hold Lasix unless pulmonary edema	May use balanced fluid IF CVP < 8 AND evidence of hypovolemia (not just oliguria); hold Lasix
Avoid Nephrotoxic meds	Standard care	No NSAIDS or ACE/ARBs	No NSAIDS or ACE/ARBs Adjust doses (narcotics)*
Cardiac management	Usual care	Monitor SCVO2 if h/o abnormal LV Fx	Monitor SVO2, Echo or PA catheter if < 55% – Inotropes to keep CI >2.2
Recheck markers	NA	24 hrs	12 hrs

Chapter 2.3: Evaluation and general management of patients with and at ris

Don't wait 3 months!

2.3.4: Evaluate patients 3 months after AKI for resolution, new onset, or worsening of pre-existing CKD. (*Not Graded*)

- **If patients have CKD, manage these patients as detailed in the KDOQI CKD Guideline (Guidelines 7-15). (*Not Graded*)**
- **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 3 for patients at increased risk for CKD. (*Not Graded*)**

Chapter 3.1: Hemodynamic monitoring and support for prevention and management of AKI

3.1.1: In the absence of hemorrhagic shock, we suggest using isotonic crystalloids rather than colloids (albumin or starches) as initial management for expansion of intravascular volume in patients at risk for AKI or with AKI. (*2B*)

3.1.2: We recommend the use of vasopressors in conjunction with fluids in patients with vasomotor shock with, or at risk for, AKI. (*1C*)

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

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Context Administration of traditional chloride-liberal intravenous fluids may precipitate acute kidney injury (AKI).

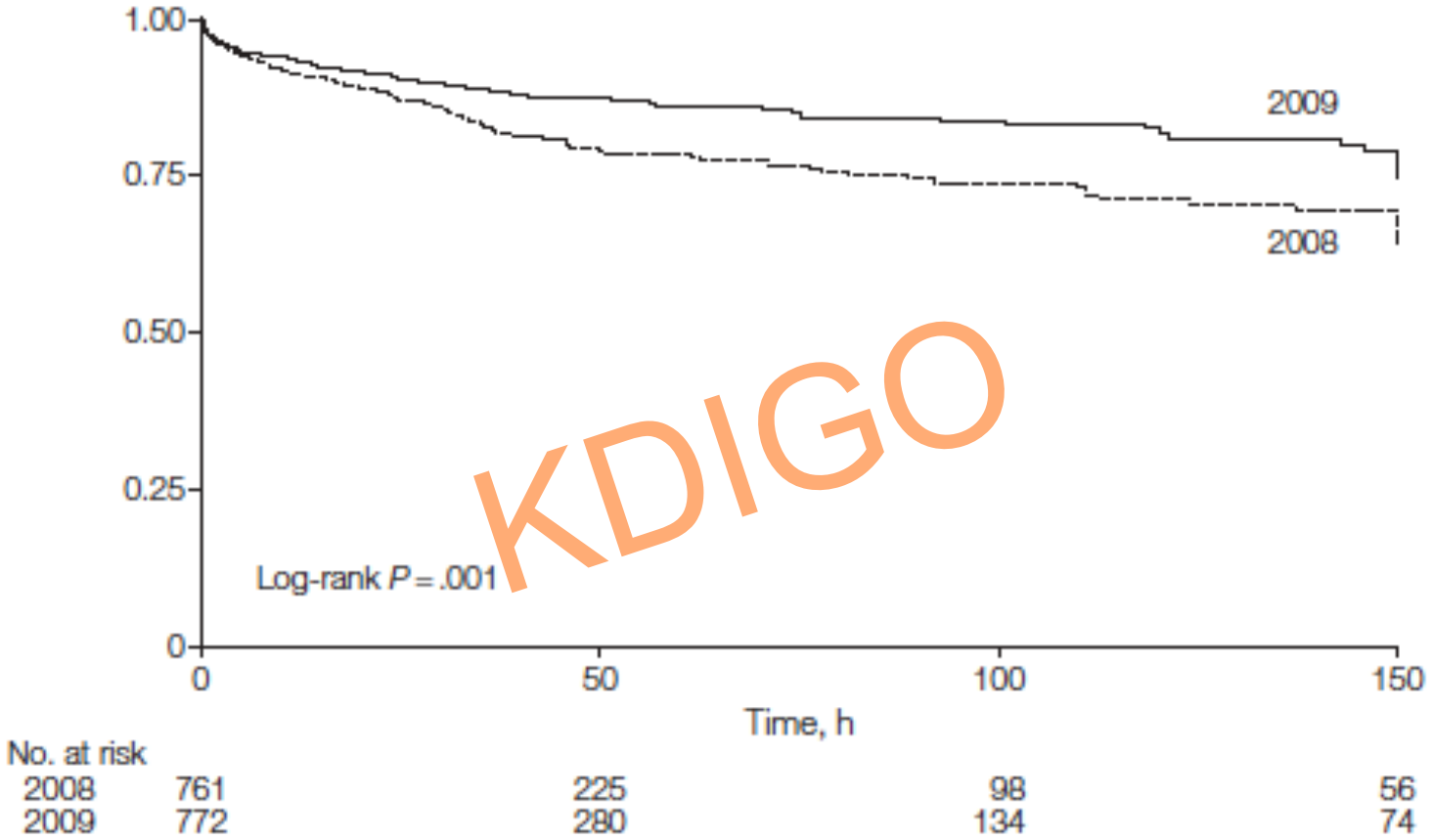
Objective To assess the association of a chloride-restrictive (vs chloride-liberal) intravenous fluid strategy with AKI in critically ill patients.

Design, Setting, and Patients Prospective, open-label, sequential period pilot study of 760 patients admitted consecutively to the intensive care unit (ICU) during the control period (February 18 to August 17, 2008) compared with 773 patients admitted consecutively during the intervention period (February 18 to August 17, 2009) at a university-affiliated hospital in Melbourne, Australia.

THE ADMINISTRATION OF INTRAvenous chloride is ubiquitous

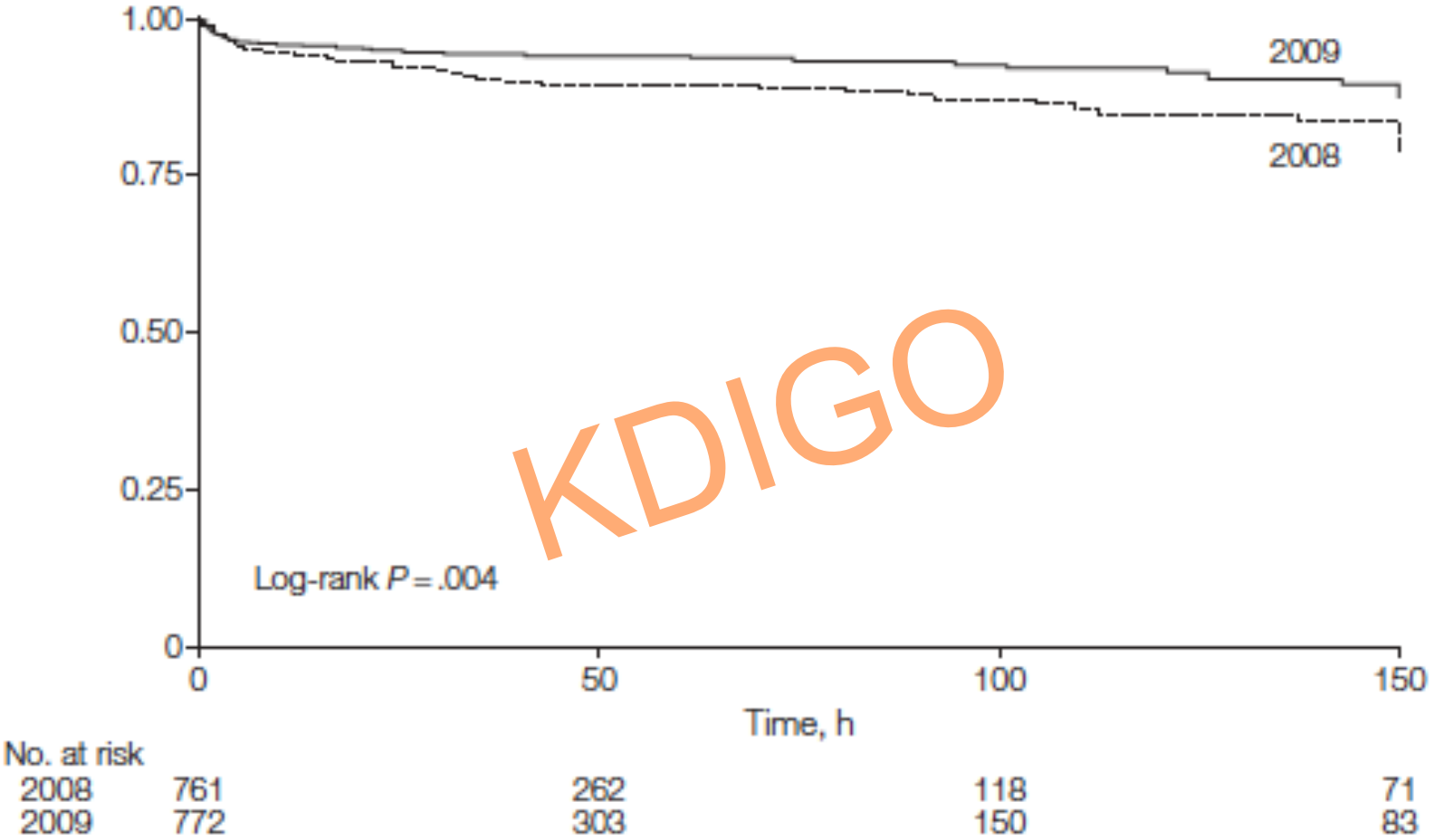
JAMA, October 17, 2012—Vol 308, No. 15

Risk for AKI (KDIGO Stage 2-3)



Covariate-adjusted Risk for Stage 2-3 AKI (OR 0.52 [95% CI, 0.37-0.75]; P = 0.001)

Risk for RRT



Covariate-adjusted Risk RRT (OR 0.52 [95% CI, 0.33-0.81]; P=0.004).

Chapter 3.1: Hemodynamic monitoring and support for prevention and management of AKI

3.1.3: We suggest using protocol-based management of hemodynamic and oxygenation parameters to prevent development or worsening of AKI in high-risk patients in the perioperative setting (*2C*) or in patients with septic shock (*2C*).

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Randomized Trial of Protocol-Based Care for Early Septic Shock

The ProCESS Investigators

ABSTRACT

BACKGROUND

In a single-center study published more than a decade ago involving patients presenting to the emergency department with severe sepsis and septic shock, mortality was markedly lower among those who were treated according to a 6-hour protocol of early goal-directed therapy (EGDT), in which intravenous fluids, vasopressors, inotropes, and blood transfusions were adjusted to reach central hemodynamic targets, than among those receiving usual care. We conducted a trial to determine whether these findings were generalizable and whether all aspects of the protocol were necessary.

The members of the writing committee (Donald M. Yealy, M.D., John A. Kellum, M.D., David T. Huang, M.D., Amber E. Barnato, M.D., Lisa A. Weissfeld, Ph.D., and Francis Pike, Ph.D., University of Pittsburgh, Pittsburgh; Thomas Terndrup, M.D., Ohio State University, Columbus; Henry E. Wang, M.D., University of Alabama at Birmingham, Birmingham; Peter C. Hou, M.D., Brigham and Women's Hospital, Boston; Frank LoVecchio, D.O., Maricopa

Outcomes

Table 2. Outcomes.*

Outcome	Protocol-based EGDT (N=439)	Protocol-based Standard Therapy (N=446)	Usual Care (N=456)	P Value†
Death — no./total no. (%)				
In-hospital death by 60 days: primary outcome	92/439 (21.0)	81/446 (18.2)	86/456 (18.9)	0.83‡
Death by 90 days	129/405 (31.9)	128/415 (30.8)	139/412 (33.7)	0.66
New organ failure in the first week — no./total no. (%)				
Cardiovascular	269/439 (61.3)	284/446 (63.7)	256/456 (56.1)	0.06
Respiratory	165/434 (38.0)	161/441 (36.5)	146/451 (32.4)	0.19
Renal	12/382 (3.1)	24/399 (6.0)	11/397 (2.8)	0.04
Duration of organ support — days§				
Cardiovascular	2.6±1.6	2.4±1.5	2.5±1.6	0.52
Respiratory	6.4±8.4	7.7±10.4	6.9±8.2	0.41
Renal	7.1±10.8	8.5±12	8.8±13.7	0.92

Chapter 3.3: Glycemic control and nutritional support

3.3.1: In critically ill patients, we suggest insulin therapy targeting plasma glucose 110-149 mg/dl (6.1- 8.3 mmol/l). *(2C)*

3.3.2: We suggest achieving a total energy intake of 20-30 kcal/kg/d in patients with any stage of AKI. (*2C*)

3.3.3: We suggest to avoid restriction of protein intake with the aim of preventing or delaying initiation of renal replacement therapy (RRT). (*2D*)

Chapter 3.3: Glycemic control and nutritional support

3.3.4: We suggest administering 0.8-1.0 g/kg/d of protein in noncatabolic AKI patients without need for dialysis *(2D)*, 1.0-1.5 g/kg/d in patients with AKI on RRT *(2D)*, and up to a maximum of 1.7 g/kg/d in patients on continuous renal replacement therapy and in hypercatabolic patients (*2D*).

3.3.5: We suggest providing nutrition preferentially via the enteral route in patients with AKI. (*2C*)

Chapter 3.4: Use of diuretics in AKI

3.4.1: We recommend not using diuretics to prevent AKI. (*1B*)

3.4.2: We suggest not using diuretics to treat AKI, except in the management of volume overload. (*2C*)

Chapter 3.5: Vasodilator therapy: dopamine, fenoldopam & natriuretic peptides

3.5.1: We recommend not using low-dose dopamine to prevent or treat AKI. (*1A*)

3.5.2: We suggest not using fenoldopam to prevent or treat AKI. (*2C*)

3.5.3: We suggest not using atrial natriuretic peptide to prevent *(2C)* or treat *(2B)* AKI.

Chapter 3.6: Growth factor intervention

3.6.1: We recommend not using recombinant human (rh)IGF-1 to prevent or treat AKI. (*1B*)

Chapter 3.7: Adenosine receptor antagonists

3.7.1: We suggest that a single dose of theophylline may be given in neonates with severe perinatal asphyxia, who are at high risk of AKI. (*2B*)

Chapter 3.8: Prevention of aminoglycoside- and amphotericin-related AKI

3.8.1: We suggest not using aminoglycosides for the treatment of infections unless no suitable, less nephrotoxic, therapeutic alternatives are available. (*2A*)

3.8.2: We suggest that, in patients with normal kidney function in steady state, aminoglycosides are administered as a single dose daily rather than multiple-dose daily treatment regimens. (*2B*)

Chapter 3.8: Prevention of aminoglycoside- and amphotericin-related AKI

3.8.3: We recommend monitoring aminoglycoside drug levels when treatment with multiple daily dosing is used for more than 24 hours. (*1A*)

3.8.4: We suggest monitoring aminoglycoside drug levels when treatment with single-daily dosing is used for more than 48 hours. (*2C*)

3.8.5: We suggest using topical or local applications of aminoglycosides (e.g., respiratory aerosols, instilled antibiotic beads), rather than i.v. application, when feasible and suitable. (*2B*)

Chapter 3.8: Prevention of aminoglycoside- and amphotericin-related AKI

3.8.6: We suggest using lipid formulations of amphotericin B rather than conventional formulations of amphotericin B. (*2A*)

3.8.7: In the treatment of systemic mycoses or parasitic infections, we recommend using azole anti-fungal agents and/or the echinocandins rather than conventional amphotericin B, if equal therapeutic efficacy can be assumed. (*1A*)

Chapter 3.9: Other methods of prevention of AKI in the critically ill

3.9.1: We suggest that off-pump coronary artery bypass graft surgery not be selected solely for the purpose of reducing perioperative AKI or need for renal replacement therapy. (*2C*)

3.9.2: We suggest not using N-acetylcysteine (NAC) to prevent AKI in critically ill patients with hypotension. (*2D*)

3.9.3: We recommend not using oral or i.v. N-acetylcysteine (NAC) for prevention of postsurgical AKI. (*1A*)

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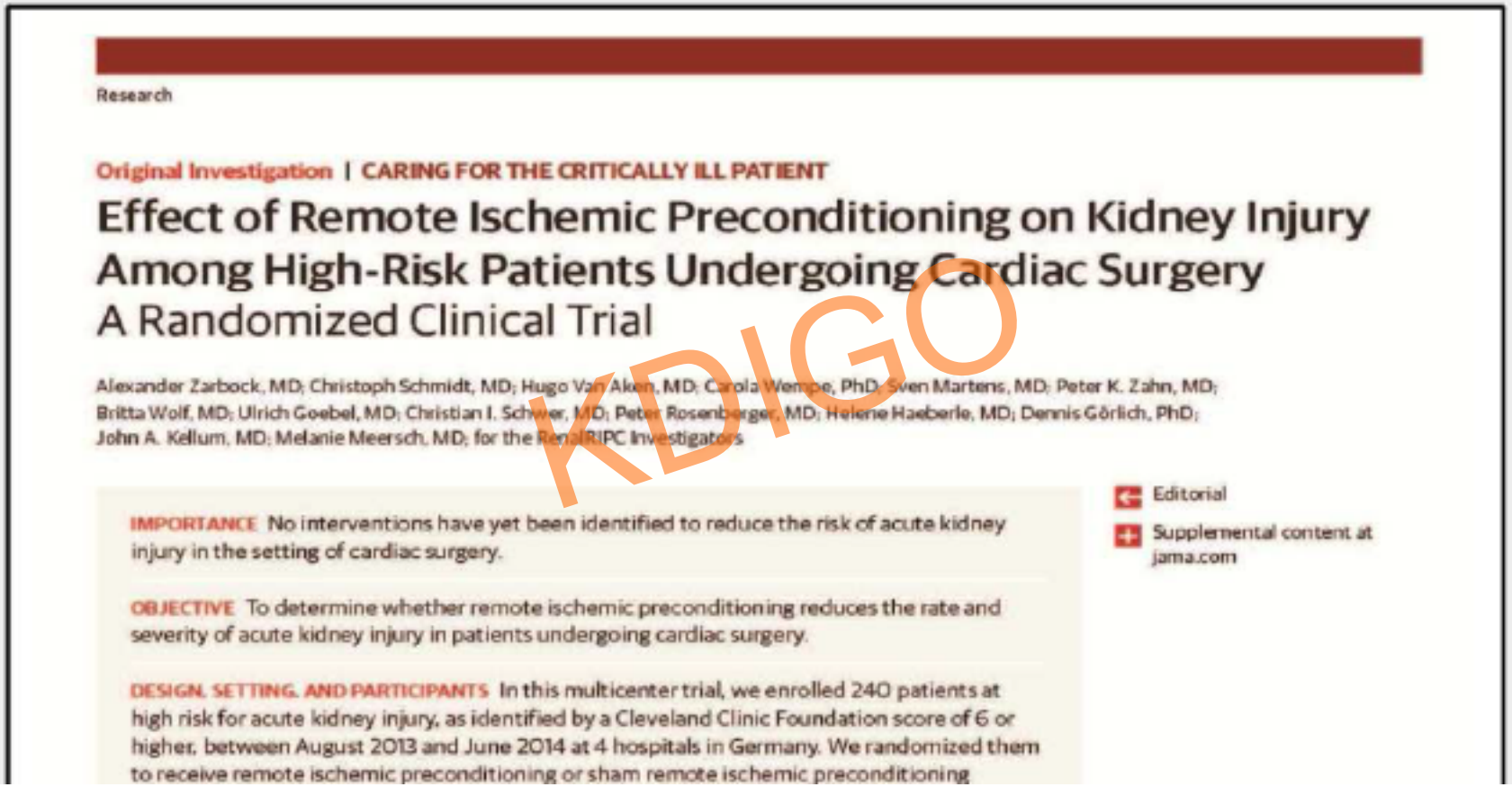

Research

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

Editorial

Supplemental content at jama.com

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Contrast-induced AKI

Chapter 4.3: Nonpharmacological prevention strategies of CI-AKI

4.3.1: Use the lowest possible dose of contrast medium in patients at risk for CI-AKI. *(Not Graded)*

4.3.2: We recommend using either iso-osmolar or low-osmolar iodinated contrast media, rather than high-osmolar iodinated contrast media in patients at increased risk of CI-AKI. *(1B)*

Chapter 4.4: Pharmacological prevention strategies of CI-AKI

4.4.1: We recommend i.v. volume expansion with either isotonic sodium chloride or sodium bicarbonate solutions, rather than no i.v. volume expansion, in patients at increased risk for CI-AKI. (*1A*)

4.4.2: We recommend not using oral fluids alone in patients at increased risk of CI-AKI. (*1C*)

Chapter 4.4: Pharmacological prevention strategies of CI-AKI

4.4.3: We suggest using oral N-acetylcysteine (NAC), together with i.v. isotonic crystalloids, in patients at increased risk of CI-AKI. (*2D*)

4.4.4: We suggest not using theophylline to prevent CI-AKI. (*2C*)

4.4.5: We recommend not using fenoldopam to prevent CI-AKI. (*1B*)

Thank you