

Akutes
Nierenversagen



Martin Bernardi

ANÄSTHESIE FORUM



ALPBACH

REPETITORIUM

Definition



- Akut auftretende Abnahme der Filtration
 - innerhalb von Stunden bis Tagen
 - prinzipiell rückbildungsfähig
- Prä-, intra-, postrenal
- Nach normaler Nierenfunktion
- CKD (acute on chronic renal failure)



Acute Kidney
Disease

Kidney
Damage

Renal
Failure

Renal
Insufficiency

Acute Tubular
Necrosis

Acute Renal
Failure

Acute Kidney Injury

Acute Renal
Impairment

Renal Illness

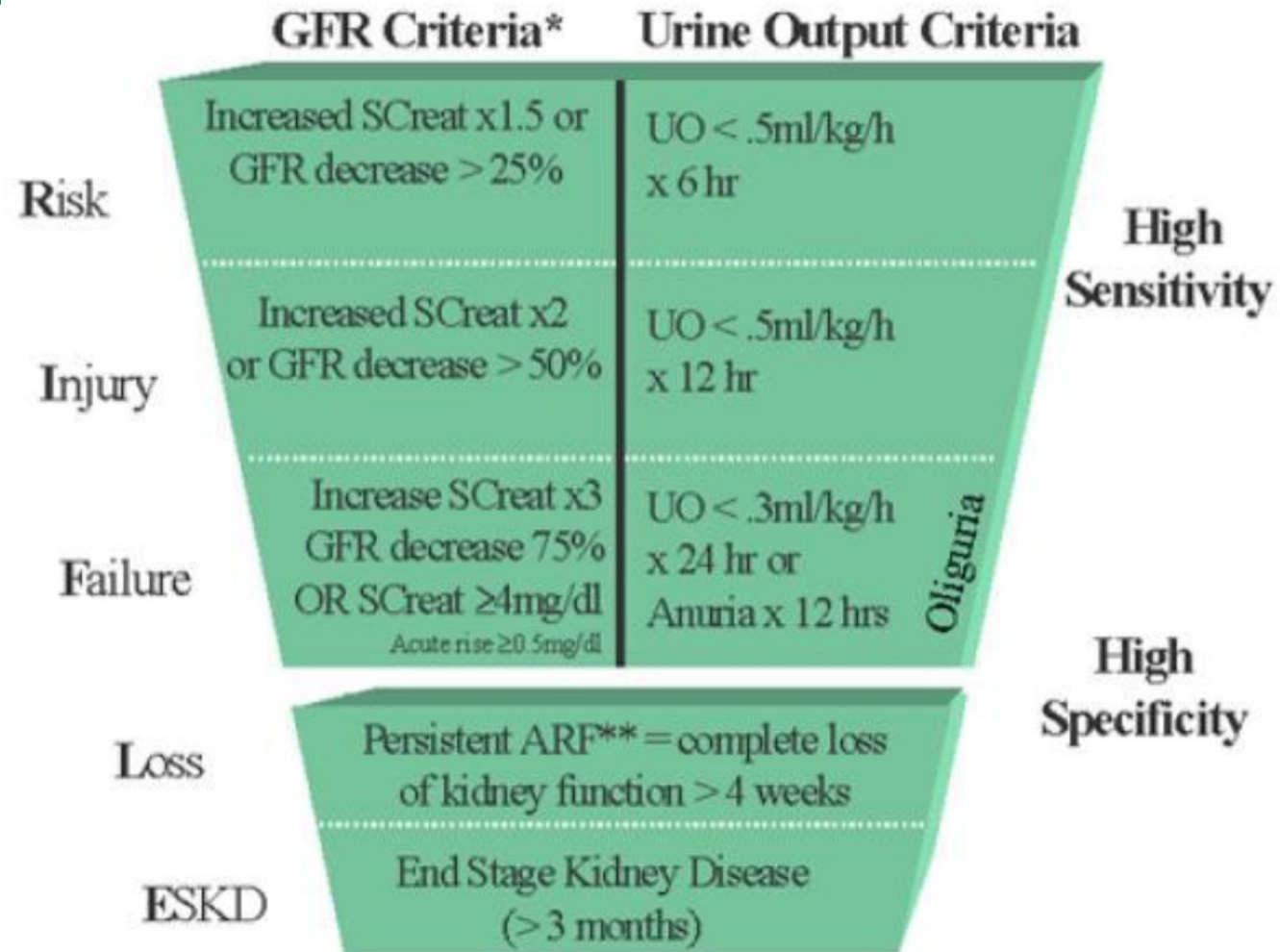
Renal
Deficiency

Acute Renal
Shutdown

Renal
Damage

Kidney
Disorder

RIFLE



Bellomo R. et al. Crit Care 2004



Table 2

Classification/staging system for acute kidney injury^a

Stage	Serum creatinine criteria	Urine output criteria
1	Increase in serum creatinine of more than or equal to 0.3 mg/dl ($\geq 26.4 \mu\text{mol/l}$) or increase to more than or equal to 150% to 200% (1.5- to 2-fold) from baseline	Less than 0.5 ml/kg per hour for more than 6 hours
2 ^b	Increase in serum creatinine to more than 200% to 300% (> 2 - to 3-fold) from baseline	Less than 0.5 ml/kg per hour for more than 12 hours
3 ^c	Increase in serum creatinine to more than 300% (> 3 -fold) from baseline (or serum creatinine of more than or equal to 4.0 mg/dl [$\geq 354 \mu\text{mol/l}$] with an acute increase of at least 0.5 mg/dl [$44 \mu\text{mol/l}$])	Less than 0.3 ml/kg per hour for 24 hours or anuria for 12 hours

^aModified from RIFLE (Risk, Injury, Failure, Loss, and End-stage kidney disease) criteria [26]. The staging system proposed is a highly sensitive interim staging system and is based on recent data indicating that a small change in serum creatinine influences outcome. Only one criterion (creatinine or urine output) has to be fulfilled to qualify for a stage. ^b200% to 300% increase = 2- to 3-fold increase. ^cGiven wide variation in indications and timing of initiation of renal replacement therapy (RRT), individuals who receive RRT are considered to have met the criteria for stage 3 irrespective of the stage they are in at the time of RRT.



Staging of AKI based on the KDIGO Guidelines

Stage	Serum creatinine	Urine output
1	1.5–1.9 times the baseline value OR ≥0.3 mg/dl (≥26.5 mmol/l) increase within 48 hours	<0.5 ml/kg/h for 6–12 h
2	2.0–2.9 times the baseline value	<0.5 ml/kg/h for ≥12 h
3	3.0 times the baseline value OR Increase in serum creatinine to ≥4.0 mg/dl (≥353.6 mmol/l) OR Initiation of renal replacement therapy OR In patients <18 years, decrease in the estimated GFR to <35 ml/min per 1.73 m ²	<0.3 ml/kg/h for ≥24 h OR Anuria for ≥12 h

Inzidenz



- 8-16% aller hospitalisierten Patienten
- 30-50% ICU PatientInnen
- Erhöhtes Risiko für CKD
- Erhöhte Lang- und Kurzzeit-Mortalität

Inzidenz



SEVEN-DAY PROFILE PUBLICATION

Intensive Care Med (2015) 41:1411–1423
DOI 10.1007/s00134-015-3934-7

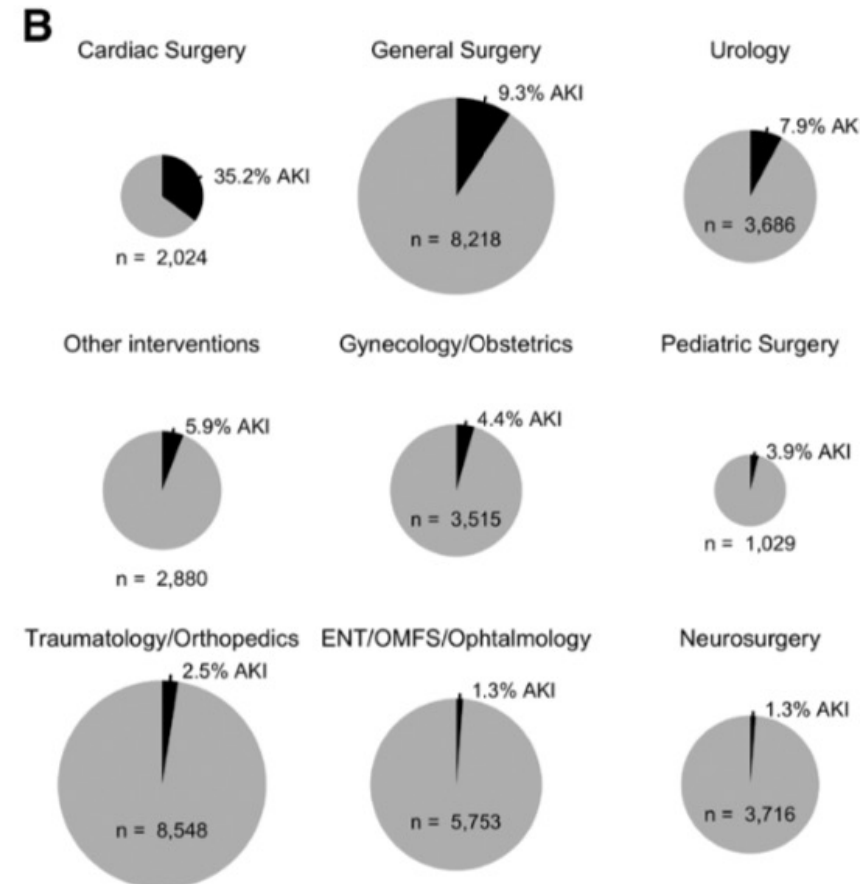
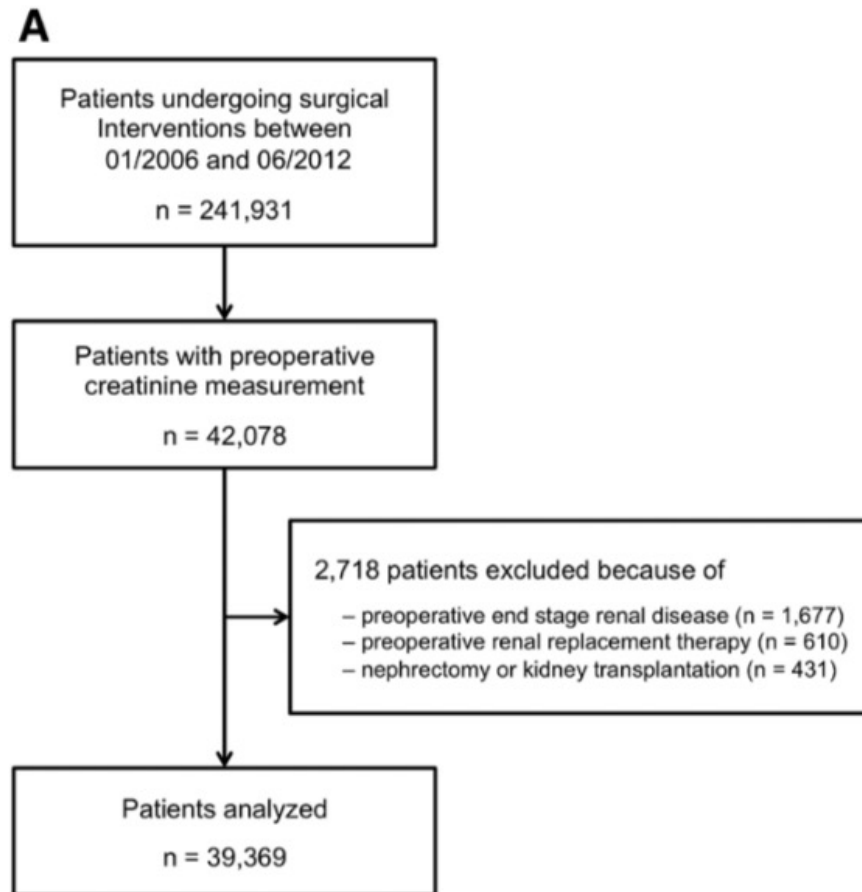


Epidemiology of acute kidney injury in critically ill patients: the multinational AKI-EPI study

Table 2 Variables at the time of acute kidney injury ($n = 666$)

Etiology of AKI	
Sepsis	271 (40.7 %)
Hypovolemia	227 (34.1 %)
Drug related	96 (14.4 %)
Cardiogenic shock	88 (13.2 %)
Hepatorenal syndrome	21 (3.2 %)
Obstruction of the urine outflow tract	9 (1.4 %)
Predisposing factors for AKI	
Diuretic treatment	216 (32.4 %)
NSAID administration	79 (11.9 %)
Aminoglycoside administration	45 (6.8 %)
Glycopeptide administration	9 (1.4 %)
Amphotericin administration	0 (0 %)
Radiocontrast media administration	14 (2.1 %)

Inzidenz

Outcome

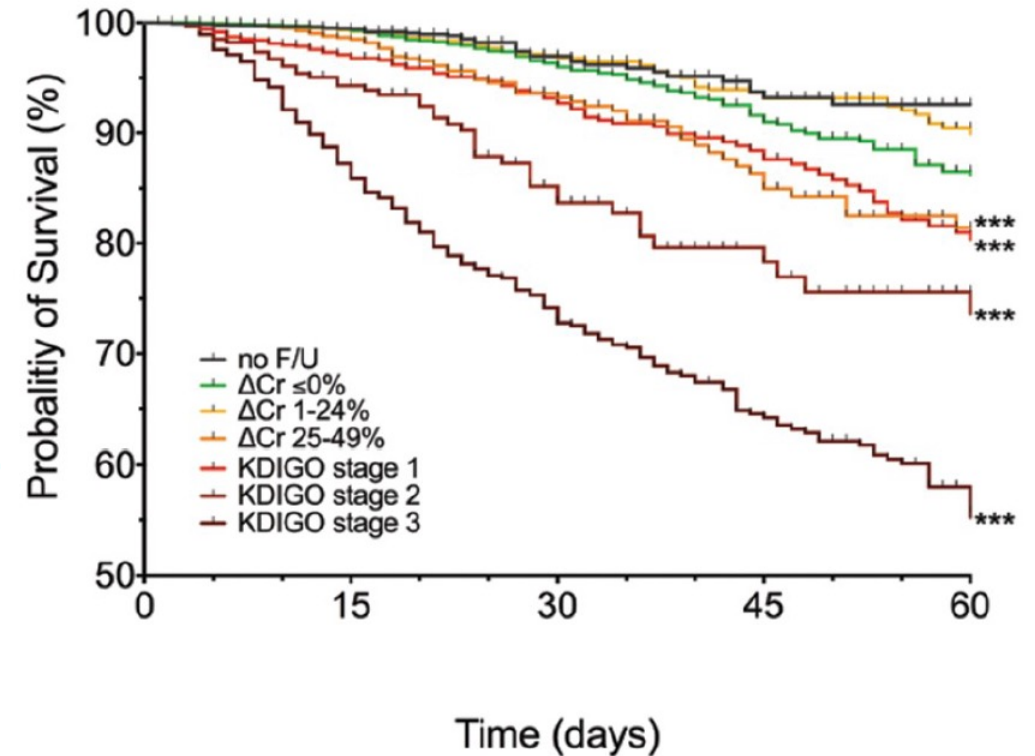


- Hohe Mortalität
 - 10-30%
 - 50% im Rahmen MOF
- 50% Restitutio
- 25-50% kompensierte Retention
- 10-15% chronisch dialysepflichtig

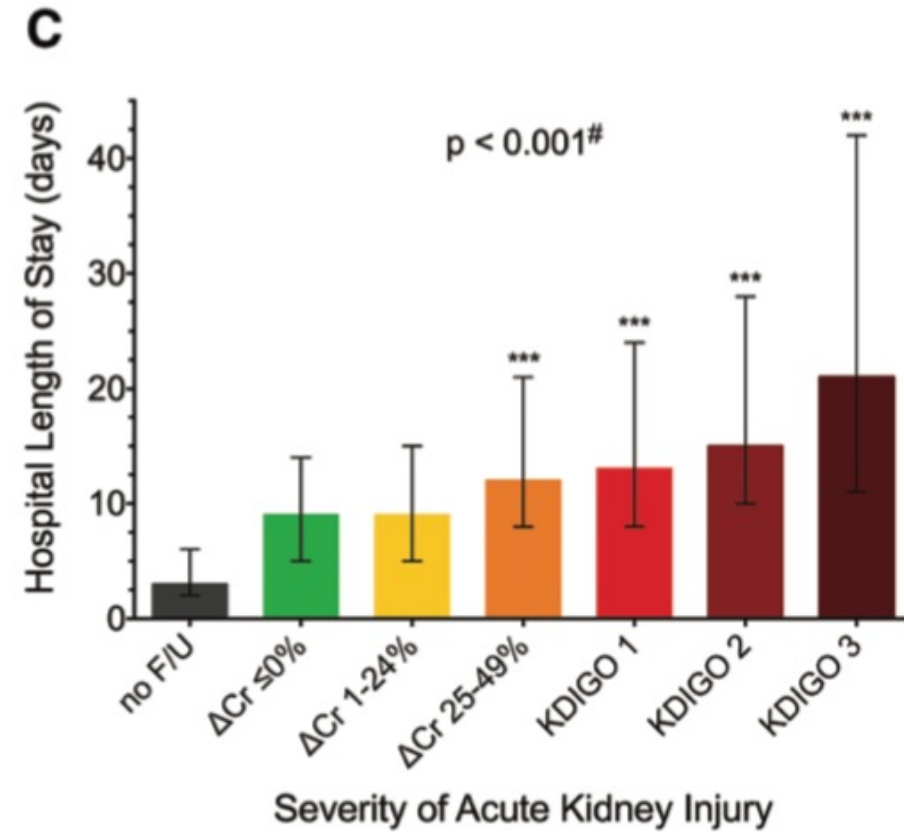
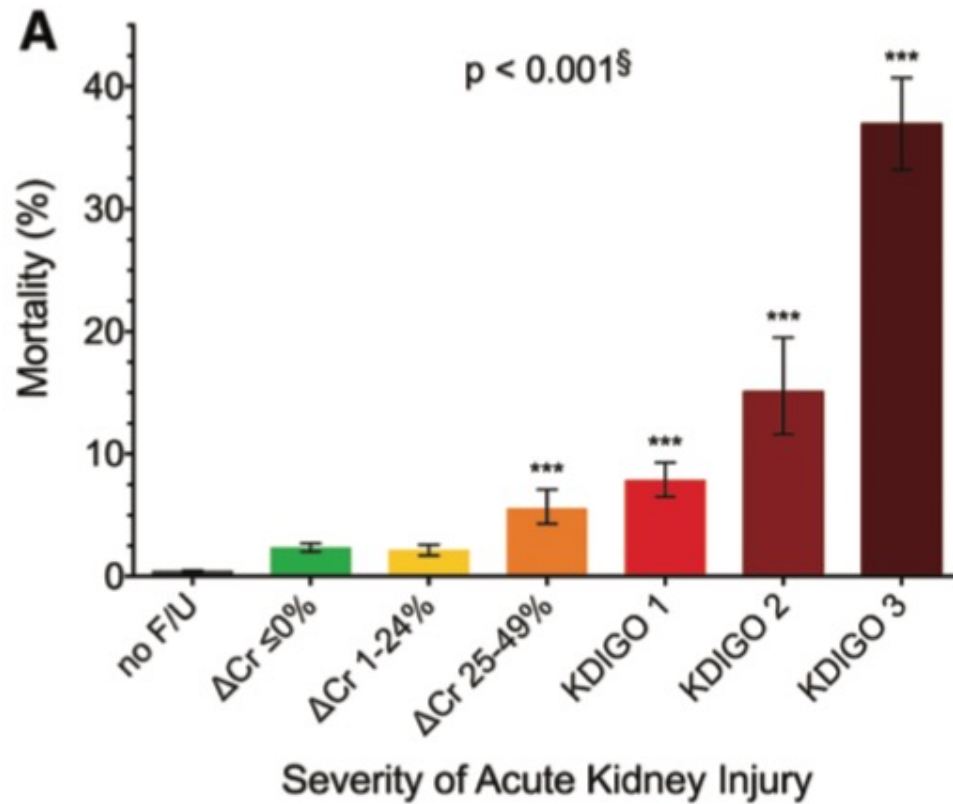
Outcome

Minor Postoperative Increases of Creatinine Are Associated with Higher Mortality and Longer Hospital Length of Stay in Surgical Patients

Felix Kork, M.D., M.Sc., Felix Balzer, M.D., M.Sc., Claudia D. Spies, M.D., Klaus-Dieter Wernecke, Ph.D., Adit A. Ginde, M.D., M.P.H., Joachim Jankowski, Ph.D., Holger K. Eltzschig, M.D.



Outcome



Folgen



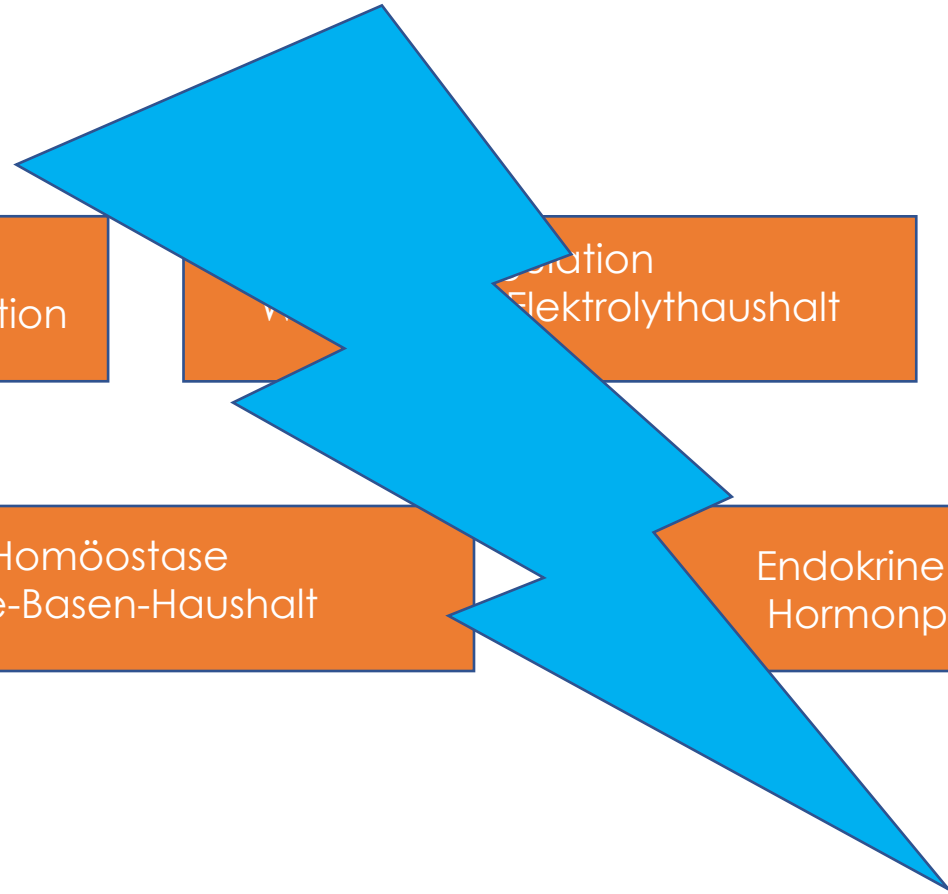
Ausscheidung
Harnkonzentrierung/Reabsorption

Regulation
Elektrolythaushalt

Blutdruckregulation
Das RAAS-System

Homöostase
Säure-Basen-Haushalt

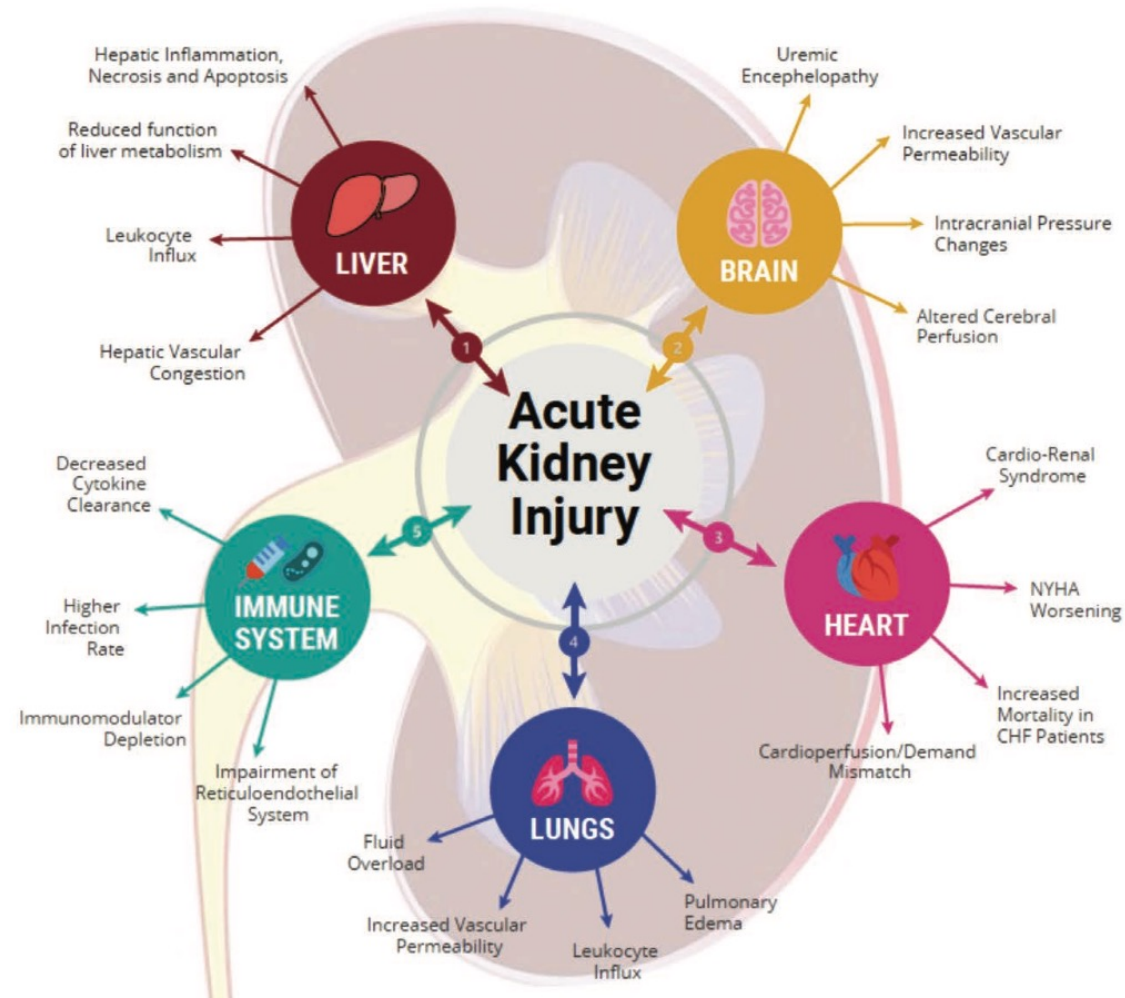
Endokrine Funktion -
Hormonproduktion



Acute Kidney injury



Consequences of acute kidney injury on remote organ functions



Gumbert et al. Anesthesiology 2020

AKI – was nun...



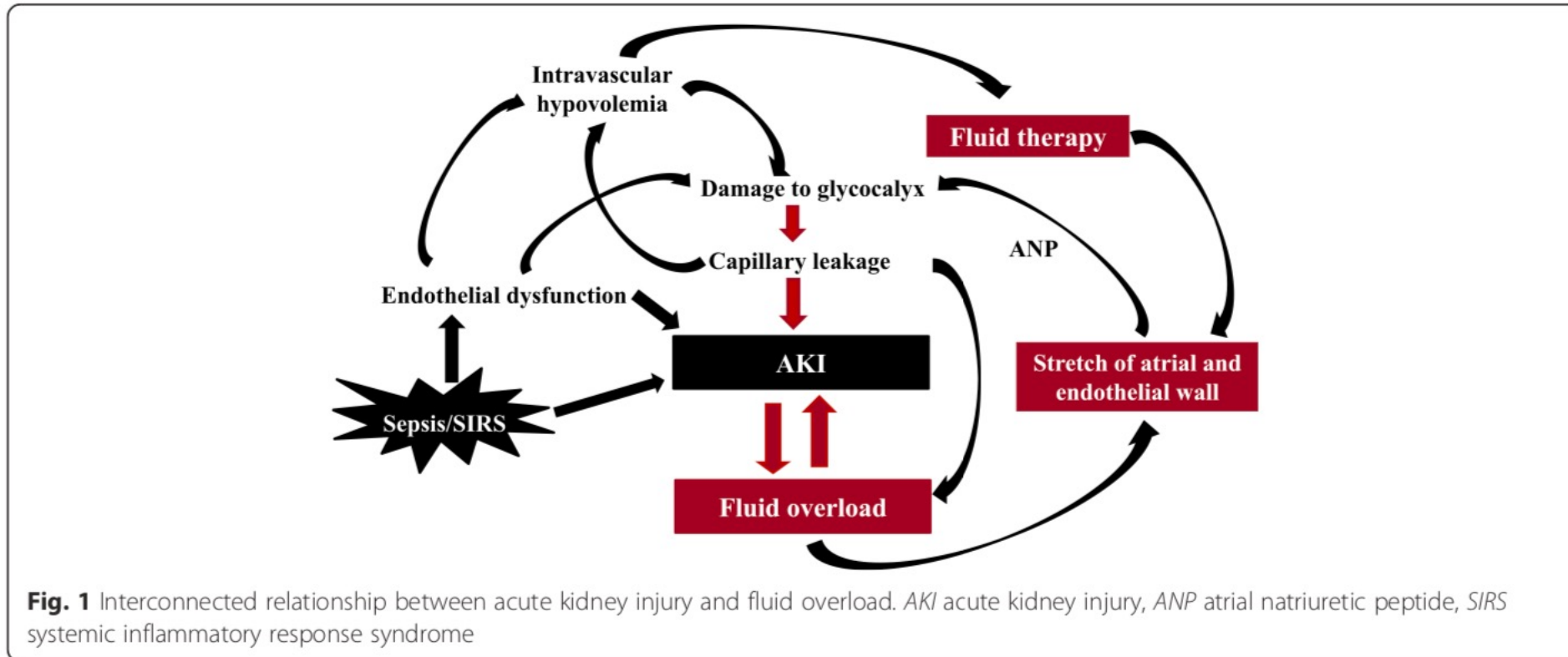
	AKI Stage			
	High Risk	1	2	3
Discontinue all nephrotoxic agents when possible				
Ensure volume status and perfusion pressure				
Consider functional hemodynamic monitoring				
Monitor Serum creatinine and urine output				
Avoid hyperglycemia				
Consider alternatives to radiocontrast procedures				
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				

Prävention



- Medikamentöse Prävention nicht möglich
- Optimierung der renalen Perfusion
- Euvolämie
- Diuretika nur bei erhaltener Diurese zur Korrektur einer Hypervolämie
 - Hyperhydratation kann eine Nierenschädigung oder Verschlechterung der Nierenfunktion hervorrufen
- Einsatz von Diuretika zur Prävention der AKI ist mangels Wirksamkeit abzuraten
- Kontrastmittelgabe zur radiologischen Diagnostik oder Therapie dringend erforderlich, soll auch bei AKI-(Risiko-)Patienten nicht darauf verzichtet werden

Volumenstatus



Volumentherapie

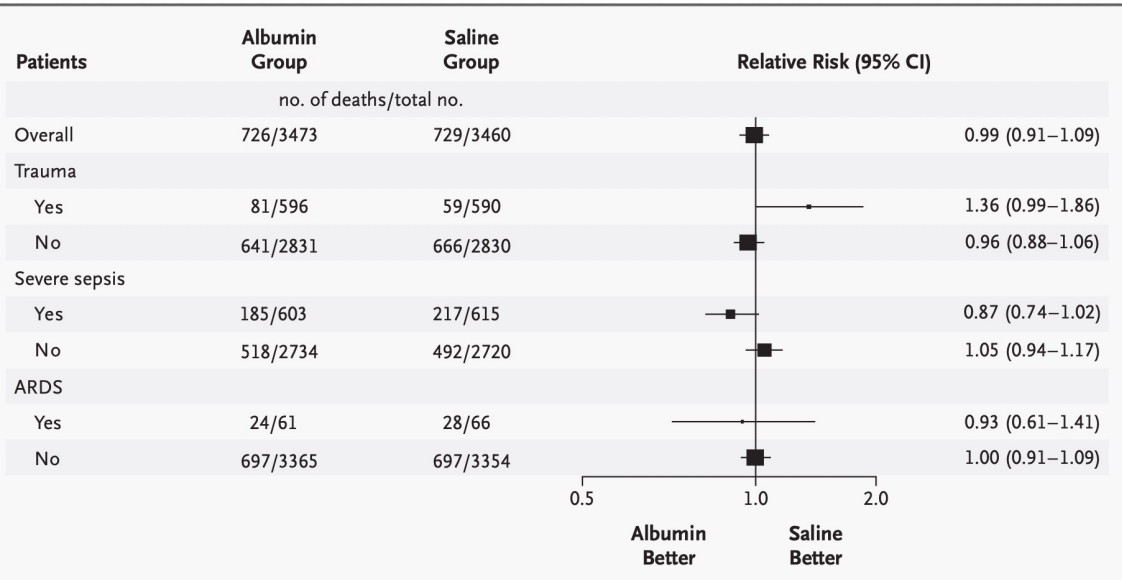
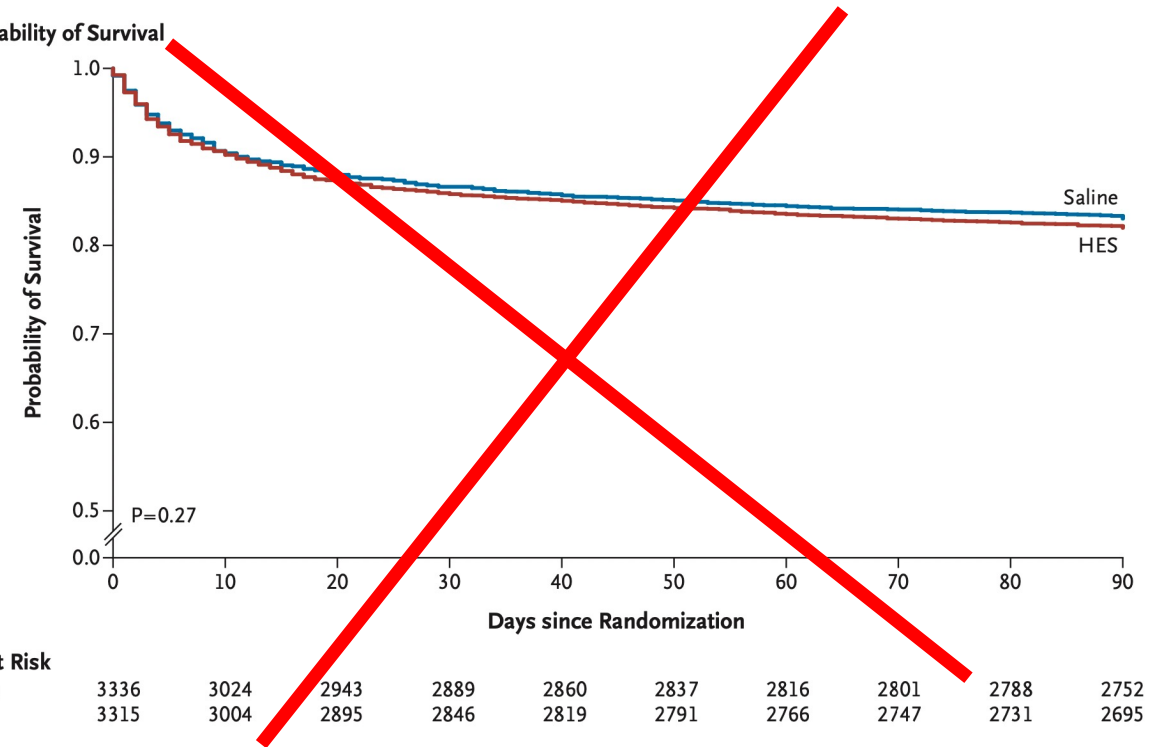


Figure 2. Relative Risk of Death from Any Cause among All the Patients and among the Patients in the Six Predefined Subgroups.

The size of each symbol indicates the relative number of events in the given group. The horizontal bars represent the confidence intervals (CI). ARDS denotes the acute respiratory distress syndrome.

A Probability of Survival



Finfer S et al. NEJM 2004
Myburgh JA et al. NEJM 2012

HES



12 January 2018
EMA/4068/2018

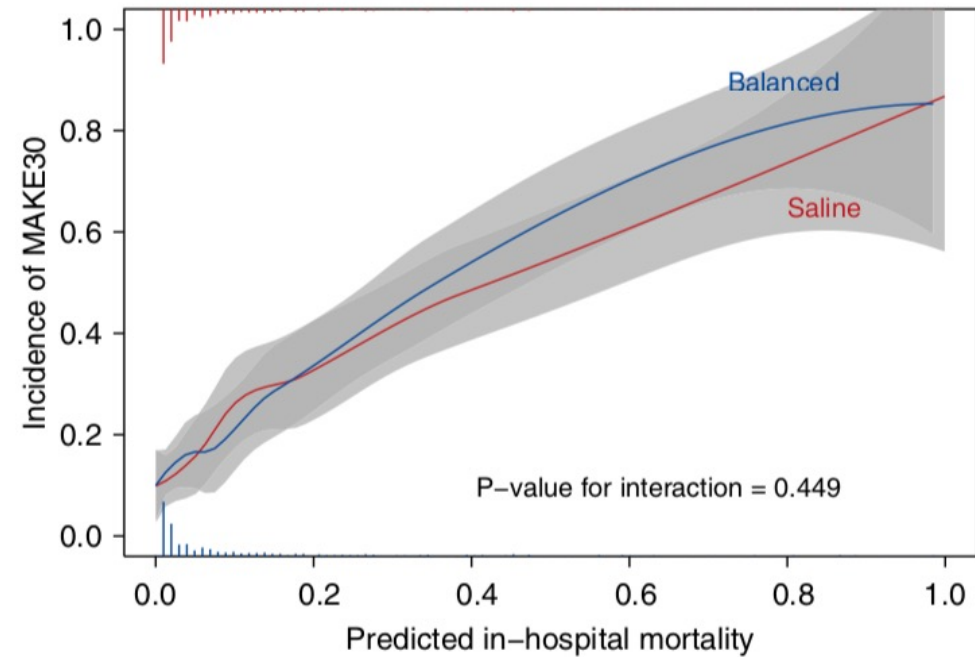
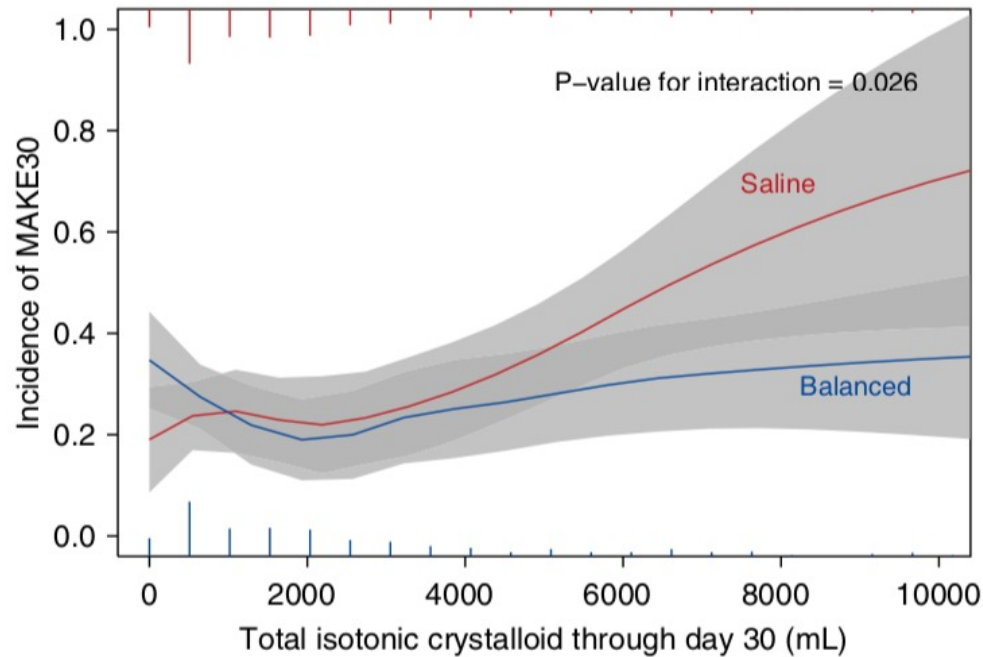


EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

PRAC recommends suspending hydroxyethyl-starch solutions for infusion from the market

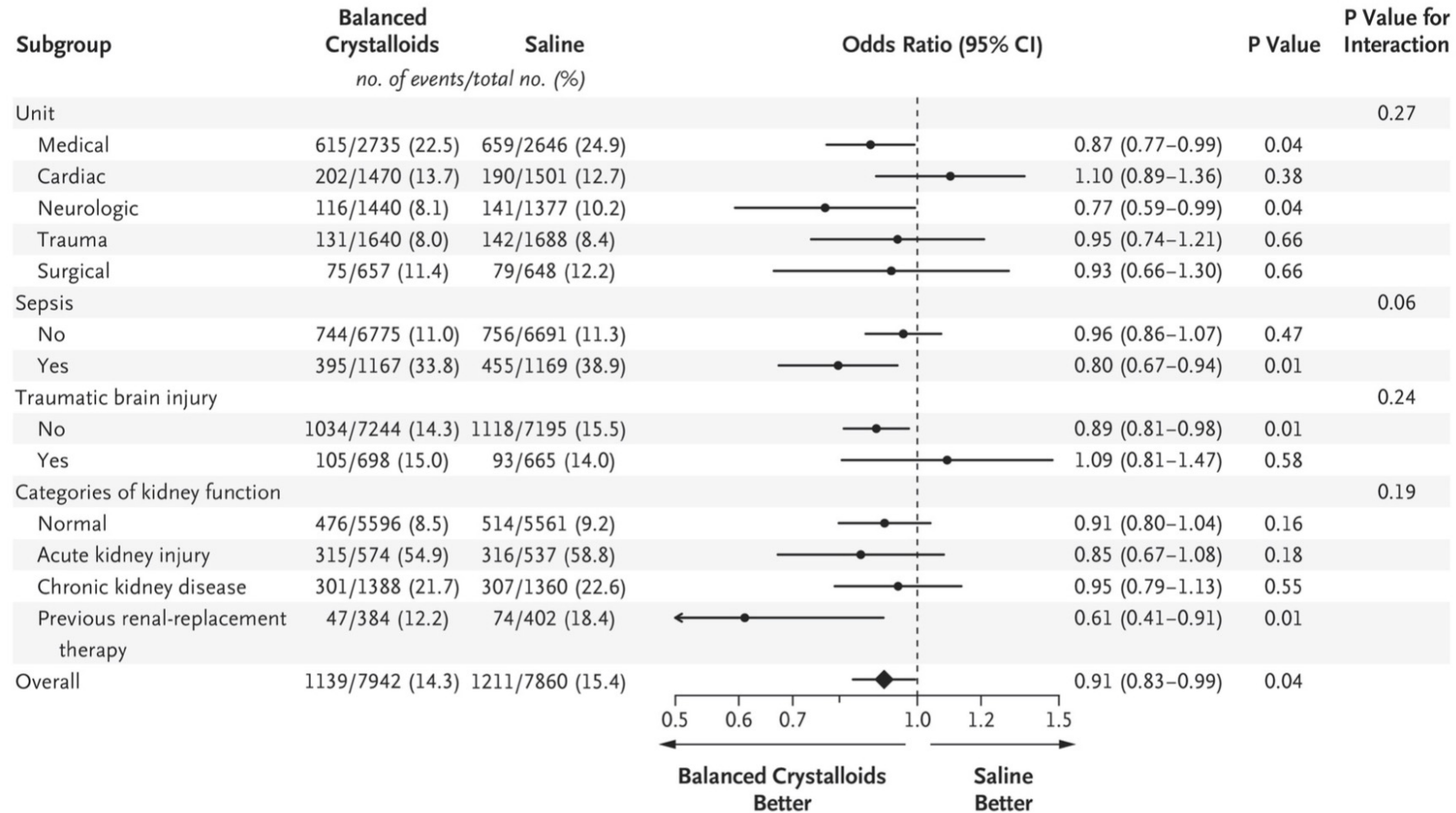
Review finds measures to protect patients have not been sufficiently effective

Volumentherapie



- NaCl 0,9% vs balanciertes Kristalloid
- MAKE30 (in-hospital mortality, receipt of new RRT, or persistent renal dysfunction)

Volumentherapie



Hyperhydratation



Table 2. ROC Analysis for RRT Requirement After LVAD

	AUC-ROC
Plasma NGAL (pre)	0.83 [0.54–0.95]#
Plasma NGAL (0h)	0.86 [0.66–0.95]#
Serum Cre (pre)	0.70 [0.39–0.90]
Serum Cre (0h)	0.67 [0.33–0.89]
Cre score	0.77 [0.40–0.95]
TB (pre)	0.44 [0.16–0.77]
TB score	0.78 [0.57–0.91]#
CVP (pre)	0.80 [0.56–0.93]#
CVP at 12h	0.89 [0.70–0.97]#
Urine volume (0–6h)	0.82 [0.51–0.95]#

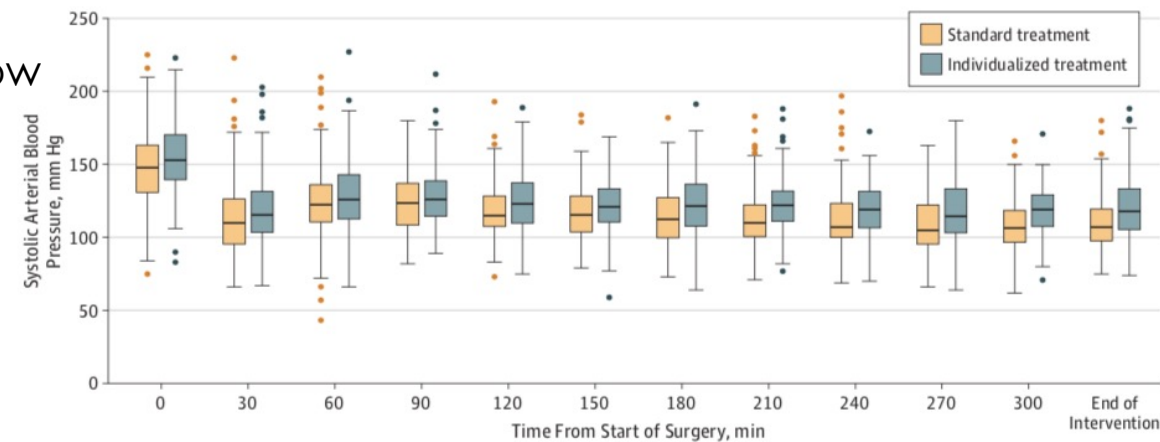
Perfusionsdruck



JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Individualized vs Standard Blood Pressure Management Strategies on Postoperative Organ Dysfunction Among High-Risk Patients Undergoing Major Surgery A Randomized Clinical Trial

- Standard treatment group
 - ephedrine iv 6-mg boluses for any decrease in SBP below 80 mm Hg or lower than 40% from the patient's reference value
- Individualized treatment group
 - SBP within $\pm 10\%$ of the reference value using a continuous infusion of norepinephrine
- Primary outcome
 - composite of SIRS + at least 1 organ system dysfunction



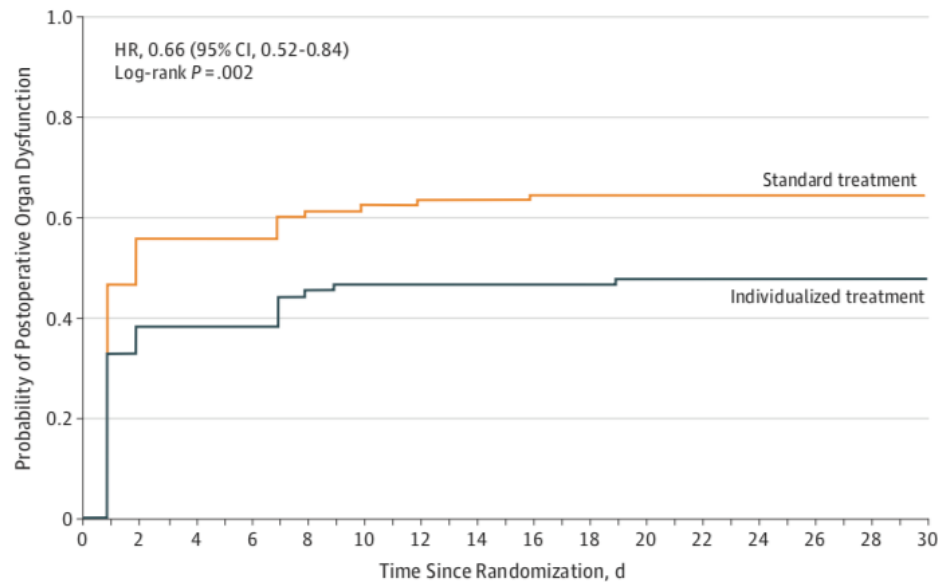
No. of patients	0	30	60	90	120	150	180	210	240	270	300	End of Intervention
Standard treatment	145	143	144	144	140	136	128	119	113	96	86	145
Individualized treatment	147	144	145	145	140	133	122	113	99	82	72	147

Futier E et al. JAMA 2017

Perfusionsdruck



Variable	Individualized Treatment (n = 147)	Standard Treatment (n = 145)	Between-Group Absolute Difference, % (95% CI)	Unadjusted Relative Risk (95% CI)	P Value	Adjusted Relative Risk (95% CI) ^a	P Value
Primary Outcome							
Primary composite outcome, No. (%) ^b	56 (38.1)	75 (51.7)	-14 (-25 to -2)	0.74 (0.57 to 0.95)	.02	0.73 (0.56 to 0.94)	.02



No. at risk	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30
Standard treatment	145	78	65	58	54	54	54	54	54	54	54	54	54	54	54	53
Individualized treatment	147	99	91	82	80	80	80	80	80	80	80	80	80	80	80	79

Renal dysfunction (RIFLE stage of risk or higher) occurred in 48 patients (32.7%) in the individualized treatment group and 71 patients (49.0%) in the standard treatment group (absolute risk difference, -16%; 95% CI, -27% to -5%; adjusted relative risk, 0.70; 95% CI, 0.53 to 0.92; $P = .01$). All-

Conclusions

Among patients predominantly undergoing abdominal surgery who were at increased postoperative risk, management targeting an individualized systolic blood pressure, compared with standard management, reduced the risk of postoperative organ dysfunction.

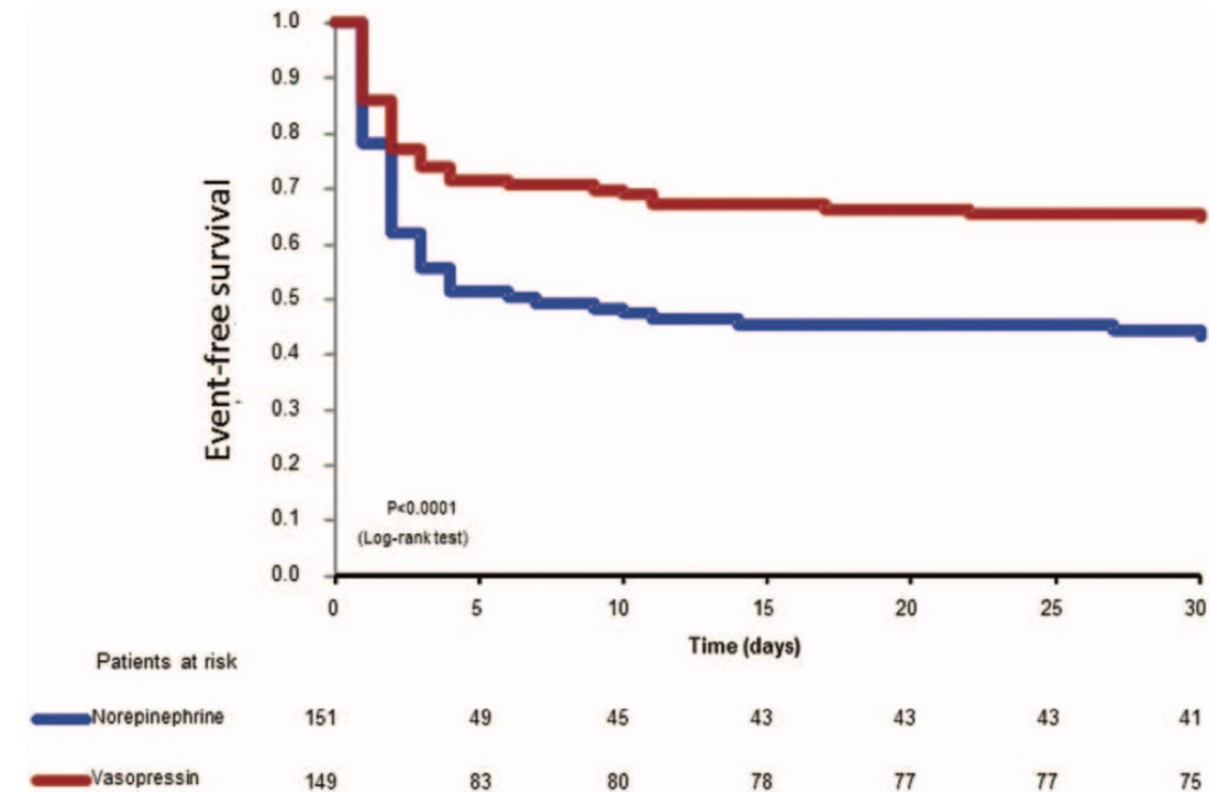
Vasopressorthherapie

CRITICAL CARE MEDICINE

Vasopressin versus Norepinephrine in Patients with Vasoplegic Shock after Cardiac Surgery

The VANCS Randomized Controlled Trial

Variable	Norepinephrine (n = 151)	Vasopressin (n = 149)	Unadjusted Odds Ratio or Hazard Ratio or Between- group Difference (95% CI)	P Value	Adjusted* Odds Ratio or Hazard Ratio or Between- group Difference (95%CI)	P Value
Primary outcome, n (%)	74 (49.0)	48 (32.2)	0.55 (0.38 to 0.80)	0.0014	0.52 (0.36 to 0.75)	0.0005
30-d mortality	24 (15.9)	23 (15.4)	0.99 (0.56 to 1.76)	0.98	1.11 (0.62 to 1.96)	0.73
MV > 48 h	13 (8.6)	8 (5.4)	0.62 (0.26 to 1.49)	0.28	0.62 (0.26 to 1.51)	0.30
Sternal wound infection	15 (9.9)	7 (4.7)	0.46 (0.19 to 1.13)	0.09	0.48 (0.19 to 1.18)	0.11
Reoperation	10 (6.6)	10 (6.7)	0.8 (0.52 to 1.23)	0.31	0.79 (0.51 to 1.22)	0.28
Stroke	4 (2.6)	4 (2.7)	1.03 (0.26 to 4.11)	0.97	1.08 (0.27 to 4.39)	0.91
Acute renal failure	54 (35.8)	15 (10.3)	0.26 (0.15 to 0.46)	< 0.0001	0.26 (0.15 to 0.46)	< 0.0001
Secondary outcomes, n (%)						
Infection	23 (15.2)	16 (10.7)	0.67 (0.34 to 1.33)	0.25	0.71 (0.35 to 1.42)	0.33
Septic shock	13 (8.6)	9 (6.0)	0.68 (0.28 to 1.65)	0.40	0.73 (0.3 to 1.81)	0.50
Atrial fibrillation	124 (82.1)	95 (63.8)	0.38 (0.22 to 0.65)	0.0004	0.37 (0.22 to 0.64)	0.0004
Ventricular arrhythmias	32 (21.2)	27 (18.1)	0.82 (0.46 to 1.46)	0.50	0.8 (0.45 to 1.43)	0.45
Length of ICU stay (d), median (IQR)	6 (4 to 9)	5 (4 to 7)	-2.42 (-4.11 to -0.73)	0.0050	-2.28 (-3.94 to -0.62)	0.0071
Length of hospital stay (d), median (IQR)	13 (10 to 20)	10 (8 to 12)	-3.76 (-6.1 to -1.42)	0.0016	-3.66 (-6.01 to -1.32)	0.0022



Nephrotoxine



- Laufende Medikation regelmäßig evaluieren
- ACE-Hemmer und ATII-Blocker pausieren
- Nephrotoxische Pharmaka absetzen
 - Aminoglykoside: tägl. Einzelgaben
 - Vancomycin: kontinuierliche Infusion
 - Kombination von Vancomycin mit Pipitaz höheres Risiko

Kontrastmittel-assoziiertes AKI



Intensive Care Med (2023) 49:205–215

<https://doi.org/10.1007/s00134-022-06966-w>

ORIGINAL

Renal outcomes following intravenous contrast administration in patients with acute kidney injury: a multi-site retrospective propensity-adjusted analysis



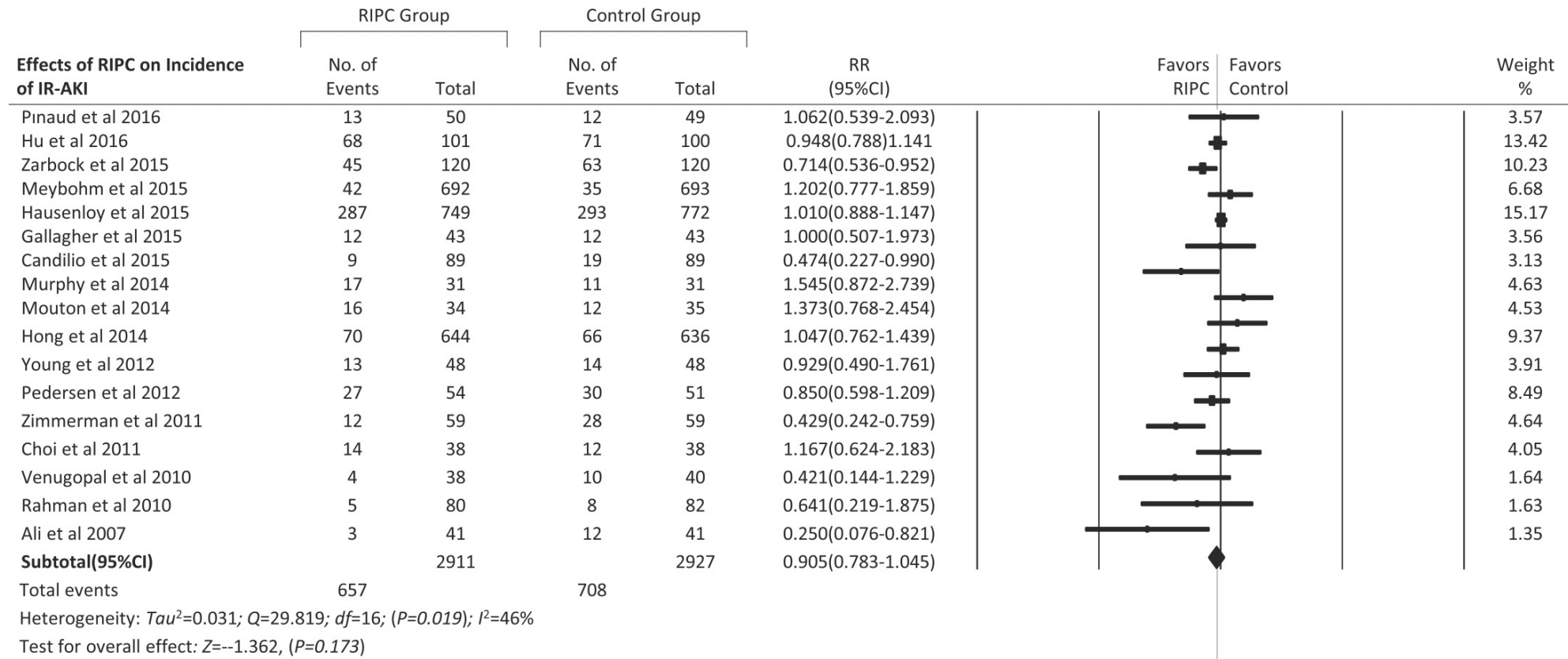
Michael R. Ehmann^{1*}, Jonathon Mitchell¹, Scott Levin¹, Aria Smith¹, Steven Menez², Jeremiah S. Hinson¹ and Eili Y. Klein^{1,3}

Conclusions

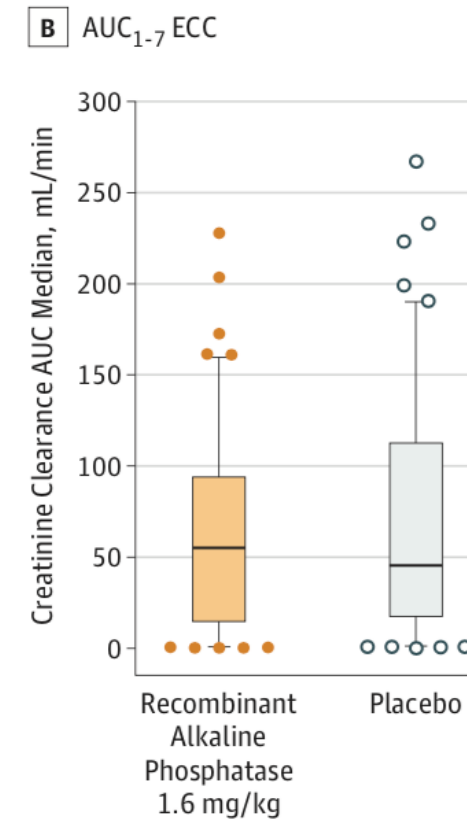
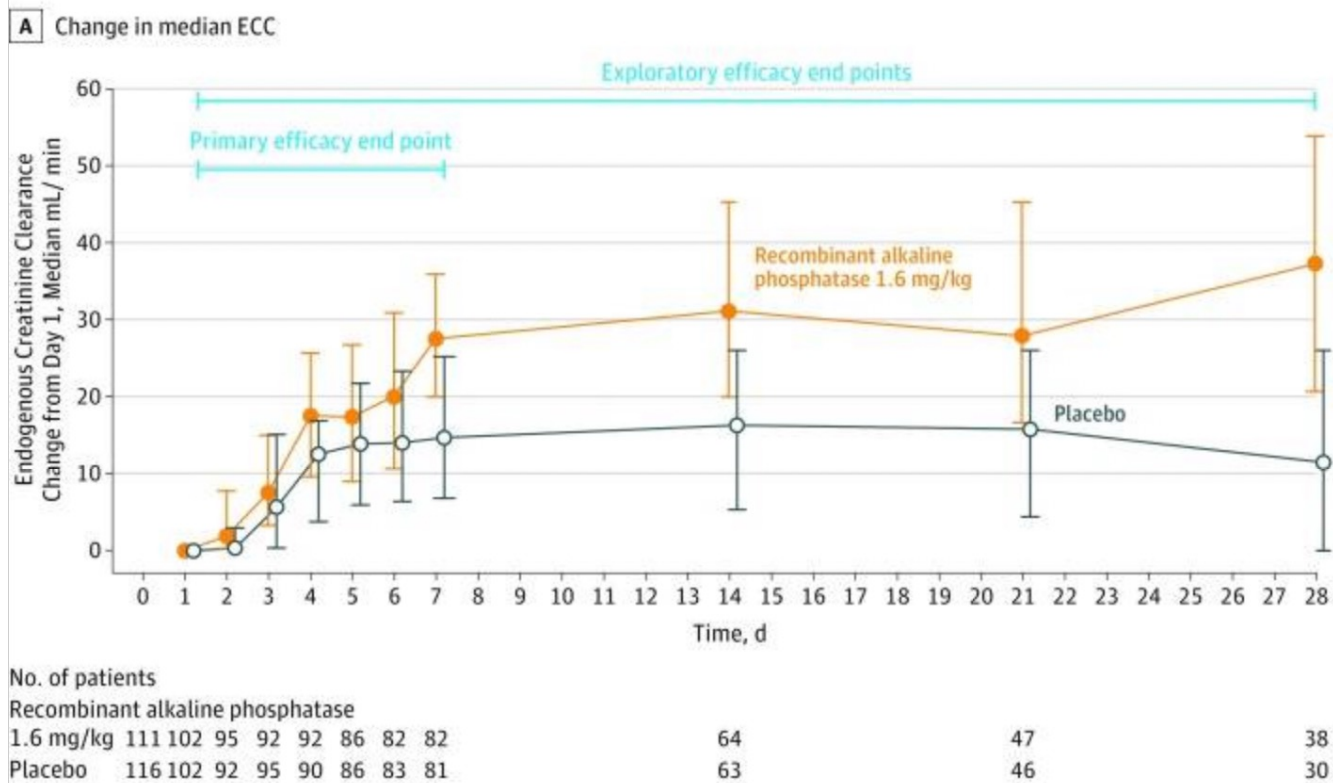
Among nearly 14,500 patients who met KDIGO sCr-based criteria for AKI on arrival to the ED, we found no independent association between the administration of CM and persistence of AKI or an increased risk of dialysis initiation within 180 days. Our findings suggest that the recent ACR-NKF consensus recommendations for use of IV CM in patients with stable renal disease may also be applied to patients with pre-existing AKI [16, 17].

- Risiko bei isoosmolaren Kontrastmittel sehr gering
- Wichtige diagn. Untersuchungen od. Interventionen nicht verzögern

Prävention – Remote ischemic preconditioning



Prävention – Alkalische Phosphatase



Prävention – Care bundles



- High-risk Patient:innen
- Renoprotektive Maßnahmen
 - Vermeidung von nephrotox. Substanzen
 - Keine ACEI/ARB für 48h
 - Vermeiden von Hyperglykämie
 - Engmaschiges SCr & UO Monitoring
 - Erweitertes hämodynamisches Monitoring
 - Optimierter Volumenstatus
 - KM-Alternativen

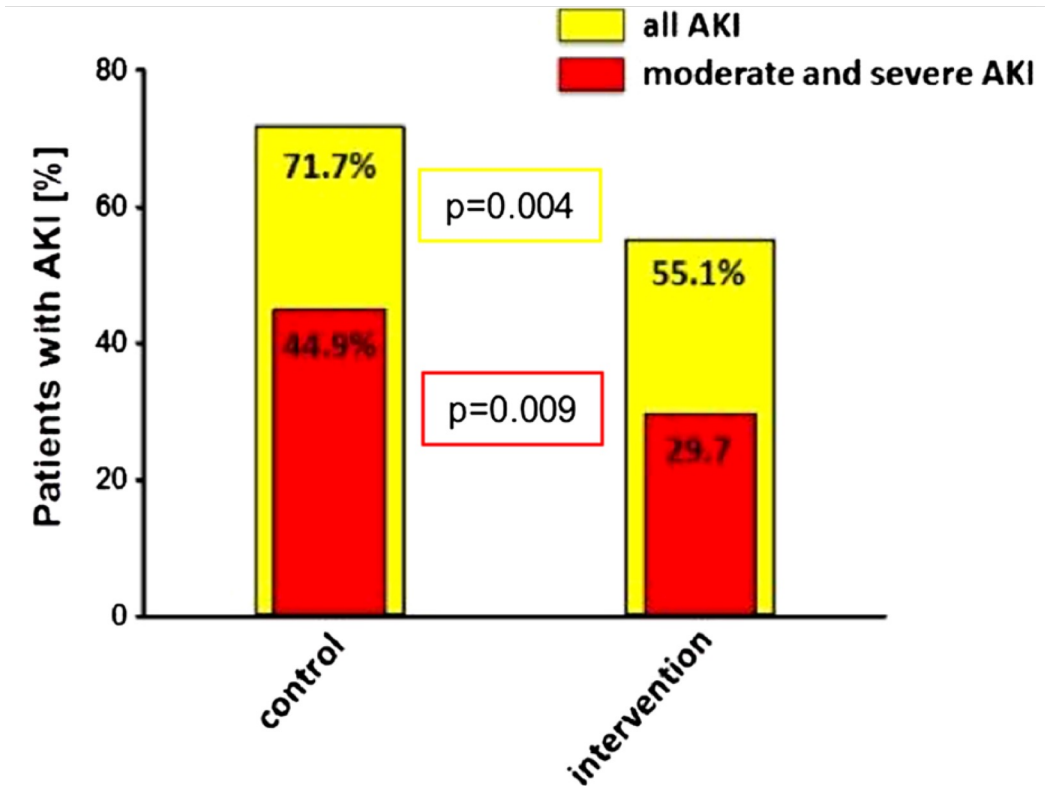


Fig. 2 Occurrence of cardiac surgery-associated AKI. Rate of CSA-AKI in control and intervention groups

Meersch M et al. ICM 2017


Prävention – Care bundles




Intensive Care Med (2017) 43:1551–1561
DOI 10.1007/s00134-016-4670-3

SEVEN-DAY PROFILE PUBLICATION

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



Melanie Meersch¹, Christoph Schmidt¹, Andreas Hoffmeier², Hugo Van Aken¹, Carola Wempe¹, Joachim Gerss³ and Alexander Zarbock^{1*} 

Prevention of Cardiac Surgery–Associated Acute Kidney Injury by Implementing the KDIGO Guidelines in High-Risk Patients Identified by Biomarkers: The PrevAKI-Multicenter Randomized Controlled Trial

Zarbock, Alexander MD[‡]; Küllmar, Mira MD^{*}; Ostermann, Marlies MD[†]; Lucchese, Gianluca MD[†]; Baig, Kamran MD[‡]; Cennamo, Armando MD[‡]; Rajani, Ronak MD[‡]; McCorkell, Stuart MD[‡]; Arndt, Christian MD[‡]; Wulf, Hinnerk MD[‡]; Iqbal, Marc MD[‡]; Monaco, Fabrizio MD^{||}; Di Prima, Ambra Licia MD^{||}; García Alvarez, Mercedes MD^{||}; Italiano, Stefano MD^{||}; Miralles Bagan, Jordi MD^{||}; Kunst, Gudrun MD[‡]; Nair, Shrijit MD[‡]; L'Acqua, Camilla MD^{**}; Hoste, Eric MD^{††}; Vandenberghe, Wim MD^{††}; Honore, Patrick M. MD^{‡‡}; Kellum, John A. MD^{§§}; Forni, Lui G. MD^{|||}; Grieshaber, Philippe MD^{¶¶}; Massoth, Christina MD^{*}; Weiss, Raphael MD^{*}; Gerss, Joachim PhD^{###}; Wempe, Carola PhD^{*}; Meersch, Melanie MD^{*}

[Author Information](#) 

Anesthesia & Analgesia: August 2021 - Volume 133 - Issue 2 - p 292-302
doi: 10.1213/ANE.0000000000005458

RANDOMIZED CONTROLLED TRIALS

Biomarker-guided Intervention to Prevent Acute Kidney Injury After Major Surgery

The Prospective Randomized BigPAK Study

Göcze, Ivan MD^{*}; Jauch, Dominik MD[‡]; Götz, Markus MD^{*}; Kennedy, Pascal^{*}; Jung, Bettina MD[‡]; Zeman, Florian[§]; Gnewuch, Carsten MD^{||}; Graf, Bernhard M. MD^{||}; Gnann, Wolfgang^{**}; Banas, Bernhard MD[‡]; Bein, Thomas MD^{||}; Schlitt, Hans J. MD^{*}; Bergler, Tobias MD[‡]

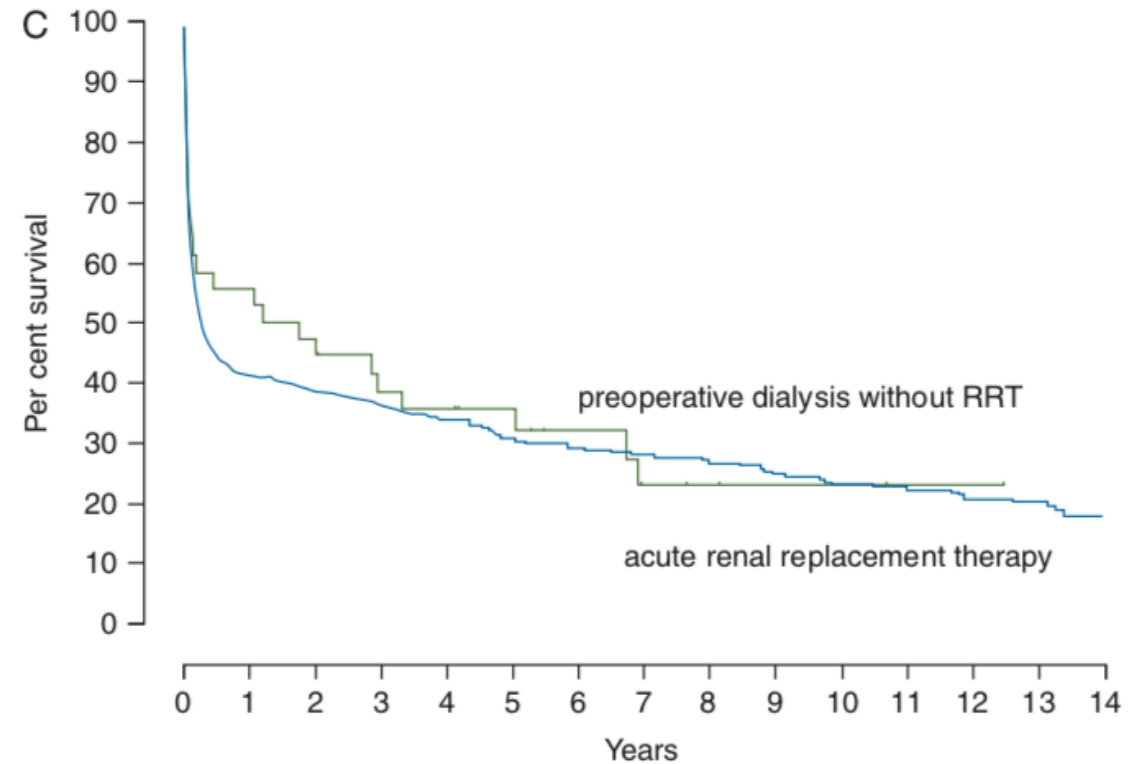
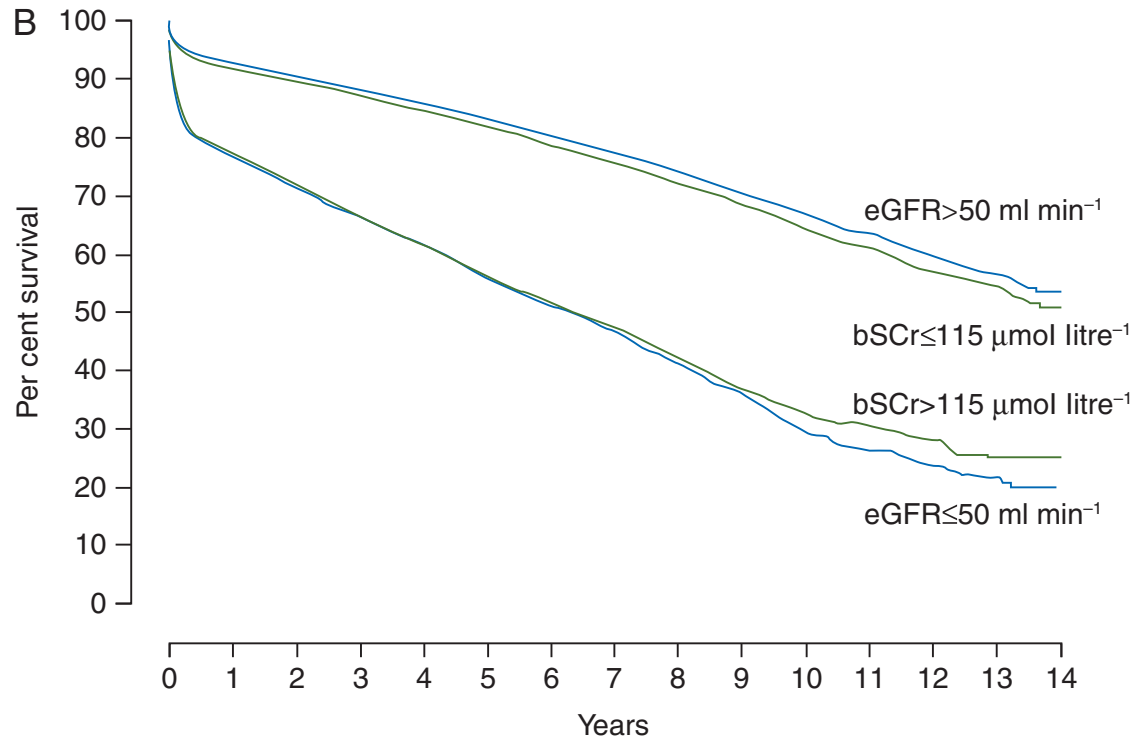
Präoperative Risikofaktoren



- Nierenfunktion beeinflusst Kurz- und Langzeitüberleben
- Erhöhtes präoperatives Serumkreatinin ist ein unabhängiger Risikofaktor

Variables	Univariate		Multivariate			
	HR (95% CI)	P-value	Short-term survival (≤150 days)		Long-term survival (>150 days)	
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Preoperative risk factors						
bSCR ($\mu\text{mol litre}^{-1}$)	1.29 (1.26–1.32)	<0.0001				
bSCR _{high} ($\mu\text{mol litre}^{-1}$)	2.61 (2.43–2.80)	<0.0001	1.59 (1.38–1.83)	0.0027	1.46 (1.32–1.62)	<0.0001
eGFR (ml min^{-1})	0.97 (0.975–0.978)	<0.0001				
eGFR _{low} (ml min^{-1})	2.86 (2.67–3.06)	<0.0001				
CKD Stage 1 (ml min^{-1})	1					
Stage 2	1.94 (1.72–2.19)	<0.0001				
Stage 3	3.83 (3.42–4.30)	<0.0001				
Stage 4	7.89 (6.70–9.30)	<0.0001				
Stage 5	8.32 (6.84–10.12)	<0.0001				
Female	1.20 (1.12–1.29)	<0.0001			0.87 (0.79–0.95)	0.0024
Age (yr)	1.06 (1.05–1.06)	<0.0001	1.04 (1.03–1.05)	<0.0001	1.05 (1.05–1.06)	<0.0001
BMI (kg m^{-2})	0.97 (0.97–0.98)	<0.0001				
Congestive heart failure	2.00 (1.85–2.17)	<0.0001	1.42 (1.22–1.65)	0.0002		
Diabetes	1.59 (1.48–1.71)	<0.0001			1.37 (1.25–1.50)	<0.0001
Angina pectoris (absence of)	1		1			
Angina, stable	0.76 (0.70–0.82)	<0.0001	0.70 (0.58–0.83)	<0.0001		
Angina, unstable	0.96 (0.88–1.05)	0.3984	1.21 (1.02–1.44)	0.0289		
Infarction	1.25 (1.17–1.35)	<0.0001				
LVEF >50%	1				1	
LVEF 30–50%	1.49 (1.39–1.60)	<0.0001			1.27 (1.17–1.39)	<0.0001
LVEF <30%	2.44 (2.18–2.74)	<0.0001			1.65 (1.42–1.92)	<0.0001
Atrial fibrillation	1.96 (1.81–2.13)	<0.0001			1.52 (1.38–1.69)	<0.0001
PAOD	1.47 (1.37–1.57)	<0.0001			1.20 (1.10–1.30)	<0.0001
COPD	1.55 (1.42–1.70)	<0.0001			1.40 (1.25–1.56)	<0.0001
History of CKD	2.76 (2.48–3.06)	<0.0001			1.30 (1.12–1.51)	0.0006
EuroSCORE	1.20 (1.19–1.21)	<0.0001				
Logistic EuroSCORE	1.07 (1.035–1.039)	<0.0001				
Medications						
Diuretics	1.90 (1.78–2.04)	<0.0001			1.27 (1.16–1.38)	<0.0001
ACE-inhibitors	1.19 (1.11–1.28)	<0.0001				

Präoperative Risikofaktoren



Bernardi MH et al. Br J Anaesth 2015

Perioperative Risikofaktoren



Original Investigation

FREE

March 8, 2022

Predictive Accuracy of a Perioperative Laboratory Test-Based Prediction Model for Moderate to Severe Acute Kidney Injury After Cardiac Surgery

Sevag Demirjian, MD¹; C. Allen Bashour, MD²; Andrew Shaw, MB²; et al

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Duration from end of surgery to metabolic panel draw (hour)

Pre-operative serum creatinine (mg/dl)

Post-operative serum creatinine (mg/dl)

Post-operative serum albumin (mg/dl)

Post-operative BUN (mg/dl)

Post-operative serum potassium (mmol/L)

Post-operative serum sodium (mmol/L)

Post-operative serum bicarbonate (mmol/L)

	Result	Probability
1	AKI ^{2/3} in 3 days	46.6%
2	AKI ^{2/3} in 14 days	41.9%
3	AKI ^D in 3 days	37.2%
4	AKI ^D in 14 days	41%

<https://riskcalc.org/AKIpostCardiacSurgery/>

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Postoperative Früherkennung



EJA

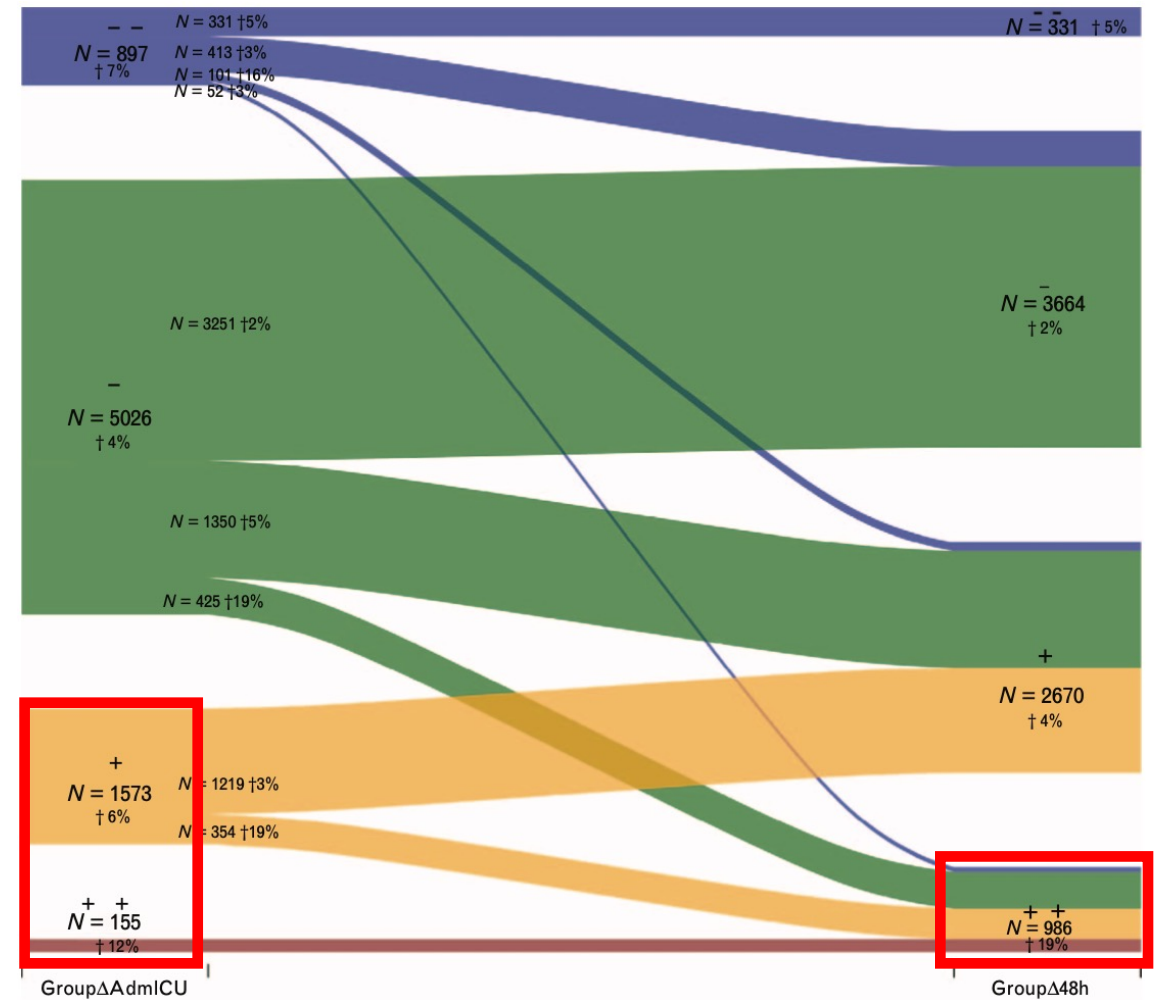
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ORIGINAL ARTICLE

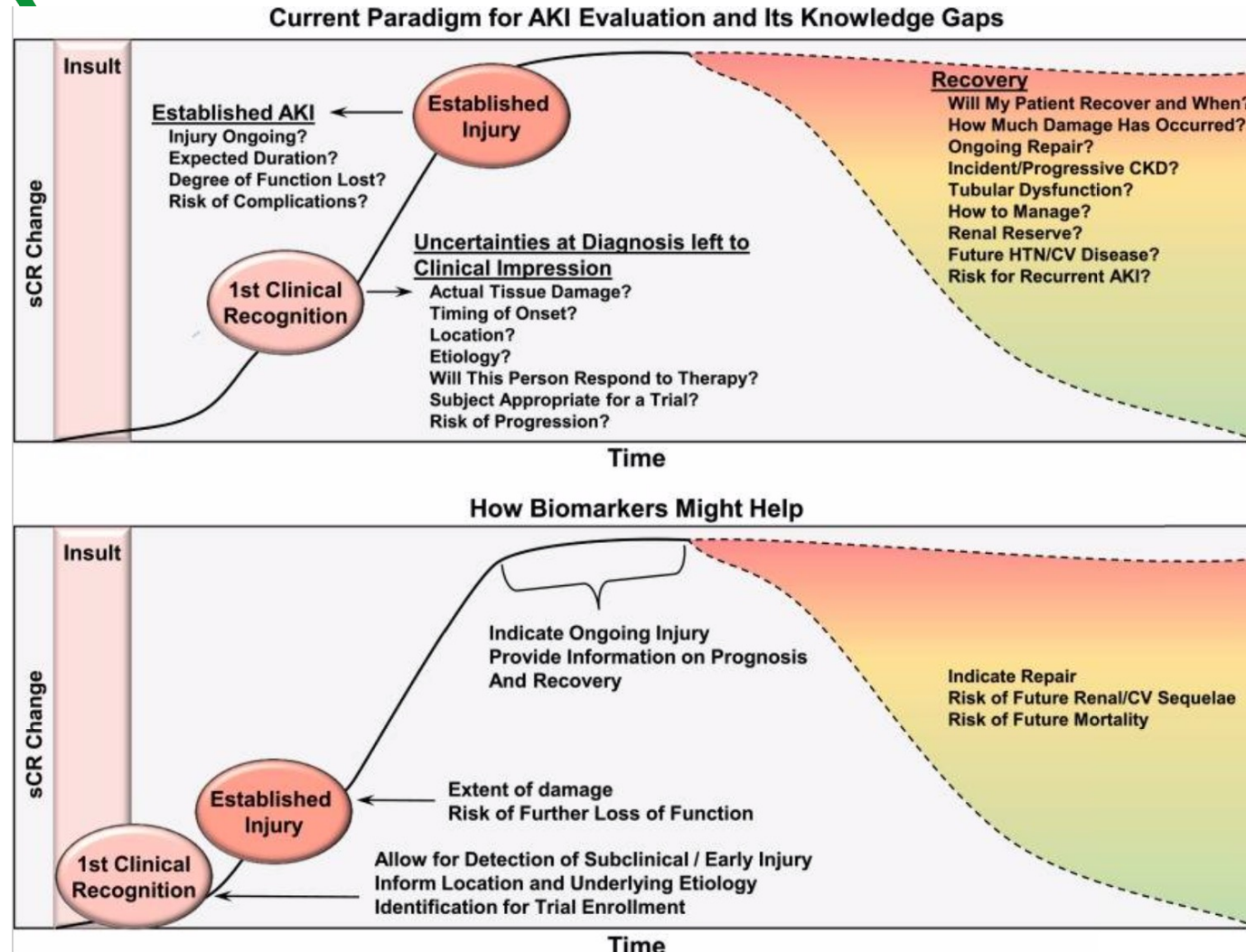
Very early changes in serum creatinine are associated with 30-day mortality after cardiac surgery

A cohort study

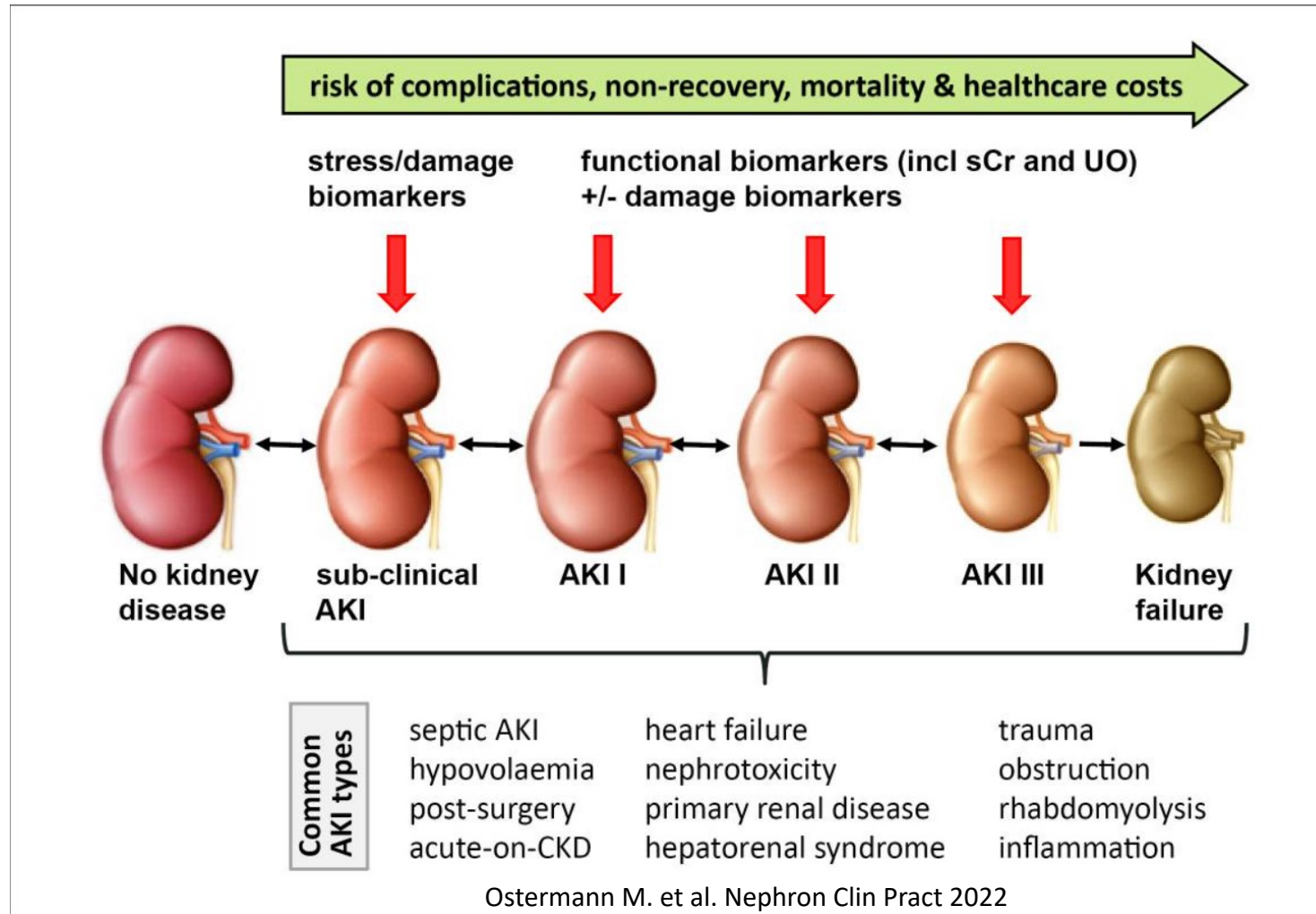
Martin H. Bernardi, Robin Ristl, Thomas Neugebauer, Michael J. Hiesmayr, Wilfred Druml and Andrea Lassnigg



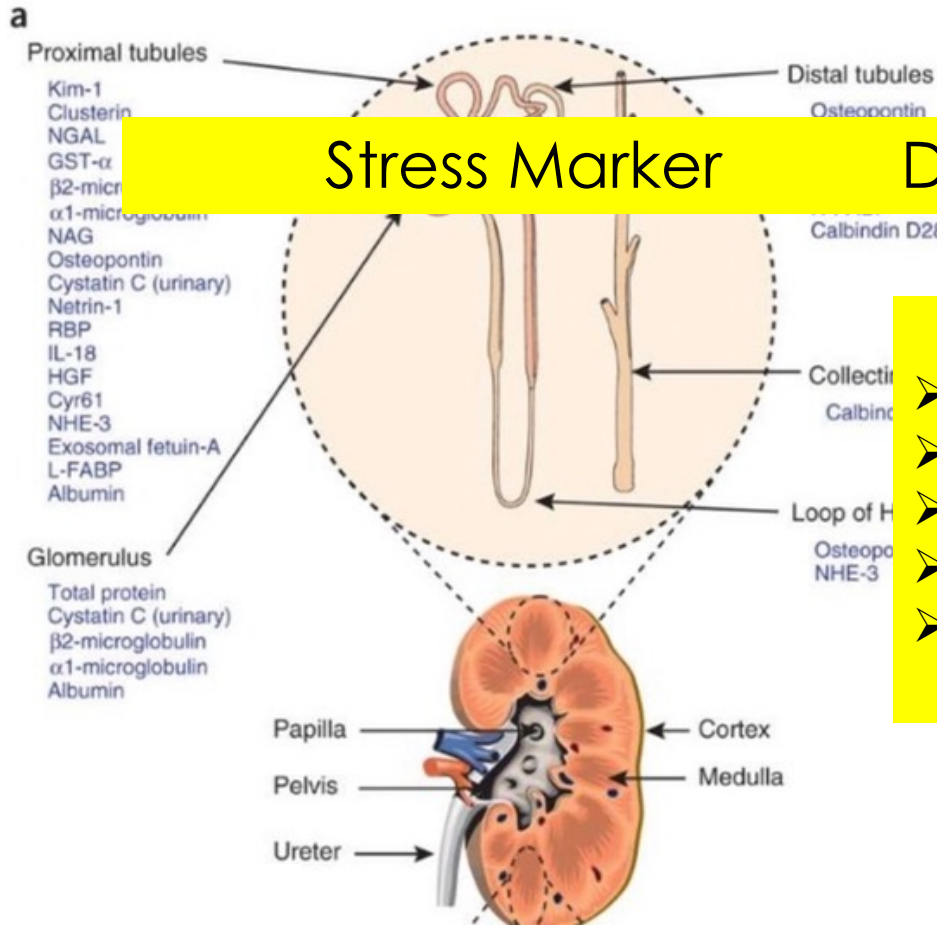
Biomarker



Biomarker



Biomarker



Stress Marker

Damage Marker

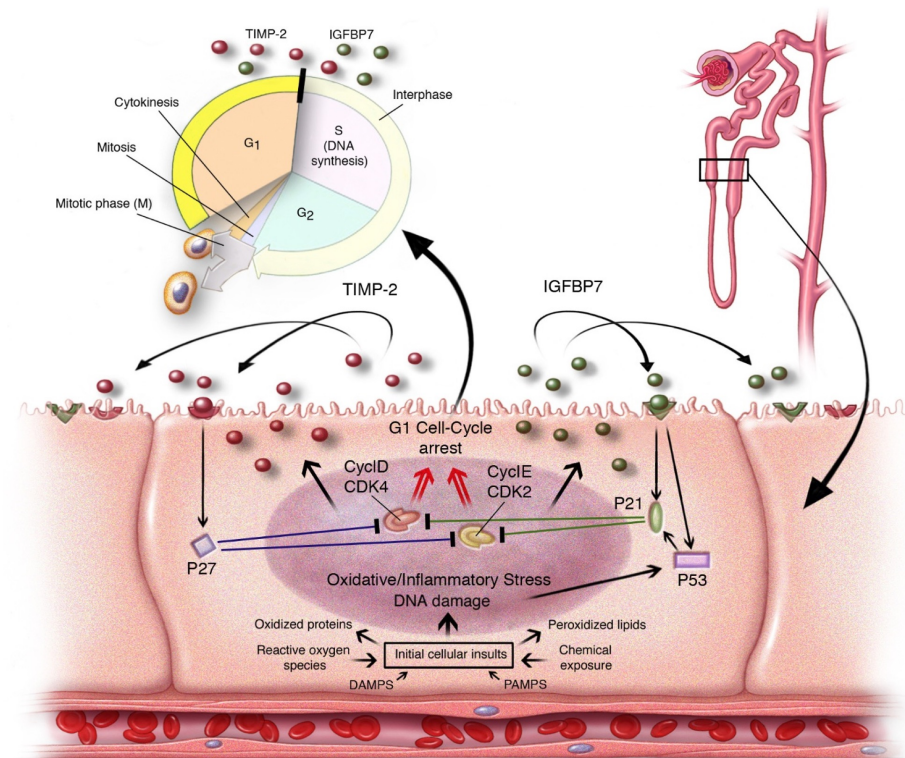
Functional Marker

- Risk assessment
- Prediction
- Diagnosis
- Severity
- Recovery


AKI biomarker	Biological role	Source	Stress marker ^a	Damage marker ^b	Functional marker ^c	Risk assessment	Prediction of AKI	Diagnosis of AKI	Severity of AKI	Kidney recovery
Alanine aminopeptidase; alkaline phosphatase; γ-glutamyl transpeptidase	Enzymes located on the brush border villi of the proximal tubular cells; released into urine after tubular damage	Coca et al, ² 2008		Urine				X	X	
Calprotectin	Cytosolic calcium-binding complex; derived from neutrophils and monocytes; detectable in urine in intrinsic AKI	Charlton et al, ³ 2014; Heller et al, ⁴ 2011		Urine				X		
C-C motif chemokine ligand 14	Pro-inflammatory chemokine; released into urine following stress or damage of tubular cells	Hoste et al, ⁵ 2020		Urine						X
Chitinase 3-like protein 1	39 kDa intracellular protein of glycoside hydrolase family; expressed by endothelial cells, macrophages, and neutrophils	De Loor et al, ⁶ 2016		Urine and plasma				X		
Cystatin C	13 kDa cysteine protease inhibitor produced by nucleated human cells; freely filtered	Coca et al, ² 2008; Ho et al, ⁷ 2015; Ravn et al, ⁸ 2019			Plasma			X	X	
Dickkopf-3	38 kDa stress-induced, kidney tubular epithelia-derived glycoprotein; secreted into urine under tubular stress conditions	Schunk et al, ⁹ 2019	Urine			X	X			
α glutathione S-transferase	Cytoplasmic enzyme in proximal tubule	Koynar et al, ¹⁰ 2010		Urine				X		
hepcidin	2.78 kDa peptide hormone predominantly produced in hepatocytes; freely filtered	Ho et al, ¹¹ 2015		Urine and plasma			X	X		
Tissue metalloproteinase-2; insulin-like growth factor binding protein-7	Metalloproteinases released during cell cycle arrest	Kashani et al, ¹² 2013; Ostermann et al, ¹³ 2018; Joannidis et al, ¹⁴ 2019	Urine			X	X	X		
Proinflammatory cytokine	released tubular damage	Coca et al, ² 2008; Ho et al, ⁷ 2015		Urine		X	X			
Glycoprotein produced by tubular cells; released into urine after tubular damage		Coca et al, ² 2008; Ho et al, ⁷ 2015; Koynar et al, ¹⁰ 2010		Urine		X	X	X		
Lipid chaperone; freely filtered in proximal tubule; released after tubular cell damage		Ho et al, ⁷ 2015		Urine and plasma			X			
Stranded non-coding individual microRNAs are especially in association with AKI and fibrosis		Fan et al, ¹⁵ 2019		Urine and plasma			X			
MicroRNAs released from tubular epithelial cells, podocytes and podocytes; released		Moledina et al, ¹⁶ 2017		Urine					X	
Enzyme; released into urine after tubular damage		Charlton et al, ³ 2014		Urine			X			
Cytokines: (1) monomeric 25 kDa protein produced by neutrophils and monocytes; (2) dimeric 135 kDa protein produced by monocytes		Coca et al, ² 2008; Ho et al, ⁷ 2015; Charlton et al, ³ 2014		Urine and plasma			X	X		
Proinflammatory molecule minimally filtered by normal tubular cells of normal kidneys; released into urine after tubular damage		Ramesh et al, ¹⁷ 2010		Urine				X		
Osteopontin	Glycoprotein expressed in tubular cells and interstitial infiltrating cells in areas of tubulointerstitial damage	Lorenzen et al, ¹⁸ 2011		Plasma			X	X		
Proenkephalin A	Endogenous polypeptide hormone in adrenal medulla, nervous system, immune system and renal tissue; freely filtered	Legrand et al, ¹⁹ 2019		Plasma			X	X	X	
Retinol binding protein	21 kDa glycoprotein; synthesized by liver; filtered by glomeruli and reabsorbed by proximal tubules; released into urine following tubular damage	Charlton et al, ³ 2014		Plasma						
Tumor necrosis factor	Pro-inflammatory cytokine; released after tubular damage	Ho et al, ⁷ 2015		Plasma			X			

TIMP2*IGFBP7

- IGFBP7 – insulin-like growth factor-binding protein 7
- TIMP-2 – tissue inhibitor of metalloproteinases-2
- „Cell cycle arrest“ Biomarkers
- Identifikation von Hochrisikopatient:innen



Biomarker



- Eventuell frühere Risikoerkennung

- Frühzei

- Redukt

Derzeit nicht
empfohlen!

- Hilfestellung bei Entscheidung zum Start/Stop einer RRT

Indikationen einer Nierenersatztherapie



Urgent indications (in the absence of contraindications to RRT)

Severe hyperkalemia unresponsive to medical measures for potassium removal (e.g., $K^+ \geq 6.0$ mmol/l, rapidly rising, or cardiac toxicity)
Severe acidemia and metabolic acidosis (e.g., $pH \leq 7.2$ or serum bicarbonate ≤ 12 mmol/l despite normal or low arterial pCO_2)
Refractory hypoxemia due to fluid overload (e.g., diuretic-resistant pulmonary edema)
Symptoms or complications attributable to uremia (e.g., pericarditis, encephalopathy)
Concomitant intoxication with a dialyzable drug/toxin

Relative indications (in the absence of life-threatening complications of AKI)

Advanced nonkidney organ dysfunction worsened or exacerbated by excessive fluid accumulation (i.e., impaired respiratory function)
Anticipated solute burden (e.g., tumor lysis syndrome; rhabdomyolysis; intravascular hemolysis)
Need for large volume fluid administration (i.e., nutrition, medications or blood products)

Relative contraindications

Low likelihood for benefit (i.e., futile prognosis)
Patient receiving palliative care and/or approaching end-of-life
High likelihood of nonrecovery of kidney function in patient who is not a candidate for long-term dialysis

Nierenersatztherapie Early vs. Late



Feature	ELAIN [36]	AKIKI [17]	IDEAL-ICU [33]	STARRT-AKI [18 ^{***}]
Country	Germany	France	France	Multi-National
No. of sites	1	31	24	168
No. of participants	231	620	488 ^a	3019
Setting/population	Mixed medical/surgical ICU (94.8% surgical)	Mixed medical/surgical ICU (79.7% medical)	Mixed medical/surgical ICU (septic shock)	Mixed medical/surgical ICU
ARR for sample size calculation	18%	15%	10%	6%
Control group mortality	55%	55%	55%	44%
Interventions:				
Early (accelerated)	KDIGO stage 2 (within 8 h)	KDIGO stage 3 (within 6 h)	RIFLE-failure (within 12 h)	KDIGO stage 2 (within 12 h)
Delayed (conservative)	KDIGO stage 3 (within 12 h)	Specific criteria/emergent indications	Specific criteria 48–60 h after eligibility or emergent indications	Specific criteria/emergent indications
Actual inter-arm time difference in RRT initiation (h)	19.5	55	44	25
Received RRT in delayed	90.8%	51.0%	62.0%	61.8%
RRT modality	CRRT	Physician discretion (initial IHD 55%)	Physician discretion	Physician discretion
SOFA score at enrollment	~16.0	~10.9	~12.3	~11.7
Primary endpoint	90-day mortality	60-day mortality	90-day mortality	90-day mortality
Early (accelerated)	39.3%	48.5%	58.0%	43.9%
Delayed (conservative)	54.7%	49.7%	54.0%	43.7%
Effect estimate	HR, 0.66 (95% CI 0.45–0.97)	HR, 1.03 (95% CI 0.82–1.29)	RR, 1.08 ^b (95% CI 0.90–1.30)	RR, 1.00 (95% CI 0.93–1.09)
Kidney recovery	RRT dependence at 90 days	RRT dependence at 60 days	RRT dependence at 90 days	RRT dependence at 90 days
Early (accelerated)	53.6%	2.0%	2.0%	10.4%
Delayed (conservative)	38.7%	5.0%	3.0%	6.0%
Effect estimate	OR, 0.55 (95% CI 0.32–0.93)	RR, 0.53 ^b (95% CI 0.20–1.41)	RR, 0.83 ^b (95% CI 0.28–2.46)	RR, 1.74 (95% CI 1.24–2.43)
Adverse events	Aggregate	CRBSI	Indication for emergent RRT ^c	Aggregate
Early (accelerated)	75.0%	10.0%	–	23.0%
Delayed (conservative)	68.5%	3.0%	17%	16.5%
Effect estimate	RR, 1.18 ^b (95% CI 0.86–1.61)	RR, 1.35 ^b (95% CI 1.08–1.68)	–	RR, 1.40 (95% CI 1.21–1.62)

Danke für die
Aufmerksamkeit!



Martin Bernardi

ANÄSTHESIE FORUM



ALPBACH

REPETITORIUM
