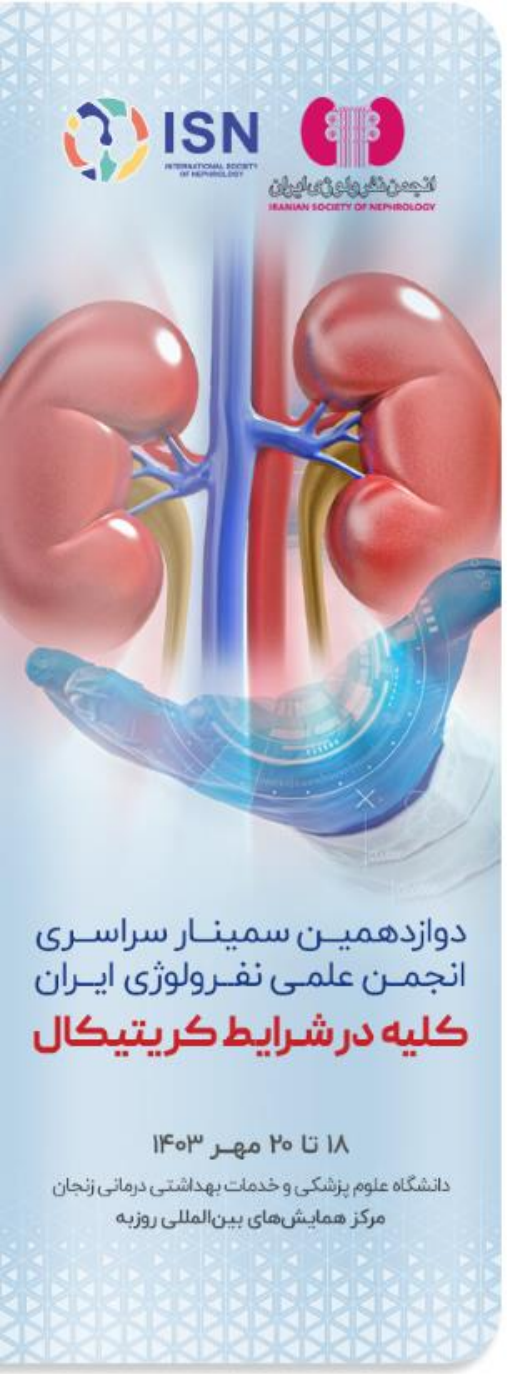

AKI in Cardiac Surgery

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Outlines

- Definition
- Pathogenesis
- Outcome
- Risk factors and Prediction
- Prevention and Treatment

Expanded Challenges in Cardiac Surgery

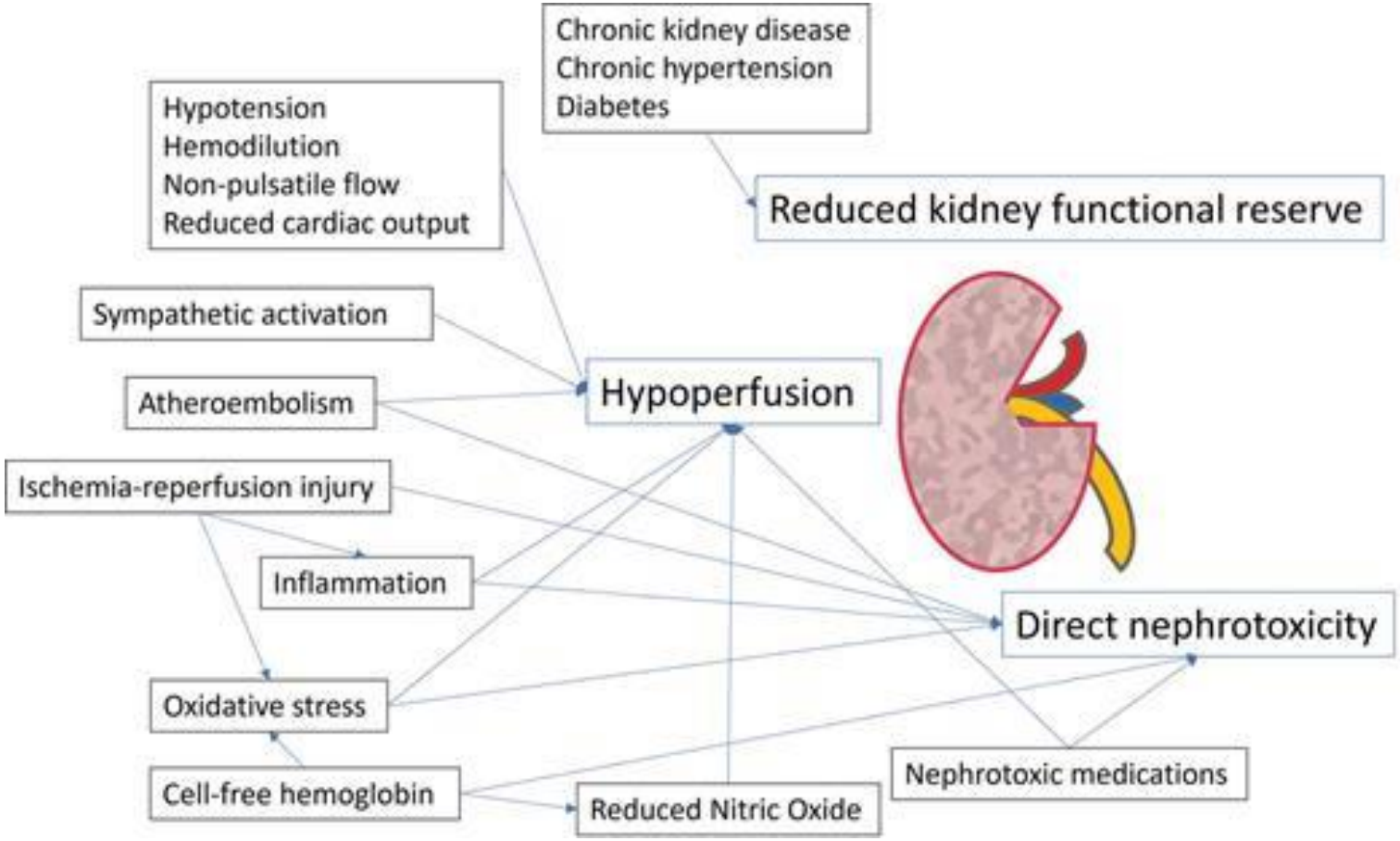
- Older patients
- Multiple procedures within operation
- Reoperation
- Comorbidities
- Coagulopathies
- New supportive technology(LVAD,ECMO,..)

Defining acute kidney injury

RIFLE		AKIN		KDIGO		Urine output*
Criteria	Creatinine definition	Criteria	Creatinine definition	Criteria	Creatinine definition	
Risk	≥1.5-fold increase from baseline SCr or decrease in GFR ≥25%	Stage 1	≥0.3 mg/dL increase or ≥1.5-fold increase from baseline SCr within 48 hrs	Stage 1	≥0.3 mg/dL increase within 48 hrs or 1.5–1.9 times baseline within 7 days	<0.5 mL/kg/h for >6 hours
Injury	≥2-fold increase from baseline SCr or decrease in GFR ≥50%	Stage 2	≥2-fold increase from baseline SCr	Stage 2	2.0–2.9 times baseline within 7 days	<0.5 mL/kg/h for 12 hours
Failure	≥3-fold increase from baseline SCr or increase to ≥4 mg/dL or decrease in GFR ≥75%	Stage 3	≥3-fold increase from baseline SCr or increase to ≥4.0 mg/dL with an acute increase of >0.5 mg/dL or initiation of RRT	Stage 3	≥3 times baseline within 7 days or increase to ≥4.0 mg/dL with an acute increase of >0.5 mg/dL or initiation of RRT	<0.3 mL/kg/h for 24 hours or anuria for >12 hours

RIFLE: risk, injury, failure, loss, end-stage kidney disease; AKIN: acute kidney injury network; KDIGO: kidney disease: improving global outcomes; SCr: serum creatinine; GFR: glomerular filtration rate; RRT: renal replacement therapy.
*Urine output criteria are common to three definitions.

Pathogenesis




WHY IS THAT
IMPORTANT?

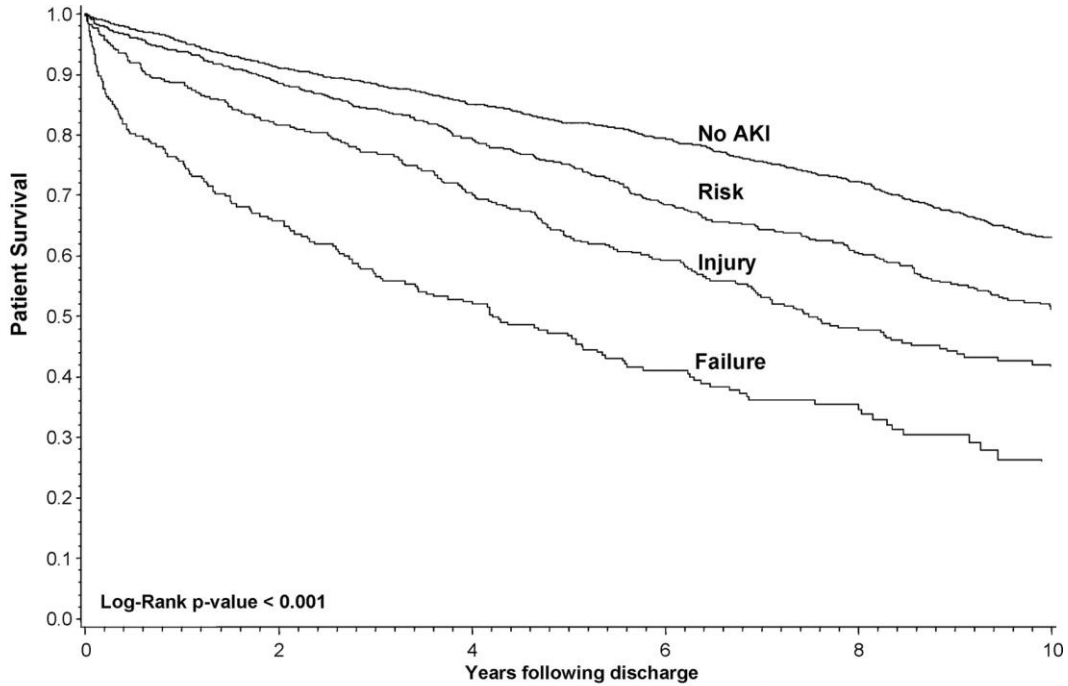
Circulation
Volume 119, Issue 18, 12 May 2009; Pages 2444-2453
https://doi.org/10.1161/CIRCULATIONAHA.108.800011

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, and Azra Bihorac, MD

Abstract: ***Background***— Long-term survival after acute kidney injury (AKI) is poorly studied. We report the relationship between long-term mortality and AKI with small changes in serum creatinine during hospitalization after various cardiothoracic surgery procedures.***Methods and Results***— This was a retrospective study of 2973 patients with no history of chronic kidney disease who were discharged from the hospital after cardiothoracic surgery between 1992 and 2002. AKI was defined by the RIFLE classification (Risk, Injury, Failure, Loss, and End stage), which requires at least a 50% increase in serum creatinine and stratifies patients into 3 grades of AKI: Risk, injury, and failure. Patient survival was determined through the National Social Security Death Index. Long-term survival was analyzed with a risk-adjusted Cox proportional hazards regression model. Survival was worse among patients with AKI and was proportional to its severity, with an adjusted hazard ratio of 1.23 (95% CI 1.06 to 1.42) for the least severe RIFLE risk class and 2.14 (95% CI 1.73 to 2.66) for the RIFLE failure class compared with patients without AKI. Survival was worse among all subgroups of cardiothoracic surgery with AKI except for valve surgery. Patients with complete renal recovery after AKI still had an increased adjusted hazard ratio for death of 1.28 (95% CI 1.11 to 1.48) compared with patients without AKI.***Conclusions***— The risk of death associated with AKI after cardiothoracic surgery remains high for 10 years regardless of other risk factors, even for those patients with complete renal recovery. Improved renal protection and closer postdischarge follow-up of renal function may be warranted.



Follow Up (years)		T=0	T=2	T=4	T=6	T=8	T=10
At risk (n)	No AKI	1708	1555	1454	1075	770	465
	Risk	637	564	504	364	259	165
	Injury	386	315	265	181	121	61
	Failure	242	159	125	79	42	15

Review Article

The Impact of Acute Kidney Injury on Chronic Kidney Disease After Cardiac Surgery: A Systematic Review and Meta-analysis

Rasmus Bo Lindhardt[*,†,1], Sebastian Buhl Rasmussen[*,†], Lars Peter Riber[†,‡], Jens Flensted Lassen[†,§], Hanne Berg Ravn[*,†]

[*]*Department of Anesthesiology and Intensive Care, Odense University Hospital, Odense, Denmark*
[†]*Department of Clinical Research, Health Faculty, University of Southern Denmark, Odense, Denmark*
[‡]*Department of Cardiac, Thoracic and Vascular Surgery, Odense University Hospital, Odense, Denmark*
[§]*Department of Cardiology, Odense University Hospital, Odense, Denmark*

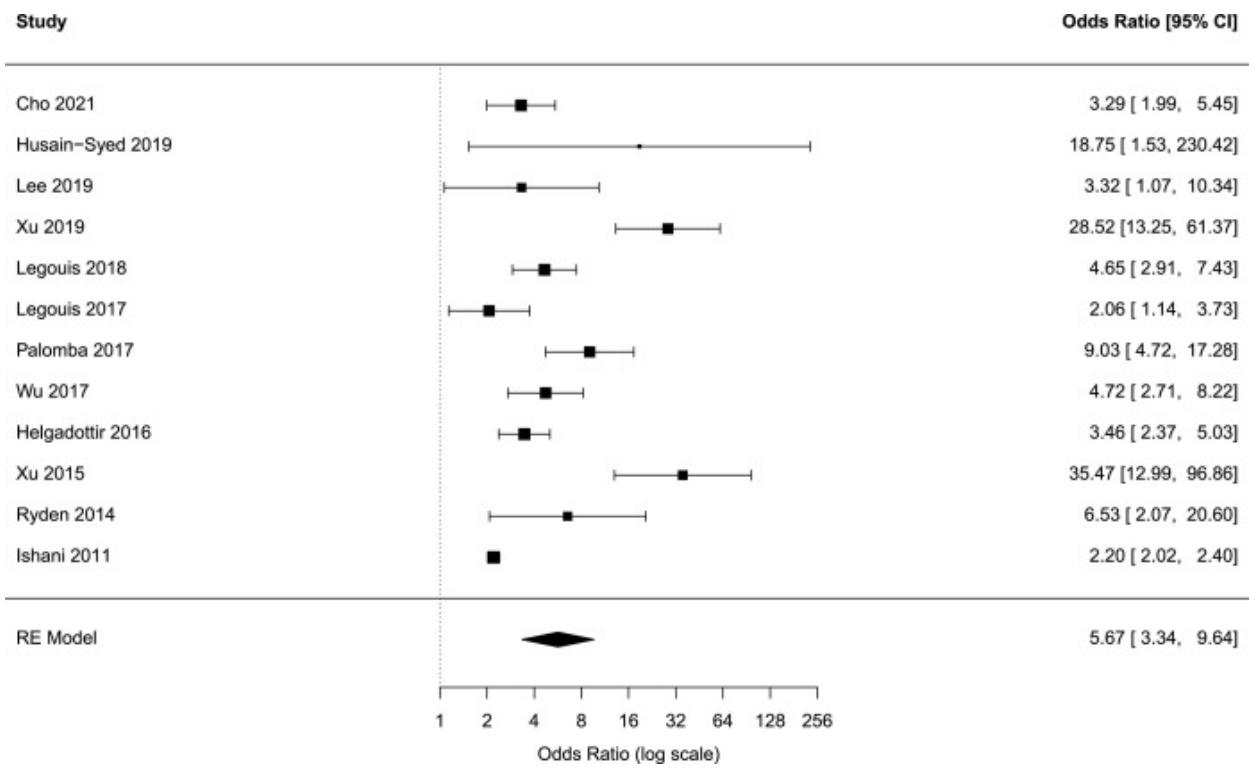
Objectives: To evaluate the impact of acute kidney injury on transition to chronic kidney disease (CKD) after cardiac surgery and to determine frequency of incident CKD in these patients.

Design: A systematic review and meta-analysis of observational studies.

Setting: Electronic databases Medline and Embase were systematically searched from 1974 to February 6, 2023.

Participants: Eligible studies were original observational studies on adult cardiac surgery patients, written in the English language, and with clear kidney disease definitions. Exclusion criteria were studies with previously transplanted populations, populations with preoperative kidney impairment, ventricular assist device procedures, endovascular procedures, a kidney follow-up period of <90 days, and studies not presenting necessary data for effect size calculations.

Interventions: Patients developing postoperative acute kidney injury after cardiac surgery were compared with patients who did not develop



5-fold increased odds of developing CKD.

New-onset CKD in 1/4 patients

CSA-AKI Prediction

- Several risk scores to predict AKI:
  - Cleveland Clinic score
  - Mehta score
  - Simplified Renal Index (SRI) score

- No guidelines for use of a specific prediction model

- Poor for predicting non-RRT AKI

- Rahmanian
- Palomba
- Aronson
- Thakar
- Mehta
- Fortescue
- Wijeysundera

Comparison and clinical suitability of eight prediction models for cardiac surgery-related acute kidney injury Get access >

Harmke D. Kiers ✉, Mark van den Boogaard, Micha C.J. Schoenmakers, Johannes G. van der Hoeven, Henry A. van Swieten, Suzanne Heemskerk, Peter Pickkers

Nephrology Dialysis Transplantation, Volume 28, Issue 2, February 2013, Pages 345–351,

The Thakar model offers the best discriminative value to predict CSA-AKI and is applicable in a preoperative setting and for all patients undergoing cardiac surgery.

CLINICAL NEPHROLOGY

A Clinical Score to Predict Acute Renal Failure after Cardiac Surgery

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

Author Information

Journal of the American Society of Nephrology 16(1):p 162-168, January 2005. | **DOI:** 10.1681/ASN.2004040331

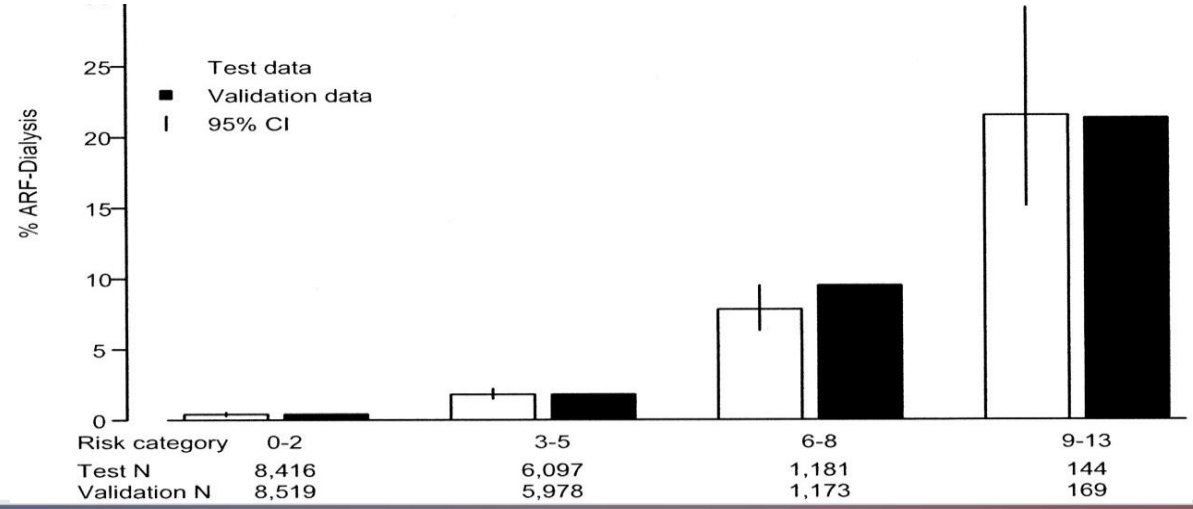
33,217 patients underwent open-heart surgery at the Cleveland Clinic Foundation (1993 to 2002)

The primary outcome was ***ARF that required dialysis***

Table 1. Logistic model parameter estimates, score points, and AUC for each risk factor included in the scoring modela

Risk Factor	Estimate (CI)	*P* Value	Points	AUC for Single Variable
Female gender	0.48 (0.21–0.75)	<0.001	1	55.3
Congestive heart failure	0.48 (0.20–0.76)	<0.001	1	63.9
Left ventricular ejection fraction <35%	0.39 (0.07–0.71)	0.016	1	56.4
Preoperative use of IABP	1.08 (0.49–1.67)	<0.001	2	52.6
COPD	0.70 (0.37–1.04)	<0.001	1	54.8
Insulin-requiring diabetes	0.40 (0.05–0.76)	0.026	1	54.4
Previous cardiac surgery	0.54 (0.28–0.81)	<0.001	1	57.5
Emergency surgery	1.13 (0.65–1.60)	<0.001	2	54.3
Surgery type				
valve only	0.45 (0.10–0.80)	0.013	1	63.3
CABG + Valve	0.86 (0.53–1.19)	<0.001	2	
other cardiac surgeries	1.02 (0.56–1.49)	<0.001	2	
Preoperative creatinine 1.2 to <2.1 mg/dl	0.92 (0.64–1.21)	<0.001	2	68.6
Preoperative creatinine ≥2.1 mg/dl	2.66 (2.28–3.04)	<0.001	5	

[a] CI, confidence interval; AUC, area under the receiver operating characteristic curve; IABP, intra-aortic balloon pump; COPD, chronic obstructive pulmonary disease.



Cleveland Clinic Score		Mehta Score		Simplified Renal Index	
Derivation Cohort: 15,838 cardiac surgery patients, Single U.S. Center, 1993–2002		Derivation Cohort: 449,524 cardiac surgery patients, database of > 600 centers, 2002–2004		Derivation Cohort: 10,751 cardiac surgery patients, single Canadian center, 1999–2004	
Validation Cohort: 17,379 cardiac surgery patients from the same center and time period		Validation Cohort: 86,009 cardiac surgery patients from the same database, 2005		Validation Cohort: 9,380 cardiac surgery patients, two Canadian centers, 1999–2003	
Variable	**Points**	**Variable**	**Points**	**Variable**	**Points**
Female sex	1	Age ≥ 55	0–10	Preoperative glomerular filtration rate	1–2
Congestive heart failure	1	Non-White race	2	Diabetes requiring medications	1
Left ventricular ejection fraction < 35%	1	Preoperative serum creatinine	5–40	Left ventricular ejection fraction ≤40%	1
Preoperative intra-aortic balloon pump	2	New York Heart Association Class IV heart failure	3	Previous cardiac surgery	1
Chronic obstructive pulmonary disease	1	Diabetes treated with oral medications	2	Preoperative intra-aortic balloon pump	1
Insulin-dependent diabetes	1	Insulin-dependent diabetes	5	Nonelective surgery	1
Previous cardiac surgery	1	Chronic obstructive pulmonary disease	3	Type of surgery	0–1
Emergency surgery	2	Recent myocardial infarction	3		
Type of surgery	0–2	Previous cardiac surgery	3		
Preoperative serum creatinine	0–5	Cardiogenic shock	7		
		Type of surgery	0–7		
Score range	0–17	**Score range**	0–85	**Score range**	0–8

Calculator | About | References

Dialysis Risk After Cardiac Surgery (Cleveland Clinic Score by Thakar)

Estimate risk of dialysis after cardiac surgery.

Questions

1. **Gender?**
2. Heart Failure?
3. Ejection Fraction <35%?
4. Preoperative Use of IABP?
5. COPD Requiring Medical Therapy?
6. Diabetes Requiring Insulin?
7. Past Cardiac Surgery?
8. Preoperative CKD: Creatinine?
9. Emergency Surgery?

Biomarkers

- **serum creatinine** :

✓diagnostic criteria for CSA- AKI

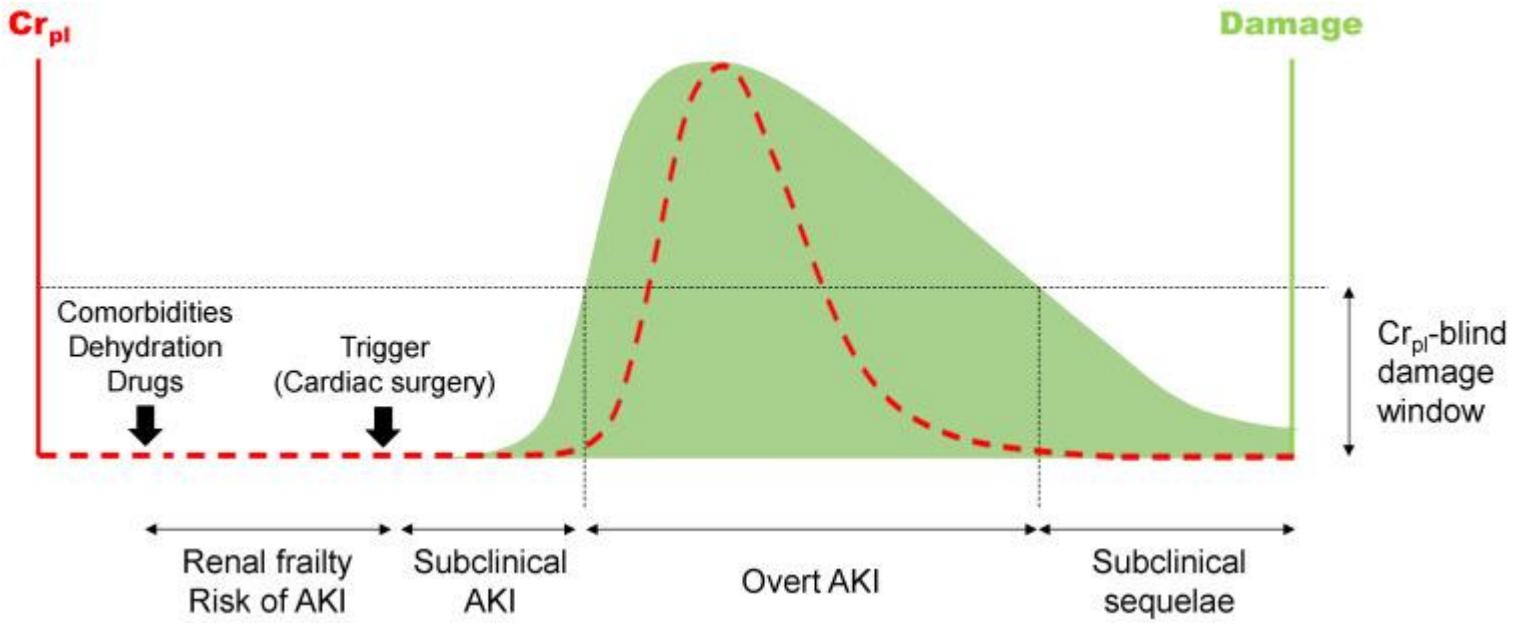
✓Diminished accuracy in non–steady state conditions

- **Other AKI-related biomarkers**

Better prediction

Earlier detection

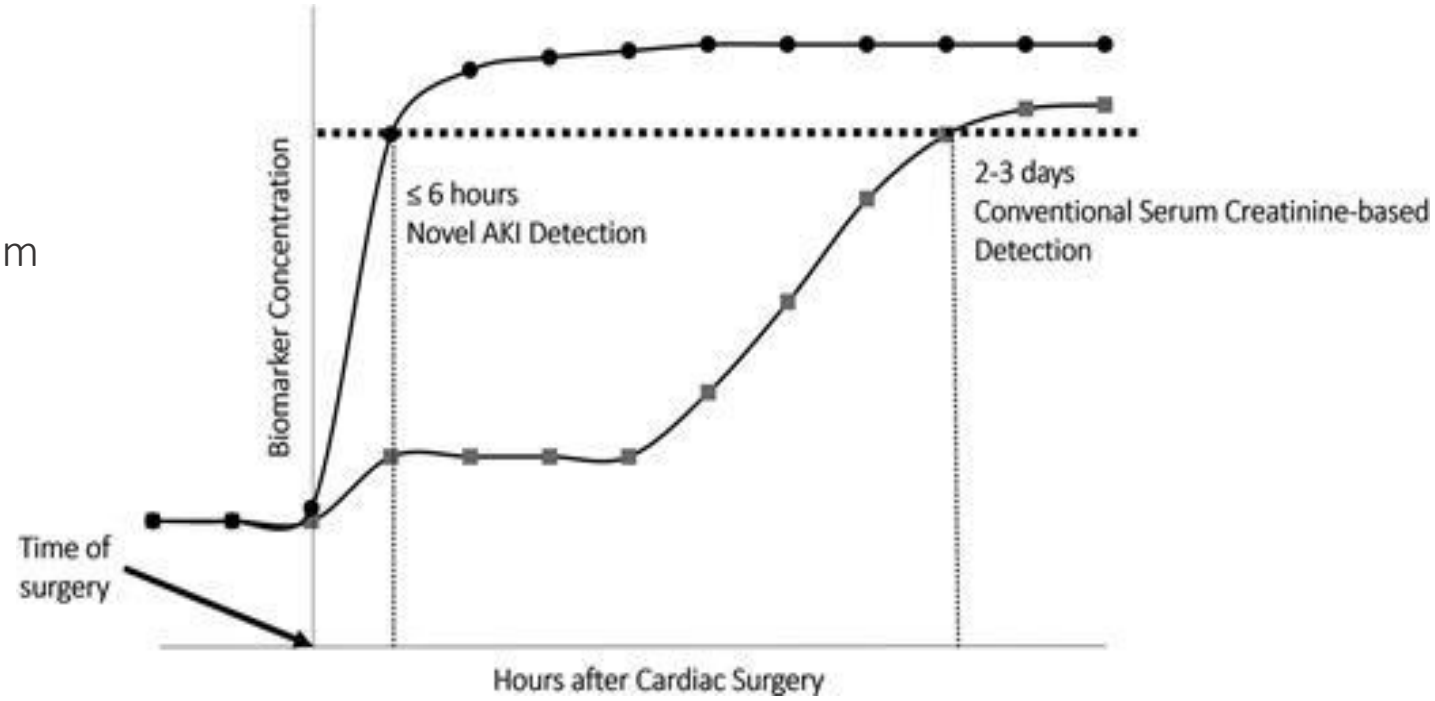
Perform inconsistently



Stages of AKI potentially subject to diagnosis

- Diagnosis of Cardiac Surgery-Associated Acute Kidney Injury: State of the Art and Perspectives, 2022

- Timeline highlighting the potential for novel biomarkers to identify AKI as compared to serum creatinine-based criteria



Acute Kidney Injury after Cardiac Surgery: Prediction, Prevention, and Management (Sreekanth R. Cheruku)

Biomarker	Source	Pathophysiology	Utility in Cardiac Surgery	Limitations
Neutrophil gelatinase-associated lipocalin	Blood, urine	Upregulated in the proximal tubules after ischemic or nephrotoxic injury to the kidneys	Early detection of AKI	More specific in children and adults without chronic kidney disease.
Cystatin C	Blood	Functional biomarker with decreased clearance in AKI	Early detection of AKI Unaffected by differences in muscle mass.	Some studies have indicated that Cystatin C has lower predictive value.
Interleukin-18	Urine	Mediates ischemic and inflammatory kidney injury in the proximal tubules	Early detection of AKI	Some studies have indicated that interleukin-18has lower predictive value.
Kidney injury molecule-1	Urine	Rapidly expressed in proximal tubular cells after ischemic kidney injury	Early detection of AKI	Some studies have indicated that it peaks up to 2–3 days after kidney injury.
[Tissue inhibitor of metalloproteinase]x[insulin-like growth factor-binding protein 7]	Urine	Induces cell cycle arrest in renal tubular cells	Early detection of AKI Better sensitivity and specificity in predicting AKI.	Some studies have indicated that these biomarkers have lower specificity.
C-C motif chemokine ligand 14	Urine	Mediates inflammatory kidney injury in the proximal tubules	Predicts persistent AKI and the need for renal replacement therapy- and can be used as a marker for progression of AKI to chronic kidney disease	Does not provide early detection of AKI

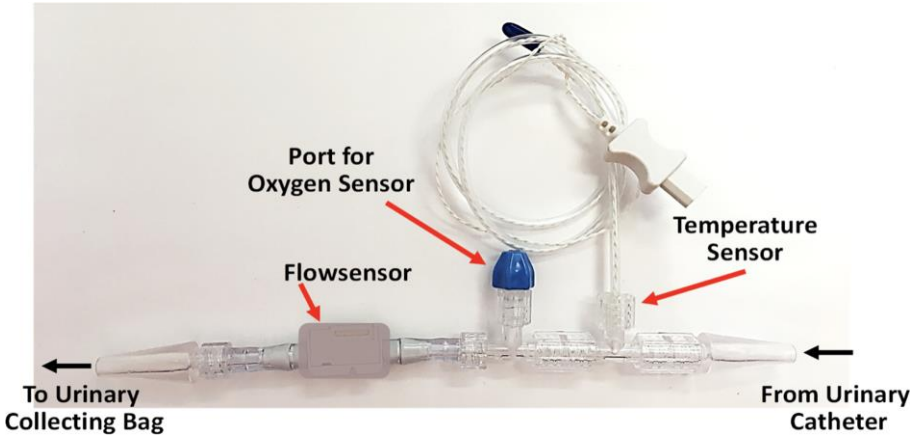
AKI, acute kidney injury

- Early rise in serum **cystatin C** : increase requiring RRT
- **IL18** : elevated in CSA- AKI, as early as 4 to 6h after CPB
- Combination of **KIM-1** and **IL-18** : excellent predictive value
- **Tissue inhibitor of metalloproteinase** & **insulin-like growth factor -binding protein**: superior sensitivity and specificity in predicting KDIGO stage 2 to 3 AKI
- **C-C motif chemokine ligand 14** : renal nonrecovery

Other Predicting Tests

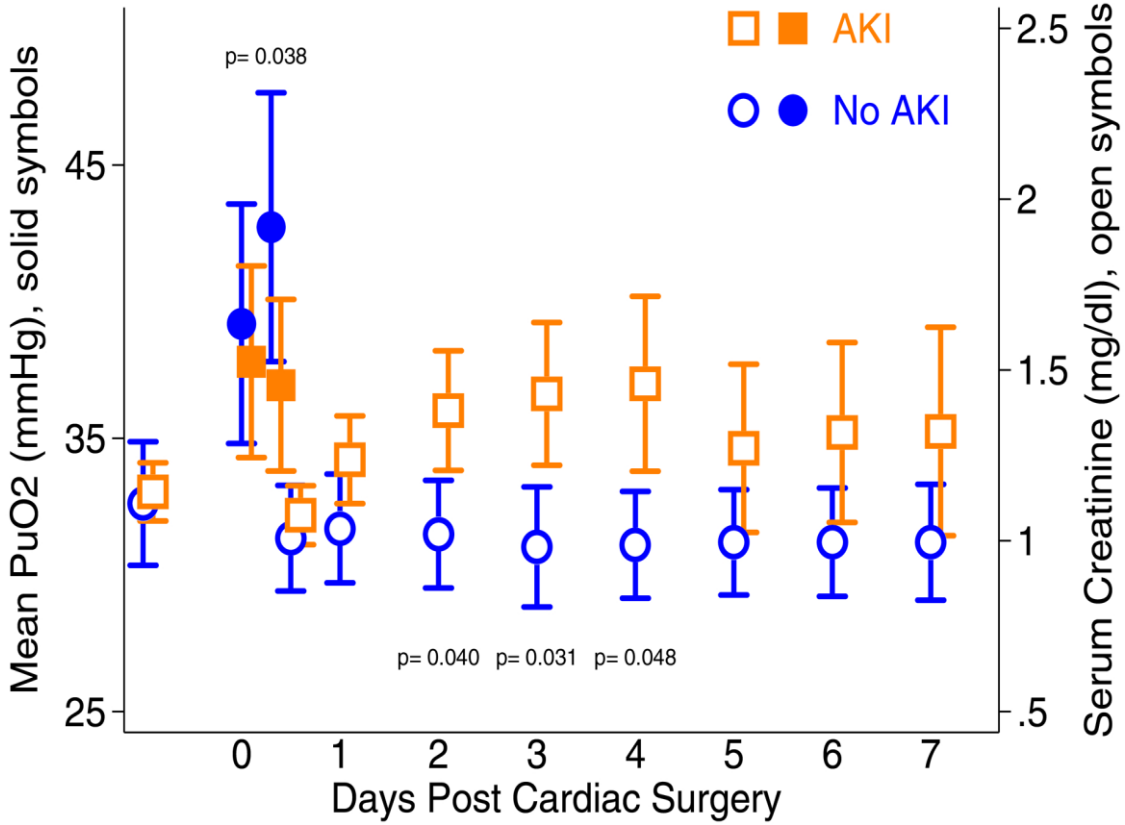
- Renal Functional Reserve
- Noninvasive Urine Oximetry

Noninvasive Urine Oximetry



Noninvasive urine oxygen monitoring and the risk of acute kidney injury in cardiac surgery

Natalie A. Silverton, MD FRCPC FASE,[1] Lars R. Lofgren, BS,[1] Isaac E. Hall, MD MS,[2] Gregory J. Stoddard, MPH MBA,[3] Natalia P. Melendez,[4] Michael Van Tienderen, DO,[1] Spencer Shumway,[6] Bradley J. Stringer,[1] Woon-seok Kang, MD,[5] Carter Lybbert,[7] and Kai Kuck, PhD[1]



Renal Functional Reserve

Proposed roles of renal functional reserve as a biomarker

- ✓ Detection of subclinical kidney disease in high-risk groups such as patients with hypertension, diabetes mellitus, or systemic sclerosis
- ✓ Preoperative clinical risk assessment for AKI in individuals undergoing high-risk surgery (e.g., cardiac surgery)
- ✓ Assessment of level of renal recovery after AKI
- ✓ Pre donation risk stratification among living kidney donors

Renal functional reserve: from physiological phenomenon to clinical biomarker and beyond(2020)

Preoperative Strategies to Prevent CSA-AKI

- **Pharmacological Interventions**:

  No specific drugs proven effective

- **Optimization of Preoperative Medication**:Avoid nephrotoxins

  ACE inhibitors/ARBs: Controversial

- **Prehabilitation**:

  Recommended to begin at least 4 weeks pre-surgery.

  Focus on education, nutrition, exercise

  Evidence of benefits remains unclear.

Pharmacological Interventions

- **No specific drugs proven effective for preventing CSA-AKI**
- Various agents evaluated (e.g., corticosteroids, N-acetylcysteine, dopamine) but none routinely recommended.
- **Dexmedetomidine**:Mixed results; potential nephroprotective effects but caution due to hypotension.
- **Atrial Natriuretic Peptide (ANP) :**Low-dose may reduce RRT needs
- high doses linked to adverse events
- **Levosimendan**:Limited impact on AKI
- some evidence for reduced RRT need in specific trials.

Intraoperative Strategies for Preventing CSA-AKI

- Optimal Target of Mean Arterial Pressure (MAP)
- Inotropic and Vasopressor Support
- Transfusion Strategies
- Remote Ischaemic Preconditioning (RIPC)
- Goal-Directed Oxygen Delivery on CPB
- CPB Rewarming Temperature

- **MAP Considerations:**
  - MAP < 65 mmHg for >10 min linked to increased RRT risk.
  - Controversy: Meta-analyses show weak association between intraoperative hypotension and AKI.
  - Recommended MAP: 50-80 mmHg during CPB (EACTS guidelines)

- **Inotropic and Vasopressor Support:**
- Inotropes improve renal perfusion in low cardiac output.
- Vasopressors increase renal perfusion pressure in hypotension.
- Vasopressin vs. Norepinephrine: Ongoing debate on first-line treatment for vasoplegia

.

- **Fluid Management:**
- Complex balance: Avoid both excessive fluid accumulation and hypovolemia.
- Higher positive fluid balance linked to increased AKI.
- Restrictive fluid strategies may reduce complications

•Goal-Directed Therapy:

•Aims to optimize cardiac output and oxygen delivery.
•Associated with reduced AKI incidence post-surgery

•Transfusion Strategies:

•Restrictive transfusion strategy (Hct ≥ 24%) shows noninferior outcomes compared to liberal strategies.
•Current guideline: Transfusion if Hb < 6.0 g/dL

.

•Remote Ischaemic Preconditioning (RIPC):

•Controversial role in AKI prevention.
•Mixed results from studies

CPB

- Initial Evidence :Off-pump CABG suggested to reduce AKI risk
- Recent RCT Findings : No significant difference in AKI prevention compared to on-pump surgery

➢ **Off-Pump CABG Benefits**: Reduced bleeding and respiratory complications

➢ **Off-pomp Concerns** :Increased early revascularization ,Lower graft patency rates

Trials:

ROOBY: No survival or renoprotective benefits, Higher rate of cardiac death

CORONARY :No significant difference in AKI prevention compared to on-pump surgery

HEPCON : limited overall effect of CPB on AKI.

Anemia and Transfusion of Packed RBC

- Anemia and transfusions increase AKI risk in cardiac surgery
- Combined effects elevate risk more than either factor alone

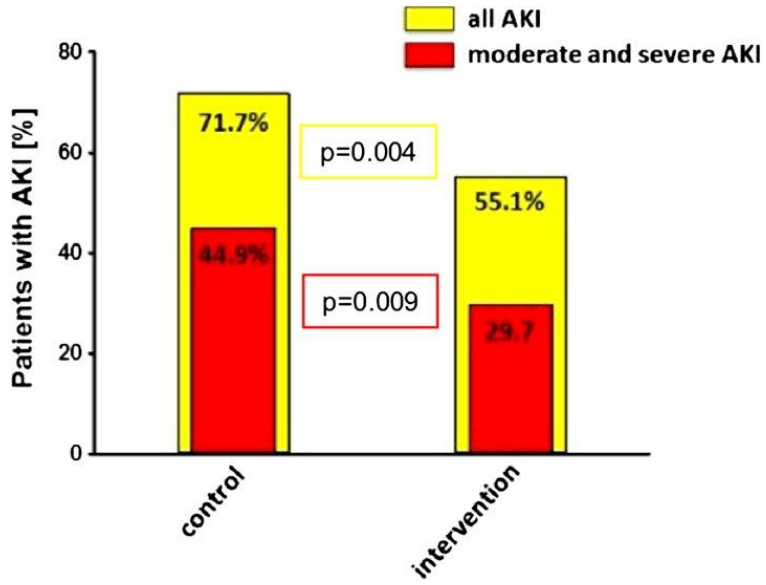
- **Transfusion Strategies** : Restrictive: Hematocrit ≥ 24%
- Guidelines :Transfusion recommended if hemoglobin < 6 g/dl
  Acceptable hematocrit: 21% - 24% with adequate oxygen delivery.

Postoperative strategies:KDIGO Bundle of Care for AKI

Randomized Controlled Trial > Intensive Care Med. 2017 Nov;43(11):1551-1561.
doi: 10.1007/s00134-016-4670-3. Epub 2017 Jan 21.

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], Alexander Zarbock [4]



FEATURED ARTICLES: ORIGINAL CLINICAL RESEARCH REPORT

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,

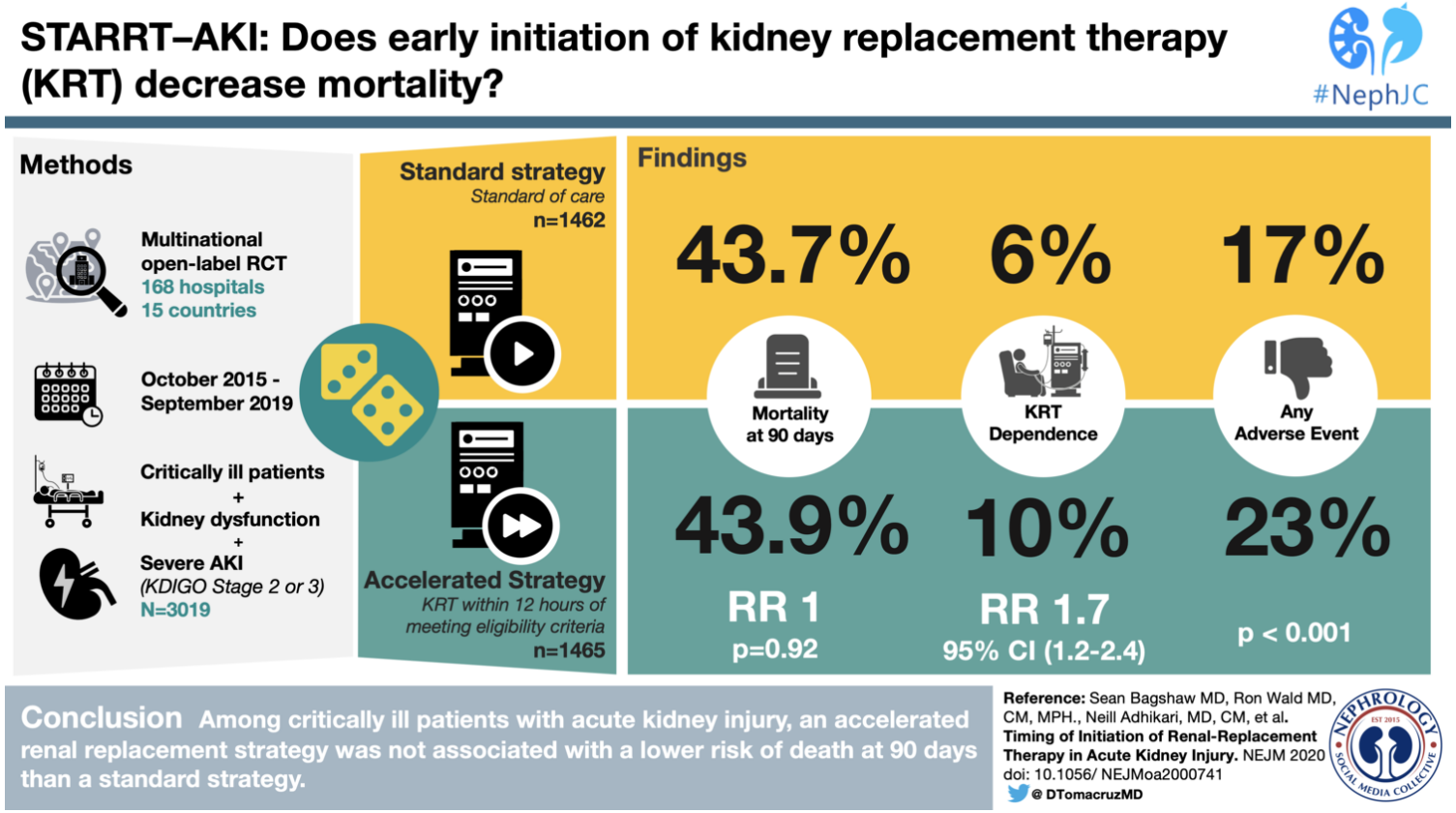
- **Incidence of stage 2 and 3 AKI was significantly lower in the KDIGO bundle group**

KDIGO Bundle of Care for AKI

- **Early Risk Assessment**: Identify patients at high risk for AKI preoperatively.
- **Monitoring Kidney Function** :Regularly check serum creatinine and urine output post-surgery.
- **Optimized Fluid Management** :Tailor fluid therapy to maintain adequate renal perfusion.
- **Medication Management**: Review and adjust nephrotoxic medications; avoid if possible.
- **Nutritional Support**: Ensure adequate nutrition to support recovery.
- **Multidisciplinary Approach**: A medical team for coordinated care

RRT Initiation in CSA-AKI

Best Practices and Considerations?



Early RRT may lead to higher long-term dependence.
Delayed RRT strategies show better outcomes

RRT in CSA-AKI

- **Current Best Practices**:

  Reserve RRT for refractory issues: Electrolyte imbalances ,Acid-base disturbances ,Volume overload

  - ❖ Delayed RRT strategies show better outcomes
  - ❖ For patients with high likelihood of RRT, early initiation is preferred
  - ❖ Importance of Monitoring

- **RRT Modalities**:

  both Intermittent and continuous RRT options

  CRRT preferred for hemodynamically unstable patients

Cytosorb Filters in Cardiac Surgery

•**Extracorporeal Cytokine Removal:**
•Intended to reduce inflammatory products during cardiac surgery.

•**Current Findings:**
•Studies show **no significant benefits** in patient outcomes.
•Limited ability to remove cell-free hemoglobin.

•**Usage Restrictions:**
•Effective only in specific scenarios with extracorporeal circulation.

•**Conclusion:**
•Current evidence does not support routine use in cardiac surgery.
•Further research may be needed to explore potential benefits.

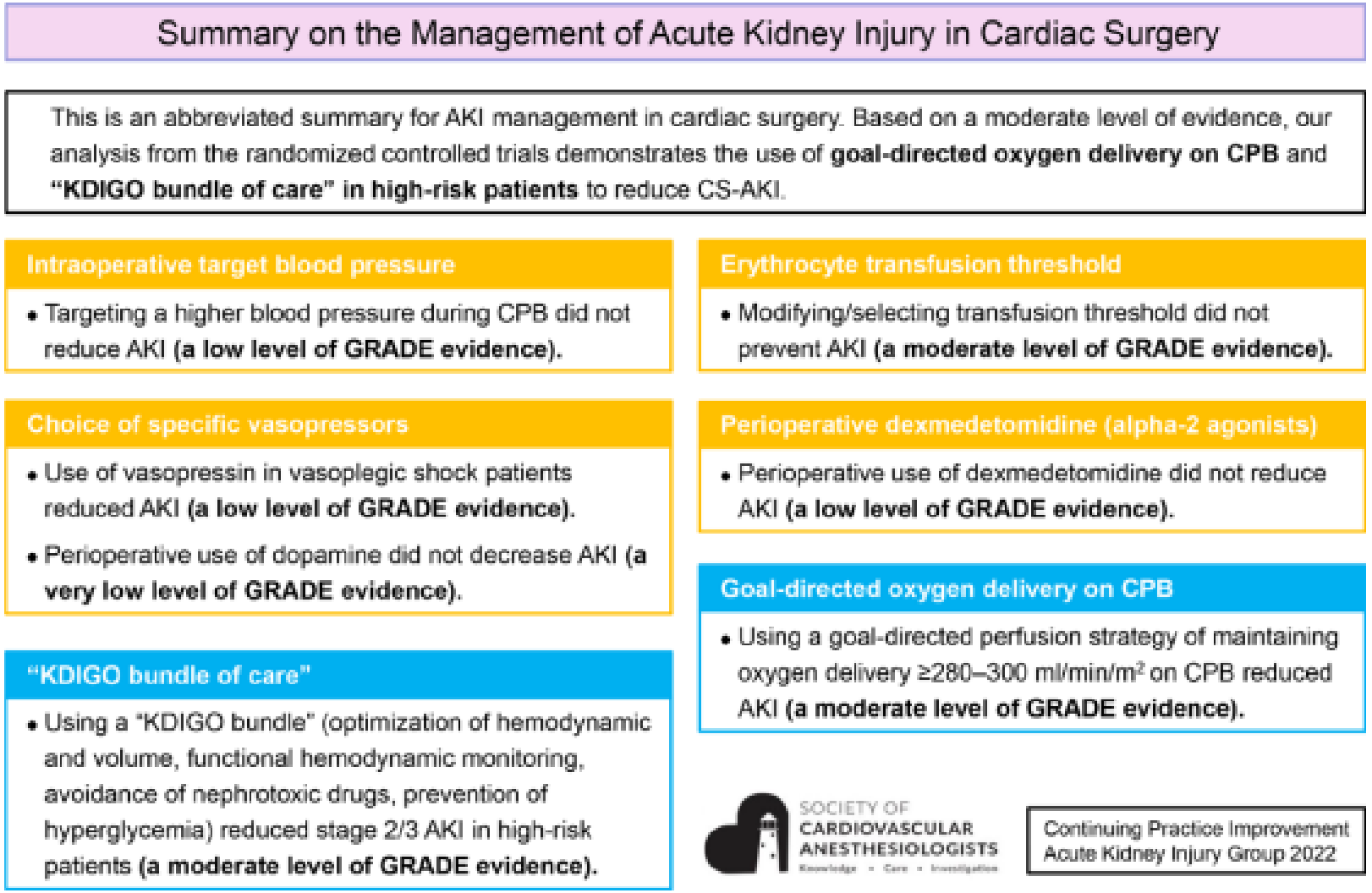


Figure 3. Summary on the management of CS-AKI. CPB indicates cardiopulmonary bypass; CS-AKI, cardiac surgery-associated acute kidney injury; GRADE, Grading of Recommendations, Assessment, Development and Evaluation; KDIGO, Kidney Disease Improving Global Outcomes.

Home Messages

- CSA-AKI associated with poor outcome
- Clinical AKI is the tip of the iceberg
- Preventing Aki can reduce long term complication
- Early interventions and prevention is critical

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