Avoiding Kidney Injury: Cardiac Surgery

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Objectives

- Discuss incidence and impact of cardiac surgery-associated acute kidney injury (CSA-AKI) & Chronic Kidney Disease in patients undergoing cardiac surgery
- Review the pathophysiology related to cardiac surgery and risk for developing AKI
- Summarize recommendations supported by the literature for recognizing and preventing CSA-AKI

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For more information...

- For a more in-depth overview of kidney disease, including staging and definitions, reference: MPOG Avoiding Kidney Injury - Overview, Pathophysiology, Definitions
- For other specialty specific recommendations, reference the following sections of the toolkit:
  - Avoiding Kidney Injury - Pediatrics
  - Avoiding Kidney Injury - Obstetrics
  - Avoiding Kidney Injury - Recommendations for Adult Surgical Patients

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Incidence of CSA-AKI

- 5-50% of patients develop AKI after cardiac surgery [1,5]
  - **28%** (287/1030) patients: 2013 single-center registry, AKIN criteria [2]
  - **36%** (819/2,284) patients: 2018 single-center prospective cohort study, KDIGO criteria [3]
  - **36%** (931/2,575) patients: 2017 single-center retrospective analysis, KDIGO criteria [4]
  - **50%** (221/443) patients: 2015 single-center retrospective study, RIFLE definition [5]
- In a study of 3,869 cardiac surgery patients, 22% developed stage 1 AKI (AKIN definition) [6]

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Impact of CSA-AKI

- 2-5% of cardiac surgery patients require renal replacement therapy postoperatively [3]
- Five-year risk of death was 27% among cardiac surgery patients with AKI compared to 12.1% in patients without AKI [2]
- In a study of valve and valve+CABG operations, postoperative renal injury of AKI stage 1 or higher found to be associated with an increase in long-term mortality (HR: 2.27 for valve; HR: 1.65 for valve+CABG; HR: 1.56 for CABG) [7]
- Further, an increase in creatinine by only 10% during the first week after valve operation is associated with an increased risk for long-term mortality (≤ 18 years) [7]

Impact of CSA-AKI

Table 7. Hospital Outcomes in Propensity-Matched Patients

Outcomes	No AKI (n = 833)	Stage I AKI (n = 833)	*p* Value
Intensive care unit stay, days	2.71 ± 3.89	5.28 ± 10.72	<0.0001
Length of ventilation, hours	19.31 ± 58.67	41.77 ± 125.0	<0.0001
Length of hospital stay, days	14.73 ± 18.31	17.95 ± 20.19	0.0007
CNS complications	68 (8.16)	127 (15.25)	<0.0001
Atrial fibrillation	67 (8.04)	140 (16.81)	<0.0001
Postoperative pneumonia	3 (0.36)	17 (2.04)	0.001
Sternal wound infection	5 (0.60)	27 (3.24)	<0.0001

Values are mean ± SD or n (%).

AKI = acute kidney injury; CNS = central nervous system.

Table 8. Predictors of Mortality

Predictors	OR	95% CI	*p* Value
Acute kidney injury	8.454	4.712–15.167	<0.0001
Preoperative creatinine	1.004	1.003–1.006	<0.0001
Preoperative hemoglobin	1.01	1.03–1.005	0.004
Hypertension	4.27	1.58–11.36	0.0009
Operative priority urgent	1.7	1.001–2.86	0.002
Operative priority emergent	2.464	1.121–5.414	0.002
CARE score	6.32	3.44–11.62	0.005

CARE = Cardiac Anesthesia Risk Evaluation; CI = confidence interval; OR = odds ratio.

Cardiac surgery patients who developed Stage 1 AKI also experienced increased hospital mortality, post-op complications, & longer length of stay. [6]

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Impact of CSA-AKI

- Mortality rates among cardiovascular patients requiring postoperative renal replacement therapy are between 40-70% [8]

- In a review of cases for 1,078,036 patients undergoing CABG, valve-replacement surgery or both from the Nationwide Inpatient Sample from 2008-2011 (United States only) [9]
  - 1 in every 10 patients developed AKI after cardiac operation
  - 10-fold greater in-hospital mortality
  - Twofold greater length of stay
  - On average, $36,453 greater index hospitalization costs

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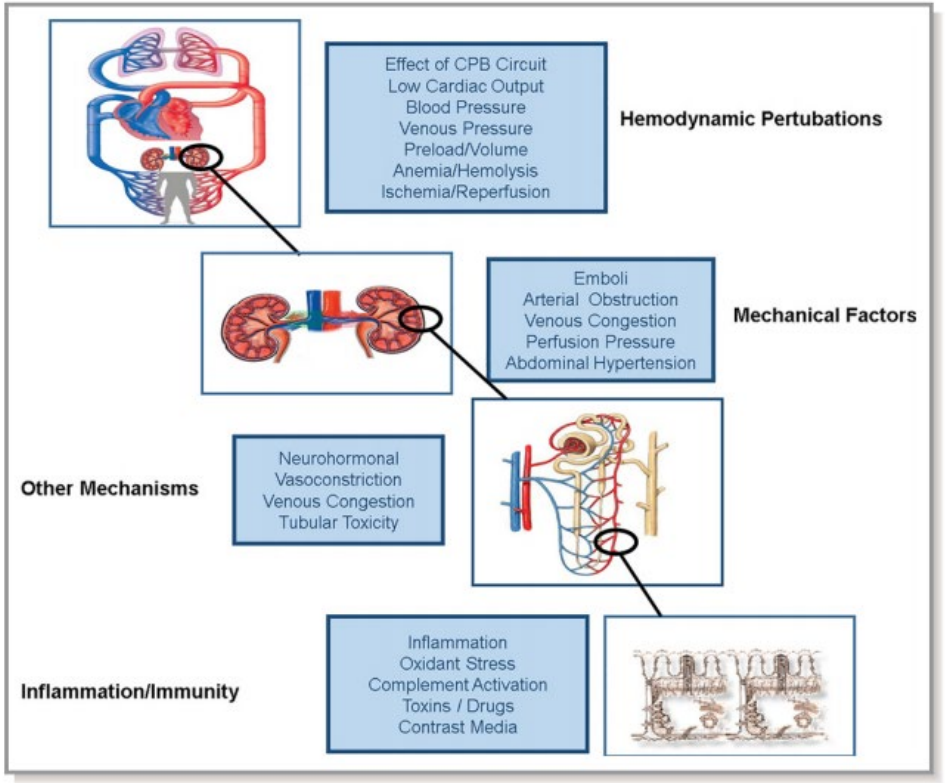
Pathophysiology of AKI related to Cardiopulmonary bypass



There are many variables associated with cardiac surgery & cardiopulmonary bypass:

- Nonpulsatile blood flow
- Hemodilution
- Transfusion load
- Release of free hemoglobin & free iron from hemolysis
- Prolonged hypothermia
- Inflammatory response
- Venous congestion

All of these factors can contribute to acute kidney injury. [10]

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Incidence of CKD after Cardiac Surgery

In a review of 29,388 cardiac surgery patients using the VASQIP registry: [8]

- 31% (9125) patients had CKD at time of surgery
- CKD defined as average eGFR <60mL/min/1.73m^2 for at least 3 months
- In remaining 20,263 patients without CKD at baseline:
  - 25% of patients with NO increase in postop creatinine developed CKD
  - 33% of patients with an increase of 1-24% in postop creatinine developed CKD
  - 44% of patients with an increase of 25-49% in postop creatinine developed CKD
  - 51% of patients with an increase of 50-99% in postop creatinine developed CKD
  - 53% of patients with an increase of ≥100% in postop creatinine developed CKD

Considerations for Preventing CSA-AKI [10]

Preop

- Assess Risk Factors
- Statin initiation: not supported
- Maintain normoglycemia
- Hold ACE inhibitors & ARBs

Intraop

- Maintain Normoglycemia
- Avoid hydoxyethyl starch
- Use balanced crystalloid solutions to replace fluid losses
- Avoid hyperthermic perfusion during CPB
- Avoid significant hemodilution during CPB & limit blood transfusions

Postop

- Avoid dopamine
- Discontinue ACEIs & ARBs for the first 48 hours after surgery
- Monitor sCr and urine output
- Maintain normoglycemia
- Avoid radiocontrast agents

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Preoperative Considerations

1. **Assess risk factors**
2. **Determine baseline kidney function**
3. **Assess for anemia**
4. **Assess for albuminuria**
5. **Statin initiation:** Not proven to reduce risk of AKI[10-12]
   - High-dose atorvastatin did not reduce AKI overall after cardiac surgery (Statin AKI Cardiac Surgery RCT- 2016)[13]
   - Preop treatment with a statin was not associated with postop AKI, RRT, or mortality [14]
6. **Maintain Normoglycemia**
7. **Hold ACE inhibitors and ARBs [10-12; 15-16]**
   - TRIBE-AKI study found increase in AKI in patients receiving ACEIs and ARBs (no ACEIs or ARBs: 31% incidence compared to 34% in held ACEIs/ARBs vs. 42% incidence with continued ACEIs/ARBs) [15]
   - Large meta-analysis (29 studies) found preop use of ACE/ARB until day of surgery increased odds of developing AKI [16]

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CSA-AKI Risk Factors [17]

Preop	Intraop	Postop
Advanced Age	Complex surgery	Vasopressor exposure
Female	Cardiopulmonary bypass	Inotrope exposure
Hypertension	Low HCT in CPB	Blood transfusion
Hyperlipidemia	Aortic cross clamp time*	Anemia
Chronic Kidney Disease	Hypoperfusion	Hypovolemia
Liver Disease	Hypovolemia	Venous congestion
Peripheral Vascular Disease	Venous congestion	Cardiogenic shock
Previous Stroke	Emboli	
Smoking hx	Inotropes Exposure	
Diabetes		
Anemia		

* Cardiopulmonary bypass lasting 3 hours or longer was associated with a nearly fourfold elevated risk in renal dysfunction (unadjusted relative risk, 3.7 [CI, 2.8 to 4.9]) compared with cardiopulmonary bypass lasting less than 2 hours. [18]

Intraoperative Considerations

1. Maintain normoglycemia
2. Avoid hydroxyethyl starch
3. Use balanced crystalloid solutions & vasopressors to maintain hemodynamics
4. Avoid hyperthermic perfusion during CPB
5. Avoid significant hemodilution during CPB
6. Limit blood transfusions

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Intraoperative Considerations:

1. Maintain normoglycemia

- AKI may further complicate glycemic control as it is associated with insulin resistance and reduced renal clearance of insulin [19]
- Aortic cross-clamp time and blood transfusion as independent risk factors of postoperative hyperglycemia after cardiac surgery in non-diabetics [20]
- In a study of 510 patients undergoing cardiovascular surgery and found the incidence of AKI to be higher in patients with high HbA1c levels preoperatively; Every 1% increase over 6% in HgA1c levels increased the risk of renal complications by 24% [21]
- Glycemic variability, a standard deviation of all POC-BG readings, is associated with increased postoperative LOS-ICU, rise in creatinine, and AKI [22]

Intraoperative Considerations:

1. **Maintain normoglycemia (continued)**
   - In a randomized controlled trial, moderate glucose control defined as 127-179 mg/dl was found to be preferable to tight control ≤ 126 in patients undergoing CABG [23]
   - Incidence of AKI was higher in patients with time-weighted average intraop glucose of >150mg/dl (8%) as compared to patients with blood glucose 110-150 mg/dl (3%) [24]
   - KDIGO - recommends maintaining blood glucose between 110 - 149 mg/dL in critically ill patients [25]
   - Tight glucose control (<150mg/dl) is seen as *controversial* as risks of hypoglycemia are significant: NICE-SUGAR meta-analysis [26]
   - Society of Thoracic Surgeons (STS) Practice Guidelines recommend **maintaining serum glucose levels ≤ 180 mg/dL for at least 24 hours after cardiac surgery** [27]

Intraoperative Considerations:

2. **Hydroxyethyl Starch (HES) studies show mixed results**
   - Hydroxyethyl starch-containing solutions may increase AKI occurrence
     - Scandinavian Starch for Severe Sepsis/Septic Shock (6S) Trial [28]
   - Crystalloid versus Hydroxyethyl Starch Trial (CHEST) published in 2012 initially found an increased need for renal replacement therapy in patients receiving HES vs. crystalloids; later analysis (2016) did not find this to be true- **no difference in patient outcomes** [29]
   - Need for further research, should be used cautiously

Intraoperative Considerations:

3. **Use Vasopressors & crystalloids to maintain hemodynamic stability:**
    - Either norepinephrine or vasopressin can be used for hemodynamic support in the patient post-cardiac surgery [30]
    - European Society of Intensive Care Medicine recommendations: [11]
        - Norepinephrine recommended as first-choice vasopressor to protect kidney function

          (Grade 1B evidence)
        - Suggest vasopressin in patients with vasoplegic shock after cardiac surgery (Grade 2C evidence)
        - Controlled fluid resuscitation in volume depletion, while avoiding volume overload using balanced crystalloids (Grade 1C/2C)
    - American Heart Association - Cardiac and Vascular Surgery- Associated Acute Kidney Injury Consensus Guidelines recommend:[10]
        - Use of balanced crystalloid solutions guided by measures of fluid responsiveness (Grade 1B)

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Goal-Directed Perfusion Trial (GIFT)[31]

- Multicenter RCT conducted at 9 institutions in Europe, Australia, New Zealand, and the United States

- 350 cardiac surgery patients with cardiopulmonary bypass ≥ 90 minutes
  - Intervention group: Maintain DO_2 value ≥ 280mL ▪ min^{-1} ▪ m^{-2} during CPB; Adjust arterial pump flow based on Hct value to maintain DO_2; Transfuse 1U PRBC if SvO_2 <68% and/or the oxygen extraction rate was >40%
  - Control group: Arterial pump flow based on body surface area and temp, target value of 2.4L ▪ min^{-1} ▪ m^{-2} at normothermia. Transfusion trigger based on Hct value alone.

- Lower incidence of AKIN Stage 1 AKI in GDP group; same incidence for stage 2 & 3

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Goal Directed Resuscitation in Cardiac Surgery [32]

126 cardiac surgery patients undergoing CABG or valve surgery were randomized to two groups:

- Control group: 64 patients receiving usual care
- Goal directed therapy group: 62 patients receiving protocol-based care (see graphic)

Outcomes:

- 30-day mortality and major complications reduced in the GDT group (27% compared to 45% in the control) p=0.037
- However, no significant difference in AKI requiring dialysis or hemofiltration

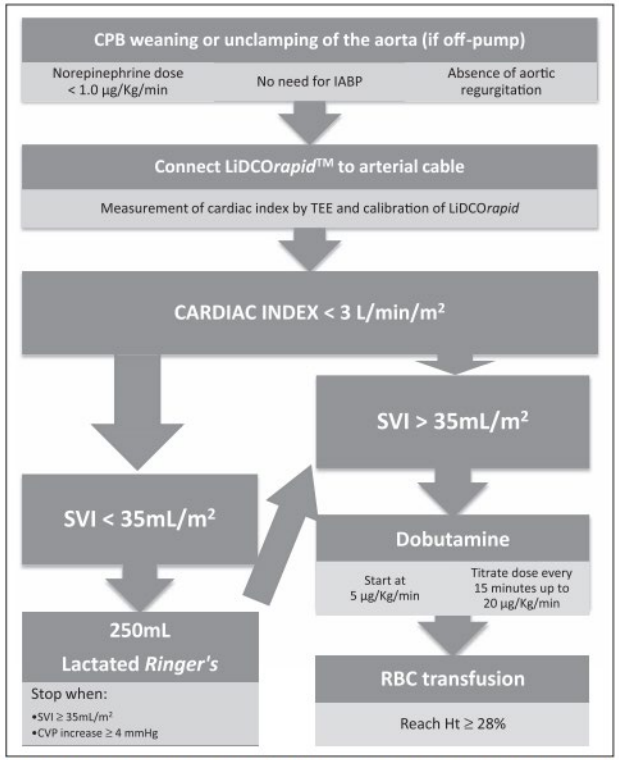

Figure 1. Algorithm of the goal-directed therapy (GDT) group. CPB = cardiopulmonary bypass, CVP = central venous pressure, Ht = hematocrit, IABP = intraaortic balloon pump, SVI = stroke volume index, TEE = transesophageal echocardiogram.

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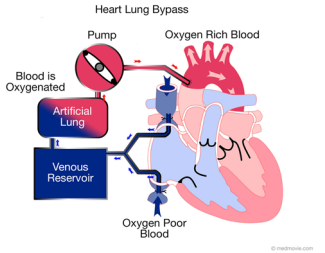
Intraoperative Considerations



4. **Avoid periods of hyperthermic perfusion**
   - CABG patients re-warmed on CPB to 37℃ had a higher incidence of renal dysfunction (17%) as compared to patients re-warmed to 34℃ (9%); n=223 [33]

5. **Avoid significant hemodilution**
   - Hemodilution during CPB is an independent risk factor for AKI in adult cardiac surgery [34]
   - In a retrospective analysis of 16,790 cardiac surgery patients, relative risk of AKI increased by 7% for every percentage point decrease in nadir HCT during CPB [35]

6. **Limit blood transfusions**
   - Transfusion of ≥ 2 units of packed red blood cells has been associated with higher incidence of AKI[36]
   - In 2 different RCTs, patients were randomized to liberal (Hg<9.5) or restrictive (Hb<7.5) groups intraoperatively and postoperatively and there was no difference in postop AKI [37-38]

PrevAKI Study [39]

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

Cardiac surgery, n = 276

Successfully reduced AKI in cardiac population through 3 primary interventions:

1. Optimized hemodynamics:
   - Dobutamine or epinephrine for cardiac index <3.0
   - Norepinephrine for MAP <65
2. Avoided hyperglycemia
3. Held ACEi/ARB for 48 hours after surgery

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Postoperative Considerations

1. **Avoid low-dose dopamine to treat/prevent AKI**
   - In a meta-analysis of 58 studies examining dopamine use, 24 studies included outcomes: low-dose dopamine was not associated with the prevention of acute renal failure [40]
   - A second meta-analysis of 61 studies established similar findings: low-dose dopamine increased urine output but did not prevent renal dysfunction [41]

2. **Monitor sCr and urine output for early detection of AKI[10]**

3. **Maintain blood glucose**
   - Society of Thoracic Surgeons (STS) Practice Guidelines recommend maintaining serum glucose levels ≤ 180 mg/dL for at least 24 hours after cardiac surgery [27]

4. **Avoid radiocontrast agents**
   - Contrast dose > 240 mg/kg resulted in greater incidence of CSA-AKI for patients who underwent cardiac catheterization ≤7 days before cardiac surgery than those > 7 days before cardiac surgery (39% vs. 29%, p = 0.025) [42]

Interventions requiring more research

- Beta-blockers may lead to decreased risk of renal dysfunction after cardiac surgery
  - Preop beta-blocker use was not associated with postop AKI [43]
  - In a large North American observational analysis (629,877 patients), preoperative beta-blocker therapy was associated with a slightly lower risk of renal failure in patients undergoing CABG (3% vs. 4%) [44]

- Unclear if fenoldopam reduces risk of AKI in patients undergoing cardiac surgery [45-46]
  - Meta-analysis including 7 trials and 1,107 patients undergoing cardiac surgery: fenoldopam associated with decreased incidence of AKI but increased incidence of hypotension; no change in hospital mortality or RRT requirements [45]
  - A multicenter, randomized, double-blind, placebo controlled, parallel-group study was stopped for futility as fenoldopam did not reduce 30-day mortality or need for RRT but was associated with increased rate of hypotension [46]

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Interventions requiring more research

- Volatile anesthetics may protect against AKI [47-48]
  - A meta-analysis of 10 trials with 1600 patients found that volatile anesthetics significantly reduced AKI incidence compared with control data (relative risk: 0.65; 95% CI, 0.43-0.97; P=0.04) [47]

- Remote Ischemic Preconditioning [49-51]
  - Application of controlled ischemia to remote tissues or organs to create a protective adaptive response in distant organs
  - Mixed results in studies -> differing protocols, patient populations, and study design
  - Further investigation needed before adopting into practice

Interventions requiring more research

- Alpha-2 agonists
  - A study in pediatric patients undergoing congenital cardiac surgery showed that dexmedetomidine was associated with lower instances of acute kidney injury [52]
  - A meta-analysis stated that dexmedetomidine may be promising as an agent to prevent postoperative renal dysfunction after cardiac surgery [53]

- Intraoperative FiO2
  - The ROCS trial is examining the impact of hyperoxia on end organ injury during cardiac surgery [54]
  - A subanalysis of an ongoing RCT did not find a significant increase in AKI with intraoperative hyperoxia during **non-cardiac** surgery [55]

Summary of Considerations for preventing AKI after Cardiac Surgery

1. Assess Risk Factors for AKI
2. Establish Baseline Renal Function
3. Maintain Blood Glucose
4. Avoid Hydroxyethyl Starch
5. Maintain Hemodynamics: Balanced crystalloids & vasopressors
6. Avoid hyperthermic perfusion & significant hemodilution during CPB
7. Limit Blood Transfusions
8. Avoid Low-dose Dopamine to treat/prevent AKI
9. Continue to monitor creatinine and urine output postoperatively
10. Avoid Radiocontrast Agents: Postpone surgery if possible after contrast

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