AKI in Cardiac Surgery

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CSA-AKI: Cardiac Surgery associated Acute Kidney Injury Definition

- Any patient who has undergone cardiac surgery in the previous 7 days and meets the KDIQO criteria for Acute Kidney Injury can be considered to have Cardiac Surgery-related Acute Kidney Injury
- CSA-AKI can be classified as type 1 Cardiorenal Syndrome (acute CRS)

KDIGO

Kidney disease improving Global o

SCr, UO, GFR

Stage 1

SCr increased $\geq$ 0.3 mg/dL within 48 h
SCr increased by 1.5 × to 1.9 × , which is known or presumed to have occurred withi
prior 7 d
UO < 0.5 mL/kg/h for 6–12 h

Stage 2

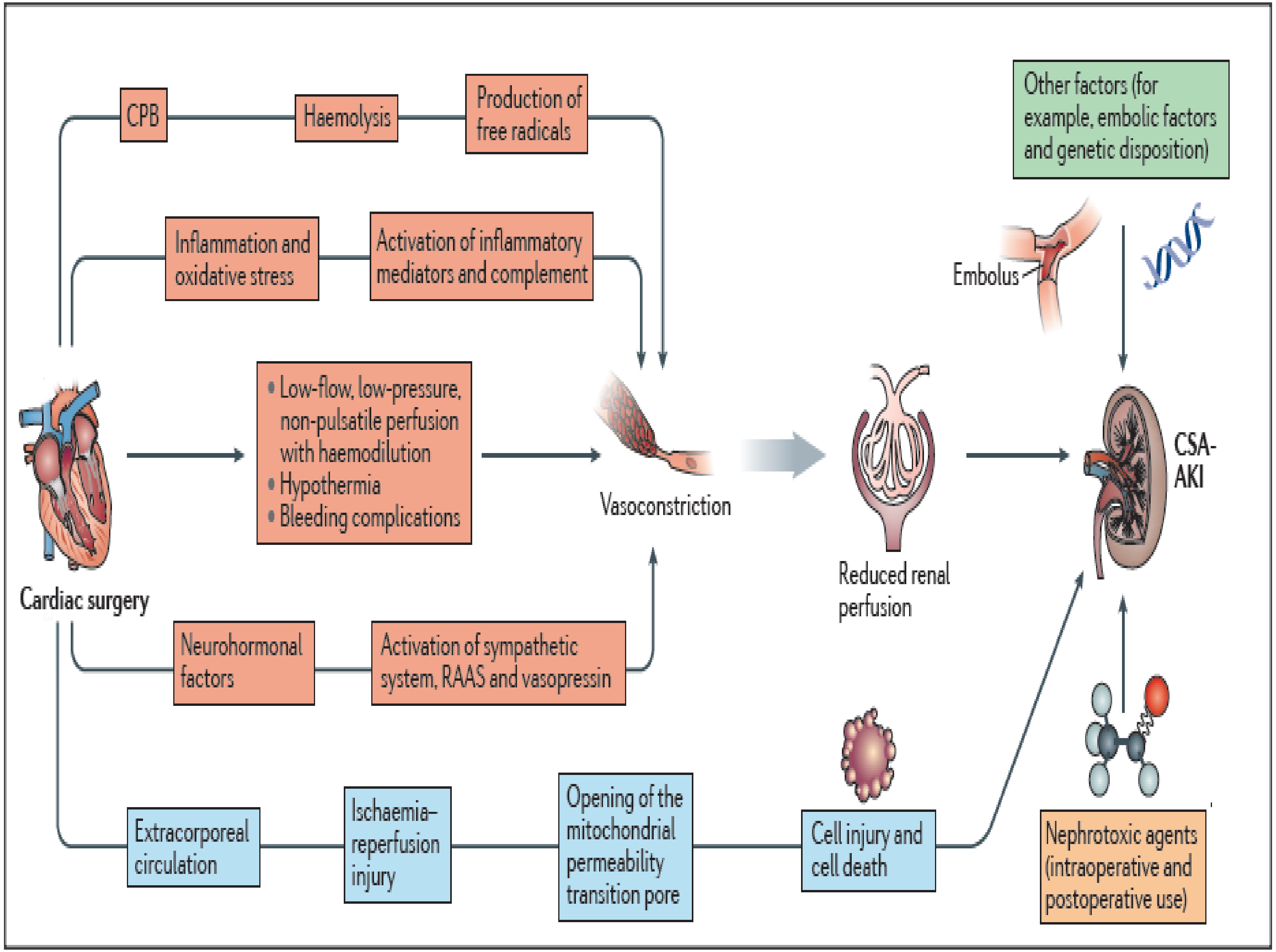
SCr increased by 2.0 × to 2.9 ×
UO < 0.5 mL/kg/h for 12 h

Stage 3

SCr increased by $\geq$ 3.0 ×
SCr $\geq$ 4 mg/dL
Initiation of RRT
UO < 0.3 mL/kg/h for 24 h
Anuria for 12 h
eGFR < 35 mL/min/1.73 m^2(in patients < 18

Pathophysiology

- Renal hypoperfusion
- Ischaemia - reperfusion Injury



CSA - AKI

- The incidence of CSA-AKI is as high as 40% (studies based on KDIQO criteria)
- The second leading cause of AKI in the Intensive Care Units (ICU)
- Approximately 3% of patients require Renal Replacement Therapy (RRT) – 30day mortality : 60%
- 25% will develop CKD
- 5-year survival 54%, 7-year survival 38%
- It is independently associated with 3-8 times higher mortality, prolonged ICU hospitalization
- Highest cost ($1 billion in 2022 in the United States)

Diagnosis of CSA-AKI

- Early diagnosis is critical
- AKI has no specific treatment
- However, current diagnostic criteria are not suitable for rapid identification of AKI.

Biomarkers

Figure 2. New, biomarker-enhanced definition of acute kidney injury according to the Acute Disease Quality Initiative Consensus Conference proposal, modified from Ostermann et al.

Functional criteria	Stage	Damage criteria
No change or sCr level increase <0.3mg/dl and no UO criteria	1S	Biomarker positive
SCr level increase ≥0.3mg/dl ≤48h or ≥150% for ≤7d and/or UO <0.5ml/kg/h for >12h	1A	Biomarker negative
	1B	Biomarker positive
SCr level increase >200% and/or UO <0.5ml/kg/h for >12h	2A	Biomarker negative
	2B	Biomarker positive
SCr level increase >300% (≥4.0mg/dl with an acute increase of ≥0.5mg/dl) and/or UO <0.3ml/kg/h for >24h or anuria for >12h and/or RRT	3A	Biomarker negative
	3B	Biomarker positive

- > 60 biomarkers in serum and urine
- Urine biomarkers more rapidly detect subclinical AKI
- No validated diagnostic thresholds have been established
- They have not been put into clinical practice
- ADQI (Acute Disease Quality Initiative) proposed the inclusion of biomarkers in KDIGO staging

Ostermann M, Zarbock A, Goldstein S, Kashani K, Macedo E, Murugan R, et al. Recommendations on acute kidney injury biomarkers from the acute disease quality initiative consensus conference: a consensus statement. JAMA Netw Open. 2020

Biomarkers in CSA-AKI

Table 6. Sensitivity Analyses Showing Recalculated Composite AUROC When Studies Restricted to Those Measuring Biomarkers Earlier Versus Later

	All Studies		Earlier: ≤6 Hours		Later: >6 Hours	
Biomarker	Composite AUROC (95% CI)	No. of Studies	Composite AUROC (95% CI)	No. of Studies	Composite AUROC (95% CI)	No. of Studies
Urine						
NGAL	0.72 (0.66-0.79)	16	0.74 (0.65-0.83)	11	0.69 (0.59-0.79)	5
Cystatin C	0.63 (0.37-0.89)	3	—	—	—	—
NAG	0.69 (0.60-0.79)	4	—	—	—	—
KIM-1	0.72 (0.59-0.84)	6	0.68 (0.61-0.75)	5	—	—
IL-18	0.66 (0.56-0.76)	5	—	—	0.66 (0.51-0.80)	4
L-FABP	0.72 (0.60-0.85)	6	0.73 (0.50-0.96)	4	—	—
α-GST	0.57 (0.46-0.68)	3	0.57 (0.46-0.68)	3	—	—
π-GST	0.65 (0.48-0.82)	3	0.65 (0.48-0.82)	3	—	—
Plasma						
NGAL	0.71 (0.64-0.77)	6	0.73 (0.44-1.00)	3	0.69 (0.60-0.78)	3
Cystatin C	0.69 (0.63-0.74)	5	0.65 (0.51-0.79)	4	—	—

Abbreviations: AUROC, area under the receiver operating characteristic curve; CI, confidence interval; GST, glutathione *S*-transferase; IL, interleukin; KIM, kidney injury molecule; L-FABP, liver-type fatty acid binding protein; NAG, *N*-acetyl-β-D-glucosaminidase; NGAL, neutrophil gelatinase-associated lipocalin.

- **CCA (TIMP-2, IGFBP7)** : cell cycle arrest : Tissue inhibitor of metalloproteinases-2 (TIMP-2) and Insulin-like growth factor-binding protein 7 (IGFBP7)
- Commercially available
- The PrevAKI multicenter RCT showed a reduction in the incidence of stages 2 and 3 AKI after cardiac surgery, after detecting high-risk patients defined as [TIMP 2]×[IGFBP7]≥0.3

Urinary, Plasma, and Serum Biomarkers' Utility for Predicting Acute Kidney Injury Associated With Cardiac Surgery in Adults: A Meta-analysis Julie Ho et al, Am J Kidney Dis. 2015

Zarbock A, et al. Prevention of cardiac surgery-associated acute kidney injury by implementing the KDIGO guidelines in high-risk patients identifed by biomarkers: the PrevAKI-multicenter randomized controlled trial. Anesth Analg. 2021

Imaging Indicators

- Renal arterial Resistance Index (RRI) =(systolic velocity—diastolic velocity)/systolic velocity
- Intraoperative RRI increase > 0.68 appeared to be an independent predictor of postoperative AKI. 70% sensitivity

Kajal K, et al. Intraoperative evaluation of renal resistive index with transesophageal echocardiography for the assessment of acute renal injury in patients undergoing coronary artery bypass grafting surgery: a prospective observational study. Ann Card Anaesth. 2022

- Intraparenchymal renal resistive index variation (IRRIV) = the percentage reduction of RRI after abdominal pressure (10% of DB).
- IRRIV predicted subclinical AKI after cardiac surgery with 46.1% sensitivity but 100% specificity

Samoni Set al. Ultrasonographic intraparenchymal renal resistive index variation for assessing renal functional reserve in patients scheduled for cardiac surgery: a pilot study. Blood Purif. 2022

- Severe venous congestion in the kidney presents with a monophasic diastolic wave. Intrarenal venous blood flow patterns are an independent predictor of AKI and mortality

Beaubien-Souligny et al. Alterations in portal vein fow and intrarenal venous fow are associated with acute kidney injury after cardiac surgery: a prospective observational cohort study. J Am Heart Assoc. 2018

Prediction algorithms

- Diagnostic accuracy 70-80%
- Machine learning tools
- Biomarkers, imaging indicators,
- Key risk factors

Model	Risk factors included	AUC/C-statistic in first-time report	Reference
Coulson et al. (2020)	Preoperative model for AKI: ·Preoperative haemoglobin ·Preoperative creatinine ·Age ·NYHA status ·BMI Postoperative model for AKI ·Preoperative haemoglobin ·Preoperative creatinine ·Perfusion time ·NYHA status ·BMI Preoperative model for RRT: ·Preoperative creatinine ·Previous cardiac surgery ·NYHA status ·Type of surgery Postoperative model for RRT: ·Perfusion time ·Preoperative creatinine ·Intra-aortic balloon pump	0.68 for preoperative model for AKI 0.70 for postoperative model for AKI 0.80 for preoperative model for RRT 0.85 for postoperative model for RRT	[43]
Wang et al. (2022)	·Postoperative creatinine ·Aortic cross-clamping time ·Emergency surgery ·Preoperative cystatin C	c-statistic of 0.851 for AKI requiring RRT	[44]
Demirjian et al. (2022)	·Preoperative serum creatinine ·Postoperative serum creatinine ·Postoperative serum albumin ·Postoperative blood urea nitrogen ·Postoperative serum potassium ·Postoperative serum sodium ·Postoperative serum bicarbonate	0.876 for moderate to severe AKI (KIDGO stage 2 or 3) within 72 h after cardiac surgery 0.854 for moderate to severe AKI within 14 days 0.916 for AKI requiring dialysis within 72 h 0.900 for AKI requiring dialysis within 14 days	[46]
Chen et al. (2020)	·Interferon-γ ·Interleukin-16 ·Mip-1α (macrophage inflammatory protein-1α)	C-statistic of 0.87 for severe AKI (AKIN stage 2 or 3)	[47]
Zhang et al.(2022)	·Age ·Male ·Preoperative serum creatinine ·Preoperative neutrophil to lymphocyte ratio ·Preoperative blood glucose ·Preoperative high-density lipoprotein ·Intraoperative urine output ·Conventional ultrafiltration ·Central venous pressure ·Perfusion flow ·Intubated PaO_2/FiO_2 ratio ·Postoperative haemoglobin ·Postoperative serum potassium ·Postoperative lactic dehydrogenase	0.824	[48]

AKI acute kidney injury, *ARF* acute renal failure, *BMI* body mass index, *FiO_2* inspired oxygen fraction, *NYHA* New York heart association, *PaO_2* partial pressure of oxygen, *RRT* renal replacement therapy

Risk Factors

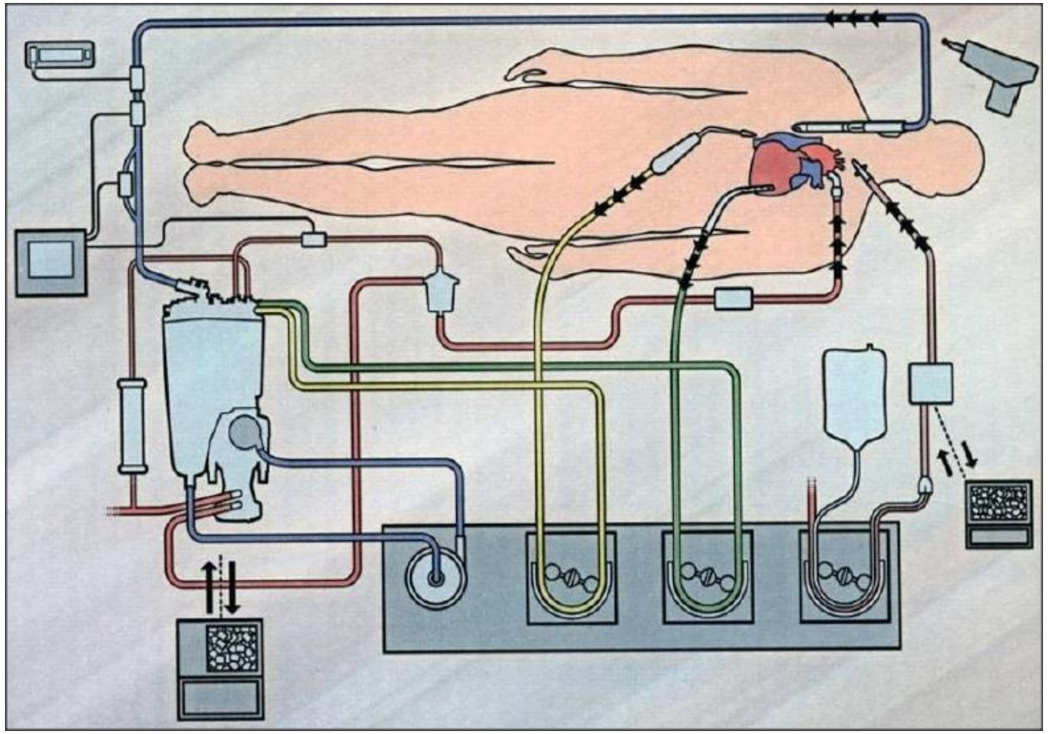
Table 2 Common risk factors for AKI after cardias surgery, adapted from [37–39]

	Patient-related	Procedure-related (surgery, anaesthesia, CPB-related)
Preoperative	•Gender •Advanced age •Severe cardiac disease •Previous cardiac surgery •Active congestive heart failure •Cardiogenic shock •NYHA class III/IV •Left ventricular ejection fraction < 35% •Left main coronary artery disease •Anaemia •Coexisting disease (Peripheral vascular disease, hypertension, generalized atherosclerotic disease, chronic obstructive pulmonary disease, previous cerebrovascular accidents, diabetes mellitus, chronic kidney disease, chronic liver disease) •Nephrotoxins (ACEis/ARBs, antibiotics, diuretics, or NSAIDs)	•Preoperative contrast media exposure •Preoperative insertion of intra-aortic balloon pump •Emergency status
Intraoperative		•Type of surgery (valvular, valvular and coronary, emergency and redo surgery) •CPB (non-pulsatile, low-flow, low-pressure perfusion) •Hypotension •Hypothermia •Deep hypothermic circulatory arrest CPB duration •Cross-clamp duration •Anaemia (Haemodilution, Haemolysis) •Transfusion load •Embolism
Postoperative		•Low cardiac output •Hypovolemia •Hypotension •Intense vasoconstriction •Atheroembolism (requiring Intra-aortic balloon pump) •Sepsis •Nephrotoxins •Cardiogenic Shock

ACEis angiotensin-converting enzyme inhibitors;, *AKI* acute kidney injury, *ARBs* angiotensin receptor blockers, *CPB* cardiopulmonary bypass, *NSAIDs* nonsteroidal anti-inflammatory drugs, *NYHA* New York heart association

CPB: cardiopulmonary bypass

- To use or not heart – lung machine
- On – pump vs Off – pump



Off-pump vs on-pump

- CORONARY trial (AKIN/RIFLE)
- 4752 pts
- 30 days
- Primary endpoint: No statistically significant difference in AKI requiring RRT
- Secondary endpoint: off-pump: fewer AKI episodes **But** more revascularization episodes (PCI or CABG)

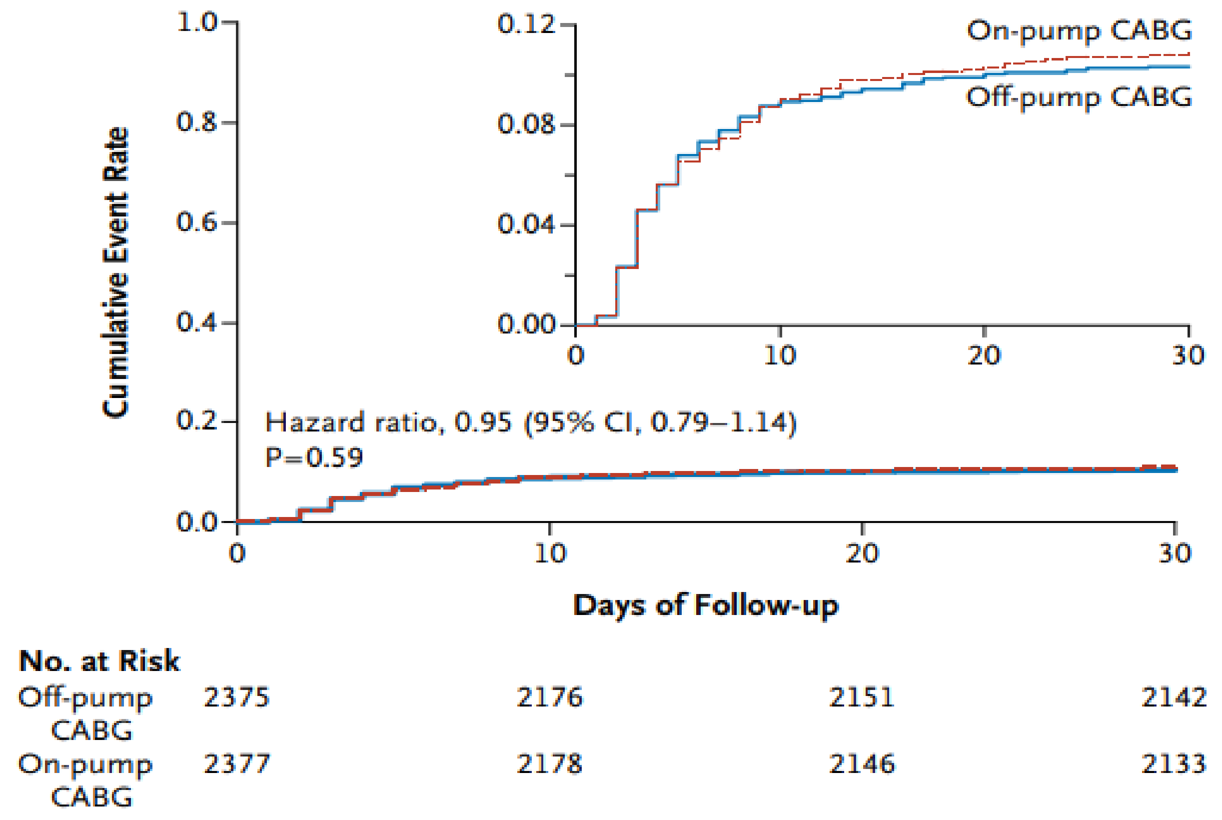


Figure 2. Kaplan–Meier Curves for the Primary Composite Outcome at 30 Days.

The primary composite outcome was death, myocardial infarction, stroke, or new renal failure requiring dialysis.

Off-pump vs on-pump

- COPCABE trial
- 2539 pts > 75yrs
- 30 days and 1 year

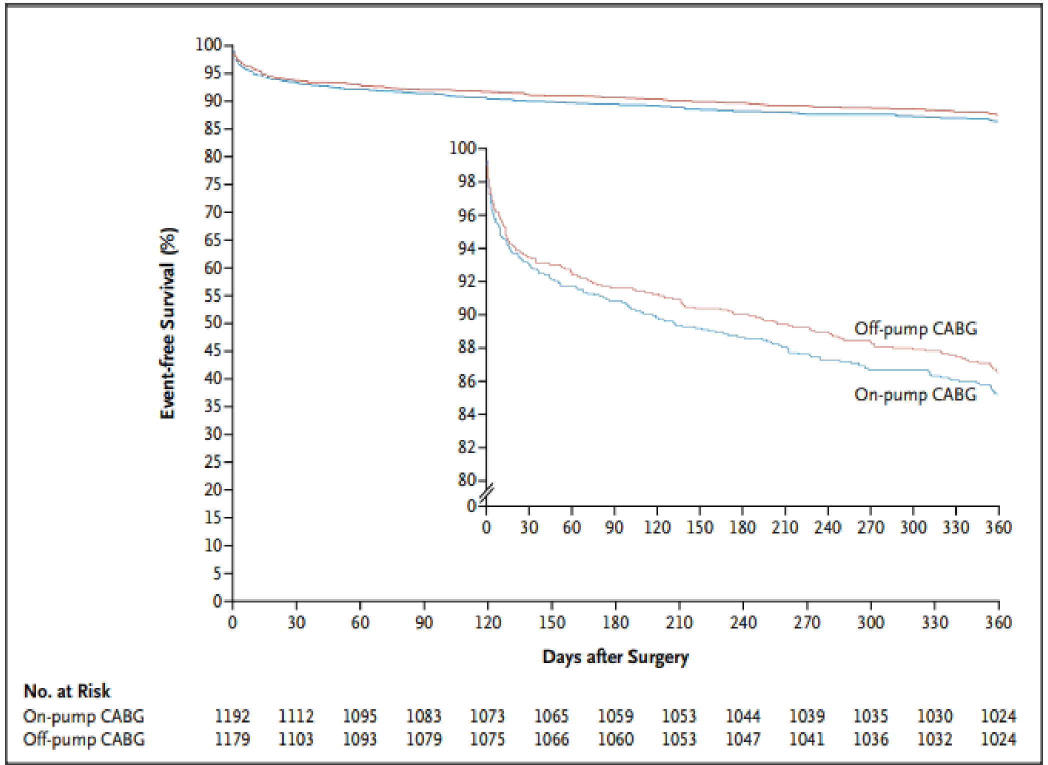


Table 3. Trial End Points (Modified Intention-to-Treat Analysis).*

End Point	Off-Pump CABG	On-Pump CABG	Odds Ratio or Hazard Ratio (95% CI)†	P Value
	no./total no. (%)			
At 30 days‡				
Primary composite end point§	93/1187 (7.8)	99/1207 (8.2)	0.95 (0.71–1.28)	0.74
Individual components				
Death	31/1187 (2.6)	34/1207 (2.8)	0.92 (0.57–1.51)	0.75
Myocardial infarction	18/1187 (1.5)	20/1207 (1.7)	0.92 (0.51–1.66)	0.79
Stroke	26/1187 (2.2)	32/1207 (2.7)	0.83 (0.50–1.38)	0.47
Repeat revascularization	15/1187 (1.3)	5/1207 (0.4)	2.42 (1.03–5.72)	0.04
New renal-replacement therapy	29/1187 (2.4)	37/1207 (3.1)	0.80 (0.49–1.29)	0.36
At 12 mo¶				
Primary composite end point§	154/1179 (13.1)	167/1191 (14.0)	0.93 (0.76–1.16)	0.48
Individual components				
Death	83/1179 (7.0)	95/1191 (8.0)	0.88 (0.65–1.18)	0.38
Myocardial infarction	25/1179 (2.1)	28/1191 (2.4)	0.90 (0.53–1.54)	0.70
Stroke	41/1179 (3.5)	52/1191 (4.4)	0.79 (0.53–1.19)	0.26
Repeat revascularization	36/1179 (3.1)	24/1191 (2.0)	1.52 (0.90–2.54)	0.11
New renal-replacement therapy	34/1179 (2.9)	42/1191 (3.5)	0.82 (0.52–1.28)	0.37

Off-pump vs on-pump

- HEPCON trial
- 120pts
- Conventional Extracorporeal Circulation (CECC) vs minimized extracorporeal circulation (MECC) vs off-pump coronary artery bypass grafting (OPCAB)
- At 72 hours no difference between the 3 surgical techniques.
- AKI independent of the surgical technique at 48 hours .

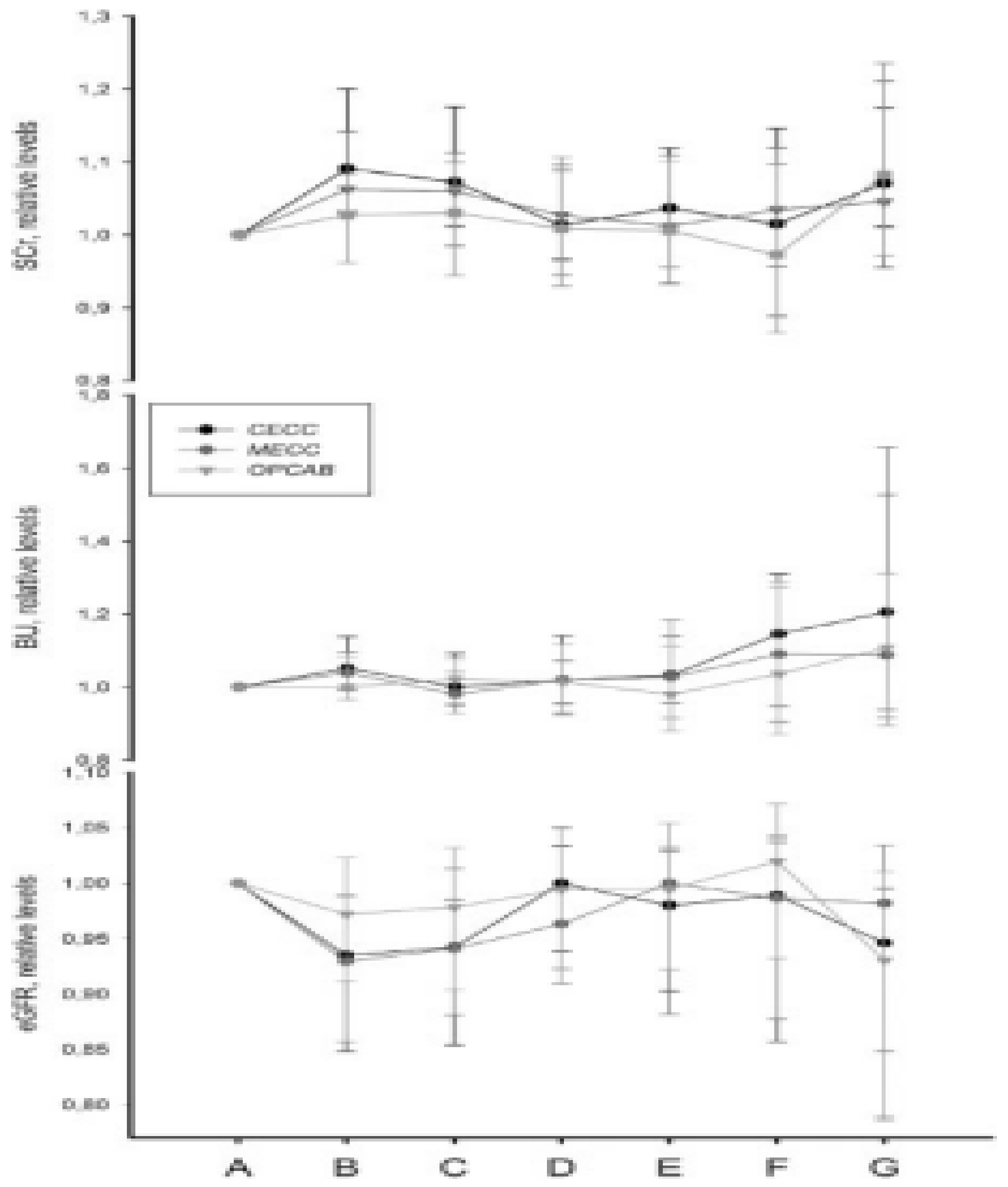


Fig. 3 Time courses of kidney function parameters (relative to baseline). Levels before anesthesia (A), before protamine administration (B), at ICU arrival (C), 6 hours (D), 12 hours (E), 24 hours (F), and 72 hours after ICU arrival. Abbreviations: BU, blood urea; CECC, conventional extracorporeal circulation; eGFR, estimated glomerular filtration rate; ICU, intensive care unit; MECC, minimized extracorporeal circulation; OPCAB, off-pump coronary artery bypass; SCr, serum creatinine.

CPB: pulsatile vs non-pulsatile

- Pulsatile flow in the extracorporeal circulation creates higher circuit pressures, provides a higher mean arterial pressure to the patient, and possibly better microvascular blood flow. But it also creates greater shear forces that lead to greater hemolysis

Zihui Tan et al.Pulsatile Versus Nonpulsatile Flow During Cardiopulmonary Bypass: Extent of Hemolysis and Clinical Significance ASAIO j. Sep/Oct 2020

- Intravascular hemolysis leads to an acute increase in free hemoglobin, which through consumption of NO causes reduced renal perfusion. Free hemoglobin is directly toxic to the tubule.

Vermeulen Windsant, I. C. et al. Hemolysis during cardiac surgery is associated with increased intravascular nitric oxide consumption and perioperative kidney and intestinal tissue damage. *Front. Physiol.* ***5, 340 (2014).***

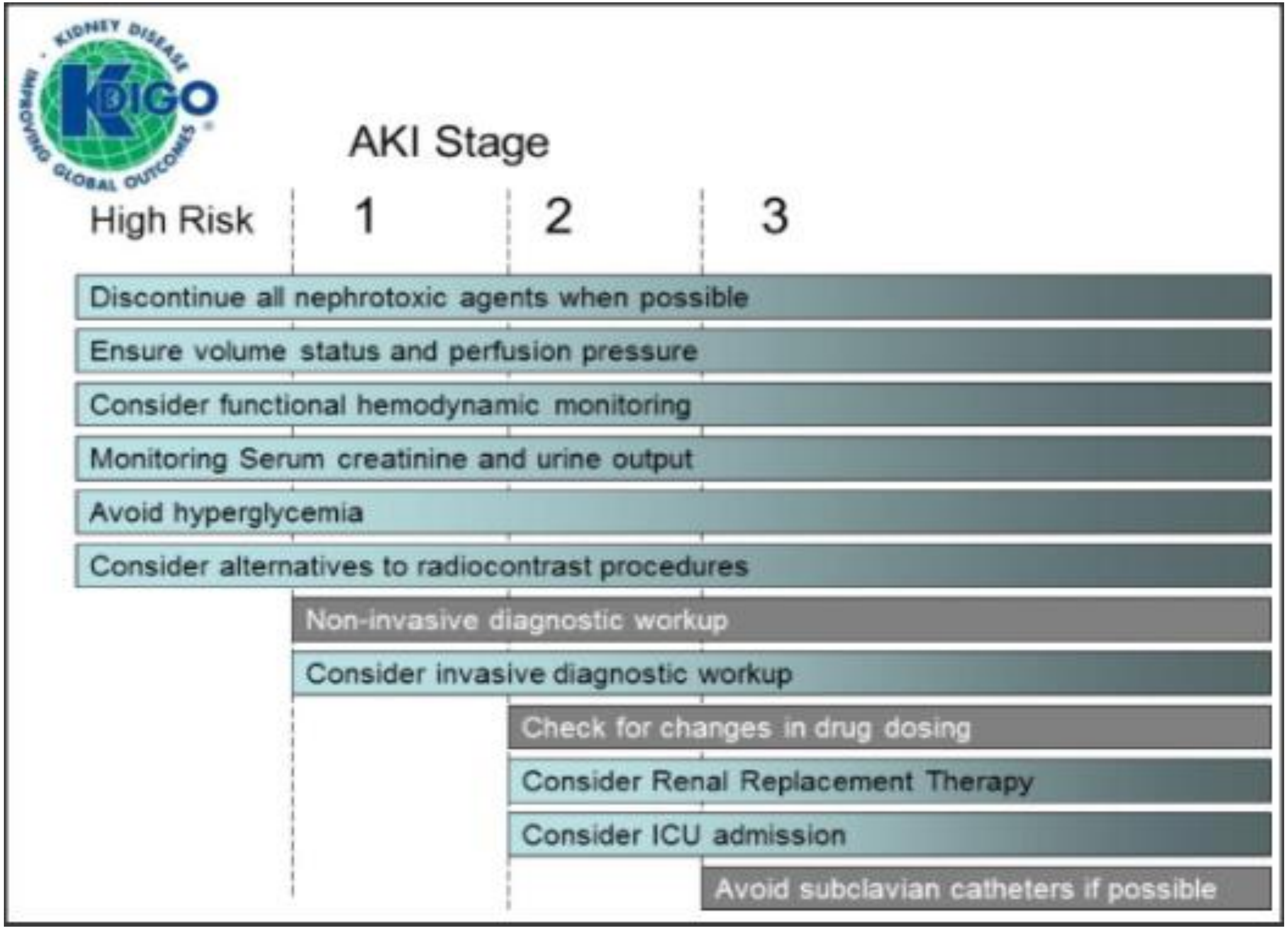
CPB: pulsatile vs non-pulsatile

- 2489 pts
- KDIQO criteria
- No difference in the incidence of AKI between the two methods
- No difference in AKI stages
- No difference in the incidence of AKI with prolonged use of either method

CSA-AKI and Other Outcomes by Group

Outcome	Nonpulsatile	Pulsatile	p Value
All patients (n = 2,489):	Total n = 1,223	Total n = 1,266	
AKI (any stage)	292 (23.9%)	321 (25.4%)	0.392
No AKI	931 (76.1%)	945 (74.6%)	0.120
AKI (stage 1)	166 (13.6 %)	189 (14.9%)	
AKI (stage 2)	36 (2.9%)	55 (4.3%)	
AKI (stage 3)	90 (7.4%)	77 (6.1%)	
Preexisting CKD stage 3 (n = 602):	Total n = 287	Total n = 315	
AKI (any stage)	131 (45.6%)	141 (44.8%)	0.828
AKI (stage 2 or 3)	61 (21.3%)	63 (20.0%)	0.704
Postoperative renal replacement therapy	47 (16.4%)	36 (11.4%)	0.079
Perfusion time > 2 h	Total n = 244	Total n = 247	
AKI (any stage)	77 (31.6%)	87 (35.2%)	0.389
Perfusion time > 3 h	Total n = 47	Total n = 44	
AKI (any stage)	23 (48.9%)	17 (38.6%)	0.323
Other outcomes:			
Postoperative stroke	19 (1.6%)	13 (1.0%)	0.244
30-day mortality	18 (1.5%)	17 (1.3)	0.785
Median length of hospital stay (IQR)	9 (7-14)	9 (6-13)	0.027

Management



KIDNEY DISEASE · IMPROVING GLOBAL OUTCOMES
KDIGO
AKI Stage
High Risk
1
2
3
Discontinue all nephrotoxic agents when possible
Ensure volume status and perfusion pressure
Consider functional hemodynamic monitoring
Monitoring 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

Society of Cardiovascular Anesthesiologists Clinical Practice Update for Management of Acute Kidney Injury Associated With Cardiac Surgery

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Summary on the Management of Acute Kidney Injury in Cardiac Surgery

This is an abbreviated summary for AKI management in cardiac surgery. Based on a moderate level of evidence, our analysis from the randomized controlled trials demonstrates the use of **goal-directed oxygen delivery on CPB** and **"KDIGO bundle of care" in high-risk patients** to reduce CS-AKI.

Intraoperative target blood pressure

- Targeting a higher blood pressure during CPB did not reduce AKI **(a low level of GRADE evidence).**

Choice of specific vasopressors

- Use of vasopressin in vasoplegic shock patients reduced AKI **(a low level of GRADE evidence).**
- Perioperative use of dopamine did not decrease AKI **(a very low level of GRADE evidence).**

"KDIGO bundle of care"

- Using a "KDIGO bundle" (optimization of hemodynamic and volume, functional hemodynamic monitoring, avoidance of nephrotoxic drugs, prevention of hyperglycemia) reduced stage 2/3 AKI in high-risk patients **(a moderate level of GRADE evidence).**

Erythrocyte transfusion threshold

- Modifying/selecting transfusion threshold did not prevent AKI **(a moderate level of GRADE evidence).**

Perioperative dexmedetomidine (alpha-2 agonists)

- Perioperative use of dexmedetomidine did not reduce AKI **(a low level of GRADE evidence).**

Goal-directed oxygen delivery on CPB

- Using a goal-directed perfusion strategy of maintaining oxygen delivery ≥280–300 ml/min/m^2 on CPB reduced AKI **(a moderate level of GRADE evidence).**

SOCIETY OF CARDIOVASCULAR ANESTHESIOLOGISTS
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Acute Kidney Injury Group 2022

Goal-directed perfusion strategy

- The concept of goal-directed oxygen delivery (GDP) refers to maintaining oxygen delivery above a critical value during CPB.
- The recommended critical value during moderate hypothermia is 260–272 mL/min/m2
- The EACTS/EACTA/EBCP guidelines state that the pump flow rate should be adjusted according to the arterial oxygen content to maintain a minimum threshold.

Recommendations	Class[a]	Level[b]	Ref[c]
checked based on oxygenation and metabolic parameters (SvO_2, O_2ER, NIRS, VCO_2 and lactates).			
The pump flow rate should be adjusted according to the arterial oxygen content in order to maintain a minimal threshold of DO_2 under moderate hypothermia.	IIa	B	199,202–204
Pump flow rates may be settled based on lean mass in obese patients.	IIb	B	200

Observational Study > Am J Kidney Dis. 2023 Jun;81(6):675-683.e1.
doi: 10.1053/j.ajkd.2022.11.009. Epub 2022 Dec 29.

Early Postoperative Acetaminophen Administration and Severe Acute Kidney Injury After Cardiac Surgery

Chao Xiong [1], Yuan Jia [1], Xie Wu [1], Yanyan Zhao [2], Su Yuan [3], Fuxia Yan [4], Daniel I Sessler [5]

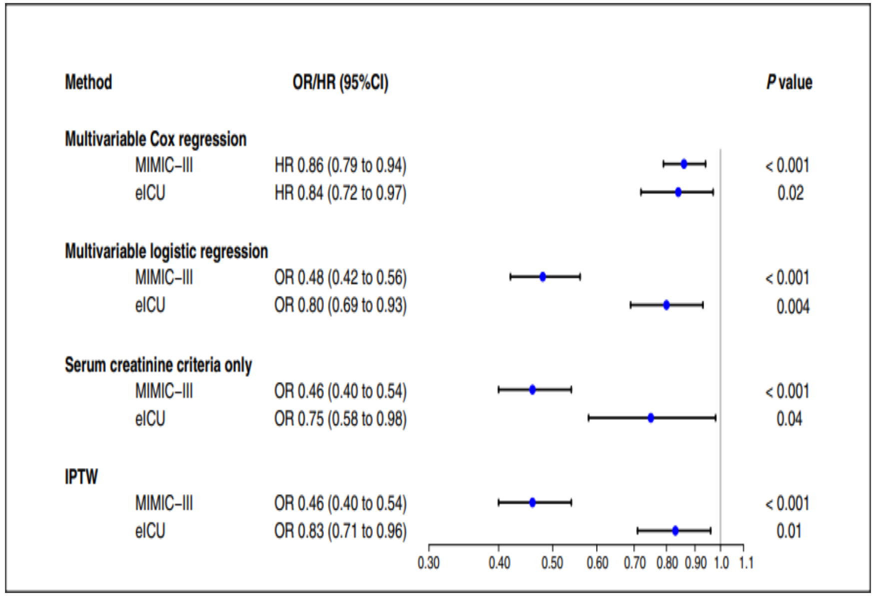
The overall incidence of severe AKI was 58% (3,390 patients) in the MIMIC-III cohort and 37% (1,431 patients) in the eICU cohort.

The benefit was consistent across sensitivity and subgroup analyses.

Table 2. Incidence of Severe AKI in Each Study Registry According to Acetaminophen Exposure

	MIMIC-III (n = 5,791)			eICU (n = 3,840)		
	Nonexposed Group (n = 1,606)	Exposed Group (n = 4,185)	*P*	Nonexposed Group (n = 1,103)	Exposed Group (n = 2,737)	*P*
Severe AKI by Scr and UO criteria	1,205 (75.0%)	2,185 (52.2%)	<0.001	445 (40.3%)	986 (36.0%)	0.01
Severe AKI by Scr criteria only	365 (22.7%)	496 (11.9%)	<0.001	107 (9.7%)	201 (7.3%)	0.02

Data are presented as n (%). Pearson χ^2 tests were used to perform univariable analyses for outcomes. Scr and UO criteria are from the KDIGO AKI definition. Abbreviations: AKI, acute kidney injury; eICU, eICU Collaborative Research Database; MIMIC-III, Medical Information Mart for Intensive Care III; Scr, serum creatinine; UO, urine output.



We have no dosage available

Renal Replacement Therapy (RRT)

- Central role in the treatment of CSA-AKI
- Continuous – RRT: the most used methods in ICUs

- Continuous volume control
- Hemodynamic stability

Renal Replacement Therapy (RRT)

Table 3 | **Conventional criteria for initiation of renal replacement therapy in acute kidney injury**

Indications	Criteria
Clinical	• Anuria (negligible urine output for 6 h) • Severe oliguria (urine output <200 ml over 12 h) • Volume overload (especially pulmonary oedema that is unresponsive to diuretics) • Clinical complications of uraemia (for example, encephalopathy, pericarditis and neuropathy)
Laboratory	• Hyperkalaemia (potassium concentration >6.5 mmol/l) • Severe metabolic acidosis (pH <7.2 despite normal or low partial pressure of carbon dioxide in arterial blood) • Pronounced azotaemia (urea concentrations >30 mmol/l or creatinine concentrations >300 μmol/l)

What is the correct start time

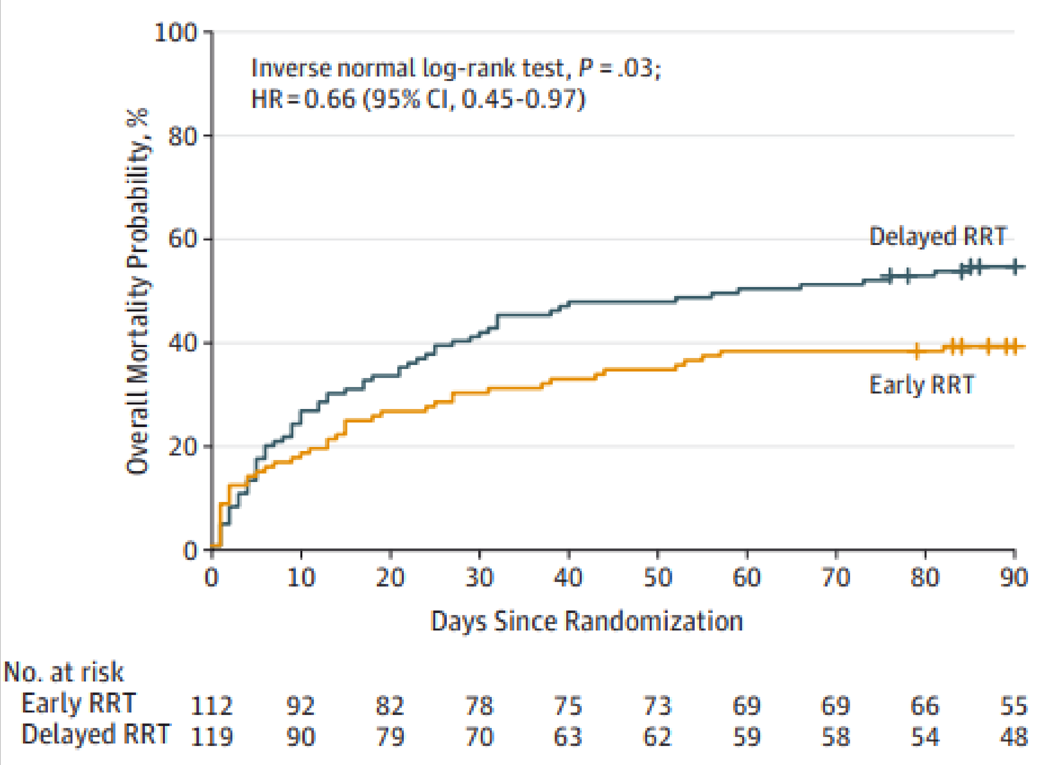
What is the correct dose

What is the appropriate method

Time to start

- ELAIN trial
- 231 pts – 108 patients after cardiac surgery
- Early onset: 8 hours from KDIQO stage 2 diagnosis
- Delayed onset: 12 hours from KDIQO stage 3 diagnosis
- Early initiation of renal function replacement significantly reduced mortality at 90 days

Figure 2. Mortality Probability Within 90 Days After Study Enrollment for Patients Receiving Early and Delayed Initiation of Renal Replacement Therapy (RRT)



Zarbock, A. et al. Effect of early versus delayed initiation of renal replacement therapy on mortality in critically ill patients with acute kidney injury: the ELAIN randomized clinical trial. *JAMA* ***(2016).***

Time to start

- 203 pts
- Early start < 3 days from the surgery
- Delayed start > 3 days

- Patients who underwent early RRT had better survival rates, better renal function at discharge, and shorter hospital stays

Table 4. Hospital mortality according to initiation of RRT after cardiac surgery

	Early RRT (≤3 days; n = 95)	Late RRT (>3 days; n = 77)	p value
Hospital mortality, n	59 (53.2%)	74 (80.4%)	
Crude OR (95% CI)	1.00 (Ref.)	4.32 (2.05–9.08)	<0.001
Age- and sex-adjusted OR (95% CI)	1.00 (Ref.)	4.26 (2.00–9.06)	<0.001
Multivariate-adjusted OR[1] (95% CI)	1.00 (Ref.)	4.06 (1.64–10.03)	0.002

[1] Adjusted for age, sex, hospital, hypertension, Euroscore, urine output 48 h, percentage change in creatinine at 48 h, days of RRT, baseline MDRD <30 ml/min.

Table 5. Estimates (regression coefficients and 95% CI) for length of hospital stay according to initiation of RRT after cardiac surgery

	Early RRT (≤3 days; n = 95)	Late RRT (>3 days; n = 77)	p value
Hospital LOS, days	25.4 (28.6)	38.2 (33.2)	
Crude (β-coefficient)	0 (Ref.)	+12.9 (+2.9 to +22.9)	0.012
Age and sex adjusted (β-coefficient)	0 (Ref.)	+13.9 (+3.8 to +24.1)	0.007
Multivariate-adjusted model[1] (β-coefficient)	0 (Ref.)	+11.7 (+1.4 to +21.9)	0.026

[1] Adjusted for age, sex, hospital, hypertension, Euroscore, urine output 48 h, percentage change in creatinine at 48 h, days of RRT, baseline MDRD <30 ml/min.

Table 6. Estimates (regression coefficients and 95% CI) of percentage change in creatinine (%ΔCr) according to initiation of RRT after cardiac surgery

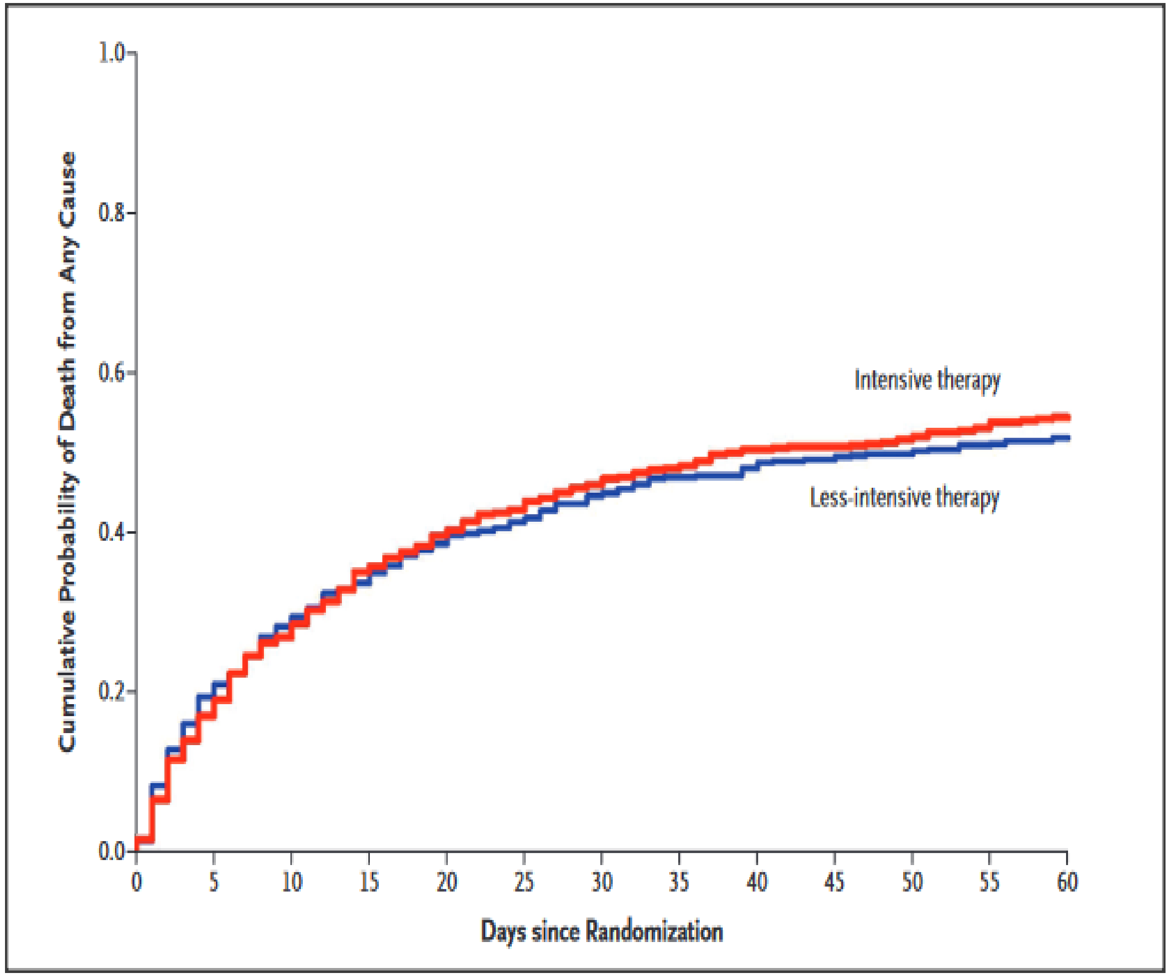
	Early RRT (≤3 days)	Late RRT (>3 days)	p value
Percentage change in creatinine (%ΔCr)	48.0 (176)	68.5 (124)	
Crude (β-coefficient)	0 (Ref.)	+24.12 (–22.40 to +70.65)	0.307
Age and sex adjusted (β-coefficient)	0 (Ref.)	+23.09 (–23.95 to +70.12)	0.334
Multivariate-adjusted model[1] (β-coefficient)	0 (Ref.)	+67.7 (+28.5 to +106.4)	0.001

Percentage change in creatinine (%ΔCr) was defined as the difference between the preoperative value and creatinine level at hospital discharge represented as a percentage of the preoperative value.
[1] Adjusted for age, sex, hospital, hypertension, Euroscore, urine output 48 h, percentage change in creatinine at 48 h, days of RRT, baseline MDRD <30 ml/min.

Garcia-Fernandez, N. et al. Timing of renal replacement therapy after cardiac surgery: a retrospective multicenter Spanish cohort study. *Blood Purif.* ***(2011).***

Dosage

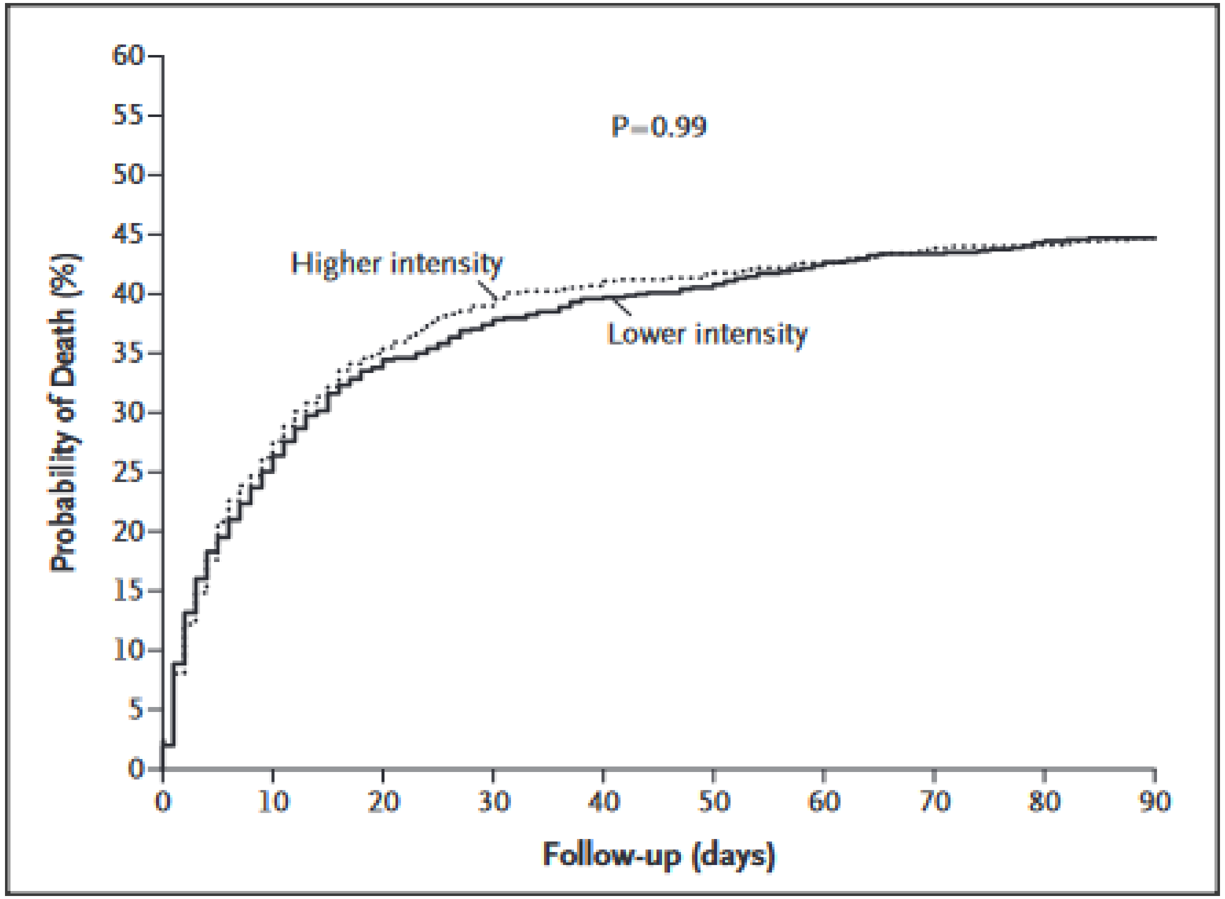
- **ATN study** : 1124 pts – 463 pts with CSA-AKI
- High – intensity :daily IHD or CVVHD with 35ml/kg/hr
- Low-intensity : IHD 3times/wk or CVVHD with 20ml/kg/hr
- No difference in mortality, improvement of renal function
- Meta-analysis: patients who received more extensive RRT needed more days of mechanical ventilation



Dosage

- Renal study: 1508 pts – 269 pts with CSA-AKI
- CVVHD 40ml/kg/hr vs CVVHD 25ml/kg/hr

- No difference in mortality at 28 and 90 days
- No difference in duration of needed RRT or improvement in renal function



Method

- 80 pts with CSA-AKI
- CVVHDF with 35ml/kg/hr vs EDD (extended daily dialysis) 6-8 hrs

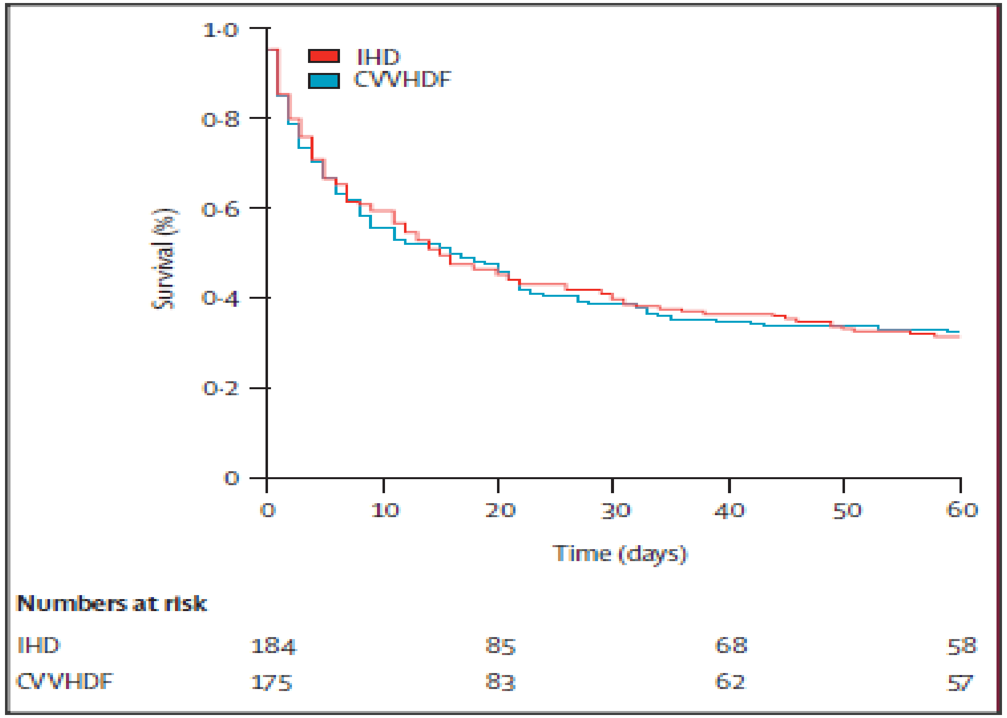
Table 2 Patients' outcome

Variables	EDD group (n = 40)	CVVHDF group (n = 40)	*P*-value
Mortality rate at day 30	7 (17.5)	9 (22.5)	NS
Length of stay in the ICU (days)	23 ± 5	19 ± 8	NS
Renal recovery in survivors	21 (63.63)	23 (74.19)	NS
Ultrafiltration volume (ml/72 h)	5680 ± 750	6300 ± 870	NS
Cost of RRT ($)	984.6 ± 615.4	4384.6 ± 2135.3	<0.001

Badawy, S., H. A. & Samir, E. M. A prospective randomized comparative pilot trial on extended daily dialysis versus continuous venovenous hemodiafiltration in acute kidney injury after cardiac surgery. *Egypt. J. Cardiothorac. Anesth.* ***(2013).***

Method

- 360 pts -107 pts with CSA-AKI
- CVVHDF (500ml/hr) vs IHD 4hrs/48hrs (low blood flow, low temperature, high sodium concentration)



	Intermittent haemodialysis	Continuous venovenous haemodiafiltration	p value
Survival			
Day 28	41·8% (34·7–49·0)	38·9% (31·6–46·1)	0·65
Day 60 (primary endpoint)	31·5% (24·8–38·2)	32·6% (25·6–39·5)	0·98
Day 90	27·2% (20·8–33·6)	28·5% (21·8–35·2)	0·95
Renal support duration (days)	11 (8–13)	11 (8–14)	0·84
Length of ICU stay (days)	20 (16–23)	19 (15–22)	0·73
Length of hospital stay (days)	30 (24–35)	32 (22–42)	0·66

Values are mean (95% CI). ICU=intensive-care unit.

Table 3: Outcomes according to treatment group

Vinsonneau, C. et al. Continuous venovenous haemodiafiltration versus intermittent haemodialysis for acute renal failure in patients with multiple-organ dysfunction syndrome: a multicentre randomised trial. *Lancet* ***(2006).***

Summarizing

- High-risk patients with multiple comorbidities
- Early detection
- Immediate support
- KDIQO approach
- Open discussion on timing, dosage, method of RRT

Our purpose: the reduction of morbidity and mortality