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Asan Medical Center

CARDIAC ASSOCIATED ACUTE KIDNEY INJURY PREVENTION

ASAN MEDICAL CENTER
Department of Thoracic and Cardiovascular Surgery
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CONTENTS

INTRODUCTION

Cardiac Surgery Associated AKI (CSA-AKI)

- **Common complication**
  - **5 – 42%** of cardiac surgery patients undergoing CPB
  - **1 – 5%** of those require renal replacement therapy (RRT)
  - Associated with decreased survival

INTRODUCTION

Cardiac Surgery Associated AKI (CSA-AKI)

- **Diagnosis**
  - **KDIGO criteria** (Kidney Disease Improving Global Outcomes)

Stage	Creatinine	Urine Output
1	1.5–1.9 times baseline, OR Increase in SCr by ≥0.3 mg/dL	<0.5 mL/kg/h × 6–12 h
2	2.0–2.9 times baseline	<0.5 mL/kg/h for ≥12 h
3	≥3 times baseline, OR SCr ≥4 mg/dL, OR Initiation of RRT	<0.3 mL/kg/h for ≥24 h, OR Anuria ≥ 12 h

PATHOPHYSIOLOGY

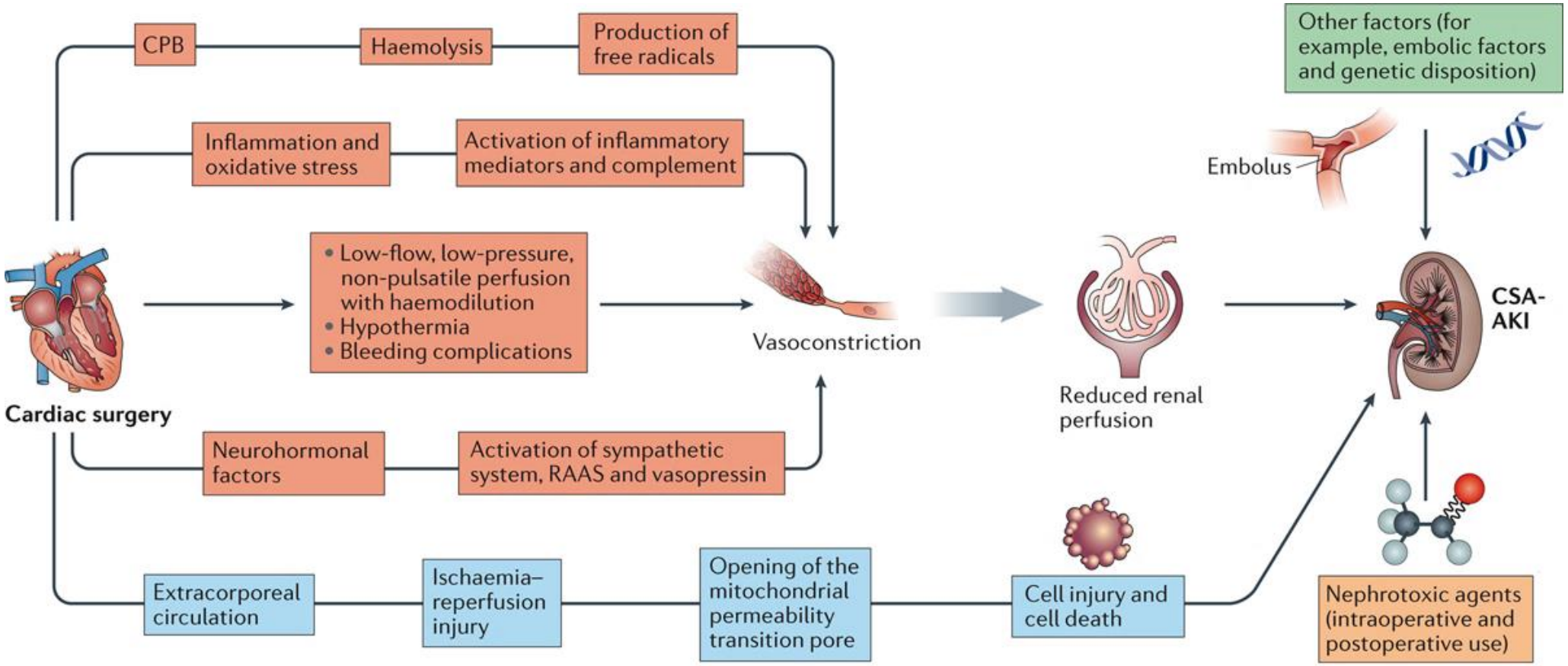
Pathophysiology of CSA-AKI

- **Complex**
- **Multifactorial**
- **Poorly understood**

- **Major injury pathways**
  - Hypoperfusion, ischemia-reperfusion injury
  - Inflammation, oxidative stress, hemolysis
  - Neurohumoral activation, nephrotoxins, mechanical factors

PATHOPHYSIOLOGY

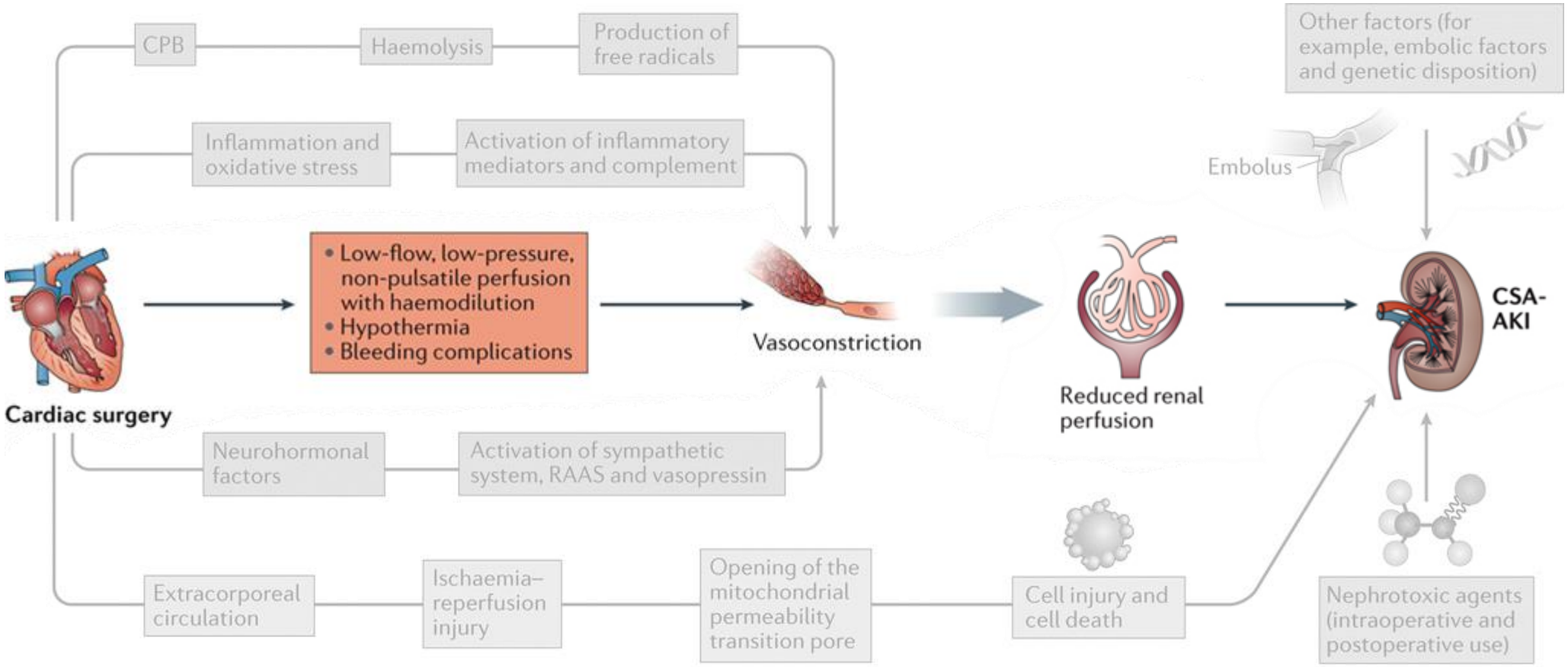
Pathophysiology of CSA-AKI



Nat Rev Nephrol. 2017 Nov;13(11):697-711

PATHOPHYSIOLOGY

Pathophysiology of CSA-AKI



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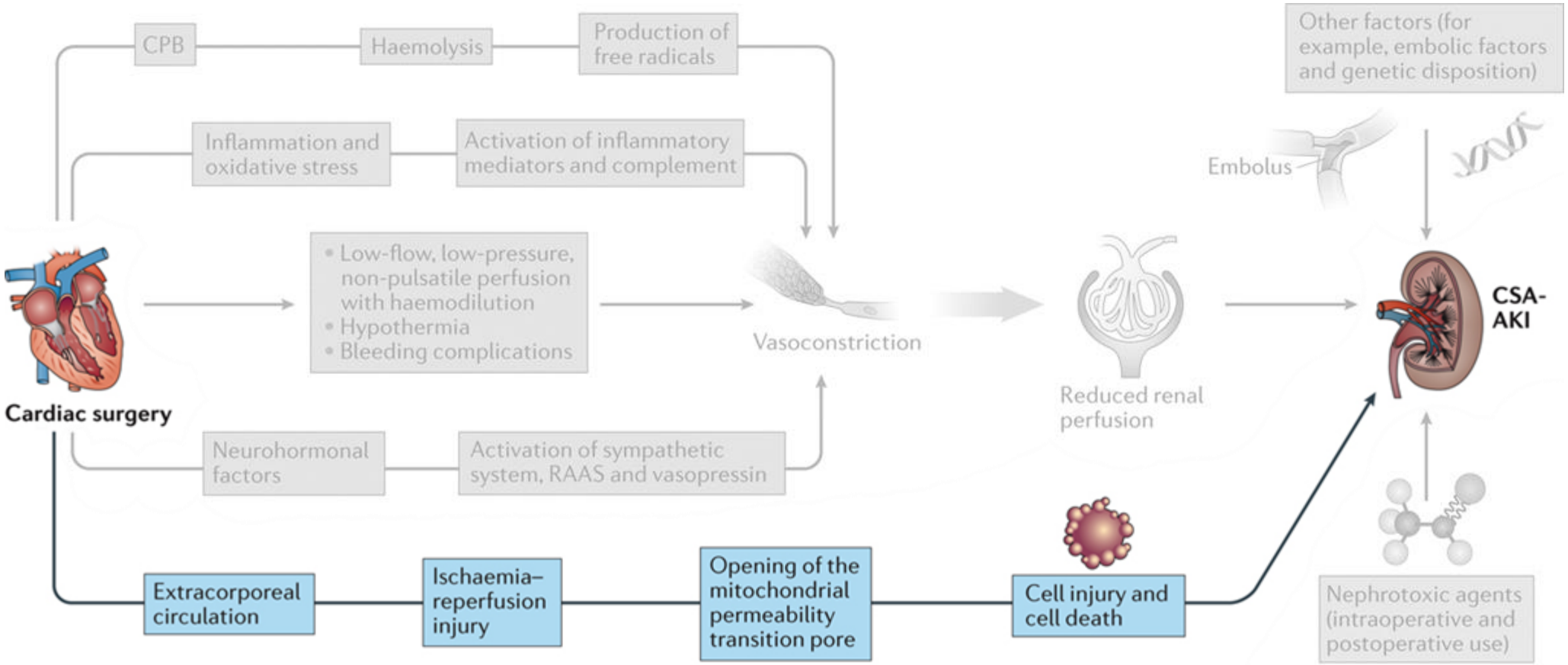

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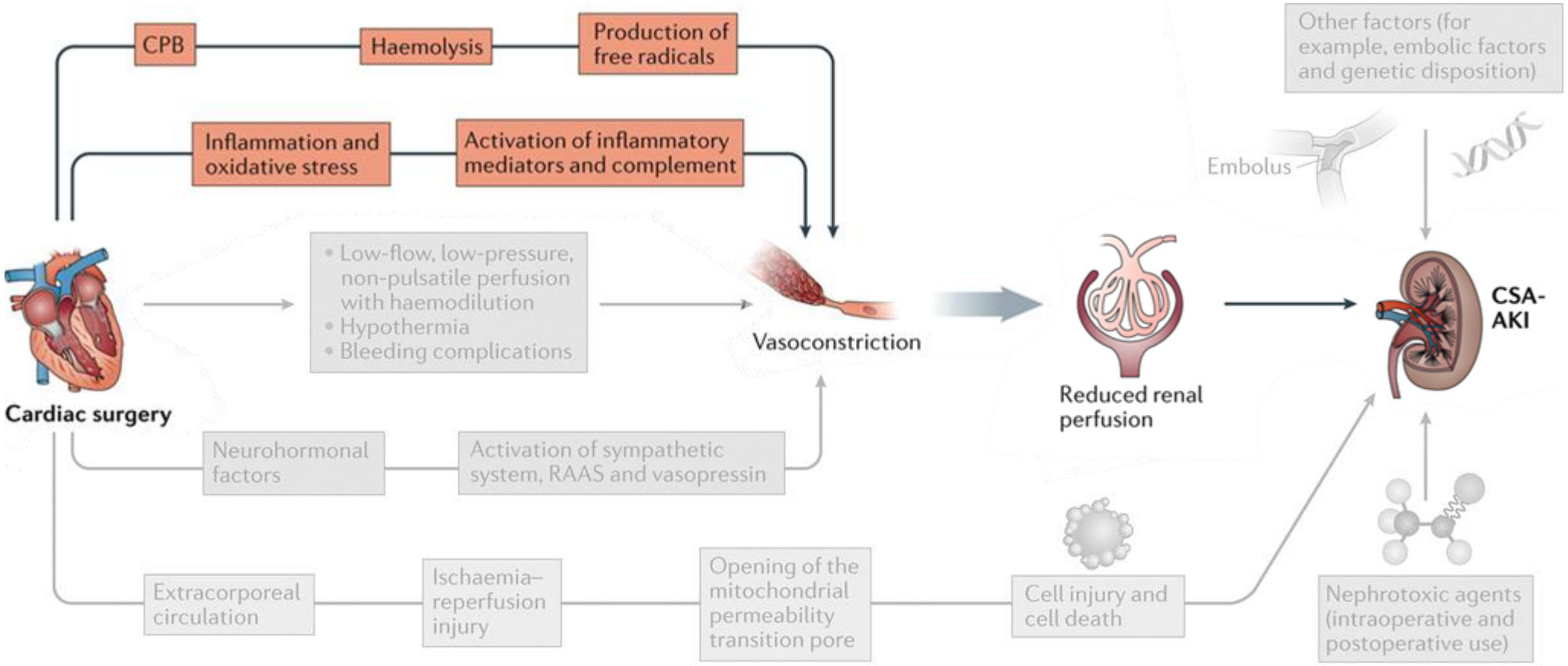

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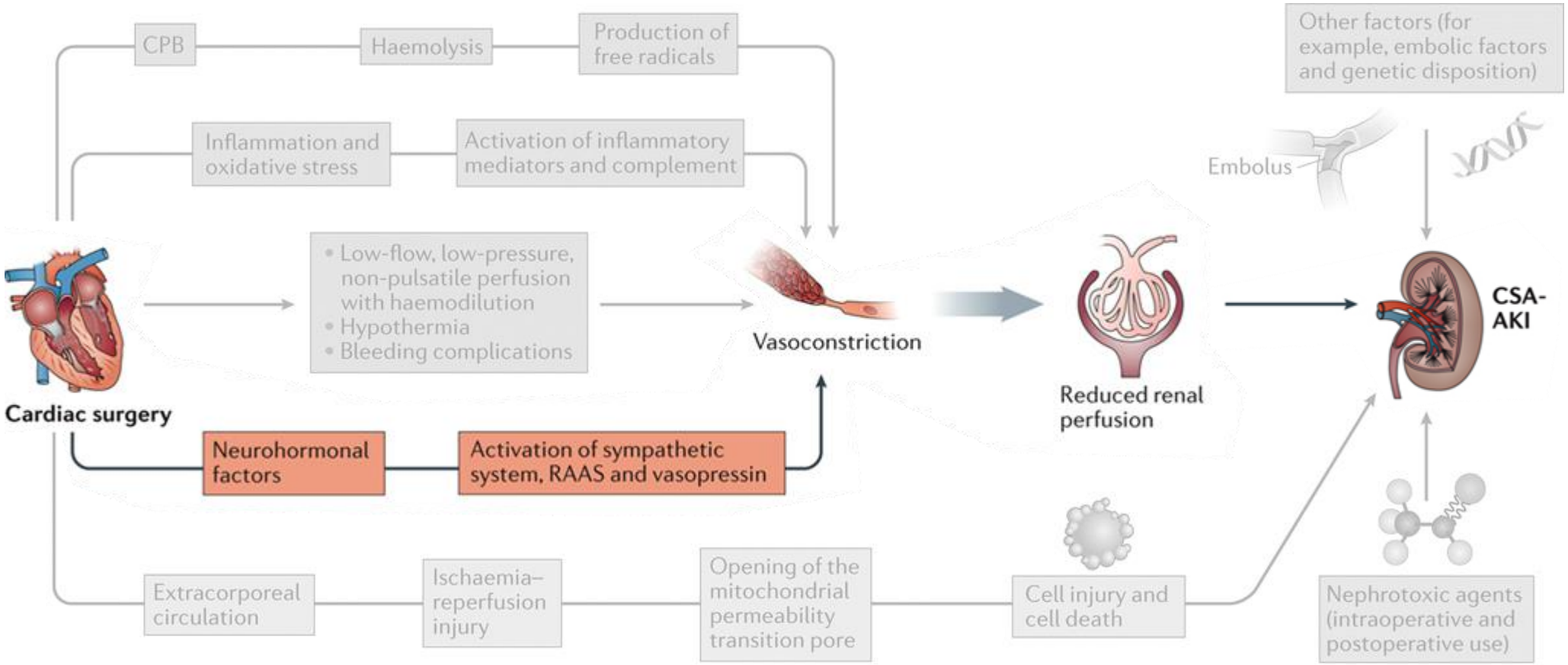

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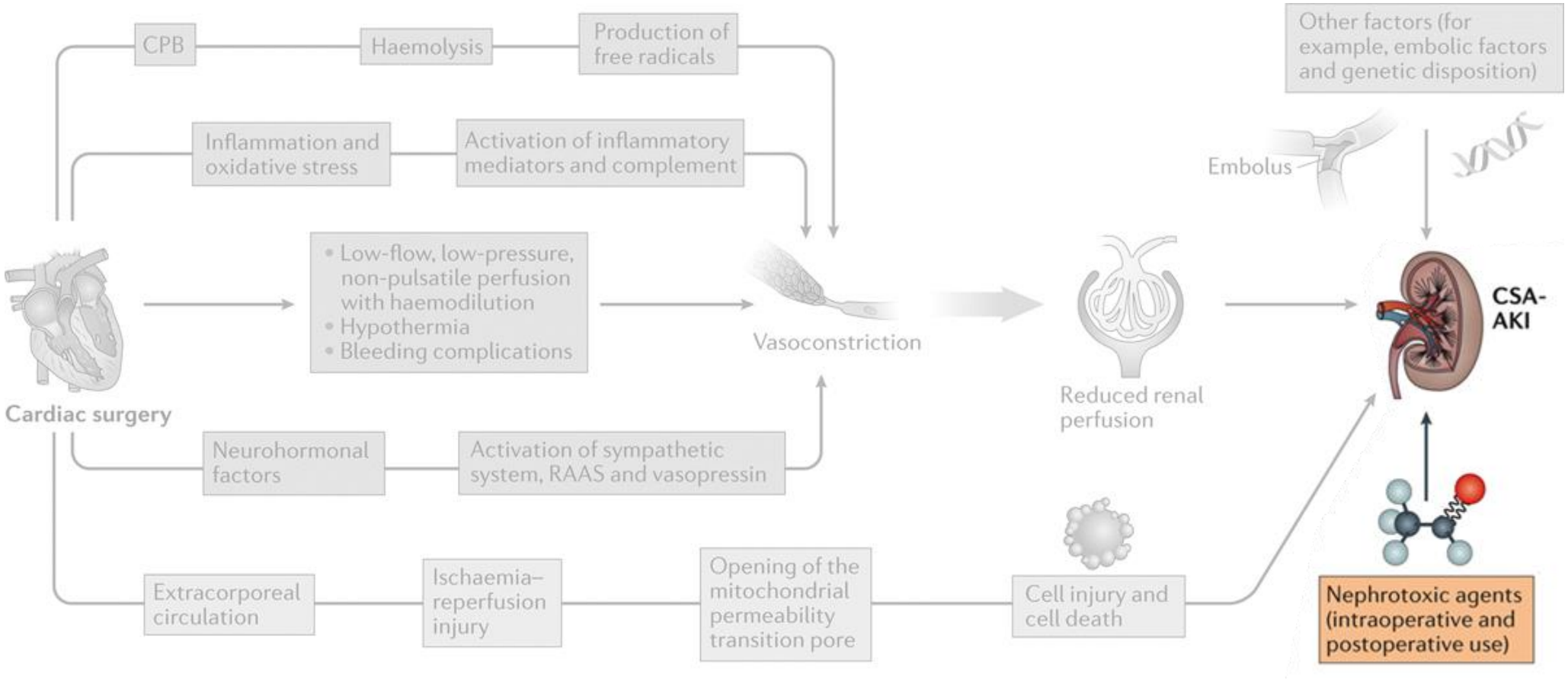

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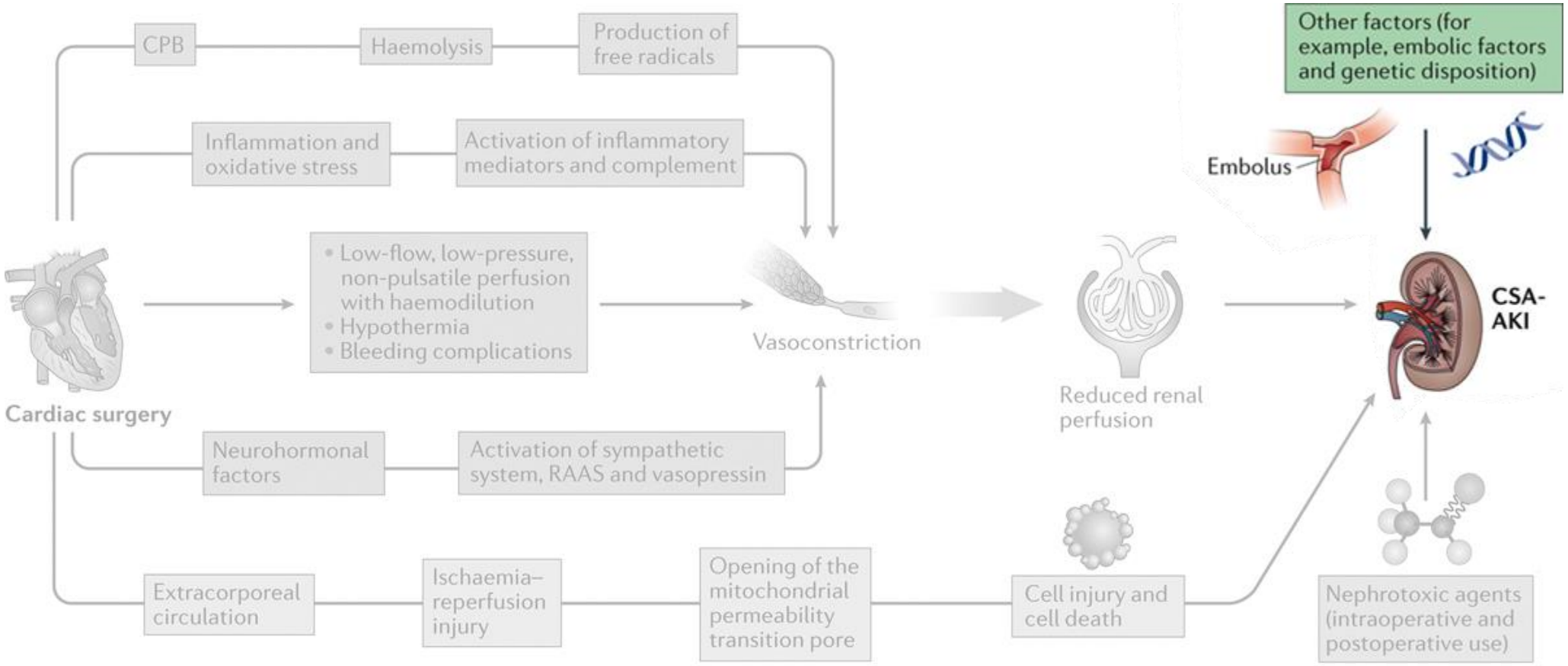

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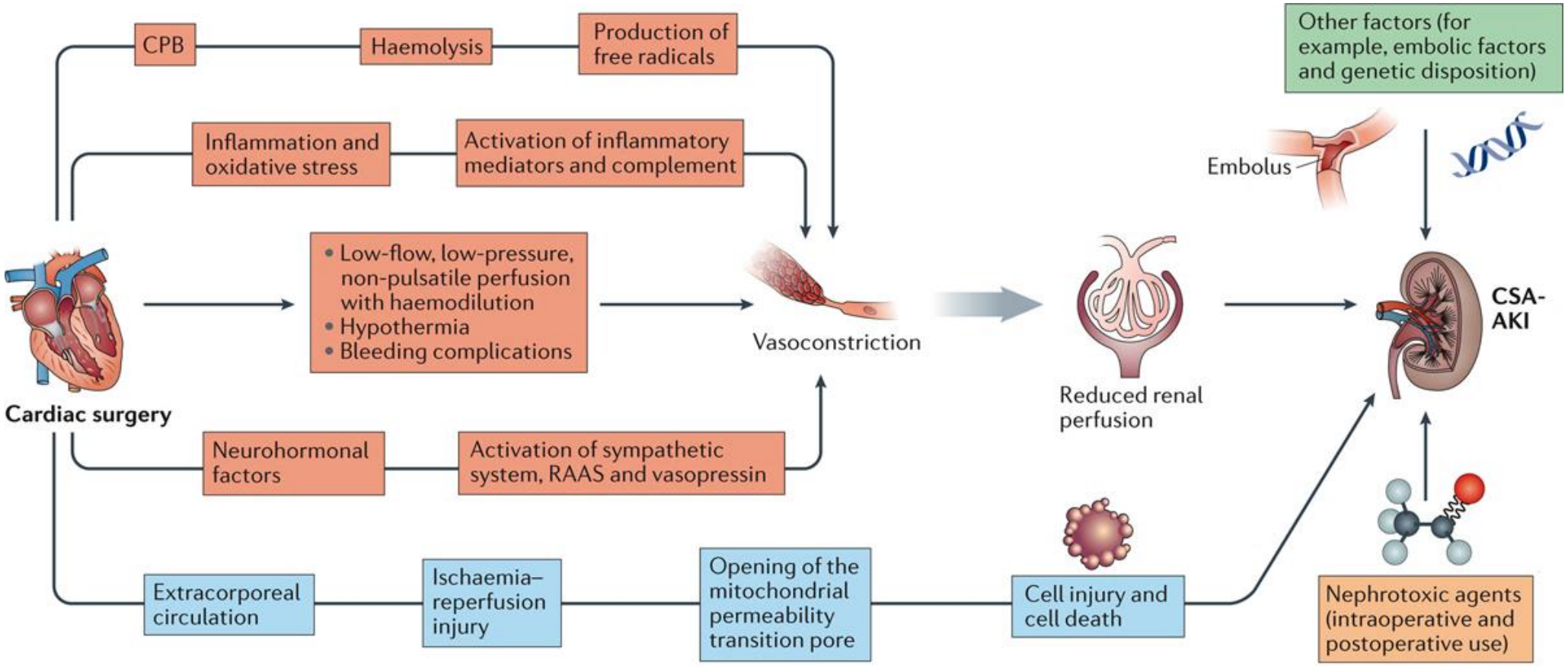


Nat Rev Nephrol. 2017 Nov;13(11):697-711

PREVENTION

Prevention Strategies of CSA-AKI

- Pharmacologic strategies
- Hemodynamics / Fluid management strategies
- Other strategies

PREVENTION

Pharmacologic Strategies

- **Dexmedetomidine** (α2-adrenergic receptor agonist)
  - Sedative, analgesic, anti-sympathetic effects
  - inflammatory cytokines levels, damage associated molecular patterns ↓
    → prevent renal tubular damage

  - **CSA-AKI Incidence ↓**
    - especially in patients > 60 years-old
    - administered immediately after induction
    - maintained intraoperatively

Meta-analysis (9 RCT, n=1308)

Effect of Dexmedetomidine on Cardiac Surgery-Associated Acute Kidney Injury: A Meta-Analysis With Trial Sequential Analysis of Randomized Controlled Trials

Ke Peng, MD[*,†], David Li, MD[†], Richard L. Applegate II, MD[†], David A. Lubarsky, MD, MBA[†], Fu-hai Ji, MD, PhD[*], Hong Liu, MD, FASE[†,1]

[*]*Department of Anesthesiology, First Affiliated Hospital of Soochow University, Suzhou, Jiangsu, China*
[†]*Department of Anesthesiology and Pain Medicine, University of California Davis Health, Sacramento, CA*

PREVENTION

Pharmacologic Strategies

- **Atrial Natriuretic Peptide**
  - Inhibit renin–angiotensin–aldosterone system and sympathetic nervous system → prevent vasoconstriction

Meta-analysis (14 trials, n=2207)

- **CSA-AKI incidence ↓**
- **RRT ↓**
- **30-day mortality ↓**

Pharmacological interventions for the prevention of renal injury in surgical patients: a systematic literature review and meta-analysis

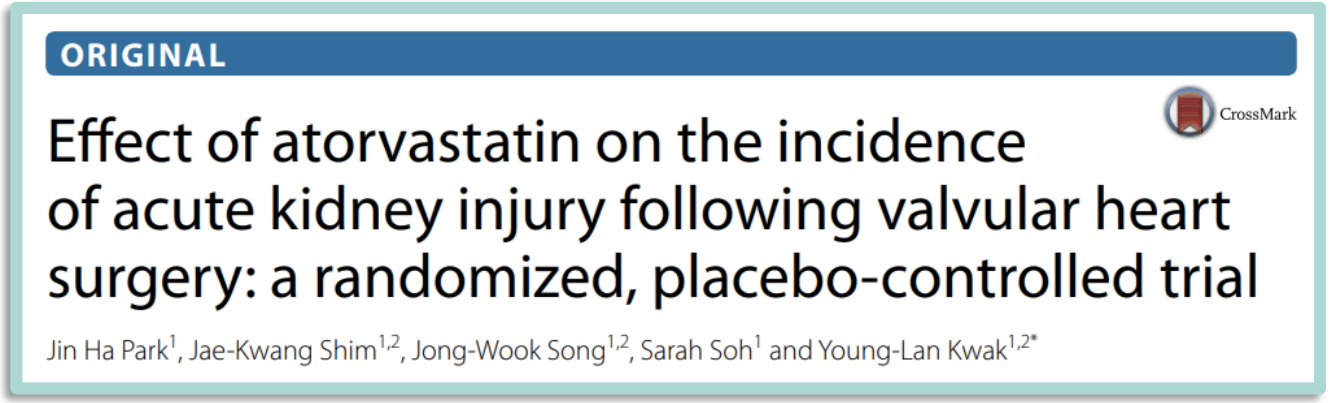
Suraj Pathak*, Guido Olivieri, Walid Mohamed, Riccardo Abbasciano, Marius Roman, Sara Tomassini, Florence Lai, Marcin Wozniak and Gavin J. Murphy

Department of Cardiovascular Sciences, National Institute for Health Research Leicester Biomedical Research Unit in Cardiovascular Medicine, University of Leicester, Leicester, UK

Pharmacologic Strategies

- **Statins**
  - Anti-inflammatory and antioxidant activities

Single Center RCT , n=200



- Control group : **26 / 100 (26%)**
- Statin group : **21 / 100 (21%)**

- **Statin treatment not associated with reduced incidence of CSA-AKI**

Intensive Care Med. 2016 Sep;42(9):1398-407

Pharmacologic Strategies

- **Fenoldopam**
  (selective dopamine D1 receptor agonist)
  - Smooth muscle relaxation, vasodilation, sodium reabsorption inhibition in renal tubules → renal vasodilatory effect

Multicenter RCT, n=667

Original Investigation

Effect of Fenoldopam on Use of Renal Replacement Therapy Among Patients With Acute Kidney Injury After Cardiac Surgery
A Randomized Clinical Trial

Tiziana Bove, MD; Alberto Zangrillo, MD; Fabio Guarracino, MD; Gabriele Alvaro, MD; Bruno Persi, MD; Enivarco Maglioni, MD; Nicola Galdieri, MD; Marco Comis, MD; Fabio Caramelli, MD; Daniela C. Pasero, MD; Giovanni Pala, MD; Massimo Renzini, MD; Massimiliano Conte, MD; Gianluca Paternoster, MD; Blanca Martinez, MD; Fulvio Pinelli, MD; Mario Frontini, MD; Maria C. Zucchetti, MD; Federico Pappalardo, MD; Bruno Amantea, MD; Annamaria Camata, MD; Antonio Pisano, MD; Claudio Verdecchia, MD; Erika Dal Checco, MD; Claudia Cariello, MD; Luana Faita, MD; Rubia Baldassarri, MD; Anna M. Scandroglio, MD; Omar Saleh, MD; Rosalba Lembo, MSc; Maria G. Calabrò, MD; Rinaldo Bellomo, MD; Giovanni Landoni, MD

- Control group : **60 / 329 (18%)**
- Fenoldopam group : **69 / 338 (20%)**

- **Not effective in AKI prevention, instead associated with hypotension**

JAMA. 2014 Dec 3;312(21):2244-53

PREVENTION

Pharmacologic Strategies

- **Failed to show preventive effects on CSA-AKI**
  (Introduced → evaluated → abandoned)

  - **Exogenous Erythropoetin**
  - **Intravenous bicarbonate/Urinary alkalization**
  - **Albumin**
  - **Corticosteroids**
  - **Etc**

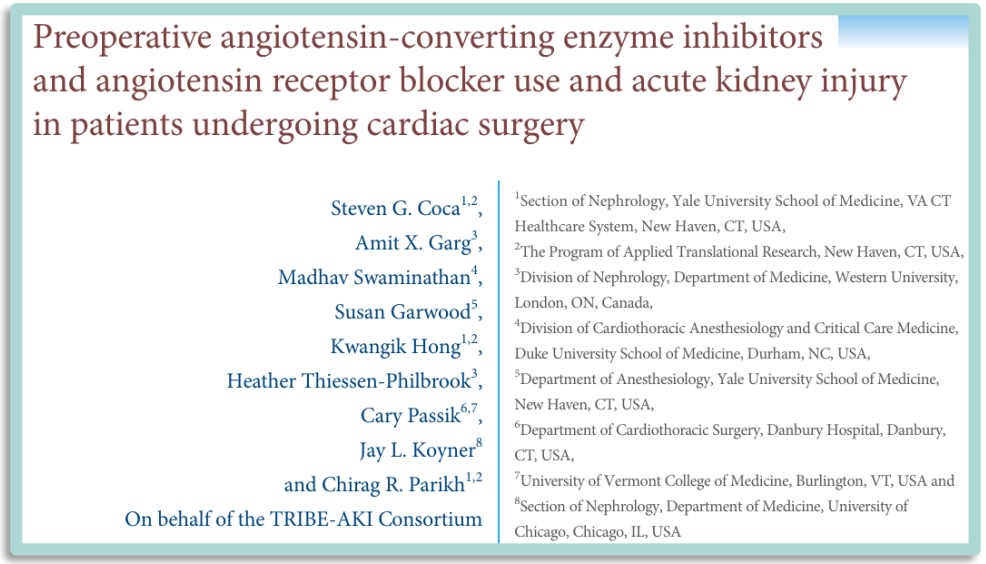
PREVENTION

Pharmacologic Strategies (Nephrotoxins)

- **Preoperative ACEi and ARB**
  - Higher risk of intraoperative hypotension
  - Most studies show association with postoperative AKI
    - No exposure group : 31%
    - Held group : 34%
    - **Continued group : 42%**

- **Recommend ACEi/ARB discontinuation at least 24h before operation**

Multicenter Prospective Study, n=1594



Preoperative angiotensin-converting enzyme inhibitors and angiotensin receptor blocker use and acute kidney injury in patients undergoing cardiac surgery

Steven G. Coca[1,2], Amit X. Garg[3], Madhav Swaminathan[4], Susan Garwood[5], Kwangik Hong[1,2], Heather Thiessen-Philbrook[3], Cary Passik[6,7], Jay L. Koyner[8] and Chirag R. Parikh[1,2]

On behalf of the TRIBE-AKI Consortium

[1]Section of Nephrology, Yale University School of Medicine, VA CT Healthcare System, New Haven, CT, USA, [2]The Program of Applied Translational Research, New Haven, CT, USA, [3]Division of Nephrology, Department of Medicine, Western University, London, ON, Canada, [4]Division of Cardiothoracic Anesthesiology and Critical Care Medicine, Duke University School of Medicine, Durham, NC, USA, [5]Department of Anesthesiology, Yale University School of Medicine, New Haven, CT, USA, [6]Department of Cardiothoracic Surgery, Danbury Hospital, Danbury, CT, USA, [7]University of Vermont College of Medicine, Burlington, VT, USA and [8]Section of Nephrology, Department of Medicine, University of Chicago, Chicago, IL, USA

Nephrol Dial Transplant. 2013 Nov;28(11):2787-99

Pharmacologic Strategies (Nephrotoxins)

- **NSAID**
  - No preventive effects on CSA-AKI
  - Increases risk of AKI due to reduced prostaglandin synthesis and alterations in renal microcirculation causing renal hypoxia

Review

Nonsteroidal Anti-Inflammatory Drugs and the Kidney

Walter H. Hörl

Division of Nephrology and Dialysis, Department of Medicine III, Medical University of Vienna, Währinger Gürtel 18-20, A-1090 Vienna, Austria; E-Mail: walter.hoerl@meduniwien.ac.at; Tel.: +43-1-40400 4390; Fax: +43-1-40400-4392

Pharmaceuticals (Basel). 2010 Jul 21;3(7):2291-2321

PREVENTION

Hemodynamic/ Fluid Management Strategies

- **Hemodynamic stability / adequate intravascular blood volume** crucial for renal protection
- **Dynamic fluid shifts / venous congestion**: common after operation
- Renal perfusion: sensitive to changes in arterial blood flow and renal afterload

Single Center Prospective Study, n=282

- **Reduced MAP, increased fluid balance** independently associated with increased mortality and RRT

Perioperative Hemodynamic Instability and Fluid Overload are Associated with Increasing Acute Kidney Injury Severity and Worse Outcome after Cardiac Surgery

Anja Haase-Fielitz[a, c] Michael Haase[b, d] Rinaldo Bellomo[g] Paolo Calzavacca[g]
Anke Spura[c] Hassina Baraki[e] Ingo Kutschka[e] Christian Albert[f]

Blood Purif. 2017;43(4):298-308

Hemodynamic/ Fluid Management Strategies

- Optimization of intravascular blood volume
  - Volume status Assessment
    - Point-of-care-ultrasound (POCUS)
    - Fluid responsiveness
    - Arterial pulse-contour analysis

- **Dynamic measures from POCUS :** better estimate of volume status than CVP

Single Center Prospective Study, n=124

Intensivist Use of Hand-Carried Ultrasonography to Measure IVC Collapsibility in Estimating Intravascular Volume Status: Correlations with CVP

S Peter Stawicki, MD, Benjamin M Braslow, MD, FACS, Nova L Panebianco, MD, James N Kirkpatrick, MD, Vicente H Gracias, MD, FACS, Geoffrey E Hayden, MD, Anthony J Dean, MD

J Am Coll Surg. 2009 Jul;209(1):55-61

Hemodynamic/ Fluid Management Strategies

- **Diuretics**
  - Control group vs. Intermittent furosemide group : No difference

Single Center RCT, n=123

A study of the efficacy of furosemide as a prophylaxis of acute renal failure in coronary artery bypass grafting patients: A clinical trial

Fatemeh Bayat[(1)], Zahra Faritous[(2)], Nahid Aghdaei[(2)], Ali Dabbagh[(3)]

  - Selective administration of diuretics, only for managing fluid overload
  - **No prophylactic or routine use of diuretic therapy**

ARYA Atheroscler. 2015 May;11(3):173-8

PREVENTION

Hemodynamic/ Fluid Management Strategies

- **Fluids**
  - High-chloride fluids : significantly higher risk of AKI

Meta-analysis (21 trials, n=6253)

Meta-analysis of high- *versus* low-chloride content in perioperative and critical care fluid resuscitation

M. L. Krajewski[1], K. Raghunathan[1,2], S. M. Paluszkiewicz[3], C. R. Schermer[4] and A. D. Shaw[5]

[1]Department of Anesthesiology, Duke University Medical Center, and [2]Anesthesiology Service, Durham VA Medical Center, Durham, North Carolina, [3]Boston Strategic Partners, Boston, Massachusetts, [4]Baxter Healthcare Corporation, Deerfield, Illinois, and [5]Department of Anesthesiology, Vanderbilt University Medical Center, Nashville, Tennessee, USA

Correspondence to: Professor A. D. Shaw, Division of Cardiothoracic Anesthesiology, Vanderbilt University Medical Center, Nashville, Tennessee 37232–8274, USA (e-mail: andrew.shaw@vanderbilt.edu)

  - **Balanced crystalloid solutions** significantly decreases stage 1 AKI

PREVENTION

Other Strategies

- **Hyperglycemia**
  - Increased production of inflammatory cytokines and superoxide

- **Glycemic control**
  - **AKI incidence ↓**
  - **RRT ↓**
  - **30-day mortality ↓**

Single Center Retrospective Study, n=1050

Tight perioperative glucose control is associated with a reduction in renal impairment and renal failure in non-diabetic cardiac surgical patients

Patrick Lecomte[1], Bruno Van Vlem[2], Jose Coddens[1], Guy Cammu[1], Guy Nollet[1], Frank Nobels[3], Hugo Vanermen[4] and Luc Foubert[1]

[1]Department of Anaesthesiology and Critical Care Medicine, Onze-Lieve-Vrouw Hospital, Moorselbaan 164, 9300 Aalst, Belgium
[2]Department of Nephrology, Onze-Lieve-Vrouw Hospital, Moorselbaan 164, 9300 Aalst, Belgium
[3]Department of Endocrinology, Onze-Lieve-Vrouw Hospital, Moorselbaan 164, 9300 Aalst, Belgium
[4]Department of Cardiothoracic and Vascular Surgery, Onze-Lieve-Vrouw Hospital, Moorselbaan 164, 9300 Aalst, Belgium

Crit Care. 2008;12(6):R154

Other Strategies

- **KDIGO bundle**
  - Discontinue nephrotoxins, optimize hemodynamics/fluid status, avoid hyperglycemia, monitor SCr and urine output

- **CSA-AKI incidence ↓**
- **CSA-AKI Severity ↓**

Single Center RCT, n=276

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*]

Intensive Care Med. 2017 Nov;43(11):1551-1561

Other Strategies

- **KDIGO bundle**
  - **Incidence of stage 2 and 3 AKI ↓**

Multicenter RCT, n=278

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

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

SUMMARY

CONCLUSION

- **CSA-AKI :** Common, pathophysiology complex
- **KDIGO Bundle**
  - Significantly reduces incidence/severity of CSA-AKI
  - Application of KDIGO Bundle important
- **Further Research :** Needed to identify effective interventions for CSA-AKI prevention optimization

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