Improving Outcomes With RRT: Effective Management of Patients with Cardiac Surgery–Associated AKI

Baxter Critical Care Institute

GBU-AT00-220030 V1.0 07/22

Purpose and intended use of this module

Each module of the “Improving Outcomes With RRT” series discusses one of the clinical challenges faced by clinicians when managing patients with AKI. These modules are intended as a high-level, data-driven overview of when and why these challenges may occur, the burden they place on patients, and the strategies currently in use to manage them.

While the content of these modules may include references to guidelines published by external organizations, they are intended for informational purposes **only** and are **not** a substitute for local clinical practice guidelines and/or regulations.

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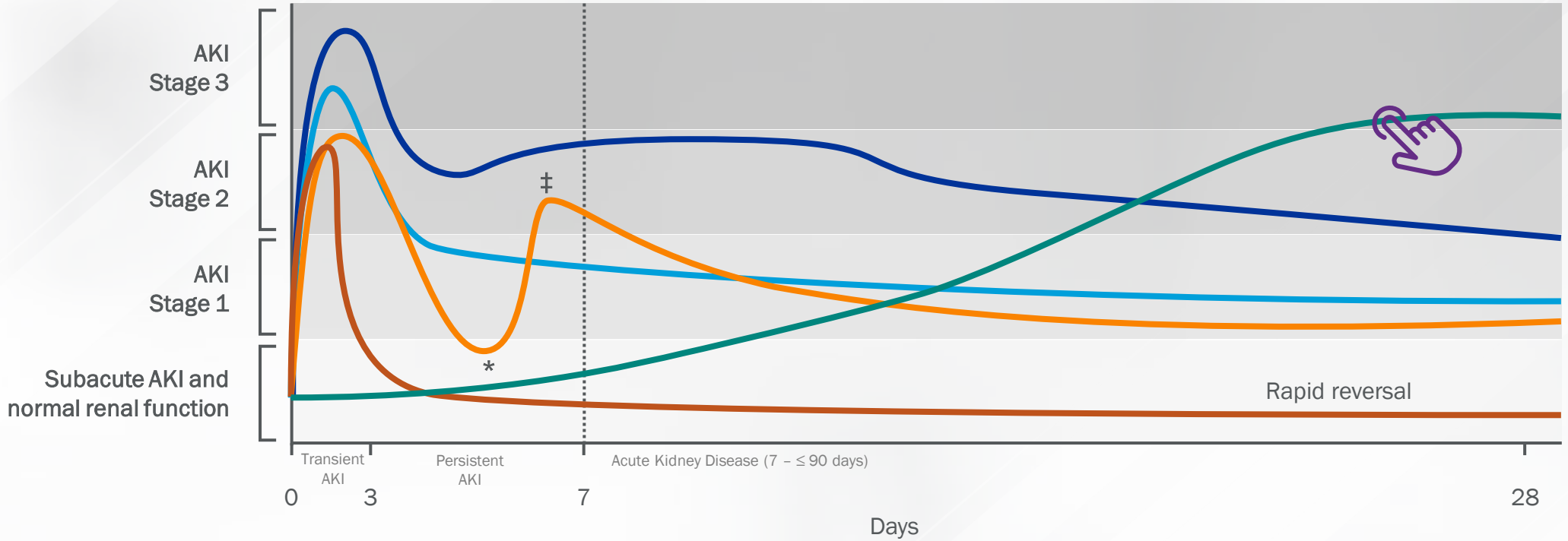
AKI, acute kidney injury; CSA-AKI, cardiac surgery–associated acute kidney injury; RRT, renal replacement therapy.

AKI is a heterogeneous syndrome; each patient with AKI has a unique trajectory of disease progression

The potential trajectories of AKI can include complete recovery of renal functional capacity, partial recovery, or progression to renal disease[1–4]



AKD, acute kidney disease.

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3. Kellum JA, *et al. Am J Respir Crit Care Med*. 2017; 195:784–791; 4. Chawla LS, *et al. Nat Rev Nephrol.* 2017; 13:241–257.

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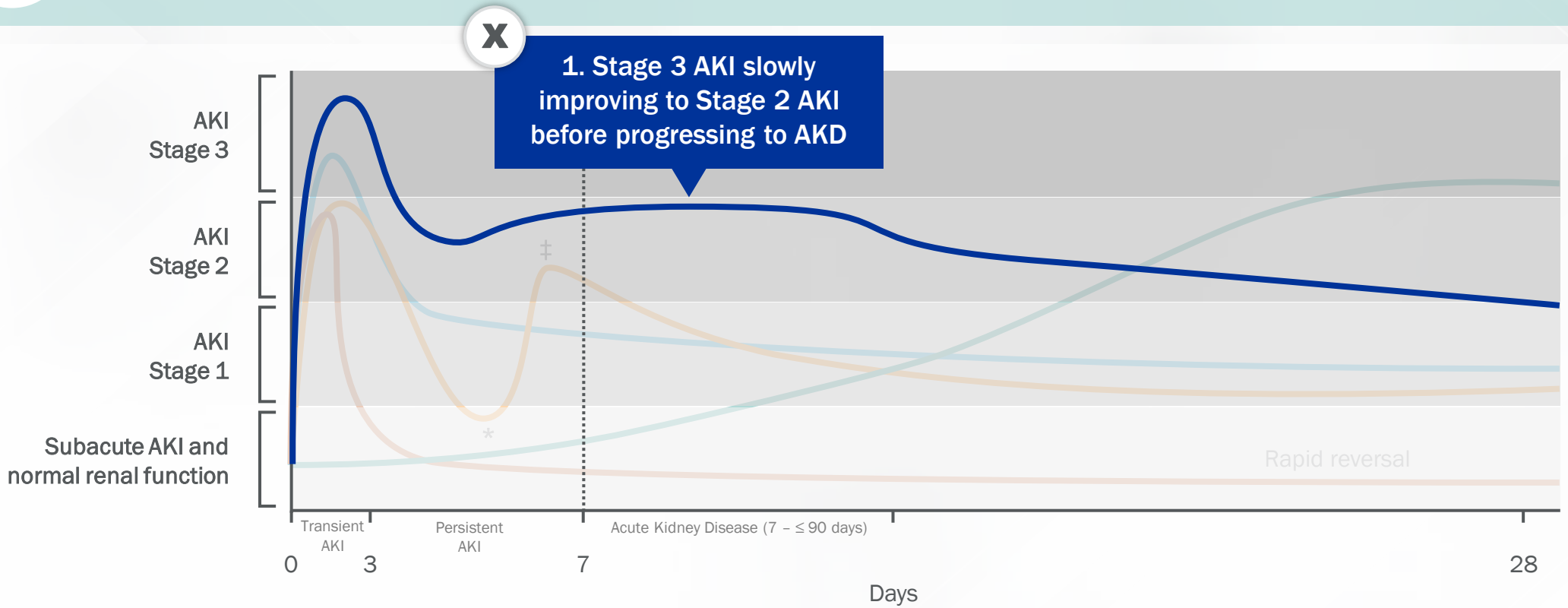

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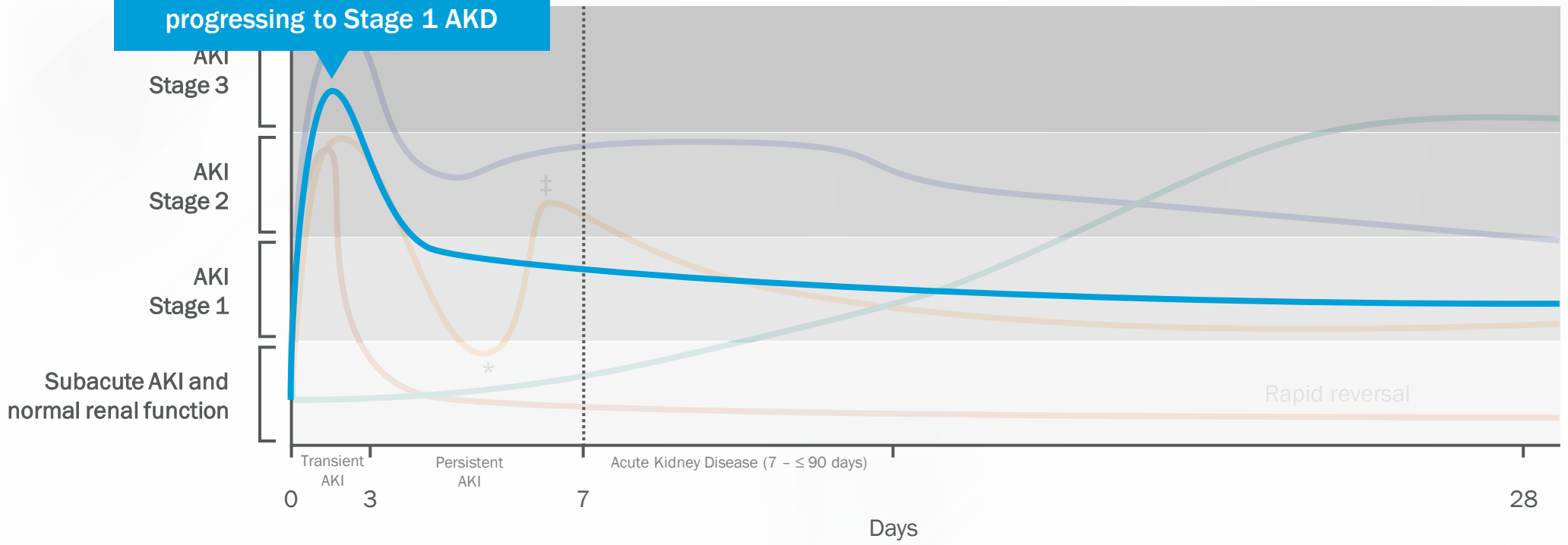
2. Stage 1 AKI progressing to Stage 3, then improving rapidly to Stage 1 AKI before progressing to Stage 1 AKD



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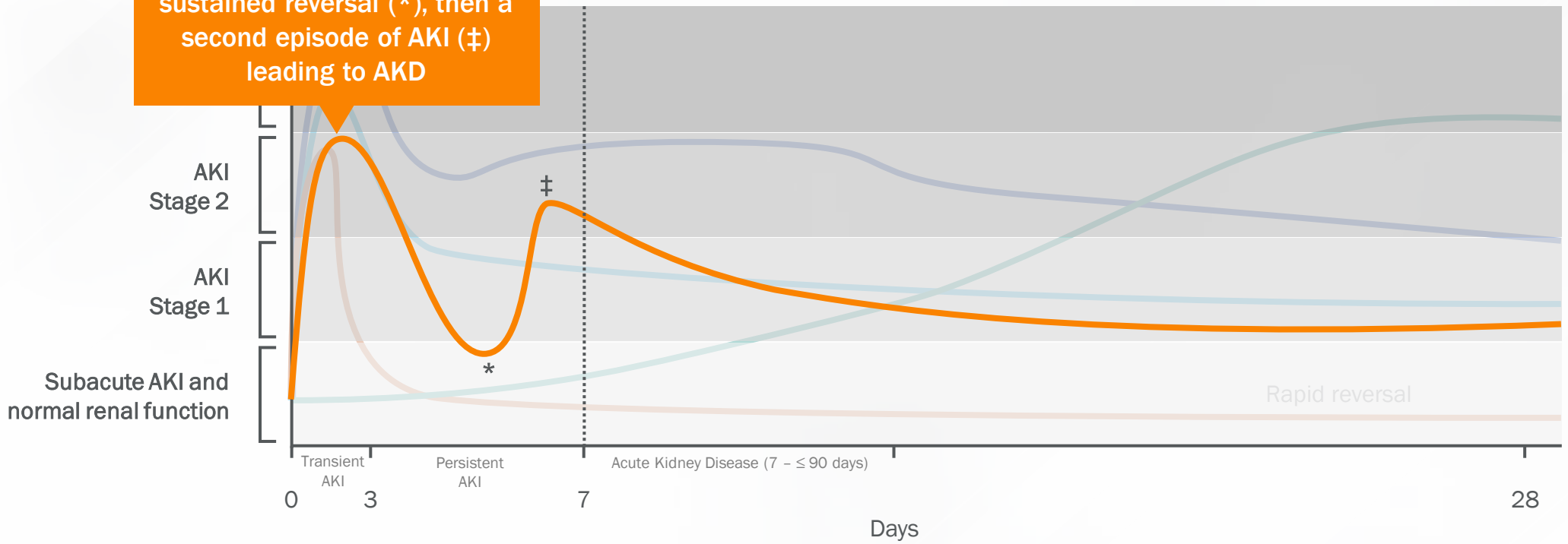
3. An episode of persistent AKI followed by a period of sustained reversal (*), then a second episode of AKI (‡) leading to AKD



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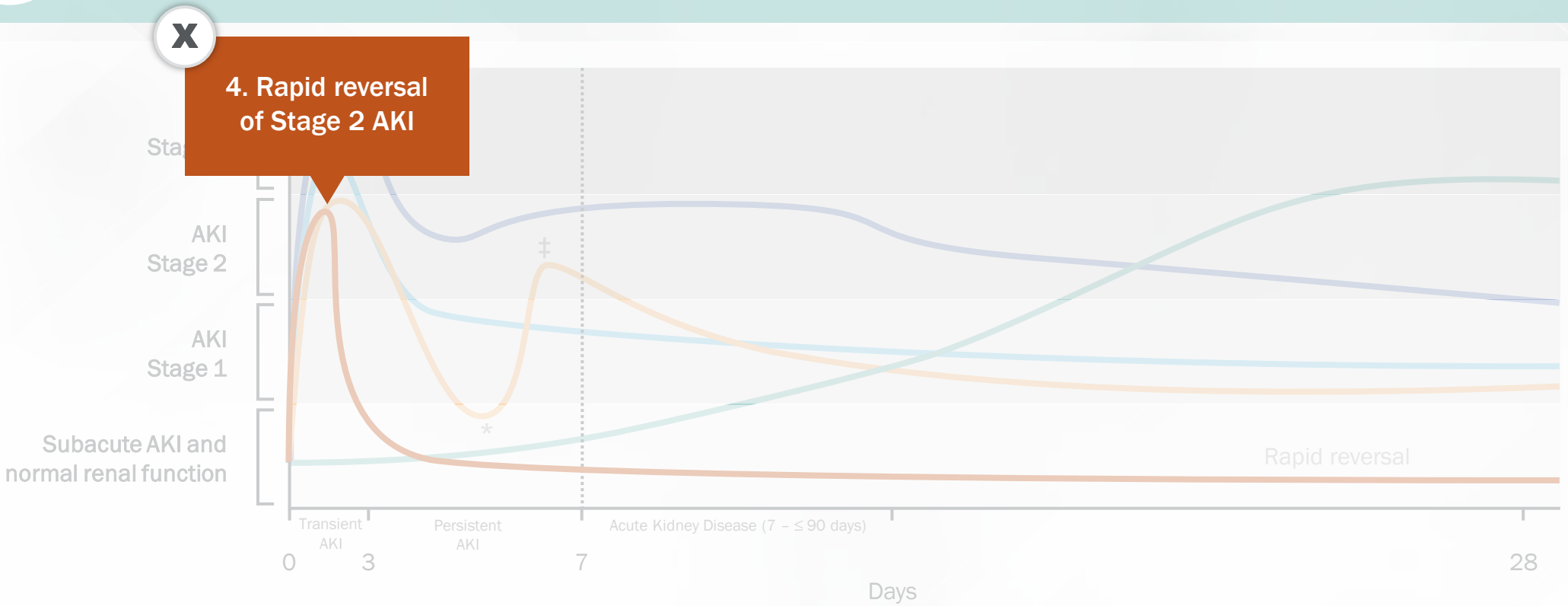

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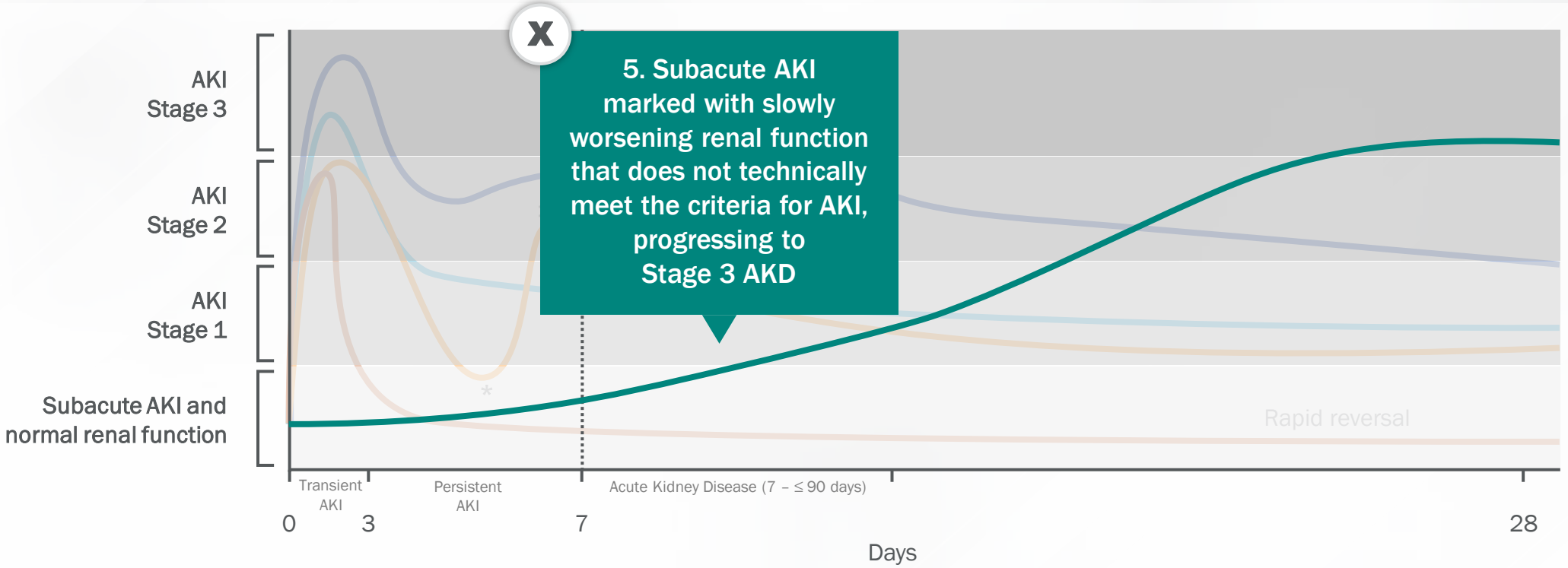

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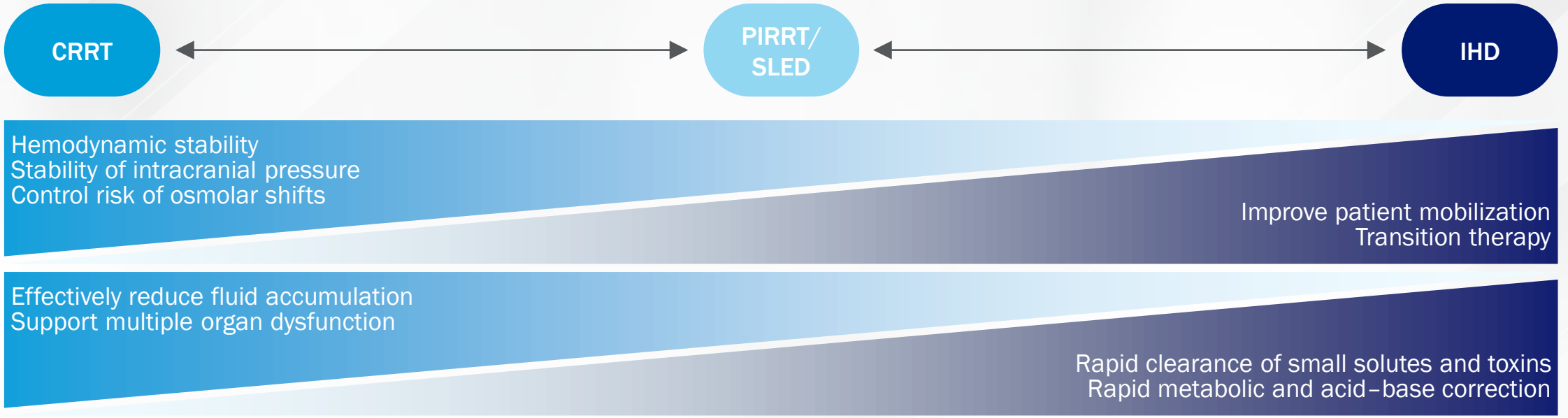
RRT represents a cornerstone of treatment for patients with severe AKI

RRT represents a major component of AKI management, particularly in severe cases, with different modalities available to address the patient's evolving clinical needs during the course of disease[1–3]



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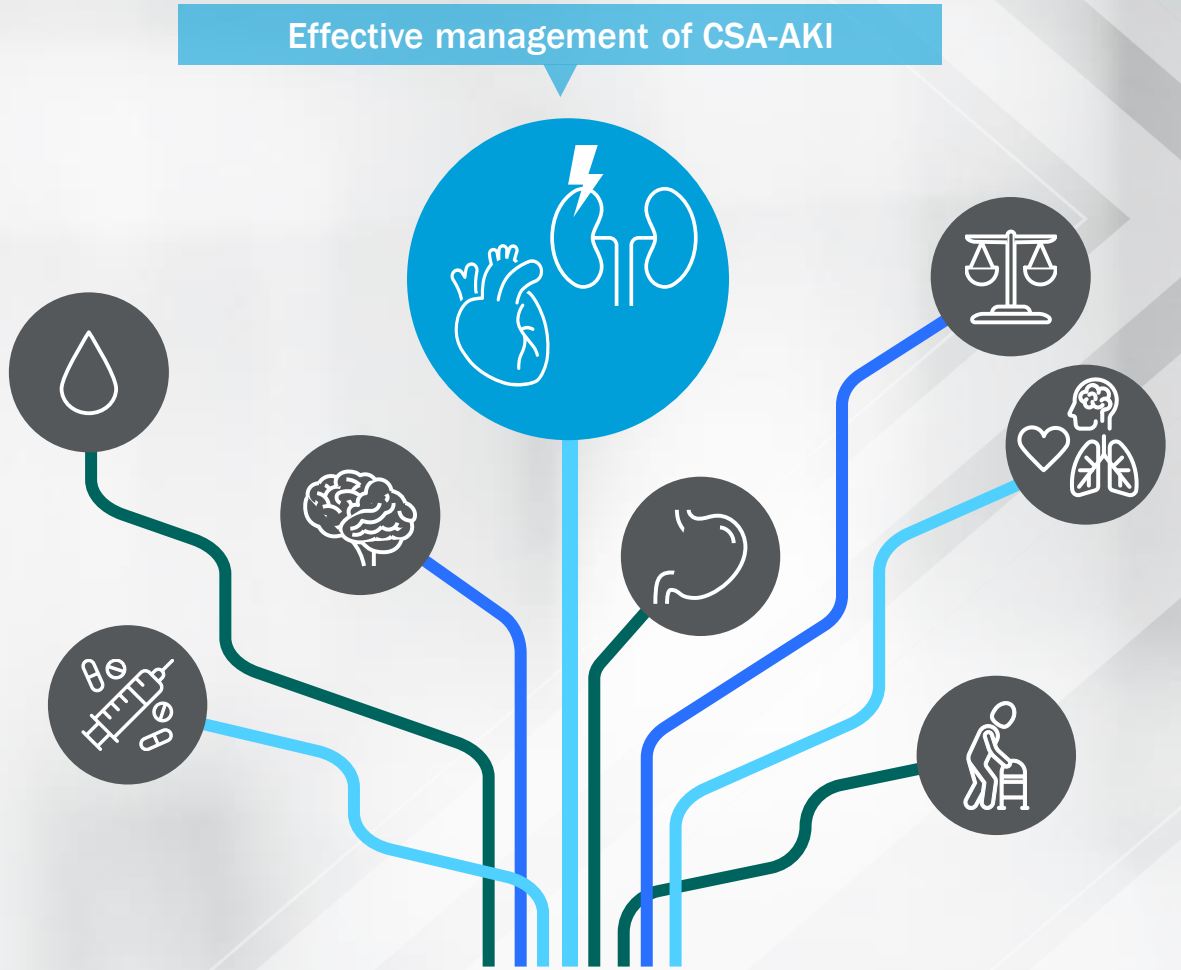
CRRT, continuous renal replacement therapy; IHD, intermittent hemodialysis; PIRRT, prolonged intermittent renal replacement therapy; RRT, renal replacement therapy; SLED, sustained low-efficiency dialysis.

1. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. *Kidney Int Suppl*. 2012; 2:1–138; 2. Ronco C, *et al. Crit Care.* 2015; 19:146;
3. Ostermann M, *et al*. *Blood Purif.* 2016; 46:224–237.

An individualized approach to care may help to address the unique clinical goals of each patient with AKI and improve outcomes

This module provides an overview of one of the many clinical challenges in managing patients with AKI, along with management strategies that may help improve outcomes



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CSA-AKI, cardiac surgery–associated acute kidney disease.

This module provides a brief overview of the burden of CSA-AKI and some of the management options

Clinical challenges in CSA-AKI:

Patients undergoing **cardiac surgery are at risk of developing AKI**[1–7]

Following cardiac surgery, patients with AKI are at an **increased risk of morbidity and mortality** vs. patients without AKI[2–4,7–10]

Patients with CSA-AKI may require RRT to help manage fluid overload[11–13]

In patients with CSA-AKI who are hemodynamically unstable, **using RRT can be challenging** as sudden shifts in fluid balance may be poorly tolerated[11]

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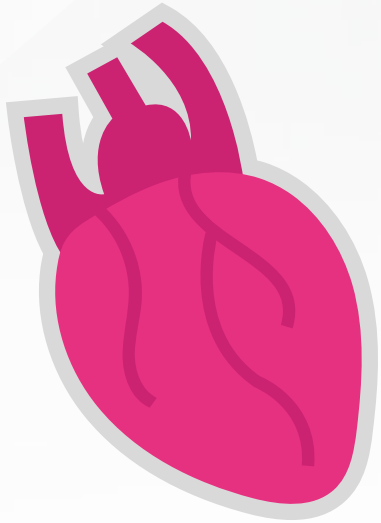
CSA-AKI, cardiac surgery–associated acute kidney injury; RRT, renal replacement therapy.

1. Hu J, *et al*. *J Cardiothorac Vasc Anesth*. 2016; 30:82–89; 2. Brown JR, *et al. Ann Thorac Surg*. 2010; 90:1142–1148; 3. Chew STH, *et al. BMC Nephrol*. 2017; 18:60; 4. Xu JR, *et al. Medicine (Baltimore)*. 2015; 94:e2025; 5. Bastin AJ, *et al. J Crit Care*. 2013; 28:389–396; 6. Hobson C, *et al. Ann Surg*. 2015; 261:1207–1214; 7. Xie X, *et al. Int Med*. 2017; 56:275–282; 8. Dasta JF, *et al. Nephrol Dial Transplant*. 2008; 23:1970–1974; 9. Pickering JW, *et al. Am J Kidney Dis*. 2015; 65:283–293; 10. Brown JR, *et al. Ann Thorac Surg*. 2016; 102:1482–1489; 11. Nadim MK, *et al. J Am Heart Assoc*. 2018; 7:e008834; 12. Haase-Fielitz A, *et al. Blood Purif*. 2017; 43:298–308; 13. Bellomo R, *et al. Cardiology*. 2001;96:169–76.

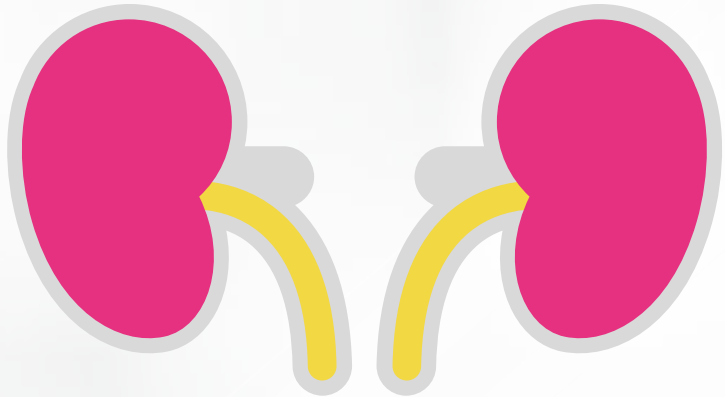
AKI is a common complication of cardiac surgery

A large proportion of patients who undergo cardiac surgery develop AKI[1–7]

AKI occurs in ~20–40% of patients after cardiac surgery[1–7]



~2–9% of patients with CSA-AKI require RRT[5–9]



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CSA-AKI has a high clinical and economic burden

In patients who have undergone cardiac surgery, the development of AKI is associated with an increased risk of morbidity and mortality[1–7]

Increased length of ICU stay[1]

Increased risk of unplanned hospital readmission[2]

Increased risk of progression to CKD or ESRD[3,4]

Increased risk of both short-term and long-term mortality[2–7]

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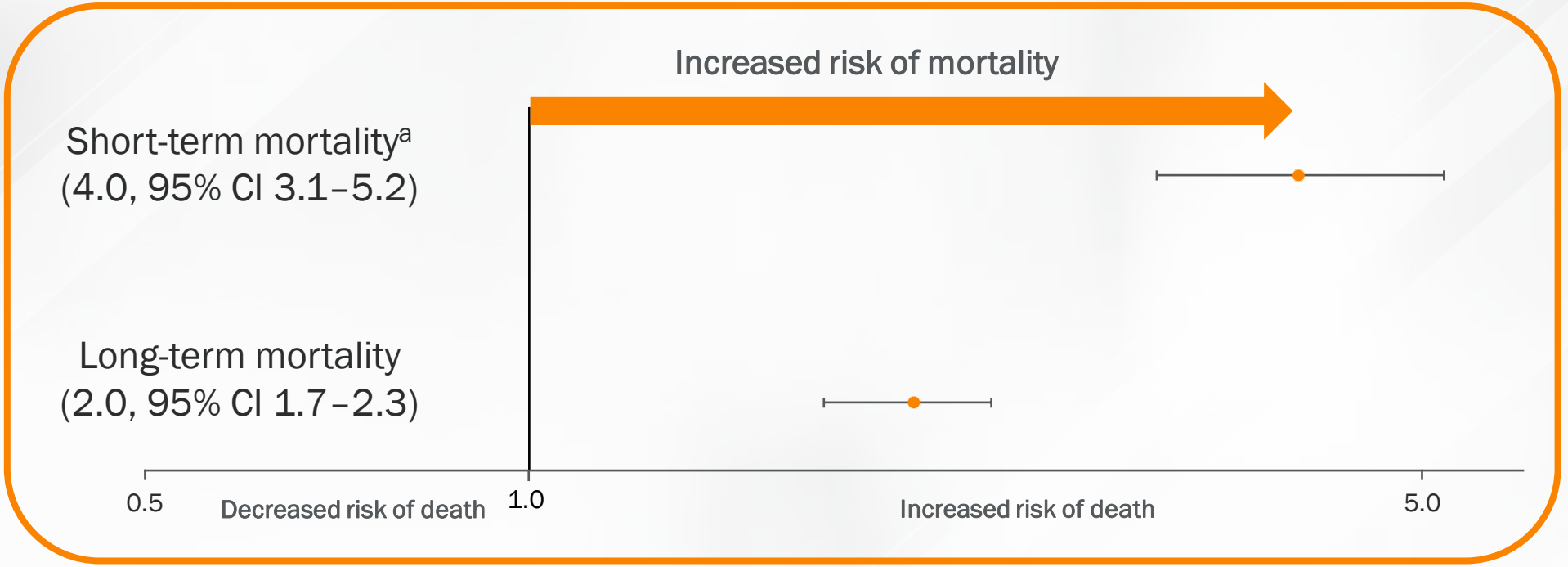
CKD, chronic kidney disease; CSA-AKI, cardiac surgery–associated acute kidney injury; ESRD, end-stage renal disease; ICU, intensive care unit.

1. Dasta JF, *et al. Nephrol Dial Transplant.* 2008; 23:1970–1974; 2. Brown JR, *et al. Ann Thorac Surg.* 2016; 102:1482–1489; 3. Chew STH, *et al. BMC Nephrol.* 2017; 18:60; 4. Xu JR, *et al. Medicine.* 2015; 94:e2025; 5. Brown JR, *et al. Ann Thorac Surg.* 2010; 90:1142–1148; 6. Xie X, *et al. Intern Med.* 2017; 56:275–282; 7. Pickering JW, *et al. Am J Kidney Dis.* 2015; 65:283–293.

CSA-AKI is associated with an increased risk of both short-term and long-term mortality

A meta-analysis of observational studies found that CSA-AKI was associated with an increased risk of both short-term (24 cohorts, N = 94,141) and long-term (12 cohorts, N = 69,797) mortality[1]



Study details

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[a] In-hospital or <90 days.

CI, confidence interval; CPB, cardiopulmonary bypass; CSA-AKI, cardiac surgery–associated acute kidney injury.

Pickering JW, *et al. Am J Kidney Dis.* 2015; 65:283–293.

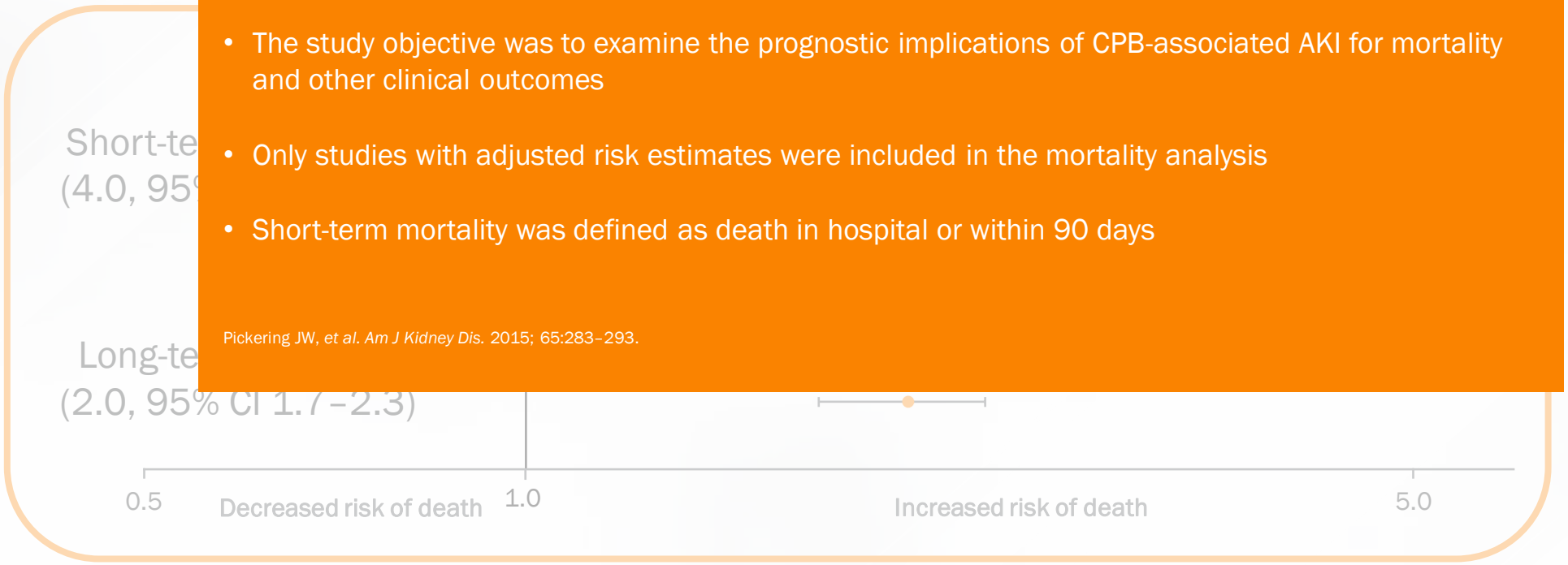
CSA-AKI is associated with an increased risk of both short-term and long-term mortality

A meta-ana… of both short-… …isk

- Systematic review and meta-analysis, including 46 studies reporting on 47 cohorts comprising 242,388 patients
- The study objective was to examine the prognostic implications of CPB-associated AKI for mortality and other clinical outcomes
- Only studies with adjusted risk estimates were included in the mortality analysis
- Short-term mortality was defined as death in hospital or within 90 days

Pickering JW, *et al. Am J Kidney Dis.* 2015; 65:283–293.

Study details



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Why do patients undergoing cardiac surgery develop AKI?

Many risk factors for CSA-AKI are unique to cardiac surgery

Patient risk factors[1–4]

- Advanced age
- Female sex
- High BMI
- CKD
- Hypertension
- DM requiring insulin
- COPD
- Peripheral vascular disease
- Cerebrovascular disease
- Sepsis
- Congestive heart failure
- Ascites

Procedure-related risk factors[1–4]

- Long duration of surgery
- Vasopressor exposure
- Packed red blood cell transfusion
- Intraaortic balloon pump
- Intraoperative hypotension
- Nephrotoxic agents
- Longer length of cardiopulmonary bypass
- Hemodilution
- Longer cross-clamp time

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BMI, body mass index; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus.

1. Meersch M, *et al. Anesth Analg.* 2017; 125:1223–1232; 2. O'Neal JB, *et al. Crit Care.* 2016; 20:187; 3. Nadim MK, *et al. J Am Heart Assoc.* 2018;7:e008834; 4. Wang Y & Bellomo R. *Nat Rev Nephrol.* 2017; 13:697–711.

Several pathophysiologic mechanisms are associated with the development of CSA-AKI

Hemodynamic perturbations

- Effect of CPB circuit
- Low cardiac output
- Blood pressure
- Venous pressure
- Preload/volume
- Anemia/hemolysis
- Ischemia/reperfusion

Mechanical factors

- Emboli
- Arterial obstruction
- Venous congestion
- Perfusion pressure
- Abdominal hypertension

Immunity/inflammation

- Inflammation
- Oxidative stress
- Complement activation
- Toxins/drugs
- Contrast media

Other mechanisms

- Neurohormonal
- Vasoconstriction
- Venous congestion
- Tubular toxicity

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CPB, cardiopulmonary bypass; CSA-AKI, cardiac surgery–associated acute kidney injury.
Nadim MK, *et al. J Am Heart Assoc.* 2018; 7:e008834.

Patients who undergo cardiac surgery can develop a positive fluid balance

Fluids and vasopressors are typically used to restore hemodynamic stability in patients undergoing cardiac surgery; however, these can result in a positive fluid balance, which contributes to AKI[1,2]

During or after cardiac surgery, patients may experience a significant shift in fluids from the intravascular to the extravascular space[3]

This fluid shift, in combination with the potentially large volumes of fluid that may be needed to restore hemodynamic stability, can result in a **positive fluid balance**[2,4]

Total perioperative (0–24 h) fluid balance by AKI severity[2]

AKI severity	Fluid balance (mL)
RIFLE-0 (no AKI)	1,520 ± 2,190
RIFLE-R	2,200 ± 2,460
RIFLE-I	2,100 ± 2,930
RIFLE-F	4,000 ± 1,950

Single-center, prospective cohort study (2017) of 282 adult cardiac surgery patients, $P = 0.004$ across RIFLE categories.[2]

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RIFLE, Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease.

1. Stephens RS & Whitman GJR. *Crit Care Med.* 2015; 43:1477–1497; 2. Haase-Fielitz A, *et al. Blood Purif.* 2017; 43:298–308; 3. Strunden MS, *et al. Ann Intensive Care.* 2011; 1:2; 4. Nadim MK, *et al. J Am Heart Assoc.* 2018; 7:e008834.

Achieving target fluid balance in patients with CSA-AKI can be challenging, and may require fluid removal with RRT

ADQI provides guidance on fluid removal strategies in critically ill patients

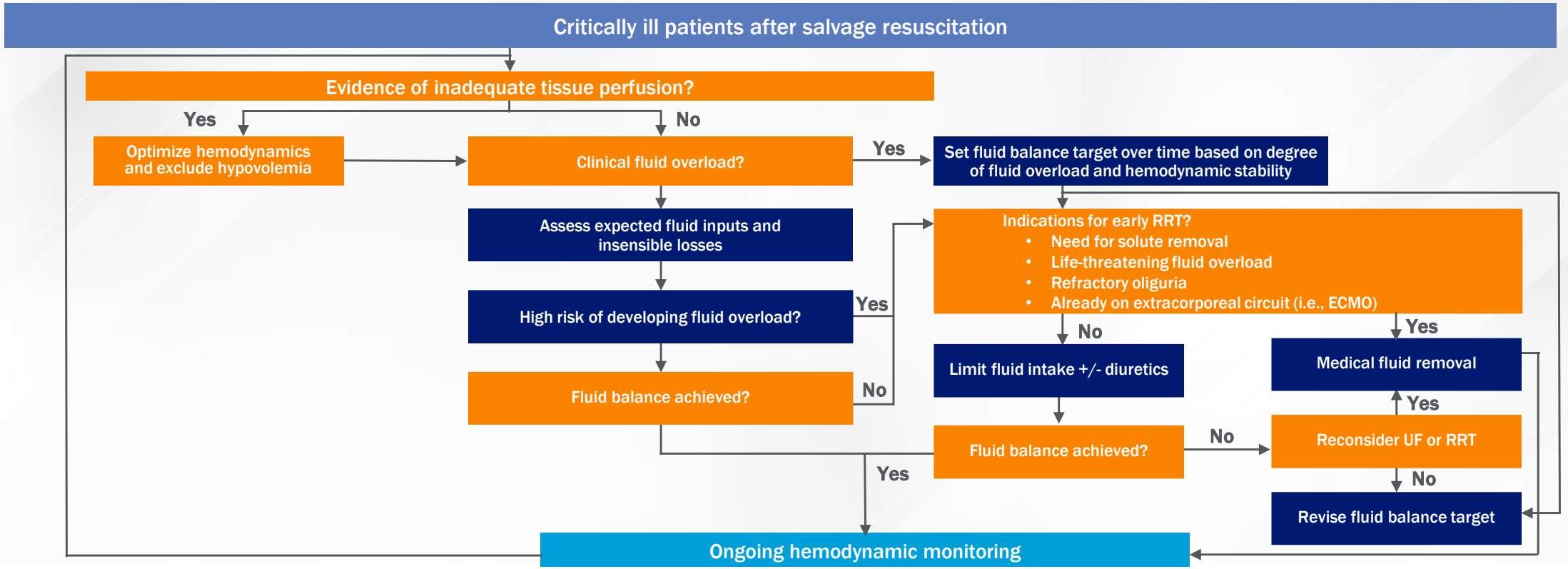

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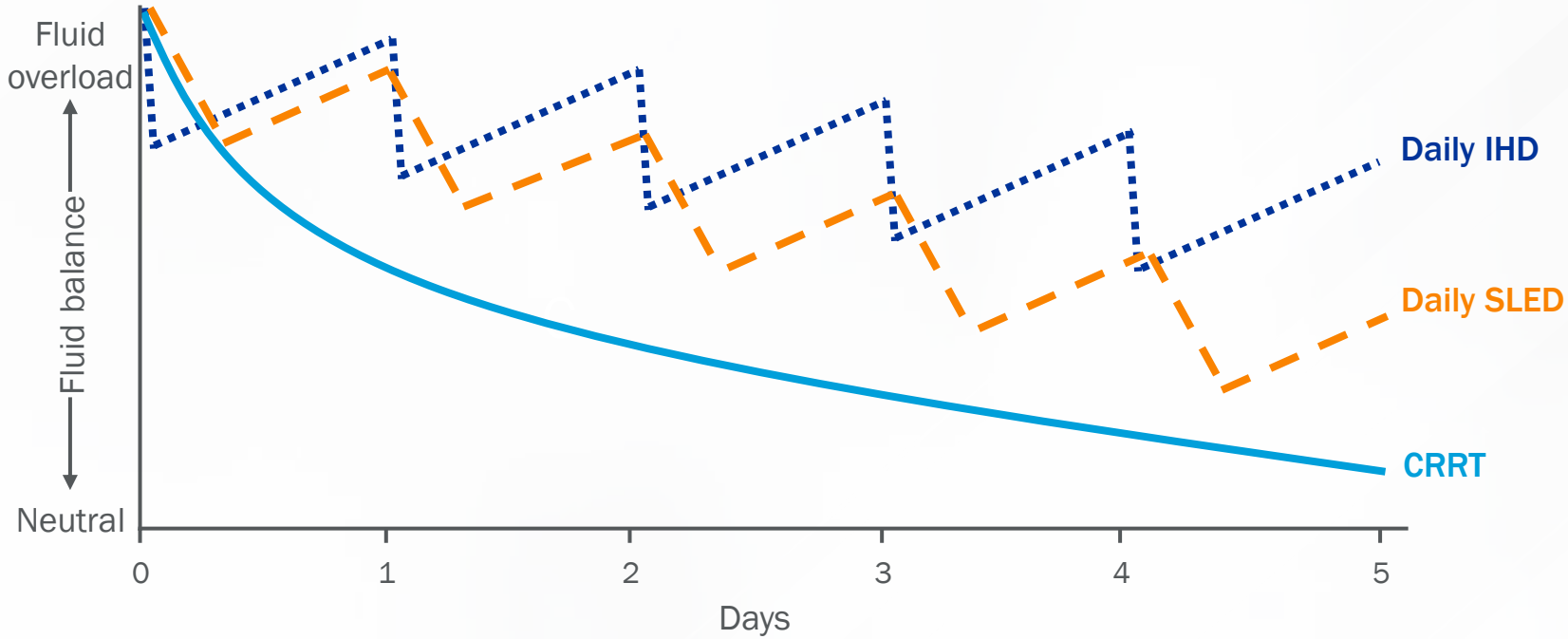
Image source: Nadim MK, *et al. J Am Heart Assoc.* 2018; 7:e008834.

ADQI, Acute Disease Quality Initiative; CSA-AKI, cardiac surgery–associated acute kidney injury; ECMO, extracorporeal membrane oxygenation; RRT, renal replacement therapy; UF, ultrafiltration.
Nadim MK, *et al. J Am Heart Assoc.* 2018; 7:e008834.

CRRT is the preferred RRT modality for patients with CSA-AKI who are hemodynamically unstable[1]

In patients with AKI, including CSA-AKI, fluid removal with RRT can be challenging due to the risk of the treatment worsening the patient's hemodynamic status.[2] Undesirable fluctuations in fluid balance may occur with certain modalities, particularly intermittent modalities such as IHD[3,4]

CRRT removes fluid in a slow and continuous manner, in theory reducing the likelihood of fluctuations in intravascular fluid volume, thereby helping to maintain hemodynamic stability[3,5,6]



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AKI, acute kidney injury; CRRT, continuous renal replacement therapy; CSA-AKI, cardiac surgery–associated AKI; IHD, intermittent hemodialysis; RRT, renal replacement therapy; SLED, sustained low-efficiency dialysis.

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ADQI guidelines recommend the use of CRRT for patients with CSA-AKI who are hemodynamically unstable

Guidelines indicate that CRRT is the preferred modality for patients with CSA-AKI who are hemodynamically unstable[1]

20th International Consensus Conference of the ADQI Group: CSA-AKI

"We recommend the use of continuous therapies in patients with hemodynamic instability and in situations in which shifts in fluid balance are poorly tolerated (Grade 1B)"[1,a]

Click here to learn more about using CRRT for greater hemodynamic stability

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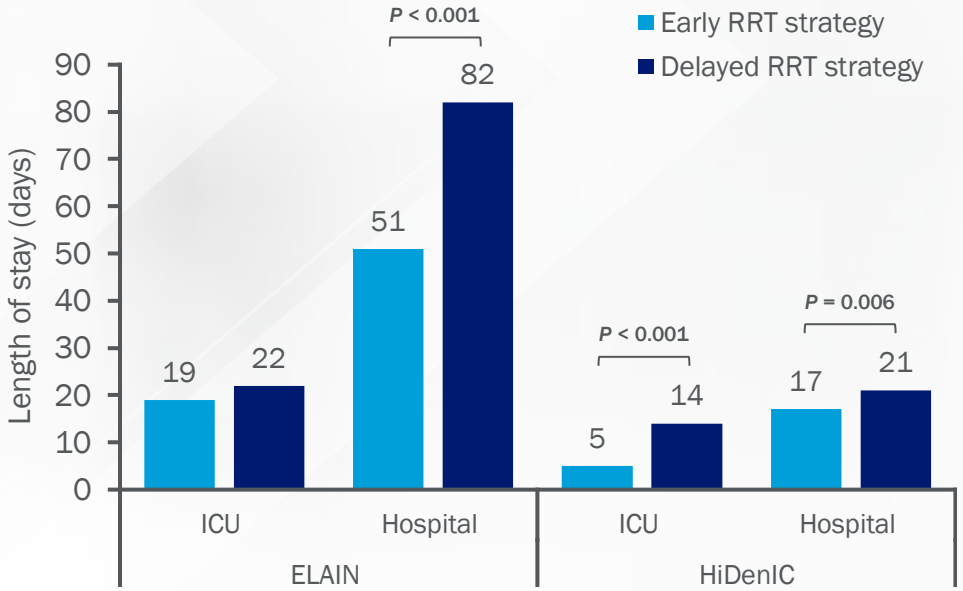
[a] Grade 1B recommendations are strong recommendations based on moderate evidence.

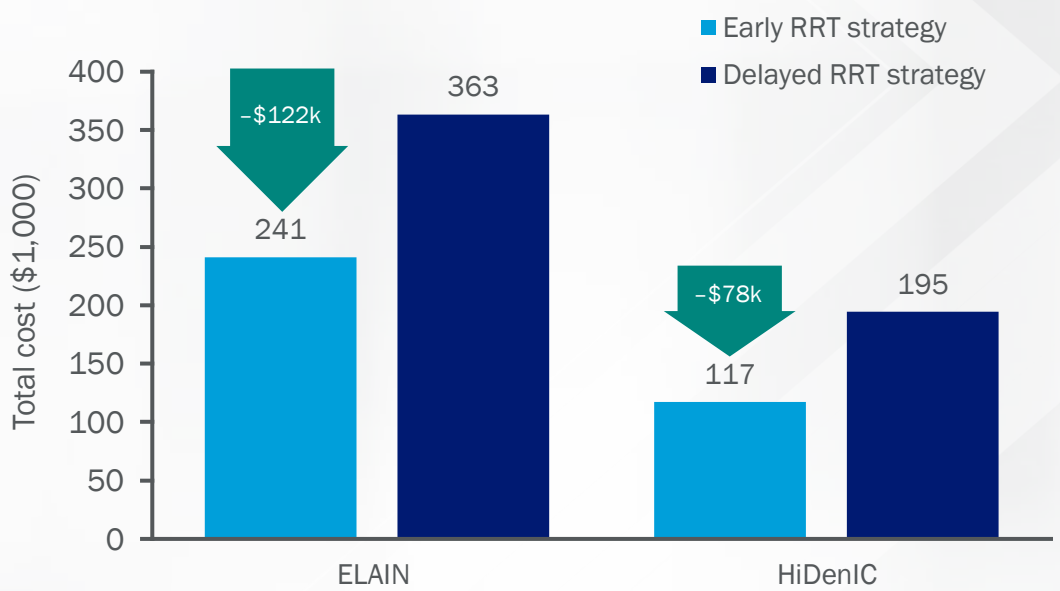
ADQI, Acute Disease Quality Initiative; CRRT, continuous renal replacement therapy; CSA-AKI, cardiac surgery–associated acute kidney injury.

1. Nadim MK, *et al. J Am Heart Assoc*. 2018; 7:e008834.

Early initiation of RRT may lead to cost savings in patients with CSA-AKI

In a cost–consequences economic model of patients with CSA-AKI predominantly treated with CRRT, early RRT initiation (<24 hr) showed considerable cost savings, mainly due to significantly reduced hospital and ICU length of stay compared with an expectant strategy with potential delayed initiation[1]





However, evidence overall suggests that pre-emptive RRT initiation (prior to clinical indications) does not improve outcomes of patients with severe AKI,[3–6] and current ADQI guidelines recommend an individualized approach to care[7]

The cost–consequences model was a decision tree comparison of post-AKI (KDIGO Stage 2) length of stay (LoS). Clinical parameters were primarily informed by the ELAIN trial,[2] in which 46.7% of patients had CSA-AKI (n = 231). Early initiation was within 8 hours of Stage 2 AKI diagnosis, and delayed initiation was within 12 hours of AKI Stage 3 diagnosis or no initiation at all. Findings were confirmed with data from CSA-AKI patients who received CRRT from a large observational US database (High-Density Intensive Care, HiDenIC), in which 96.3% had AKI Stage 2 or 3 within 48 hours of surgery start time; 50 (37.3%) patients received early RRT and 84 (62.7%) patients received delayed RRT (n = 134). Early initiation was defined as receiving RRT within 24 hours after first AKI Stage 2 or 3, and late initiation was defined as beyond 24 hours until 10 days post-AKI. Resource utilization was determined by RRT duration, ICU LoS, and hospital LoS. All resources were costed from a US healthcare perspective. Daily cost estimates were derived from published literature and expressed in US$ 2020.

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ADQI, Acute Disease Quality Initiative; AKI, acute kidney injury; CRRT, continuous renal replacement therapy; CSA-AKI, cardiac surgery–associated acute kidney injury; ELAIN, Early versus late initiation of renal replacement therapy in critically ill patients with acute kidney injury; HiDenIC, High-Density Intensive Care; ICU, intensive care unit; KDIGO, Kidney Disease: Improving Global Outcomes; LoS, length of stay; RRT, renal replacement therapy.

1. Ethgen O, *et al. J Crit Care*. 2022; 69:153977; 2. Zarbock, *et al. JAMA*. 2016; 315:2190–2199; 3. STARRT-AKI Investigators. *N Engl J Med*. 2020; 383:240–251; 4. Gaudry S, *et al. N Engl J Med*. 2016; 375:122–133; 5. Gaudry S, *et al. Lancet*. 2020; 395:1506–1515; 6. Barbar SD, *et al. N Engl J Med*. 2018;379:1431–1442; 7. Nadim MK, *et al. J Am Heart Assoc*. 2018; 7:e008834.

Summary of key points

- AKI is a common complication of cardiac surgery[1]
- CSA-AKI is associated with high clinical and economic burden, including increased risk of mortality[2–4]
- A diverse range of patient- and procedure-related risk factors contribute to the pathophysiologic mechanisms of CSA-AKI[1,5–7]
- Achieving target fluid balance in patients with CSA-AKI can be challenging, and may require fluid removal with RRT[7]
- CRRT is the preferred RRT modality for patients with severe hemodynamic instability, and is recommended by ADQI guidelines for patients with CSA-AKI who are hemodynamically unstable[7–9]
- Early initiation of CRRT may lead to cost savings in patients with CSA-AKI[10]

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ADQI, Acute Disease Quality Initiative; CRRT, continuous renal replacement therapy; CSA-AKI, cardiac surgery–associated acute kidney injury; RRT, renal replacement therapy.

1. Wang Y & Bellomo R. *Nat Rev Nephrol*. 2017; 13:697–711; 2. Dasta JF, *et al. Nephrol Dial Transplant.* 2008; 23:1970–1974; 3. Brown JR, *et al. Ann Thorac Surg*. 2016; 102:1482–1489; 4. Pickering JW, *et al. Am J Kidney Dis*. 2015; 65:283–293; 5. Meersch M, *et al*. *Anesth Analg*. 2017; 125:1223–1232; 6. O'Neal JB, *et al*. *Crit Care.* 2016; 20:187; 7. Nadim MK, *et al. J Am Heart Assoc.* 2018; 7:e008834; 8. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. *Kidney Int Suppl*. 2012; 2:1–138; 9. Murugan R, *et al. Blood Purif*. 2016; 42:266–278; 10. Ethgen O, *et al. J Crit Care*. 2022; 69:153977.

References and abbreviations

ADQI, Acute Disease Quality Initiative; AKD, acute kidney disease; AKI, acute kidney injury; BMI, body mass index; CI, confidence interval; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CPB, cardiopulmonary bypass; CRRT, continuous renal replacement therapy; CSA-AKI, cardiac surgery–associated acute kidney injury; DM, diabetes mellitus; ECMO, extracorporeal membrane oxygenation; ELAIN, early versus late initiation of renal replacement therapy in critically ill patients with acute kidney injury; ERSD, end-stage renal disease; HiDenIC, High-Density Intensive Care; ICU, intensive care unit; IHD, intermittent hemodialysis; LoS, length of stay; PIRRT, prolonged intermittent renal replacement therapy; RIFLE, Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease; RRT, renal replacement therapy; SLED, sustained low-efficiency dialysis; UF, ultrafiltration.

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GBU-AT00-220030 v2.0 03/23