Contrast-associated acute kidney injury

The impact on clinical outcomes and hospital resources

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Approximately every

40 seconds,

someone in America will have an MI[1]*

In 2019, ≈720,000 had a new coronary event (first hospitalized MI or CHD death), and ≈335,000 had a recurrent event[1]

Imaging of the coronary vasculature for these patients depends on the use of iodinated contrast, which may put them at risk for CA-AKI[2]

*AHA computation

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References:

1. Benjamin EJ et al. Circulation. 2019;139(10):e56-e528.
2. McCullough PA et al. J Am Coll Cardiol. 2016;68(13):1465-1473.

AHA, American Heart Association
AKI, acute kidney injury
CHD, coronary heart disease
CA-AKI, contrast-associated AKI
MI, myocardial infarction

About CA-AKI

How CA-AKI can affect you and your patients

Reducing the risk of CA-AKI

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AKI, acute kidney injury
CA-AKI, contrast-associated AKI

About CA-AKI

- How acute kidney injury after contrast administration is defined
- How the risk of CA-AKI following percutaneous coronary intervention varies
- Why the kidneys are especially vulnerable to injury from iodinated CM
- Why the kidneys of “high-risk” patients may respond differently
- How the risk of CA-AKI can vary with baseline renal function
- What effect a combination of risk factors can have on CA-AKI incidence
- How CA-AKI can lead to other problems
- Why CA-AKI is a growing concern

How CA-AKI can affect you and your patients

Reducing the risk of CA-AKI

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AKI, acute kidney injury
CA-AKI, contrast-associated AKI
CM, contrast medium/media

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AKI, acute kidney injury
CA-AKI, contrast-associated AKI
PCI, percutaneous coronary intervention

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AKI, acute kidney injury
CA-AKI, contrast-associated AKI
NCDR, National Cardiovascular Data Registry

How acute kidney injury after contrast administration is defined

Post-contrast AKI describes a sudden deterioration in renal function that occurs within 48 hours following the intravascular administration of iodinated CM[1]

AKIN suggests a diagnosis of AKI is made if one of the following occurs within 48 hours of a nephrotoxic event such as intravascular iodinated CM exposure:[2]

- Absolute SCr increase ≥0.3 mg/dL
- Relative increase in SCr ≥50% (≥1.5-fold above baseline)
- Urine output reduced to ≤0.5 mL/kg/hour for more than 6 hours

It has been suggested that the terms CA-AKI or CIN be reserved for cases where a causal relationship can be shown between the administered CM and the deterioration in renal function[1]

– in clinical practice it is usually difficult to distinguish CA-AKI from PC-AKI[1]

AKI, acute kidney injury
AKIN, Acute Kidney Injury Network
CA-AKI, contrast-associated AKI
CIN, contrast-induced nephropathy
CM, contrast medium/media
PC-AKI, post-contrast AKI
SCr, serum creatinine

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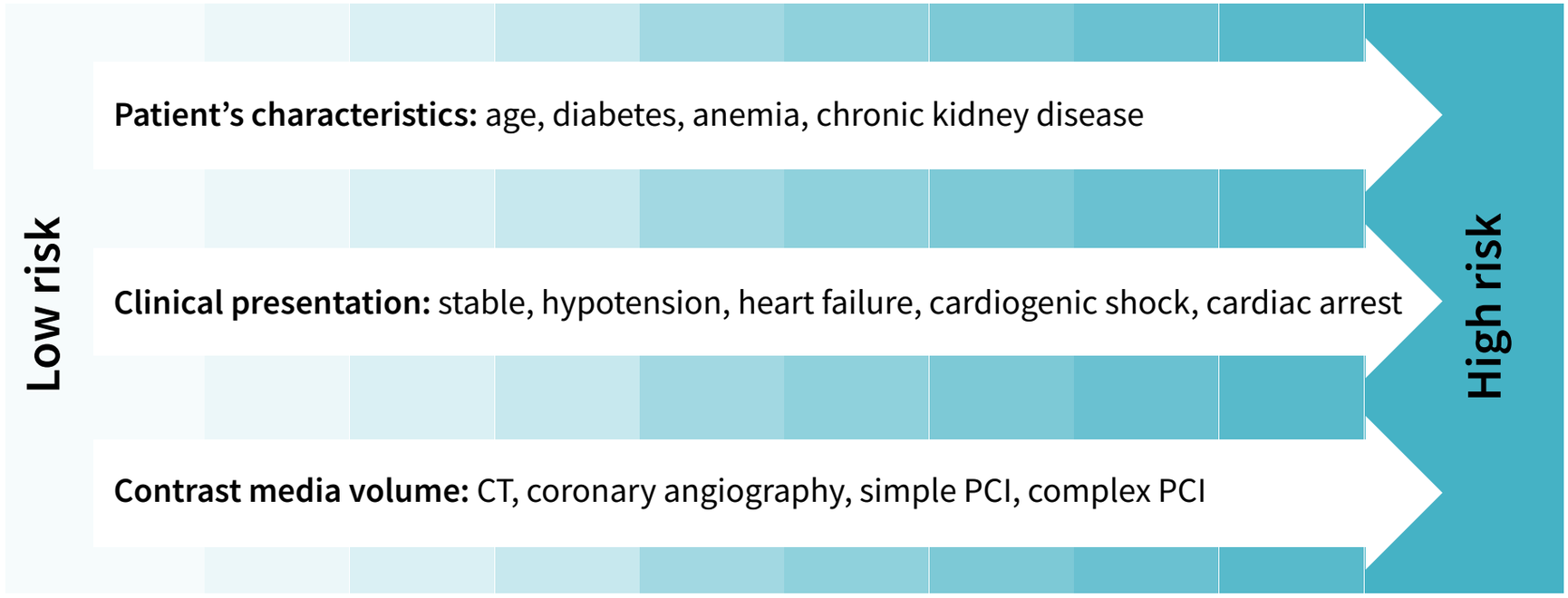
References:
1. van der Molen AJ et al. Eur Radiol. 2018;28(7):2845-2855.
2. Mehta RL et al. Crit Care. 2007;11(2):R31.

How the risk of CA-AKI following percutaneous coronary intervention varies

CA-AKI risk varies as a function of a patient's characteristics, clinical presentation, and the volume of CM used[1]



Adapted from Azzalini L et al. 2017.

The rate of CA-AKI reported for patients undergoing PCI ranges from less than 3% in patients with normal renal function increasing up to 40% in those with CKD[2]

AKI, acute kidney injury
CA-AKI, contrast-associated AKI
CKD, chronic kidney disease
CM, contrast medium
CT, computed tomography
PCI, percutaneous coronary intervention

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References:
1. Azzalini L et al. Can J Cardiol. 2017;33(10):1125-1228.
2. Azzalini L et al. Can J Cardiol. 2016;32(2):247-255.

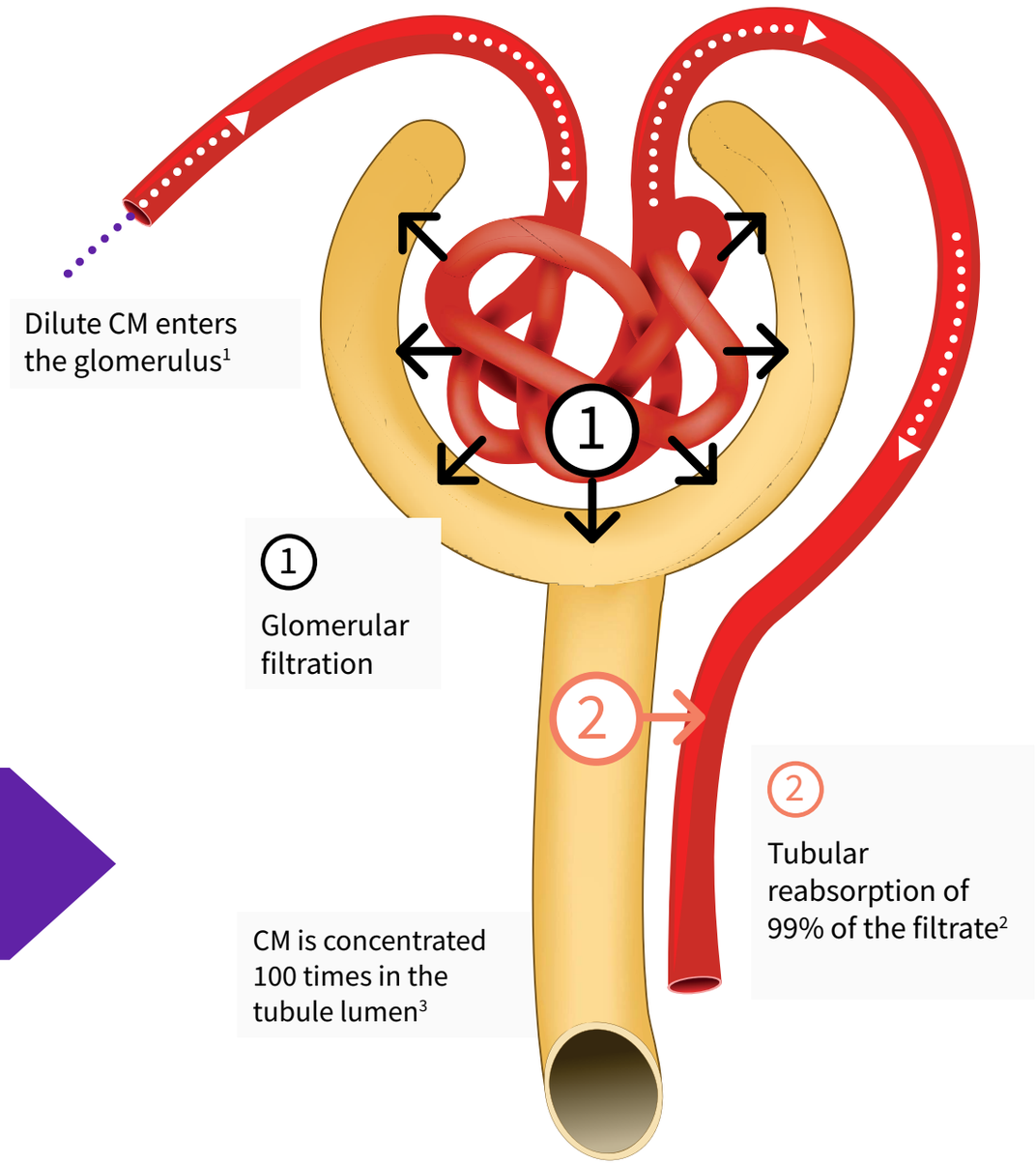
Why the kidneys are especially vulnerable to injury from iodinated CM

After intravascular injection, CM is diluted in the bloodstream and immediately distributed throughout the extracellular fluid[1]

1. Being poorly bound to serum albumin, the contrast agent is freely filtered by renal glomeruli[1]

2. Robust tubular reabsorption of the filtrate leads to a many-fold increase in the luminal CM concentration relative to that in the plasma[2]

No other organ is exposed to such high concentration of contrast as that hosted by the kidneys[2]



CM, contrast medium/media

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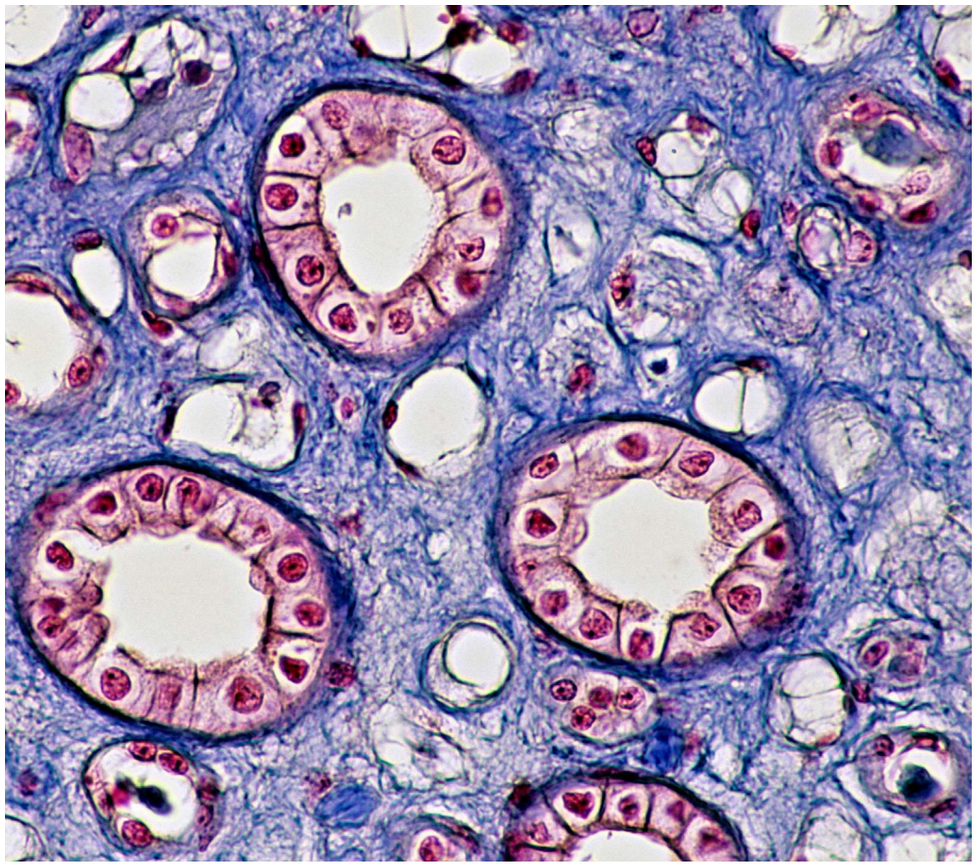
References:

1. Andreucci M et al. Drug Healthc Patient Saf. 2017;9:25-37.
2. Hiremath S, Velez JC. Curr Opin Nephrol Hypertens. 2020;29(1):152-160
3. Berg KJ. Scand J Urol Nephrol. 2000;34(5):317-22.

Why the kidneys of “high-risk” patients may respond differently

Contrast agents are directly toxic to tubular epithelial cells, leading to loss of function and both apoptosis and necrosis[1]



In healthy patients[2]

- there is a robust tubular repair capability
- exposure to CM may not have any clinical consequences

In patients with CKD and diabetes mellitus[2]

- the number of functioning nephrons is reduced
- the ability to regenerate tubular epithelial cells is impaired
- routine cardiac procedures can cause CA-AKI that is clinically meaningful

AKI, acute kidney injury
CA-AKI, contrast-associated AKI
CKD, chronic kidney disease
CM, contrast medium/media

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References:

1. Mehran R et al. N Engl J Med. 2019;380(22):2146-2155
2. McCullough PA et al. J Am Coll Cardiol. 2016;68:1465–1473.

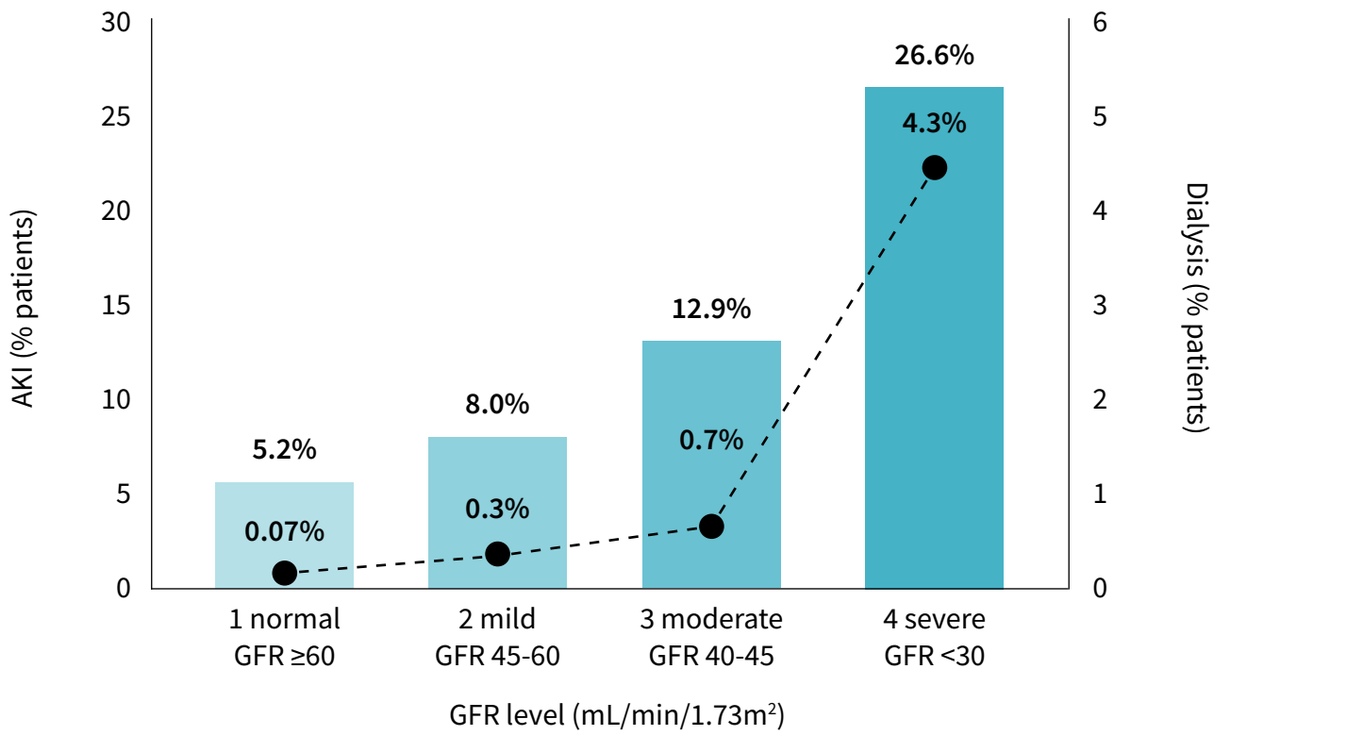
How the risk of CA-AKI can vary with baseline renal function

A large national cohort study of post-PCI patients found AKI developed in 7.1% of patients, 0.3% of whom required acute dialysis[1]

The incidence of AKI sharply increases as CKD progresses and eGFR worsens[1]

Data from 985,737 consecutive patients at 1,253 sites participating in the NCDR CathPCI Registry® from June 2009 through June 2011

AKI was defined as an absolute increase of ≥0.3 mg/dL or ≥1.5-fold relative increase in SCr



Adapted from Tsai TT et al. 2014.

AKI, acute kidney injury
AKI-D, AKI dialysis
CA-AKI, contrast-associated AKI
CKD, chronic kidney disease
eGFR: estimated GFR
GFR, glomerular filtration rate
NCDR, National Cardiovascular Data Registry
PCI, percutaneous coronary intervention
SCr, serum creatinine

Reference:
1. Tsai TT et al. JACC Cardiovasc Interv. 2014;7(1):1-9.

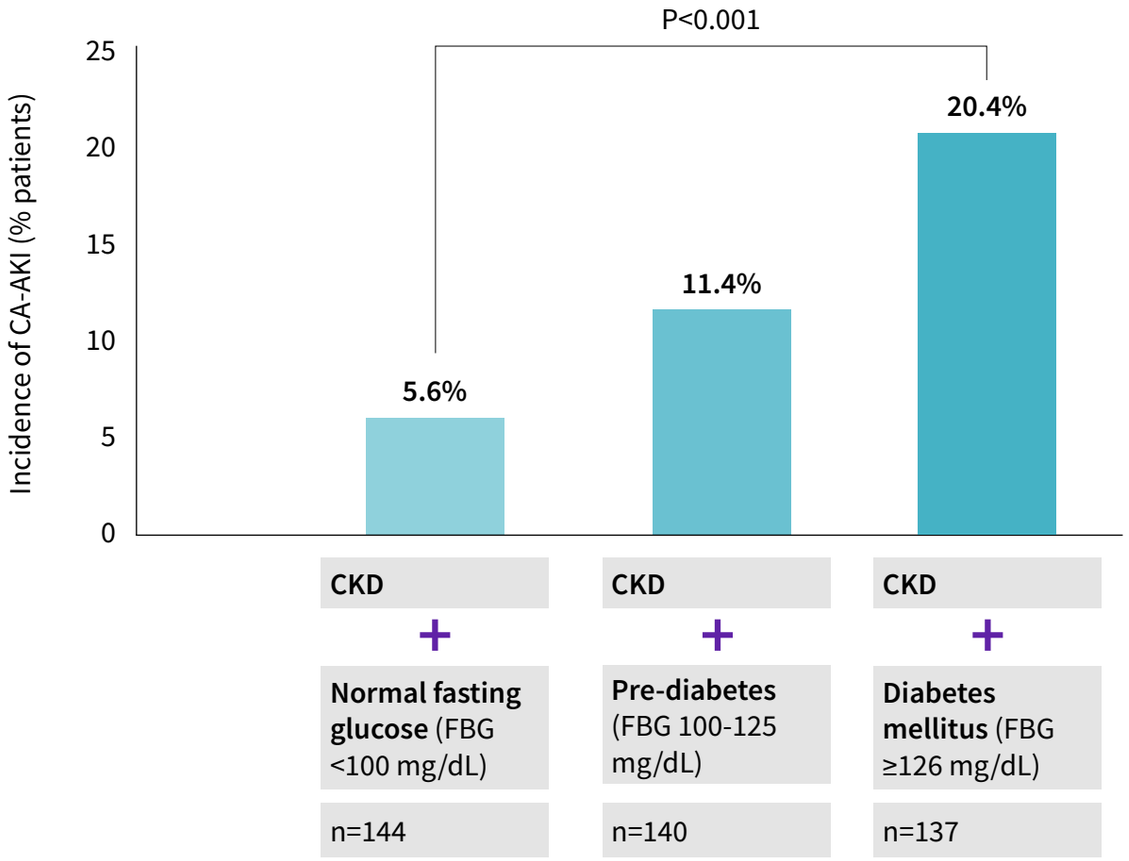
What effect a combination of risk factors can have on CA-AKI incidence

CKD and diabetes are principal risk factors for CA-AKI[1]

CKD patients who also have diabetes mellitus are at increased risk for developing CA-AKI[2]

Single center, prospective cohort study of 421 patients with CKD (91% stage 3) referred for non-emergency diagnostic coronary angiography.

CA-AKI was defined as an increase of ≥25% in SCr within 48 hours



Adapted from Toprak O et al. 2007.

AKI, acute kidney injury
CA-AKI, contrast-associated AKI
CKD, chronic kidney disease
FBG, fasting blood glucose
KDIGO, Kidney Disease: Improving Global Outcomes
SCr, serum creatinine

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References:
1. KDIGO AKI Work Group. Kidney Int Suppl. 2012;2:1–138.
2. Toprak O et al. Nephrol Dial Transplant. 2007;22(3):819-826.

How CA-AKI can lead to other problems

CA-AKI has been associated with increased hospital stay and cost, irreversible kidney injury, need for dialysis, and death:[1]

AKI is associated with incident and progressive chronic kidney disease[2]

CKD may lead to, or exacerbate, the risk for cardiovascular disease[2]

The composite endpoint of major adverse renal and cardiovascular events (MARCE) has recently been introduced to take account of the multifaceted nature of CA-AKI-related adverse outcomes[3,4]

Once CA-AKI is established there may be no specific treatment, hence the goal is prevention[3]

AKI, acute kidney injury
CA-AKI, contrast-associated AKI
CKD, chronic kidney disease
CVD, cardiovascular disease
MARCE, major adverse renal and cardiovascular events defined as renal failure with dialysis, myocardial infarction, stroke, heart failure, renal/cardiac hospitalization, or death

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References:
1. Azzalini L et al. Can J Cardiol. 2016;32(2):247-255.
2. Keuffel E et al. J Med Econ. 2017;21(4):356-364.
3. Almendarez M et al. JACC Cardiovasc Interv. 2019;12(19):1877-1888.
4. Chawla LS et al. Clin J Am Soc Nephrol. 2014;9(3):448-456.

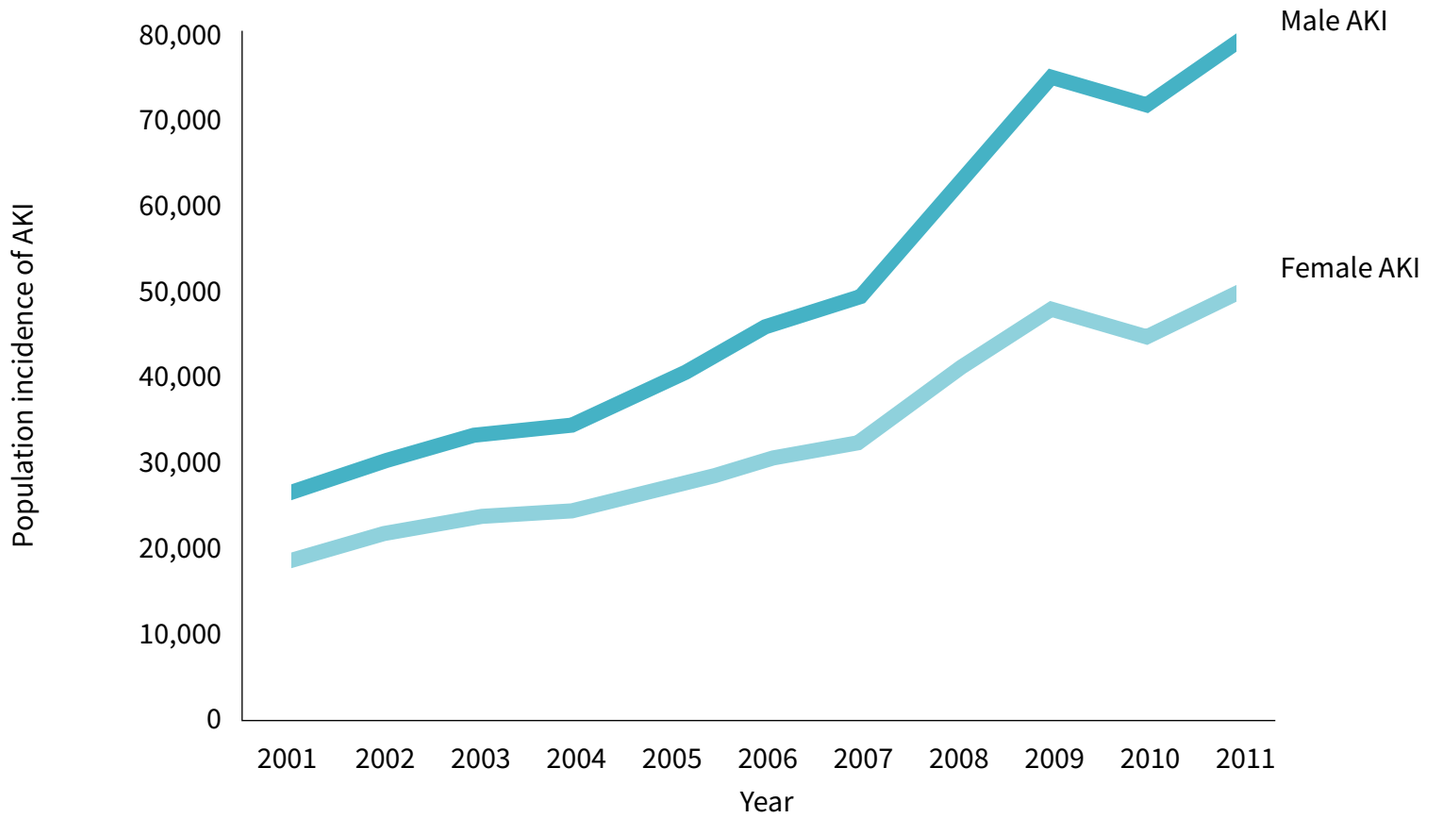
Why CA-AKI is a growing concern

Vulnerable patient populations (such as the elderly, and patients with diabetes or heart disease) are growing, as is the complexity of procedures being performed[1]

The incidence of AKI among cardiac catheterization and PCI patients has increased sharply in the United States[2]

Analysis of discharge data from the NIS, a nationally representative, stratified sample

The database included 46 states, 1,049 hospitals, and >8 million discharge records in 2011



Adapted from Brown JR et al. 2016.

AKI, acute kidney injury
CA-AKI, contrast-associated AKI
PCI, percutaneous coronary intervention
NIS, National Inpatient Sample

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References:

1. Keuffel E et al. J Med Econ. 2017;21(4):356–364.
2. Brown JR et al. J Am Heart Assoc. 2016;5(3):e002739.

The potential impact of CA-AKI on short-term outcomes

Some studies have asserted CA-AKI is a predictor of adverse outcomes and mortality after primary PCI in STEMI[1]

Impact of CA-AKI on short-term outcomes after PCI in STEMI[1]

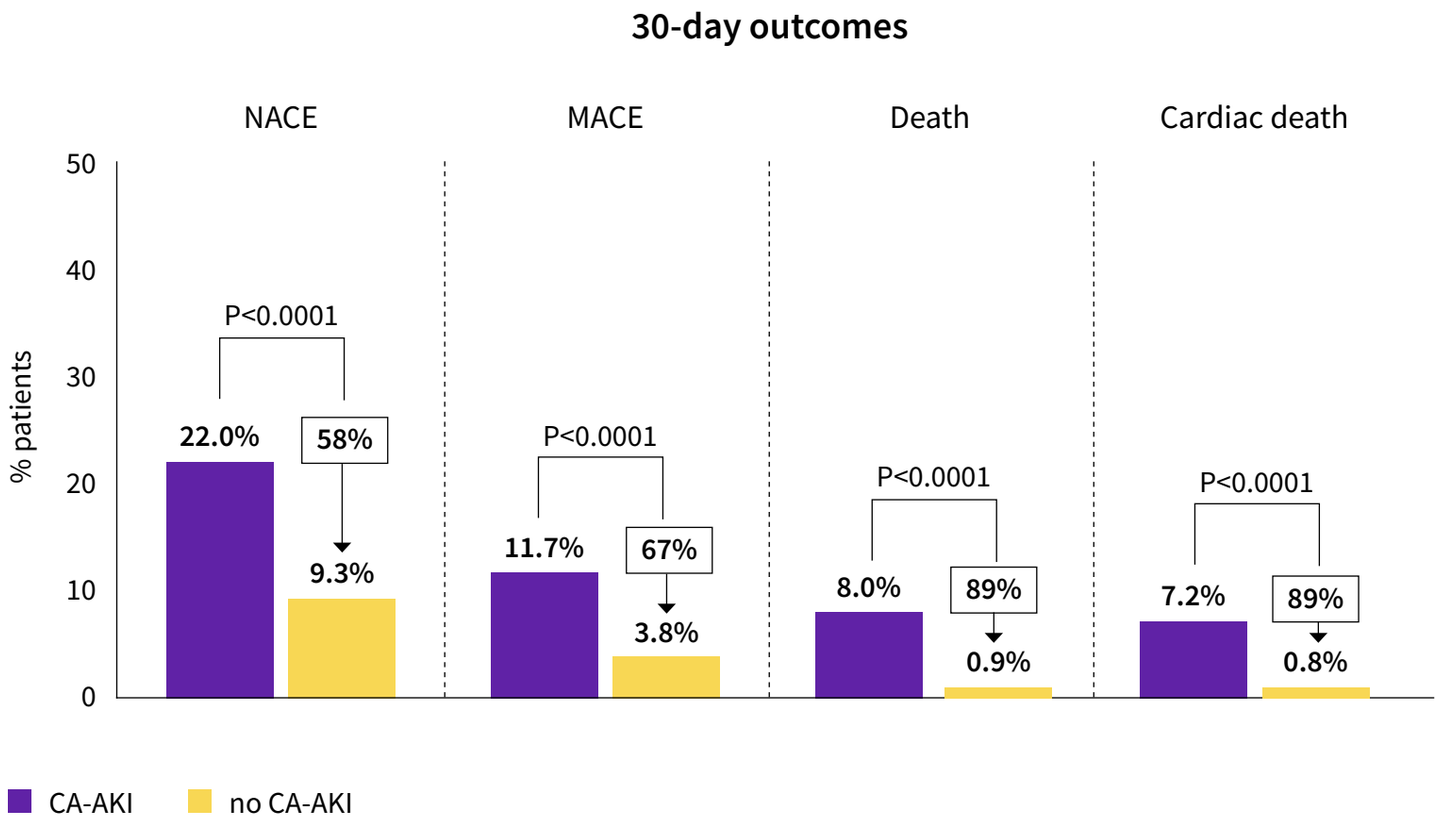
Prospective, open-label, randomized study of 3,602 STEMI patients undergoing PCI

16.1% developed CA-AKI

MACE: death, re-infarction, target vessel revascularization for ischaemia, or stroke

NACE: a combination of major bleeding or MACE

CA-AKI: increase in SCr ≥0.5 mg/dL or ≥25% from baseline within 48 hours of CM exposure



Adapted from Narula A et al. 2014.

AKI, acute kidney injury
CA-AKI, contrast-associated AKI
CM, contrast medium/media
MACE, major adverse cardiac events
MI, myocardial infarction
NACE, net adverse clinical events
PCI, percutaneous coronary intervention
SCr, serum creatinine
STEMI, ST-segment elevation MI

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Reference:
1. Narula A et al. Eur Heart J. 2014; 35(23): 1533-40.

The potential impact of CA-AKI on long-term outcomes

CA-AKI is a powerful independent predictor of adverse outcomes and mortality after primary PCI in STEMI[1]

Impact of CA-AKI on long-term outcomes after PCI in STEMI[1]

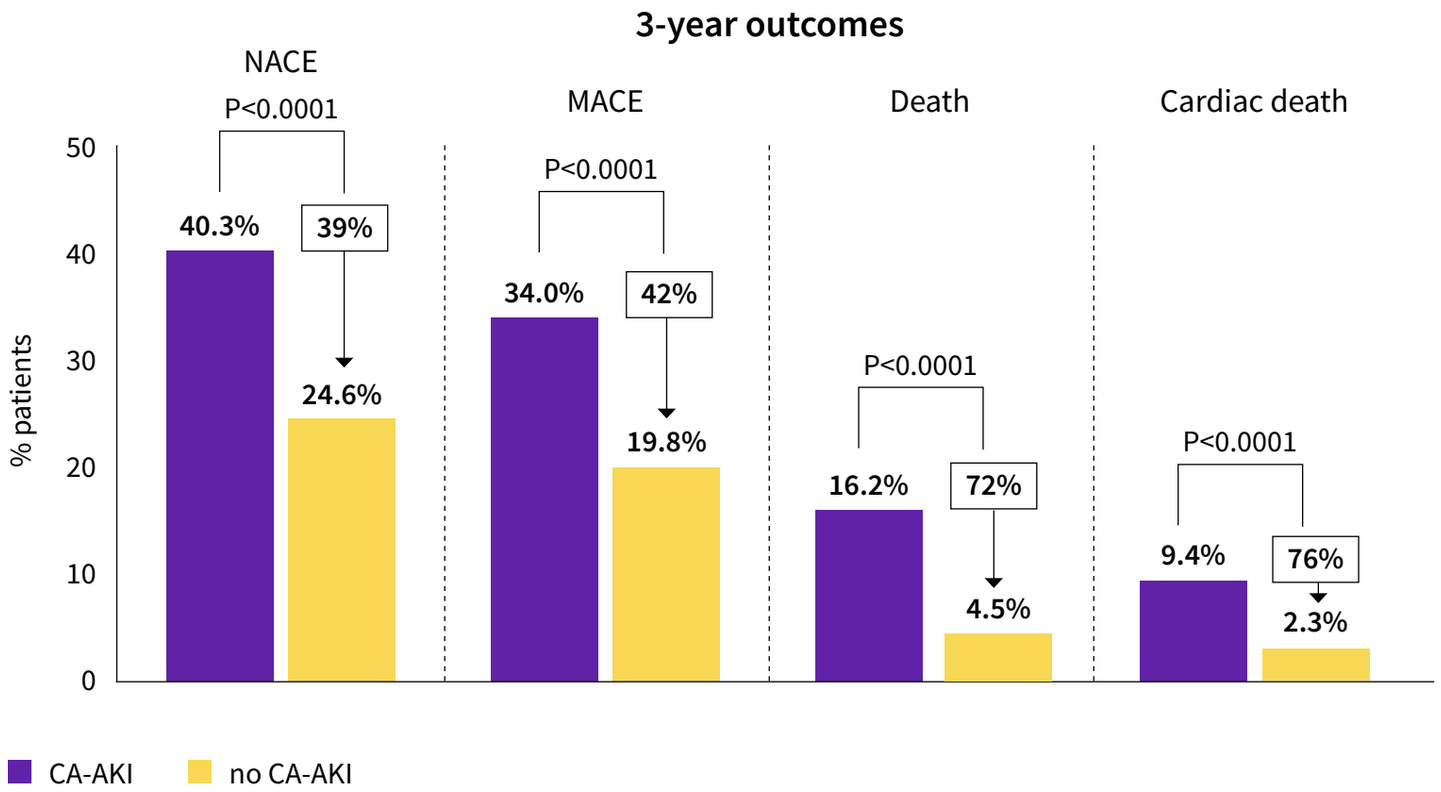
Prospective, open-label, randomized study of 3,602 STEMI patients undergoing PCI

16.1% developed CA-AKI

MACE: death, re-infarction, target vessel revascularization for ischaemia, or stroke

NACE: a combination of major bleeding or MACE

CA-AKI: increase in SCr ≥0.5 mg/dL or ≥25% from baseline within 48 hours of CM exposure



Adapted from Narula A et al. 2014.

AKI, acute kidney injury
CA-AKI, contrast-associated AKI
CM, contrast medium/media
MACE, major adverse cardiac events
MI, myocardial infarction
NACE, net adverse clinical events
PCI, percutaneous coronary intervention
SCr, serum creatinine
STEMI, ST-segment elevation MI

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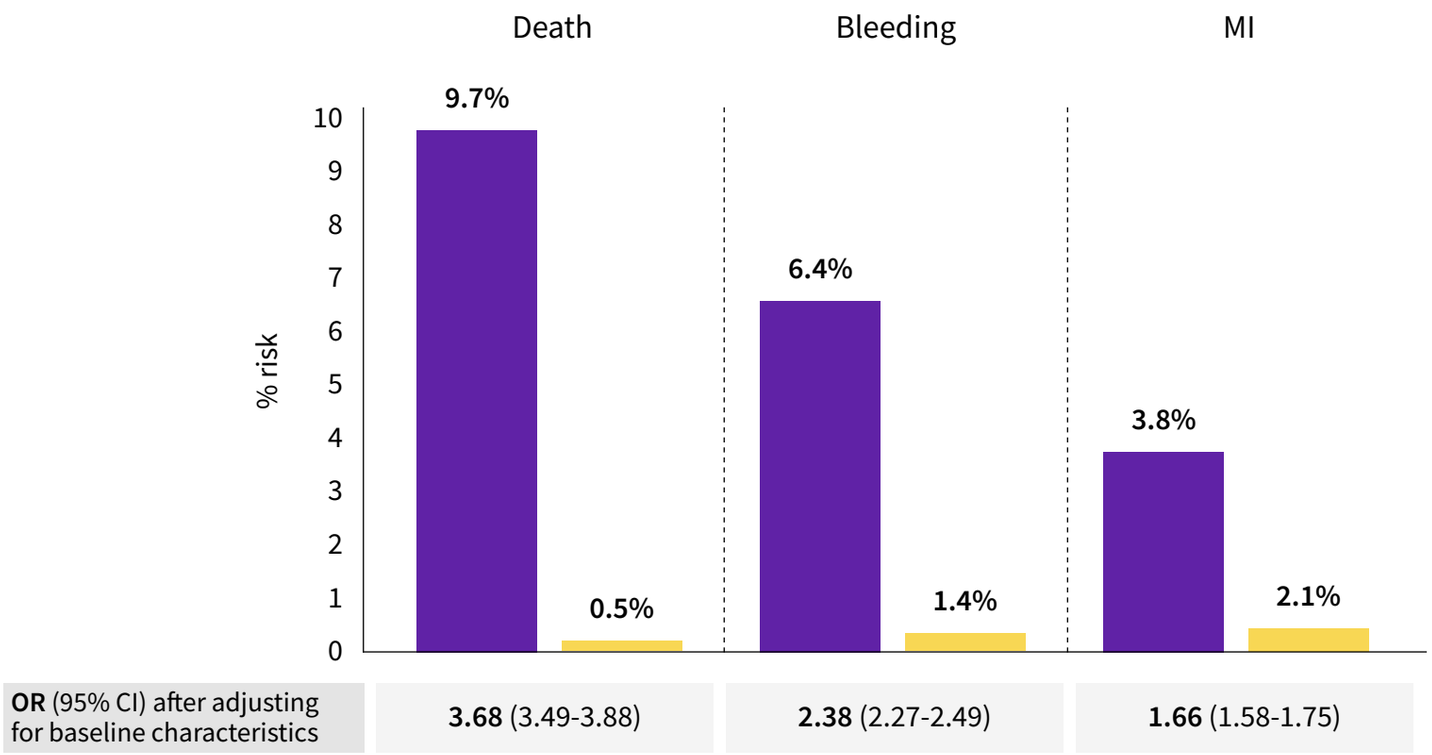
Reference:

1. Narula A et al. Eur Heart J. 2014; 35(23): 1533-40.

Real-world data support the need for strategies to minimize the risk of post-contrast AKI in PCI patients

Risk of death, bleeding, and myocardial infarction in PCI patients with/without post-contrast AKI[1]

Data from 985,737 consecutive patients at 1,253 sites participating in the NCDR CathPCI Registry® from June 2009 through June 2011[1]



Adapted from Tsai TT et al. 2014.

AKI, acute kidney injury
CI, confidence interval
MI, myocardial infarction
NCDR, National Cardiovascular Data Registry
OR, odds ratio
PCI, percutaneous coronary intervention

AKI is common and independently associated with other adverse events and would justify a national effort to improve prevention as a foundation for greater safety and better PCI outcomes[1]

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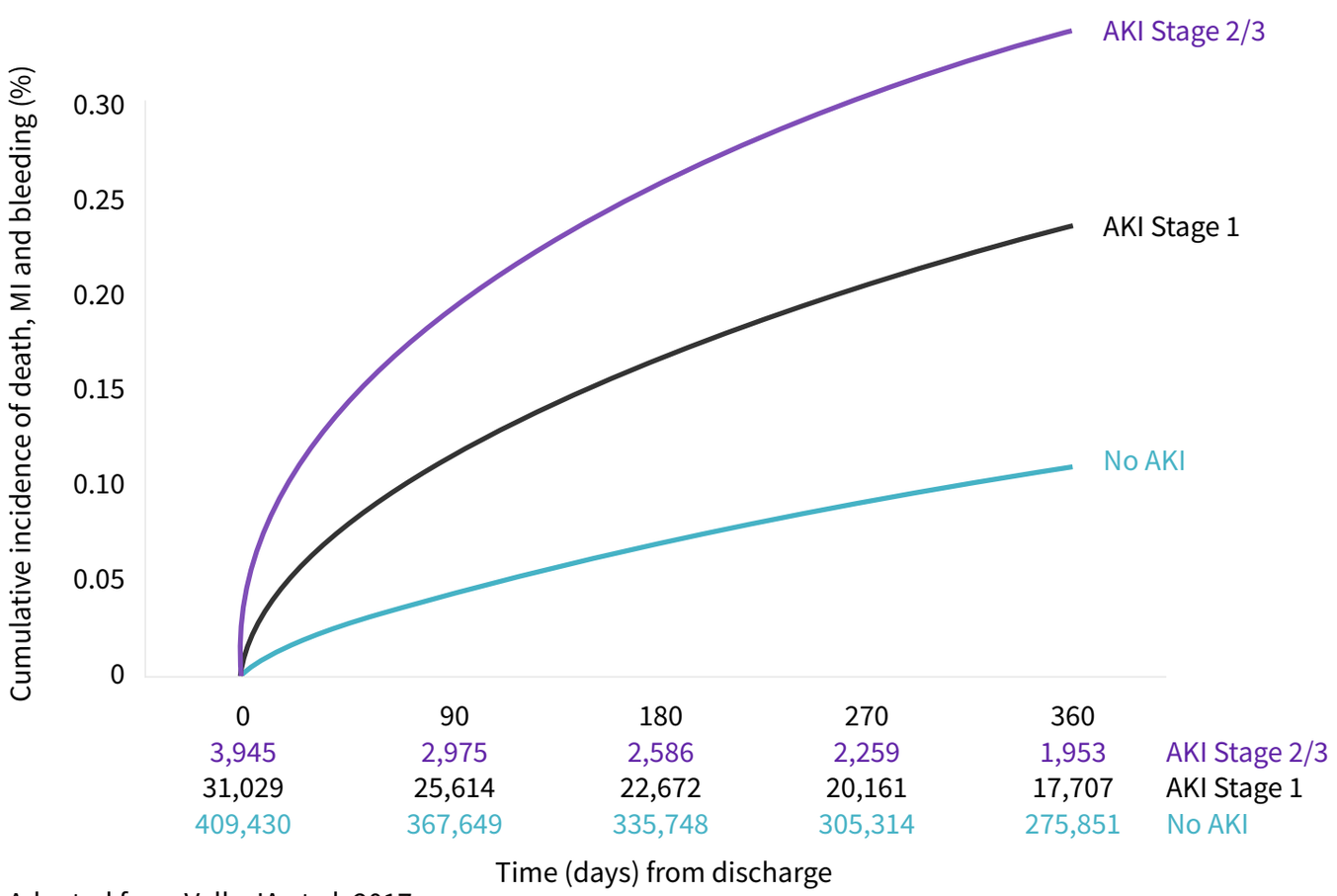
Reference:
1. Tsai TT et al. JACC Cardiovasc Interv. 2014;7(1):1-9.

Morbidity and mortality may occur after hospital discharge

Cumulative incidence of adverse events post-discharge, by presence and severity of in-hospital AKI[1]

Data from 453,475 patients undergoing PCI at 1,127 sites participating in the NCDR CathPCI Registry® from June 2004 through June 2009.



Adapted from Valle JA et al. 2017.

AKI, acute kidney injury
MI, myocardial infarction
NCDR, National Cardiovascular Data Registry
PCI, percutaneous coronary intervention

Post-PCI AKI should be recognized as a significant risk factor not only for in-hospital adverse events but also after hospital discharge[1]

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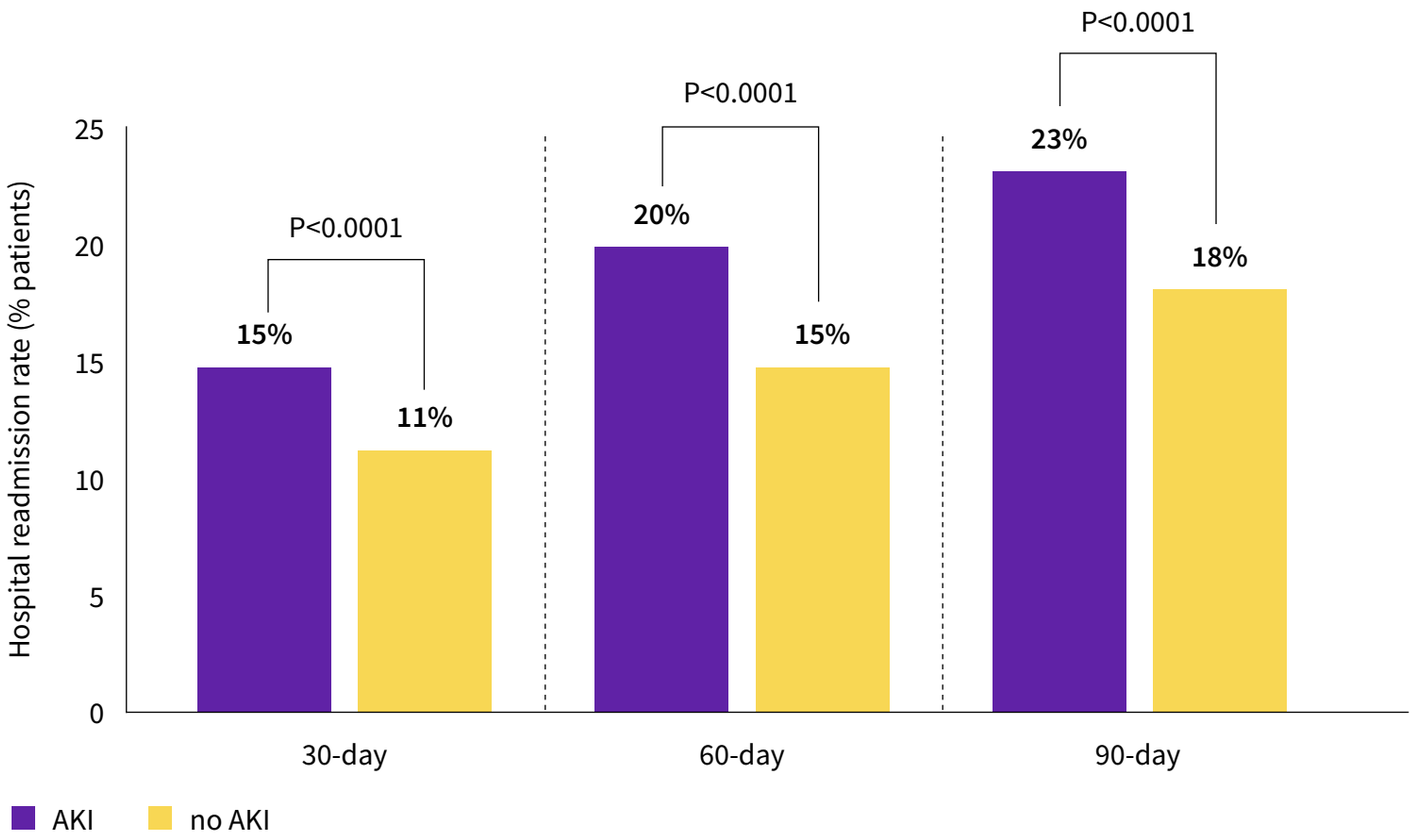
Reference:
1. Valle JA et al. Circ Cardiovasc Interv. 2017;10(4). pii: e004439.

Survivors of hospital-acquired AKI experience higher odds of early hospital readmission

Hospital readmission rates among patients with and without AKI during the index hospitalization[1]

Retrospective cohort study of adults discharged from a tertiary acute-care facility from October 2000 through September 2007.



Adapted from Koulourdis I et al. 2015.

The development of AKI during hospitalization might be an unrecognized, albeit important, care-related determinant of hospital readmissions[1]

AKI, acute kidney injury

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Reference:
1. Koulouridis I et al. Am J Kidney Dis. 2015;65(2):275–282.

The economic burden of hospital-acquired AKI is high

Data from the 2012 NIS was used to compare hospitalization costs and LOS for patients with and without AKI[1]

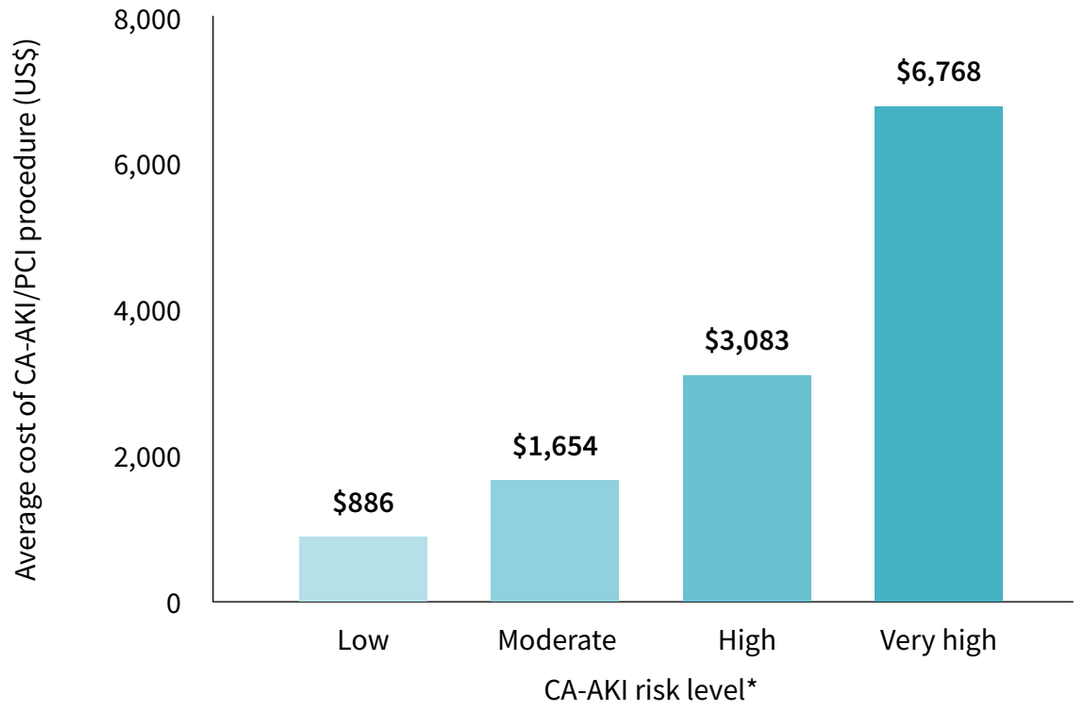
n=29,763,649 adult hospitalizations without ESRD

Adapted from Silver SA et al. 2017.

	Impact on LOS	Impact on hospitalization cost
AKI	+ 3.2 days	+ $7,933
AKI-D	+ 11.5 days	+ $42,077

A decision analytic model estimated the in-hospital and 1-year costs of CA-AKI[2]

Long-term healthcare costs increase with CA-AKI risk level[2]



* Risk levels based on Mehran risk scores[3]

Adapted from Subramanian S et al. 2007.

AKI, acute kidney injury
AKI-D, AKI dialysis
CA-AKI, contrast-associated AKI
ESRD, end-stage renal disease
LOS, length of stay
NIS, National Inpatient Sample
PCI, percutaneous coronary intervention

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References:
1. Silver SA et al. J Hosp Med. 2017;12(2):70-76.
2. Subramanian S et al. J Med Econ. 2007;10(2):119-134.
3. Mehran R et al. J Am Coll Cardiol. 2004;44:1393–1399.

Strategies to mitigate the risk of CA-AKI

- Screening patients
- Periprocedural hydration
- Limiting contrast volume
- Risks/benefits of chosen CM

AKI, acute kidney injury
CA-AKI, contrast-associated AKI
CM, contrast medium/media

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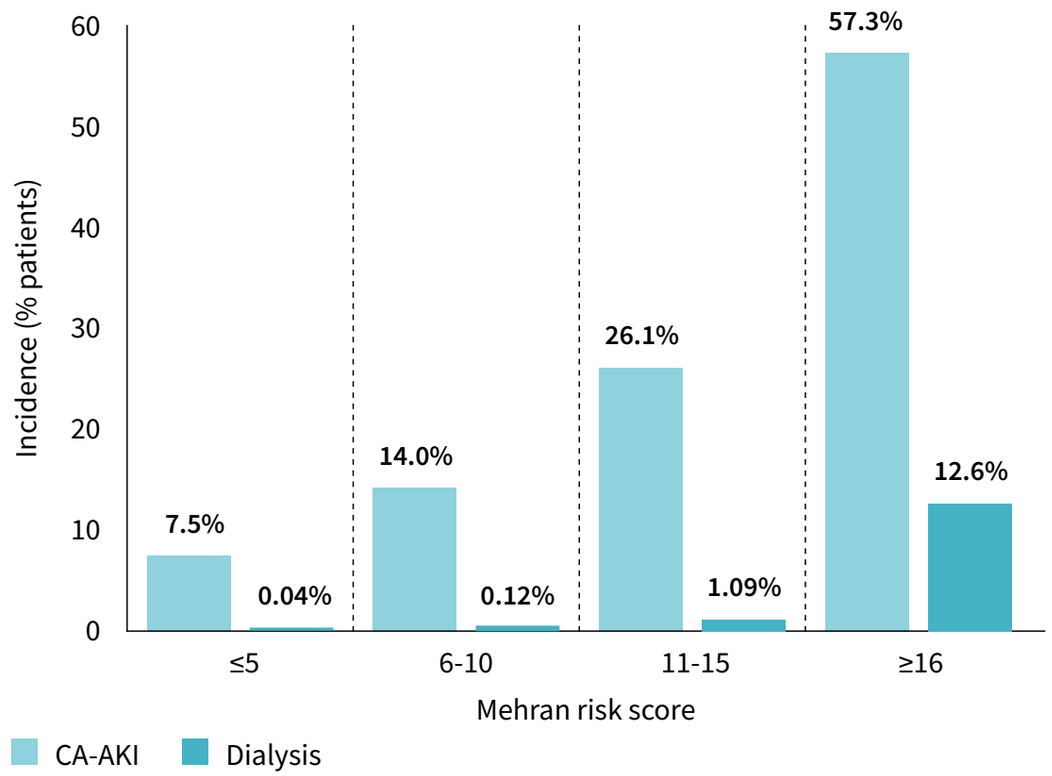
Screening for patient risk – Mehran

Several investigators have looked at the use of risk scores to guide preventive strategies, the most comprehensive of which is the Mehran risk score[1]

Mehran risk score for CA-AKI[2]

Variable	Points
Hypotension	5
Intra-aortic balloon pump	5
Chronic heart failure	5
Age >75 years	4
Anemia	3
Diabetes	3
Contrast media volume	1 for each 100 mL
Serum creatinine >1.5 mg/dl	4
or eGFR <60 ml/min//1.73 m^2	2 for 40-60 4 for 20-40 6 for <20

Adapted from Mehran R et al. 2004.



The Mehran score was more recently validated in a contemporary cohort of ACS patients; the CA-AKI rate predicted by the model closely approximated the observed rate[3]

ACS, acute coronary syndrome
AKI, acute kidney injury
CA-AKI, contrast-associated AKI

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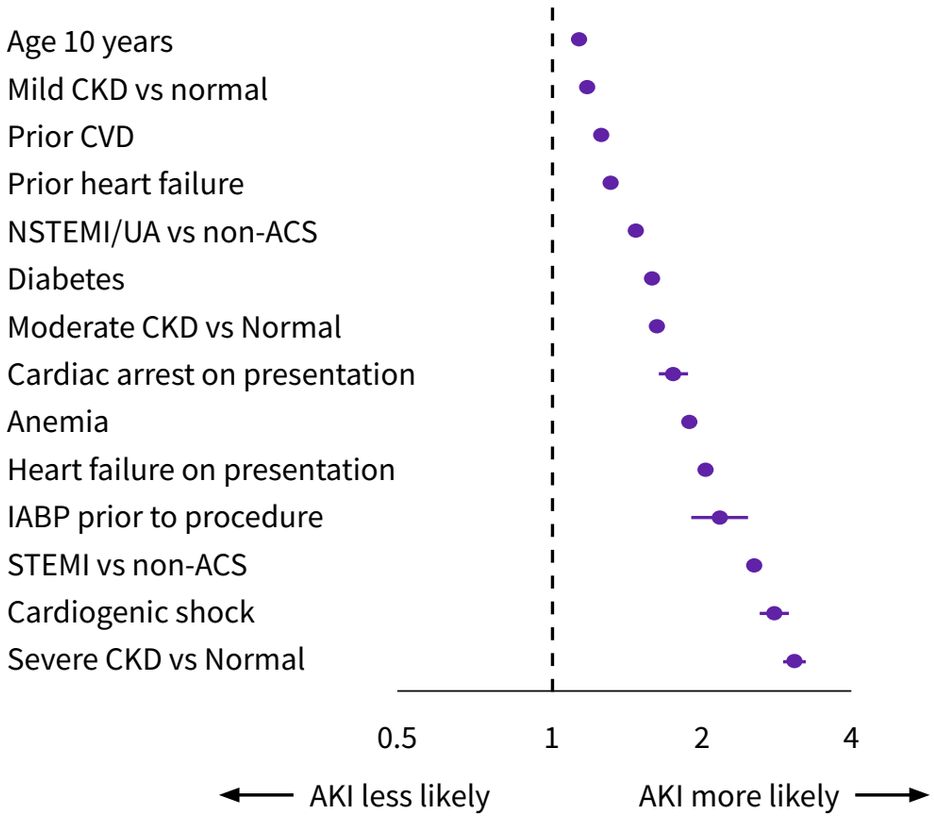
References:
1. Azzalini L et al. Can J Cardiol. 2016;32(2):247-255.
2. Mehran R et al. J Am Coll Cardiol. 2004;44:1393–1399.
3. Abellás-Sequeiros RA et al. J Cardiol. 2016;67(3):262-7.

Screening for patient risk – NCDR model

Data from the large NCDR cohort were assessed to understand the incidence, predictors, and outcomes of AKI post-PCI

NCDR risk model for post-contrast AKI[1]



Focusing on pre-procedure variables to best estimate the periprocedure risk of AKI, can enhance the patient consent process and risk/benefit evaluations[1]

Adapted from Tsai TT et al. 2014.

ACS, acute coronary syndrome
AKI, acute kidney injury
CKD, chronic kidney disease
CVD, cardiovascular disease
IABP, intra-aortic balloon pump
MI, myocardial infarction
NCDR, National Cardiovascular Data Registry
NSTEMI, non-ST-segment elevation MI
PCI, percutaneous coronary intervention
STEMI, ST-segment elevation MI
UA, unstable angina

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Reference:
1. Tsai TT et al. JACC Cardiovasc Interv. 2014;7(1):1-9.

Administering periprocedural hydration

- Volume expansion and treatment of dehydration are well-established interventions in the prevention of CA-AKI[1]
- Intravenous saline hydration during primary PCI reduced the relative risk of CA-AKI to almost 50%[1]

Two common referenced hydration protocols[2-4]

	Clinical practice guidelines	Hemodynamic-guided fluid administration
Name	ACCF/AHA/SCAI Practice Guidelines for PCI	POSEIDON Trial Hydration Protocol
Type	Normal saline (isotonic crystalloid)	Sliding scale hydration based on intracardiac pressure measurement (LVEDP)
Preprocedure	Intravenous administration: 1-1.5 mL/kg/h for 3-12 hours	Bolus infusion at 3 mL/kg for 1 hour
Intraprocedure and Postprocedure	Postprocedure: Intravenous administration: 1-1.5 mL/kg/hr for 6-24 hours	• 5 mL/kg/h for LVEDP <13 mm Hg • 3 mL/kg/h for LVEDP 13-18 mm Hg • 1.5 mL/kg/h for LVEDP >18 mm Hg • Continued 4 hours postprocedure
Reference	Levine GN et al. JACC 2011; 24: e44-e122	Brar SS et al. Lancet 2014; 383: 1814-1823

ACCF, American College of Cardiology Foundation;
AHA, American Heart Foundation
AKI, acute kidney injury
CA-AKI, contrast-associated AKI
LVEDP, left ventricular end diastolic pressure
PCI, percutaneous coronary intervention;
SCAI, Society for Cardiovascular Angiography and Interventions.

Focusing on pre-procedure variables to best estimate the periprocedure risk of AKI can enhance the patient consent process and risk/benefit evaluations[5]

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References:
1. Jurado-Román A et al. Am J Cardiol. 2015;115(9):1174–1178.
2. Levine GN et al. J Am Coll Cardiol. 2011;58(24):e44–122.
3. Brar SS et al. Lancet. 2014;383(9931):1814–1823.
4. ClinicalTrials.gov Identifier: NCT01218828. https://clinicaltrials.gov/ct2/show/NCT01218828. Accessed July 13, 2022.
5. Tsai TT et al. JACC Cardiovasc Interv. 2014;7(1):1-9.

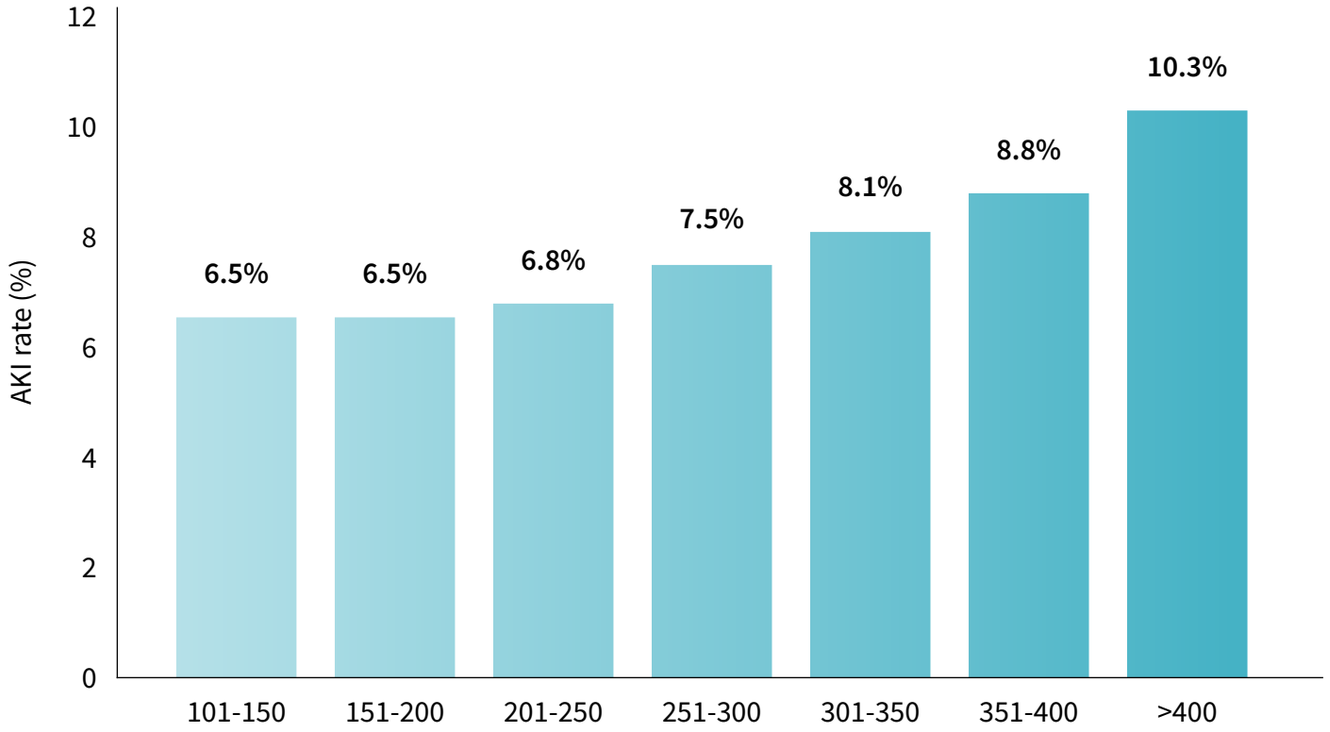
Limiting contrast volume in high-risk patients

Evidence suggests that there is a nearly linear relationship between the magnitude of contrast reduction and the expected reduction in AKI[1]

Relationship between increasing contrast volume and AKI[2]

Cross-sectional study using the NCDR CathPCI Registry® to identify in-hospital care for PCI in the US

Participants included 1,349,612 patients who underwent PCI performed by 5,973 physicians in 1,338 hospitals from June 2009 through June 2012



Adapted from Amin AP et al. 2017.

AKI, acute kidney injury
NCDR, National Cardiovascular Data Registry
PCI, percutaneous coronary intervention

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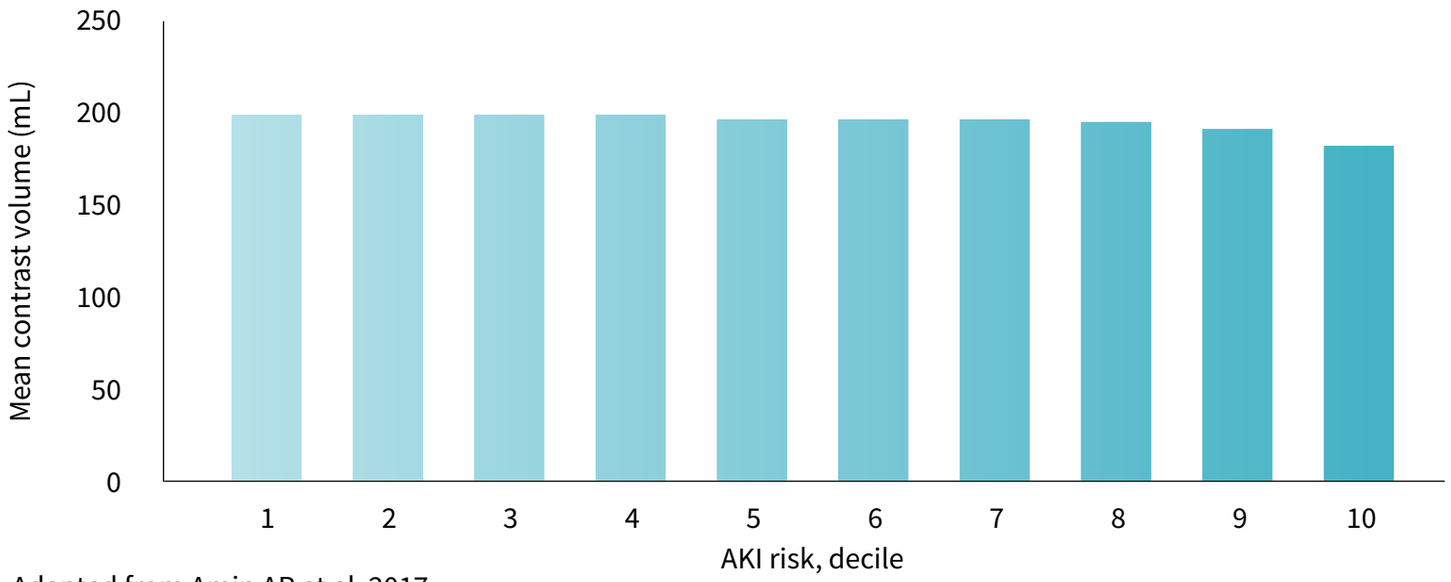
References:
1. Gurm HS et al. J Invasive Cardiol. 2016;28(4):142-6
2. Amin AP et al. JAMA Cardiol. 2017;2(9):1007-1012 (+online supplementary content)

Limiting contrast volume in all patients

Data from CathPCI Registry® show that:

- physicians vary markedly in their use of contrast[1]
- they appear not to use substantially less contrast in patients with higher risk for AKI[1]
- AKI rates also vary greatly among physicians[1]

Mean contrast volume used by AKI risk[1]



Adapted from Amin AP et al. 2017.

The absence of an adjustment in contrast volume for patients at higher risk for AKI underscores an important opportunity to reduce AKI[1]

AKI, acute kidney injury
NCDR, National Cardiovascular Data Registry
PCI, percutaneous coronary intervention

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Reference:
1. Amin AP et al. JAMA Cardiol. 2017;2:1007–1012.

Reviewing benchmarked data can help inform best practice

NCDR®
NATIONAL CARDIOVASCULAR DATA REGISTRY

In-hospital AKI rate is an important quality metric in the NCDR CathPCI Registry®[1]

Executive Summary

CathPCI Registry®

National Outcomes Report (999997) compared to rolling four quarters (R4Q) for US Hospitals ending 2014Q3

Section II: Quality Metrics - to support self assessment and quality improvement at the provider, hospital, and/or healthcare system level.

PCI in-hospital risk adjusted AKI (all patients)

My Hospital	US Hospital 50th percentile	US Hospitals 90th percentile
....	6.13	2.85

Your hospital's PCI in-hospital risk adjusted AKI rate for all patients adjusted using the NCDR risk adjustment model.

AKI, acute kidney injury
NCDR, National Cardiovascular Data Registry
PCI, percutaneous coronary intervention

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Reference:
1. The CathPCI Registry. https://cvquality.acc.org/NCDR-Home/registries/hospital-registries/cathpci-registry. Accessed July 13, 2022.

Clinical society recommendations

	KDIGO	AHA	ACCF	SCAI
Screen for patient risk[1-3]	✓	✓	✓	✓
Administer periprocedural hydration[1-3]	✓	✓	✓	✓
Limit contrast volume in high-risk patients[1-3]	✓	✓	✓	✓
Consider the risks and benefits of the contrast media[1,3]	✓			

ACCF, American College of Cardiology Foundation
AHA, American Heart Association
KDIGO, Kidney Disease Improving Global Outcomes
SCAI, The Society for Cardiovascular Angiography and Interventions

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References:
1. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. Kidney Int Suppl. KDIGO Clinical Practice Guideline for Acute Kidney Injury. 2012;2:1–138.
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