Baxter

ACUTE KIDNEY INJURY

A SERIOUS RENAL COMPLICATION[1-4]

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AKI AWARENESS

DEFINITION OF AKI

According to the KDIGO Clinical Practice Guideline,[5] AKI is defined as any of the following (not graded):

- Increase in SCr by ≥0.3 mg/dL (≥26.5 μmol/L) within 48 hours; or
- Increase in SCr to ≥1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or
- Urine volume <0.5 mL/kg/h for 6 hours

INCIDENCE OF AKI

- Worldwide, approximately **20%** of hospitalized patients have AKI[6]
- Approximately **20–60%** of adult* ICU patients have AKI; about **15–25%** of these patients receive RRT[7-10]
- Approximately **27%** of paediatric and young adult ICU patients develop AKI during the first week after admission[11]
- AKI may be under-recognized in hospitalized patients in some countries[12-15]
- The incidence of dialysis-requiring AKI has increased in some countries[16-18]

*One study included patients aged >15 years.

AKI encompasses even small changes in kidney function, is common among ICU patients, and may be underdiagnosed[5-7,11-15,19,20]

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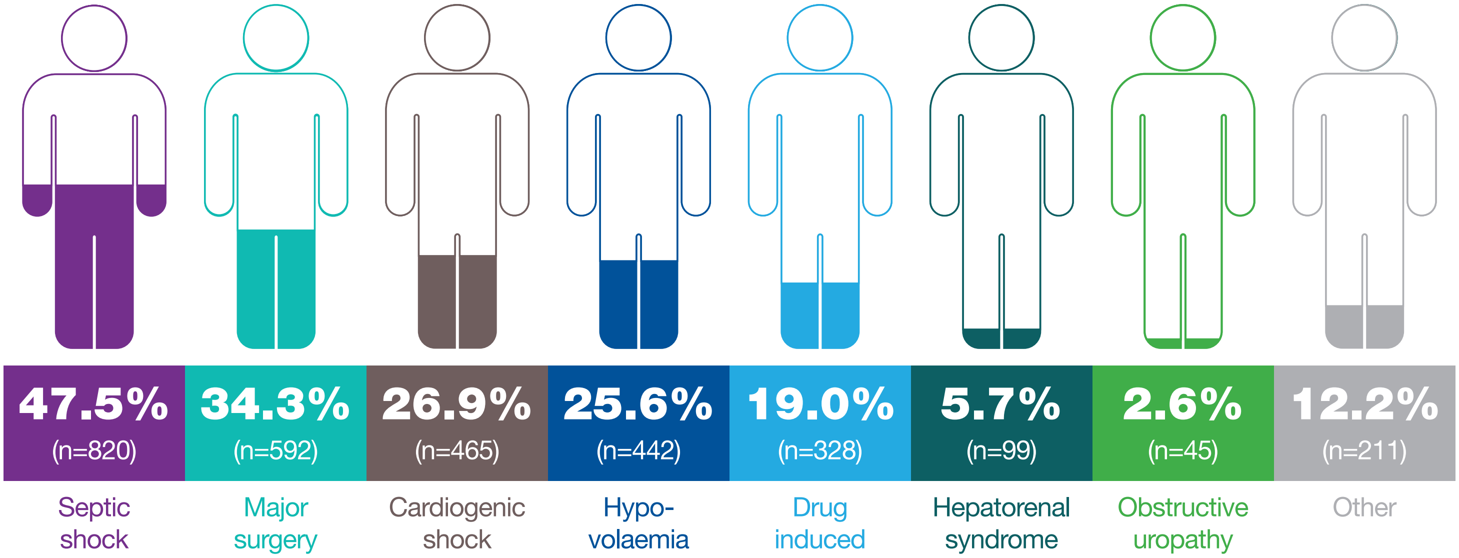
MAJOR FACTORS CONTRIBUTING TO AKI IN THE ICU SETTING[21]



Data are from a prospective observational study of AKI in ICU patients from September 2000 to December 2001 at 54 hospitals in 23 countries. AKI was defined as urine output <200 mL in 12 hours and/or BUN >84 mg/dL (>30 mmol/L). Factors contributing to AKI for 1726 patients are shown above as % (n); more than one factor may have been reported for each patient.[21]

Many factors may contribute to AKI in the ICU[21]

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AKI AWARENESS

NATURAL HISTORY OF AKI[22]

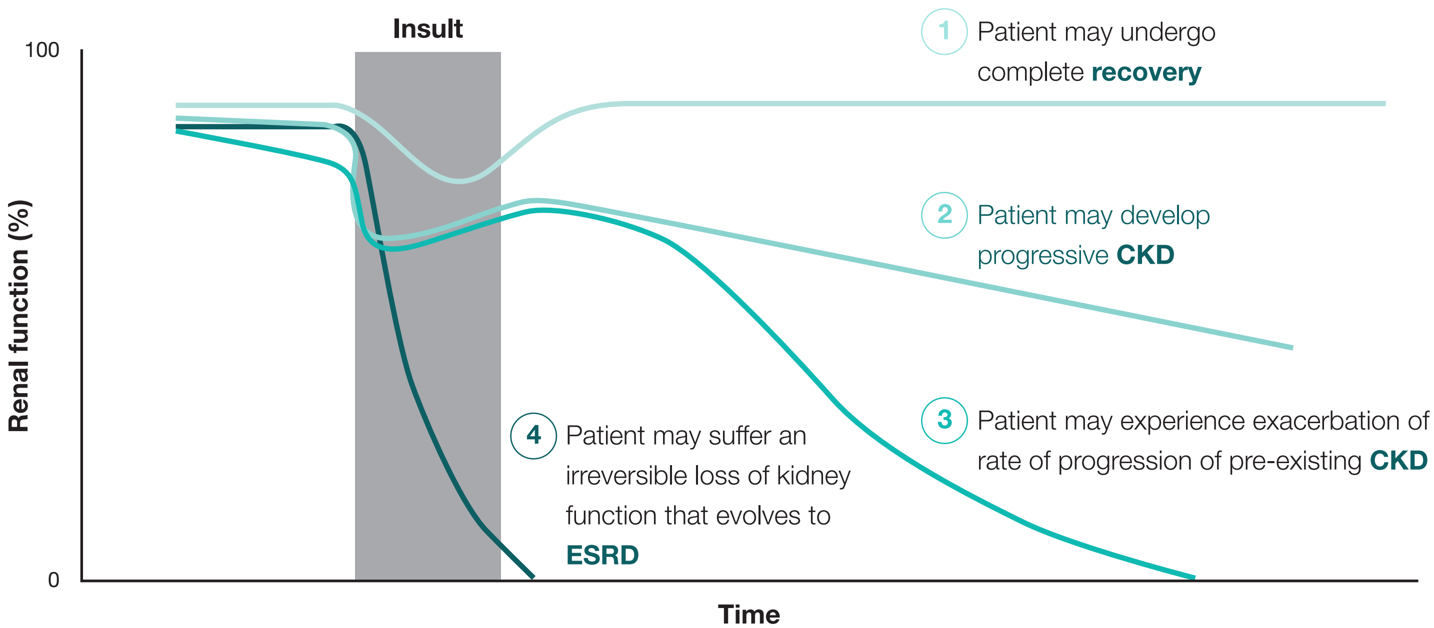

Figure adapted from Cerdá J, et al. *Clin J Am Soc Nephrol*. 2008;3(3):881-886.

The graphic above depicts potential courses of a patient after AKI.[22]

KEY STUDY TAKEAWAY

AKI may progress to or worsen CKD, or result in ESRD[22]

AKI is associated with an increased risk of CKD, including ESRD[23-25]

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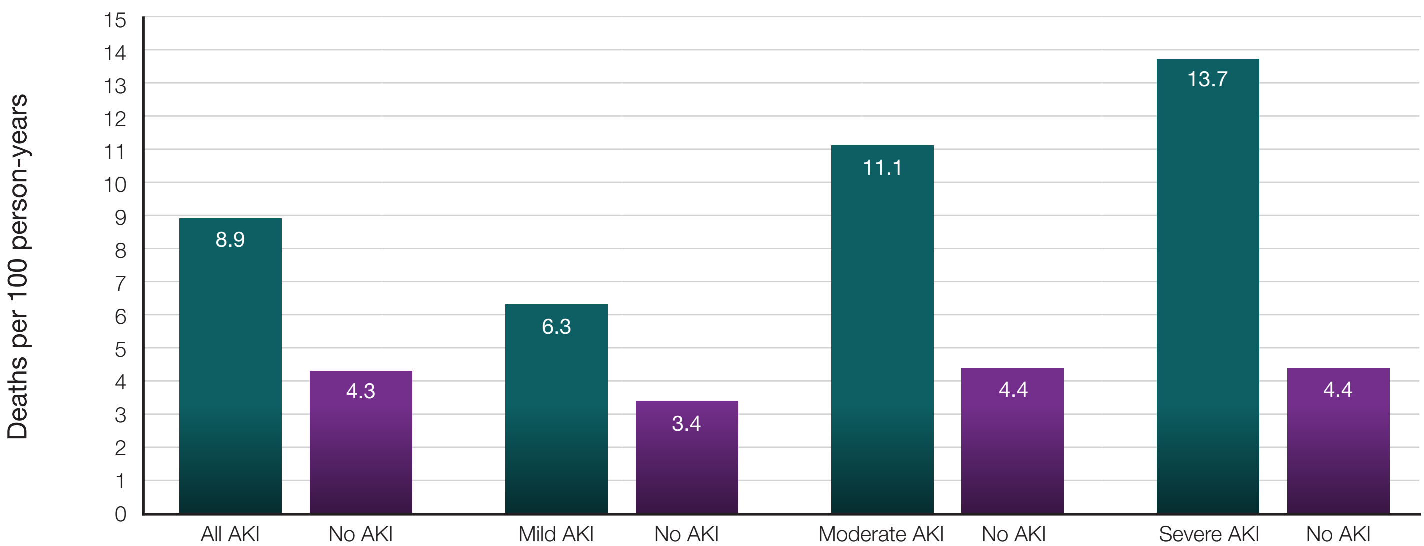
AKI-ASSOCIATED MORTALITY[1]



	All AKI	No AKI	Mild AKI	No AKI	Moderate AKI	No AKI	Severe AKI	No AKI
No. of studies	15		3		6		7	
N	7665	87,014	3972	9908	2928	67,488	1079	13,351
Pooled RRs for mortality by AKI severity	**2.59** (95% CI 1.97, 3.42)		**1.67** (95% CI 1.41, 1.98)		**2.73** (95% CI 1.81, 4.14)		**3.04** (95% CI 2.13, 4.33)	

The above data are from a meta-analysis of 15 studies that reported long-term mortality of both patients who survived hospitalization with AKI and patients who survived hospitalization without AKI. Mortality was further analysed according to AKI severity: mild AKI (increase in creatinine level >25% or decrease in creatinine clearance >10%), moderate AKI (increase in creatinine level by >50%, >100%, or >1 mg/dL; or creatinine concentration >1.7 mg/dL), and severe AKI (requiring RRT).[1]

Even mild AKI is associated with an increased risk of long-term mortality, while moderate or severe AKI is associated with a 3-fold increase in mortality vs no AKI[1]

THERAPY

POTENTIAL APPLICATIONS FOR RRT[5]

Renal replacement

- Traditional approach based on utilization of RRT with little or no residual kidney function

Life-threatening indications*

- Hyperkalaemia
- Acidaemia
- Pulmonary oedema
- Uraemic complications

Non-emergent indications

- Solute control
- Fluid removal
- Correction of acid–base abnormalities

Renal support†

- Volume control
- Nutrition
- Drug delivery
- Solute modulation
- Regulation of acid–base and electrolyte status

*The KDIGO Clinical Practice Guideline recommends initiating RRT emergently for life-threatening changes in fluid, electrolyte, or acid-base balance (recommendation is not graded but is based on wide acceptance that these conditions necessitate emergent dialysis).

†Based on the utilization of RRT as an adjunct to enhance kidney function, modify fluid balance, and control solute levels.

There are a variety of potential applications for RRT[5]

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DIALYSIS-REQUIRING AKI AMONG ICU PATIENTS

AN **ESTIMATED**

2–14%

OF **ICU PATIENTS**

MAY REQUIRE RRT

FOR AKI[6-10]

While estimates vary by study, dialysis-requiring AKI is common among critically ill patients[6-10]

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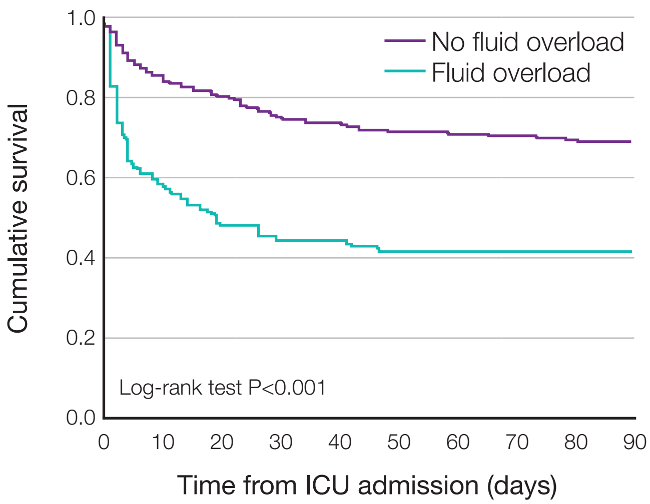
THERAPY

FLUID OVERLOAD MAY ADVERSELY IMPACT AKI PATIENT PROGNOSIS[26,27]

Fluid overload at RRT initiation for AKI has been associated with an increased risk of 90-day mortality[27]



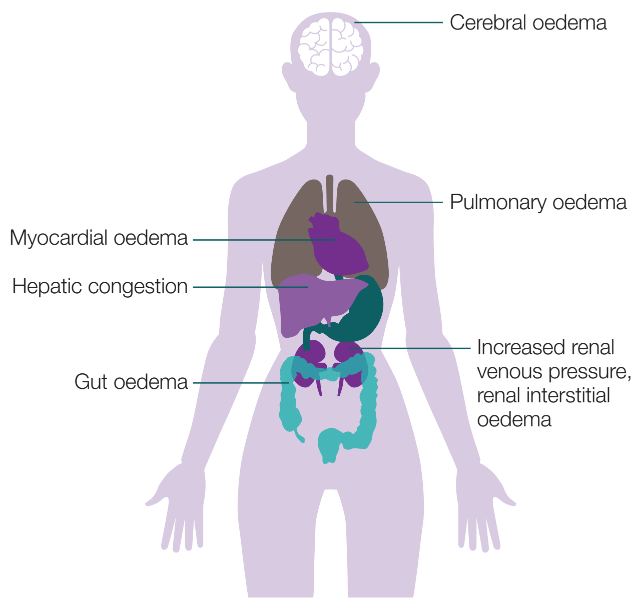
Vaara ST, et al. *Crit Care.* 2012;16(5):R197.

Prospective, observational cohort study of 296 adults treated with RRT in 17 Finnish ICUs from September 2011 to February 2012. Fluid overload was defined as cumulative fluid accumulation >10% of baseline weight. Presence of fluid overload was identified as a factor associated with 90-day mortality; adjusted OR: 2.626 (95% CI 1.301, 5.299); P=0.007.[27]

KEY STUDY TAKEAWAY

Fluid overload in AKI patients was independently associated with mortality[27]

Consequences of fluid overload may lead to organ dysfunction[28]



Prowle JR, et al. *Nat Rev Nephrol.* 2010;6(2):107-115.

KEY STUDY TAKEAWAY

Fluid overload may be associated with serious complications in multiple organs[28]

RRT may be used as part of a fluid management strategy to help avoid or control fluid overload in AKI patients[5,29]

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FLUID ACCUMULATION OVER TIME WITH CRRT AND IHD IN THE PICARD STUDY[30,*]

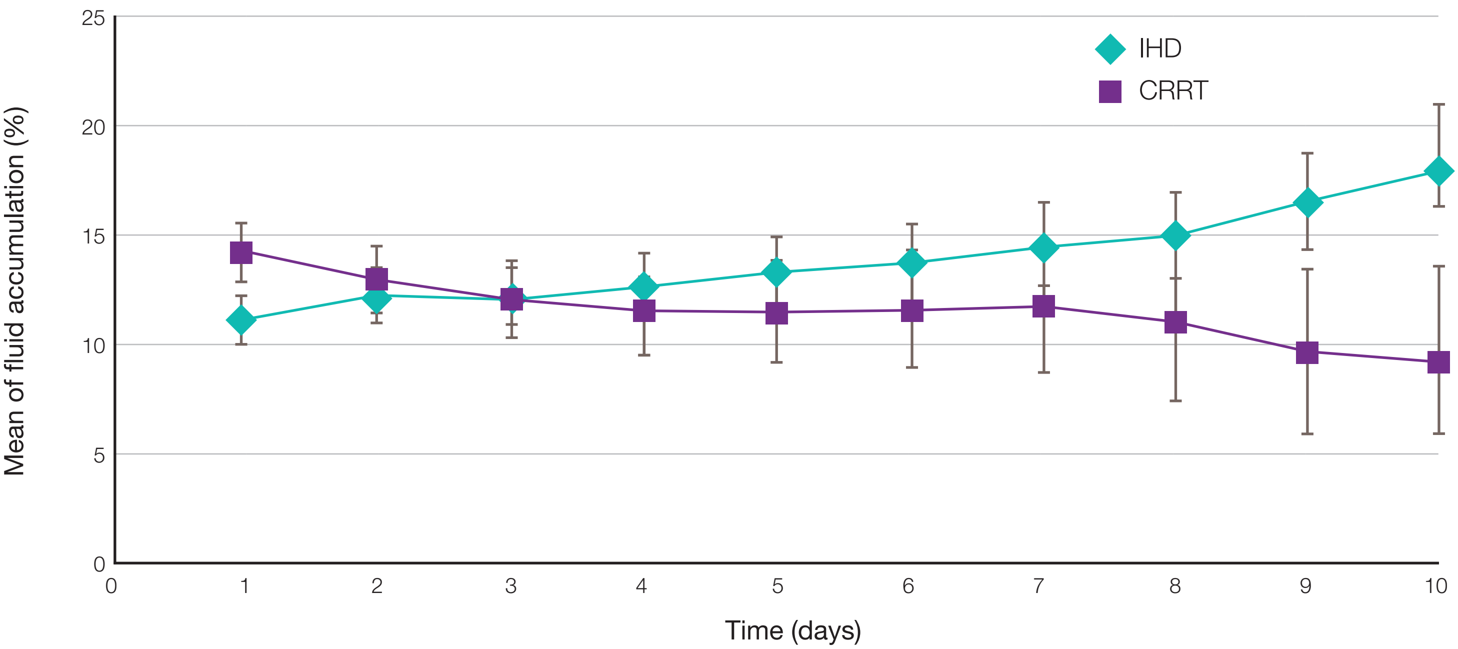

Figure adapted from Bouchard J, et al. *Kidney Int*. 2009;76(4):422-427.
*Details of data collection and statistical analysis were not reported.

PICARD was a prospective, observational study of 618 critically ill patients with AKI at five centres in North America from February 1999 to August 2001. The objective was to determine whether fluid accumulation is associated with mortality and non-recovery of kidney function.[30]

KEY STUDY TAKEAWAY

Patients who received CRRT had reduced accumulation over time compared with those who received IHD[30,*]

CRRT is a preferred RRT by many clinicians for patients with AKI who are haemodynamically unstable[5,31]

LONG-TERM OUTCOMES

ACUTE RRT MODALITY TYPE MAY IMPACT THE RISK OF LONG-TERM DIALYSIS DEPENDENCE[32-35]

INCIDENCE OF CHRONIC DIALYSIS BY INITIAL RRT MODALITY FOR PATIENTS WITH AKI SURVIVING TO 90 DAYS[32]

CRRT (n=2004)		**IHD (n=2004)**		**HR (95% CI)** (CRRT vs IHD)
Events (%)	Incidence per 100 person-years	Events (%)	Incidence per 100 person-years	
435 (22)	6.5	533 (27)	8.2	0.75 (0.65, 0.87) P<0.0001

Retrospective, multicentre, cohort study of critically ill adults who initiated dialysis for AKI between 1996 and 2009. Patients initially treated with CRRT were propensity matched with those initially treated with IHD, and rates of dialysis dependence from day 90 to the end of the follow-up period were compared. The follow-up period was until death or 31 March, 2011. Dialysis dependence was defined as the receipt of dialysis for at least 90 days.[32]

KEY STUDY TAKEAWAY

Patients treated with IHD had a higher risk of chronic dialysis following an initial AKI episode compared with patients treated with CRRT[32]

Use of CRRT for AKI management has been associated with a lower risk of chronic dialysis compared with IHD[32-35]

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CUMULATIVE COST OF DIALYSIS DEPENDENCE BY INITIAL AKI TREATMENT MODALITY[36]

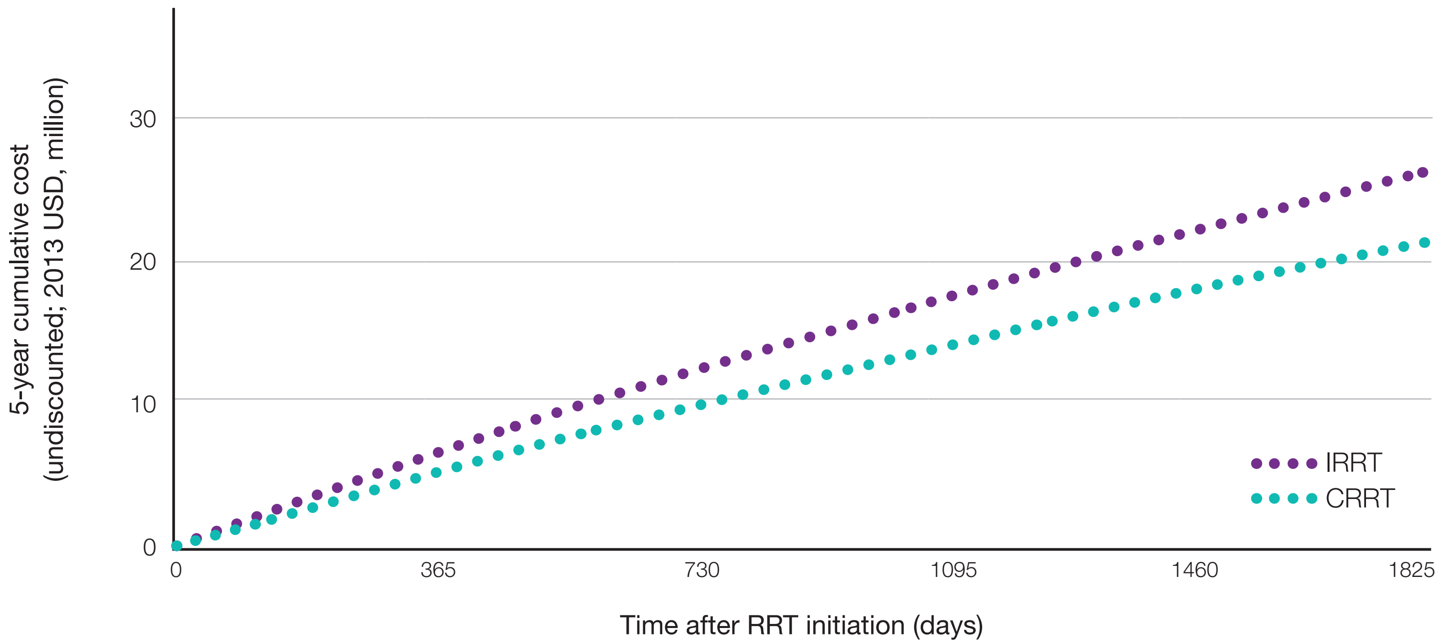


Figure adapted from Ethgen O, et al. *Nephrol Dial Transplant*. 2015;30(1):54-61.

Health outcomes and healthcare costs were modelled and averaged for 1000 patients initiated on CRRT and 1000 patients initiated on IRRT. All costs were inflated to 2013 USD.[36]

KEY STUDY TAKEAWAY

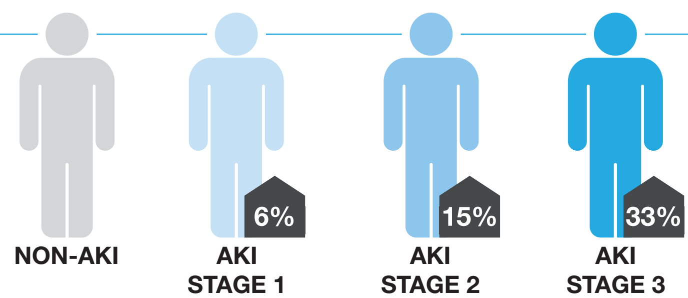
The cost of dialysis dependence was consistently lower with CRRT as the initial modality compared with IRRT[36]

The long-term cost of AKI may be lower for patients initially treated with continuous therapy compared with those treated with intermittent therapies[36]

AKI AND ECONOMIC IMPLICATIONS

AKI MAY BE ASSOCIATED WITH A SUBSTANTIAL FINANCIAL BURDEN[37-39,*]

PATIENTS **WITH AKI** HAD SIGNIFICANTLY **HIGHER DAILY COSTS** COMPARED WITH PATIENTS **WITHOUT AKI**[38,†]



Acute medical condition	Adjusted mean cost difference in 2012 USD (95% CI)[a]
AKI-D[b]	11,016 (10,468, 11,564)
Sepsis	4822 (4696, 5068)
VTE	3782 (3611, 3953)
Acute pancreatitis	1802 (1676, 1929)
AKI[c]	1795 (1692, 1899)
Pneumonia	1705 (1584, 1825)
Stroke	1427 (1281, 1573)
MI	14 (–91, 119)
GI bleed	–860 (–961, –759)

THE INCREMENTAL **COST OF AKI-D OR AKI WAS HIGHER** THAN MANY OTHER CONDITIONS FOUND IN HOSPITALIZED PATIENTS[39,‡]

[a]Compared with reference group without the condition of interest.
[b]Compared with patients without AKI.
[c]AKI group includes patients with AKI-D.

*Costs for hospitalized AKI patients may vary by country.
†Multicentre, retrospective cohort study of 659,945 adult hospital admissions across central China in 2013.[38]
‡A 2012 US multicentre, retrospective study of 29,763,649 adult hospitalizations involving patients without ESRD.[39]

KEY STUDY TAKEAWAY

AKI was expensive relative to other acute medical conditions[39]

While expenditures may vary by country, AKI is a costly condition[37-39]

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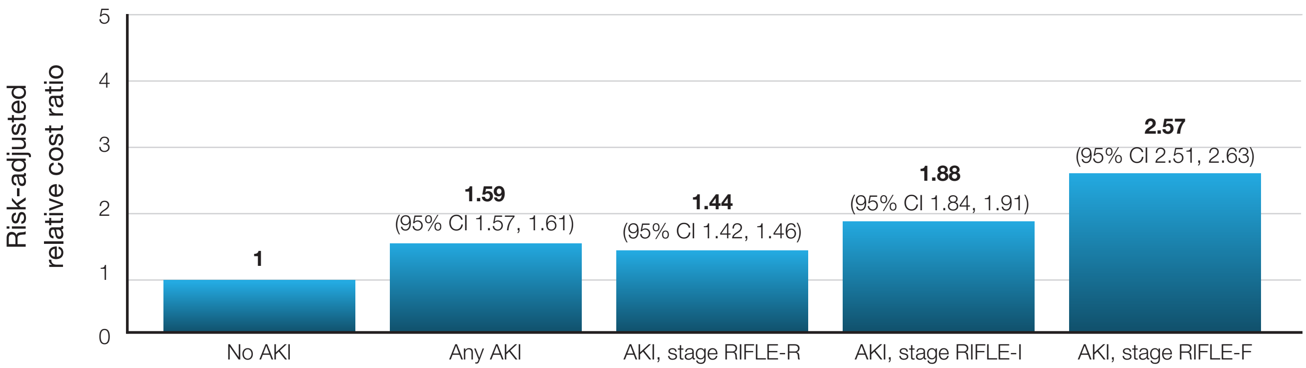
COST ASSOCIATED WITH POSTOPERATIVE AKI[40,*]

RISK-ADJUSTED AVERAGE COST OF POSTOPERATIVE CARE FOR SURGICAL PATIENTS WAS $42,600 FOR AKI VERSUS $26,700 FOR NO AKI, REPRESENTING **159% HIGHER HOSPITAL COSTS FOR AKI VERSUS NO AKI**[40]



P<0.001 for all groups compared with the no AKI group.

*Data are from the USA; costs may vary by location.

In a retrospective US cohort study of 50,314 adult patients undergoing major inpatient surgery with no history of CKD, AKI developed in approximately 39% of patients, with approximately 9% of them receiving RRT.[40]

KEY STUDY TAKEAWAY

AKI added significantly to postoperative hospital costs, even among patients with mild AKI[40]

Postoperative AKI is associated with a substantial financial burden[40]

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To learn more about AKI and CRRT,

please visit: **www.baxter.com/healthcare-professionals/critical-care**

[1]Coca SG, et al. *Am J Kidney Dis.* 2009;53(6):961-973. [2]Ricci Z, et al. *Kidney Int.* 2008;73(5):538-564. [3]Chawla LS, et al. *Clin J Am Soc Nephrol.* 2014;9(3):448-456. [4]Brown JR, et al. *Ann Thorac Surg.* 2016;102(5):1482-1489. [5]Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. *Kidney Int Suppl.* 2012;2(1):1-138. [6]Susantitaphong P, et al. *Clin J Am Soc Nephrol.* 2013;8(9):1482-1493. [7]Hoste EAJ, et al. *Intensive Care Med.* 2015;41(8):1411-1423. [8]Srisawat N, et al. *Am J Nephrol.* 2015;41(1):81-88. [9]Garzotto F, et al. *Crit Care.* 2016; 20(1):196. [10]Bouchard J, et al. *Clin J Am Soc Nephrol.* 2015;10(8):1324-133. [11]Kaddourah A, et al. *N Engl J Med.* 2017;376(1):11-20. [12]Yang L, et al. *Lancet.* 2015;386(10002):1465-1471. [13]Campbell CA, et al. *Intern Med J.* 2019 Feb 28. doi: 10.1111/imj.14264. [Epub ahead of print]. [14]Park S, et al. *Am J Kidney Dis.* 2017;71(1):9-19. [15]West Midlands Acute Medicine Collaborative. *Clin Med* (London). 2019;19(2):109-113. [16]Wald R, et al. *Am J Kidney Dis.* 2015;65(6):870-877. [17]Hsu RK, et al. *J Am Soc Nephrol.* 2012;24(1):37-42. [18]Pavkov ME, et al. *MMWR Morb Mortal Wkly Rep.* 2018;67(10):289-293. [19]Meran S, et al. *Clin Kidney J.* 2014;7(2):144-150. [20]Cheng X, et al. *BMC Nephrol.* 2017;18(1):203. [21]Uchino S, et al. *JAMA.* 2005;294(7):813-818. [22]Cerdá J, et al. *Clin J Am Soc Nephrol.* 2008;3(3):881-886. [23]Ishani A, et al. *J Am Soc Nephrol.* 2009;20(1):223-228. [24]Coca SG, et al. *Kidney Int.* 2012;81(5):442-448. [25]Wald R, et al. *JAMA.* 2009;302(11):1179-1185. [26]Zhang L, et al. *J Crit Care.* 2015;30(4):860.e7-860.e.13. [27]Vaara ST, et al. *Crit Care.* 2012;16(5):R197. [28]Prowle JR, et al. *Nat Rev Nephrol.* 2010;6(2):107-115. [29]Murugan R, et al. *Blood Purif.* 2016;42(3):266-278. [30]Bouchard J, et al. *Kidney Int.* 2009;76(4):422-427. [31]Ostermann M, et al. *Blood Purif.* 2016;42(3):224-237. [32]Wald R, et al. *Crit Care Med.* 2014;42(4):868-877. [33]Bell M, et al. *Intensive Care Med.* 2007;33(5):773-780. [34]Cartin-Ceba R, et al. *Intensive Care Med.* 2009;35(12):2087-2095. [35]Lin YF, et al. *Am J Surg.* 2009;198(3):325-332. [36]Ethgen O, et al. *Nephrol Dial Transplant.* 2015;30(1):54-61. [37]National Clinical Guideline Centre (UK). Acute Kidney Injury: Prevention, Detection and Management Up to the Point of Renal Replacement Therapy. 2013; NICE Clinical Guidelines, No. 169. Introduction. [38]Xu X, et al. *Clin J Am Soc Nephrol.* 2015;10(9):1510-1518. [39]Silver SA, et al. *J Hosp Med.* 2017;12(2):70-76. [40]Hobson C, et al. *Ann Surg*. 2015;261(6):1207-1214.

AKI, acute kidney injury; **AKI-D**, dialysis-requiring AKI; **BUN**, blood urea nitrogen; **CI**, confidence interval; **CKD**, chronic kidney disease; **CRRT**, continuous renal replacement therapy; **ESRD**, end-stage renal disease; **GI**, gastrointestinal; **HR**, hazard ratio; **ICU**, intensive care unit; **IHD**, intermittent haemodialysis; **IRRT**, intermittent renal replacement therapy; **KDIGO**, Kidney Disease Improving Global Outcomes; **MI**, myocardial infarction; **OR**, odds ratio; **RIFLE**, risk, injury, failure, loss of kidney function, and end-stage kidney disease; **RR**, rate ratio; **RRT**, renal replacement therapy; **SCr**, serum creatinine; **VTE**, venous thromboembolism

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