Published in final edited form as:
Curr Opin Nephrol Hypertens. 2007 May ; 16(3): 227–236. doi:10.1097/MNH.0b013e3280dd8c35.

The incidence and prognostic significance of acute kidney injury

Sushrut S. Waikar[a], **Kathleen D. Liu**[b], and **Glenn M. Chertow**[b]

[a] Renal Division, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts

[b] Division of Nephrology, Department of Medicine, University of California San Francisco, San Francisco, California, USA

Abstract

Purpose of review—Acute kidney injury is an increasingly common and potentially catastrophic complication in hospitalized patients. This review summarizes the major epidemiologic studies that have informed our understanding of the incidence and prognostic significance of acute kidney injury.

Recent findings—Early observational studies from the 1980s and 1990s established the general epidemiologic features of acute kidney injury, including the incidence, prognostic significance and predisposing medical and surgical conditions. Recent multicenter observational cohorts and administrative databases have enhanced our understanding of the overall disease burden of acute kidney injury and trends in its epidemiology. An increasing number of clinical studies focusing on specific types of acute kidney injury (e.g. following exposure to intravenous contrast, sepsis and major surgery) have provided further details into this heterogeneous syndrome.

Summary—In light of the increasing incidence and prognostic significance of acute kidney injury, new strategies for prevention and treatment are desperately needed.

Keywords

acute kidney injury; acute renal failure; epidemiology; incidence; outcomes

Introduction

Acute renal failure (ARF), often referred to as 'acute kidney injury' (AKI), is characterized by sudden (i.e. hours to days) impairment of kidney function. AKI is now understood to be an increasingly common and potentially catastrophic complication in hospitalized patients. This review summarizes recent epidemiologic studies of AKI, including early observational studies, recent large cohort studies and administrative/claims database investigations.

Early epidemiologic studies of acute kidney injury

The first prospective cohort studies of AKI were performed in individual centers and provided insights into the frequency, causes and prognostic significance of AKI. Hou *et al.* [1], in 1983, found that 4.9% of hospitalized patients developed AKI [defined as a relative increase in serum creatinine (SCr) of 0.5, 1.0 or 1.5 mg/dl, depending on the baseline SCr]. The major causes of hospital-acquired AKI were decreased renal perfusion (42%), major surgery (18%), contrast nephropathy (12%) and aminoglycoside antibiotics (7%). The crude

Correspondence to Sushrut S. Waikar, MD, MPH, Brigham and Women's Hospital, MRB-4, 75 Francis Street, Boston, MA 02115, USA, Tel: +617 732 8474; fax: +617 732 6392; swaikar@partners.org.

in-hospital mortality rate was 25% and was higher in those with more significant degrees of AKI.

Nash *et al*. [2] updated their initial study of hospital-acquired AKI almost two decades later. They reported that 7.2% of patients developed AKI – higher than the 4.9% in the original study performed at a different institution, although the in-hospital mortality rate (19.4%) was slightly lower. The most common causes of AKI in the follow-up study were decreased renal perfusion (39%; defined broadly to include congestive heart failure, cardiac arrest, and volume contraction), nephrotoxin administration (16%), contrast administration (11%) and major surgery (9%).

Multicenter observational cohort studies of acute kidney injury

Regardless of how carefully conducted, single-center studies are inherently limited in terms of sample size and external validity (i.e. generalizability to AKI at other medical centers). Recognizing this limitation, investigators have launched multicenter epidemiologic investigations of AKI.

The first multicenter observational studies of AKI were published in the mid-1990s by Liano *et al.* [3] and Brivet *et al.* [4]. Results from the two most recent multicenter studies are described below.

The Program to Improve Care in Acute Renal Disease (PICARD) investigators [5] performed a 31-month-long, prospective observational cohort study of patients at five academic medical centers in the United States from 1999 to 2001. Eligible patients were those in the intensive care unit for whom nephrologic consultation was obtained; AKI was defined as an increase in SCr of at least 0.5 mg/dl if baseline was less than or equal to 1.5 mg/dl, or an increase of at least 1.0 mg/dl if baseline SCr was between 1.6 and 4.9 mg/dl.

A total of 618 patients were enrolled in PICARD. One of the most illustrative findings in PICARD was the degree of heterogeneity of patients with AKI across the five medical centers in terms of baseline characteristics, processes of care and in-hospital mortality. In-hospital mortality associated with AKI from ATN and nephrotoxins ranged from a low of 24% to a high of 62%. Substantial differences in process of care were also evident across the five sites (e.g. medication use, dialytic modality, timing of initiation of dialysis). Despite the many differences, however, the presumed causes of AKI were relatively similar among institutions. Fully half of patients were labeled as having ATN with no specified precipitant. The next most common causes included nephrotoxin administration (26%), cardiac disease (20%, including myocardial infarction, cardiogenic shock, and congestive heart failure), ATN from hypotension (20%), ATN from sepsis (19%), unresolved prerenal factors (16%) and liver disease (11%).

The largest and most inclusive cohort study of AKI to date was conducted by the Beginning and Ending Supportive Therapy for the Kidney (BEST Kidney) investigators [6••]. They prospectively studied patients admitted to 54 intensive care units across 23 countries over 15 months, beginning in September 2000. The study population was patients with severe AKI: inclusion criteria were treatment with renal replacement therapy or AKI defined as oliguria of less than 200 ml in 12 h or blood urea nitrogen (BUN) of more than 84 mg/dl. Of 29 269 patients admitted to the intensive care units, 5.7% had AKI. Similar to the PICARD experience, 30% had preexisting chronic kidney disease (CKD) not requiring dialysis. The most common causes of AKI were septic shock (48%), major surgery (34%), cardiogenic shock (27%), hypovolemia (26%) and nephrotoxin administration (19%). (Multiple causes were allowed on the data collection form, accounting for the sum >100%.)

The overall in-hospital mortality rate in the BEST Kidney cohort study was 60%. As with PICARD, mortality varied widely across centers. Among countries contributing more than 100 patients to the cohort, in-hospital mortality ranged from 51 to 77%. A multivariable logistic regression model to identify independent correlates of in-hospital mortality yielded several previously identified risk factors also found in PICARD [7] or the French Study Group [4], including delayed AKI, age, sepsis and a generic disease severity score that included both BUN and urine output.

Administrative database studies

Medical administrative and claims databases afford investigators the opportunity to study AKI in vast numbers of patients over multiple years admitted to a wide spectrum of hospitals, including those not ordinarily represented in prospective cohort studies. The major limitation of most administrative databases is the lack of detailed clinical and laboratory information. Waikar *et al.* [8] performed a validation study of the accuracy of International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes for acute renal failure using linked administrative and laboratory data from nearly 100 000 patient discharges from three Boston-area teaching hospitals. Compared with a 100% change in serum creatinine during hospitalization, they found the ICD-9-CM code for ARF (584.x) to have high specificity (97.7%) and negative predictive value (96.1%), but low sensitivity (35.4%) and moderate positive predictive value (47.9%). The ICD-9-CM codes for ARF requiring dialysis (584.x +39.95) were very accurate (>90% for each measure) compared with detailed review of 150 charts.

Two studies to date have utilized large administrative or claims databases to study trends in the epidemiology of AKI in the United States. Xue *et al.* [9••] used inpatient claims data from a 5% sample of Medicare beneficiaries to investigate the incidence and mortality of acute renal failure between 1992 and 2001. Waikar *et al.* [10••] used the Nationwide Inpatient Sample (NIS) (a nationally representative database of hospital discharges) to study AKI from 1988 to 2002. Using the same ICD-9-CM codes to identify AKI and a similar and partially overlapping study population, the two studies found a marked rise in the incidence and fall in the mortality associated with AKI and AKI requiring dialysis. Among Medicare beneficiaries, the incidence of AKI rose from 14 to 35 per 1000 discharges between 1992 and 2001; in the NIS, which, unlike the Medicare database, includes patients under the age of 65, the incidence of AKI rose from 4 to 21 per 1000 discharges between 1988 and 2002. Both studies showed a statistically significant decline in mortality, in contrast to the prevailing wisdom and a recent systematic review [11], which suggest that mortality rates have remained unchanged over decades. In the NIS study, in-hospital mortality in patients with AKI requiring dialysis (AKI-D) declined from 41% in 1988 to 28% in 2002. Consistently lower mortality over time was seen in every ARF subgroup examined, including sepsis, acute myocardial infarction, pneumonia, coronary artery bypass grafting and cardiac catheterization. The extent to which changes in coding practice for ARF contributed to these trends was not clear.

Liangos *et al.* [12] used the National Hospital Discharge Survey (NHDS) (a nationally representative hospital discharge database different from the NIS database used by Waikar *et al.* [10••]) to study AKI in patients admitted in 2001. Using the same diagnosis codes, they reported that 19 per 1000 discharges had AKI, and that 21% died in hospital – virtually identical to the findings in the NIS. Both NIS and NHDS studies documented that patients with AKI have a median length of stay of 7 days, and that approximately a quarter are discharged to skilled nursing facilities. The NHDS study also showed that the development of AKI added 2 days on average to the length of hospital stay, even after adjusting for numerous covariates. Costs attributable to AKI were not reported in the NIS, NHDS or the

Medicare analyses. Costs were addressed in a study by Fischer *et al.* [13] involving administrative data from 23 Massachusetts hospitals. They reported that uncomplicated ARF (i.e. excluding patients in the intensive care unit) had the third highest median direct hospital costs ($2600) after acute myocardial infarction and stroke.

The study from the NIS estimated the incidence of AKI at 288 per 100 000 US population in 2002; the incidence of AKI-D was estimated to be 27 per 100 000 population. Other investigators have performed population-based epidemiology studies and estimated AKI-D rates of 45 per 100 000 (Manchester, UK) [14], 20 per 100 000 (Scotland) [15] and 8 per 100 000 (Australia) [16].

Epidemiology in disease-specific states

Estimates of the incidence of AKI and associated mortality have been performed in numerous conditions, including sepsis, contrast nephropathy, major surgery and nephrotoxic antibiotic administration. Several of the largest studies are summarized in Table 1 [17–27,28••,29–44]. A striking and consistent finding is the marked increase in mortality associated with the development of AKI. Studies that have identified risk factors for the development of AKI or AKI-D using multivariable regression models are described in Table 2 [7,17,18,21–24,28••,31,38,44–51]. Attempts at deriving risk factors or prediction rules for AKI-associated mortality are described in Table 3 [6••,7,19,51–57].

Small changes in serum creatinine

One of the first studies to examine the independent association between AKI and mortality showed that in patients undergoing radiocontrast procedures, an increase in SCr of at least 25% to at least 2 mg/dl was associated with a 5.5-fold higher odds of death, after adjustment for comorbid medical conditions [58]. Recent studies have explored whether the association between AKI and mortality extends to less severe kidney injury, as assessed by smaller increases in SCr. In a consecutive sample of 19 982 adults admitted to an urban medical center, Chertow *et al.* [59] found that patients with an increase in SCr of just 0.3–0.4 mg/dl had a 70% higher multivariable-adjusted odds of death than patients with little or no change in SCr. Other investigators have reported comparable findings in patients with congestive heart failure [60,61] and those undergoing cardiac surgery [29,30,43,62]. Brown and colleagues [29] studied 1391 undergoing coronary artery bypass grafting (CABG) to investigate the prognostic significance of varying cut-offs for perioperative SCr increases. Compared with patients with less than a 25% change in SCr, those with a 50–99% increase in SCr had a 6.6-fold increased risk of death at 90 days, adjusted for age and sex. They did not find a significant mortality difference in the group with a 25–49% increase in SCr [hazard ratio (HR) 1.80; 95% confidence interval (CI) 0.73–4.44].

In recognition of the potential clinical importance of small changes in kidney function, and the need to standardize definitions of AKI for clinical and research purposes, the Acute Kidney Dialysis Quality Initiative [63] has proposed the RIFLE criteria for the classification of AKI. The RIFLE criteria provide a graded definition of AKI severity, starting at the lowest stage (‘Risk’, defined as oliguria for over 6 h or an increase in SCr of at least 50%). Progressively more severe injury, as defined by an increase in SCr or duration and severity of oliguria, is denoted by ‘Injury’ and ‘Failure’. The final two stages correspond to prolonged need for renal replacement therapy for more than 4 weeks (‘Loss’) or more than 3 months (‘ESRD’).

Whether the RIFLE criteria will be widely adopted in medicine will depend upon the demonstration of its utility and validity. Research has begun on the incidence and prognosis associated with the various stages of RIFLE [64–70]. One large study of 5383 intensive care

unit admissions at a single center used an integrated database with physiologic and laboratory information to show that over two-thirds of all patients had some evidence of AKI during admission, and that over half of the patients with 'Risk' progressed; the hazard ratio for in-hospital mortality according to maximum RIFLE classification was not significant for 'Risk', of borderline statistical significance for 'Injury' (HR 1.4; 95% CI 1.0–1.9) and significant for 'Failure' (HR 2.7; 95% CI 2.0–3.6) [70].

Acute kidney injury in the setting of chronic kidney disease

The fact that an already damaged organ is at heightened risk of acute injury is intuitive. Indeed, elevated baseline SCr has been consistently observed to be a risk factor for the development of AKI in a number of settings, including radiocontrast administration, open heart surgery and sepsis. Patients with CKD constitute a large fraction of patients with AKI in cohort studies. One-third of patients in the PICARD cohort [7] had CKD stage IV or above. Similarly, in the BEST cohort [6••], 30% of patients had CKD (defined as 'any abnormal serum level of creatinine or creatinine clearance prior to hospitalization'), while 15% had unknown baseline renal function. In the cohort study by Nash *et al*. [2], 151 of 332 patients with AKI had SCr values above 1.2 at baseline. Interestingly, patients with CKD have been reported to have lower in-hospital mortality than patients without CKD who develop AKI. This finding has been noted in large databases as well as in studies to identify predictors of mortality following AKI. In the NIS study [10••], 22% of patients with CKD and AKI-D died in hospital, compared with 30% of patients without CKD. In the PICARD cohort [7], the presence of stage IV CKD conferred a 43% (95% CI 16–61%) lower adjusted odds of in-hospital mortality; underlying CKD was not associated with lower odds of death after AKI in the BEST-Kidney cohort [6••]. Used as a continuous variable, higher baseline SCr has also been associated with lower mortality in studies examining outcomes following AKI [7,53]. Reasons that may underlie this seemingly paradoxical finding include confounding by malnutrition (and lower SCr values from low muscle mass), and unrecorded differences in disease severity among persons with and without CKD who develop AKI. In other words, a lesser injury (or fewer associated complications) may result in AKI in the setting of underlying CKD. Conversely, underlying CKD appears to increase the risk of nonrecovery after AKI. In a population-based surveillance study of AKI from Calgary [71], among all patients with AKI who required dialysis 1 year following admission, 63% had preexisting CKD (median preadmission SCr 2.6 mg/dl). Similar findings were observed in PICARD (data not shown).

Summary

AKI is an increasingly common and potentially catastrophic complication in hospitalized patients. Early observational studies from the 1980s and 1990s established the general epidemiologic features of AKI, including the incidence, prognostic significance and predisposing medical and surgical conditions. Recent multicenter observational cohorts and administrative databases have enhanced our understanding of the overall disease burden of AKI and trends in its epidemiology. An increasing number of clinical studies focusing on specific types of AKI (e.g. in the setting of intravenous contrast, sepsis and major surgery) have provided further details into this heterogeneous syndrome.

Despite an increasingly sophisticated understanding of the epidemiology and pathobiology of AKI, current prevention strategies are inadequate and treatment options outside of renal replacement therapy are nonexistent. New strategies for the prevention and treatment of AKI are desperately needed and should be facilitated by ongoing clinical and basic studies of AKI pathogenesis, biomarker discovery/validation and novel therapeutic approaches.

Abbreviations

AKI	acute kidney injury
AKI-D	acute kidney injury requiring dialysis
ARF	acute renal failure
BUN	blood urea nitrogen
CABG	coronary artery bypass grafting
CI	confidence interval
CKD	chronic kidney disease
HR	hazard ratio
ICD-9-CM	International Classification of Diseases, 9th Revision, Clinical Modification
NHDS	National Hospital Discharge Survey
NIS	Nationwide Inpatient Sample
SCr	serum creatinine

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

• of special interest

•• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 293).

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Curr Opin Nephrol Hypertens. Author manuscript; available in PMC 2011 January 26.

Table 1

Incidence and mortality of AKI in selected conditions

Author, year [ref.]	Setting	Definition of AKI	Incidence	In-hospital mortality
Sepsis				
Yegenaga *et al.* 2004 [17]	ICU admissions with sepsis/SIRS (*N* = 217)	SCr increase to >2 mg/dl SCr rise from ≤1.0 to ≥2.0 mg/dl	AKI: 13% AKI-D: 6% AKI: 30% AKI-D: 11%	No AKI: 24% AKI: 72% AKI-D: 69% No AKI: 28% AKI: 57%
Hoste *et al*. 2003 [18]	Surgical ICU admissions with sepsis (*N* = 185)			
Neveu *et al*. 1996 [19]	ICU admissions with ARF and sepsis (*N* = 345)	100% increase in SCr to >3.5 mg/dl or BUN ≥100 mg/dl, or 100% increase in BUN or SCr	(not reported; 46% of all AKI was in the setting of sepsis)	AKI from sepsis: 74% Nonseptic AKI: 45%
Rangel-Frausto *et al*. 1995 [20]	ICU admissions with sepsis/SIRS (*N* = 2527)	Acute SCr increase >2 mg/dl, need for dialysis, or doubling of SCr	AKI: 9% for SIRS, 51% for culture + septic shock	3–46%, depending on severity AKI mortality not reported
Percutaneous coronary intervention (PCI)				
Marenzi *et al*. 2004 [21]	ST-elevation AMI treated with primary PCI (*N* = 208)	Increase in SCr >0.5 mg/dl	AKI: 19% AKI-D: 3%	AKI: 31% No AKI: 0.6%
Mehran *et al*. 2004 [22]	PCI (*N* = 8357)	Increase in SCr ≥25% or ≥0.5 mg/dl	AKI: 13%	Not reported
Rihal *et al*. 2002 [23]	PCI (*N* = 7586)	Increase in SCr ≥0.5 mg/dl	AKI: 3.3% AKI-D: 0.3%	AKI: 22% No AKI: 1%
McCullough *et al.* 1997 [24]	PCI (*N* = 1826)	Increase in SCr >25%	AKI: 14% AKI-D: 0.8%	No AKI: 1% AKI: 7% AKI-D: 36%
IV contrast for radiologic examination				
Mitchell *et al.* 2007 [25]	CT angiography to rule out pulmonary embolism in the emergency dept (*N* = 1224)	Increase in SCr >25% or 0.5 mg/dl within 7 days	AKI: 4% of entire cohort, 12% of those with two SCr measurements AKI-D: 0%	Not reported
Parfrey *et al.* 1989 [26]	i.v. contrast for cardiac arteriography or CT examination (*N* = 220)	Increase in SCr >25%	AKI in +DM −CKD: 2.4% +DM+CKD: 8.8% −DM +CKD: 6.4%	Not reported
Cramer *et al.* 1985 [27]	CT of the brain with (*N* = 193) and without (*N* = 233) i.v. contrast	Increase in SCr ≥50% to at least 1.2 mg/dl	AKI in i.v. contrast: 2.1% AKI no i.v. contrast: 1.3%	Not reported
Cardiac surgery				
Mehta *et al.* 2006 [28••]	Cardiac surgery (*N* = 449 524)	Need for dialysis	AKI: not reported AKI-D: 1.4%	No AKI-D: 2.3% AKI-D: 43.6%
Brown *et al*. 2006 [29]	Patients undergoing CABG (without valve replacement) (*N* = 1391)	Increase in SCr <25%, 25–49%, 50–99%, ≥100%	25–49%: 16% 50–99%: 7% ≥100%: 5%	(90-day mortality adjusted HR, ref. = <25% increase in SCr) 25–49%: 1.8 50–99%: 12.2 ≥100%: 5%: 30.8
Loef *et al.* 2005 [30]	CABG or valvular surgery (*N* = 843)	Increase in SCr ≥25% within 7 days of surgery	AKI: 17.2% AKI-D: 0.7%	No AKI: 1.1% AKI: 14.5% AKI-D: 83.3%

Author, year [ref.]	Setting	Definition of AKI	Incidence	In-hospital mortality
Thakar *et al*. 2005 [31]	Open-heart surgery (*N* = 18 838)	Need for dialysis	AKI: not reported AKI-D: 1.7%	Not reported
Bove *et al*. 2004 [32]	Cardiopulmonary bypass/CABG (including valve replacement) (*N* = 5068)	Increase in SCr ≥100%	AKI: 3.4% AKI-D: 1.9%	No AKI: 2.7% AKI: 46.2% AKI-D: 63.8%
Ryckwaert *et al*. 2002 [33]	CABG or valvular surgery (*N* = 591)	Increase in SCr ≥20% within 3 days of surgery	AKI: 15.6% AKI-D: 1.4%	No AKI: 1.0% AKI: 12.0% AKI-D: 37.5%
Chertow *et al.* 1997 [34]	CABG or valvular surgery (*N* = 43 642)	Need for dialysis	AKI: not reported AKI-D: 1.1%	(30-day mortality) No AKI: 4.3% AKI: not reported AKI-D: 63.8%
Mangano *et al*. 1998 [35]	CABG or valvular surgery (*N* = 2222)	Increase in SCr of ≥0.7 mg/dl to at least 2.0 mg/dl	AKI: 7.7% AKI-D: 1.4%	No AKI: 0.9% AKI: 19% AKI-D: 63.8%
Nephrotoxic antibiotics				
Fowler *et al*. 2006 [36]	Daptomycin (*N* = 124) or gentamicin +PCN/vanco (*N* = 126)	Decrease in CrCl to <50 ml/min, or decrease in CrCl of 10 ml/min if below 50 at baseline	AKI, daptomycin: 11% AKI, gentamicin: 26.3%	Not reported
Bates *et al*. 2001 [37,38]	Amphotericin B (*N* = 707) (64 received liposomal preparation)	Increase in SCr of ≥50% to at least 2.0 mg/dl (severe: peak SCr at least 3.0 mg/dl)	AKI: 30% Severe AKI: 13%	No AKI: 14% AKI: 54%
Wingard *et al.* 1999 [39]	Amphotericin B for aspergillosis (*N* = 239)	Increase in SCr of ≥100%	AKI: 53% AKI-D: 14.5%	No AKI-D: 57% AKI-D: 76%
Leehey *et al.* 1993 [40]	Aminoglycosides (*N* = 243)	Increase in SCr of 0.5 mg/dl and 100% over baseline	AKI: 20.6% AKI-D: 1.2%	Not reported
Smith *et al.* 1980 [41]	Gentamicin and tobramycin (*N* = 146)		AKI: 19.2%	Not reported
Aortic aneurysm repair				
Prinssen *et al.* 2004 [42]	Open (*N* = 174) or endovascular (*N* = 171) AAA repair	Increase in SCr ≥20%	AKI: 13% (both groups)	Not reported
Ryckwaert *et al*. 2003 [43]	Infra-renal aortic abdominal surgery (*N* = 215)	Increase in SCr ≥20%	AKI: 20% AKI-D: 2.8%	No AKI: 1.2% AKI: 9.3% AKI-D: 50%
Godet *et al.* 1997 [44]	Thoracic or thoracoabdominal aortic surgery (*N* = 475)	Increase in SCr to >1.7 mg/dl or 30% over baseline	AKI: 25% AKI-D: 8%	AKI: 38% AKI-D: 56%

Abbreviations: AAA, abdominal aortic aneurysm; AKI, acute kidney injury; AKI-D, acute kidney injury requiring dialysis; AMI, acute myocardial infarction; BUN, blood urea nitrogen; CABG, coronary artery bypass grafting; CKD, chronic kidney disease; CT, computed tomography; DM, diabetes mellitus; HR, hazard ratio; ICU, intensive care unit; i.v., intravenous; PCI, percutaneous coronary intervention; PCN, penicillin; SCr, serum creatinine; SIRS, systemic inflammatory response syndrome.

Curr Opin Nephrol Hypertens. Author manuscript; available in PMC 2011 January 26.

Table 2

Predictors of the development of acute kidney injury

Author, year [ref.]	Clinical setting	*N* (% with AKI outcome)	AKI definition	Identified risk factors in multivariable models
Davidson *et al*. 1989 [45]	Diagnostic cardiac catheterization	1162 (6%)	Increase in SCr ≥0.5 mg/dl	Older age and baseline SCr ≥1.2
Rich and Crecelius 1990 [46]	Cardiac catheterization, age ≥70, including percutaneous coronary intervention	183 (11%)	Increase in SCr ≥0.5 mg/dl	Contrast volume >200 ml, serum albumin <3.5 mg/dl, diabetes, serum sodium <135 mmol/l, SCr >1.5, NYHA class III or IV
Lautin *et al*. 1991 [47]	Femoral arteriography	394 (22%)	Increase in SCr >0.3 mg/dl and 20% over baseline	Diabetes, baseline SCr >1.5 mg/dl
McCullough *et al.* 1997 [24]	Percutaneous coronary intervention	1826 (0.77%)	Need for dialysis	Lower baseline CrCl, diabetes, contrast volume
Gruberg *et al*. 2001 [48]	Percutaneous coronary intervention	7690 (0.66%)	Need for dialysis	Non-Q-wave MI, saphenous vein graft intervention, peak postprocedural SCr, IABP, contrast volume, lower baseline CrCl
Rihal *et al*. 2002 [23]	Percutaneous coronary intervention	7586 (3.3%)	Increase in SCr ≥0.5 mg/dl	Older age, higher baseline SCr, CHF, DM, shock, MI, PVD, contrast volume
Mehran *et al*. 2004 [22]	Percutaneous coronary intervention	8357 (13.1%)	Increase in SCr ≥25% or ≥0.5 mg/dl	Hypotension, IABP, CHF, CKD, DM, age >75, anemia, contrast volume
Marenzi *et al*. 2004 [21]	Percutaneous coronary intervention for acute MI	208 (19%)	Increase in SCr >0.5 mg/dl	Age ≥75, anterior acute MI, time-to-reperfusion ≥6 h, contrast volume, IABP
Chertow *et al.* 1998 [49]	Coronary artery bypass grafting	42 773 (1.1%)	Need for dialysis	Valve surgery, lower preoperative CrCl, IABP, prior heart surgery, NYHA class IV, PVD, LVEF <35%, pulmonary rales, COPD, SBP ≥160 (CABG only)
Thakar *et al*. 2005 [31]	Coronary artery bypass grafting	33 217 (1.7%)	Need for dialysis	Female sex, CHF, IABP, COPD, insulin-requiring diabetes, previous cardiac surgery, emergency/valve surgery, higher preoperative SCr
Mehta *et al.* 2006 [28••]	Coronary artery bypass grafting	449 524 (1.4%)	Need for dialysis	Higher preoperative SCr, older age, type of surgery (+/− valve), diabetes, recent MI, nonwhite race, chronic lung disease, prior CABG, NYHA class IV, cardiogenic shock
Hoste *et al*. 2003 [18]	Sepsis	185 (16%)	Increase in SCr to at least 2 mg/dl	pH <7.3 and SCr >1.0 mg/dl on day of sepsis diagnosis
Yegenaga *et al.* 2004 [17]	Sepsis	257 (11%)	Increase in SCr to at least 2.0 mg/dl or urine output <400 ml/24 h	Older age, higher SCr, higher CVP, serum bilirubin >1.5 mg/dl
Chawla *et al.* 2005 [50]	Sepsis	194 (18%)	>75% increase in SCr (baseline ≤2.0 mg/dl) or >50% increase (baseline >2.0 mg/dl)	Low serum albumin, high A–a gradient, active cancer
Chertow *et al.* 1998 [51]	Established AKI (placebo arm of RCT)	256 (57%)	Need for dialysis or death	Oliguria, low serum albumin, acute MI, mechanical ventilation, arrhythmias
Chertow *et al.* 2006 [7]	Established AKI	618 (64%)	Need for dialysis	Younger age, oliguria, higher BUN, liver failure
Godet *et al.* 1997 [44]	Thoracoabdominal aortic surgery	475 (25%)	Increase in SCr to at least 1.7 mg/dl or ≥30% increase if preexisting CKD	Age >50, preoperative SCr >1.3, ischemia duration >30 min, use of Cell-saver, >5 units pRBC transfusion

Author, year [ref.]	Clinical setting	*N* (% with AKI outcome)	AKI definition	Identified risk factors in multivariable models
Bates *et al*. 2001 [38]	Amphotericin B	643 (27%)	Increase in SCr ≥50% to at least 2.0 mg/dl	ICU stay at initiation of therapy, use of cyclosporine, maximum daily dose of amphotericin B

Abbreviations: AKI, acute kidney injury; A–a, alveolar-arterial; BUN, blood urea nitrogen; CABG, coronary artery bypass grafting; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CrCl, creatinine clearance; IABP, intraaortic balloon pump; ICU, intensive care unit; MI, myocardial infarction; NYHA, New York Heart Association; PICARD, Program to Improve Care in Acute Renal Disease; RCT, randomized controlled trial; pRBC, packed red blood cells; PVD, peripheral vascular disease; SCr, serum creatinine.

Curr Opin Nephrol Hypertens. Author manuscript; available in PMC 2011 January 26.

Table 3

Predictors of mortality after acute kidney injury

Author, year [ref.]	Clinical setting	*N* (% mortality)	AKI definition	Identified risk factors for mortality in multivariable models
Liano *et al*. 1993 [52]	Hospital	328 (53%)	Increase in SCr to at least 2.0 mg/dl (baseline <1.5 mg/dl)	Coma, mechanical ventilation, hypotension, oliguria, jaundice, nephrotoxic etiology (protective), normal consciousness (protective)
Chertow *et al*. 1995 [53]	Intensive care unit	132 (70%)	Need for dialysis	Mechanical ventilation, malignancy, nonrespiratory organ system failure
Neveu *et al*. 1996 [19]	Intensive care unit	345 (59%)	Increase in SCr to at least 3.5 mg/dl or BUN to at least 100 mg/dl, or >100% increase in SCr	Sepsis as cause of AKI, occurrence of AKI during intensive care unit stay, oliguria, mechanical ventilation, generic severity of illness score, preadmission health status
Paganini *et al*. 1996 [54]	Intensive care unit	512 (67%)	Need for dialysis	Male sex, mechanical ventilation, hematologic dysfunction, bilirubin >2.0 mg/dl, absence of surgery, higher SCr on first dialysis treatment, increasing number of failed organ systems, increased BUN from time of admission
Chertow *et al*. 1998 [51]	Placebo arm of randomized, controlled trial	256 (36%)	Increase in SCr of ≥1.0 mg/dl	Male sex, mechanical ventilation, oliguria, acute myocardial infarction, stroke/seizure, hypertension (protective), low serum bicarbonate
Metnitz *et al*. 2002 [55]	Intensive care unit	839 (63%)	Need for dialysis	Mechanical ventilation, cardiopulmonary resuscitation, treatment of complicated metabolic acidosis/alkalosis, enteral nutrition (protective)
Mehta *et al*. 2002 [56]	Intensive care unit	605 (52%)	BUN ≥40 mg/dl or SCr ≥2.0 mg/dl; increase in SCr ≥1.0 mg/dl if preexisting CKD	Older age, male sex, nonrenal organ failure (respiratory, liver, and hematologic), lower SCr, higher BUN, oliguria, higher heart rate
Lins *et al*. 2004 [57]	Intensive care unit	293 (51%)	Increase in SCr to at least 2.0 mg/dl, or ≥50% increase in SCr if preexisting CKD	Older age, lower serum albumin, higher INR value, mechanical ventilation, CHF, higher serum bilirubin, sepsis, hypotension
Uchino *et al*. 2005 [6••]	Intensive care unit	1738 (60%)	BUN >84 mg/dl or oliguria <200 ml in 12 h	Older age, delay between admission and inclusion into study, mechanical ventilation, generic severity of illness score, vasopressor use, metabolic diagnosis (protective), hematologic diagnosis, septic shock, cardiogenic shock, hepatorenal syndrome
Chertow *et al*. 2006 [7]	Intensive care unit	618 (37%)	Increase in SCr ≥0.5 or 1.0 mg/dl if baseline CKD	At diagnosis: older age, CKD stage IV (protective), high BUN, liver failure, sepsis

Abbreviations: AKI, acute kidney injury; BUN, blood urea nitrogen; CHF, congestive heart failure; CKD, chronic kidney disease; NYHA, New York Heart Association; SCr, serum creatinine.