

Risk of recurrent acute kidney injury

Suppl. Appendix 1

Search strategies

Medline search strategy

1 exp Acute Kidney Injury/

2 ((acute) adj3 (renal or kidney) adj3 (insufficienc* or injur* or failur*)).mp.

3 (acute adj3 dialys*).mp

4 (acute adj3 renal replac*).mp

5 Aki.ti,ab

6 Arf.ti,ab

7 Recurrence/

8 (recurr* or repeat or re-occur* or re occur*).mp.

9 1 or 2 or 3 or 4 or 5 or 6 (68898)

10 7 or 8 (803145)

11 9 and 10 (1768)

12 prognos*.mp

13 predict*.mp

14 course*.mp

15 outcome*.mp

16 recover*.mp

17 (follow-up or follow up or follow*up).mp

18 ((regression or predict* or multivariable) adj (analys* or model*)).mp.

19 exp Cohort Studies/

20 ((longitudinal or retrospective or prospective or cross sectional or cohort or randomi*ed) adj (study or studies or review or analys* or cohort*)).mp.

21 ((validat* or rule* or scor* or risk or decision or clinical) adj5 (model*)).mp.

22 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 (6269282)

23 11 and 22 (1036)

24 (exp animal/ or nonhuman/) not exp human/

25 23 not 24 (1025)

26 limit 25 to (english language and “all adult (19 plus years)”) (558)

Risk of recurrent acute kidney injury

EMBASE search strategy

1 exp acute kidney failure/

2 (acute) adj3 (renal or kidney) adj3 (insufficienc* or injur* or failur*).mp.

3 (acute adj3 dialys*).mp

4 (acute adj3 renal replac*).mp

5 Aki.ti,ab

6 Arf.ti,ab

7 recurrent disease/

8 recurrent disease.mp.

9 (recurr* or repeat or re-occur* or re occur*).mp.

10 1 or 2 or 3 or 4 or 5 or 6

11 7 or 8 or 9

12 10 and 11

13 prognos*.mp

14 predict*.mp

15 course*.mp

16 outcome*.mp

17 recover*.mp

18 (follow-up or follow up or follow*up).mp

19 ((regression or predict* or multivariable) adj (analys* or model*)).mp.

20 ((longitudinal or retrospective or prospective or cross sectional or cohort or randomi*ed) adj (study or studies or review or analys* or cohort*)).mp.

21 ((validat* or rule* or scor* or risk or decision or clinical) adj5 (model*)).mp.

22 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21

23 12 and 22

24 (exp animal/ or nonhuman/) not exp human/

25 23 not 24

26 limit 25 to (english language and adult <18 to 64 years>)

CINAHL (EBSCO host) search strategy

S1 ((acute) N3 (renal or kidney) N3 (insufficienc* or injur* or failur*))

S2 (recurr* or repeat or re-occur* or re occur*)

Risk of recurrent acute kidney injury

S3 ((MM "Models, Statistical") or TI ((predict* or validat* or rule* or scor*) or ((predict* or multicomponent or multivariable) N3 model*) or (predict* N3 (outcome* or risk* or model*)) or ((history or variable* or criteria or scor* or characteristic* or finding* or factor* or value*) N3 (predict* or model* or decision* or identif* or prognos*)) or (decision* N3 (model* or clinical* or logistic model*)) or (prognostic N3 (history or variable* or criteria or scor* or characteristic* or finding* or factor* or model*)) or (observ* N3 (variation or model*))) or AB ((predict* or validat* or rule* or scor*) or ((predict* or multicomponent or multivariable) N3 model*) or (predict* N3 (outcome* or risk* or model*)) or ((history or variable* or criteria or scor* or characteristic* or finding* or factor* or value*) N3 (predict* or model* or decision* or identif* or prognos*)) or (decision* N3 (model* or clinical* or logistic model*)) or (prognostic N3 (history or variable* or criteria or scor* or characteristic* or finding* or factor* or model*)) or (observ* N3 (variation or model*))))

S4 S1 AND S2 AND S3

Cochrane library search strategy

#1 (acute) near (renal or kidney) near (insufficienc* or injur* or failur*)

#2 (recurr* or repeat or re-occur* or re occur*)

#3 MeSH descriptor: [Models, Statistical] explode all trees

#4 (((predict* or multicomponent or multivariable) near model*) or (predict* near (outcome* or risk* or model*)) or ((history or variable* or criteria or scor* or characteristic* or finding* or factor* or value*) near (predict* or model* or decision* or identif* or prognos*)) or (decision* near (model* or clinical* or logistic model*)) or (prognostic near (history or variable* or criteria or scor* or characteristic* or finding* or factor* or model*)) or (observ* near (variation or model*)))

#5 #3 or #4

#6 #1 and #2 and #5

Web of Science

#1 TS= (acute kidney injur* OR acute renal injur* OR acute kidney failure* OR acute renal failure* OR acute kidney insufficienc*)

#2 TS= (recurr* or repeat or re-occur* or re occur*)

#3 TS= (predict* or prognos* or course or outcome* or multicomponent or multivariable or risk or factor*)

#4 #1 and #2 and #3

Suppl. Table S1a. Characteristics of included studies on AKI recurrence within the same hospital admission

Publication Year	Author	Country	Aims	Study design	Population	N with initial AKI	N with r-AKI	AKI definition	Recurrence definition
2014	Harris et al.	USA	To assess AKI recurrence after recovery from initial AKI in critically ill patients + risk factors of AKI recurrence	Retrospective cohort study	Critically ill patients (admitted to non-cardiac, non-trauma surgical ICU)	296	68	RIFLE creatinine criteria	Any subsequent renal event (following AKI recovery) during the index admission. Recurrent AKI defined as a ≥ 1.5 fold increase in creatinine following recovery from previous AKI episode
2015	Warnock et al.	USA	To categorize hospital acquired-AKI based on the timing of minimum and peak inpatient serum creatinine and describe the association with inpatient mortality	Retrospective analysis of an administrative data	Adults admitted to a medical centre over 4 years	18,348	2,243	Acute Kidney Injury Network (AKIN) serum criteria (an increase of ± 0.3 mg/dL between peak and minimum serum creatinine)	Transient hospital-acquired AKI patients who recovered and then developed hospital-acquired AKI during an admission. AKI was defined as an increase of 0.3mg/dL from baseline creatinine

Risk of recurrent acute kidney injury

2016	Kellum et al	USA	To assess different patterns of AKI reversal in critically ill patients + how they relate to recovery and post discharge outcomes	Retrospective cohort study	Patients admitted to ICU	16,968	6,322	KDIGO (Kidney Disease Improving Global Outcomes) criteria serum creatinine and urine output criteria.	Relapse occurring during hospital admission that may not resolve before hospital discharge. Recurrent AKI defined as an increase of ≥ 1.5 fold creatinine following recovery or presence of oliguria (urine output < 5 ml/kg/hr)
2017	Rodrigo et al	Spain	To explore rate and consequences of AKI recurrence in patients admitted to ICU with severe sepsis. To compare outcomes of recurrent AKI with no AKI, 1 AKI	Prospective cohort study	Patients admitted to ICU with severe sepsis	331	79	KDIGO serum creatinine criteria	≥ 2 AKI episodes during ICU stay. Recurrent AKI defined as a new spontaneous rise of ≥ 0.3 mg/dl within 48 hours from the lowest serum creatinine after the previous AKI episode

Suppl. Table S1b. Characteristics of included studies on post-discharge AKI recurrence

Publication Year	Author	Country	Aims	Study design	Population	N with initial AKI	N with r-AKI	Duration of follow up	AKI definition	Recurrence definition
2011	Thakar et al	USA	To examine the effects of AKI episodes during multiple hospitalizations on the risk of chronic kidney disease (CKD) in a cohort with diabetes mellitus (DM).	Retrospective cohort study	Patients with diabetes mellitus	530	157	10 years (median: 62.3 months)	AKIN creatinine criteria: a 0.3 mg/dl or a 1.5-fold increase in creatinine relative to admission	Additional AKI episodes following index AKI in hospital. AKI was defined as ≥ 1.5 fold increase in creatinine relative to the admission creatinine for the hospitalisation
2014	Xie	Canada	To assess factors associated with outpatient nephrology follow-up after the development of AKI on patients who had a nephrology in-hospital consultation	Retrospective cohort study	Patients who had a nephrology in-hospital consultation and were discharged	170	70	4 years (median: 19 months)	KDIGO serum creatinine criteria: an increase in serum creatinine >0.3 mg/dl within 2 days or 50% within 7 days	Recurrent AKI post discharge in AKI patients with nephrology inpatient consultation. AKI was defined as ≥ 2 fold increase in serum creatinine within 48 hours

Risk of recurrent acute kidney injury

2016	Siew et al	USA	To explore risk factors for recurrent AKI present during index hospitalisations and how this relates to hospitalisation with recurrent AKI within 12 months of discharge from index hospitalisation	Retrospective cohort study	Patients hospitalised for at least 24 hours, where hospitalisation was complicated by AKI	11,683	2,954	1 year	a 0.3 mg/dl or 50% increase from a baseline creatinine measure	Hospitalization with recurrent AKI within 12 months of discharge from the index hospitalization. Recurrent AKI was defined as defined as a 0.3 mg/dl or 50% increase in serum creatinine from the lowest of either the most recent serum creatinine beginning at discharge from the index AKI hospitalization or the admission creatinine of the recurrent AKI hospitalization
2017	Valle et al	USA	To assess incidence of percutaneous coronary intervention associated AKI (PCI-AKI) + outcomes post PCI-AKI	Retrospective cohort study	Patients undergoing PCI	39,850	5,365	1 year	AKIN serum creatinine criteria	Recurrent renal injury after hospital discharge in patients with post-PCI AKI (defined as >0.4 mg/dL or ≥ 1.5 fold increase in serum creatinine from creatinine after previous AKI episode)

Risk of recurrent acute kidney injury

2017	Horne et al.	UK	To characterise the effect of acute kidney injury (AKI) on long-term changes in renal function in a general hospital population	Prospective matched parallel group cohort study	Hospitalised patients (with or without AKI)	194	64	3 years	AKIN serum creatinine and urine output criteria	Not clear, though follow up was 3 years (suggesting AKI after discharge). AKI defined based on AKIN criteria
2018	Rodriguez et al	Spain	To determine the impact of repeated AKI episodes in renal outcomes during 4 years follow-up	Retrospective cohort study	Patients with an AKI diagnosis in hospital who recovered fully prior to discharge	359	122	4 years (median)	Acute Dialysis Quality Initiative criteria: increase in SCr by ≥ 0.3 mg/dl (≥ 26.5 mmol/L) within 48 hours; or increase in SCr to ≥ 1.5 times baseline serum creatinine	Recurrent AKI after discharge from initial AKI hospital admission. AKI was defined as an increase in serum creatinine of 0.3mg/dl within 48 hours or up to 1.5 times baseline creatinine

Suppl. Table S2. Quality assessment of studies by domain using Newcastle-Ottawa scale.

	Representativeness of exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of Outcome	Was follow up long enough for outcomes to occur	Adequacy of follow up of cohorts
Thakar et al., 2011								
Harris et al., 2014								
Xie et al., 2014								
Warnock 2015								
Siew et al., 2016								
Kellum et al., 2017								
Rodrigo et al., 2017								
Valle et al., 2017								
Horne et al., 2017								
Rodriguez et al. 2018								

Green icon = low risk of bias. Yellow icon = unclear risk, red icon = high risk of bias.

Suppl. Table S3a. Risk factors associated with AKI recurrence within the same hospital admission. Only factors evaluated in at least 2 studies are shown here.

Publication Year	Author	Study quality	Population	Number of AKI patients with recurrent AKI	Multivariable model	Risk factors for recurrent AKI within same hospital admission						
						Age	Lower baseline eGFR	Higher serum creatinine in first AKI episode	Diabetes	Heart disease	Acute Physiology and chronic health evaluation score	AKI severity
2014	Harris et al.	Poor	ICU	68/296	No	n.s.		n.s.	n.s.		n.s.	n.s.
2015	Warnock et al	Good	Hospital	2243/12101	yes	not reported						
2016	Kellum et al	Good	ICU	3826/16968	yes	+			+	+	+	
2017	Rodrigo et al	Good	ICU	79/331	yes	+	+				+	+

Abbreviations: ICU: Intensive Care Unit, n.s = not significant, + = positively associated with increased risk of AKI recurrence.

Risk of recurrent acute kidney injury

Suppl. Table S3b. Risk factors associated with AKI recurrence post discharge from hospital. Only factors evaluated in at least 2 studies are shown here.

Publication Year	Author	Study quality	Population	Number of AKI patients with recurrent AKI	Risk factors for recurrent AKI post-discharge							
					Multivariable model	Age	Lower baseline eGFR	Higher serum creatinine in first AKI episode	Diabetes	Heart disease	Acute Physiology and chronic health evaluation	AKI severity
2014	Xie et al	Fair	Hospital	70/170	yes				-			
2016	Siew et al	Good	Hospital	2954/11683	yes		+		+	+		+
2017	Valle et al	Good	PCI	5365/39850	yes							+
2018	Rodriguez et al	Fair	Hospital	122/359	yes			+	+	+		

Abbreviations: PCI: percutaneous coronary intervention, n.s = not significant, + = positively associated with increased risk of AKI recurrence, - = negatively associated with increased risk of AKI recurrence.

Suppl. Table S4. Risk factors associated with AKI recurrence (a) within the same hospital admission and (b) post discharge from hospital*(a)*

	Harris et al., 2014	Kellum et al., 2016	Rodrigo et al., 2017	Warnock et al., 2015
Study quality	Poor	Good	Good	Good
Number of AKI patients with recurrent AKI	68/296	3826/16968	79/331	2243/12101
Population	ICU	ICU	ICU	Hospital
<i>Risk factor</i>				
Age	n.s	+	+	not reported
Sex	n.s			
Duration of dialysis/ RRT	n.s			
Ethnicity		+		
Lower baseline eGFR			+	
Higher serum creatinine in first AKI episode	n.s			
Lower mean albumin				
Acute rejection episode				
Living related donor				
Deceased donor				
Diabetes	n.s	+		
Cardiac disease		+		
Ischaemic heart disease				
Acute coronary syndrome				
Congestive heart failure				
Coronary artery disease				
Chronic kidney disease	n.s			
Hypertension	n.s			
Advanced liver disease				
Malignancy				
HIV				
Dementia				
Acute Physiology and chronic health evaluation score	n.s	+	+	
Suspected sepsis		+		
Mechanical ventilation		+		
Volume depletion				
Inpatient abdominal surgery				
AKI on admission	+			
AKI severity	n.s		+	
Post PCI AKI				
Lack of nephrology care				

Abbreviations: ICU: Intensive Care Unit, n.s = not significant, + = positively associated with increased risk of AKI recurrence. Shaded rectangles indicate covariates included in multivariable models

Risk of recurrent acute kidney injury

(b)

	Siew et al., 2016	Valle et al., 2017	Xie et al., 2014	Rodriguez et al, 2018
Study quality	Good	Good	Fair	Fair
Number of AKI patients with recurrent AKI	2954/11683	5365/39850	70/170	122/359
Population	Hospital	PCI	Hospital	Hospital
<i>Risk factor</i>				
Age				
Sex				
Duration of dialysis/ RRT				
Ethnicity				
Lower baseline eGFR	+			
Higher serum creatinine in first AKI episode				+
Lower mean albumin	+			
Acute rejection episode				
Living related donor				
Deceased donor				
Diabetes	+		-	+
Cardiac disease				
Ischaemic heart disease				+
Acute coronary syndrome	+			
Congestive heart failure	+			
Coronary artery disease	+			
Chronic kidney disease				
Hypertension				
Advanced liver disease	+			
Malignancy	+			
HIV	+			
Dementia	+			
Acute Physiology and chronic health evaluation score				
Suspected sepsis				
Mechanical ventilation				
Volume depletion	+			
Inpatient abdominal surgery	-			
AKI on admission				
AKI severity	+	+		
Post PCI AKI		+		
Lack of nephrology follow up care			+	

Abbreviations: PCI: percutaneous coronary intervention, + = positively associated with increased risk of AKI recurrence, - = negatively associated with increased risk of AKI recurrence. Shaded rectangles indicate covariates included in multivariable models.

Horne & Thakar omitted as these papers did not assess risk factors for recurrence.