KDIGO CLINICAL PRACTICE GUIDELINE FOR ACUTE KIDNEY INJURY

Online Supplementary Tables
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Abbreviations and Acronyms for Supplemental Tables

Δ	Change
↓	Decrease
↑	Increase
AAA	Abdominal aortic aneurysm
ACRF	Acute-on-chronic renal failure
AKI	Acute kidney injury
ANP	Atrial natriuretic peptide
ARF	Acute renal failure
CABG	Coronary artery bypass graft
CAD	Coronary artery disease
CI	Confidence interval
CI-AKI	Contrast-induced acute kidney injury
CKD	Chronic kidney disease
CM	Contrast medium
CrCl	Creatinine clearance
CRRT	Continuous renal replacement therapy
CT	Computerized tomography
CTS	Cardiothoracic surgery
CV	Cardiovascular
CVVH	Continuous venovenous hemofiltration
CVVHDF	Continuous venovenous hemodiafiltration
D/5	5% glucose
ERT	Evidence Review Team
eQB	Effective blood flow
GFR	Glomerular filtration rate
HCO_3	Bicarbonate
HD	Hemodialysis
HF	Hemofiltration
HVPD	High volume peritoneal dialysis
i.a.	Intrarterial
ICU	Intensive care unit
IHD	Intermittent hemodialysis
IQR	Intraquartile range
ITT	Intention-to-treat
i.v.	Intravenous
LMWH	Low molecular weight heparin
NA	Not applicable
NAC	N-acetylcysteine
nd	Not documented
NS	Not significant
OR	Odds ratio
PCI	Percutaneous coronary intervention
PTCA	Percutaneous transluminal coronary angioplasty
pts	Patients
RBC	Red blood cell
RCT	Randomized controlled trial
RIFLE	Risk, Injury, Failure, Loss, End stage renal disease
RR	Relative risk
RRT	Renal replacement therapy
RVP	Return venous pressure
S_{Cr}	Serum creatinine
UF	Ultrafiltration

Supplementary table 1: Summary table of RCTs examining the effect of starch for the prevention of AKI

Outcome	Author Year Country	Age	Baseline kidney function	Setting	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1	Arm 2					
Sepsis Patients														
Mortality														
28 d	Brunkhorst [17] 2008 Germany	65	S_{Cr} 126.4 µmol/l	ICU	28 d	262	274	10% Hydroxyethyl starch	Ringer's lactate	Per protocol	27% (24%)	1.13 (0.84-1.50)	NS (0.48)	Fair
90 d											41% (34%)	1.21 (0.97-1.50)	NS (0.09)	Fair
RRT														
RRT	Brunkhorst [17] 2008 Germany	65	S_{Cr} 126.4 µmol/l	ICU	nd	261	272	10% Hydroxyethyl starch	Ringer's lactate	Per protocol	31% (19%)	1.63 (1.20-2.21)	0.001	Fair
AKI														
Doubling of baseline S_{Cr}	Brunkhorst [17] 2008 Germany	65	S_{Cr} 126.4 µmol/l	ICU	nd	261	272	10% Hydroxyethyl starch	Ringer's lactate	Per protocol	35% (23%)	1.52 (1.16-2.00)	0.002	Fair

Supplementary table 2: Evidence profile of RCTs examining insulin vs. conventional glucose therapy for the prevention of AKI

Outcome	# of studies and study design	Total N (treatment)	Methodological quality of studies per outcome	Consistency across studies	Directness of the evidence generalizability/ applicability	Other considerations	Summary of findings		
							Quality of evidence for outcome	Qualitative and quantitative description of effect	Importance of outcome
Mortality	2 RCT (High)	6558 (3257)	No limitations	No important inconsistencies	No uncertainty	None	High	No benefit	Critical (Crucial)
	1 SR (29 trials)	8315	No limitations						
RRT	2 RCT (High)	6558 (3257)	No limitations	No important inconsistencies	No uncertainty	None	High	No benefit	Critical
	1 SR (29 trials)	3629	No limitations						
AKI	1 RCT (High)	536 (247)	Some limitations (-1)[a]	N/A	No uncertainty	Sparse (-1)	Low	Uncertain	High
Balance of potential benefits and harm No benefit. Possible harm from hypoglycemia.							Quality of overall evidence High		

Annotations:

a. Study was not blinded.

Supplementary table 3: Summary table of RCTs examining the effect of insulin for the prevention of AKI

Outcome	Author Year Country	Age	Baseline kidney function	Setting	Study duration	No. analyzed (No randomized)		Intervention/Control (target blood glucose)		Concomitant medication	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1	Arm 2					
Critically Ill Patients														
Mortality														
Mortality by 90 d	NICE-SUGAR [56] 2008 Australia, New Zealand & Canada	60	nd	ICU	90 d	3010 (3054)	3012 (3050)	Intensive glucose (81-108 mg/dl)	Conventional glucose (≤180 mg/dl)	nd	28% (25%)	1.10[a] (1.01-1.20)	0.02	Good
Mortality by 28 d											22% (21%)	1.07[a] (0.97-1.18)	NS (0.17)	Good
RRT														
RRT	NICE-SUGAR [56] 2008 Australia, New Zealand & Canada	60	nd	ICU	90 d	3010 (3054)	3012 (3050)	Intensive glucose (81-108 mg/dl)	Conventional glucose (≤180 mg/dl)	nd	15% (15%)	1.06[a] (0.94-1.20)	NS (0.34)	Good
Days of RRT											0.8 (0.8)	--	NS (0.39)	Good
Sepsis Patients														
Mortality														
90 d	Brunkhorst [17] 2008 Germany	65	S_{Cr} 126.4 µmol/l	ICU	28 d	247 (247)	289 (290)	Intensive insulin (80-110 mg/dl)	Conventional insulin (180-200 mg/dl)	Per protocol	40% (35%)	1.14 (0.92-1.42)	NS (0.31)	Fair
28 d											25% (26%)	0.96 (0.72-1.29)	NS (0.74)	Fair
RRT														
RRT	Brunkhorst [17] 2008 Germany	65	S_{Cr} 126.4 µmol/l	ICU	nd	244 (247)	289 (290)	Intensive insulin (80-110 mg/dl)	Conventional insulin (180-200 mg/dl)	Per protocol	28% (23%)	1.22 (0.91-1.63)	NS (0.19)	Fair
AKI														
Doubling of baseline S_{Cr}	Brunkhorst [17] 2008 Germany	65	S_{Cr} 126.4 µmol/l	ICU	nd	244 (247)	289 (290)	Intensive insulin (80-110 mg/dl)	Conventional insulin (180-200 mg/dl)	Per protocol	31% (27%)	1.15 (0.88-1.50)	NS (0.25)	Fair

Annotations:

*Calculated by ERT with raw data from original studies when available. When study reported only event rates, calculations were done using percentages.

a. NICE-SUGAR: Mortality by 90 d, OR 1.14 (95% CI 1.02-1.28); Mortality by 28 d, OR 1.09 (95% CI 0.96-1.23); RRT, OR 0.9 (95% CI -0.9-2.7)

Supplementary table 4: Summary table of RCTs examining the effect of dopamine vs. placebo for the treatment of AKI

Outcome	Author Year Country	Age	Baseline kidney function	Setting	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication	Event rate Arm 1 (Arm 2)	RR* (95% CI)	P value	Quality
						Arm 1	Arm 2	Arm 1	Arm 2					
Critically Ill Patients														
Mortality														
Survival to ICU discharge											67% (64%)	1.04 (0.89-1.22)	NS (0.61)	Fair
Survival to hospital discharge	Bellomo [9] 2000 Australia	63	S_{Cr} 183 µmol/l	ICU	nd	161 (163)	163 (165)	Dopamine	Placebo	nd	57% (60%)	0.96 (0.80-1.15)	NS (0.66)	Fair
Mortality											43% (40%)	1.06 (0.82-1.37)	nd	Fair
RRT														
RRT	Bellomo [9] 2000 Australia	63	S_{Cr} 183 µmol/l	ICU	nd	161 (163)	163 (165)	Dopamine	Placebo	nd	22% (25%)	0.89 (0.60-1.32)	NS (0.55)	Fair

Annotations:
* Calculated by ERT with raw data from original studies when available. When study reported only event rates, calculations were done using percentages.

Supplementary table 5: Evidence profile of RCTs examining fenoldopam vs. control for the prevention of AKI

Outcome	# of studies and study design	Total N (treatment)	Methodological quality of studies per outcome	Consistency across studies	Directness of the evidence generalizability/ applicability	Other considerations	Summary of findings		
							Quality of evidence for outcome	Qualitative and quantitative description of effect	Importance of outcome
Mortality	1 RCT (High)	300 (150)	No limitations	N/A	No uncertainty	Sparse (-1)	Moderate	No significant difference however single study in sepsis.	Critical
RRT	3 RCTs (High)	653 (325)	No limitations	No important inconsistencies	No uncertainty	Imprecision (-1) [a]	Moderate	Trend to less RRT (borderline benefit in the one study in sepsis patients and very low event rates in the two studies in CTS patients).	Critical
AKI	3 RCTs (High)	653 (325)	No limitations	No important inconsistencies	No uncertainty	None	High	Consistent benefit for kidney function in all three studies, but variable outcome definitions.	High (Crucial)

Balance of potential benefits and harm

Benefit for prevention of AKI with fenoldopam, but major concerns about potential for harm from hypotension and tachycardia.

Quality of overall evidence

High

Annotations:

a. Low event rates in CTS studies

Supplementary table 6: Summary table of RCTs examining the effect of fenoldopam for the prevention of AKI

Outcome	Author Year Country	Age	Baseline kidney function	Setting	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1	Arm 2					
CTS Patients														
RRT														
5 d	Caimmi [19] 2003 Italy	70	S_{Cr} 1.82 mg/dl GFR 51 ml/min	CTS	5 d	80 (80)	80 (80)	Fenoldopam	Conventional maintenance	nd	0% (4%)	0.14 (0.01-2.72)	NS (>0.1)	Fair
Mean 13 d	Cogliati [22] 2007 Italy	70	S_{Cr} 1.8 mg/dl GFR 40 ml/min	CTS	Mean 13 d	95 (95)	98 (98)	Fenoldopam	Normal saline	Per protocol	0% (8%)	0.06 (0.00-1.04)	0.004	Good
AKI														
↑S_{Cr} to 1.5X basal	Caimmi [19] 2003 Italy	70	S_{Cr} 1.82 mg/dl GFR 51 ml/min	CTS	5 d	80 (80)	80 (80)	Fenoldopam	Conventional maintenance	nd	0% (31%)	0.02 (0.00-0.32)	<0.01	Fair
↑S_{Cr} to >2 mg/dl with ΔS_{Cr} >0.7 mg/dl, 48 h	Cogliati [22] 2007 Italy	70	S_{Cr} 1.8 mg/dl GFR 40 ml/min	CTS	Mean 13 d	95 (95)	98 (98)	Fenoldopam	Normal saline	Per protocol	13% (28%)	0.46 (0.25-0.85)	0.02	Good
Sepsis Patients														
Mortality														
Mean 8 d	Morelli [54] 2005 Italy	58	S_{Cr} 89.8 µmol/l GFR 81 ml/min	Sepsis	Mean 8 d	150 (150)	150 (150)	Fenoldopam	Placebo	nd	35% (44%)	0.79 (0.59-1.05)	NS (0.1)	Good
RRT														
Mean 8 d	Morelli [54] 2005 Italy	58	S_{Cr} 89.8 µmol/l GFR 81 ml/min	Sepsis	Mean 8 d	150 (150)	150 (150)	Fenoldopam	Placebo	nd	7% (14%)	0.56 (0.38-0.83)	0.056	Good
AKI														
↑S_{Cr} >150 µmol/l during drug infusion[a]	Morelli [54] 2005 Italy	58	S_{Cr} 89.8 µmol/l GFR 81 ml/min	Sepsis	Mean 8 d	150 (150)	150 (150)	Fenoldopam	Placebo	nd	19% (34%)	0.57 (0.38-0.84) [p 0.005]	0.006	Good

Annotations

* Calculated by ERT with raw data from original studies when available. When study reported only event rates, calculations were done using percentages.

a. Drug infused until one of the following events occurred: the patient died, serious adverse effect attributed to the study drug or patient discharged from ICU.

Supplementary table 7: Evidence profile of RCTs of fenoldopam vs. placebo for the treatment of AKI

Outcome	# of studies and study design	Total N (treatment)	Methodological quality of studies per outcome	Consistency across studies	Directness of the evidence generalizability/ applicability	Other considerations	Summary of findings		
							Quality of evidence for outcome	Qualitative and quantitative description of effect	Importance of outcome
Mortality	1 RCT (High)	155 (80)	No limitations	N/A	No uncertainty	Imprecision (-1)[a]	Moderate	No benefit in a mixed ICU population	Critical
RRT	2 RCTs (High)	255 (130)	No limitations	No important inconsistencies	No uncertainty	Imprecision (-1)[a]	Moderate	No benefit	Critical (Crucial)
ΔAKI	1 RCT (High)	100 (50)	No limitations	N/A	Some uncertainty (-1)[c]	Imprecision (-1)[a]	Low	Benefit for kidney function	High
		Balance of potential benefits and harm No benefit						Quality of overall evidence Moderate	

Annotations:

a. Low event rates. Only one study for mortality.
b. Presumably study aimed to include people with AKI but mean baseline creatinine was only 1.2 mg/dl
c. 10% change in creatinine is a relatively small change

Supplementary table 8: Summary table of RCTs of examining the effect of fenoldopam for the treatment of AKI

Outcome	Author Year Country	Age	Baseline kidney function	Setting	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication	Event rate Arm 1 (Arm 2)	RR* (95% CI)	P value	Quality
						Arm 1	Arm 2	Arm 1	Arm 2					
Critically Ill Patients														
Mortality														
21 d	Tumlin [86] 2005 US	64	S_{Cr} 1.17 mg/dl	ICU	21 d	80 (82)	75 (78)	Fenoldopam	Placebo	Per protocol	13% (25%)	0.54 (0.28-1.06)	NS (0.068)	Good
RRT														
4 d	Brienza [14] 2006 Italy	69	S_{Cr} 1.78 mg/dl	ICU	4 d	50 (50)	50 (50)	Fenoldopam	Dopamine	Per protocol	4% (6%)	0.67 (0.12-3.82)	NS	Good
21 d	Tumlin [86] 2005 US	64	S_{Cr} 1.17 mg/dl	ICU	21 d	80 (82)	75 (78)	Fenoldopam	Placebo	Per protocol	16% (25%)	0.64 (0.34-1.21)	NS (0.16)	Good
AKI														
↑S_{Cr} >10%	Brienza [14] 2006 Italy	69	S_{Cr} 1.78 mg/dl	ICU	4 d	50 (50)	50 (50)	Fenoldopam	Dopamine	Per protocol	16% (38%)	0.42 (0.20-0.87)	<0.05	Good
↓S_{Cr} >10%											66% (46%)	1.43 (1.00-2.06)	<0.05	Good

Annotations:
* Calculated by ERT with raw data from original studies when available. When study reported only event rates, calculations were done using percentages.

Supplementary table 9: Summary table of RCTs of nesiritide vs. control for the prevention of AKI

Outcome	Author Year Country	Age	Baseline kidney function	Setting	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1	Arm 2					
CTS Patients														
Mortality														
180 d	Mentzer [50] 2007 Multi	63	S_{Cr} 1.07 mg/dl GFR 82 ml/min	CTS	180 d	141 (152)	138 (151)	Nesiritide	Placebo	Per protocol	7% (15%)	0.48[a] (0.22-1.05)	Log rank test 0.046	Fair
AKI														
AKI (no definition but not RRT)	Mentzer [50] 2007 Multi	63	S_{Cr} 1.07 mg/dl GFR 82 ml/min	CTS	180 d	141 (152)	138 (151)	Nesiritide	Placebo	Per protocol	7% (12%)	0.58 (0.27-1.21)	nd	Poor

Annotations:
*Calculated by ERT with raw data from original studies when available. When study reported only event rates, calculations were done using percentages.
a. Mentzer: Mortality 180 d, HR 0.44 (95% CI 0.19-1.01)

Supplementary table 10: Evidence profile of RCTs examining anaritide vs. control for the prevention of AKI

Outcome	# of studies and study design	Total N (treatment)	Methodological quality of studies per outcome	Consistency across studies	Directness of the evidence generalizability/ applicability	Other considerations	Summary of findings		
							Quality of evidence for outcome	Qualitative and quantitative description of effect	Importance of outcome
Mortality	2 RCTs (High)	272 (138)	Serious limitations (-2)	No important inconsistencies	No uncertainty	Imprecision (-1)[b]	Very low	Uncertain	Critical
RRT	2 RCTs (High)	272 (138)	Serious limitations (-2)	No important inconsistencies	No uncertainty	Imprecision (-1)[b]	Very low	Uncertain	Critical
AKI	1 RCT (High)	148 (75)	Serious limitations (-2)[a]	N/A	No uncertainty	Imprecision (-1)[b]	Very low	Uncertain	High (Crucial)
		Balance of potential benefits and harm Uncertain						Quality of overall evidence Very low	

Annotations:
a. No definition of AKI
b. Wide confidence intervals

Supplementary table 11: Summary table of RCTs examining the effect of anaritide vs. control for the prevention of AKI

Outcome	Author Year Country	Age	Baseline kidney function	Setting	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1	Arm 2					
CTS Patients														
Mortality														
30 d	Sezai [75] 2006 Japan	63	nd	CTS	30 d	75 (75)	73 (73)	ANP	Normal Saline	nd	0% (0%)	0.97 (0.02-48)	nd	Fair
In-hospital mortality	Sezai [74] 2007 Japan	69	nd	CTS	Mean 18 d	63 (63)	61 (61)	h-ANP	Normal saline	Per protocol	6% (8%)	0.75 (0.21-2.74)	NS (0.692)	Poor
Late postoperative death (2 y)											3% (7%)	0.43 (0.08-2.29)	NS (0.32)	Poor
Cumulative survival rate (2 y)											91% (85%)	1.07 (0.94-1.22)	NS (0.368)	Poor
RRT														
Need for HF	Sezai [75] 2006 Japan	63	nd	CTS	30 d	75 (75)	73 (73)	ANP	Normal saline	nd	0% (1%)	0.32 (0.01-7.84)	nd	Poor
Need for HF	Sezai [74] 2007 Japan	69	nd	CTS	Mean 18 d	63 (63)	61 (61)	h-ANP	Normal saline	Per protocol	0% (3%)	0.26 (0.01-5.71)	nd	Poor
AKI														
AKI (no definition)	Sezai [75] 2006 Japan	63	nd	CTS	30 d	75 (75)	73 (73)	ANP	Normal saline	nd	0% (1%)	0.32 (0.01-7.84)	nd	Poor

Annotations:
*Calculated by ERT with raw data from original studies when available. When study reported only event rates, calculations were done using percentages.
a. Mentzer: Mortality 180 d, HR 0.44 (95% CI 0.19-1.01)

Supplementary table 12: Evidence profile of RCTs examining anaritide vs. placebo for the treatment of AKI

Outcome	# of studies and study design	Total N (treatment)	Methodological quality of studies per outcome	Consistency across studies	Directness of the evidence generalizability/ applicability	Other considerations	Summary of findings		
							Quality of evidence for outcome	Qualitative and quantitative description of effect	Importance of outcome
Mortality	2 RCTs (High)	720 (351)	No limitations	No important inconsistencies	No uncertainty	None	High	No benefit. For the oliguric patient subgroup in one study, there was benefit for dialysis-free survival by 21 days.	Critical
RRT	2 RCTs (High)	720 (351)	No limitations	No important inconsistencies	No uncertainty	None	High	No benefit. For one study in oliguric patients, trend to a decrease in dialysis by 14 days. For the oliguric patient subgroup in the other study, there was a benefit for dialysis by 14 days.	Critical
AKI	0 RCT	--	--	--	--	--	--	--	High
		Balance of potential benefits and harm No benefit						Quality of overall evidence High	

Supplementary table 13: Summary table of RCTs examining the effect of ANP vs. placebo for the treatment of AKI

Outcome	Author Year Country	Age	Baseline kidney function	Setting	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication	Event rate Arm 1 (Arm 2)	RR* (95% CI)	P value	Quality
						Arm 1	Arm 2	Arm 1	Arm 2					
Predominantly Critically Ill Patients														
Mortality														
Mortality by 21 d	Allgren [4] 1997 US	62	S_{Cr} 4.4 mg/dl	ICU and non ICU	60 d	248 (248)	256 (256)	ANP	Placebo	None	29% (26%)	1.12 (0.84-1.48)	NS (0.41)	Good
Dialysis-free survival by 21 d[a]											43% (47%)	0.91 (0.69-1.22)	NS (0.35)	Good
Mortality by 60 d	Lewis [44] 2000 US	64	S_{Cr} 4.3 mg/dl CrCl 8 ml/min	ICU and non ICU	60 d	108 (108)	114 (114)	ANP	Placebo	nd	60% (56%)	1.07 (0.86-1.34)	NS (0.541)	Good
Mortality by 21 d											51% (40%)	1.27 (0.95-1.70)	NS (0.112)	Good
Dialysis-free survival by 21 d											21% (15%)	1.40 (0.79-2.48)	NS (0.22)	Good
RRT														
Dialysis by 14 d[a]	Allgren [4] 1997 US	62	S_{Cr} 4.4 mg/dl	ICU and non ICU	60 d	248 (248)	256 (256)	ANP	Placebo	None	44% (42%)	1.05 (0.86-1.28)	NS (0.75)	Good
Dialysis by 14 d	Lewis [44] 2000 US	64	S_{Cr} 4.3 mg/dl CrCl 8 ml/min	ICU and non ICU	60 d	108 (108)	114 (114)	ANP	Placebo	nd	64% (77%)	0.83 (0.70-0.99)	0.054	Good

Annotations:

* Calculated by ERT with raw data from original studies when available. When study reported only event rates, calculations were done using percentages.

In the Allgren study, dialysis-free survival at 21 days and dialysis by 14 days was lower in the ANP vs. placebo in the subgroup with oliguria.

Supplementary table 14: Summary table of RCTs examining the effect of erythropoietin vs. placebo for the prevention of AKI

Outcome	Author Year Country	Age	Baseline kidney function	Setting	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication	Event rate Arm 1 (Arm 2)	RR* (95% CI)	P value	Quality
						Arm 1	Arm 2	Arm 1	Arm 2					
Mortality														
Death in 7 d	Endre [24] 2010 Australia & New Zealand	65	S_{Cr} 0.79 mg/dl GFR 91 ml/min	ICU	30 d	70 (84)	63 (78)	EPO	Placebo	None	9 (11%) [13 (17%)]	0.62 (0.29-1.36)	NS (0.36)	B
Death in 30 d											16 (19%) [17 (22%)]	0.85 (0.47-1.53)	NS (0.70)	B
RRT														
Dialysis in 30 d	Endre [24] 2010 Australia & New Zealand	65	S_{Cr} 0.79 mg/dl GFR 91 ml/min	ICU	30 d	70 (84)	63 (78)	EPO	Placebo	None	5 (6%) [3 (4%)]	1.50 (0.37-6.02)	NS (0.72)	B
AKI														
↑ S_{Cr} ≥50% or 0.3 mg/dl by 7 d	Endre [24] 2010 Australia & New Zealand	65	S_{Cr} 0.79 mg/dl GFR 91 ml/min	ICU	30 d	70 (84)	63 (78)	EPO	Placebo	None	41 (49%) [38 (49%)]	0.97 (0.73-1.29)	NS (1.0)	B
AKIN-creatinine											38 (45%) [37 (47%)]	0.92 (0.69-1.25)	NS (0.88)	B
AKIN-UO											59 (70%) [40 (51%)]	1.33 (1.07-1.64)	0.016	B
AKIN-Total											66 (79%) [54 (69%)]	1.10 (0.98-1.24)	NS (0.21)	B
RIFLE-creatinine [↑S_{Cr} ≥50% sustained for >24 h by 7 d]											20 (24%) [15 (19%)]	1.20 (0.67-2.14)	NS (0.57)	B

Supplementary table 15: Evidence profile of RCT examining on vs. off pump cardiothoracic surgery

Outcome	# of studies and study design	Total N (treatment)	Methodological quality of studies per outcome	Consistency across studies	Directness of the evidence generalizability/ applicability	Other considerations	Summary of findings		
							Quality of evidence for outcome	Qualitative and quantitative description of effect	Importance of outcome
Mortality	7 RCTs (High)	3453 (1720)	Some limitations (-1)	No important inconsistencies	No uncertainty	Imprecision (-1)[a]	Low	Uncertain	Critical
RRT	6 RCTs (High)	3353 (1670)	Some limitations (-1)	No important inconsistencies	No uncertainty	Imprecision (-1)[a]	Low	Uncertain	Critical
AKI	3 RCTs (High)	481 (243)	Some limitations (-1)	No important inconsistencies	No uncertainty	Sparse (-1) Imprecision (-1)[a]	Very low	Two studies show no benefit of having an off pump surgery and one study showed benefit.	High (Crucial)
		Balance of potential benefits and harm Uncertain						Quality of overall evidence Very low	

Annotations:
a. Wide confidence intervals

Supplementary table 16: Summary table of RCTs examining the effect of on vs. off pump CABG for the prevention of AKI

Outcome	Author Year Country	Age	Baseline kidney function	Setting	Study duration	No. analyzed (No randomized)		Intervention/Control		Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1	Arm 2				
Mortality													
In operating room	Puskas [64] 2003 US	62	nd	CTS	30 d	99 (99)	98 (98)	On pump	Off pump	0% (0%)	1.01 (0.02-50.41)	nd	Fair
In hospital <30 d										2% (1%)	1.98 (0.18-21.48)	NS (>0.999)	Fair
In hospital >30 d										0% (2%)	0.20 (0.01-4.07)	NS (0.246)	Fair
Out of hospital <30 d										0% (0%)	1.01 (0.02-50.41)	nd	Fair
In-hospital mortality	Al-Ruzzeh [3] 2006 UK	63	nd	CTS	6 mo	84 (84)	84 (84)	On pump	Off pump	0% (1%)	0.33 (0.01-8.07)	NS (1)	Fair
Deaths	Sajja [72] 2007 India	60	S_{Cr} 1.48 mg/dl	CTS	5 d	60 (60)	56 (56)	On pump	Off pump	5% (0%)	6.53 (0.35-123.68)	nd	Fair
Death	Straka [80] 2004 Czech	63	nd	CTS	30 d	184 (184)	204 (204)	On pump	Off pump	1% (2%)	0.55 (0.10-2.99)	NS (0.39)	Fair
Deaths 30 d post-op	Tatoulis [82] 2006 Australia	66	nd	CTS	30 d	50 (50)	50 (50)	On pump	Off pump	0% (0%)	1.00 (0.02-49.42)	nd	Fair
All-cause mortality at 1 mo	van Dijk [88] 2001 Netherlands	62	S_{Cr} 1.01 mg/dl	CTS	30 d	139 (139)	142 (142)	On pump	Off pump	0% (0%)	1.02 (0.02-51.13)	nd	Fair
30 d death after surgery or before discharge	Shroyer [76] 2009 US [a]	63	nd	CTS	1 y	1104 (1104)	1099 (1099)	Off-pump	On-pump	2% (1%)	1.38 (0.68-2.80)	0.47	Good
All-cause within 1 y										4% (3%)	1.43 (0.90-2.26)	0.15	Good
RRT													
New dialysis	Puskas [64] 2003 US	62	nd	CTS	30 d	99 (99)	98 (98)	On pump	Off pump	0% (1%)	0.33 (0.01-8.00)	NS (>0.246)	Fair
HF	Al-Ruzzeh [3] 2006 UK	63	nd	CTS	6 mo	84 (84)	84 (84)	On pump	Off pump	6% (2%)	2.50 (0.50-12.53)	NS (0.27)	Poor
HD	Sajja [72] 2007 India	60	S_{Cr} 1.48 mg/dl	CTS	5 d	60 (60)	56 (56)	On pump	Off pump	5% (0%)	6.53 (0.35-123.68)	nd	Fair
HD	Straka [80] 2004 Czech	63	nd	CTS	30 d	184 (184)	204 (204)	On pump	Off pump	1% (1%)	1.11 (0.16-7.79)	NS (0.65)	Fair

HD	van Dijk [88;88] 2001 Netherlands	62	S_{Cr} 1.01 mg/dl	CTS	30 d	139 (139)	142 (142)	On pump	Off pump	1% (0%)	3.06 (0.13-74.60)	NS (0.31)	Poor
Renal failure requiring dialysis within 30 d	Shroyer [76] 2009 US	63	nd	CTS	1 y	1104 (1104)	1099 (1099)	Off-pump	On-pump	1% (1%)	0.90 (0.37-2.20)	NS (0.82)	Good
AKI													
New renal failure (↑S_{Cr} ≥2.0 mg/dl or ↑S_{Cr} 50%)	Puskas [64] 2003 US	62	nd	CTS	30 d	99 (99)	98 (98)	On pump	Off pump	2% (1%)	1.98 (0.18-21.48)	NS (>0.999)	Fair
Renal impairment	Al-Ruzzeh [3] 2006 UK	63	nd	CTS	6 mo	84 (84)	84 (84)	On pump	Off pump	17% (10%)	1.75 (0.78-3.95)	NS (0.15)	Poor
↑S_{Cr}≥ 20%, 1 or 5 d	Sajja [72] 2007 India	60	S_{Cr} 1.48 mg/dl	CTS	5 d	60 (60)	56 (56)	On pump	Off pump	62% (30%)	2.14 (1.38-3.32)	<0.001	Fair

Annotations:

*Calculated by ERT with raw data from original studies when available. When study reported only event rates, calculations were done using percentages.

a. Shroyer study: 30-d death after surgery or before discharge: RR 1.38 (95% CI 0.68 to 2.80); All-cause mortality at 1 y: RR 1.41 (95% CI 0.90 to 2.24); Renal failure requiring dialysis within 30 d: 0.90 (0.37 to 2.20)

Supplementary table 17: Evidence profile of RCTs examining NAC vs. placebo in the prevention of AKI

Outcome	# of studies and study design	Total N (treatment)	Methodological quality of studies per outcome	Consistency across studies	Directness of the evidence generalizability/ applicability	Other considerations	Summary of findings		
							Quality of evidence for outcome	Qualitative and quantitative description of effect	Importance of outcome
Mortality	5 RCTs (High)	968 (486)	No limitations	No important inconsistencies	No uncertainty	Imprecision (-1)[a]	Moderate	Uncertain	Critical
RRT	5 RCTs (High)	968 (486)	No limitations	No important inconsistencies	No uncertainty	Imprecision (-1)[a]	Moderate	Uncertain	Critical
AKI	5 RCTs (High)	968 (486)	No limitations	No important inconsistencies	No uncertainty	None	High	No benefit	High (Crucial)
		Balance of potential benefits and harm No benefit					Quality of overall evidence High		

Annotations:
a. Low event rates with wide confidence intervals

Supplementary table 18: Summary table of RCTs examining the effect of NAC vs. placebo in the prevention of AKI

Outcome	Author Year Country	Age	Baseline kidney function	Setting	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1	Arm 2					
Critically Ill Patients														
Mortality														
Mean 16 d	Komisarof [39] 2007 US	60	S_{Cr} 1.29 mg/dl	Critically ill	Mean 16 d	71 (71)	71 (71)	NAC	Placebo	nd	10% (10%)	1.00 (0.37-2.70)	NS (1.00)	Good
RRT														
Mean 16 d	Komisarof [39] 2007 US	60	S_{Cr} 1.29 mg/dl	Critically ill	Mean 16 d	71 (71)	71 (71)	NAC	Placebo	nd	3% (3%)	1.00 (0.14-6.90)	NS (1.00)	Good
AKI														
↑S_{Cr} ≥ 0.5 mg/dl during hospitalization	Komisarof [39] 2007 US	60	S_{Cr} 1.29 mg/dl	Critically ill	Mean 16 d	71 (71)	71 (71)	NAC	Placebo	nd	16% (17%)	0.92 (0.43-1.94)	NS (0.82)	Good
↑S_{Cr} 50% during hospitalization											13% (17%)	0.75 (0.34-1.67)	NS (0.4782)	Good
CTS Patients														
Mortality														
In-hospital	Sisillo [78] 2008 Italy	74	S_{Cr} 1.27 mg/dl GFR 46 ml/min	CTS	nd	129 (129)	125 (125)	NAC	Placebo	Per protocol	4% (3%)	1.21 (0.33-4.41)	NS (0.77)	Good
90 d	Wijeysundera [93] 2007 Canada	74	S_{Cr} 131 µmol/l eGFR 42 ml/min	CTS	90 d	88 (89)	87 (88)	NAC	Placebo	Per protocol	0% (8%)	0.07 (0.00-1.14)	0.007	Good
30 d	Adabag [1] 2008 US	70	S_{Cr} 1.9 mg/dl GFR 40 ml/min	CTS	30 d	50 (50)	52 (52)	NAC	Placebo	nd	4% (6%)	0.69 (0.12-3.98)	NS (0.68)	Good
In-hospital	Burns [18] 2005 Canada	69	S_{Cr} 1.1 mg/dl	CTS	8 d	148 (148)	147 (147)	NAC	Placebo	Per protocol	3% (3%)	1.24 (0.34-4.53)	NS (>0.99)	Good
RRT														
In-hospital	Sisillo [78] 2008 Italy	74	S_{Cr} 1.27 mg/dl GFR 46 ml/min	CTS	nd	129 (129)	125 (125)	NAC	Placebo	Per protocol	8% (5%)	1.61 (0.61-4.31)	NS (0.33)	Good
In-hospital (median 8 d)	Wijeysundera [93] 2007 Canada	74	S_{Cr} 131 µmol/l eGFR 42 ml/min	CTS	90 d	88 (89)	87 (88)	NAC	Placebo	Per protocol	1% (4%)	0.33[a] (0.03-3.11)	NS (0.37)	Fair
30-d	Adabag [1] 2008 US	70	S_{Cr} 1.9 mg/dl GFR 40 ml/min	CTS	30 d	50 (50)	52 (52)	NAC	Placebo	nd	6% (4%)	1.56 (0.27-8.95)	NS (0.68)	Good
In-hospital	Burns [18] 2005 Canada	69	S_{Cr} 1.1 mg/dl	CTS	8 d	148 (148)	147 (147)	NAC	Placebo	Per protocol	1% (2%)	0.33 (0.03-3.15)	NS (0.37)	Good

Outcome	Author Year Country	Age	Baseline kidney function	Setting	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1	Arm 2					
AKI														
↑S_{Cr} >25%	Sisillo [78] 2008 Italy	74	S_{Cr} 1.27 mg/dl GFR 46 ml/min	CTS	3 d	129 (129)	125 (125)	NAC	Placebo	Per protocol	40% (52%)	0.78 (0.59-1.01)	NS (0.06)	Good
5 d	Adabag [1] 2008 US	70	S_{Cr} 1.9 mg/dl GFR 40 ml/min	CTS	30 d	50 (50)	52 (52)	NAC	Placebo	nd	44% (37%)	1.20 (0.75-1.94)	NS (0.44)	Good
30 d											14% (14%)	1.04 (0.39-2.75)	NS (0.94)	Good
↑S_{Cr} >0.5 mg/dl or >25% at 5 d (ITT)	Burns [18] 2005 Canada	69	S_{Cr} 1.1 mg/dl	CTS	8 d	148 (148)	145 (147)	NAC	Placebo	Per protocol	30% (29%)	1.03[∞] (0.72-1.46)	NS (0.89)	Good
↑S_{Cr} >0.5 mg/dl or >25% at 5 d (per protocol analysis)											30% (28%)	1.07 (0.74-1.53)	NS (0.71)	Good
↑S_{Cr} ≥ 44 µmol/l or 25% by 72 h	Wijeysundera [93] 2007 Canada	74	S_{Cr} 131 µmol/l eGFR 42 ml/min	CTS	90 d	88 (89)	87 (88)	NAC	Placebo	Per protocol	28% (32%)	0.88[a] (0.56-1.39)	NS (0.59)	Fair

Annotations:

*Calculated by ERT with raw data from original studies when available. When study reported only event rates, calculations were done using percentages.

[∞]Calculated estimate was same as estimate reported in the study.

a. Wijeysundera: In-hospital (median 8 d), the difference in medians between NAC vs. placebo 0.32 (95% bootstrap non-parametric CI 0.007-4.12); ↑S_{Cr} ≥ 44 µmol/l or 25% by 72 h, OR 0.84 (95% CI 0.42-1.68)

Supplementary table 19: Evidence profile of RCTs examining the effect of intrarterial isosmolar vs. low osmolar contrast agent on the prevention of CI-AKI

Outcome		# of studies and study design	Total N (treatment)	Methodological quality of studies per outcome	Consistency across studies	Directness of the evidence generalizability/ applicability	Other considerations	Summary of findings: Quality of evidence for outcome	Summary of findings: Qualitative and quantitative description of effect	Summary of findings: Importance of outcome
Mortality	Low osmolar, non-ionic	3 RCTs (High)	867 (436)	No limitations	No important inconsistencies	No uncertainty	Imprecision (-1)[a]	Moderate	Uncertain	Critical
	Low osmolar, ionic	1 RCT	146 (72)	No limitations	N/A	No uncertainty	Sparse and Imprecision (-2)	Low	Uncertain	
RRT Non-ionic		3 RCTs (High)	946 (478)	No limitations	No important inconsistencies	No uncertainty	Imprecision (-1)[a]	Moderate	Uncertain	Critical
CI-AKI	Low osmolar, non-ionic	9 RCTs (High)	2305 (1171)	No limitations	No important inconsistencies	No uncertainty	None	High	Seven studies showed no benefit for non-ionic isosmolar CM (iodixanol) compared to non-ionic low osmolar CM. Two studies showed benefit for non-ionic isosmolar CM (iodixanol).	High (Crucial)
	Low osmolar, ionic	2 RCTs (High)	421 (212)	No limitations	Important inconsistencies (-1)	No uncertainty	Sparse (-1)	Low	One study showed benefit for non-ionic isosmolar CM (iodixanol) compared to ionic low osmolar CM (ioxaglate). Another study showed no benefit for iodixanol compared to ioxaglate.	

Balance of potential benefits and harm	Quality of overall evidence
No or no consistent benefit for non-ionic isosmolar (iodixanol) CM compared to low osmolar ionic or non-ionic CM.	Moderate

Annotations:

a. Low event rates with wide confidence intervals

b. For the outcome of increase in creatinine of 0.5 mg/dl, there was only a trend towards benefit. For the combination of increase in creatinine of 0.5 mg/dl or 25%, there was a statistically significant benefit for iodixanol.

Supplementary table 20: Evidence profile of RCTs examining the effect of intravenous isosmolar vs. low osmolar contrast agent on the prevention of CI-AKI

Outcome	# of studies and study design	Total N (treatment)	Methodological quality of studies per outcome	Consistency across studies	Directness of the evidence generalizability/ applicability	Other considerations	Summary of findings		
							Quality of evidence for outcome	Qualitative and quantitative description of effect	Importance of outcome
Mortality	1 RCT	117 (61)	No limitations	N/A	No uncertainty	Sparse and Imprecision (-2)[a]	Low	Uncertain	Critical
RRT	3 RCTs (High)	418 (209)	No limitations	No important inconsistencies	No uncertainty	Sparse and Imprecision (-2)[a]	Low	Uncertain	Critical
CI-AKI	4 RCTs (High)	666 (334)	No limitations	No important inconsistencies	No uncertainty	Imprecision (-1)[a]	Moderate	No benefit. Two study favoring iodixanol. Two study favoring control.	High (Crucial)
		Balance of potential benefits and harm No benefit						Quality of overall evidence Moderate	

Annotations:

a. Low event rates with wide confidence intervals

Supplementary table 21: Summary table of RCTs examining the effect of isosmolar vs. low osmolar contrast agent on the prevention of CI-AKI

Outcome	Author Year Country	Age	Baseline kidney function	DM%	Procedure	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
							Arm 1	Arm 2	Arm 1	Arm 2					
Intrarterial: Low osmolar Non-ionic															
Mortality															
7 d	Aspelin [5] 2003 Multi	71	$S_{Cr:}$ 1.49 mg/dl GFR: 50 ml/min	100	Coronary or aortofemoral angiography	7 d	64 (64)	65 (65)	Iodixanol	Iohexol	i.v. fluids recommended	0% (3%)	0.20 (0.01-4.15)	nd	Fair
7 d	Solomon [79] 2007 US & Canada	72	S_{Cr} 1.46 mg/dl GFR: 49 ml/min	38	Cardiac catheterization	7 d	210 (236)	204 (230)	Iodixanol	Iopamidol	Isotonic sodium bicarbonate solution	0% (0%)	0.97 (0.02-49)	nd	Good
6 mo	Wessely [92] 2009 Germany	75	S_{Cr} 1.36 mg/dl GFR 46 ml/min	38	PCI	6 mo	162 (162)	162 (162)	Iodixanol	Iomeprol	nd	6 (4%) [7 (4%)]	0.86 (0.29-2.50)	NS (0.78)	Good
RRT															
7 d	Solomon [79] 2007 US & Canada	72	S_{Cr} 1.46 mg/dl GFR: 49.3 ml/min	38	Cardiac catheterization	7 d	210 (236)	204 (230)	Iodixanol	Iopamidol	Isotonic sodium bicarbonate solution	0% (0%)	0.97 (0.02-49)	nd	Good
7 d	Nie [57] 2008 China	61	S_{Cr} 1.48 mg/dl GFR 46 ml/min	27	Cardiac catheterization	7 d	106 (108)	102 (108)	Iodixanol	Iopromide	i.v. fluids	0% (2%)	0.32 (0.01-7.79)	nd	Good
6 mo	Wessely [92] 2009 Germany	75	S_{Cr} 1.36 mg/dl GFR 46 ml/min	38	PCI	6 mo	162 (162)	162 (162)	Iodixanol	Iomeprol	nd	3 (2%) [1 (1%)]	3.00 (0.32-28.54)	NS (0.31)	Good
CI-AKI															
↑ S_{Cr} 0.5 mg/dl by 3 d	Aspelin [5] 2003 Multi	71	$S_{Cr:}$ 1.49 mg/dl GFR: 50 ml/min	100	Coronary or aortofemoral angiography	7 d	64 (64)	65 (65)	Iodixanol	Iohexol	i.v. fluids recommended	3% (26%)	0.12 (0.03-0.50)	0.002	Good
↑ S_{Cr} 1.0 mg/dl by 3 d												0% (15%)	0.05 (0.00-0.81)	nd	B
↑S_{Cr} ≥0.5 mg/dl (44.2 µmol/l) by 45-120 h	Solomon [79] 2007 US & Canada	72	S_{Cr} 1.46 mg/dl GFR: 49 ml/min	38	Cardiac catheterization	7 d	210 (236)	204 (230)	Iodixanol	Iopamidol	Isotonic sodium bicarbonate solution	7% (4%)	1.51 (0.67-3.41)	NS (0.39)	Good
↑S_{Cr} ≥25%	Hardiek [30] 2008 US	65	S_{Cr} 0.91 mg/dl GFR 105 ml/min	100	Angiography	7 d	54 (54)	48 (48)	Iodixanol	Iopamidol	i.v. fluids	13% (21%)	0.62 (0.26-1.51)	NS (0.29)	Good

Outcome	Author Year Country	Age	Baseline kidney function	DM%	Procedure	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
							Arm 1	Arm 2	Arm 1	Arm 2					
↑S_{Cr} ≥0.5 mg/dl or ≥25% by 3 d	Nie [57] 2008 China	61	S_{Cr} 1.48 mg/dl GFR 46 ml/min	27	Cardiac catheterization	7 d	106 (108)	102 (108)	Iodixanol	Iopromide	i.v. fluids	6% (17%)	0.34 (0.14-0.83)	0.011	Good
↓CrCl 20% by 48 h	Feldkamp [26] 2006 Germany	60	S_{Cr} 1.04 mg/dl	42	Cardiac catheterization	48 h	105 (105)	116 (116)	Iodixanol	Iopromid	i.v. fluids	20% (22%)	0.91 (0.54-1.52)	NS (0.80)	Good
↑S_{Cr} 25% by 48 h												9% (7%)	1.29 (0.52-3.16)	NS (0.83)	Good
↑S_{Cr} >0.5 mg/dl by 3 d "Evaluable group"	Rudnick [71] 2008 US	71	S_{Cr} 1.99 mg/dl GFR 37 ml/min	52	Cardiac catheterization	28 d	156 (173)	143 (164)	Iodixanol	Ioversol	NAC in some	22% (24%)	0.92 (0.60-1.39)	NS (0.78)	Good
↑S_{Cr} >0.5 mg/dl by 3 d "ITT group"												20% (21%)	0.95 (0.62-1.46)	NS (0.89)	Good
Day 2 ↑S_{Cr} ≥44 mol/l (0.5 mg/dl) or 25%	Juergens [34] 2009 Australia	70	S_{Cr} 144.1 µmo/l GFR 49 mmol/l	35	Cardiac catheterization	7 d	100 (108)	91 (94)	Iopromide	Iodixanol	NAC	15% (12%)	1.24 (0.60-2.56)	NS (0.56)	Good
Day 2 ↑S_{Cr} ≥44 mol/l												7% (3%)	2.12 (0.57-7.97)	NS (0.34)	Good
↑S_{Cr} ≥88 mol/l												1% (2%)	0.46 (0.04-4.93)	NS (0.61)	Good
↑S_{Cr} ≥0.5 mg/dl (44.2 µmol/l) by 3 d	Laskey [42] 2009 Multi	69	S_{Cr} 1.6 mg/dl GFR 45 mmol/l	100	Cardiac catheterization	7 d	214 (263)	203 (263)	Iodixanol	Iopamidol	i.v. fluids	11% (10%)	1.14 (0.65-2.00)	NS (0.7)	Good
↑S_{Cr} ≥0.5 mg/dl or >25%	Wessely [92] 2009 Germany	75	S_{Cr} 1.36 mg/dl GFR 46 ml/min	38	PCI	6 mo	162 (162)	162 (162)	Iodixanol	Iomeprol	nd	36 (22%) [45 (28%)]	0.80 (0.55-1.17)	NS (0.25)	Good
Severe CIN (↑S_{Cr}≥ 1 mg/dl)												10 (6%) [6 (4%)]	1.67 (0.62-4.48)	NS (0.30)	Good
Intrarterial: Low Osmolar Ionic															
Mortality															
In-hospital	Mehran [49] 2009 US	71	S_{Cr} 1.86 mg/dl GFR 45 ml/min	51	Coronary angiography	3 d	72 (72)	74 (74)	Iodixanol	Ioxaglate	NAC (70%)	3% (0%)	5.14 (0.25-105.19)	NS (0.24)	Good
30 d												6% (1%)	4.23 (0.48-36.92)	NS (0.20)	Good
CI-AKI															
↑S_{Cr} ≥25%	Jo [33] 2006	66	S_{Cr} 1.38	34	Cardiac	48 h	140	135	Iodixanol	Ioxaglate	i.v. fluids	8%	0.46	0.021	Good

Outcome	Author Year Country	Age	Baseline kidney function	DM%	Procedure	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
							Arm 1	Arm 2	Arm 1	Arm 2					
or ≥0.5 mg/dl by 2 d	Korea		mg/dl GFR 45 ml/min		catheterization		(151)	(149)				(17%)	(0.23-0.91)		
↑S_{Cr} ≥0.5 mg/dl by 2 d												4% (9%)	0.40 (0.15-1.11)	NS (0.067)	Good
↑S_{Cr} ≥0.5 mg/dl	Mehran [49] 2009 US	71	S_{Cr} 1.86 mg/dl GFR 45 ml/min	51	Coronary angiography	3 d	72 (72)	74 (74)	Iodixanol	Ioxaglate	NAC (70%)	16% (18%)	0.89 (0.43-1.82)[b]	NS (0.82)	Good
↑S_{Cr} ≥1.0 mg/dl												1% (5%)	0.20 (0.02-2.45)[c]	NS (0.36)	Good
↑S_{Cr} ≥25%												16% (24%)	0.67 (0.34-1.30)[d]	NS (0.28)	Good
↑S_{Cr} ≥0.5 mg/dl or ≥25%												16% (24%)	0.67 (0.34-1.30)[e]	NS (0.28)	Good
Intravenous: Low Osmolar Non-ionic															
Mortality															
90 d[a]	Nguyen [55] 2008 US	63	S_{Cr} 1.77 mg/dl GFR 52 ml/min	38	CT scan	90 d	61 (65)	56 (61)	Iodixanol	Iopromide	None	5% (4%)	1.38 (0.24-7.94)	NS (0.720)	Fair
RRT															
72 h	Barrett [7] 2006 US & China	67	S_{Cr} 1.6 mg/dl GFR 44 ml/min	20	CT scan	72 h	76 (82)	77 (84)	Iodixanol	Iopamidol	Volume supplementation	0% (0%)	1.01 (0.05-50)	nd	Fair
7 d	Thomsen [84] 2008 Multi	67	S_{Cr} 1.7 mg/dl GFR 41 ml/min	28	CT scan of the liver	7 d	72 (92)	76 (91)	Iodixanol	Iomeprol	nd	0% (0%)	1.06 (0.02-52)	NS	Fair
90 d	Nguyen [55] 2008 US	63	S_{Cr} 1.77 mg/dl GFR 52 ml/min	38	CT scan	90 d	61 (65)	56 (61)	Iodixanol	Iopromide	None	0% (0%)	0.92 (0.02-46)	NS	Fair
CI-AKI															
↑S_{Cr} ≥0.5 mg/dl by 72 h	Barrett [28] 2006 US & China	67	S_{Cr} 1.6 mg/dl GFR 44 ml/min	20	CT scan	72 h	76 (82)	77 (84)	Iodixanol	Iopamidol	Volume supplementation	3% (0%)	4.74 (0.23-97)	NS (0.3)	Fair
↑S_{Cr} ≥25%, by 72 h												4% (4%)	1.01* (0.21-4.86)	NS (0.4)	Fair
↑S_{Cr} ≥25% by 48-72 h	Kuhn [40] 2008 US & China	70	S_{Cr} 1.46 mg/dl GFR 48 ml/min	100	CT scans	3 d	125 (131)	123 (132)	Iodixanol	Iopamidol	i.v. fluids	6% (5%)	0.84* (0.29-2.44)	NS (1.0)	Fair
↓GFR 25%												2%	0.98*	NS	Fair

Outcome	Author Year Country	Age	Baseline kidney function	DM%	Procedure	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
							Arm 1	Arm 2	Arm 1	Arm 2					
by 48-72 h												(2%)	(0.20-4.78)	(1.0)	
↑S_{Cr} ≥0.5 mg/dl by 48-72 h	Thomsen [84] 2008 Multi	67	S_{Cr} 1.7 mg/dl GFR 41 ml/min	28	CT scan of the liver	7 d	72 (92)	76 (91)	Iodixanol	Iomeprol	nd	7% (0%)	11.61 (0.65-206)	0.025	Fair
↑ S_{Cr} ≥25% by 48-72 h												7% (5%)	1.32 (0.37-4.72)	NS (0.74)	Fair
↓CrCl ≥25% by 48-72 h												3% (1%)	2.11 (0.20-23)	NS (0.61)	Fair
S_{Cr} ≥0.5 mg/dl by 3 d	Nguyen [55] 2008 US	63	S_{Cr} 1.77 mg/dl GFR 52 ml/min	38	CT scan	90 d	61 (65)	56 (61)	Iodixanol	Iopromide	None	5% (19%)	0.28 (0.08-0.95)	0.037	Fair
S_{Cr}≥1.0 mg/dl by 3 d												3% (3%)	0.92 (0.13-6.30)	NS (0.931)	Fair

Annotations

* Calculated by ERT with raw data from original studies when available. When study reported only event rates, calculations were done using percentages.

a. All deaths were deemed unrelated to the contrast media by an independent panel

b. Mehran study reported a RR of 0.88 (95% CI 0.42 to 1.85)

c. Mehran study reported a RR of 0.32 (95% CI 0.03 to 2.99)

d. Mehran study reported a RR of 0.66 (95% CI 0.33 to 1.31)

e. Mehran study reported a RR of 0.66 (95% CI 0.33 to 1.31)

Supplementary table 22: Evidence profile of RCTs examining effect of i.v. sodium bicarbonate vs. control for the prevention of CI-AKI

Outcome	# of studies and study design	Total N (treatment)	Methodological quality of studies per outcome	Consistency across studies	Directness of the evidence generalizability/ applicability	Other considerations	Summary of findings		
							Quality of evidence for outcome	Qualitative and quantitative description of effect	Importance of outcome
Mortality	3 RCT (High)	936 (471)	No limitations	No important inconsistencies	No uncertainty	Imprecision (-1)[a]	Moderate	Uncertain	Critical
RRT	6 RCTs (High)	1419 (710)	No limitations	No important inconsistencies	No uncertainty	Imprecision (-1)[a]	Moderate	Uncertain	Critical
CI-AKI	12 RCTs (High)	2441 (1224)	No limitations	Important inconsistencies (-1)	No uncertainty	None	Moderate	Six studies showed a benefit for bicarbonate while 6 studies did not.	High (Crucial)
		Balance of potential benefits and harm Possible but inconsistent benefit.						Quality of overall evidence Moderate	

Annotations:

a. Low event rates with wide confidence intervals

Supplementary table 23: Summary table of RCTs examining the effect of i.v. sodium bicarbonate on the prevention of CI-AKI

Outcome	Author Year Country	Age	Baseline kidney function	Procedure	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1	Arm 2					
Mortality														
Cumulative mortality (N=353)	Brar [13] 2008 US	71	S_{Cr} 1.49 mg/dl GFR 48 ml/min	Cardiac catheterization	6 mo	165 (175)	158 (178)	Bicarbonate	Normal saline	NAC in 50% of patients	2% (4%)	0.55 (0.16-1.83)	NS (0.54)	Fair
30 d	Maioli [45] 2008 Italy	74	S_{Cr}1.20 mg/dl GFR 42 ml/min	Cardiac catheterization	30 d	250 (250)	252 (252)	Bicarbonate	Normal saline	NAC	2% (1%)	1.34 (0.30-5.95)	NS (0.69)	Good
7 d	Recio-Mayoral [66] 2007 Spain & UK	65	S_{Cr} 1.0 mg/dl GFR 75 ml/min	Cardiac catheterization	7 d	56 (56)	55 (55)	Bicarbonate	Normal saline	NAC	2% (7%)	0.25 (0.03-2.13)	NS (0.21)	Fair
RRT														
6 mo	Brar [13] 2008 US	71	S_{Cr} 1.49 mg/dl GFR 48 ml/min	Cardiac catheterization	6 mo	165 (175)	158 (178)	Bicarbonate	Normal saline	NAC in 50% of patients	1% (3%)	0.48 (0.16-1.83)	NS (0.32)	Fair
During hospital stay	Merten [51] 2004 US	67	S_{Cr} 1.89 mg/dl GFR 41 ml/min	Cardiac catheterization, CT and others	9 mo	60 (69)	59 (68)	Bicarbonate	Normal saline	None	0% (0%)	0.98 (0.02-48.76)	nd	Fair
14 d	Adolph [2] 2008 Germany	70	S_{Cr} 1.54 mg/dl	Cardiac catheterization	14 d	71 (72)	74 (76)	Bicarbonate	Normal saline	None	0% (0%)	0.98 (0.02-48.76)	nd	Fair
HF by 30 d	Maioli [45] 2008 Italy	74	S_{Cr}1.20 mg/dl GFR 42 ml/min	Cardiac catheterization	30 d	250 (250)	252 (252)	Bicarbonate	Normal saline	NAC	0.4% (0.4%)	1.01 (0.06-16.03)	NS (0.99)	Good
7 d	Recio-Mayoral [66] 2007 Spain & UK	65	S_{Cr} 1.0 mg/dl GFR: 75 ml/min	Cardiac catheterization	7 d	56 (56)	55 (55)	Bicarbonate	Normal saline	NAC	2% (6%)	0.33 (0.04-3.05)	NS (0.36)	Fair
5 d	Briguori [15] 2007 Italy	70	S_{Cr} 1.95 mg/dl GFR 32 ml/min	CAD or peripheral angiography	5 d	108 (117)	111 (118)	Bicarbonate	Normal saline	NAC	1% (1%)	1.03 (0.07-16.23)	NS	Good
CI-AKI														
↓GFR >25%. 1 d-4 d	Brar [13] 2008 US	71	S_{Cr} 1.49 mg/dl GFR 48 ml/min	Cardiac catheterization	6 mo	165 (175)	158 (178)	Bicarbonate	Normal saline	NAC in 50% of patients	13% (15%)	0.91[a] (0.53-1.57)	NS (0.75)	Good
↓GFR≥25%, 2 d	Merten [51] 2004 US	67	S_{Cr} 1.89 mg/dl GFR 41 ml/min	Cardiac catheterization, CT and others	9 mo	60 (69)	59 (68)	Bicarbonate	Normal saline	None	2% (14%)	0.12 (0.02-0.95)	0.02	Good

Outcome	Author Year Country	Age	Baseline kidney function	Procedure	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1	Arm 2					
↑S_{Cr}>0.5 mg /dl or GFR>25% above baseline, 0 d-1 or 2 d	Adolph [2] 2008 Germany	70	S_{Cr} 1.54 mg/dl	Cardiac catheterization	14 d	71 (72)	74 (76)	Bicarbonate	Normal saline	None	4% (3%)	1.56 (0.27-9.08)	NS (0.61)	Good
↑S_{Cr} >25% or 0.5 mg/dl after 48 h	Ozcan [60] 2007 Turkey	69	S_{Cr} 1.39 mg/dl GFR 50 ml/min	Cardiac catheterization	48 h	88 (88)	88 (88)	Bicarbonate	Normal saline	None	5% (14%)	0.33[b] (0.11-0.99)	0.036	Fair
↑ S_{Cr} >25% or 0.5 mg/dl after 48 h adjusted by Mehran risk score											5% (14%)	0.36[b] (0.13-1.02)	0.043	Fair
↑S_{Cr} ≥0.5 mg/dl by 5 d	Maioli [45] 2008 Italy	74	S_{Cr}1.20 mg/dl GFR 42 ml/min	Cardiac catheterization	30 d	250 (250)	252 (252)	Bicarbonate	Normal saline	NAC	10% (12%)	0.87 (0.52-1.44)	NS (0.59)	Good
↑S_{Cr} ≥25% by 5 d											15% (21%)	0.71 (0.49-1.04)	NS (0.08)	Good
↑S_{Cr} ≥25% by 2 d											10% (15%)	0.67 (0.42-1.07)	NS (0.09)	Good
↑S_{Cr} ≥ 0.5 mg/dl in 3 d	Recio-Mayoral [66] 2007 Spain & UK	65	S_{Cr} 1.0 mg/dl GFR 75 ml/min	Cardiac catheterization	7 d	56 (56)	55 (55)	Bicarbonate	Normal saline	NAC	2% (22%)	0.065 (0.008-0.52)	0.0009	Fair
↑S_{Cr} >25%	Briguori [15] 2007 Italy	70	S_{Cr} 1.95 mg/dl GFR 32 ml/min	CAD or peripheral angiography	5 d	108 (117)	111 (118)	Bicarbonate	Normal saline	NAC	2% (10%)	0.19 (0.04-0.82)	0.019	Good
↑S_{Cr} ≥0.5 mg/dl											1% (11%)	0.09 (0.01-0.65)	0.003	Good
↓eGFR ≥25%											1% (9%)	0.10 (0.01-0.79)	0.009	Good
↑S_{Cr} ≥50%	Pakfetrat [61] 2009 Iran	58	S_{Cr} 1.1 mg/dl GFR 72 ml/min	Coronary angiography	48 h	96 (96)	96 (96)	Bicarbonate	Normal saline	nd	4% (17%)	0.25 (0.09-0.72)	0.03	Good
↑S_{Cr} ≥0.5 mg/dl or ↑S_{Cr} >25% by 2 d	Vasheghani-Farahani [89] 2009 Iran	63	S_{Cr} 1.63 mg/dl GFR 46 ml/min	Coronary angiography	5 d	135 (135)	130 (130)	Bicarbonate	Normal saline	nd	7% (6%)	1.24[c] (0.48-3.23)	0.60	Good

Outcome	Author Year Country	Age	Baseline kidney function	Procedure	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1	Arm 2					
↑S_{Cr} ≥0.5 mg/dl or ↑S_{Cr} >25% by 5 d											9% (7%)	1.32[c] (0.55-3.19)	0.60	Good
↑S_{Cr}>25% or >0.5 mg/dl by 3 d	Tamura [81] 2009 Japan	72	S_{Cr} 1.36 mg/dl GFR 40 ml/min	Elective coronary procedure	3 d	72 (72)	72 (72)	Bicarbonate	Normal Saline	None	1% (13%)	0.11 (0.01-0.85)	0.017	Good
↑S_{Cr}>25% or >0.5 mg/dl by 2 d	Rosenstock [70] 2010 US	71	S_{Cr} 1.7 mg/dl GFR 43 ml/min	Cardiac or vascular angiography	2 d	136/142		Bicarbonate	Normal saline + dextrose	None	Total: 2 (1.5%)	--	nd	Poor
↑S_{Cr}≥25% by 5 d	Castini [21] 2010 Italy	70	S_{Cr} 1.59 mg/dl GFR 47 ml/min	Coronary angiography and/or percutaneous coronary intervention	5 d	52 (52)	51 (51)	Bicarbonate _ dextrose	Saline	None	14% (14%)	0.98 (0.37-2.60)	NS	Good
↑S_{Cr} ≥0.5 mg/dl by 5 d											12% (8%)	1.47 (0.44-4.91)	NS	

Annotations:

* Calculated by ERT with raw numbers from original studies when available. When study reported only event rates, calculations were done using percentages.

a. Brar: RR 0.94 (95%CI 0.55-1.60)

b. Ozcan: ↑S_{Cr} >25% or 0.5 mg/dl after 48 hrs, RR 0.30 (0.09-0.97) p=0.036; ↑ S_{Cr} >25% or 0.5 mg/dl after 48 hrs adjusted by Mehran risk score, RR 0.29 (95%CI 0.09-0.96) p=0.043

c. Farahani: ↑S_{Cr} ≥0.5 mg/dl or ↑S_{Cr} >25% on day 2 (ITT): OR 1.26 (0.045-3.5) p=0.060; ↑S_{Cr} ≥0.5 mg/dl or ↑S_{Cr} >25% on day 5 (ITT): OR 1.3 (0.5-3.4) p=0.60

Supplementary table 24: Evidence profile of RCTs examining the effect of NAC vs. placebo on the prevention of CI-AKI

Outcome	# of studies and study design	Total N (treatment)	Methodological quality of studies per outcome	Consistency across studies	Directness of the evidence generalizability/ applicability	Other considerations	Summary of findings		
							Quality of evidence for outcome	Qualitative and quantitative description of effect	Importance of outcome
Mortality	6 RCTs (High)	1476 (798)	No limitations	No important inconsistencies	No uncertainty	Imprecision (-1)[a]	Moderate	Uncertain	Critical
RRT	11 RCTs (High)	2547 (1326)	No limitations	No important inconsistencies	No uncertainty	Imprecision (-1)[a]	Moderate	Uncertain	Critical
CI-AKI	19 RCTs (High)	3755 (1915)	No limitations	Important inconsistencies (-1)[b]	No uncertainty	None	Moderate	Possible benefit. Six studies showed statistically significant benefit while fourteen studies did not.	High
			Balance of potential benefits and harm Possible benefit					Quality of overall evidence Moderate	

Annotations:
a. Low event rates with wide confidence intervals
b. Some show statistically significant benefit while others do not.

Supplementary table 25: Summary table of RCTs examining the effect of NAC vs. placebo on the prevention of CI-AKI

Outcome	Author Year Country	Age	Baseline kidney function	Procedure	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1[d]	Arm 2					
Mortality														
In-hospital	Carbonell [20] 2007 Spain	63	S_{Cr} 0.94 mg/dl GFR:86 ml/min	Cardiac catheterization	nd	107 (107)	109 (109)	NAC	Placebo	i.v. fluids	3% (5%)	0.60 (0.16-2.32)	NS (0.45)	Fair
In-hospital	Marenzi [46] 2006 Italy	63	S_{Cr} 1.06 mg/dl GFR 75 ml/min	Angioplasty	72 h	115 (116)	119 (119)	Standard NAC	Control	i.v. fluids	4% (11%)	0.40 (0.15-1.08)	NS (0.07)	Fair
In-hospital						118 (119)	119 (119)	High-dose NAC	Control	i.v. fluids	3% (11%)	0.23 (0.07-0.80)	0.02	Fair
In-hospital	Miner [52] 2004 Canada	71	S_{Cr} 124 µmol GFR 46 ml/min	Coronary angiography	9 mo	95 (95)	85 (85)	NAC	Placebo	i.v. fluids	0% (2%)	0.18 (0.01-3.68)	NS (nd)	Fair
9 mo											4% (4%)	1.19 (0.27-5.18)	NS (0.81)	Fair
7 d	Rashid [65] 2004 UK	72	S_{Cr} 109 µmol/l GFR 51 ml/min	Angiography or angioplasty	7 d	46 (46)	48 (48)	NAC	Placebo	i.v. fluids	2% (0%)	3.13 (0.13-75)	nd	Fair
In hospital	Reinecke [67] 2007 Germany	67	S_{Cr} 1.4 mg/dl GFR 49 mg/dl	Cardiac catheterization	Median 553 d	114 (146)	115 (140)	NAC	Control	i.v. fluids	1% (1%)	1.01 (0.21-4.89)	NS (0.991)	Fair
30 d											1% (2%)	0.34 (0.04-3.19)	NS (0.342)	Fair
6 d	Gomes [29] 2005 Brazil	64	S_{Cr} 123.76 µmol/l GFR 59 ml/min	Cardiac catheterization	Median 6 d	77 (77)	79 (79)	NAC	Placebo	i.v. fluids	7% (3%)	2.56 (0.51-12.83)	NS (0.42)	Fair
6 mo follow-up	Thiele [83] 2010 Germany	68	S_{Cr} 81 µmol/l CrCl 85 ml/min	PCI	6 mo	126 (126)	123 (125)	NAC	Placebo	i.v. hydration	12 (10%) [12 (10%)]	0.98 (0.46-2.09)	NS	Fair
RRT														
5 d	Briguori [16] 2002 Italy	64	S_{Cr}:1.52 mg/dl GFR 56 ml/min	Coronary or peripheral angiography	5 d	92 (92)	91 (91)	NAC	Control	i.v. fluids	0% (1%)	0.33 (0.01-7.99)	nd	Fair
In CI-AKI patients	Carbonell [20] 2007 Spain	63	S_{Cr} 0.94 mg/dl GFR 86 ml/min	Cardiac catheterization	nd	107 (107)	109 (109)	NAC	Placebo	i.v. fluids	0% (0%)	1.02 (0.02-51)	NS	Fair
7 d	Kay [35] 2003 China	69 (median)	Median S_{Cr} 1.24 mg/dl GFR 45 ml/min	Coronary angiography, coronary angiography and PCI, or PCI	7 d	98 (98)	102 (102)	NAC	Control	i.v. fluids	0% (0%)	1.04 (0.02-52)	nd	Fair

Outcome	Author Year Country	Age	Baseline kidney function	Procedure	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1[d]	Arm 2					
72 h	Marenzi [46] 2006 Italy	63	S_{Cr} 1.06 mg/dl GFR 75 ml/min	Angioplasty	72 h	115 (116)	119 (119)	Standard NAC	Control	i.v. fluids	4% (11%)	0.34 (0.07-1.67)	NS (0.187)	Fair
72 h						118 (119)	119 (119)	High-dose NAC	Control	i.v. fluids	3% (11%)	0.17 (0.02-1.37)	NS (0.09)	Fair
Urgent, in-hospital	Miner [52] 2004 Canada	71	S_{Cr} 124 µmol/l GFR 46 ml/min	Coronary angiography	9 mo	95 (95)	85 (85)	NAC	Placebo	i.v. fluids	1% (0%)	2.69 (0.11-65)	NS	Fair
Long-term											1% (1%)	0.89 (0.06-14.09)	NS (0.937)	Fair
7 d	Rashid [65] 2004 UK	72	S_{Cr} 109 µmol/l GFR 51 ml/min	Angiography or angioplasty	7 d	46 (46)	48 (48)	NAC	Placebo	i.v. fluids	0% (2%)	0.35 (0.01-8.32)	nd	Fair
7 d	Shyu [77] 2002 Taiwan	70	S_{Cr} 2.8 ml/min GFR 24 mg/dl	Coronary angiography	7 d	60 (60)	61 (61)	NAC	Placebo	i.v. fluids	0% (2%)	0.34 (0.01-8.16)	nd	Fair
8 d	Webb [91] 2004 Canada	71	S_{Cr} 141 µmol/l GFR 44 ml/min	Cardiac catheterization or percutaneous coronary intervention	8 d	242 (242)	245 (245)	NAC	Placebo	i.v. fluids	3% (2%)	1.50 (0.48-4.65)	NS (0.483)	Fair
In hospital	Reinecke [67] 2007 Germany	67	S_{Cr} 1.4 mg/dl GFR 49 mg/dl	Cardiac catheterization	Median 553 d	114 (146)	115 (140)	NAC	Control	i.v. fluids	2% (1%)	1.01 (0.06-15.93)	NS (0.995)	Fair
6 d	Gomes [29] 2005 Brazil	64	S_{Cr} 123.76 µmol/l GFR 59 ml/min	Cardiac catheterization	Median 6 d	77 (77)	79 (79)	NAC	Placebo	i.v. fluids	3% (0%)	5.13 (0.25-105)	NS (0.24)	Fair
30 d	Ochoa [58] 2004 US	73	S_{Cr} 2.02 mg/dl	Cardiac catheterization	30 d	36 (36)	44 (44)	NAC	Placebo	i.v. fluids	0% (0%)	1.22 (0.02-60)	nd	Poor
RRT	Thiele [83] 2010 Germany	68	S_{Cr} 81 µmol/l CrCl 85 ml/min	PCI	6 mo	126 (126)	123 (125)	NAC	Placebo	i.v. hydration	4 (3%) [1 (1%)]	3.90 (0.44-34.45)	NS (0.37)	Fair
CI-AKI														
↑S_{Cr} >0.5 mg/dl by 48 h	Boccalandro [11] 2003 US	66	S_{Cr} 1.8 mg/dl GFR 54 ml/min	Cardiac catheterization	48 h	73 (73)	105 (106)	NAC	Placebo	i.v. fluids	13% (12%)	1.11 (0.51-2.39)	NS (0.84)	Fair
↑S_{Cr} >25% by 48 h	Briguori [16] 2002 Italy	64	S_{Cr} 1.52 mg/dl GFR 56 ml/min	Coronary or peripheral angiography	5 d	92 (92)	91 (91)	NAC	Control	i.v. fluids	7% (11%)	0.59 (0.23-1.57)	NS (0.22)	Fair
↑S_{Cr} ≥0.5 mg/dl or	Carbonell [20] 2007	63	S_{Cr} 0.94 mg/dl GFR 86 ml/min	Cardiac catheterization	nd	107 (107)	109 (109)	NAC	Placebo	i.v. fluids	10% (10%)	1.02 (0.46-2.25)	NS (0.5)	Good

Outcome	Author Year Country	Age	Baseline kidney function	Procedure	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1[d]	Arm 2					
>25% by 48 h	Spain													
↑S_{Cr} >25% by 48 h	Kay [35] 2003 China	69 (median)	Median S_{Cr} 1.24 mg/dl GFR 45 ml/min	Coronary angiography, coronary angiography and PCI, or PCI	7 d	98 (98)	102 (102)	NAC	Control	i.v. fluids	4% (12%)	0.35[a] (0.12-1.04)	0.03	Good
↑S_{Cr} ≥25% by 72 h	Marenzi [46] 2006 Italy	63	S_{Cr} 1.06 mg/dl GFR 75 ml/min	Angioplasty	72 h	115 (116)	119 (119)	Standard NAC	Control	i.v. fluids	15% (33%)	0.45 (0.27-0.75)	0.002	Good
↑S_{Cr} ≥25% by 72 h						118 (119)	119 (119)	High-dose NAC	Control	i.v. fluids	8% (33%)	0.26 (0.14-0.49)	<0.001	Good
↑S_{Cr} ≥25% by 48-72 h	Miner [52] 2004 Canada	71	S_{Cr} 124 µmol/l GFR 46 ml/min	Coronary angiography	9 mo	95 (95)	85 (85)	NAC	Placebo	i.v. fluids	10% (22%)	0.45 (0.22-0.94)	0.04	Fair
↑S_{Cr} >25% by 2 d	Poletti [63] 2007 Switzerland	70	S_{Cr} 146 µmol/l	CT scans	7 d	44 (50)	43 (50)	NAC	Placebo	i.v. fluids	5% (21%)	0.28 (0.06-1.27)	0.02	Good
↑S_{Cr} ⩾0.5 mg/dl or >25% by 48 h	Rashid [65] 2004 UK	72	S_{Cr} 109 µmol/l GFR 51 ml/min	Angiography or angioplasty	7 d	46 (46)	48 (48)	NAC	Placebo	i.v. fluids	6% (6%)	0.89 (0.17-4.65)	NS (0.89)	Good
↑S_{Cr} 0.5 mg/dl by 48 h	Shyu [77] 2002 Taiwan	70	S_{Cr} 2.8 ml/min GFR 24 mg/dl	Coronary angiography	7 d	60 (60)	61 (61)	NAC	Placebo	i.v. fluids	3% (25%)	0.13 (0.08-0.20)	<0.001	Good
↓GFR >5 ml/min by 2-8 d	Webb [91] 2004 Canada	71	S_{Cr} 141 µmol/l GFR 44 ml/min	Cardiac catheterization or percutaneous coronary intervention	8 d	242 (242)	245 (245)	NAC	Placebo	i.v. fluids	23% (21%)	1.10 (0.78-1.53)	NS (0.594)	Good
↑S_{Cr} ≥0.5 mg/dl by 24 h	Reinecke [67] 2007 Germany	67	S_{Cr} 1.4 mg/dl GFR 49 mg/dl	Cardiac catheterization	Median 553 d	140 (146)	137 (140)	NAC	Control	i.v. fluids	3% (6%)	1.12 (0.42-3.00)	NS (0.824)	Fair
↑S_{Cr} ≥44.2 µmol/l by 48 h	Gomes [29] 2005 Brazil	64	S_{Cr} 123.76 µmol/l GFR 59 ml/min	Cardiac catheterization	Median 6 d	77 (77)	79 (79)	NAC	Placebo	i.v. fluids	10% (10%)	1.03 (0.41-2.60)	NS (1.00)	Good
↑S_{Cr} 0.5 mg/dl or	Kefer [36] 2003	61	S_{Cr} 1.10 mg/dl	Cardiac catheterization	24 h	53 (53)	51 (51)	i.v. NAC	Placebo	i.v. fluids	4% (5%)	0.64 (0.11-3.68)	NS (0.98)	Fair

Outcome	Author Year Country	Age	Baseline kidney function	Procedure	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1[d]	Arm 2					
25%	Belgium													
↑S_{Cr} ≥0.5 mg/dl or >25% by 48 h	Ochoa [58] 2004 US	73	S_{Cr} 2.02 mg/dl	Cardiac catheterization	30 d	36 (36)	44 (44)	NAC	Placebo	i.v. fluids	8% (25%)	0.33[b] (0.10-1.10)	0.05	Poor
↑S_{Cr} ≥0.5 mg/dl or >25% by 48 h	Ozcan [60] 2008 Turkey	69	S_{Cr} 1.39 mg/dl GFR 50 ml/min	Cardiac catheterization	48 h	88 (88)	88 (88)	NAC	Control	i.v. fluids	13% (14%)	0.93[c] (0.44-1.96)	NS (0.82)	Fair
↑S_{Cr} 0.5 mg/dl by 48 h	Baskurt [8] 2009 Turkey	67	S_{Cr} 1.3 mg/dl GFR 51 ml/min	Cardiac catheterization	10 d	73 (73)	72 (72)	NAC	Control	i.v. fluids	10% (7%)	1.38 (0.46-4.15)	NS	Good
↑S_{Cr} >0.5 mg/dl or >25% by 72 h	Ferrario [27] 2009 Italy	75	GFR 40 ml/min	Cardiac catheterization or peripheral angiography	72 h	99 (103)	101 (104)	NAC	Placebo	i.v. fluids	8 (8%) [6 (6%)]	1.36 (0.49-3.78)	NS (0.9)	Good
↑S_{Cr} ≥0.5 mg/dl or >25% by 48 h	Kim [37] 2010 Korea	62	S_{Cr} 1.03 mg/dl	Cardiac catheterization	48 h	80 (80)	86 (86)	NAC	Placebo	NS	3 (4%) [7 (8%)]	0.46 (0.12-1.72)	NS (0.235)	Fair
↑S_{Cr} ≥25% by 72 h	Thiele [83] 2010 Germany	68	S_{Cr} 81 µmol/l CrCl 85 ml/min	PCI	6 mo	126 (126)	123 (125)	NAC	Placebo	i.v. hydration	18 (14%) [25 (20%)]	0.70 (0.40-1.22)	NS (0.28)	Good
CIN in patients with CrCl ≤60 ml/min			CrCl ≤60 ml/min			24 (126)	23 (125)				25%[e] (13%)	1.92 (0.54-6.77)	NS (0.46)	Good
CIN in patients with CrCl >60 ml/min			CrCl >60 ml/min			102 (126)	100 (125)				10%[e] (20%)	0.49 (0.24-0.99_	NS (0.08)	Good
↑S_{Cr}≥25% by 5 d	Castini [21] 2010 Italy	71	S_{Cr} 1.57 mg/dl GFR 49 ml/min	Coronary angiography and/or percutaneous coronary intervention	5 d	53 (53)	51 (51)	NAC	Saline	None	17% (14%)	1.24 (0.50-3.07)	NS	Good
↑S_{Cr} ≥0.5 mg/dl by 5 d											9% (8%)	1.20 (0.34-4.23)	NS	

Annotations:

* Calculated by ERT with raw data from original studies when available. When study reported only event rates, calculations were done using percentages.

a. Kay: ↑S_{Cr} >25% by 48 h, RR 0.32 (95% CI 0.10-0.96)
b. Ochoa: ↑S_{Cr} ≥0.5 mg/dl or >25% by 48 h, RR 3.7 (95% CI 0.94-14.4)
c. Ozcan: ↑S_{Cr} ≥0.5 mg/dl or >25% by 48 h, RR 0.95 (95% CI 0.37-2.17)
d. NAC was administered orally unless otherwise noted
e. Estimated from figure

Supplementary table 26: Evidence profile of RCTs examining the effect of theophylline vs. placebo on the prevention of CI-AKI

Outcome	# of studies and study design	Total N (treatment)	Methodological quality of studies per outcome	Consistency across studies	Directness of the evidence generalizability/ applicability	Other considerations	Summary of findings		
							Quality of evidence for outcome	Qualitative and quantitative description of effect	Importance of outcome
Mortality	0 RCTs	--	--	--	--	--	--	--	Critical
RRT	1 RCT (High)	157 (80)	No limitations	No important inconsistencies	No uncertainty	Sparse (-1) Imprecise (-1)	Low	Uncertain	Critical
CI-AKI	4 RCTs (High)	502 (252)	No limitations	Important inconsistencies (-1)[a]	No uncertainty	Sparse (-1)	Low	Uncertain	High (Crucial)
		Balance of potential benefits and harm Uncertain						Quality of overall evidence Low	

Annotations:

a. Two studies by Huber [31;32] and one by Baskurt [8] showed benefit while one study did not (Dussol).

Supplementary table 27: Summary table of RCTs examining the effect of theophylline vs. placebo on the prevention of CI-AKI

Outcome	Author Year Country	Age	Baseline kidney function	Procedure	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication	Event rate Arm 1 (Arm 2)	RR* (95% CI)	P value	Quality
						Arm 1	Arm 2	Arm 1	Arm 2					
RRT														
RRT	Dussol [23] 2006 France	65	S_{Cr} 214 µmol/l GFR 35 ml/min	Coronary angiography (36%)	2 d	80 (80)	77 (77)	Theophylline	Control	i.v. fluids	0% (0%)	0.96 (0.02-47.91)	nd	Good
CI-AKI														
↑S_{Cr} ≥0.5 mg/dl by 48 hrs	Huber [31] 2002 Germany	67	S_{Cr} 2.07 mg/dl	70% i.a.; 30% i.v.	2 d	50 (50)	50 (50)	Theophylline	Placebo	i.v. fluids, NAC in 20%	4% (16%)	0.25 (0.06-1.12)	0.046	Good
↑S_{Cr} ≥0.5 mg/dl by 48 hrs	Huber [32] 2003 Germany	68	S_{Cr} 1.65 mg/dl	Coronary angiography	2 d	50 (50)	50 (50)	Theophylline	Placebo	i.v. fluids	4% (20%)	0.20 (0.05-0.87)	0.0138	Good
S_{Cr} ≥0.5 mg/dl by 48 h	Dussol [23] 2006 France	65	S_{Cr} 214 µmol/l GFR 35 ml/min	Coronary angiography (36%)	2 d	80 (80)	77 (77)	Theophylline	Control	i.v. fluids	8% (5%)	1.44 (0.42-4.92)	NS	Good
S_{Cr} ≥1.0 mg/dl by 48 h											3% (1%)	1.93 (0.18-20.80)		
↑S_{Cr} ≥0.5 mg/dl by 48 h	Baskurt [8] 2009 Turkey	67	S_{Cr} 1.3 mg/dl GFR 51 ml/min	Cardiac catheterization	10 d	72 (72)	73 (73)	Theophylline	Control	NAC	0% (10%)	0.07 (0.00-1.16)	nd	Good

Annotations:

* Calculated by ERT with raw numbers from original studies when available. When study reported only event rates, calculations were done using percentages.

Supplementary table 28: Evidence profile of RCTs examining the effect of hemodialysis or hemofiltration on the prevention of CI-AKI

Outcome	# of studies and study design	Total N (treatment)	Methodological quality of studies per outcome	Consistency across studies	Directness of the evidence generalizability/ applicability	Other considerations	Summary of findings		
							Quality of evidence for outcome	Qualitative and quantitative description of effect	Importance of outcome
Mortality	4 RCTs (High)	514 (256)	No limitations	Important inconsistencies (-1)	No uncertainty	Imprecision (-1)[a]	Low	Uncertain. Two studies by Marenzi [47;48] showed benefit for HF (either post or pre/post dye). Two other studies showed no benefit.	Critical
RRT	5 RCTs (High)	596 (298)	No limitations	Important inconsistencies (-1)	No uncertainty	Imprecision (-1)[a]	Low	Uncertain. Two studies by Marenzi [47;48] and one by Lee [43] showed benefit for HF (either post or pre/post dye). Two other studies showed no benefit.	Critical (Crucial)
		Balance of potential benefits and harm Uncertain						Quality of overall evidence Low	

Annotations:

a. Wide confidence intervals

Supplementary table 29: Summary table of RCTs examining the effect of hemodialysis or hemofiltration on the prevention of CI-AKI

Outcome	Author Year Country	Age	Baseline kidney function	Procedure	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1	Arm 2					
Mortality														
In-hospital	Marenzi [48] 2003 Italy	69	S_{Cr} 3.0 mg/dl GFR 26 ml/min	Cardiac catheterization or PTCA and stenting	12 mo	58 (58)	56 (56)	HF	Isotonic saline	None	2% (14%)	0.12 (0.02-0.93)	0.02	Fair
12 mo											10% (30%)	0.34 (0.14-0.80)	0.01	Fair
6 d	Vogt [90] 2001 Switzerland	69	S_{Cr} 308 µmol/l GFR 20 ml/min	Renal angioplasty, peripheral angioplasty, computerized tomography, cardiac catheterization, or other	6 d	54 (55)	57 (58)	HD	No HD	Isotonic saline	2% (2%)	1.06 (0.07-16)	NS (1.00)	Fair
In-hospital	Reiniecke [67] 2007 Germany	67	S_{Cr} 1.4 mg/dl GFR 49 mg/dl	Cardiac catheterization	18 mo	113 (138)	115 (140)	HD	No HD	Isotonic saline & D/5	2% (1%)	3.05 (0.32-29)	NS (0.33)	Fair
30 d											2% (2%)	1.02 (0.21-4.94)	NS (0.98)	Fair
In-hospital	Marenzi [47] 2006 Italy	71	S_{Cr} 3.6 mg/dl GFR 20 ml/min	Aortic angiography, peripheral angioplasty, renal angioplasty, others	3 d	31 (31)	30 (30)	Pre/post HF	Control	Isotonic saline	0% (20%)	0.07 (0.00-1.27)	nd	Fair
In-hospital						31 (31)	30 (30)	Post HF	Control	Isotonic saline	10% (20%)	0.48 (0.13-1.76)	nd	Fair
RRT														
RRT until hospital discharge	Marenzi [48] 2003 Italy	69	S_{Cr} 3.0 mg/dl GFR 26 ml/min	Cardiac catheterization or PTCA and stenting	12 mo	58 (58)	56 (56)	HF	Isotonic saline hydration	None	3% (25%)	0.14 (0.03-0.58)	<0.001	Fair
RRT at 12 mo											2% (5%)	0.32 (0.03-3.00)	0.01	Fair
Additional RRT within 6 d	Vogt [90] 2001 Switzerland	69	S_{Cr} 308 µmol/l GFR 20 ml/min	Renal angioplasty, peripheral angioplasty, computerized tomography, cardiac catheterization, or other	6 d	54 (55)	57 (58)	HD	No HD	Isotonic saline hydration	15% (5%)	2.81 (0.79-10)	NS (0.12)	Fair
Additional RRT during hospitalization	Reiniecke [67] 2007 Germany	67	S_{Cr} 1.4 mg/dl GFR 49 mg/dl	Cardiac catheterization	18 mo	113 (138)	115 (140)	HD	No HD	Isotonic saline & D/5	2% (1%)	3.05 (0.32-29)	NS (0.33)	Fair

Outcome	Author Year Country	Age	Baseline kidney function	Procedure	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1	Arm 2					
Additional RRT during hospitalization	Lee [43] 2007 Taiwan	65	S_{Cr} 4.9 mg/dl CrCl 13 ml/min	Cardiac catheterization	10 d (mean)	42 (42)	40 (40)	HD	Control	Isotonic saline	2% (35%)	0.07 (0.01-0.49)	0.001	Good
RRT at hospital discharge											0% (13%)	0.09 (0.00-1.52)	0.018	Good
Additional RRT during hospitalization	Marenzi [47] 2006 Italy	71	S_{Cr} 3.6 mg/dl GFR 20 ml/min	Aortic angiography, peripheral angioplasty, renal angioplasty, others	3 d	31 (31)	30 (30)	Pre/post HF	Control	Isotonic saline	0% (30%)	0.05 (0.00-0.84)	nd	Fair
Additional RRT during hospitalization						31 (31)	30 (30)	Post HF	Control	Isotonic saline	10% (30%)	0.32 (0.10-1.08)	NS (0.06)	Fair

Annotations:

* Calculated by ERT with raw numbers from original studies when available. When study reported only event rates, calculations were done using percentages.

∞Calculated estimate was same as estimate reported in the study.

Supplementary table 30: Summary table of RCTs examining the effect of early vs. late CVVH in the treatment of AKI

Outcome	Author Year Country	Age	Baseline kidney function	Setting	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication/ therapy	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1	Arm 2					
Mortality														
28 d survival	Bouman [12] 2002 Netherlands	68	CrCl 68 ml/min	ICU	28 d	35 (35)	36 (36)	Early low volume HF (24-36 l/d) [20 ml/kg/h]	Late low volume HF (24-36 l/d) [19 ml/kg/h]	nd	31% (25%)	1.24 (0.58-2.63)	nd	Fair
ICU survival					Mean 12 d in survivors			Early low volume HF (24-36 l/d) [20 ml/kg/h]	Late low volume HF ((24-36 l/d) [19 ml/kg/h]		37% (31%)	1.19 (0.62-2.29)	nd	Fair
Hospital survival								Early low volume HF (24-36 l/d) [20 ml/kg/h]	Late low volume HF (24-36 l/d) [19 ml/kg/h]		51% (39%)	1.31 (0.78-2.20)	nd	Fair
Kidney function														
Median duration of renal failure (days)	Bouman [12] 2002 Netherlands	68	CrCl 68 ml/min	ICU	nd	35 (35)	36 (36)	Early low volume HF (24-36 l/d) [20 ml/kg/h]	Late low volume HF (24-36 l/d) [19 ml/kg/h]	nd	5.7 (6.6)	IQR 2-6-12.7 (2.9-12.2)	nd	Fair
Duration of renal failure in hospital survivors (days)								Early low volume HF (24-36 l/d) [20 ml/kg/h]	Late low volume HF (24-36 l/d) [19 ml/kg/h]		3.2 (5.6)	IQR 2.4-5.4 (3.1-8.5)	nd	Fair

Annotations:
* Calculated by ERT with raw data from original studies when available. When study reported only event rates, calculations were done using percentages.

Supplementary table 31: Evidence profile of RCTs examining the effect of citrate vs. heparin/nadroparin in CRRT for AKI

Outcome	# of studies and study design	Total N (treatment)	Methodological quality of studies per outcome	Consistency across studies	Directness of the evidence generalizability/ applicability	Other considerations	Summary of findings		
							Quality of evidence for outcome	Qualitative and quantitative description of effect	Importance of outcome
Hemofilter survival	4 RCTs (High)	298 (142)	Some limitations (-1)[a]	Important inconsistencies (-1)	No uncertainty	None	Low	Two studies showing benefit for citrate vs. heparin. One study of citrate vs. heparin showed no difference. One study of citrate vs. nadroparin showed no difference.	High
Bleeding	4 RCTs (High)	298 (142)	Some limitations (-1)[a]	No important inconsistencies	No uncertainty	None	Moderate	Benefit with less bleeding in the citrate arms.	Critical (Crucial)
Transfusions	3 RCTs (High)	278 (134)	Some limitations (-1)[a]	Important inconsistencies (-1)	No uncertainty	None	Low	On average, no difference in 3 studies. One study with statistically significant difference.	High
Metabolic complications	4 RCTs (High)	298 (142)	Some limitations (-1)[a]	No important inconsistencies	No uncertainty	None	Moderate	Calcium was lower and bicarbonate was higher in the citrate arms compared to the heparin arms.	High
Balance of potential benefits and harm Benefit for citrate compared to heparin with less bleeding and better circuit survival. With citrate, lower calcium and higher bicarbonate level.							Quality of overall evidence Moderate		

Annotation:

a. Relatively small number of patients and/or circuits.

Supplementary table 32: Summary table of RCTs examining the effect of citrate vs. heparin/nadroparin in CRRT for AKI

Outcome	Author Year Country	Age	Baseline kidney function	Setting	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication/ therapy	Categorical outcomes	Continuous outcomes	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1	Arm 2						
Hemofilter survival															
Hemofilter failure	Kutsogiannis [41] 2000 Canada	67	Highest S_{Cr} 335 µmol/l	ICU	nd	16 (16) [36 circuits]	14 (14) [43 circuits]	Citrate	Heparin	None	33% (58%)	--	0.57 (0.34-0.97)	nd	Fair
Hemofilter survival time, h											--	125 (38)	--	<0.001	Fair
Hemofilter clotting											17% (54%)	--	0.31[c] (0.14-0.68)	0.002	Fair
Median circuit survival time, h	Monchi [53] 2004 Belgium	67	S_{Cr} 28.5 mg/l	ICU	Maximum of 10 d per patient	8 (8) [26 circuits]	12 (12) [23 circuits]	Citrate	Heparin	None	--	70 (40)	--[d]	0.0007	Fair
Rate of spontaneous circuit failure											57% (87%)	--	0.66 (0.45-0.95)	0.03	Fair
Median circuit survival time, h											--	140 (45)	--	<0.0001	Fair
Median circuit survival time until clotting, h	Betjes [10] 2007 Netherlands	58	S_{Cr} 574 mmol/l	ICU	Maximum of 9 d per patient	21 (21) [70 circuits]	27 (27) [72 circuits]	Citrate	Heparin	None	--	36 (38)	--	nd	Fair
Median circuit survival time, h	Oudemans-van Straaten [59] 2009 Netherlands	73	S_{Cr} 2.3 mg/dl	ICU	3 mo	97 (107)[f]	103 (108)[f]	Citrate	Nadroparin	Per protocol	--	27 (26)	--[e]	NS (0.68)	Good
Bleeding															
Incidence of definite/occult hemorrhage	Kutsogiannis [41] 2000 Canada	67	Highest S_{Cr} 335 µmol/l	ICU	nd	16 (16)	14 (14)	Citrate	Heparin	None	0.01 (0-0.04) [0.13 (0.04-0.23)]	--	--[c]	0.06	Fair
Major bleeding	Monchi [53] 2004 Belgium	67	S_{Cr} 28.5 mg/l	ICU	Maximum of 10 d per patient	8 (8) [26 circuits]	12 (12) [23 circuits]	Citrate	Heparin	None	0% (8%)	--	0.49 (0.02-10.66)	nd	Fair
Major bleeding	Betjes [10] 2007 Netherlands	58	S_{Cr} 574 mmol/l	ICU	Maximum of 9 d per patient	21 (21) [70 circuits]	27 (27) [72 circuits]	Citrate	Heparin	None	0% (37%)	--	0.06 (0.00-0.98)	<0.01	Fair

Outcome	Author Year Country	Age	Baseline kidney function	Setting	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication/ therapy	Categorical outcomes	Continuous outcomes	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1	Arm 2						
Bleeding	Oudemans-van Straaten [59] 2009 Netherlands	73	S_{Cr} 2.3 mg/dl	ICU	3 mo	97 (107)	103 (108)	Citrate	Nadroparin	Per protocol	6% (16%)	--	0.40 (0.16-0.98)	0.08	Good
Transfusions															
RBC transfusions	Kutsogiannis [41] 2000 Canada	67	Highest S_{Cr} 335 µmol/l	ICU	nd	16 (16)	14 (14)	Citrate	Heparin	None	0.17 (0.10-0.25) [0.33 (0.18-0.49)]	--	-- [c]	NS (0.13)	Fair
RBC transfusion per CVVH day	Betjes [10] 2007 Netherlands	58	S_{Cr} 574 mmol/l	ICU	Maximum of 9 d per patient	21 (21) [70 circuits]	27 (27) [72 circuits]	Citrate	Heparin	None	0.43 (0.88)	--	--	0.01	Fair
RBC transfusion during CVVH period	Oudemans-van Straaten [59] 2009 Netherlands	73	S_{Cr} 2.3 mg/dl	ICU	3 mo	97 (107)	103 (108)	Citrate	Nadroparin	Per protocol	56 (62)	--	0.96 (0.76-1.21)	NS (0.89)	Good
RBC transfusion per CVVH day											0.27 (0.36)	--	--	NS (0.31)	Good
Metabolic complications															
Hypocalcemia	Kutsogiannis [41] 2000 Canada	67	Highest S_{Cr} 335 µmol/l	ICU	nd	16 (16)	14 (14)	Citrate	Heparin	None	13% (0%)	--	4.39 (0.23-84.23)	nd	Fair
Metabolic alkalosis											19% (0%)	--	6.15 (0.35-109.37)	nd	Fair
Hypocalcemia	Monchi [53] 2004 Belgium	67	S_{Cr} 28.5 mg/l	ICU	Maximum of 10 d per patient	8 (8) [26 circuits]	12 (12) [23 circuits]	Citrate	Heparin	None	13% (0%)	--	4.41 (0.20-953.97)	nd	Fair
Metabolic alkalosis											13% (0%)	--	4.41 (0.20-953.97)	nd	Fair
Hypocalcemia	Betjes [10] 2007 Netherlands	58	S_{Cr} 574 mmol/l	ICU	Maximum of 9 d per patient	21 (21) [70 circuits]	27 (27) [72 circuits]	Citrate	Heparin	None	10% (0%)	--	6.40 (0.32-126.36)	nd[b]	Fair

Outcome	Author Year Country	Age	Baseline kidney function	Setting	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication/ therapy	Categorical outcomes	Continuous outcomes	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1	Arm 2						
Hypocalcemia	Oudemans-van Straaten [59] 2009 Netherlands	73	S_{Cr} 2.3 mg/dl	ICU	3 mo	97 (107)	103 (108)	Citrate	Nadroparin	Per protocol	[a]	--	--	<0.001	Good

Annotations:

* Calculated by ERT with raw numbers from original studies when available. When study reported only event rates, calculations were done using percentages.

a. Initial hypocalcemia was less often corrected in the citrate group.

b. The mean ionized calcium concentration was slightly lower in the citrate arm. 2 hypocalcemic episodes in the citrate arm without apparent clinical problems which could be rapidly reversed.

c. Kutsogiannis: Hemofilter clotting: HR 0.37 (95% CI 0.20-0.70); Incidence of definite/occult bleeding: RR 0.17 (95% CI 0.03-1.04); RBC transfusion: RR 0.53 (95% CI 0.24-1.20)

d. Monchi: Median circuit survival time: IQR 44-140 (17-48)

e. Oudesman: Median circuit survival time: IQR 13-47 (15-43)

f. Median time on CVVH per patients was 58 and 63 hours for citrate vs. nadroparin respectively.

Supplementary table 33: Summary table of RCTs examining the effect of access placement with tunneled versus non-tunneled catheters on AKI

Outcome	Author Year Country	Age	Baseline kidney function	Setting	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication/ therapy	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1	Arm 2					
Catheter related complications and performance														
Insertion failure	Klouche [38] 2006 France	61	nd	ICU	Mean dialysis 12 d	15[a] (19)	15[a] (15)	Tunneled femoral catheter	Non-tunneled femoral catheter	CVVHDF, IHD with LMWH anticoagulation	27% (0%)	9.00 (0.53-153.38)	<0.01	Poor
Elapsed time for catheter insertion in min											46 (23)	--	<0.05	Poor
Hematomas											27% (7%)	4.00 (0.50-31.74)	<0.05	Poor
Thrombosis											0% (7%)	0.33 (0.01-7.57)	<0.05	Poor
Infections											0% (13%)	0.20 (0.01-3.84)	<0.05	Poor
Interruptions due to catheter dysfunction											13% (40%)	0.33 (0.08-1.39)	<0.05	Poor
Need for reversal catheter											33% (67%)	0.50 (0.22-1.11)	<0.05	Poor
Blood flow rate %											0.99 (0.99)	--	NS	Poor
Recirculation rate %											9.4 (11.1)	--	NS	Poor
Blood flow rate (RVP/eQB)											0.62 (0.69)	--	<0.01	Poor
Prescribed Kt/V											1.2 (1.3)	--	NS	Poor
Delivered Kt/V											1.2 (1.1)	--	NS	Poor
Ratio of prescribed to delivered Kt/V											106 (90)	--	<0.05	Poor
Clearance ratio %											88 (82)	--	<0.05	Poor

Outcome	Author Year Country	Age	Baseline kidney function	Setting	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication/ therapy	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1	Arm 2					
Catheter survival														
Catheters needed per patient	Klouche [38] 2006 France	61	nd	ICU	Mean dialysis 12 d	15[a] (19)	15[a] (15)	Tunneled femoral catheter	Non-tunneled femoral catheter	CVVHDF, IHD with LMWH anticoagulation	1 (1.86)	--	<0.05	Poor
Catheter survival rate at middle of dialysis time											100% (65%)	1.50 (1.05-2.15)	<0.05	Poor
Catheter survival rate at 10 d use											100% (40%)	2.50 (1.35-4.65)	<0.05	Poor

Annotations:

*Calculated by ERT with raw data from original studies when available. When study reported only event rates, calculations were done using percentages.

a. Number of actual dialysis sessions in each arm was 89 IHD sessions and 42 CVVHDF sessions in the tunneled catheter arm and 63 IHD sessions 51 CVVHDF sessions in the non-tunneled arm. However, the number of sessions analyzed was 75 IHD sessions and 42 CVVHDF sessions in the tunneled arm and 40 IHD sessions and 46 CVVHDF sessions in the non-tunneled arm.

Supplementary table 34: Summary table of RCTs examining the effect of jugular vs. femoral access placement on AKI

Outcome	Author Year Country	Age	Baseline kidney function	Setting	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication/ therapy	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1	Arm 2					
Procedure-related outcomes														
Ultrasound-guided insertion	Parienti [62] 2008 France	65	nd	ICU	nd	366 (375)	370 (375)	Jugular	Femoral	nd	2% (0%)	15.16 (0.87-265)	NS	Good
No of attempts (median)											1 (1-2) [1 (1-2)]	--	NS	Good
Mean time required for insertion (min)											15 (13)	--	NS	Good
First attempt of the right side											71% (57%)	1.24 (1.11-1.38)	NS	Good
Failure on 1st side											9% (5%)	1.91 (1.10-3.32)	0.02	Good
Crossover											5% (2%)	2.27 (1.00-5.17)	0.05	Good
Days of insertion											7 (6)	--	NS	Good
Rate of arterial puncture											5% (4%)	1.58 (0.74-2.95)	NS	Good
Rate of hematoma formation											4% (1%)	3.29 (1.08-9.98)	0.03	Good
Infectious complications														
Incidence of catheter colonizations/1000 catheter days	Parienti [62] 2008 France	65	nd	ICU	nd	366 (375)	370 (375)	Jugular	Femoral	nd	35.7 (40.8)	[a]	NS (0.31)	Good
Incidence of catheter related blood stream infections /1000 catheter days											2.3 (1.5)	--	NS (0.42)	Good
Thrombosis														
Symptomatic deep vein thrombosis	Parienti [62] 2008 France	65	nd	ICU	nd	75 (375)	76 (375)	Jugular	Femoral	nd	1% (1%)	1.01 (0.14-7.14)	NS	Good
Rates of thrombosis											23% (11%)	2.15 (0.99-4.69)	NS (0.16)	Good

Annotations:
*Calculated by ERT with raw data from original studies when available. When study reported only event rates, calculations were done using percentages.
a. Hazards ratio: 0.85 (95% CI 0.62-1.16)

Supplementary table 35: Summary table of RCTs examining the effect of dialysis modality (continuous vs. intermittent RRT) in AKI

Outcome	Author Year Country	Age	Baseline Kidney function	Setting	Study Duration	No. analyzed (No randomized)		Intervention/Control		Concomitant Medication/ Therapy	Event Rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1 prescribed [delivered]	Arm 2 prescribed [delivered]					
Mortality														
In-hospital	Gabriel [28] 2008 Brazil	64	S_{Cr} 5.8 mg/dl	ICU & non-ICU	In-hospital	60 (60)	60 (60)	HVPD Kt/V 0.65 [Kt/V 3.6]	HD Kt/V 1.2 [Kt/V 4.7]	nd	58% (53%)	1.09 (0.80-1.50)	NS (0.48)	Fair
AKI														
Recovery of kidney function in survivors	Gabriel [28] 2008 Brazil	64	S_{Cr} 5.8 mg/dl	ICU & non-ICU	In-hospital	60 (60)	60 (60)	HVPD Kt/V 0.65 [Kt/V 3.6]	HD Kt/V 1.2 [Kt/V 4.7]	nd	83% (77%)	1.09 (0.91-1.30)	NS (0.84)	Poor
Recovery of kidney function														
Resolution of AKI in survivors (d)	Gabriel [28] 2008 Brazil	64	S_{Cr} 5.8 mg/dl	ICU & non-ICU	In-hospital	60 (60)	60 (60)	HVPD Kt/V 0.65 [Kt/V 3.6]	HD Kt/V 1.2 [Kt/V 4.7]	nd	7.2 (10.6)	--	0.04	Poor

Annotations:
*Calculated by ERT with raw data from original studies when available. When study reported only event rates, calculations were done using percentages.

Supplementary table 36: Summary table of RCTs examining the effect of bicarbonate vs. lactate as buffer for CVVH replacement fluid on acidosis in AKI

Outcome	Author Year Country	Age	Baseline kidney function	Setting	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication/ therapy	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1	Arm 2					
Metabolic														
Blood HCO_3 level, mmol/l	Barenbrock [6] 2000 Germany	59	S_{Cr} 3.3 mg/dl	ICU	5 d	61 (61)	56 (56)	Bicarbonate buffer	Lactate buffer	Heparin and vasopressors	23.7 (21.8)	--	<0.01	Good
Blood lactate level, mg/dl											17.4 (28.7)	--	<0.05	Good
i.v. Bicarbonate, mmol/ml/24 h											13 (68)	--	<0.01	Good
Events														
Hypotensive episodes, mean no of events per 24 h	Barenbrock [6] 2000 Germany	59	S_{Cr} 3.3 mg/dl	ICU	5 d	61 (61)	56 (56)	Bicarbonate buffer	Lactate buffer	Heparin and vasopressors	0.26 (0.60)	--	<0.005	Fair
CV events											15% (38%)	0.39 (0.20-0.79)	<0.01	Poor

Annotations:
*Calculated by ERT with raw data from original studies when available. When study reported only event rates, calculations were done using percentages.

Supplementary table 37: Evidence profile of RCTs examining the effect of dose of continuous and intermittent RRT on AKI

Outcome	# of studies and study design	Total N (treatment)	Methodological quality of studies per outcome	Consistency across studies	Directness of the evidence generalizability/ applicability	Other considerations	Summary of findings		
							Quality of evidence for outcome	Qualitative and quantitative description of effect	Importance of outcome
Mortality	7 RCTs (High)	3635 (1881)	No limitations	Important inconsistencies (-1)[a]	Direct	None	Moderate	Continuous: No benefit of UF dose greater than 20 ml/kg/d with the exception of one study that showed a benefit of higher dose (≥35 ml/kg/d vs. 20 ml/kg/d). Intermittent: No benefit of daily vs. alternate daily dose with Kt/V >1.2 per treatment.	Critical
AKI/RRT dependence	6 RCTs (High)	3413 (1769)	No limitations	None	Direct	None	High	Continuous and Intermittent: No difference for RRT duration or recovery of kidney function between high intensity and low intensity RRT.	Critical
Balance of potential benefits and harm No benefit for higher dose compared to lower dose. (Continuous RRT 20 ml/kg/d and intermittent RRT alternate daily treatment with Kt/V >1.2).							Quality of overall evidence Moderate		

Annotation:
a. One study (Ronco[69]) shows benefit for higher-dose arms.

Supplementary table 38: Summary table of RCTs examining the effect of dose of continuous and intermittent RRT on AKI

Outcome	Author Year Country	Age	Baseline kidney function	Setting	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication/ therapy	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1 (prescribed) [delivered]	Arm 2 (prescribed) [delivered]					
Continuous and intermittent RRT														
Mortality														
Mortality, all-cause, 60 d†	VA/NIH Acute Renal Failure Trial Network [87] 2008 US	60	S_{Cr} 1.1 mg/dl GFR ≥45 in 88%	ICU	60 d	563 (563)	561 (561)	Intensive RRT[a] (35 ml/kg/d) Daily dose (Kt/V 1.2-1.4) [Kt/V 1.31]	Less intensive RRT[b] (20 ml/kg/d) Alternate daily dose (Kt/V 1.2-1.4) [Kt/V 1.32]	UF on non-dialysis days for volume overload when on intermittent therapy	54% (52%)	1.04[d] (0.93-1.16)	NS (0.47)	Good
Mortality, in-hospital, 60 d†											51% (48%)	1.07[d] (0.95-1.20)	NS (0.27)	Good
AKI/RRT dependence														
RRT-free days through day 28	VA/NIH Acute Renal Failure Trial Network [87] 2008 US	60	S_{Cr} 1.1 mg/dl GFR ≥45 in 88%	ICU	60 d	553 (563)	555 (561)	Intensive RRT[a] (35 ml/kg/d) Daily dose (Kt/V 1.2-1.4) [Kt/V 1.31]	Less intensive RRT[b] (20 ml/kg/d) Alternate daily dose (Kt/V 1.2-1.4) [Kt/V 1.32]	UF on non-dialysis days for volume overload when on intermittent therapy	6 (7)	--	NS (0.07)	Good
RRT-dependent, no recovery of renal function											76% (73%)	1.04 (0.97-1.12)	nd	Good
Complete recovery											15% (18%)	0.84 (0.64-1.09)	NS (0.24)	Good
Partial recovery											9% (9%)	0.98 (0.68-1.43)		Good
Continuous RRT														
Mortality														
28 d	RENAL Replacement Therapy Study [68] 2009 Australia & NZ	65	S_{Cr} 3.8 mg/dl GFR 54 ml/min	ICU	90 d	721 (747)	743 (761)	Intensive RRT (40 ml /kg/h) [33 ml/kg/h]	Lower intensity RRT (25 ml/kg/h) [22 ml/kg/h]	Vasoactive drugs IHD	39% (37%)	1.07 (0.87–1.32)	NS (0.52)	Good
90 d											45% (45%)	1.00 (0.81–1.23)	NS (0.99)	
In-ICU											35% (34%)	1.03 (0.83–1.27)	NS (0.81)	
In-hospital											9% (10%)	0.913 (0.65–1.29)	NS (0.60)	
Outside-hospital											0.4% (0.3%)	1.55 (0.26–9.28)	NS (0.63)	
In-ICU by 30 d†	Tolwani [85] 2008 US	58	S_{Cr} 4.2 mg/dl	ICU	30 d	100 (100)	100 (100)	High dose CVVHDF (35 ml/kg/h) [29 ml/kg/h]	Low dose CVVHDF (20 ml/kg/d) [17 ml/kg/h]	None	51% (44%)	1.16 (0.86-1.55)	NS (0.32)	Fair
In-ICU											60% (55%)	1.09 (0.86-1.39)	NS (0.47)	Fair
In-hospital											64% (60%)	1.07 (0.86-1.33)	NS (0.56)	Fair

Outcome	Author Year Country	Age	Baseline kidney function	Setting	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication/ therapy	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1 (prescribed) [delivered]	Arm 2 (prescribed) [delivered]					
28 d†	Bouman [12] 2002 Netherlands	68	CrCl 68 ml/min	ICU	28 d	35 (35)	35 (35)	Early high volume HF (72-96 l/d) [48 ml/kg/h]	Early low volume HF (24-36 l/d) [20 ml/kg/h]	nd	26% (31%)	0.84 (0.40-1.77)	nd[c]	Fair
In-ICU											29% (37%)	0.78 (0.40-1.54)	nd[c]	Fair
In-hospital											37% (51%)	0.73 (0.42-1.25)	nd[c]	Fair
15 d†	Ronco [69] 2000 Italy	61	S_{Cr} 309.4 µmol/l	ICU	15 d	140 (140)	139 (139)	High dose (45 ml/h/kg) [42 ml/kg/h 68 l/24 h]	Intermediate dose (35 ml/h/kg) [34 ml/kg/h 56 l/24 h]	nd	42% (43%)	0.98 (0.74-1.28)	NS (0.87)	Fair
15 d†						140 (140)	146 (146)	High dose (45 ml/kg/d) [42 ml/kg/h 68 l/24 h]	Low dose (20 ml/kg/d) [19 ml/kg/h 31 l/24 h]	nd	42% (59%)	0.49 (0.35-0.69)	0.0013	Fair
15 d†						139 (139)	146 (146)	Intermediate dose (35 ml/kg/d) [34 ml/kg/h 56 l/24 h]	Low dose (20 ml/kg/d) [19 ml/kg/h 31 l/24 h]	nd	43% (59%)	0.51 (0.36-0.72)	0.0007	Fair
AKI/RRT dependence														
RRT dependence at 28 d	RENAL Replacement Therapy Study [68] 2009 Australia & NZ	65	S_{Cr} 3.8 mg/dl GFR 54 ml/min	ICU	90 d	721 (747)	743 (761)	Intensive RRT (40 ml /kg/h) [33 ml/kg/h]	Lower intensity RRT (25 ml/kg/h) [22 ml/kg/h]	Vasoactive drugs IHD	15% (12%)	1.22 (0.83–1.79)	NS (0.31)	Good
RRT dependence at 90 d											7% (4%)	1.59 (0.86–2.92)	NS (0.14)	
RRT days (mean)											13 (12)	--	NS (0.14)	
RRT days (mean)	Ronco [69] 2000 Italy	61	S_{Cr} 309.4 µmol/l	ICU	nd	140 (140)	139 (139)	High dose (45 ml/h/kg) [42 ml/kg/h 68 l/24 h]	Intermediate dose (35 ml/h/kg) [34 ml/kg/h 56 l/24 h]	nd	12 (13)	--	nd	Fair
RRT days (mean)						140 (140)	146 (146)	High dose (45 ml/kg/d) [42 ml/kg/h 68 l/24 h]	Low dose (20 ml/kg/d) [19 ml/kg/h 31 l/24 h]	nd	12 (11)	--	nd	Fair
RRT days (mean)						139 (139)	146 (146)	Intermediate dose (35 ml/kg/d) [34 ml/kg/h	Low dose (20 ml/kg/d) [19 ml/kg/h 31 l/24 h]	nd	13 (11)	--	nd	Fair

Outcome	Author Year Country	Age	Baseline kidney function	Setting	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication/ therapy	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1 (prescribed) [delivered]	Arm 2 (prescribed) [delivered]					
								56 l/24 h]						
Full recovery of kidney function in survivors					15 d post-HF	140 (140)	139 (139)	High dose (45 ml/h/kg) [42 ml/kg/h 68 l/24 h]	Intermediate dose (35 ml/h/kg) [34 ml/kg/h 56 l/24 h]	nd	90% (92%)	0.98 (0.91-1.05)	nd	Fair
Full recovery of kidney function in survivors						140 (140)	146 (146)	High dose (45 ml/kg/d) [42 ml/kg/h 68 l/24 h]	Low dose (20 ml/kg/d) [19 ml/kg/h 31 l/24 h]	nd	90% (95%)	0.95 (0.89-1.01)	nd	Fair
Full recovery of kidney function in survivors						139 (139)	146 (146)	Intermediate dose (35 ml/kg/d) [34 ml/kg/h 56 l/24 h]	Low dose (20 ml/kg/d) [19 ml/kg/h 31 l/24 h]	nd	92% (95%)	0.97 (0.91-1.03)	nd	Fair
Full recovery of kidney function in nonsurvivors						140 (140)	139 (139)	High dose (45 ml/h/kg) [42 ml/kg/h 68 l/24 h]	Intermediate dose (35 ml/h/kg) [34 ml/kg/h 56 l/24 h]	nd	20% (19%)	1.05 (0.65-1.70)	nd	Fair
Full recovery of kidney function in nonsurvivors						140 (140)	146 (146)	High dose (45 ml/kg/d) [42 ml/kg/h 68 l/24 h]	Low dose (20 ml/kg/d) [19 ml/kg/h 31 l/24 h]	nd	20% (20%)	1.00 (0.63-1.59)	nd	Fair
Full recovery of kidney function in nonsurvivors						139 (139)	146 (146)	Intermediate dose (35 ml/kg/d) [34 ml/kg/h 56 l/24 h]	Low dose (20 ml/kg/d) [19 ml/kg/h 31 l/24 h]	nd	19% (20%)	0.95 (0.59-1.52)	nd	Fair
Renal recovery at ICU discharge	Tolwani [85] 2008 US	58	S_{Cr} 4.2 mg/dl	ICU	30 d	100 (100)	100 (100)	High dose CVVHDF (35 ml/kg/d) [29 ml/kg/h]	Standard dose CVVHDF (20 ml/kg/d) [17 ml/kg/h]	None	28% (37%)	0.76 (0.50-1.13)	NS (0.17)	Fair
Renal recovery at hospital discharge											29% (41%)	0.71 (0.48-1.04)	NS (0.75)	Fair
Duration of renal failure (days)	Bouman [12] 2002 Netherlands	68	CrCl 68 ml/min	ICU	nd	35 (35)	35 (35)	Early high volume HF (72-96 l/d)	Early low volume HF (24-36 l/d)	nd	5.5 (5.7)	--	nd	Fair

Outcome	Author Year Country	Age	Baseline kidney function	Setting	Study duration	No. analyzed (No randomized)		Intervention/Control		Concomitant medication/ therapy	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1 (prescribed) [delivered]	Arm 2 (prescribed) [delivered]					
								[48 ml/kg/h]	[20 ml/kg/h]					
Duration of renal failure in survivors (days)											4.3 (3.2)	--	nd	Fair
Duration of renal failure in survivors (days)											3.2 (5.6)	--	nd	Fair
Intermittent RRT														
Mortality														
14 d	Faulhaber-Walter [25] 2009 Germany	50	S_{Cr} 3.09 mg/dl	ICU	28 d	81 (81)	75 (76)	Intensified Extended Dialysis	Standard Extended Dialysis	nd	30% (29%)	1.00 (0.81-1.22)	NS (0.97)	Good
28 d											44% (39%)	0.91 (0.69-1.18)	NS (0.47)	Good
AKI/RRT dependence														
Renal recovery from survivors	Faulhaber-Walter [25] 2009 Germany	50	S_{Cr} 3.09 mg/dl	ICU	28 d	81 (81)	75 (76)	Intensified Extended Dialysis	Standard Extended Dialysis	nd	60% (63%)	0.86 (0.57-1.31)	NS (0.77)	Good
CVVH vs. CVVHD														
Mortality														
28 d survival	Saudan [73] 2006 Switzerland	65	S_{Cr} 388 µmol/l	ICU	90 d	102 (102)	104 (104)	CVVH (25 ml/kg/h)	CVVHDF (CVVH: 24 ml/kg/h, HD: 18 ml/kg/h)	Nutritional support	59% (39%)	1.51 (1.13-2.02)	0.03	Poor
90 d survival											59% (34%)	1.74 (1.27-2.37)	0.0005	Poor
ΔKidney function														
Renal recovery	Saudan [73] 2006 Switzerland	65	S_{Cr} 388 µmol/l	ICU	90 d	102 (102)	104 (104)	CVVH (25 ml/kg/h)	CVVHDF (CVVH: 24 ml/kg/h, HD: 18 ml/kg/h)	Nutritional support	78% (71%)	1.10 (0.94-1.29)	NS (0.62)	Poor

Annotations:

* Calculated by ERT with raw data from original studies when available. When study reported only event rates, calculations were done using percentages.

†Primary outcome

a. Intensive RRT: IHD and SLED 6 d/wk or CVVHDF at a net ultrafiltration rate of 35 ml/kg/h

b. Less intensive RRT: IHD and SLED 3 d/wk or CVVHDF at a net ultrafiltration rate of 20 ml/kg/h

c. Comparison across the 3 arms of the study was not statistically significant. (p=0.80)

d. VA/NIH Acute Renal Failure Trial Network: Mortality, All-cause, 60 d, OR 1.09 (95% CI 0.86-1.40); Mortality, In-hospital, 60 d, OR 1.15 (95% CI 0.90-1.47)

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