

Supplementary Appendix

**Lung-kidney interactions in critically ill patients: Consensus report of the Acute  
Disease Quality Initiative (ADQI) 21 Workgroup**

**ADQI Methodology  
including ESM Tables 1-8**

## Methods

The methodology of ADQI ([www.ADQI.org](http://www.ADQI.org)) consensus meetings is well established having undergone subsequent refinements in the last two decades [1]. The ADQI consensus process relies on evidence where available, if no evidence is available, expert consensus opinion is relied on.

The ADQI method comprises four stages:

- I) Systematic search for evidence in the available literature
- II) Establishment of clinical and physiological outcomes, as well as measures to be used for comparison of different treatments
- III) Description of current practice and rationale for using current techniques
- IV) Identifying areas where evidence is lacking and therefore research is required

The topics chosen for the XXI. ADQI conference were selected based on the following criteria:

- I) Prevalence of lung-kidney interactions
- II) Current clinical practice
- III) Influence of lung-kidney interactions on outcome
- IV) To potentially develop evidence-based guidelines on lung-kidney interactions
- V) Availability of scientific evidence

ADQI methodology begins with a pre-conference comprehensive literature search and appraisal of scientific evidence to identify key themes allotted to four workgroups, in which participants were divided (ESM Table 1). Participants were chosen to have a balanced presence of nephrologists, intensivists and pulmonologists, among those individuals who had an excellent record of publication in the field in the last 5 years. Furthermore, a few individuals were chosen based on experience in managing consensus process and evidence grading. A good representation of the different continents was another criterium and the final selection was based on the availability of the invited experts. Participants were divided into the following working groups:

- I) ALI/ARDS and the kidney
- II) Mechanical ventilation (VILI) and the kidney
- III) Extracorporeal strategies for (avoiding) ALI/VILI and AKI
- IV) AKI and the lung

One group member served as the group facilitator. The conference directors circulated between the breakout groups, serving as moderators for plenary session.

During the breakout sessions, summary/consensus statements were developed, requiring each work group to identify key issues, classify current state of consensus and providing supporting evidence. The findings of each workgroup were then presented to the entire group in plenary sessions, where each statement was revised until a final version was agreed upon. After each plenary session, the workgroups revised its findings based on the consensus

reached by the whole group. To develop directives for future research, participants were asked to:

- I) Identify deficiencies in current literature
- II) Determine, where more evidence is necessary
- III) Articulate research questions for areas, where evidence is lacking

Each workgroup identified relevant studies through MEDLINE, Embase, bibliographies of review articles and other files provided by participants. Article searches was generally limited to English language articles. Efforts were made to include mainly evidence from randomized controlled trials, however, other articles were also permissible to incorporate the best available evidence.

Summary statements were then proposed and supported by evidence and/or consensus where evidence was limited. Consensus statements were iteratively developed and refined in response to feedback during plenary sessions involving all ADQI delegates, and final consensus statements were agreed.

The work groups identified core themes and key questions for presentation to all ADQI delegates during the meeting (ESM Table 2). To address the heterogeneity of reported entities of severe respiratory function in critically ill patients, we are using the combined term “acute respiratory failure/acute respiratory distress syndrome” (ARF/ARDS) throughout the paper subsuming both patients meeting the ARDS Berlin-criteria and those suffering from other forms of respiratory dysfunction like acute exacerbated chronic obstructive pulmonary disease (COPD). For studies reporting the results of animal trials, we are using the term “acute lung injury” (ALI). A comparison between different ARF/ARDS and AKI definitions is available in ESM Table 5 and ESM Table 6.

The quality of evidence was judged by using the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) criteria [2]. Recommendations were graded as either having strong (Grade 1) or weak (Grade 2) strength (ESM Table 3). Furthermore, the degree of evidence for every recommendation was classified from high (A) to very low (D), incorporating different factors including e.g. study design (ESM Table 4). If there was risk of bias, inconsistency or imprecision, evidence was downgraded. It was upgraded for large effect size or significant dose-response gradient.

After the conference, a writing committee collected and edited the individual conference reports from each workgroup. Those final reports were then summarized by the writing committee into a final conference report, which was mailed to each participant for comment and revision. After approval by each member the final conference document was submitted for publication.

## **Search strategy**

MEDLINE and Embase were searched from inception to May 2018 by each of the 4 working groups to identify key studies, addressing interactions of lung and kidney in critically ill (adult) patients. Furthermore, reference lists of identified articles were checked for additional publications of potential interest and every participant was invited to provide additional articles. The resulting publications were the basis of the conference and the consensus statements.

The following terms and text words and their combinations using modifiers ('AND', 'OR') were used:

'Kidney failure, acute', 'renal'

'Renal Insufficiency'

'Renal Plasma Flow'

'Glomerular filtration rate'

'Acidosis, Renal Tubular'

'Kidney, Artificial'

'Acute Kidney Injury'

'Renal Dialysis'

'Renal Replacement Therapy'

'Hemofiltration'

'Respiratory Distress Syndrome, Adult'

'Lung injury'

'Pneumonia'

'Pulmonary Oedema'

'Respiratory Insufficiency'

'Respiratory failure'

'Respiratory Tract Infections'

'Chronic obstructive pulmonary disease'

'COPD'

'Acute exacerbated chronic obstructive pulmonary disease'

'AE-COPD'

'Hypoxemia'

'Hypercapnia'

'Acidosis, Respiratory'

'Positive-Pressure Respiration, Intrinsic'

'Severe Acute Respiratory Syndrome'

'Extracorporeal Membrane Oxygenation'

'ECCO2R'

'Extracorporeal carbondioxide removal'

'Positive-Pressure Respiration'

'Positive end expiratory pressure'

'Tidal volume'

'Non-invasive Ventilation'

'Ventilator Weaning'

ESM Table 1 Information regarding workgroups and work product

<b>Co-Chairs</b>	<b>Group 1</b>	<b>Group 2</b>	<b>Group 3</b>	<b>Group 4</b>
Michael Joannidis (Innsbruck, Austria)	<i>ALI/ARDS and the kidney</i>	<i>Mechanical ventilation (VILI) and the kidney</i>	<i>Extracorporeal strategies for (avoiding) ALI/VILI and AKI</i>	<i>AKI and the lung</i>
Lui G. Forni (Guildford, UK)				
Claudio Ronco (Vicenza, Italy)				
John A. Kellum (Pittsburgh, PA, USA)				
<b>Facilitators</b>	John Prowle (London, UK)	Marlies Ostermann (London, UK)	Patrick M. Honore (Brussels, Belgium)	Kianoush Kashani (Minnesota, MN, USA)
	Faeq Husain-Syed (Giessen, Germany)	Sean M. Bagshaw (Edmonton, Canada)	John A. Kellum (Pittsburgh, PA, USA)	Vincenzo Cantaluppi (Novara, Italy)
	Patrick T. Murray (Dublin, Ireland)	Marco Maggiorini (Zuerich, Switzerland)	Thomas Staudinger (Vienna, Austria)	Kai Singbartl (Phoenix, AZ, USA)
	Matthias Lubnow (Regensburg, Germany)	Melanie Meersch (Muenster, Germany)	Michael Darmon (Paris, France)	Claudio Ronco (Vicenza, Italy)
	Xiaoqiang Ding (Shanghai, China)	Zaccharia Ricci (Vicenza, Italy)	Eric Hoste (Gent, Belgium)	Lui G. Forni (Guildford, UK)
	Michael Joannidis (Innsbruck, Austria)		Valentin Fuhrmann (Muenster, Germany)	Sebastian J. Klein (Innsbruck, Austria)
	Tobias Welte (Hannover, Germany)			

ESM Table 2 Core themes and questions: Respiratory failure, mechanical ventilation and the kidney

<p>1a. What is the association between acute respiratory failure and acute kidney stress/injury and function in critically ill patients?</p> <p>1b. What is the association between IMV and acute kidney stress/injury and function in critically ill patients?</p>
<p>2a. What is the incidence of AKI among critically ill patients with acute lung disease not receiving IMV? Are there important differences by baseline susceptibility, diagnostic case-mix, illness acuity or other context specific considerations?</p> <p>2b. What is the attributable risk of AKI among critically ill patients receiving IMV? Are there important differences by baseline susceptibilities, diagnostic case-mix, illness acuity or other context specific considerations?</p>
<p>3a. What are the potential physiological and/or pathophysiological mechanisms of AKI in patients with acute respiratory failure not receiving IMV?</p> <p>3b. What additional mechanisms attributable to IMV contribute to AKI?</p>
<p>4a. What are the non-extracorporeal interventions/management strategies in patients with acute respiratory failure to prevent and/or mitigate acute kidney stress/injury and loss of function and/or facilitate kidney recovery?</p> <p>4b. What are the additional strategies in mechanically ventilated patients?</p> <ul style="list-style-type: none"><li>i) Does lung-protective ventilation mitigate or prevent AKI? Should this strategy be adopted among patients with normal lung function who require a period of IMV?</li><li>ii) Does any pharmacological intervention reduce or increase the occurrence of AKI (stress/injury/dysfunction) during receipt of IMV?</li><li>iii) Does any strategy of non-invasive ventilatory support reduce or increase the occurrence of AKI (stress/injury/dysfunction)?</li><li>iv) Does AKI (stress/injury/dysfunction) impair and/or delay the capacity to wean/liberate from IMV?</li><li>v) Is there an optimal strategy to wean/liberate from IMV to prevent, mitigate worsening, or facilitate recovery from AKI?</li></ul>

Abbreviations: AKI, acute kidney injury; IMV, invasive mechanical ventilation

ESM Table 3 Grading of recommendations and implications according to GRADE

Grading of recommendations [3]	Implications		
	For patients	For clinicians	For policy makers
<b>Strong GRADE 1</b>	Most people in your situation would want the recommended course of action and only a small proportion would not	Most patients should receive the recommended course of action	The recommendation can be adopted as a policy in most situations
<b>Conditional GRADE 2</b>	The majority of people in your situation would want the recommended course of action, but many would not	Recognize that different choices will be appropriate for different patients and that you must make greater effort to help each patient to arrive at a management decision consistent with his or her values and preferences; decision aids and shared decision making are particularly useful	Policy making will require substantial debate and involvement of many stakeholders



ESM Table 4 Rating of Evidence and Definition

Evidence Rating [4]		Definition
High	A	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	B	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	C	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very Low	D	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

ESM Table 5 Comparison of RIFLE, AKIN and KDIGO AKI-definitions

	<b>RIFLE [5]</b>	<b>AKIN [6]</b>	<b>KDIGO [7]</b>
<b>Definition of AKI</b>	Increase in sCr $\geq$ 1.5 times baseline within 7 days OR UO < 0.5 ml/kg/h for 6 hours	Increase in sCr by $\geq$ 0.3 mg/dl within 48 hours OR Increase in sCr to $\geq$ 1.5 times baseline OR UO < 0.5 ml/kg/h for > 6 hours	Increase in sCr by $\geq$ 0.3 mg/dl within 48 hours OR Increase in sCr to $\geq$ 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days OR UO < 0.5 ml/kg/h for 6 hours
<b>Staging</b>	<p><b>RIFLE-Risk</b> Increase in sCr 1.5 times baseline OR GFR decrease &gt; 25% OR UO &lt; 0.5 ml/kg/h for 6 hours</p> <p><b>RIFLE-Injury</b> Increase in sCr 2.0 times baseline OR GFR decrease &gt; 50% OR UO &lt; 0.5 ml/kg/h for 12 hours</p> <p><b>RIFLE-Failure</b> Increase in sCr 3.0 times baseline OR GFR decrease 75% OR Increase in sCr to <math>\geq</math> 4.0 mg/dl (with an acute increase of <math>\geq</math> 0.5 mg/dl) OR UO &lt; 0.3 ml/kg/h for 24 hours OR Anuria for 12 hours</p> <p><b>RIFLE-Loss</b> Persistent AKI = requirement for RRT &gt; 4 weeks</p> <p><b>RIFLE-ESKD</b> Requirement for dialysis &gt; 3 months</p>	<p><b>AKIN stage 1</b> sCr 1.5-1.9 times baseline OR <math>\geq</math> 0.3 mg/dl increase OR UO &lt; 0.5 ml/kg/h for &gt; 6 hours</p> <p><b>AKIN stage 2</b> sCr 2.0-2.9 times baseline OR UO &lt; 0.5 ml/kg/h for &gt; 12 hours</p> <p><b>AKIN stage 3</b> sCr 3.0 times baseline OR Increase in sCr to <math>\geq</math> 4.0 mg/dl (with an acute increase of <math>\geq</math> 0.5 mg/dl) OR UO &lt; 0.3 ml/kg/h for <math>\geq</math> 24 hours OR Anuria for <math>\geq</math> 12 hours</p>	<p><b>KDIGO stage 1</b> sCr 1.5-1.9 times baseline OR <math>\geq</math> 0.3 mg/dl increase OR UO &lt; 0.5 ml/kg/h for 6-12 hours</p> <p><b>KDIGO stage 2</b> sCr 2.0-2.9 times baseline OR UO &lt; 0.5 ml/kg/h for <math>\geq</math> 12 hours</p> <p><b>KDIGO stage 3</b> sCr 3.0 times baseline OR Increase in sCr to <math>\geq</math> 4.0 mg/dl OR Initiation of RRT OR UO &lt; 0.3 ml/kg/h for <math>\geq</math> 24 hours OR Anuria for <math>\geq</math> 12 hours</p>

RIFLE, Risk – Injury – Failure – Loss – ESKD; ESKD, end stage kidney disease; AKIN, acute kidney injury network; KDIGO, kidney disease: improving global outcomes; sCr, serum creatinine; UO, urine output; GFR, glomerular filtration rate; RRT, renal replacement therapy.

ESM Table 6 Comparison of ALI/ARDS definitions.

	AECC definition [8]		Berlin definition [9]	
	ALI	ARDS	ARDS	
<b>Timing</b>	Acute onset	Acute onset	Within 1 week of a known clinical insult or new or worsening respiratory symptoms	
<b>Chest imaging</b>	Bilateral infiltrates seen on frontal chest radiograph	Bilateral infiltrates seen on frontal chest radiograph	Bilateral opacities—not fully explained by effusions, lobar/lung collapse, or nodules	
<b>Origin of edema</b>			Respiratory failure not fully explained by cardiac failure or fluid overload Need objective assessment (e.g., echocardiography) to exclude hydrostatic edema if no risk factor present	
<b>PAWP</b>	≤ 18 mm Hg when measured or no clinical evidence of left atrial hypertension	≤ 18 mm Hg when measured or no clinical evidence of left atrial hypertension	Removed	
<b>Oxygenation</b>	PaO <sub>2</sub> /FIO <sub>2</sub> ≤ 300 mm Hg (regardless of PEEP level)	PaO <sub>2</sub> /FIO <sub>2</sub> ≤ 200 mm Hg (regardless of PEEP level)	Mild	200 mm Hg PaO <sub>2</sub> /FIO <sub>2</sub> ≤ 300 mm Hg with PEEP or CPAP ≥ 5 cm H <sub>2</sub> O
			Moderate	100 mm Hg PaO <sub>2</sub> /FIO <sub>2</sub> ≤ 200 mm Hg with PEEP ≥ 5 cm H <sub>2</sub> O
			Severe	PaO <sub>2</sub> /FIO <sub>2</sub> ≤ 100 mm Hg with PEEP ≥ 5 cm H <sub>2</sub> O

AECC, American-European consensus conference; ALI, acute lung injury; ARDS, acute respiratory distress syndrome; PEEP, positive end-expiratory pressure; PAWP, pulmonary artery wedge pressure; CPAP, continuous positive airway pressure.

ESM Table 7 Studies reporting the incidence/outcome(s) of AKI in patients with ARF/ARDS and of ARF/ARDS in patients with AKI.

Study	Design	Cohort	Renal Endpoint	Pulmonary Endpoint	Outcome(s)
<b>AKI in patients with ARF/ARDS</b>					
Chu (2005)[10]	Retrospective observational	536 SARS patients	AKI (pCr >30% of baseline) in 6.7%	ARDS in 13.4%	ARDS independent risk factor for developing AKI (RR 37.91 [7.9–180.4])
Rocha (2005)[11]	Retrospective observational	296 patients after lung transplantation	Acute renal failure (doubling of sCr in 2 weeks) 56%	Length of MV	MV associated with AKI (OR 6.16 [1.70–22.24])
Liu (2007)[12]	Secondary analysis from RCT	876 patients	25% developed AKI (AKI Stage 2+)		AKI independent predictor of mortality (OR 3.36 [2.35–4.81])
Viera (2007)[13]	Observational retrospective	143 oncology patients MV	66.4% developed AKI (as defined by oliguria and SCr > 1.5 mg/dl)		Weaning prolonged with AKI 41 (16–97) vs 21 (7–34) hours ICU mortality rate 66.7% in patients with AKI.
Cooke (2008)[14]	Secondary analysis prospective multicentre cohort	1,113 patients with ALI	Oliguria (<500 ml/24 hr) 7.9%		Mortality 69% RR death 1.9 (1.61–2.23)
Arnaoutakis (2011)[15]	Retrospective observational	106 patients after lung transplantation	AKI (RIFLE-I or -F) in 36.7%		AKI (RIFLE-F) associated with increased mortality (RR 4.76 [1.65–13.7]); RIFLE-R or -I not associated with higher mortality
Lombardi (2011)[16]	Prospective Observational	2,783 patients on MV	28.8% AKIN criteria first 48 hours		AKI independent predictor of mortality (OR 1.65 [1.23–2.14])
Soto (2012)[17]	retrospective analysis multicentre randomized trial	751 patients with ARDS	AKI (RIFLE-R) 61.9%		AKI associated with increased mortality (OR 2.76 [1.72–4.42])
Veeravagu (2014)[18]	Retrospective observational	193,209 SAH patients		ARDS	Renal dysfunction predicted ARDS development (1.35 [1.19–1.53])
Darmon (2014)[19]	Prospective database Observational	8,029 consecutive ICU patients	AKI (31.3%)	ARDS (23.4%)	AKI more common in ARDS (44.3 vs. 27.4%) MV and ARDS independently associated with subsequent AKI (OR 4.34 [95% CI 3.71–5.10] and OR 11.01 [95% CI, 6.83 to 17.73] respectively)

Saravu (2014)[20]	Prospective observational	1,191 malaria patients	Mild AKI (peak sCr 1.6-3.0 mg/dl) 8.4% Severe AKI (peak sCr >3 mg/dl) 3.8%	MV in mild AKI 6% MV in severe AKI 26.1% Pulmonary edema/ARDS in mild AKI 6.9% Pulmonary edema/ARDS in severe AKI 4.3%	Mild and severe AKI associated with pulmonary edema/ARDS (OR 2.4 [1.01–5.9]) and 1.5 (0.3-6.6) and with MV (OR 4.7 [1.6–13.6] and 26.2 [10.3–66.4])
Saeed (2014)[21]	Retrospective observational	7,068,334 patients with acute ischemic stroke	AKI (stage I+) in 5.3%		AKI associated with MV (3.6% vs. 0.7%)
Clemens (2016)[22]	Retrospective observational	830 burns patients on MV	48.2% AKI (KDIGO)	36% (ARDS)	ARDS development in AKI patients (OR 1.73 [1.18-2.54]) AKI associated with increased mortality (OR 3.73 [2.39–5.82])
Murugan (2010) [23]	Secondary analysis prospective multicentre cohort	1836 patients with community-acquired pneumonia	34.4% AKI (RIFLE)		AKI associated with MV (18.4% vs 1%); higher mortality in hospital (11.1% vs 1.3%), at 90 days (24% vs 9.8%), at 1 year (36.3% vs 20.1%) in AKI patients
Barakat (2015) [24]	Retrospective database	189,561 patients with COPD	(ICD-10 code N17 Acute Kidney Failure)		Hospitalization for AKI in 1,610 patients (incidence rate 128/10,000 person-years); increasing AKI rates with worsening COPD severity; AKI in 1.9% of COPD exacerbations
<b>ARF/ARDS in patients with AKI</b>					
Chertow (1995)[25]	Retrospective observational	132 ICU patients on dialysis		MV 78%	MV associated with increased mortality (81% vs 29%)
Mehta (2002)[26]	Retrospective observational	605 ICU patients with renal failure		NA	Respiratory failure associated with increased mortality (OR 2.62 [1.70–4.04])
Uchino (2005)[27]	Prospective Observational	RRT or acute renal failure		76.2% MV	MV increased hospital mortality 2.11 (1.58–2.82)
Franzen (2010)[28]	Retrospective observational	39 AKI patients treated with IHD		ARDS in 44%	Pulmonary co-comorbidity associated with higher mortality (HR 2.23 [0.6–8.31]); ARDS associated with higher mortality (HR 1.83 [0.52–6.46])
<b>Physiological studies in humans</b>					

Drury (1947) [29]	Prospective interventional	4 subjects submitted to 30-minute periods of continuous pressure breathing at 10, 20, 30 and 40 mmHg			Depression of urine volume and urea clearance during and immediately after pressure breathing
Murdaugh (1959) [30]	Prospective interventional	9 subjects submitted to continuous positive pressure breathing (24-26 mmHg) 9 subjects submitted to continuous negative pressure breathing (18-22 mmHg)			8/9 subjects had diuresis with dilution of urine in response to continuous negative pressure breathing. Significant decrease in rate of urine flow, free water and osmolar clearance, sodium excretion, GFR and renal plasma flow with positive pressure ventilation.
<b>Meta-analysis</b>					
Van den Akker (2013) [31]	Systematic review and meta-analysis	31 studies (10,333 patients) reporting relation between use of invasive MV and AKI were included			Pooled OR for overall effect of MV on AKI was 3.16 (95% CI: 2.32-4.28).

Abbreviations: OR, odds ratio; SARS, severe acute respiratory syndrome; AKI, acute kidney injury; ; AKIN, Acute Kidney Injury Network; ALI, acute lung injury; ARDS, acute respiratory distress syndrome; COPD, chronic obstructive pulmonary disease; GFR, glomerular filtration rate; HR, hazard ratio; ICU, intensive care unit; IHD, intermittend hemodialysis, KDIGO, kidney disease improving global outcome; MV, mechanical ventilation; RCT, randomized clinical trial; RIFLE, risk-injury-failure-loss-end-stage kidney disease; RR, relative risk; RRT, renal replacement therapy; SAH, subarachnoid hemorrhage; SCr, serum creatinine

ESM Table 8 Studies reporting the incidence of AKI/RRT in patients treated with ECMO

Study	Design	Cohort	Renal Endpoint	Outcome(s)
Combes (2018) [32]	Randomized controlled trial (EOLIA trial)	249 adult patients with very severe ARDS randomized to receive veno-venous ECMO or conventional management (control group)		At 60 days: Patients with ECMO had significantly more days without RRT (difference 18 days [95%CI 0-51]) Patients with ECMO had significantly more days free from AKI (difference 25 days [95%CI 6-53])
Kielstein (2013) [33]	Retrospective analysis	200 adult patients undergoing ECMO treatment in medical and surgical ICUs		60% required RRT for AKI, 23% received RRT before ECMO initiation 3-month survival was significantly lower in patients requiring RRT (53% vs 17%)
Schmidt (2014) [34]	Retrospective analysis of the ELSO registry	2,355 adult patients with severe acute respiratory failure treated with ECMO	Renal dysfunction: chronic or acute renal insufficiency (sCr >1.5 mg/dl) with or without RRT	Pre-ECMO, 18% had renal dysfunction, significantly more patients who did not survive to hospital discharge had renal dysfunction (14 vs 24%) Renal dysfunction (either AKI or CKD) was associated with decreased hospital survival (OR 0.77 [95%CI 0.61-0.89])
Schmidt (2014) [35]	Retrospective observational study	172 adult patients with ECMO for cardiac (n=115) or respiratory (n=57) failure	RIFLE-R, RIFLE-I or RIFLE-F AKI 57% had AKI at ECMO initiation (RIFLE-R 13%, RIFLE-I 23%, RIFLE-F 21%) 60% received CRRT during ECMO	Need for RRT was associated with a decreased day 90 survival (67 vs. 90%) Greater RIFLE severity at ECMO initiation carried a greater 90-day mortality rate (15% in the no-AKI group to 47% in the RIFLE-F group) AKI patients had significantly higher mortality at day 90 compared to non-AKI patients (31 vs 15%)
Haneya (2015) [36]	Retrospective observational study	262 adult patients with ECMO for respiratory failure	AKI and RRT	50% required RRT for AKI, RRT patients had a higher hospital mortality compared to patients without RRT (47.3% vs 71.8%; p < 0.001) Need for RRT prior to ECMO was independent risk factor for mortality, whereas need for RRT during ECMO was not.

Peek (2009) [37]	RCT (CESAR-trial)	180 adult ARDS patients randomized to receive veno-venous ECMO (n=90) or conventional management (n=90)		80% in the ECMO group vs 84% in the conventional management group required CVVH (p = 0.61)
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Abbreviations: AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; CVVH, continuous veno-venous haemofiltration; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; OR, odds ratio; RIFLE, risk-injury-failure-loss-end-stage kidney disease; RRT, renal replacement therapy; SCr, serum creatinine.



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