

# A meta-analysis of complications and mortality of extracorporeal membrane oxygenation

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Modern extracorporeal membrane oxygenation (ECMO) was introduced into clinical practice several years ago, but owing to major refinements it is now considered the first-choice treatment in patients with refractory cardiogenic shock and/or acute lung or respiratory failure (ARF).<sup>1-3</sup> Its cost and accompanying logistical issues limit wider application of this technology. Accordingly, use of ECMO must be individualised carefully, balancing purported benefits, risks, and the likelihood of subsequent recovery without major neurological sequelae.

Despite the availability of several multicentre registries, a plethora of case reports, a wide range of clinical applications and an ample choice of devices and accessories, there has been no systematic appraisal of the risks inherent in applying ECMO in unselected patients and there is still uncertainty on the incidence and impact of complications associated with ECMO.<sup>4-7</sup> Systematic reviews and meta-analyses provide a robust and validated means of summarising clinical evidence from independent reports, and their use has been advocated to appraise more thoroughly the risk of adverse outcomes with clinical interventions.<sup>8</sup> We aimed to perform a comprehensive, up-to-date and methodologically sound systematic review and meta-analysis of the peer-reviewed literature, focusing on outcomes and complications of ECMO in adult patients.

## Methods

### Design

This systematic review complies with MOOSE (Meta-analysis of Observational Studies in Epidemiology) and PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.<sup>9-10</sup> Study search, selection, abstraction and quality assessment were all performed by two independent reviewers (GL, GB-Z), with divergences resolved after consensus.

### Search

MEDLINE/PubMed was searched for articles on complications occurring in patients during or after ECMO, with the following highly sensitive strategy: (ecmo OR ecls OR els OR (extracorporeal AND ((membrane AND oxygen\*) OR (life AND support)))) AND (fatal\* OR mortal OR death OR

## ABSTRACT

**Objective:** To comprehensively assess published peer-reviewed studies related to extracorporeal membrane oxygenation (ECMO), focusing on outcomes and complications of ECMO in adult patients.

**Design:** Systematic review and meta-analysis.

**Data sources:** MEDLINE/PubMed was searched for articles on complications and mortality occurring during or after ECMO.

**Data extraction:** Included studies had more than 100 patients receiving ECMO and reported in detail fatal or non-fatal complications occurring during or after ECMO. Primary outcome was mortality at the longest follow-up available; secondary outcomes were fatal and non-fatal complications.

**Data synthesis:** Twelve studies were included (1763 patients), mostly reporting on venoarterial ECMO. Criteria for applying ECMO were variable, but usually comprised acute respiratory failure, cardiogenic shock or both. After a median follow-up of 30 days (1st–3rd quartile, 30–68 days), overall mortality was 54% (95% CI, 47%–61%), with 45% (95% CI, 42%–48%) of fatal events occurring during ECMO and 13% (95% CI, 11%–15%) after it. The most common complications associated with ECMO were: renal failure requiring continuous venovenous haemofiltration (occurring in 52%), bacterial pneumonia (33%), any bleeding (33%), oxygenator dysfunction requiring replacement (29%), sepsis (26%), haemolysis (18%), liver dysfunction (16%), leg ischaemia (10%), venous thrombosis (10%), central nervous system complications (8%), gastrointestinal bleeding (7%), aspiration pneumonia (5%), and disseminated intravascular coagulation (5%).

**Conclusions:** Even with conditions usually associated with a high chance of death, almost 50% of patients receiving ECMO survive up to discharge. Complications are frequent and most often comprise renal failure, pneumonia or sepsis, and bleeding.

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mortality). All searches were updated on 2 January, 2012. No language restriction was enforced, and references from selected studies as well as previous systematic reviews on

the topic were manually searched for additional studies (backward snowballing).

### Selection criteria

Citations were first screened at the title and abstract level. If potentially pertinent, they were retrieved in full text and appraised. Inclusion criteria were: a) the study reported on 100 or more patients; b) patients received ECMO; and c) the study reported in detail on fatal or non-fatal complications occurring during or after ECMO. Articles were only included if all criteria were met. Exclusion criteria were: a) inclusion of < 100 patients treated by ECMO; b) selective inclusion of patients < 18 years; and c) duplicate publication (in which case only the most recent report from the same study group was included in the systematic review). Articles were excluded if one of these criteria was met.

A sample size cut-off of 100 patients was chosen pre hoc to limit the undue influence of anecdotal cases and the ensuing risk of imprecision and publication bias, in keeping with prior systematic reviews.<sup>11</sup> Where data were lacking in the selected published papers, corresponding authors were contacted by phone or email and asked to clarify and detail missing data for inclusion in the meta-analysis.

### Data abstraction and quality appraisal

Several study, patient, procedural and outcome features were abstracted, with the primary outcome of the study being mortality at the longest follow-up available. Other outcomes of interest were fatal and non-fatal complications occurring during or after ECMO. The validity of included studies was appraised with the Newcastle-Ottawa scale.<sup>12</sup>

**Table 1. Major studies excluded because of a lack of data on extracorporeal membrane oxygenation (ECMO) complications, or duplicate publication**

Study	Year	Patients receiving ECMO	Type of ECMO	Mortality
Bizzarro MJ et al <sup>14</sup>	2011	20 741	VA and VV	na
Brogan TV et al <sup>15</sup>	2009	1 473	VA and VV	50.0%
Doll N et al <sup>16</sup>	2004	219	na	na
Elsharkawy HA et al <sup>17</sup>	2010	233	na	63.9%
Farrar DJ et al <sup>18</sup>	2000	1 376	na	na
Fischer S et al <sup>19</sup>	2007	31 340	na	na
Hoefer D et al <sup>20</sup>	2006	131	na	na
Morimura N et al <sup>21</sup>	2011	105	na	6.4%
Ranucci M et al <sup>22</sup>	2004	180	na	na
Rastan AJ et al <sup>23</sup>	2010	517	na	na
Rastan AJ et al <sup>24</sup>	2006	154	na	na
Rich PB et al <sup>25</sup>	1998	100	na	na
Schaible T et al <sup>26</sup>	2012	106	VA	na
Sheu JJ et al <sup>27</sup>	2010	334	na	na
Tsai CW et al <sup>28</sup>	2008	104	na	75.9%

na = not available or applicable. VA = venoarterial. VV = venovenous.

### Data analysis

Continuous variables are reported as median (1st–3rd quartile) and categorical variables as number (%). Meta-analytic pooling was performed for outcome variables, using a

**Table 2. Included studies**

Study	Year	Location	Design	Prospective	Setting	Primary end point	Follow-up
Beiras-Fernandez A et al <sup>29</sup>	2011	Germany	Registry	No	Single centre	na	1 year
Bisdas T et al <sup>5</sup>	2011	Germany	Registry	No	Single centre	Complications	Inhospital
Camboni et al <sup>30</sup>	2011	Germany	Registry	No	Single centre	na	Inhospital
Chen YC et al <sup>31</sup>	2011	Taiwan	Registry	No	Single centre	Inhospital mortality	6 months
Foley DS et al <sup>32</sup>	2002	USA	Registry	No	Single centre	Complications	Inhospital
Hei F et al <sup>33</sup>	2011	China	Registry	No	Single centre	Inhospital mortality	Inhospital
Hemmila MR et al <sup>34</sup>	2004	USA	Registry	No	Single centre	Inhospital mortality	Inhospital
Kolla S et al <sup>35</sup>	1997	USA	Registry	No	Single centre	Inhospital mortality	Inhospital
Sun HY et al <sup>36</sup>	2010	Taiwan	Registry	No	Single centre	Infections	Inhospital
Wu MY et al <sup>37</sup>	2010	Taiwan	Registry	No	Single centre	Inhospital mortality	3 years
Wu VC et al <sup>38</sup>	2010	Taiwan	Registry	No	Multicentre	Inhospital mortality	Inhospital
Yu K et al <sup>39</sup>	2011	China	Registry	No	Single centre	na	Inhospital

na = not available or applicable.

**Table 3. Characteristics of patients in included studies**

Study	Patients	Children included	Median age of adults, years	Males	Criteria for ECMO
Beiras-Fernandez A et al <sup>29</sup>	108	Yes	43	66%	Failure in weaning CPB
Bisdas T et al <sup>5</sup>	174	Yes	46	37%	VA ECMO: CI < 2.2 L/min/m <sup>2</sup> ; SBP, < 90 mmHg; lactates, > 4.0 mmol/L during inotropic support and/or IABP. VV ECMO: ARDS unresponsive to conventional therapy
Camboni et al <sup>30</sup>	127	Yes	48	67%	Hypoxia (PaO <sub>2</sub> < 85 mmHg)
Chen YC et al <sup>31</sup>	102	No	47	61%	Cardiogenic shock
Foley DS et al <sup>32</sup>	100	Yes	38	na	Severe respiratory or cardiac instability
Hei F et al <sup>33</sup>	121	Yes	49	62%	Cardiogenic shock, failure in weaning CPB, pulmonary hypertension, cardiac and pulmonary dysfunction with hypoxia, CI < 2.0 L/min/m <sup>2</sup> despite inotropic support
Hemmila MR et al <sup>34</sup>	268	No	38	49%	ARF with PaO <sub>2</sub> /FiO <sub>2</sub> ratio < 100 on FiO <sub>2</sub> of 1.0, alveolar–arterial gradient > 600 mmHg, or transpulmonary shunt fraction > 30% despite and after optimal treatment
Kolla S et al <sup>35</sup>	100	No	34	40%	ARF with transpulmonary shunt > 30%, compliance < 0.5 mL/cm H <sub>2</sub> O/kg, mechanical ventilation < 5 days, and age younger than 60 years
Sun HY et al <sup>36</sup>	330	No	51	68%	ARF or cardiogenic shock
Wu MY et al <sup>37</sup>	110	No	60	71%	Cardiogenic shock
Wu VC et al <sup>38</sup>	102	No	48	69%	Cardiogenic shock
Yu K et al <sup>39</sup>	121	No	30	67%	Cardiogenic shock

ARDS = acute respiratory distress syndrome. ARF = acute respiratory failure. CI = cardiac index. CPB = cardiopulmonary bypass. IABP = intra-aortic balloon pump. na = not available or applicable. SBP = systolic blood pressure. VA = venoarterial. VV = venovenous.

random-effects generic inverse-variance weighting approach and reporting results as a summary point estimate and 95% confidence interval.<sup>13</sup> Statistical consistency was tested by means of  $I^2$ . Small study effects (eg, publication bias) were appraised by visual inspection of funnel plots.<sup>13</sup> Inverse-variance weighting meta-regression was used with a hypothesis-generating scope to explore for potential moderators, and results are expressed as b (95% confidence interval) and corresponding  $P$  value. Statistical significance was set at the 5% level, with 2-tailed  $P$  values reported throughout. Computations were performed with RevMan 5 (Nordic Cochrane Centre) and SPSS Statistics 20 (IBM).

## Results

A total of 2070 citations were obtained by bibliographic searches. After excluding non-pertinent studies or those not fulfilling the selection criteria (Table 1), a final set of 12 studies was included (Table 2). These studies were mostly performed in the past decade, stemming from several countries, and included a total of 1763 patients (median, 116 [1st–3rd quartile, 102–139 patients]). The median age of adults was 47 years (1st–3rd quartile, 38–48 years), and

66% (median; 1st–3rd quartile, 55%–68%) were male (Table 3). Criteria for applying ECMO were variable, but most often included cardiogenic shock, ARF, or both. Appraisal of procedural features showed that ECMO was maintained for a median of 5.9 days (1st–3rd quartile, 5.4–7.3 days), and was venoarterial in 92% (median; 1st–3rd quartile, 24%–100%) of patients (Table 4).

Analyses of outcomes, appraised at a median follow-up of 30 days (1st–3rd quartile, 30–68 days), showed that overall mortality was 54% (point estimate; 95% CI, 47%–61%;  $I^2 = 90\%$ ), with 45% (point estimate; 95% CI, 42%–48%) of fatal events occurring during ECMO and 13% (point estimate; 95% CI, 11%–15%) occurring after ECMO (Table 5; Figures 1 and 2). Several complications were described during or shortly after ECMO use, including (in decreasing order of risk): renal failure requiring continuous venovenous haemofiltration (52%), bacterial pneumonia (33%), any bleeding (33%), oxygenator dysfunction requiring system replacement (29%), sepsis (26%), haemolysis (18%), liver dysfunction (16%), leg ischaemia (10%), venous thrombosis (10%), central nervous system complications (8%), gastrointestinal bleeding (7%), aspiration pneumonia (5%), and disseminated intravascular coagulation (5%) (Table 5).

**Table 4. Procedural characteristics of included studies**

Study	VV ECMO	VA ECMO	Shift from VV to VA ECMO	ECMO duration (days)	Accesses	ECMO used	Pump (type)	Coating	Protective ventilation	Polymethyl-pentene oxygenator	Anti-coagulant therapy (target ACT)
Beiras-Fernandez A et al <sup>14</sup>	0	100%	0	5.7	RA and ascending aorta	Medtronic	Bio-Pump Medtronic (C)	Yes	No	na	Heparin (160-200 s)
Bisdas T et al <sup>5</sup>	18%	83%	0	6.0	VV and VA: femoro-femoral with arterial leg reperfusions	Maquet/Levitronix	Maquet (C)	na	Yes	na	Heparin (na)
Camboni et al <sup>15</sup>	100%	0	1%	na	RIJV and femoral vein	Maquet	Maquet (C)	na	Yes	na	Heparin (160 s)
Chen YC et al <sup>16</sup>	0	100%	0	5.5	Femoro-femoral	na	na	na	No	na	na
Foley DS et al <sup>17</sup>	53%	47%	0	9.5	VV: RIJV and femoral vein; VA: femoro-femoral	Avecor Cardiovascular	Cobe Roller Pump (R) or Sarns Delphin II (C)	na	No	na	na
Hei F et al <sup>18</sup>	0	100%	0	5.4	Adults: femoro-femoral; children: RA and ascending aorta	Medtronic Minimax/Quadrox D Jostra	(C)	na	Yes	na	Heparin (> 200 s)
Hemmila MR et al <sup>19</sup>	73%	23%	10%	5.2	VV: RA and IVC; VA: RA or IVC plus femoral or common carotid artery	na	na	na	Yes	na	Heparin (160–180 s)
Kolla S et al <sup>20</sup>	76%	24%	7%	na	VA: RIJV and common carotid artery or femoral artery and vein; VV: RIJV and femoral vein	na	(C)	na	Yes	na	Heparin (160–180 s)
Sun HY et al <sup>21</sup>	19%	8%	0	7.7	VV: RIJV and femoral vein; VA: femoro-femoral	na	na	na	No	na	na
Wu MY et al <sup>22</sup>	0	100%	0	5.4	Femoro-femoral	Capiox EBS/Medos Deltastream	(R)	na	No	na	Heparin (180–200 s)
Wu VC et al <sup>23</sup>	0	100%	0	8.8	Femoro-femoral	na	CB2505 Medtronic (C)	Yes	No	na	na
Yu K et al <sup>24</sup>	0	100%	0	6.0	Femoro-femoral	Medtronic/Quadrox D PLS	Bio Medicus BP-550 or RotaFlow R-32 (C)	Yes	No	na	Heparin (140–180 s)

ACT = activated clotting time. C = centrifugal. ECMO = extracorporeal membrane oxygenation. IVC = inferior vena cava. na = not available or applicable. R = roller. RA = right atrium. RIJV = right internal jugular vein. VA = venoarterial. VV = venovenous.

Exploratory meta-regression analyses showed that mortality appeared to increase with year of publication ( $b = 1.865$  [95% CI, 0.193–3.537];  $P = 0.032$ ), and tended to be lower in studies more frequently employing venovenous ECMO rather than venoarterial ECMO ( $b = -0.203$  [95% CI,

$-0.412$  to  $0.005$ ];  $P = 0.005$ ). It was not significantly associated with number of children ( $P = 0.159$ ), age ( $P = 0.123$ ), male sex ( $P = 0.177$ ), use of protective ventilation ( $P = 0.168$ ), ECMO duration ( $P = 0.900$ ), or follow-up duration ( $P = 0.713$ ).

**Table 5. Clinical outcomes and complications in patients receiving extracorporeal membrane oxygenation (ECMO)**

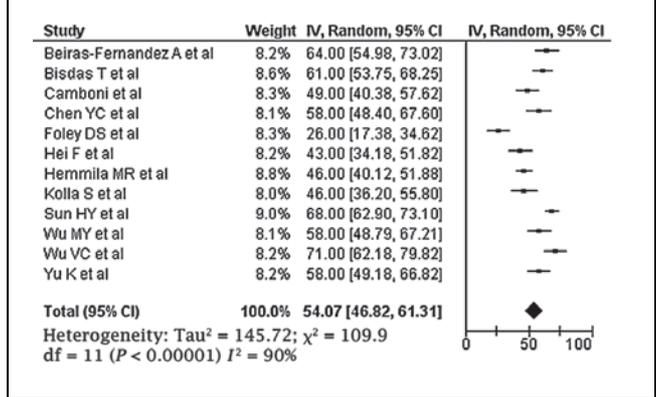
Outcome	No. of studies reporting outcome (no. of patients)	Summary point estimate (95% CI)
<b>Mortality</b>		
Overall	12 (1763)	54% (47%–61%)
During ECMO	8 (1059)	45% (42%–48%)
After ECMO	5 (734)	13% (11%–15%)
<b>Complications</b>		
Aspiration pneumonia	3 (495)	5% (3%–7%)
Bacterial pneumonia	4 (825)	33% (30%–36%)
Bleeding	5 (946)	33% (30%–36%)
Central nervous system complications	5 (720)	8% (6%–10%)
Disseminated intravascular coagulation	3 (510)	5% (3%–7%)
Gastrointestinal bleeding	4 (610)	7% (5%–9%)
Haemolysis	4 (610)	18% (15%–21%)
Leg ischaemia	5 (856)	10% (8%–12%)
Liver dysfunction	4 (610)	16% (13%–19%)
Oxygenator dysfunction requiring replacement	5 (946)	29% (26%–32%)
Renal failure requiring continuous venovenous haemofiltration	6 (828)	52% (49%–55%)
Sepsis	5 (940)	26% (23%–29%)
Venous thrombosis	1 (127)	10% (5%–15%)

**Discussion**

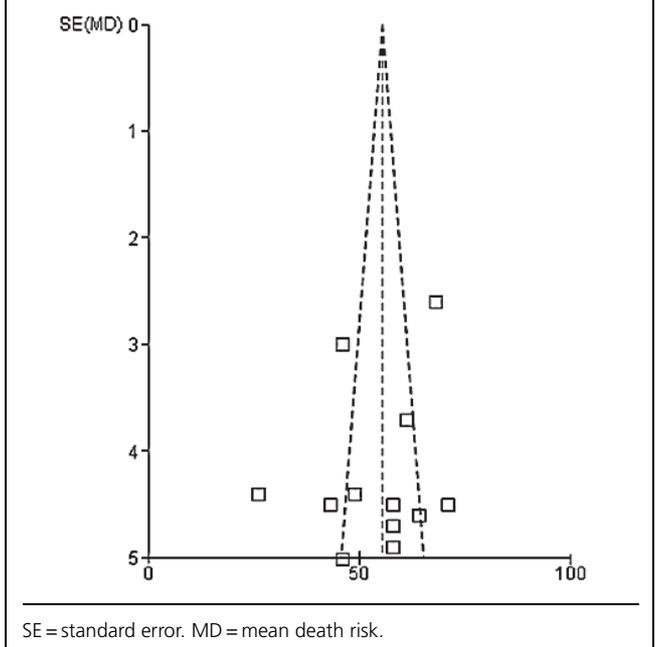
This systematic review detailing the outcomes for 1763 adult patients receiving ECMO shows that use of ECMO in critically ill patients is progressively increasing, with higher risk patients being treated more and more often. Overall outcomes indicate that ECMO is feasible in several critical conditions with different aetiologies; and despite their prohibitive baseline risk and comorbidities, almost half of patients receiving ECMO in real-world practice survive up to hospital discharge. However, ECMO is still associated with several complications, including renal failure, pneumonia or sepsis, and bleeding. Determining whether the occurrence of such events may be reduced by improving ECMO or supportive therapy, or whether they are simply secondary to the critical conditions of patients treated with ECMO, requires further dedicated studies.

The management of patients with severe cardiogenic shock or respiratory failure has been revolutionised by the introduction of ECMO, which can provide short-term support to failing hearts and lungs in newborns and children, as well as adults.<sup>1-3,40,41</sup> ECMO has been available since the

**Figure 1. Forest plot for the overall risk of death in patients receiving extracorporeal membrane oxygenation**



**Figure 2. Funnel plot for the overall risk of death in patients receiving extracorporeal membrane oxygenation**



late 1990s, but it is still used in a limited number of patients per year in any given institution, mainly because of the high cost and logistic reasons. Accordingly, it remains challenging for a clinician to precisely estimate the risk-benefit balance of ECMO and to use this estimate to individualise use of ECMO in real-world patients.

The results of our meta-analysis showed that ECMO has proven feasible. In-hospital mortality was 54%, suggesting that, despite ample room for additional improvements,

ECMO achieved remarkable results in patients at high risk of death. Yet complications were common and often potentially life-threatening. It remains unclear whether this is due to the underlying patient condition and comorbidities, or if technological improvements and changes in ancillary procedures and medications may reduce such risk. Indeed, state-of-the-art ECMO is now remarkably safe in patients without comorbidities, and future application of ECMO in awake or ambulatory patients, similar to its current application as a bridge to heart transplantation, can be envisioned. Of course, ECMO is invasive and candidates for ECMO are by definition critically ill, thus it is very hard to altogether avoid adverse events and complications in patients requiring ECMO.

The apparent increase in mortality over the years disclosed by our hypothesis-generating meta-regression analysis most likely represents the application of ECMO to sicker and more unstable patients in the recent past, rather than any detrimental effect of current ECMO technology compared with past technologies.<sup>3</sup> Accordingly, meta-regression suggested that venovenous ECMO is safer than venoarterial ECMO,<sup>41,42</sup> possibly because of its lower invasiveness, but these findings indicate a need for dedicated head-to-head randomised trials focusing on clinically relevant end points.

This study has several limitations, including those typical of systematic reviews and meta-analyses of study-level data, like inclusion of studies with heterogeneous primary outcomes. We focused specifically on studies reporting at least 100 patients receiving ECMO to enable precise and accurate prevalence and incidence estimates. However, this selection criterion has led to the exclusion of several potentially important reports, from case reports to studies with relatively small samples. Nevertheless, including such smaller studies would have increased the risk of biased estimates, given the inherent likelihood that smaller studies tend to be subject to selective reporting, publication bias, and several other methodological shortcomings.<sup>13</sup>

## Conclusion

Even with conditions usually associated with a high chance of death, almost 50% of patients receiving ECMO survive up to discharge. Nonetheless, complications are frequent and most often comprise renal failure, pneumonia or sepsis, and bleeding.

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## Competing interests

None declared.

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## References

- Bartlett RH, Roloff DW, Cornell RG, et al. Extracorporeal circulation in neonatal respiratory failure: a prospective randomized study. *Pediatrics* 1985; 76: 479-87.
- Bartlett RH, Roloff DW, Custer JR, et al. Extracorporeal life support: the University of Michigan experience. *JAMA* 2000; 283: 904-8.
- Brodie D, Bacchetta M. Extracorporeal membrane oxygenation for ARDS in adults. *N Engl J Med* 2011; 365: 1905-14.
- Peris A, Zagli G, Cianchi G, et al. Iliopsoas haematoma: unexpected life-threatening complication during extracorporeal membrane oxygenation support in H1N1-induced acute respiratory distress syndrome patients. *Br J Anaesth* 2011; 107: 819-20.
- Bisdas T, Beutel G, Warnecke G, et al. Vascular complications in patients undergoing femoral cannulation for extracorporeal membrane oxygenation support. *Ann Thorac Surg* 2011; 92: 626-31.
- Bellissima P, Bellissima G. [Pulmonary complications from pandemic AH1N1 influenza: clinical-radiological features] [Italian]. *Infez Med* 2011; 19: 20-7.
- Hervey-Jumper SL, Annich GM, Yancon AR, et al. Neurological complications of extracorporeal membrane oxygenation in children. *J Neurosurg Pediatr* 2011; 7: 338-44.
- Warren FC, Abrams KR, Golder S, Sutton AJ. Systematic review of methods used in meta-analyses where a primary outcome is an adverse or unintended event. *BMC Med Res Methodol* 2012; 12: 64.
- Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 2000; 283: 2008-12.
- Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ* 2009; 339: b2700.
- Mitchell MD, Mikkelsen ME, Umscheid CA, et al. A systematic review to inform institutional decisions about the use of extracor-

- poreal membrane oxygenation during the H1N1 influenza pandemic. *Crit Care Med* 2010; 38: 1398-404.
- 12 Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol* 2010; 25: 603-5.
  - 13 Biondi-Zoccai G, Lotrionte M, Landoni G, Modena MG. The rough guide to systematic reviews and meta-analyses. *HSR Proc Intensive Care Cardiovasc Anesth* 2011; 3: 161-73.
  - 14 Bizzarro MJ, Conrad SA, Kaufman DA, Rycus P; Extracorporeal Life Support Organization Task Force on Infections, Extracorporeal Membrane Oxygenation. Infections acquired during extracorporeal membrane oxygenation in neonates, children, and adults. *Pediatr Crit Care Med* 2011; 12: 277-81.
  - 15 Brogan TV, Thiagarajan RR, Rycus PT, et al. Extracorporeal membrane oxygenation in adults with severe respiratory failure: a multi-center database. *Intensive Care Med* 2009; 35: 2105-14.
  - 16 Doll N, Kiaii B, Borger M, et al. Five-year results of 219 consecutive patients treated with extracorporeal membrane oxygenation for refractory postoperative cardiogenic shock. *Ann Thorac Surg* 2004; 77: 151-7; discussion 157.
  - 17 Elsharkawy HA, Li L, Esa WA, et al. Outcome in patients who require venoarterial extracorporeal membrane oxygenation support after cardiac surgery. *J Cardiothorac Vasc Anesth* 2010; 24: 946-51.
  - 18 Farrar DJ. The thoratec ventricular assist device: a paracorporeal pump for treating acute and chronic heart failure. *Semin Thorac Cardiovasc Surg* 2000; 12: 243-50.
  - 19 Fischer S, Bohn D, Rycus P, et al. Extracorporeal membrane oxygenation for primary graft dysfunction after lung transplantation: analysis of the Extracorporeal Life Support Organization (ELSO) registry. *J Heart Lung Transplant* 2007; 26: 472-7.
  - 20 Hoefer D, Ruttman E, Poelzl G, et al. Outcome evaluation of the bridge-to-bridge concept in patients with cardiogenic shock. *Ann Thorac Surg* 2006; 82: 28-33.
  - 21 Morimura N, Sakamoto T, Nagao K, et al. Extracorporeal cardiopulmonary resuscitation for out-of-hospital cardiac arrest: a review of the Japanese literature. *Resuscitation* 2011; 82: 10-4.
  - 22 Ranucci M, Isgrò G, Soro G, et al. Reduced systemic heparin dose with phosphorylcholine coated closed circuit in coronary operations. *Int J Artif Organs* 2004; 27: 311-9.
  - 23 Rastan AJ, Dege A, Mohr M, et al. Early and late outcomes of 517 consecutive adult patients treated with extracorporeal membrane oxygenation for refractory postcardiotomy cardiogenic shock. *J Thorac Cardiovasc Surg* 2010; 139: 302-11, 311.e1.
  - 24 Rastan AJ, Lachmann N, Walther T, et al. Autopsy findings in patients on postcardiotomy extracorporeal membrane oxygenation (ECMO). *Int J Artif Organs* 2006; 29: 1121-31.
  - 25 Rich PB, Younger JG, Soldes OS, et al. Use of extracorporeal life support for adult patients with respiratory failure and sepsis. *ASAIO J* 1998; 44: 263-6.
  - 26 Schaible T, Kohl T, Reinshagen K, et al. Right- versus left-sided congenital diaphragmatic hernia: postnatal outcome at a specialized tertiary care center. *Pediatr Crit Care Med* 2012; 13: 66-71.
  - 27 Sheu JJ, Tsai TH, Lee FY, et al. Early extracorporeal membrane oxygenator-assisted primary percutaneous coronary intervention improved 30-day clinical outcomes in patients with ST-segment elevation myocardial infarction complicated with profound cardiogenic shock. *Crit Care Med* 2010; 38: 1810-7.
  - 28 Tsai CW, Lin YF, Wu VC, et al; NSARF Study Group. SAPS 3 at dialysis commencement is predictive of hospital mortality in patients supported by extracorporeal membrane oxygenation and acute dialysis. *Eur J Cardiothorac Surg* 2008; 34: 1158-64.
  - 29 Beiras-Fernandez A, Deutsch MA, Kainzinger S, et al. Extracorporeal membrane oxygenation in 108 patients with low cardiac output – a single-center experience. *Int J Artif Organs* 2011; 34: 365-73.
  - 30 Camboni D, Philipp A, Lubnow M, et al. Support time-dependent outcome analysis for veno-venous extracorporeal membrane oxygenation. *Eur J Cardiothorac Surg* 2011; 40: 1341-6.
  - 31 Chen YC, Tsai FC, Chang CH, et al. Prognosis of patients on extracorporeal membrane oxygenation: the impact of acute kidney injury on mortality. *Ann Thorac Surg* 2011; 91: 137-42.
  - 32 Foley DS, Pranikoff T, Younger JG, et al. A review of 100 patients transported on extracorporeal life support. *ASAIO J* 2002; 48: 612-9.
  - 33 Hei F, Lou S, Li J, et al. Five-year results of 121 consecutive patients treated with extracorporeal membrane oxygenation at Fu Wai Hospital. *Artif Organs* 2011; 35: 572-8.
  - 34 Hemmila MR, Rowe SA, Boules TN, et al. Extracorporeal life support for severe acute respiratory distress syndrome in adults. *Ann Surg* 2004; 240: 595-605.
  - 35 Kolla S, Awad SS, Rich PB, et al. Extracorporeal life support for 100 adult patients with severe respiratory failure. *Ann Surg* 1997; 226: 544-64.
  - 36 Sun HY, Ko WJ, Tsai PR, et al. Infections occurring during extracorporeal membrane oxygenation use in adult patients. *J Thorac Cardiovasc Surg* 2010; 140: 1125-32.
  - 37 Wu MY, Lin PJ, Lee MY, et al. Using extracorporeal life support to resuscitate adult postcardiotomy cardiogenic shock: treatment strategies and predictors of short-term and midterm survival. *Resuscitation* 2010; 81: 1111-6.
  - 38 Wu VC, Tsai HB, Yeh YC, et al; NSARF Study Group. Patients supported by extracorporeal membrane oxygenation and acute dialysis: acute physiology and chronic health evaluation score in predicting hospital mortality. *Artif Organs* 2010; 34: 828-35.
  - 39 Yu K, Long C, Hei F, et al. Clinical evaluation of two different extracorporeal membrane oxygenation systems: a single center report. *Artif Organs* 2011; 35: 733-7.
  - 40 Bennett CC, Johnson A, Field DJ, Elbourne D; UK Collaborative ECMO Trial Group. UK collaborative randomised trial of neonatal extracorporeal membrane oxygenation: follow-up to age 4 years. *Lancet* 2001; 357: 1094-6.
  - 41 Peek GJ, Mugford M, Tiruvoipati R, et al. Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial. *Lancet* 2009; 374: 1351-63.
  - 42 Chauhan S, Subin S. Extracorporeal membrane oxygenation, an anesthesiologist's perspective: physiology and principles. Part 1. *Ann Card Anaesth* 2011; 14: 218-29. □