Meta-analysis of the outcome after postcardiotomy venoarterial extracorporeal membrane oxygenation in adult patients

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Highlights

- One third of patients requiring VA-ECMO after adult cardiac surgery survive to discharge and most of them are alive one year after surgery.
- VA-ECMO may save the lives of significant number of patients who otherwise would succumb after adult cardiac surgery.
- Further studies are needed to identify patients who are likely to die or to have a poor quality of life after postcardiotomy VA-ECMO.

Abstract

Objective: This study was planned to pool existing data on the outcome and evaluate the efficacy of postcardiotomy venoarterial extracorporeal membrane oxygenation (VA-ECMO) in adult patients.

Design: Systematic review of the literature and meta-analysis.

Setting: Multistitutional study.

Participants: Adult patients with acute heart failure immediately after cardiac surgery.

Interventions: VA-ECMO after cardiac surgery. Studies evaluating only heart transplant patients were excluded from this analysis.

Measurements and main results: A literature search was performed to identify studies published since 2000. Thirty-one studies reported on 2986 patients (mean age, 58.1 years) who required postcardiotomy VA-ECMO. The weaning rate from VA-ECMO was 59.5% and hospital survival was 36.1% (95%CI 31.5 -40.8). The pooled rate of reoperation for bleeding was 42.9%, major neurological event 11.3%, lower limb ischemia 10.8%, deep sternal wound infection/mediastinitis 14.7% and renal replacement therapy 47.1%. The pooled mean number of transfused red blood cell units was 17.7 (95%CI 13.3-22.1). The mean stay in the intensive care unit was 13.3 days (95%CI 10.2-16.4). Survivors were significantly younger (mean, 55.7 vs. 63.6 years, p=0.015) and their blood lactate level before starting VA-ECMO was lower (mean, 7.7 vs. 10.7 mmol/L, p=0.028) than patients who died. One-year survival rate was 30.9% (95%CI 24.3-37.5).

Conclusions: Pooled data showed that VA-ECMO may salvage one third of patients unresponsive to any other resuscitative treatment after adult cardiac surgery.

Introduction

Cardiogenic shock after cardiac surgery may occur because of preoperative depressed ventricular function, intraoperative myocardial damage, incomplete coronary revascularization, myocardial stunning or hibernation, and technical factors.[1,2] High-dose inotropic support is the main treatment strategy for postcardiotomy cardiogenic shock. In case of postcardiotomy cardiogenic shock unresponsive to pharmacologic treatment, intraaortic balloon pump (IABP) is considered a valid adjunctive tool to improve cardiac performance by reducing cardiac afterload and improving coronary artery flow. However, IABP does not replace the cardiopulmonary function and venoarterial extracorporeal membrane oxygenation (VA-ECMO) is the only salvage therapy for patients with severe cardiopulmonary failure.[1,3-6] The aim of this study is to pool the available data from current studies on the outcome after VA-ECMO after adult cardiac surgery.

2. Methods

The present systematic review and meta-analysis is registered in the International prospective register of systematic reviews PROSPERO with the reference code ID=CRD42016048140.

2.1. Search Strategy

A literature review was performed through PubMed, Scopus, Sciencedirect and Google Scholar on September 2016, to identify any study being published since 2000 evaluating the outcome of patients who underwent VA-ECMO after adult cardiac surgery. The retrieval terms were ‘‘ECMO”, “extracorporeal membrane oxygenation", ECLS", "extracorporeal life support" combined with "postcardiotomy" OR "cardiac surgery" OR "coronary". Once the abstracts of potentially relevant studies were scrutinized, each study was independently evaluated by three coauthors (M.G., D.B., F.B.) for inclusion or exclusion from this analysis. Reference lists of retrieved articles were searched as well. The guidelines for Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) were applied.[7]

2.2 Treatment Definition and Inclusion/Exclusion Criteria

For the purpose of this analysis, eligible studies were those reporting on the outcome of adult patients who underwent VA-ECMO for acute heart failure and/or respiratory failure after cardiac surgery. Studies that met the Population, Interventions, Comparison and Outcomes (PICO) criteria (Tab. 1) were included in the present meta-analysis.

To enter this analysis, studies had to fulfil all these inclusion criteria: (1) provide data on patients who required VA-ECMO after cardiac surgery procedure; (2) include patients aged 18 years or older; (3) report data at least on in-hospital or 30-day mortality; (4) be a prospective or retrospective observational investigation; (5) be published in English language as a full article; (6) include at least 10 patients; (7) less than half of patients had heart transplantation; and (8) be published since 2000.

Articles were ineligible for study inclusion if they (1) reported ambiguous or inaccurate data (discrepancies between data reported in the text and tables); (2) did not provide specific information on the type of ECMO used in the study population and its related outcome; (3) did not provide specific information on the timing of insertion of VA-ECMO; (4) reported data on other than cardiac surgery interventions; (5) included pediatric patients; (6) included only patients undergoing heart transplantation. In particular, we excluded from this analysis those studies which did not clearly state that VA-ECMO was performed through any peripheral or central arterial and venous cannulation. In this regard, the definitions of cardiopulmonary resuscitation or postcardiotomy ECMO were not considered sufficient to consider the study population as having been treated with VA-ECMO. Indeed, venovenous-ECMO can also be used in some patients with respiratory failure occurring after cardiac surgery and their outcome is expected to be better outcome than those requiring VA-ECMO.

2.3. Data Extraction

Data were independently collected from the retrieved articles by two investigators (M.G. and D.B.) and checked by two investigators (F.B, and E.M.K.). Disagreement on collected data was settled by consensus between these investigators. No attempt was made to obtain specific or missing data from the authors. The following data were extracted: first author, year of publication, study period, overall number of adult cardiac surgery procedures performed during the study period, type of intervention, number of patients, gender, major comorbidities and outcome measures. VA-ECMO was considered as inserted intra- or postoperatively when not otherwise specified. The quality of the included studies was assessed by two investigators (F.B, and E.M.K.) using the National Heart, Blood, and Lung Institute (NHBLI) criteria for study quality assessment of case-control series (https://www.nhlbi.nih.gov/health-pro/guidelines/in-develop/cardiovascular-risk-reduction/tools/case_series; accessed on January 17, 2017) (Suppl. Tab. 1)

2.4. Outcome measures

The primary outcome of this analysis was hospital survival or 30-day survival. The secondary outcomes were weaning from VA-ECMO, intensive care unit stay, in-hospital stay, reoperation for bleeding, blood transfusion, major neurological events (stroke, intracranial bleeding and/or global brain ischemia), lower limb ischemia, lower limb amputation, deep sternal wound infection/mediastinitis, renal replacement therapy, implantation of ventricular assist device, heart transplantation and 1-year survival (Tab. 1). The definitions for these outcome measures were the ones adopted by the investigators of the included studies.

2.5. Statistical Analysis

Statistical analysis was performed using the Open Meta-Analyst software (Brown University, Providence, RI, USA; *http://www.cebm.brown.edu/openmeta/*). To control for the anticipated heterogeneity among observational studies, absolute values and means were pooled using random effects models. Heterogeneity across studies was evaluated using the I^2 test. The results are expressed as pooled untransformed proportions and means with their 95% confidence intervals (CI). Leave-one-out sensitivity analysis was performed to confirm consistency of the overall analysis. Mean differences were estimated to evaluate the differences in continuous variables between survivors and deaths. The impact of risk factors on hospital survival was evaluated by two-arm analysis and meta-regression. A $p<0.05$ was considered statistically significant.

3. Results

Thirty-one studies[5,6,8-37] including 2986 patients fulfilled the pre-specified selection criteria and were included in this analysis (Suppl. Fig. 1). Twenty-five studies (80.6%) were considered of good quality according to the NHBLI) criteria.

3.1. Patient characteristics and VA-ECMO management

The pooled proportion of VA-ECMO in the overall cardiac surgery population was 1.4% (95%CI 1.0-1.7, I^2 98%, 14 studies reporting on 169,329 patients). Two studies reported on patients who underwent isolated coronary artery bypass surgery, whereas the other studies reported on patients who underwent several types of cardiac surgery procedures. Sixteen studies reported the outcome of patients who required ECMO after heart transplantation among other cardiac surgery procedures (proportion of heart transplant patients, 11.6%, 95%CI 7.5-15.8, I^2 91%, 16 studies reporting on 1659 patients). The pooled proportion of heart transplant patients in the overall series was 4.4% (95%CI 3.5-5.6, I^2 89%, 28 studies reporting on 2879 patients). The mean pooled age of the patients was 58.1 years (95%CI 55.8-60.3, I^2 94%, 24 studies including 2234 patients) and 30.9% of the patients were female (95%CI 27.4-34.4, I^2 71%, 29 studies including 2903 patients) (Tab. 2). VA-ECMO was inserted at the time of surgery in 53.8% of the patients (95%CI 46.6-61.0, I^2 86%, 12 studies including 1224 patients). The primary arterial cannulation site was a peripheral artery in 79.0% of the patients (95%CI 73.8-84.3, I^2 98%, 23 studies including 2652 patients), IABP was used concomitantly in 62.2% of the patients (95%CI 48.9-75.6, I^2 99%, 19 studies including 1910 patients) and the oxygenator had to be changed in 11.4% of the patients (95%CI 7.2-15.7, I^2 82%, 8 studies including 1241 patients). Nineteen studies reported the therapeutic range of activated clotting time which was accepted being 200 sec or less in 17 studies (89.5%) and 180 sec or less in 9 studies (47.4%). The mean duration of VA-ECMO was 5.0 days (95%CI 4.1-6.0, I^2 99%, 25 studies including 2569 patients) ranging from a mean of 2.5 to 10.8 days (Tab. 2).

3.2. Early outcome

The pooled hospital survival after postcardiotomy VA-ECMO was 36.1% (Tab. 3) (Fig. 1). The leave-one-out analysis confirmed this finding (36.1%, 95%CI 31.5 -40.8). Study quality did not influence hospital survival (poor quality, 2 studies: 25.7%; fair quality, 6 studies: 40.0%; good quality, 23 studies: 36.0%; meta-regression: p=0.390). The pooled weaning rate from VA-ECMO was 59.1% (25 studies including 2197 patients; among these studies, the pooled hospital survival was 35.7%, 95%CI 31.4-40.0, I^2 74). The pooled mean stay in the intensive care unit was 13.3 days and the mean in-hospital stay was 22.5 days (Tab. 3).

The pooled rate of reoperation for bleeding was 42.9%, of major neurological event 11.3%, of lower limb ischemia 10.8%, of lower limb amputation 1.1%, of deep sternal wound infection/mediastinitis 14.7% and of renal replacement therapy 47.1%. The pooled mean number of red blood cell units was 17.7 (Tab. 3).

3.3. Post-ECMO implantation of ventricular assist devices and heart transplantation

A ventricular assist device was used after VA-ECMO in 2.3% of patients (95%CI 1.3-3.4, I^2 58%) and heart transplantation was performed in 1.9% of patients (95%CI 1.0-2.8, I^2 50%) as reported in 21 studies. Nine studies reported on the hospital survival of 45 patients who received any ventricular assist device implanted after postcardiotomy VA-ECMO. The pooled hospital survival of these patients was 45.6% (95%CI 28.0-63.1, I^2 43%) (Suppl. Fig. 2). Seven studies reported on hospital survival after heart transplantation in 18 patients after postcardiotomy VA-ECMO and its pooled rate was 66.2% (95%CI 48.2-84.1, I^2 0%) (Suppl. Fig. 3).

3.4. Baseline predictors of hospital survival

Meta-regression showed that the mid-term of study (p=0.442), proportion of VA-ECMO in the overall cardiac surgery population (single institutions included: p=0.262), mean number of VA-ECMO per year (single institutions included: p=0.631), mean duration of VA-ECMO (p=0.932), proportion of VA-ECMO inserted through a peripheral artery (p=0.704), proportion of VA-ECMO inserted later after surgery (p=0.101), proportion of IABP (p=0.926), and proportion of ventricular assist device or heart transplant after VA-ECMO (p=0.301) were not associated with hospital survival. Single institutions having higher mean number of postcardiotomy VA-ECMO per year did not have lower hospital survival rates (p=0.758).

Meta-regression showed a trend toward lower hospital survival in series with high mean age (p=0.064) (Suppl. Fig. 4). Twelve studies reported on the impact of patients' age on hospital survival after post-cardiotomy VA-ECMO. Pooled analysis showed that hospital survivors (387 patients) were significantly younger than patients who died after VA-ECMO (924 patients) (pooled mean age, 55.7 vs. 63.6 years; mean difference, -7.223 years, 95%CI -9.777- - 4.669, I^2 53%, p=0.015) (Fig. 2).

Six studies reported on the impact of the levels of blood lactate before starting VA-ECMO on hospital survival after post-cardiotomy ECMO. Pooled analysis showed that hospital survivors (211 patients) had significantly lower baseline levels of blood lactate than patients who died on VA-ECMO or after weaning from VA-ECMO (341 patients) (mean difference, -3.0 mmol/L, 95%CI –4.3- - 1.7, p=0.028 I^2 60%) (Suppl. Fig. 5). The pooled mean baseline blood lactate among survivors was 7.7 mmol/L (95%CI 4.8-10.5, I^2 97%) and the pooled mean levels of blood lactate among deaths was 10.7 mmol/L (95%CI 7.8-13.7, I^2 96%).

3.5. Impact of type of surgery on hospital survival

Two studies reported on VA-ECMO in patients who underwent isolated coronary surgery and hospital survival was 48.5% (95%CI 18.7-78.2, I^2 79%). All other series reported on mixed cardiac surgery procedures. Proportion of isolated coronary artery bypass grafting in these series was not predictive of hospital survival in meta-regression (p=0.546). The proportion of heart transplantation as a primary procedure tended to be associated with better hospital survival (meta-regression: p=0.082). Studies excluding patients with heart transplantation had a pooled hospital survival of 31.2% (95%CI 26.2-36.2, I^2 58%; 15 studies, 1220 patients), whereas it was 39.8% (95%CI 32.9-46.6, I^2 58%) in studies those including heart transplant patients (16 studies, 1659 patients) (meta-regression: p=0.060).

3.6. One-year survival

Eleven studies reported Kaplan-Meier estimates of 1-year survival including operative deaths. The pooled 1-year survival rate after postcardiotomy VA-ECMO was 30.9% (95%CI 24.3-37.5, I^2 82%, 1290 patients estimated at risk) (Suppl. Fig. 6). Three studies reporting only on patients who underwent general cardiac surgery had a 1-year pooled survival of 24.6% (95%CI 13.5-35.7, I^2 78%, 554 patients estimated at risk) and eight studies including a few heart transplant patients had 1-year pooled survival of 33.5% (95%CI 26.6-40.4, I^2 66%, 736 patients estimated at risk) (meta-regression: p=0.092).

4. Discussion

The present pooled analysis showed that VA-ECMO is a valid mean to salvage one third of patients with profound cardiogenic shock after adult cardiac surgery. Older age and hyperlactatemia before starting VA-ECMO seems to have a significant negative impact on hospital survival.

The estimated hospital survival (36.1%) was poorer than the one (55.8%) reported by Maxwell et al.[4] from the Nationwide Inpatient Sample database. However, the analysis of this administrative dataset did not include information on the type of ECMO used in these patients. This finding was not confirmed even by a more recent analysis of the same registry whose hospital survival after postcardiotomy ECMO was 40%.[3] Indeed, VA-ECMO after adult cardiac surgery is associated with higher risk of in-hospital mortality compared with other conditions.[26,31,38] This negative prognostic effect may be explained by the combined impact of the underlying cardiac disease and the extent of the surgical procedure along with any possible concomitant technical complication occurring during surgery. Despite this, VA-ECMO confirmed its value in salvaging a significant number of patients who would have most certainly died without mechanical cardiopulmonary resuscitation. The efficacy of this salvage therapy was confirmed by a satisfactory 1-year survival of 30%.

It is worth noting that hospital survival and 1-year survival were somewhat lower in series including only patients undergoing general cardiac surgery compared with series including a small number of heart transplant patients. This finding could be explained by a better outcome of patients requiring ECMO after heart transplantation as well as by larger experience in ECMO and heart failure therapies at heart transplant centers.

The present analysis showed that despite a rather high weaning rate from VA-ECMO of about 60%, the pooled hospital survival of these patients was 36%. This finding is of clinical importance because several patients likely died despite initially satisfactory hemodynamics. The retrieved studies did not provide detailed data on the causes of deaths of patients weaned from ECMO. The post-ECMO cardiorespiratory conditions at the time of weaning were possibly not optimal or deteriorated shortly after weaning. It is unknown whether a prolonged ECMO therapy would have allowed a better recovery in these patients. Furthermore, there is scarce data on the impact of VAD implantation and heart transplantation in these patients. In fact, we observed that only 4% of patients underwent implantation of a ventricular assist device or underwent heart transplantation and their pooled hospital survival was 45.6% and 66.2%, respectively.

This pooled analysis showed that 1.4% of patients undergoing adult cardiac surgery required VA-ECMO. This figure suggests that each center of cardiac surgery faces rather often the dilemma of whether to treat postcardiotomy cardiogenic shock with VA-ECMO. This prompts the need of expertise in the decision-making process as well as in the management of a relatively large number of patients. In fact, the estimated prevalence of patients requiring VA-ECMO might have been biased by a strict patient selection and the uncertainty of the benefit of this therapy as suggested by the rather young age of these patients (mean age, 58.2 years). Indeed, advanced patients' age was associated with a significantly poorer early survival. Subanalyses of patients aged 70 years or more demonstrated that a few elderly patients may still survive to discharge after postcardiotomy VA-ECMO.[10,39] This observation suggests that further studies are needed to assess whether advanced age is an absolute contraindication to postcardiotomy ECMO or whether this treatment can still be valuable in absence of significant comorbidities and critical hemodynamic conditions.

The decision of whether to institute VA-ECMO in these critically ill patients is rendered difficult by the lack of other indicators of prohibitive mortality risk. In fact, most of the studies focused on the identification of clinical variables and biomarkers of prognostic importance during ECMO, in order to understand when this therapy should be prolonged or discontinued. However, identification of risk factors predicting a prohibitive mortality risk before instituting ECMO would be of greater value to guide the decision-making process and allocation of resources in these patients. In this regard, the present findings suggest that VA-ECMO may be contraindicated in the elderly and in those patients with increased blood lactate before instituting VA-ECMO. Still, we were unable to assess whether patients undergoing a salvage operation after a cardiac arrest or acute heart failure may have a different outcome than patients more stable conditions, because the included studies did not report on the outcome of such different conditions. Indeed, the lack of data on the outcome of patients with specific baseline conditions and operative variables (for example: young patients vs. elderly patients; preserved left ventricular function vs. depressed left ventricular function; elective surgery vs. emergency/salvage surgery; isolated coronary artery bypass grafting vs. heart valve surgery vs. aortic surgery; etc.) prevented a more in depth analysis of the potential benefits and harms in these subgroups of patients.

A few limitations of this study deserve to be acknowledged. First, this is an aggregate data meta-analysis which does not allow analysis of data at patient level. This prevents the analysis of pre-, intra- and postoperative variables which may affect the early and late survival of these patients as well as the occurrence of severe adverse events such as major bleeding and neurological complications. Second, many of these studies are of small size and retrospective nature, which prevent conclusive results. Third, the lack of information on important patients' characteristics, treatment methods and outcomes prevented the pooling of important data from all available studies. Fourth, differences between institutions in terms of patient selection, volume and expertise, treatment strategy as well as availability of ventricular assist devices and heart transplant might have had a significant impact on the outcome of these patients. Indeed, the significant heterogeneity of outcomes between studies is possibly related to such inter-institutional differences. Furthermore, it is also possible that reported series are from centers with expertise with ECMO and reported outcome could not be replicated in centers with more limited experience. Fifth, most of studies are of retrospective nature and of suboptimal quality. This could be a source of significant bias in the present analysis. Sixth, only thirteen studies reported on the mid-term survival of these patients and this prevented an evaluation of the durability of this salvage therapy in a larger study population. Seventh, the retrieved studies included heterogenous procedures ranging from elective isolated coronary artery bypass grafting to emergency operation for aortic dissection. Sensitivity analyses for different types of cardiac operations were not feasible and therefore, it remains unknown whether the type of surgery may affect the outcome of postcardiotomy VA-ECMO. Finally, we excluded from this analysis those studies evaluating only the outcome of patients who required ECMO after heart transplantation. This decision was taken considering the differences in terms of baseline characteristics, causes of postoperative heart failure and outcome of heart transplant patients who required ECMO as compared with patients undergoing general cardiac surgery.[9,40] Studies reporting on a few of heart transplant patients among other patients undergoing general cardiac surgery were still included in this analysis and survival of these series were analyzed separately. In fact, exclusion of series reporting a small proportion of heart transplant patients would have introduced a possible bias related to the expertise in ECMO and heart failure therapies in heart transplant centers as well as to a significant reduction of the sample size of this analysis.

5. Conclusions

Based on the results of this pooled analysis, one third of patients requiring VA-ECMO after adult cardiac surgery survive to discharge and most of them are alive one year after surgery. This data suggests that, despite the increased burden of resources needed for the management of VA-ECMO, this aggressive treatment may save the lives of a significant number of patients who otherwise would succumb after adult cardiac surgery. Data from large prospective multicenter registries is needed to confirm these findings and identify patients who may most benefit of VA-ECMO. In particular, future studies should evaluate the benefits and harms of different strategies of cannulation, management and weaning from VA-ECMO, the value of ventricular assist device and heart transplantation in this setting as well as the long-term survival and quality of life of these patients.

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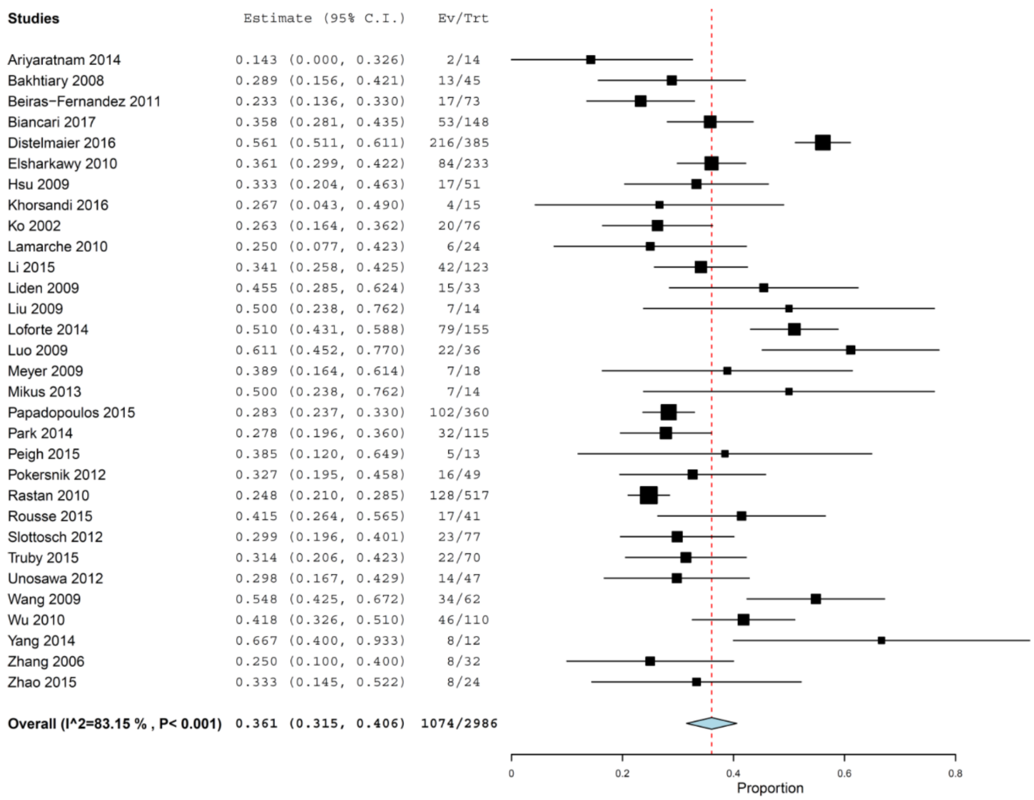


Figure 1. Forest plot of hospital survival after postcardiotomy venoarterial extracorporeal membrane oxygenation in adults.

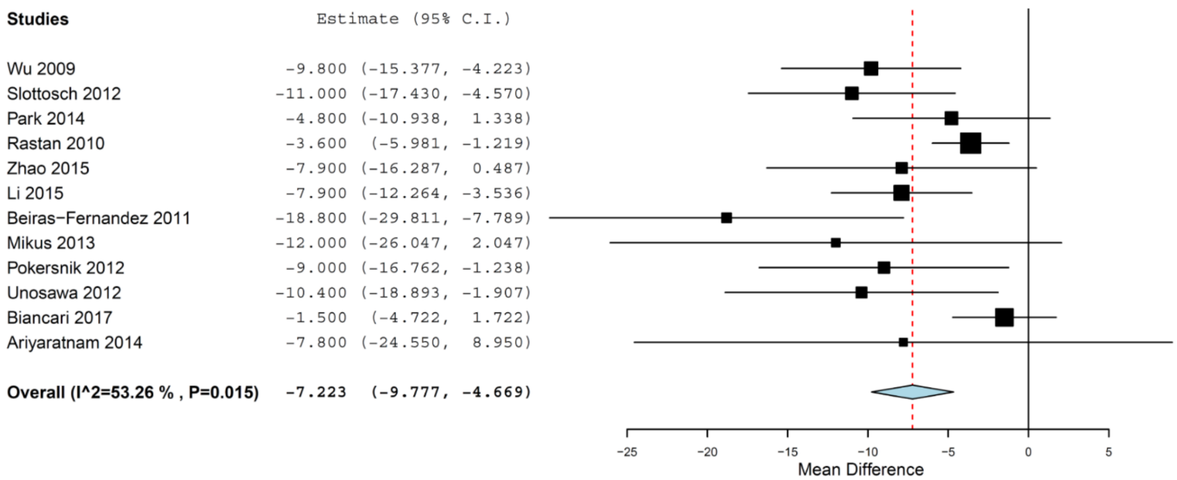


Figure 2. Forest plot summarizing the difference in age of adult patients who survived and those who died after postcardiotomy venoarterial extracorporeal membrane oxygenation.

Table 1

Participants, intervention, comparison and outcomes (PICO) of the present meta-analysis.

PICO	Description
Population	Patients who underwent any adult cardiac surgery procedure
Intervention	Venoarterial extracorporeal membrane oxygenation for acute heart and/or respiratory failure after adult cardiac surgery
Comparison	None
Outcomes	Hospital survival, 1-year survival, weaning from support, intensive care unit stay, in-hospital stay, reoperation for bleeding, blood transfusion, major neurological events, lower limb ischemia, lower limb amputation, deep sternal wound infection/mediastinitis, renal replacement therapy, implantation of ventricular assist device, heart transplantation

Table 2

Characteristics and outcomes reported in studies included in the present meta-analysis.

Author	Year	Study quality	No. of patients	Mean age (years)	ECMO started at surgery (%)	IABP (%)	Peripheral ECMO (%)	Mean ECMO duration (days)	Weaned from ECMO (%)	Hospital survival (%)	1-year survival (%)
Ariyaratnam	2014	Poor	14	65.6	-	-	-	5.6	50	14	-
Bakhtiary	2008	Good	45	60.1	67	67	82	6.4	56	29	27
Beiras-Fernandez	2011	Good	73	49.3	-	49	-	4.4	-	23	-
Biancari	2017	Good	148	65.4	51	32	60	6.4	-	36	31
Distelmaier	2016	Good	385	-	-	-	90	4	-	56	40
Elsharkawy	2010	Good	233	-	-	-	67	-	-	36	-
Hsu	2009	Good	51	63.0	-	100	-	7.5	53	33	29
Khorsandi	2016	Fair	15	-	-	-	-	5.4	-	27	-
Ko	2002	Good	76	56.8	51	58	80	10.5	55	26	25
Lamarche	2010	Good	24	52.5	67	-	63	-	63	25	-
Li	2015	Good	123	56.2	50	59	100	4.4	56	34	-
Liden	2009	Good	33	52.4	-	42	36	5.5	79	45	36
Liu	2009	Good	14	55.7	64	71	100	3.0	64	50	43
Loforte	2014	Fair	155	55.0	-	100	51	8.2	57	51	-
Luo	2009	Good	36	-	-	31	-	-	67	61	-
Meyer	2009	Poor	18	50	-	-	100	4	67	39	-
Mikus	2013	Fair	14	53.1	86	100	43	9	50	50	-
Papadopoulos	2015	Good	360	62	-	22	90	7	58	28	26
Park	2014	Good	115	61.7	36	-	100	3.0	41	28	-
Peigh	2015	Good	13	-	-	-	-	-	-	38	-
Pokersnik	2012	Good	49	65	-	59	65	3.8	55	33	-
Rastan	2010	Good	517	63.5	42	74	39	3.3	63	25	17
Rousse	2015	Good	41	47	-	12	90	-	37	41	-
Slottosch	2012	Good	77	60	44	94	100	3.3	62	30	-
Truby	2015	Good	70	-	-	-	-	-	-	31	-
Unosawa	2012	Fair	47	64.4	70	-	68	2.6	62	30	30
Wang	2009	Good	62	51	-	31	-	2.5	65	55	52
Wu	2010	Good	110	60.6	-	-	100	6.0	61	42	-
Yang	2014	Fair	12	60.4	-	100	100	5.2	100	67	-
Zhang	2006	Good	32	55.4	-	-	59	2.9	44	25	-
Zhao	2015	Fair	24	59.3	37	88	96	4.8	67	33	-

Table 3

Pooled rates of early outcomes.

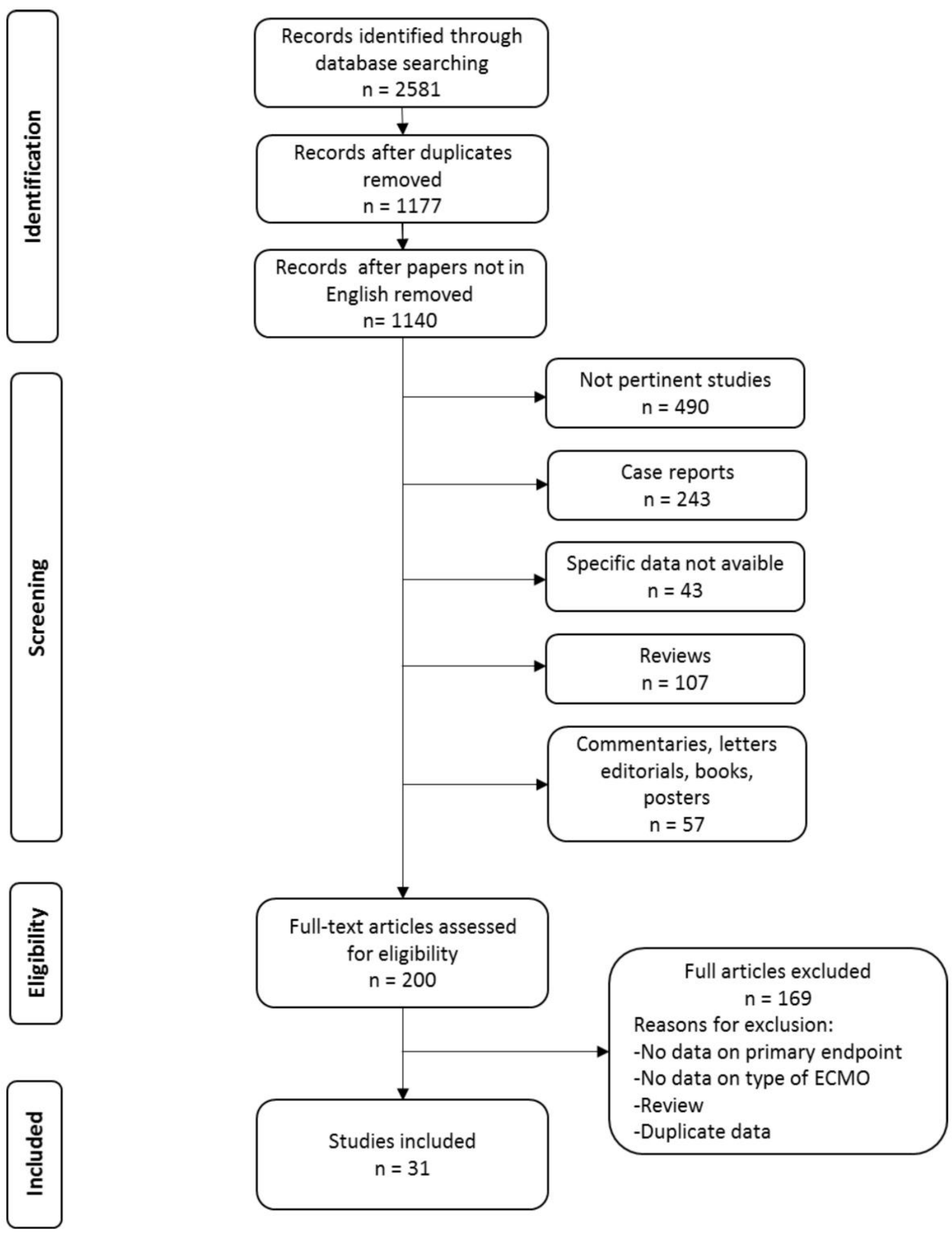
Outcomes	*No. of studies*	*No. of patients*	*Proportion / Mean (95%CI)*	I^2
Hospital survival (%)	31	2986	36.1 (31.5-40.8)	84%
Weaning from VA-ECMO (%)	24	2049	59.5 (54.6-64.3)	77%
Reoperation for bleeding (%)	18	1779	42.9 (34.2-51.5)	93%
RBC units transfused	11	1241	17.7 (13.3-22.1)	99%
Major neurological event (%)	16	1736	11.3 (7.8-14.8)	79%
Limb ischemia (%)	16	1909	10.8 (8.0-13.5)	70%
Lower limb amputation (%)	5	330	1.1 (0.0-2.3)	0%
Deep sternal wound infection/mediastinitis (%)	4	490	14.7 (4.0-25.4)	92%
Renal replacement therapy (%)	19	1979	47.1 (38.9-55.2)	92%
Ventricular assist device (%)	21	1685	2.3 (1.3-3.4)	57%
Heart transplantation (%)	21	1685	1.9 (1.0-2.8)	50%
Intensive care unit stay (days)	10	589	13.3 (10.2-16.4)	95%
In-hospital stay (days)	9	1154	22.5 (17.7-27.3)	95%

Pooled estimates are reported as percentages or means with 95%confidence intervals (95%CI); VA-ECMO: venoarterial extracorporeal membrane oxygenation; RBC: red blood cell.

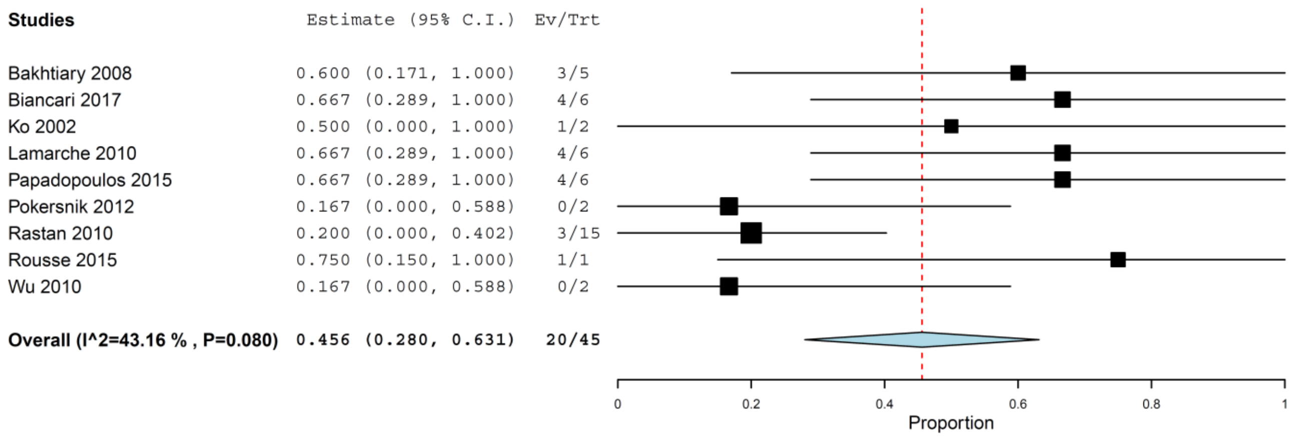
Supplementary digital content

Meta-analysis of the Outcome after Postcardiotomy Venoarterial Extracorporeal Membrane Oxygenation in Adult Patients

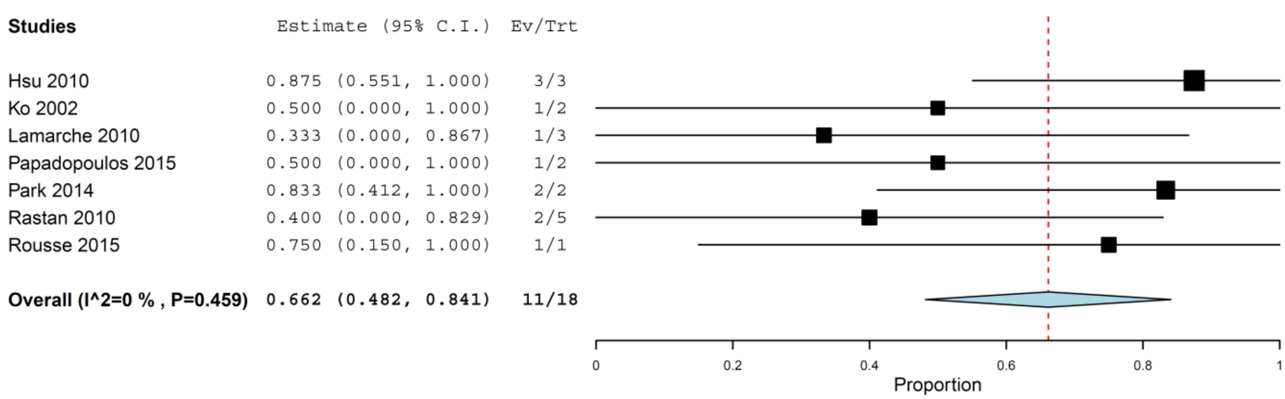
Content



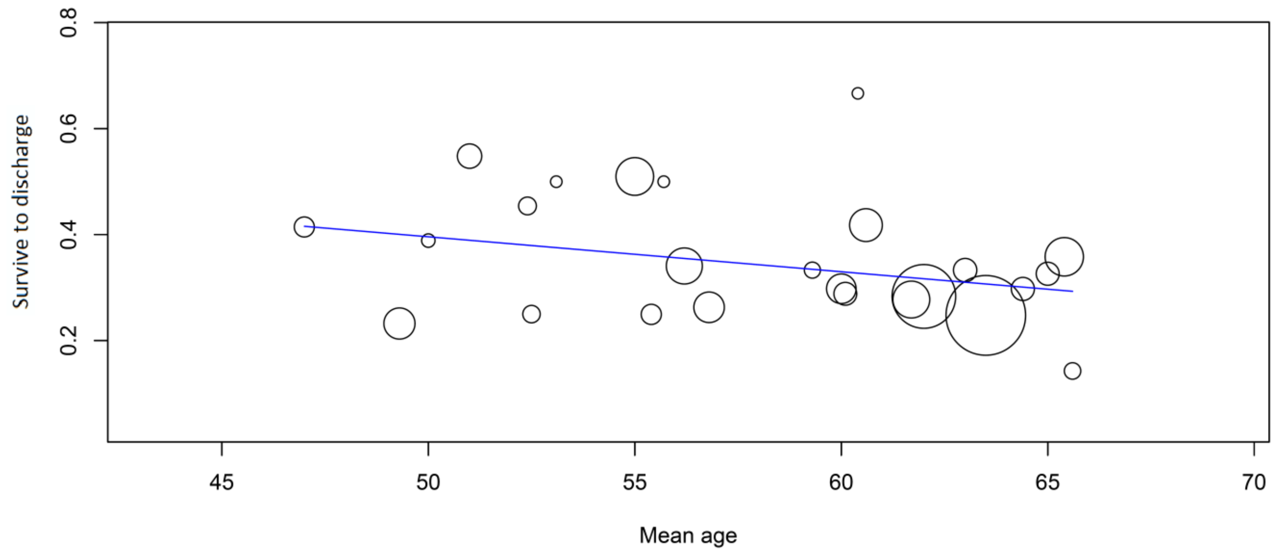
Supplementary figure 1. Flow chart of the literature search.



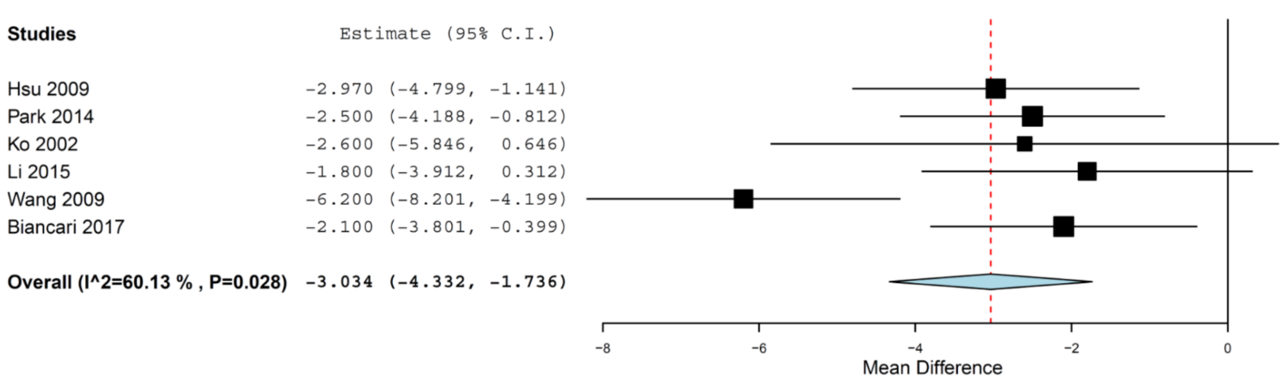
Supplementary figure 2. Forest plot of the pooled rate of hospital survival in patients who received any ventricular assist device after postcardiotomy venoarterial extracorporeal membrane oxygenation in adults.



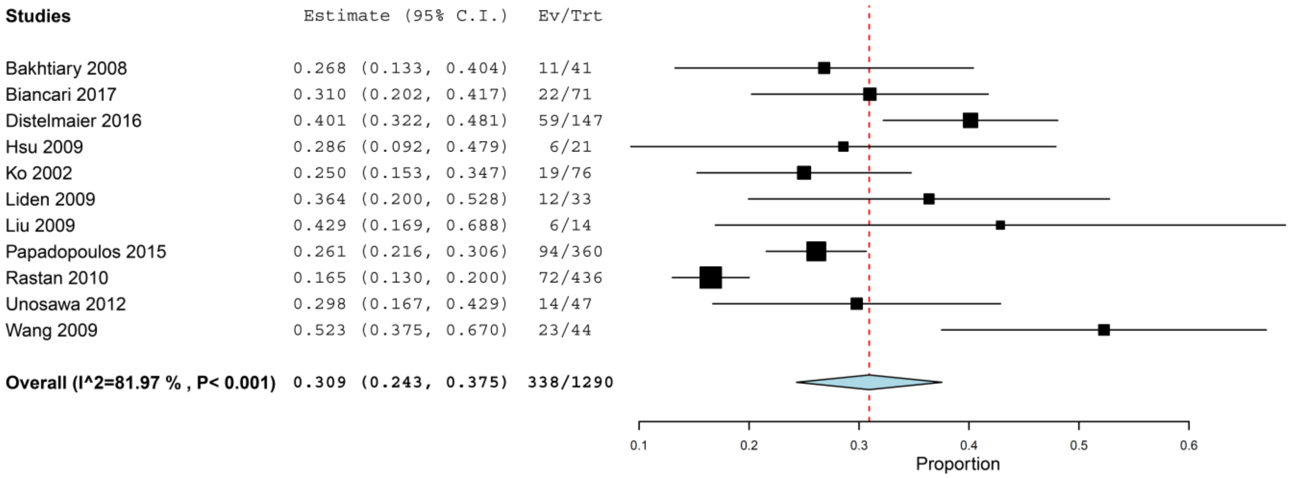
Supplementary figure 3. Forest plot of the pooled rate of hospital survival in patients who underwent heart transplantation after postcardiotomy venoarterial extracorporeal membrane oxygenation in adults.



Supplementary figure 4. L'Abbé plot showing the impact of mean age on hospital survival after postcardiotomy venoarterial extracorporeal membrane oxygenation in adults.



Supplementary figure 5. Forest plot summarizing the difference between survivors and deaths in blood lactate before starting postcardiotomy venoarterial extracorporeal membrane oxygenation.



Supplementary figure 6. Forest plot summarizing pooled 1-year survival after postcardiotomy venoarterial extracorporeal membrane oxygenation in adult patients.

	Ariyaratnam			**Bakhtiary**			**Beiras-Fernandez**			**Biancari**			**Distelmaier**			**Elsharkawy**		
Criteria	Yes	No	Other	Yes	No	Other	Yes	No	Other	Yes	No	Other	Yes	No	Other	Yes	No	Other
1. Was the study question or objective clearly stated?		x		x			x			x			x			x		
2. Was the study population clearly and fully described, including a case definition?	x			x			x			x			x			x		
3. Were the cases consecutive?			NR			NR	x			x			x					NR
4. Were the subjects comparable?	x			x			x			x			x			x		
5. Was the intervention clearly described?	x			x			x			x			x			x		
6. Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants?		x		x			x			x			x			x		
7. Was the length of follow-up adequate?	x			x			x			x			x			x		
8. Were the statistical methods well-described?	x			x			x			x			x			x		
9. Were the results well-described?		x		x			x			x			x			x		
Quality rating	Poor			Good			Good			Good			Good			Good		

Supplementary table 1. Quality assessment of studies reporting on the outcome after extracorporeal membrane oxygenation in patients who underwent adult cardiac surgery according to the National Heart, Lung, and Blood Institute criteria.

	Hsu			Khorsandi			Ko			Lamarche			Li			Liden		
Criteria	Yes	No	Other	Yes	No	Other	Yes	No	Other	Yes	No	Other	Yes	No	Other	Yes	No	Other
1. Was the study question or objective clearly stated?	x			x			x			x			x			x		
2. Was the study population clearly and fully described, including a case definition?	x			x			x			x			x			x		
3. Were the cases consecutive?			NR	x					NR	x					NR			NR
4. Were the subjects comparable?	x			x			x			x			x			x		
5. Was the intervention clearly described?	x			x			x			x			x			x		
6. Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants?	x				x		x			x			x			x		
7. Was the length of follow-up adequate?	x			x			x			x			x			x		
8. Were the statistical methods well-described?	x				x		x			x			x			x		
9. Were the results well-described?	x			x			x			x			x			x		
Quality rating	Good			Fair			Good			Good			Good			Good		

	Liu			Loforte			Luo			Meyer			Mikus			Papadopoulos		
Criteria	Yes	No	Other	Yes	No	Other	Yes	No	Other	Yes	No	Other	Yes	No	Other	Yes	No	Other
1. Was the study question or objective clearly stated?		x			x		x				x			x		x		
2. Was the study population clearly and fully described, including a case definition?	x			x			x			x			x			x		
3. Were the cases consecutive?			NR	x					NR			NR	x			x		
4. Were the subjects comparable?	x			x			x			x			x			x		
5. Was the intervention clearly described?	x			x			x			x			x			x		
6. Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants?	x				x		x				x			x		x		
7. Was the length of follow-up adequate?	x			x			x			x			x			x		
8. Were the statistical methods well-described?	x			x			x				x		x			x		
9. Were the results well-described?	x			x			x				x		x			x		
Quality rating	Good			Fair			Good			Poor			Fair			Good		

	Park			Peigh			Pokersnik			Rastan			Rousse			Slottosch		
Criteria	Yes	No	Other	Yes	No	Other	Yes	No	Other	Yes	No	Other	Yes	No	Other	Yes	No	Other
1. Was the study question or objective clearly stated?	x			x			x			x				x		x		
2. Was the study population clearly and fully described, including a case definition?	x			x			x			x			x			x		
3. Were the cases consecutive?	x					NR			NR	x			x			x		
4. Were the subjects comparable?	x			x			x			x			x			x		
5. Was the intervention clearly described?	x			x			x			x			x			x		
6. Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants?		x		x			x			x			x			x		
7. Was the length of follow-up adequate?	x			x			x			x			x			x		
8. Were the statistical methods well-described?	x			x			x			x			x			x		
9. Were the results well-described?	x			x			x			x			x			x		
Quality rating	Good			Good			Good			Good			Good			Good		

	Truby			Unosawa			Wang			Wu			Yang			Zhang		
Criteria	Yes	No	Other	Yes	No	Other	Yes	No	Other	Yes	No	Other	Yes	No	Other	Yes	No	Other
1. Was the study question or objective clearly stated?	x			x			x			x			x			x		
2. Was the study population clearly and fully described, including a case definition?	x			x			x			x			x			x		
3. Were the cases consecutive?	x					NR			NR			NR	x					NR
4. Were the subjects comparable?	x			x			x			x			x			x		
5. Was the intervention clearly described?	x			x			x			x			x			x		
6. Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants?	x				x		x				x		x				x	
7. Was the length of follow-up adequate?	x			x			x			x			x			x		
8. Were the statistical methods well-described?	x			x			x			x			x			x		
9. Were the results well-described?	x			x			x			x			x			x		
Quality rating	Good			Fair			Good			Fair			Good			Good		

	Zhao		
Criteria	Yes	No	Other
1. Was the study question or objective clearly stated?	x		
2. Was the study population clearly and fully described, including a case definition?	x		
3. Were the cases consecutive?			NR
4. Were the subjects comparable?	x		
5. Was the intervention clearly described?		x	
6. Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants?		x	
7. Was the length of follow-up adequate?	x		
8. Were the statistical methods well-described?	x		
9. Were the results well-described?	x		
Quality rating	Fair		

NR: not reported