

**Supplemental table 1:** Characteristics of the included trials (randomised trials).

<b>Study ID</b>	Kussmann 2009	Kraft 2013	Brown 2016
<b>Methods</b>	prospective randomised controlled single center trial	prospective randomised controlled single center trial	Prospective randomised single center trial
<b>Participants</b>	104 children less than 9 months of age, cardiac surgery (congenital heart disease) under hypothermic CPB	152 severely burned children (>30% TBSA) aged 7.1-9.7 years old	Patients undergoing scoliosis repair under 18 years
<b>Interventions</b>	104 children monitored with cerebral NIRS allocated to three groups: 23 children (2 control groups, control group1=12 children with integrated rSO <sub>2</sub> ≤45% (=minutes x desaturations points % ) between 0.3-39 minutes % and control group2= 11 children with integrated rSO <sub>2</sub> ≤45% between 60–383 minutes% ) versus groupe3= 81 children (experimental group) with integrated rSO <sub>2</sub> ≤45% =0 minutes %	76 children managed with PiCCO (Experimental group) for fluid and hemodynamic optimisation Versus 76 children managed with standard care (Control) for fluid and	Fluid management, boluses of 5ml/kg of plasmalyte, in goal-directed fluid therapy (GDT) protocol guided by transesophageal doppler measurement (7 patients experimental group)VERSUS Fluid management, with boluses of 5ml/kg of plasmalyte in standard care guided by clinical judgment ( 7 patients control group)
<b>Outcomes</b>	lactate at 60 minutes post-CPB, cardiac index at 6 and 18 hours post CPB, length of intubation, ICU and hospital stay, and Modified Pediatric Risk of Mortality-III (PRISM III) scores at 12 and 24 hours post-CPB	morbidity (sepsis) and mortality over 20 days of burn injury	Postsurgical kidney dysfunction, Length of hospitalisation, number of intra-operative hypotensive episodes , Incidence of intra-operative spinal cord monitoring changes from the evoked potentials
<b>Bias</b>	Unclear for blinding	Unclear for randomisation, blinding and allocation concealment	Unclear for randomisation, blinding and allocation concealment
<b>Mortality control group (n)</b>	0	19	NA
<b>Mortality experimental group (n)</b>	0	12	NA
<b>Organ dysfunction control group</b>	NA	NA	0

(n)			
Organ dysfunction experimental group (n)	NA	NA	7
Infections control group	NA	13	NA
Infections experimental group (n)	NA	7	NA
LOS control group in days mean±SD or median [IQR]	group1 7[5.5-8]; group2 9[5-21]	0.6 ± 0.1	NA
LOS experimental group in days mean±SD or median [IQR]	7[5-8]	0.6 ± 0.0	NA

NA non applicable, CPB cardiopulmonary bypass, LOS length of hospital stay, SD standard deviation, IQR interquartile range, ICU intensive care unit, TBSA total burned surface area, PiCCO pulse contour cardiac output, rSO2 regional oxygen saturation, NIRS near infrared spectroscopy

**Supplemental table 2:** characteristics of the included trials (non randomised prospective trials).

Study ID	Gist 2016	RuRuf 2015	Hatherill 1997	Dewitt 2014	Gaies 2014	Gil-Anton 2014
<b>Methods</b>	prospective observational single center trial	prospective observational single center trial	prospective observational single center trial	prospective observational single center trial	Prospective, multi-institutional observational (4 centers) cohort study	prospective observational single center trial
<b>Participants</b>	106 children aged $\leq 4$ years old or $\leq 15$ kg in cardiac surgery, congenital heart surgery or heart transplantation under CPB	59 infants $<12$ months and $<10$ kg undergoing cardiopulmonary bypass surgery for congenital heart disease for univentricular (n = 26) or biventricular (n = 33) repair	99 children with a median age of 5 months [0.38–31] after congenital heart disease surgical repair/CPB admitted PICU	64 neonates (aged 0-28 days, weighing $3.3 \pm 0.5$ kg) congenital heart disease surgery	391 children $<1$ year of age cardiac surgery/CPB treated postoperatively in the CICU	35 children median age 18 months [3-144] median weight 10kg [3.8-58] PICU post cardiac surgery /CPB
<b>Interventions</b>	12 children with a $\geq 20\%$ reduction from the baseline in renal NIRS for 20 consecutive minutes intraoperatively or within the first 24 postoperative hours(=control group)/ 94 children with $< 20\%$ reduction from the baseline in renal NIRS for 20 minutes (=experimental group)	28 infants (control group) with an intraoperative median rNIRS65 score of 598 min% (= desaturation points of renal SO <sub>2</sub> $< 65\%$ X minutes) and an intraoperative median rNIRS25 score of 131 min% (= decrease of renal rSO <sub>2</sub> of more than 25% from the baseline value X minutes )/ 31 infants (experimental group) with an intraoperative	Median Postoperative blood lactate level measurements on admission in the PICU in 9 non-survivors (control group) VERSUS 90 survivors (experimental group)	34 neonates with (control group) with average postoperative splanchnic regional oxymetry rSO <sub>2</sub> of $51.6 \pm 14.8\%$ /30 neonates (experimental group) with average postoperative splanchnic regional oxymetry rSO <sub>2</sub> of $70.3 \pm 12.0\%$ before and during enteral feedings	132 children with maximum VIS $\geq 20$ ) in the first 24h postoperatively (control group) versus 256 children with maximum VIS $< 20$ (experimental group) remark 3 children with missing VIS	PiCCO Cardiac Index monitoring during first 24 hours after admission in PICU: 17 children with CI $< 3$ L/min/m <sup>2</sup> (=control group)/18 children with CI $\geq 3$ L/min/m <sup>2</sup> (= experimental group)

		median rNIRS65 score of 158 min% and an intraoperative median rNIRS25 score of 0 min%				
<b>Outcomes</b>	Postoperative Mortality and AKI, postoperative increased AKI biomarkers, other postoperative adverse outcomes (LOS, LOSICU, LMV, VIS,)	Intraoperative and postoperative AKI	Postoperative mortality	Postoperative Morbidity= NEC	Mortality, LMV ECMO, cardiac arrest, RRT, neurologic injury, LOSICU, reinterventions under CPB	LOS LOSICU, LMV
<b>Bias</b>	High for randomisation, blinding and allocation concealment	High for randomisation, blinding and allocation concealment	High for randomisation, blinding and allocation concealment	High for randomisation, blinding and allocation concealment	High risk for blinding	High for randomisation, blinding and allocation concealment
<b>Mortality control group (n)</b>	2	0	9	NA	10	NA
<b>Mortality experimental group (n)</b>	1	0	0	NA	9	NA
<b>Organ dysfunction control group (n)</b>	AKI 3	AKI 28 (among which 3 had RRT)	NA	ECMO 4	23	NA
<b>Organ dysfunction experimental group (n)</b>	AKI 31	AKI 0 (RRT 0)	NA	ECMO 1	22	NA
<b>Infections control group</b>	NA	NA	NA	NEC 11	NA	NA
<b>Infections experimental group (n)</b>	NA	NA	NA	NEC 0	NA	NA
<b>LOS control group in days mean± SD</b>	22 [14-36]	28 [7-76]	NA	NA	NA	16 [4-50]

<b>or median [IQR]</b>						
<b>LOS experimental group in days mean± SD or median [IQR]</b>	10 [8-12]	25 [12-96]	NA	NA	NA	6[2-15]

VIS vasoactive inotropic score, AKI acute kidney injury, RTT renal replacement therapy, LMV duration of mechanical ventilation, PICU pediatric intensive care unit, ECMO extracorporeal membrane oxygenator, NEC necrotising enterocolitis, CICU Cardiac intensive care unit, LOSICU length of stay in the intensive care unit, CI cardiac index

**Supplemental table 3:** characteristics of the included trials (non randomised prospective trial).

<b>Study ID</b>	Aly 2017	Siegel 1996	Cheung 2005	Schumacher 2014	Kapoor 2016	Ladha 2016
<b>Methods</b>	prospective observational single center trial	prospective observational single center trial	prospective observational single center trial	prospective observational single center trial	prospective observational single center trial	Prospective observational
<b>Participants</b>	68 children median age 5 days [4-8], median weight 3.5 kg [3-3.8] with complex congenital heart disease, cardiac surgery children)	41 children aged 2 weeks to 16 years congenital heart disease surgical repair/CPB, PICU	85 infants aged ≤ 6 weeks with congenital heart disease intra- cardiac surgery	231 infants aged <12 months undergoing cardiac surgery/CPB, PICU	150 children (6 months to 12 years) TOF surgery	200 children weighing 5–20 kg, TOF surgery
<b>Interventions</b>	Preoperative, intraoperative and postoperative cerebral tissue oxygenation index (cTOI) measured by NIRS, blood lactate and inotrop scores: 29 children (experimental group) with mean cTOI 60 minutes off-CPB of 58%, 24 hours postoperative of 59%, mean lactate levels of 5.4 mmol/L at 60	Lactate levels on admission in the PICU in 11 patients (non survivors and patients with MOF) (control group)/ 30 patients (survivors and patients without MOF) (experimental group)	postoperative lactate levels on admission in PICU in 43 patients (experimental group) with lactate levels of 5.5±2.6 mmol/L and lactime to ≤5 mmol/L of 3±6 hours, lactime to ≤ 2mmol/L of 11±9 h VERSUS 42 patients (control group) with higher mean lactate	Lactate levels measured for the first 24 postoperative hours in 212 (experimental group) with lower initial median and peak median lactate levels VERSUS 19 (control group) with	Lactate levels, endothelin and central venous oxygen saturation ( ScVO2, vigileo ) T1= before induction of anesthesia; T2=20 minutes after protamine administration; T3 =24 hours postadmission in the ICU in 11 non-survivors (control group) and 139 survivors (experimental group)	Lactate levels and lactate clearance before surgery (T0), after surgery at admission in ICU (T1), every 6h postoperatively in ICU for 24 hours in 11 non survivors (group control) and in 189 survivors

	minutes off-CPB and of 5 mmol/L 24 hours postoperatively VERSUS 39 patients (control group) with mean cTOI 60 minutes off-CPB of 48%, 24 hours postoperatively of 49% and lactate levels of 6.5mmol/L 60 minutes off-CPB and of 8.2 mmol/L postoperatively		levels of 10.7±4.9 mmol/L and 6.3±2.4 mmol/L and lactime to ≤5mmol/L of 11±11h and 4±4 hours and lactime to ≤ 2mmol/L of 23±9 hours and 16±10 hours	higher initial median and peak median lactate levels		(experimental group)
<b>Outcomes</b>	Postoperative mortality and neurodevelopmental outcome at 6, 15 and 21 months	Postoperative Mortality and MOF	Postoperative mortality and Morbidity (early childhood neurodevelopment disability (cerebral palsy, legal blindness, hearing loss) or neurodevelopment delay (mental developmental index and or performance developmental index <70±SD) at 18 and 24 months of age) )	Postoperative mortality, morbidity ( dialysis, ECMO)	Postoperative mortality	Mortality, LMV, LOSI CU, inotrop requirements
<b>Bias</b>	High for randomisation, blinding and allocation concealment	High for randomisation, blinding and allocation concealment	High for randomisation, blinding and allocation concealment	High for randomisation, blinding and allocation concealment	High for randomisation, blinding and allocation concealment	High for randomisation, blinding and allocation concealment
<b>Mortality control group (n)</b>	14	7	14	11	11	11
<b>Mortality experimental group (n)</b>	0	0	0	0	0	0
<b>Organ</b>	25 patients with	MOF 11	28	9 ECMO, 7	NA	5 LOS, 1

<b>dysfunction control group (n)</b>	Bayley Scales of Infant Development score (BSID score)<70 (=neurodevelopmental score)				RRT		hemorrhagic shock, 2 respiratory failure, 3 MOF
<b>Organ dysfunction experimental group (n)</b>	0	MOF 0	0	0	0	NA	?
<b>Infections control group (n)</b>	NA	NA	NA	NA	NA	NA	NA
<b>Infections experimental group (n)</b>	NA	NA	NA	NA	NA	NA	NA
<b>LOS control group in days mean± SD or median [IQR]</b>	NA	NA	30±25 in non survivors; 54±46 in adverse survivors		NA	NA	NA
<b>LOS experimental group in days mean± SD or median [IQR]</b>	NA	NA	22±12		NA	NA	

MOF multiorgan failure

**Supplemental table 4:** characteristics of the included trials (retrospective trials ).

<b>Study ID</b>	Ranucci 2010	Rhodes 2017	Suemori 2016	Hosseinpour 2017	Maarslet 2012	Garcia 2016	Vida 2016	Zulueta 2013
<b>Methods</b>	Retrospective observational single center trial	Retrospective observational single center trial	Retrospective observational single center trial	Retrospective observational comparative single center trial	Retrospective observational single center trial	Retrospective observational single center trial	Retrospective observational single center trial	Retrospective observational single center trial
<b>Participants</b>	255 children <6 years, cardiac surgery with CPB	139 infants <90 days of age in cardiac surgery/CPB,	399 children median age 42 days (5-1708), cardiac	423 children median age between 3-3.5 [0.6-7] years with congenital heart disease	206 children, median age 27 days [10-1724] cardiac surgery, PICU	149 adolescent aged 10-18 years cardiac surgery	152 children with median age 128 days [17,537] cardiac surgery	22 children mean age 2.7±3.6 months congenital heart disease

		admitted to PICU	surgery	for cardiac surgery/CPB				surgery
<b>Interventions</b>	27 children (control group) with lowest central venous oxygen saturation ScVO2 obtained by connecting the PediaSat CVC to a dedicated monitor (Vigileo Edwards Lifesciences, Irvine, CA) (ScVO2<68%) and highest blood lactate levels (arterial blood samples) during CPB (>3mmol/L) /228 children (experimental group) ScVO2>68% with blood lactate levels <3mmol/L	34 children with postoperative (admission to PICU) venous to arterial carbon dioxide difference (AVCO2) of 8.3 (5.6, 14.9) mmHg with poor postoperative outcome (control group)/ 105 children with postoperative (admission to PICU) with venous to arterial carbon dioxide difference (AVCO2) of 5.4 (3.0, 8.4) mmHg without poor postoperative outcome (experimental group)	preoperative and postoperative cerebral tissue oxygenation index (TOI), postoperative normalized tissue hemoglobin index (nTHI), concentration changes in oxygenated hemoglobin ( $\Delta$ HbO2) and deoxygenated hemoglobin ( $\Delta$ HHb) measured by NIRS (360 children without major morbidity (experimental group)/ 27 children with major morbidity and 12 non survivors (control group)	maintenance of optimal hemodynamic status using vasoactive/inotropic agents intraoperatively; group 1=206 children treated using the conventional method i.e maintenance of optimal cardiac output (using markers of adequate cardiac output: urine output, serum lactate levels and ScVO2)= experimental group VERSUS group 2= 217 children treated according to maintenance of optimal perfusion pressure (= mean arterial pressure-CVP)= control group	17 Patients with lactate levels on admission in PICU of $\geq 4.5$ mmol/L (control group) VERSUS 189 patients (experimental group) with lactate levels on admission in PICU of <4.5 mmol/L	Maximum postoperative VIS at 24 h and 48 h: 122 adolescents without adverse outcome with maximum VIS at 24h 5[5-8] and maximum VIS at 48h 0 [0-5] VERSUS 27 adolescents (control group) with adverse outcome with maximum VIS at 24h 7.5[5-10.5] and maximum VIS at 48h 5[0-9.2]	postoperative rSO2 desaturation scores and lactate levels: 90 patients (experimental group) with postoperative desaturation scores <345% s / 62 patients (control group) with postoperative desaturation scores $\geq 345\%$ s	13 children with intraoperative desaturation rSO2 scores (cerebral and somatic NIRS) >3000% seconds (control group), intraoperative cerebral rSO2 desaturation score (=calculated by multiplying rSO2<50% by seconds) VERSUS 9 children with intraoperative desaturation scores <3000% seconds (experimental group)
<b>Outcomes</b>	Major postoperative morbidity (=mechanical ventilation time ; ICU stay ; neurologic	Poor outcome=ISS (inotrope score) > 15; death, cardiac arrest, and ECMO	Postoperative mortality, major morbidity (cardiac arrest events,EC	Mortality, Morbidity (= use of ECMO, and complications of poor peripheral perfusion	Mortality, Morbidity (=need for peritoneal dialysis PD), LMV, LOSICU	postoperative mortality, morbidity (resuscitation or mechanical support,	Mortality, Morbidity (delayed sternal closure, ECMO,pulmonary complication	Postoperative Mortality and morbidity (=low cardiac output





<b>Mortality control group (n)</b>	10	14	12	3	4	0	15	1
<b>Mortality experimental group (n)</b>	0	0	0	15	4	0	0	0
<b>Organ dysfunction control group (n)</b>	27 patients with major morbidity (Neurologic 3, AKI 6, Pulmonary 15, Gastroenteric 2, Cardiocirculatory (ventricular assist devices) 3)	19 AKI, ECMO 8, CPR 19	27 with major morbidity	6 (=5 ECMO, 1 hemofiltration)	8 (dialysis)	21 arrhythmia, 1 acute neurological event, 3 AKI	19 ECMO, 11 pulmonary complications, 8 arrhythmias, 4 AKI, 5 bleeding requiring surgical reinterventions, 24 delayed sternal closure, 31 LCOS	LOS 9 (among which 4 ECMO)
<b>Organ dysfunction experimental group (n)</b>	0 patients with major morbidity	30 AKI, ECMO 0, CPR 0	0 patients with major morbidity	14 (=8 ECMO, 4 Hemofiltration, 1 limb amputation, 1 laparotomy for enterocolitis)	9 (dialysis)	1 AKI	2 ECMO, 6 pulmonary complications, 4 arrhythmias, 1 AKI, 0 bleeding requiring surgical reinterventions, 5 delayed sternal closure, 5 LCOS	LOS 0
<b>Infections control group (n)</b>	sepsis (positive blood cultures) 10	NA	NA	NA	NA	5	NA	NA
<b>Infections experimental group (n)</b>	0	NA	NA	NA	NA	0	NA	NA
<b>LOS control group in days mean±SD or median [IQR]</b>	NA	30 [22-51]	NA	NA	NA	8 [5-16]	NA	NA
<b>LOS experimental</b>	NA	12[7-28]	NA	NA	NA	5[4-5]	NA	NA

ntal group in days mean±SD or median [IQR]								
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**Supplemental table 5:** Median length of hospital, LOS for Perioperative regional oxygen saturation (cerebral, renal, splanchnic, somatic) measured by NIRS.

Study ID	Experimental group median [IQR] LOS in days	Control group median [IQR] LOS in days	p-value
Gist 2016	10[8-12]	22[14-36]	
Kussmann 2009	7 [5-8]	9[5-21]	
Ruf 2015	25[12-96]	28[7-76]	
Median LOS [IQR] in days	10[8.5-17.5]	22[15.5-25]	0.25

**Supplemental table 6:** Median length of hospital, LOS for perioperative lactate level.

Study ID	Experimental group median mean±SD LOS in days	Control 1 group(non survivors) mean±SD LOS in days	Control 2 group (in adverse survivors) mean±SD LOS in days	p-value
Cheung 2005	22±12	30±25	54±46	<0.05 (authors)

**Supplemental table 7:** LOS, PiCCO.

Study ID	Experimental group mean or median LOS, in days	Control group mean or median LOS, in days	p-value
Gil-Anton 2014	6	16	
Kraft 2013	0.6	0.6	
Median [IQR] LOS in days	3.3[1.95-4.65]	8.3[4.45-12.15]	0.317

**Supplemental table 8:** LOS, maximum vasoactive inotrop score (VIS).

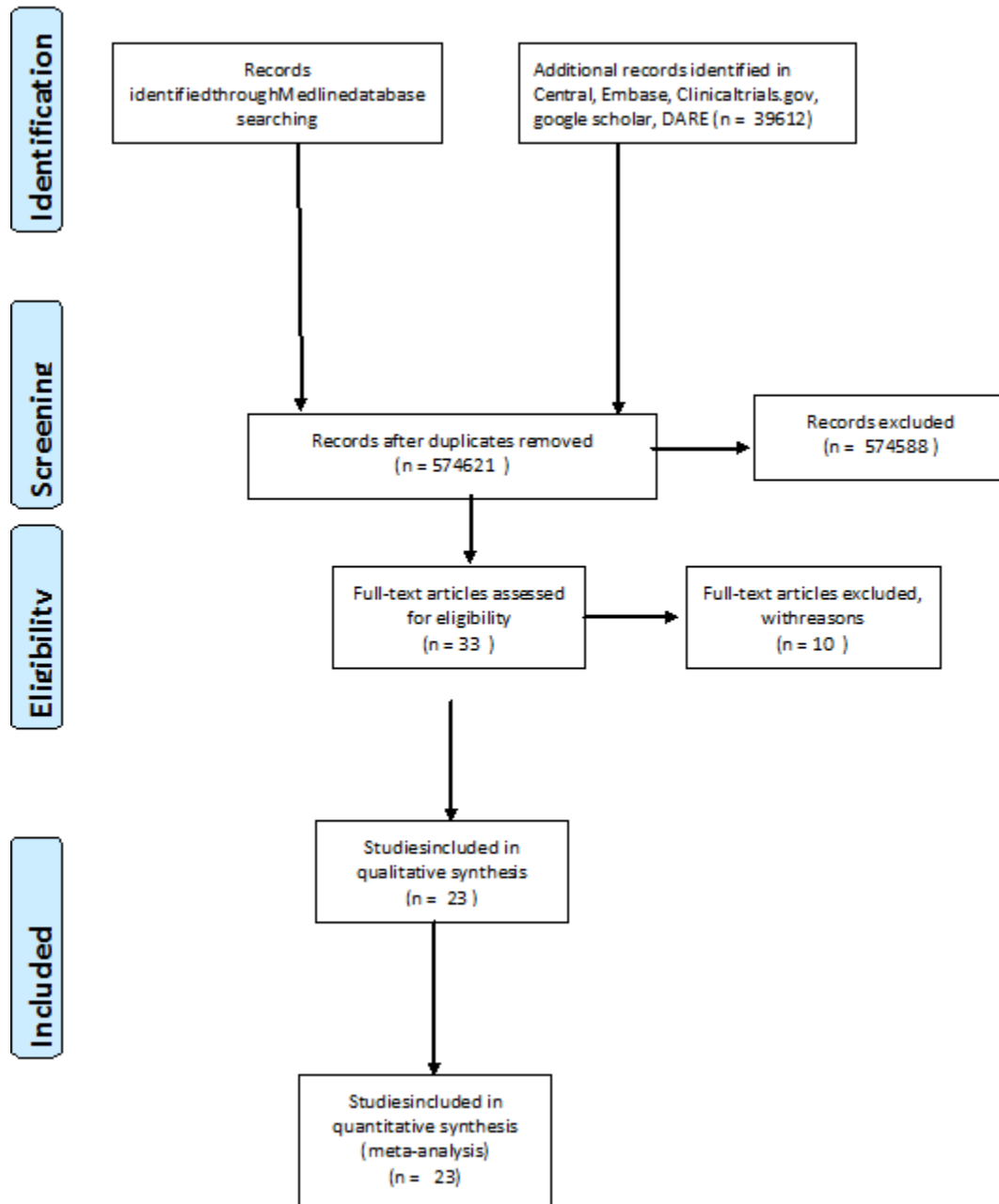
Study ID	Experimental group LOS in days median [IQR]	Control group LOS in days median [IQR]	p-value
Garcia 2016	5(4-5)	8 [5-16]	<0.001 (authors)

**Supplemental table 9:** LOS, Venous to arterial carbon dioxide difference.

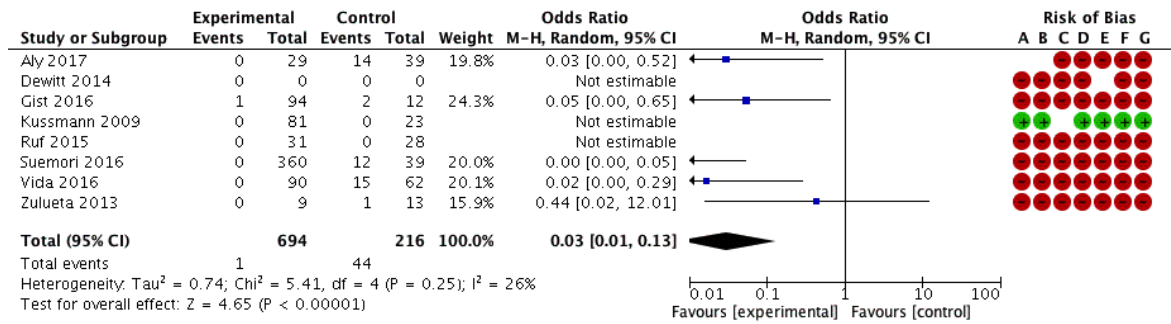
Study ID	Experimental group LOS in days median	Control group LOS in days median	p-value
Rhodes 2017	12 [7, 28]	30 [22, 51]	<0.01 (authors)

**Supplemental table 10:** LOS, All interventions included.

Study ID	Experimental group median LOS in days	Control group median LOS in days	p-value
Cheung 2005	22	55	
Garcia 2016	5	8	
Gil-Anton 2014	6	16	
Gist 2016	10	22	
Kraft 2013	0.6	0.6	
Kusmann 2009	7	9	
Rhodes 2017	12	30	
Ruf 2015	25	28	
Mean median [IQR] LOS in days	8.5[5.75-14.5]	19[8.75-28.5]	0.018



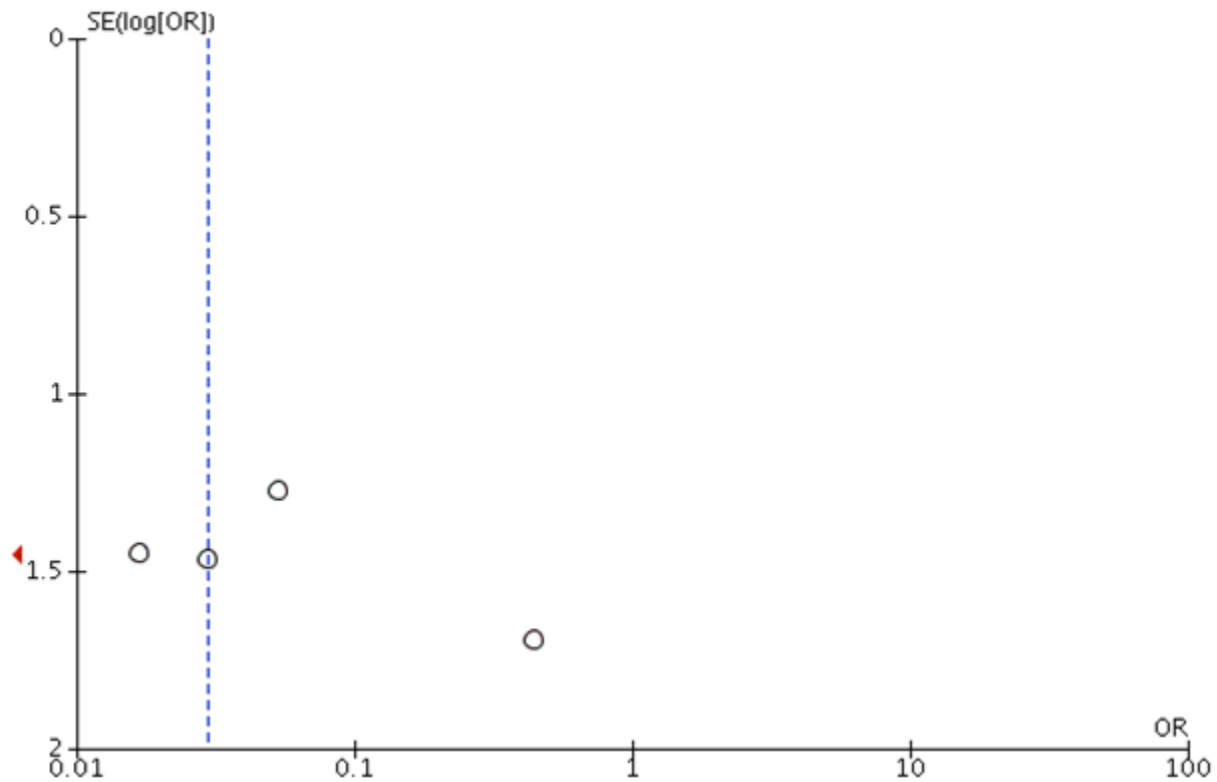
**Supplemental Figure 1:** Search flowchart according to the PRISMA statement.



**Risk of bias legend**

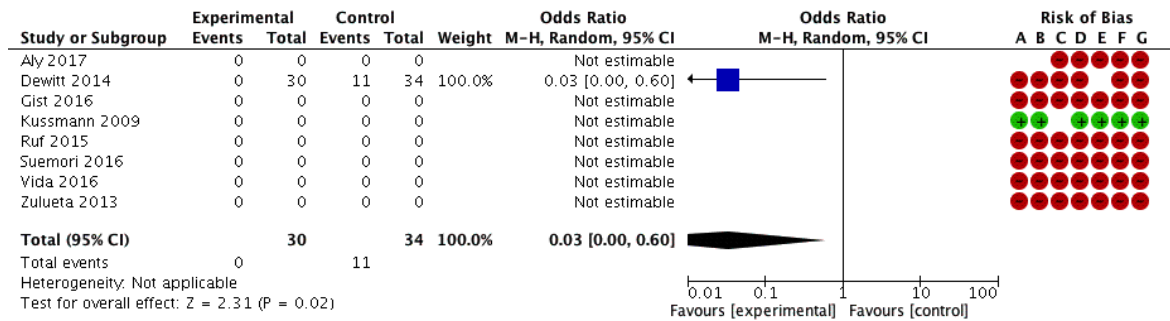
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

**Supplemental Figure 2:** Forest plot of perioperative regional oxygen saturation (cerebral, renal, splanchnic, somatic,) and mortality.



**Supplemental Figure 3:** Funnel plot of perioperative regional oxygen saturation (cerebral, renal, splanchnic, somatic,) and mortality.

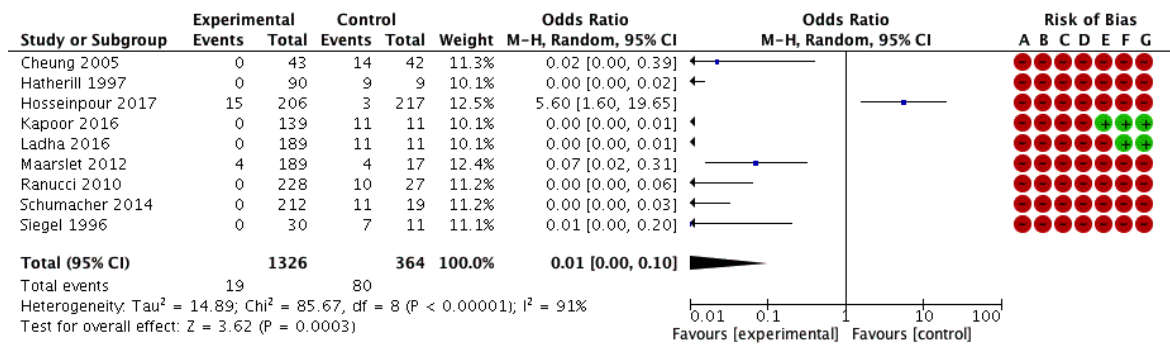




**Risk of bias legend**

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

**Supplemental Figure 6:** Forest plot of perioperative regional oxygen saturation (cerebral, renal, splanchnic, somatic) measured by NIRS and morbidity (Infections).

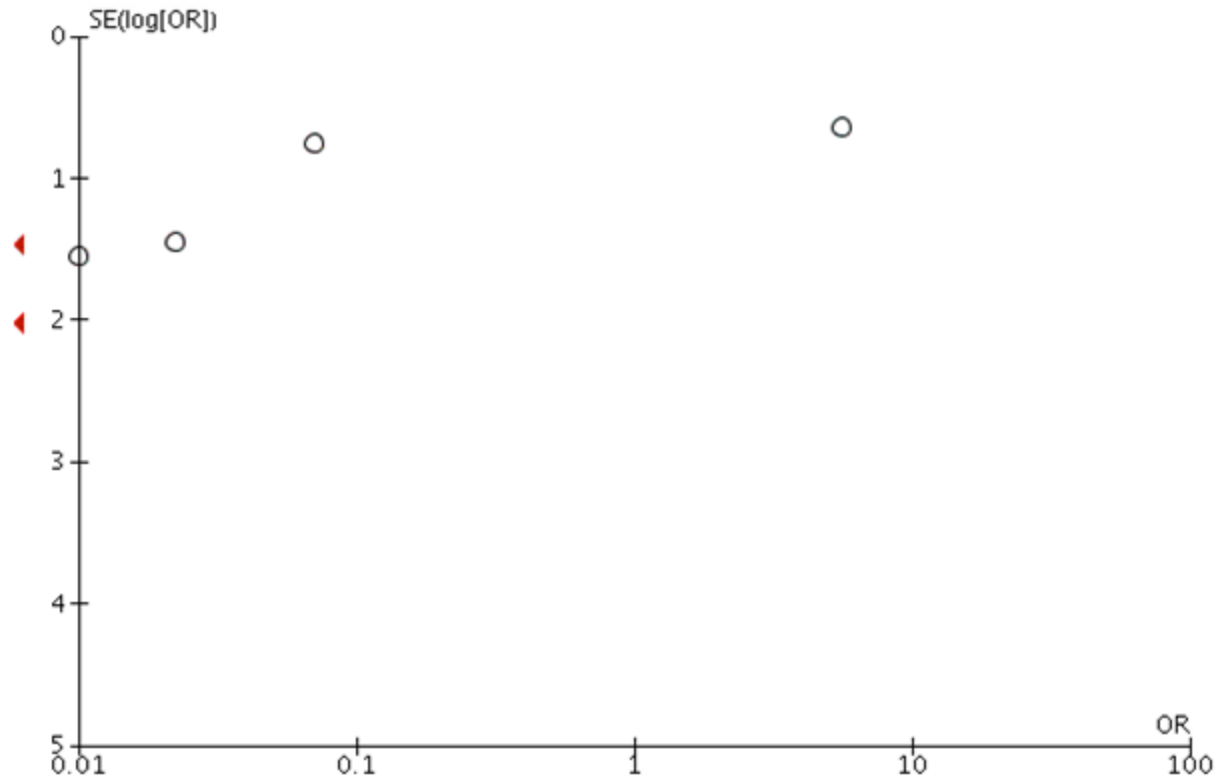


**Risk of bias legend**

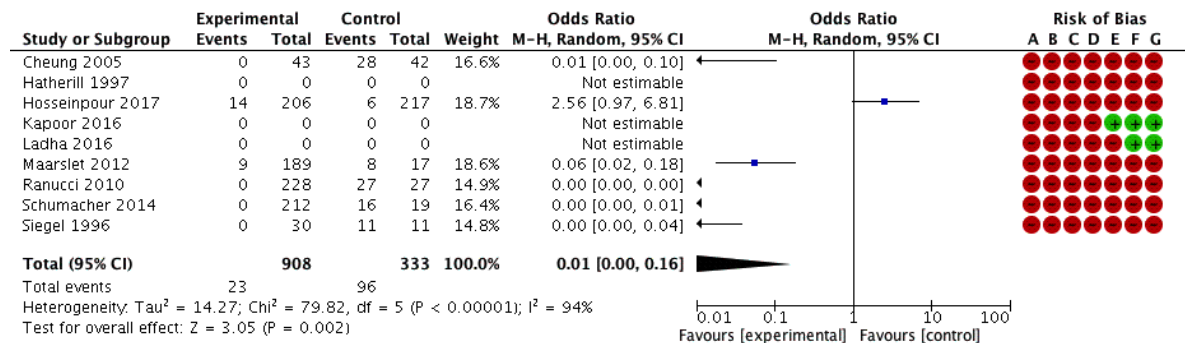
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
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- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

**Supplemental Figure 7:** Forest plot of perioperative lactate levels and mortality.





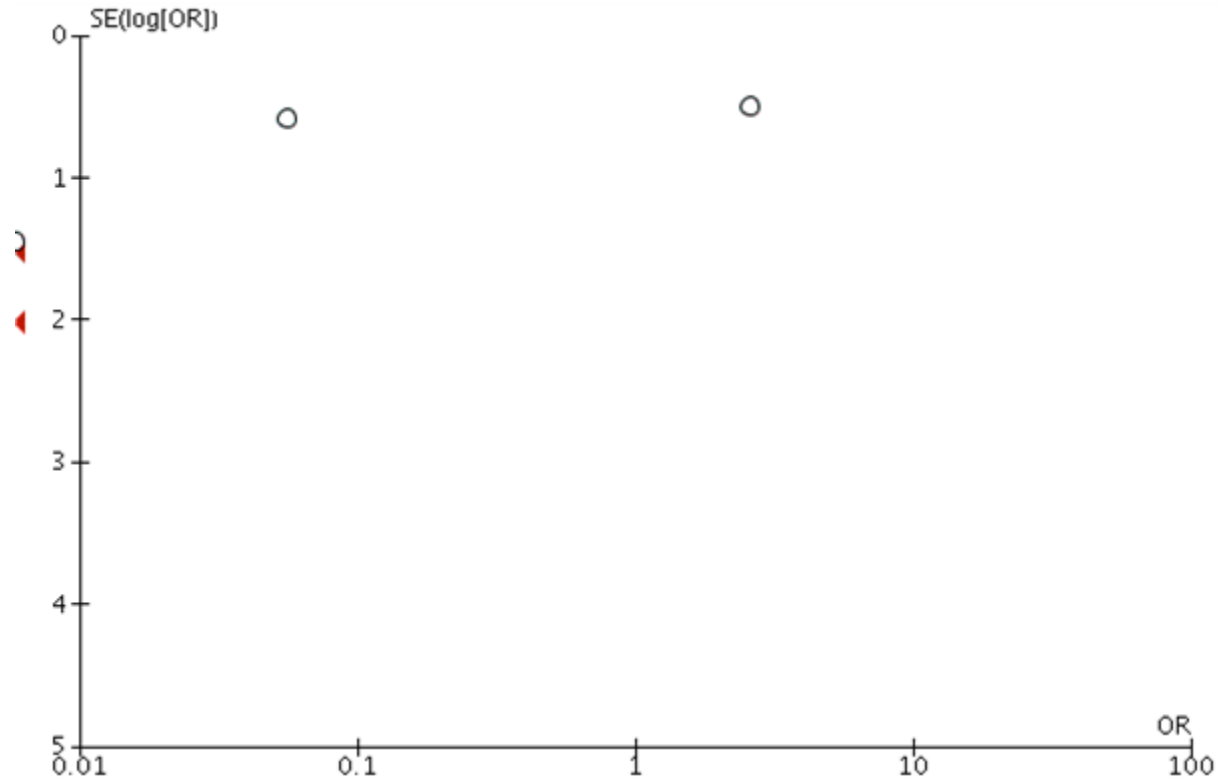
**Supplemental Figure 8:** Funnel plot of perioperative lactate levels and mortality.



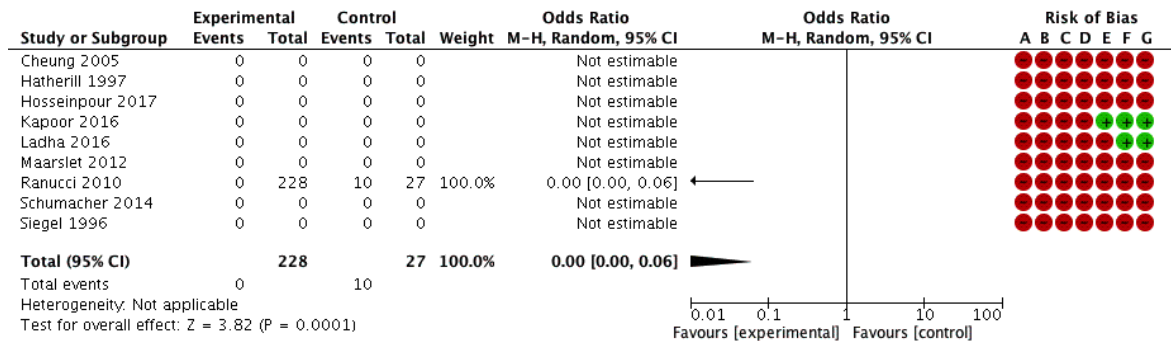
**Risk of bias legend**

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
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- (G) Other bias

**Supplemental Figure 9:** Forest plot of perioperative lactate levels and morbidity (Organ dysfunction).



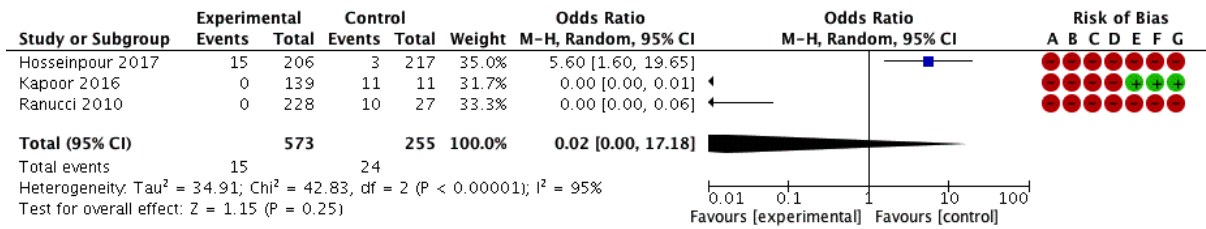
**Supplemental Figure 10:** Funnel plot of perioperative lactate levels and morbidity (Organ dysfunction).



**Risk of bias legend**

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

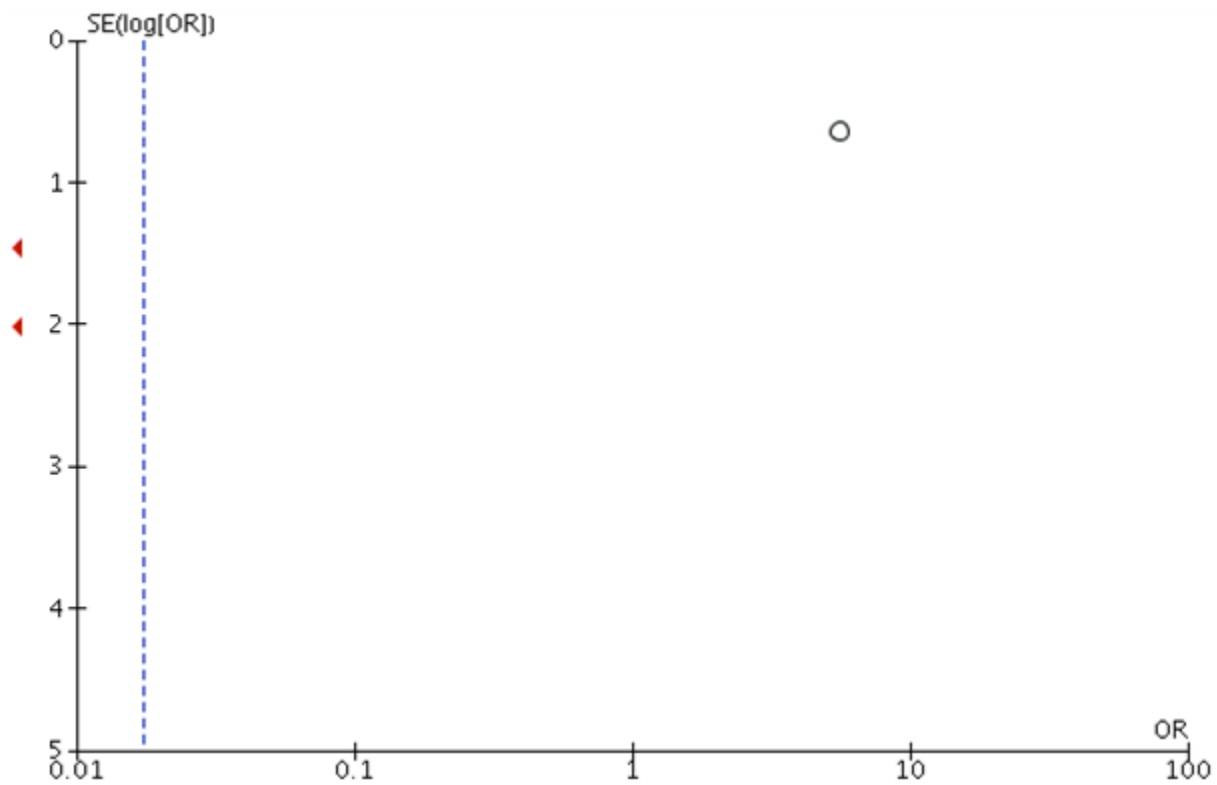
**Supplemental Figure 11:** Forest plot of perioperative lactate levels and morbidity (Infections).



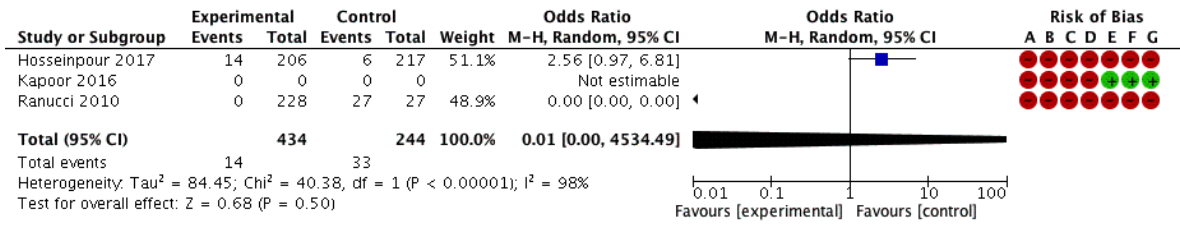
**Risk of bias legend**

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

**Supplemental Figure 12:** Forest plot of Lactate levels +ScVO2 and mortality.



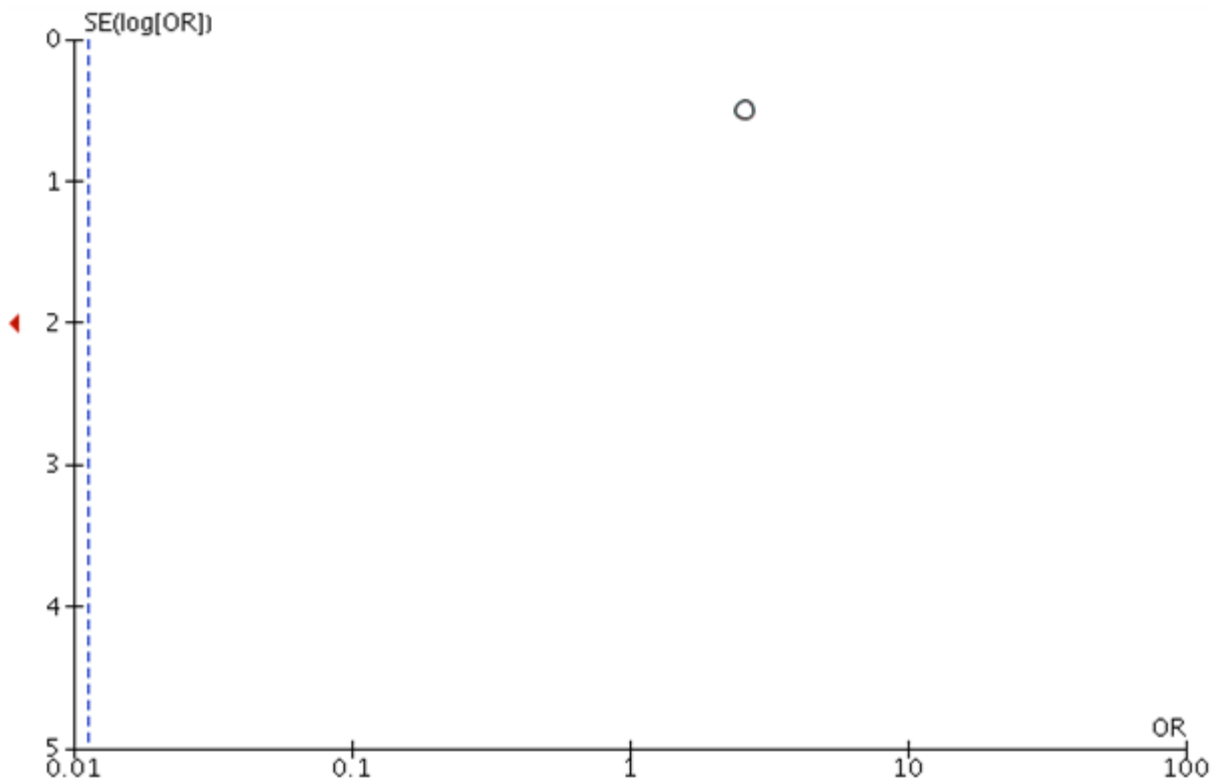
**Supplemental Figure 13:** Funnel plot of Lactate levels +ScVO2 and mortality.



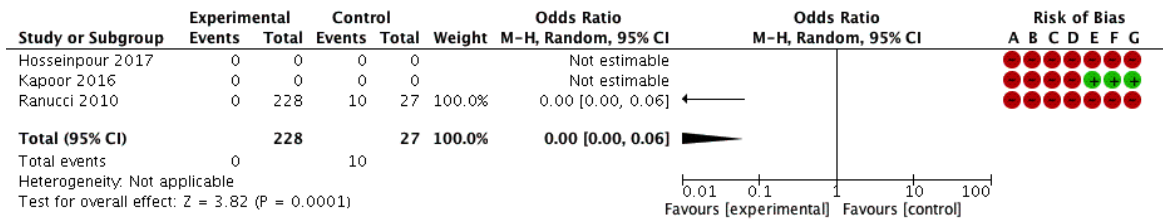
**Risk of bias legend**

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

**Supplemental Figure 14:** Forest plot of Lactate levels and ScVO2 and morbidity (organ dysfunction).



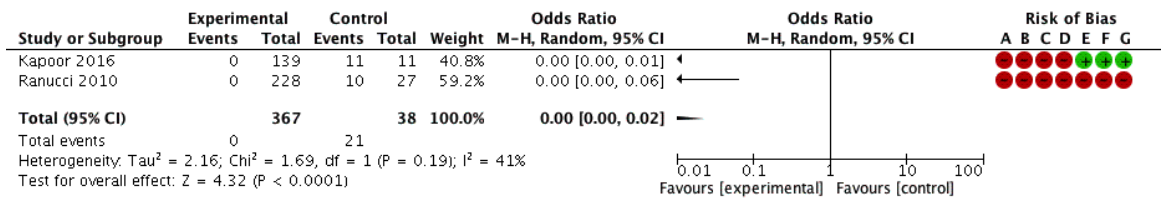
**Supplemental Figure 15:** Funnel plot of Lactate levels and ScVO2 and morbidity (organ dysfunction).



**Risk of bias legend**

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

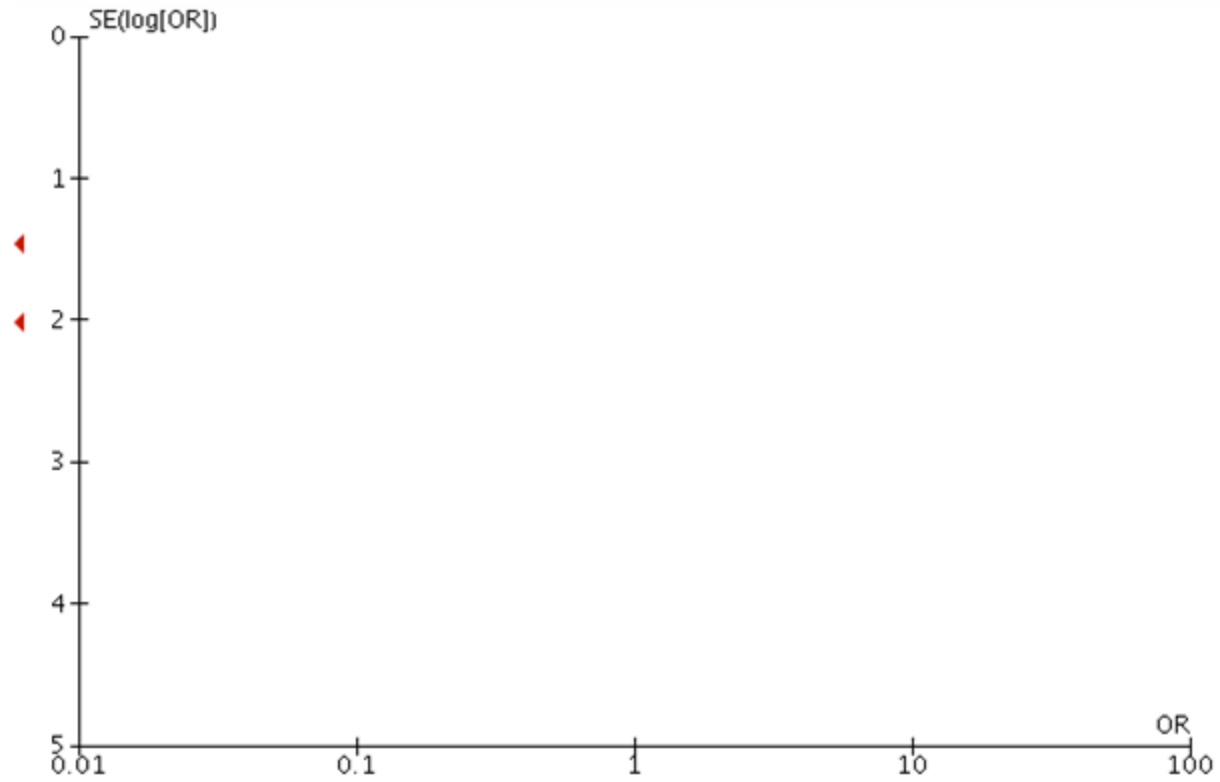
**Supplemental Figure 16:** Forest plot of Lactate levels and ScVO2 and morbidity (Infections).



**Risk of bias legend**

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

**Supplemental Figure 17:** Forest plot of Vigileo (ScVO2)+ Lactate levels and mortality.



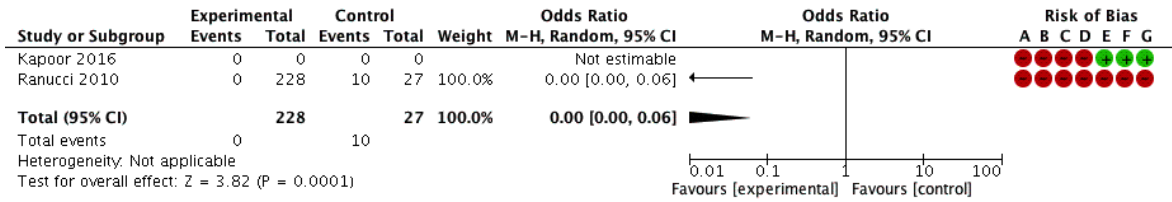
**Supplemental Figure 18:** Funnel plot of Vigileo (ScVO2) + Lactate levels and mortality.

Study or Subgroup	Experimental		Control		Weight	Odds Ratio		Odds Ratio		Risk of Bias								
	Events	Total	Events	Total		M-H, Random, 95% CI	M-H, Random, 95% CI	A	B	C	D	E	F	G				
Kapoor 2016	0	0	0	0		Not estimable				●	●	●	●	●	●			
Ranucci 2010	0	228	27	27	100.0%	0.00 [0.00, 0.00] ◀				●	●	●	●	●	●			
<b>Total (95% CI)</b>		<b>228</b>	<b>27</b>	<b>27</b>	<b>100.0%</b>	<b>0.00 [0.00, 0.00] ◀</b>												
Total events		0	27															
Heterogeneity: Not applicable																		
Test for overall effect: Z = 5.04 (P < 0.00001)																		

**Risk of bias legend**

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

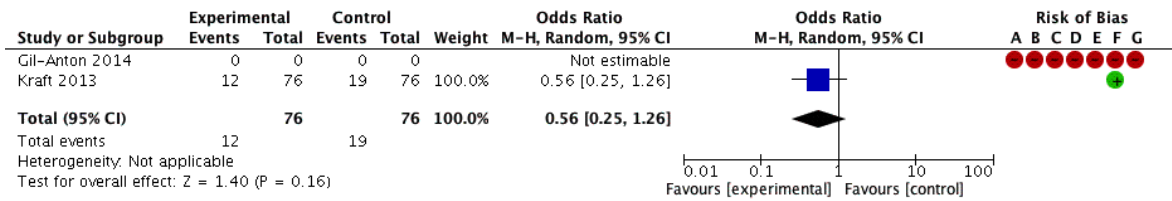
**Supplemental Figure 19:** Forest plot Vigileo (ScVO2) + Lactate levels and morbidity (Organ dysfunction).



**Risk of bias legend**

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

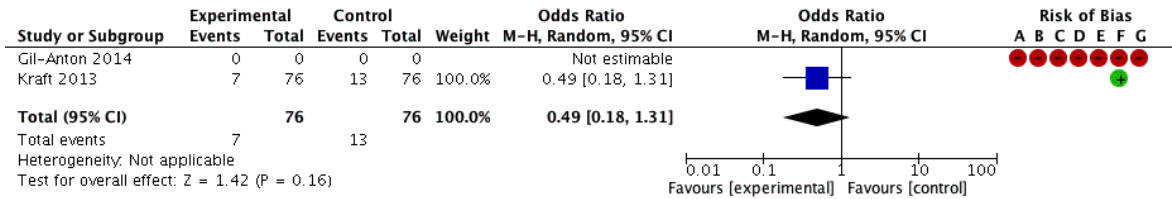
**Supplemental Figure 20:** Forest plot of Vigileo (ScVO2) + Lactate levels and morbidity (Infections).



**Risk of bias legend**

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

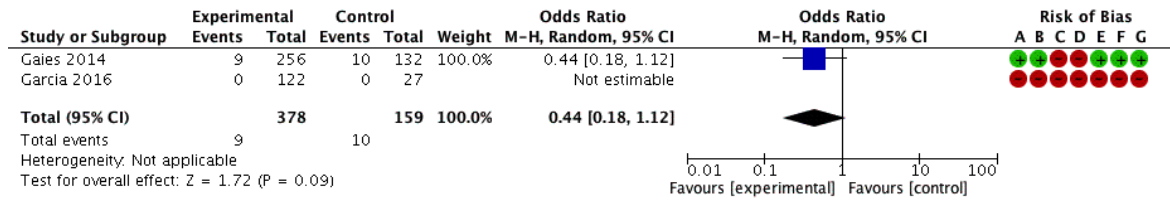
**Supplemental Figure 21:** Forest plot of PiCCO and mortality.



**Risk of bias legend**

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

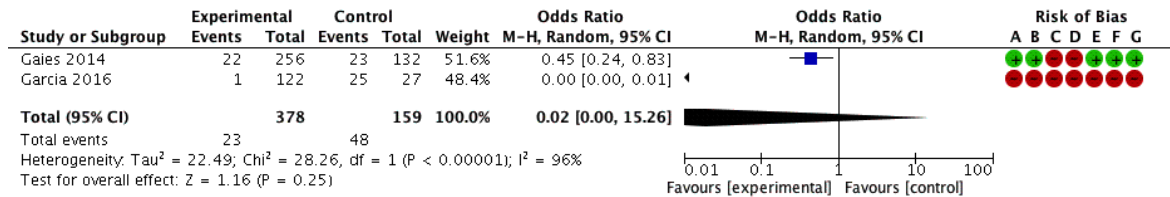
**Supplemental Figure 22:** Forest plot of comparison 5. PiCCO, outcome 5.2 Morbidity (Infections).



**Risk of bias legend**

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

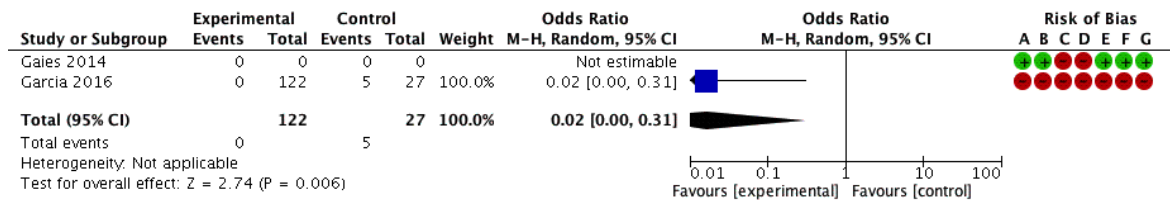
**Supplemental Figure 23:** Forest plot of maximum Vasoactive Inotrop Score (VIS) and mortality.



**Risk of bias legend**

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

**Supplemental Figure 24:** Forest plot of Maximum Vasoactive Inotrop Score (VIS) and morbidity (Organ dysfunction).

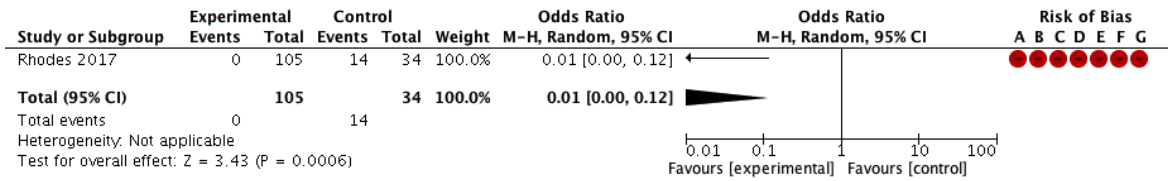


**Risk of bias legend**

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

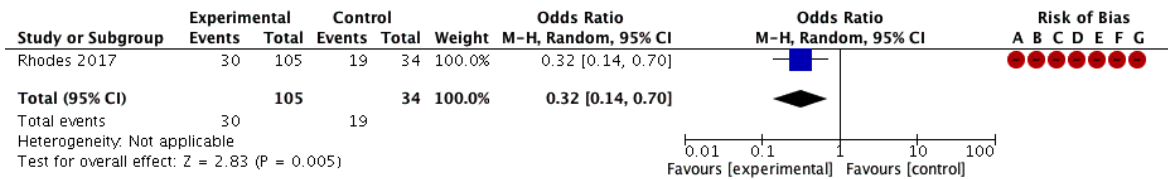
**Supplemental Figure 25:** Forest plot of maximum Vasoactive Score (VIS) and morbidity (Infections).





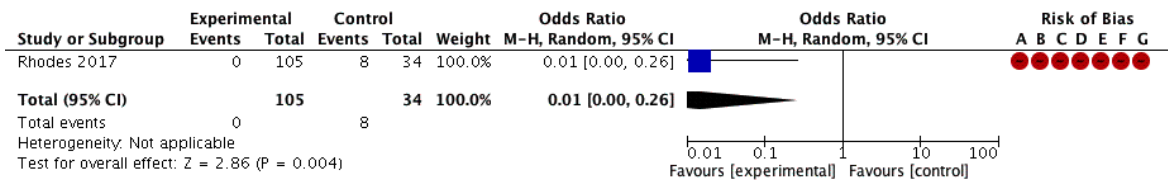
**Risk of bias legend**  
 (A) Random sequence generation (selection bias)  
 (B) Allocation concealment (selection bias)  
 (C) Blinding of participants and personnel (performance bias)  
 (D) Blinding of outcome assessment (detection bias)  
 (E) Incomplete outcome data (attrition bias)  
 (F) Selective reporting (reporting bias)  
 (G) Other bias

**Supplemental Figure 26:** Forest plot of Venous to arterial carbon dioxide difference and mortality.



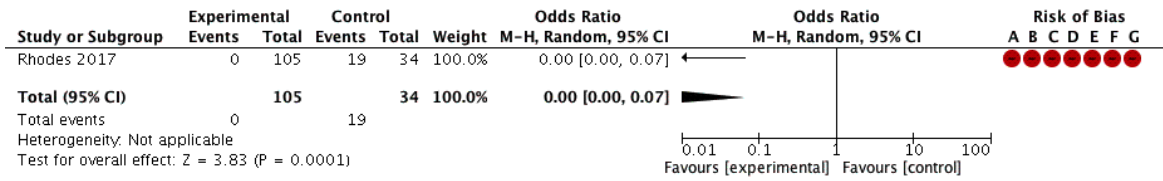
**Risk of bias legend**  
 (A) Random sequence generation (selection bias)  
 (B) Allocation concealment (selection bias)  
 (C) Blinding of participants and personnel (performance bias)  
 (D) Blinding of outcome assessment (detection bias)  
 (E) Incomplete outcome data (attrition bias)  
 (F) Selective reporting (reporting bias)  
 (G) Other bias

**Supplemental Figure 27:** Forest plot of Venous to arterial carbon dioxide difference and morbidity (organ dysfunction, acute kidney injury).



**Risk of bias legend**  
 (A) Random sequence generation (selection bias)  
 (B) Allocation concealment (selection bias)  
 (C) Blinding of participants and personnel (performance bias)  
 (D) Blinding of outcome assessment (detection bias)  
 (E) Incomplete outcome data (attrition bias)  
 (F) Selective reporting (reporting bias)  
 (G) Other bias

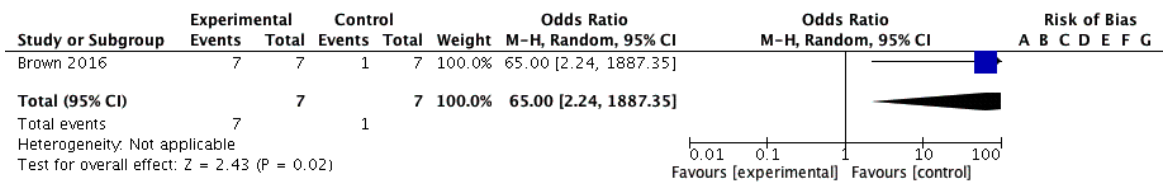
**Supplemental Figure 28:** Forest plot of venous to arterial carbon dioxide difference and morbidity (organ dysfunction, ECMO).



**Risk of bias legend**

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

**Supplemental Figure 29:** Forest plot of venous to arterial carbon dioxide difference and morbidity (CPR).



**Risk of bias legend**

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

**Supplemental Figure 30:** Forest plot of Transoesophageal doppler and morbidity (Organ dysfunction).