Study ID	Kussmann 2009	Kraft 2013	Brown 2016
Metho ds	prospective randomised controlled single center trial	prospective randomised controlled single center trial	Prospective randomised single center trial
Partici pants	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
Interv ention s	104 children monitored with cerebral NIRS allocated to three groups: 23 children (2 control groups, control group1=12 children with integrated rSO2≤45% (=minutes x desaturations points %) between 0.3-39 minutes % and control group2= 11 children with integrated rSO2 ≤45% between 60–383 minutes%) versus groupe3= 81 children (experimental group) with integrated rSO2≤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)
Outco mes	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
Bias	Unclear for blinding	Unclear for randomisaion, blinding and allocation concealment	Unclear for randomisation, blinding and allocation concealment
Morta lity contro l group (n)	0	19	NA
Morta lity experi mental group (n)	0	12	NA
Organ dysfun cion contro l group	NA	NA	0

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

(n)			
Organ dysfun cion experi mental group (n)	NA	NA	7
Infecti ons contro l group	NA	13	NA
Infecti ons experi mental group (n)	NA	7	NA
LOS contro l group in days mean <u>+</u> SD or media n [IQR]	group1 7[5.5-8]; group2 9[5-21	0.6 ± 0.1	NA
LOS experi mental group in days mean <u>+</u> SD or media n [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
Methods	prospective observational single center trial	prospective observational single center trial	prospective observation al single center trial	prospective observation al single center trial	Prospective, multi- institutional observationa l (4 centers) cohort study	prospective observational single center trial
Participan ts	106 children aged ≤ 4 years old or ≤ 15 kg in cardiac surgery, congenital heart surgery or heart transplantation under CPB	59 infants <12 months and <10kg undergoing cardiopulmon ary 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 ± 0.5 kg) congenital heart disease surgery	391 children <1 year of age cardiac surgery/CP B treated postoperativ ely in the CICU	35 children median age 18 months [3-144] median weight 10kg [3.8-58] PICU post cardiac surgery /CPB
Interventio ns	12 children with a ≥ 20% reduction from the baseline in renal NIRS for 20 consecutive minutes intra- operatively 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 SO2 < 65% X minutes) and an intraoperative median rNIRS25 score of 131 min% (= decrease of renal rSO2 of more than 25% from the baseline value X minutes)/ 31 infants (experimental group) with an intraoperative	Median Postoperati ve blood lactate level measureme nts on admission in the PICU in 9 non- survivors (control group) VERSUS 90 survivors (experiment al group)	34 neonates with (control group) with average postoperativ e splanchnic regional oxymetry rSO2 of 51.6 ± 14.8 % /30 neonates (experiment al group) with average postoperativ e splanchnic regional oxymetry rSO2 of 70.3 ± 12.0 % before and during enteral feedings	132 children with maximum VIS ≥20) in the first 24h postoperativ ely (control group) versus 256 children with maximum VIS <20 (experiment al group) remark 3 children with missing VIS	PiCCO Cardiac Index monitoring during first 24 hours after admission in PICU: 17 children with CI <3L/min/m2(=co ntrol group)/18 children with CI ≥3L/min/m2 (= experimental group)

		median				[]	
		rNIRS65					
		score of 158					
		min% and an					
		intraoperative					
		median					
		rNIRS25					
		score of 0					
		min%					
		111111%			Mortality,		
Outcomes	Postoperative Mortality and AKI, postoperative increased AKI biomakers, other postoperative adverse outcomes	Intraoperative and postoperative AKI	Postoperati ve mortality	Postoperati ve Morbidity= NEC	LMV ECMO, cardiac arrest, RRT, neurologic injury, LOSICU, reinterventio	LOS LOSICU, LMV	
	(LOS,LOSICU,L MV, VIS,)				ns under CPB		
Bias	High for randomisation, blinding and allocation concealment	High for randomisatio n, blinding and allocation concealment	High for randomisati on, blinding and allocation concealmen t	High for randomisati on, blinding and allocation concealmen t	High risk for blinding	High for randomisation, blinding and allocation concealment	
Mortality							
control	2	0	9	NA	10	NA	
group (n)							
Mortality							
experimen	1	0	0	NA	9	NA	
tal group	1	0	0	INA	9	INA	
(n)							
Organ		AKI 28 (
dysfuncion	AKI 3	among which	NA	ECMO 4	23	NA	
control		3 had RRT)	1,21	20.00		1 12 1	
group (n)		- mu ((())					
Organ							
dysfuncion	A 171 01	AKI 0 (RRT	NT 4		22	NI A	
experimen	AKI 31	0)	NA	ECMO 1	22	NA	
tal group							
(n) Infections							
control	NA	NA	NA	NEC 11	NA	NA	
group		11/1	114	THE II	114		
Infections							
experimen							
tal group	NA	NA	NA	NEC 0	NA	NA	
(n)							
LOS							
control							
group in	22 [14-36]	28 [7-76]	NA	NA	NA	16 [4-50]	
days		_				_	
mean± SD							

or median [IQR]						
LOS experimen tal group in days mean± SD or median [IQR]	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 mechanicl 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 trial	ls (non randomised prospective trial).
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Study ID	Aly 2017	Siegel 1996	Cheung 2005	Schumache r 2014	Kapoor 2016	Ladha 2016
Methods	prospective observational single center trial	prospective observation al single center trial	prospective observational single center trial	prospective observation al single center trial	prospective observational single center trial	Prospective observationa l
Participan ts	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/CP B, PICU	150 children (6 months to 12 years) TOF surgery	200 children weighing 5– 20 kg, TOF surgery
Interventi ons	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 (survivors and patients without MOF) (experiment al 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 ≤ 2 mmol/L of 11 ± 9 h VERSUS 42 patients (control group) with higher mean lactate	Lactate levels measured for the first 24 postoperati ve hours in 212 (experiment al 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 clairance before surgery (T0), after surgery at admission in ICU (T1), every 6h postoperativ ely in ICU for 24 hours in 11 non surviors (group control) and in 189 survivors

(n) Organ	25 patients with	MOF 11	28	9 ECMO, 7	NA	5 LOS, 1
Mortality experimen tal group	0	0	0	0	0	0
Mortality control group (n)	14	7	14	11	11	11
Bias	High for randomisation, blinding and allocation concealment	High for randomisati on, blinding and allocation concealmen t	High for randomisation, blinding and allocation concealment	High for randomisati on, blinding and allocation concealmen t	High for randomisation, blinding and allocation concealment	High for randomisatio n, blinding and allocation concealment
Outcomes	Postoperative mortality and neurodevelopme ntal outcome at 6, 15 and 21 months	Postoperati ve Mortality and MOF	Postoperative mortality and Morbidity (early childhood neurodevelop ment disability (cerebral palsy, legal blindness, hearing loss) or neurodevelop ment delay (mental developmental index and or performance developmental index <70±SD) at 18 and 24 months of age))	Postoperati ve mortality, morbidity (dialysis, ECMO)	Postoperative mortality	Mortality, LMV,LOSI CU, inotrop requirements
	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 \pm 4.9 mmol/L and 6.3 \pm 2.4 mmol/L and lactime to \leq 5mmol/L of 11 \pm 11h and 4 \pm 4 hours and lactime to \leq 2mmol/L of 23 \pm 9 hours and 16 \pm 10 hours	higher initial median and peak median lactate levels		(experiment al group)

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

MOF multiorgan failure

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

Study ID	Ranucci 2010	Rhodes 2017	Suemori 2016	Hosseinpour 2017	Maarslet 2012	Garcia 2016	Vida 2016	Zulueta 201 3
Methods	Retrospectiv e observationa l single center trial	Retrospect ive observatio nal single center trial	Retrospect ive observatio nal single center trial	Retrospective observational comparative single center trial	Retrospecti ve observation al single center trial	Retrospect ive observatio nal single center trial	Retrospective observational single center trial	Retrospecti ve observation al single center trial
Participa nts	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 childre n, median age 27 days [10-1724] cardiac sur gery, 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	surgery	for cardiac				surgery
		to PICU		surgery/CPB				
Intervent	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 (experiment al group) ScVO2>68 % with blood lactate levels <3mmol/L	34 children with postoperat ive (admission to PICU) venous to arterial carbon dioxide difference (AVCO2) of 8.3 (5.6, 14.9) mmHg with poor postoperat ive outcome (control group)/ 105 children with postoperat ive (admission to PICU) with venous to arterial carbon dioxide difference (AVCO2) of 5.4 (3.0, 8.4) mmHg without poor postoperat ive outcome (carbon dioxide difference (AVCO2) of 5.4 (3.0, 8.4) mmHg without poor postoperat ive	preoperati ve and postoperat ive cerebral tissue oxygenati on index (TOI), postoperat ive normalize d tissue hemoglobi n index (nTHI), concentrat ion changes in oxygenate d hemoglobi n (ΔHbO2) and deoxygena ted hemoglobi n (ΔHbO2) and deoxygena ted hemoglobi n (ΔHHb) measured by NIRS (360 children without major morbidity (experime ntal group)/ 27 children with major morbidity and 12 non survivors (control group)	maintenance of optimal hemodynamic status using vasoactive/ino tropic agents intraoperativel y; group 1=206 children treated using the conventional method i.e maintenanace 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 ≥4.5 mmol/L (control group) VERSUS 189 patiens (experimen tal group) with lactate levels on admission in PICU of <4.5 mmol/L	Maximum postoperat ive VIS at 24 h and 48 h: 122 adolescent s without adverse outcome with maximum VIS at 24h 5[5-8] and maximum VIS at 48h 0 [0-5] VERSUS 27 adolescent s (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 (experimenta l group) with postoperative desaturation scores <345%s / 62 patients (control group) with postoperative desaturation scores $\geq 345\%$ s	13 children with intraoperati ve desaturatio n rSO2 scores (cerebral and somatic NIRS) >3000 % seconds (control group), intraoperati ve cerebral rSO2 desaturatio n score (=calculate d by multiplying rSO2<50% by seconds) VERSUS 9 chldren with intraoperati ve desaturatio n scores <3000% sec onds (experiment al group)
Outcome s	Major postoperativ e morbidity (=mechanica l ventilation time ; ICU stay ; neurologic	Poor outcome=I S (inotrop score) > 15; death, cardiac arrest, and ECMO	Postoperat ive 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	postoperat ive mortality, morbidity (resuscitati on or mechanica l support,	Mortality, Morbidity (delayed sternal closure, ECMO,pulm onary complication	Postoperati ve Mortality and morbidity (=low cardiac output

	complication	within 48	MO,	(need for		arrhythmia	s, arrythmias,	syndrome
	s (stroke,	hours of	neurologic	hemofiltration,		, infection	AKI,bleeding	LCOS)
	choreoatheto	admission	al	laparotomy for		requiring	requiring	LC05)
	sis,	to PICU;	complicati	enterocolitis,		antibacteri	surgical	
	seizures);	and any	ons,	amputation)),		al therapy,	reinterventio	
	acute renal	unplanned	seizures,br	duration of		ar uterapy, acute	ns), LCOS	
	failure (need	surgical	ain	ventilation and		kidney	113), LCOS	
	for renal-	re-	infarction,	inotropic		injury or		
	replacement	interventio	sepsis)	treatment		neurologic		
	therapy);	ns during	sepsis)	ucatificiti		injury)		
	pulmonary	-				iiijui y)		
		hospital						
	complication	stay;						
	S (magazinataria	Secondary						
	(respiratory	outcomes=						
	distress	LOS,						
	syndrome;	LMV,						
	poor gas	postoperat						
	exchange	ive AKI						
	resulting in a							
	delayed							
	weaning							
	from							
	mechanical							
	ventilation;							
	pneumonia);							
	gastroenteric							
	complication							
	S							
	(necrotising							
	enterocolitis,							
	mesenteric							
	ischemia,							
	gastric							
	bleeding);							
	need for							
	extracorpore							
	al membrane							
	oxygenation							
	or							
	ventricular- assist							
	device; or							
	sepsis (with							
	positive blood							
	cultures))							
	and							
	mortality	High for	High for		High for	High for		
	High for	randomisa	randomisa		randomisati	randomisa	High for	High for
	randomisatio	tion,	tion,	High for	on,	tion,	randomisatio	randomisati
	n, blinding	blinding	blinding	randomisation,	blinding	blinding	n, blinding	on, blinding
Bias	and	and	and	blinding and	and	and	and	and
	allocation	allocation	allocation	allocation	allocation	allocation	allocation	allocation
	concealment	concealme	concealme	concealment	concealme	concealme	concealment	concealmen
	conceannent	nt	nt		nt	nt	conceannent	t
		III	IIt		IIt	IIt		

Mortality								
control	10	14	12	3	4	0	15	1
group (n)								
Mortality experime ntal group (n)	0	0	0	15	4	0	0	0
Organ dysfuncio n control group (n)	27 patients with major morbidity (Neurologic 3, AKI 6, Pulmonary 15, Gastroenteri c 2, Cardiocircul atory (ventricular assist devices) 3)	19 AKI, ECMO 8, CPR 19	27 with major morbidity	6 (=5 ECMO, 1 hemofiltration)	8 (dialysis)	21 arrythmia, 1 acute neurologic al event , 3 AKI	19 ECMO, 11 pulmonary complication s, 8 arrhythmias, 4 AKI, 5 bleeding requiring surgical reinterventio ns, 24 delayed sternal closure, 31 LCOS	LOS 9 (among which 4 ECMO)
Organ dysfuncio n experime ntal group (n)	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 complication s, 4 arrhythmias, 1 AKI, 0 bleeding requiring surgical reinterventio ns, 5 delayed sternal closure, 5 LCOS	LOS 0
Infections control group (n)	sepsis (positive blood cultures) 10	NA	NA	NA	NA	5	NA	NA
Infections experime ntal group (n)	0	NA	NA	NA	NA	0	NA	NA
LOS control group in days mean± SD or median [IQR]	NA	30 [22-51]	NA	NA	NA	8 [5-16]	NA	NA
LOS experime	NA	12[7-28]	NA	NA	NA	5[4-5]	NA	NA

ntal				
ntal				
group in				
days				
mean±				
SD or median				
median				
[IQR]				

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
Cheun g 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	
Kussmann 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.



Supplemental Figure 2: Forest plot of perioperative regional oxygen saturation (cerebral, renal, splanchnic,



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



Supplemental Figure 4: Forest plot of perioperative regional oxygen saturation measured by NIRS (cerebral, renal,

splanchnic, somatic) and morbidity (organ dysfunction).



Supplemental Figure 5: Funnel plot of perioperative regional oxygen saturation measured by NIRS (cerebral, renal, splanchnic, somatic) and morbidity (organ dysfunction).



(d) Other blas

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

	Experim	ental	Cont	rol		Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M–H, Random, 95% CI	ABCDEFG
Cheung 2005	0	43	14	42	11.3%	0.02 [0.00, 0.39]	← →	0000000
Hatherill 1997	0	90	9	9	10.1%	0.00 [0.00, 0.02]	←	
Hosseinpour 2017	15	206	3	217	12.5%	5.60 [1.60, 19.65]		0000000
Kapoor 2016	0	139	11	11	10.1%	0.00 [0.00, 0.01]	•	
Ladha 2016	0	189	11	11	10.1%	0.00 [0.00, 0.01]	•	
Maarslet 2012	4	189	4	17	12.4%	0.07 [0.02, 0.31]		0000000
Ranucci 2010	0	228	10	27	11.2%	0.00 [0.00, 0.06]	←	0000000
Schumacher 2014	0	212	11	19	11.2%	0.00 [0.00, 0.03]	←	0000000
Siegel 1996	0	30	7	11	11.1%	0.01 [0.00, 0.20]	·	000000
Total (95% CI)		1326		364	100.0%	0.01 [0.00, 0.10]		
Total events	19		80					
Heterogeneity: Tau ² =	= 14.89; C	hi ² = 85	5.67, df -	= 8 (P -	< 0.0000	1); $ ^2 = 91\%$		
Test for overall effect:	Z = 3.62	(P = 0.	0003)			F	0.01 0.1 1 10 10 avours [experimental] Favours [control]	10
							(
Risk of bias legend								
(A) Random sequence)				
(B) Allocation conceal	ment (selec	tion bia	s)					

(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 7: Forest plot of perioperative lactate levels and mortality.



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



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



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

	Experim	ental	Cont	rol		Odds Ratio	Odds Rat	io	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random,	95% CI	ABCDEFG
Cheung 2005	0	0	0	0		Not estimable			0000000
Hatherill 1997	0	0	0	0		Not estimable			0000000
Hosseinpour 2017	0	0	0	0		Not estimable			0000000
Kapoor 2016	0	0	0	0		Not estimable			
Ladha 2016	0	0	0	0		Not estimable			
Maarslet 2012	0	0	0	0		Not estimable			0000000
Ranucci 2010	0	228	10	27	100.0%	0.00 [0.00, 0.06]	←		0000000
Schumacher 2014	0	0	0	0		Not estimable			0000000
Siegel 1996	0	0	0	0		Not estimable			
Total (95% CI)		228		27	100.0%	0.00 [0.00, 0.06]			
Total events	0		10						
Heterogeneity. Not ap	plicable						0.01 0.1 1	10 100	
Test for overall effect	Z = 3.82	(P = 0.	0001)			F	avours [experimental] Fav		
Risk of bias legend (A) Random sequence (B) Allocation conceal (C) Blinding of particip (D) Blinding of outcom (E) Incomplete outcom	ment (selec pants and p ne assessm	tion bia personn ent (de	s) el (perfoi tection bi	mance	bias)				

(F) Selective reporting (reporting bias) (G) Other bias

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



(D) Blinding of outcome assessment (detection bias)

(E) Incomplete outcome data (attrition bias)

(F) Selective reporting (reporting bias)

 (\mathbf{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.



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).

	Experim	ental	Cont	rol		Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M–H, Random, 95% Cl	ABCDEFG
Hosseinpour 2017	0	0	0	0		Not estimable		0000000
Kapoor 2016	0	0	0	0		Not estimable		
Ranucci 2010	0	228	10	27	100.0%	0.00 [0.00, 0.06]	<u>←</u>	
Total (95% CI)		228		27	100.0%	0.00 [0.00, 0.06]		
Total events	0		10					
Heterogeneity: Not ap	oplicable						0.01 0.1 1 10 100	
Test for overall effect	: Z = 3.82	(P = 0.	0001)			F	Favours [experimental] Favours [control]	
Risk of bias legend								
(A) Random sequence	e generatio	n (selec	tion bias)				
(B) Allocation conceal	ment (seled	ction bia	s)					
(C) Blinding of partici	pants and p	personn	el (perfo	rmance	bias)			
(D) Blinding of outcon	ne assessm	nent (de	tection b	ias)				
(E) Incomplete outcon	ne data (at	trition b	ias)					
(F) Selective reporting	(reporting	bias)						
(C) Others black								

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



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



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

	Experimental		Cont	ol		Odds Ratio	Odds Ratio Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	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]	• • • • • • • • • • • • • • • • • • • •
Total (95% CI)		228		27	100.0%	0.00 [0.00, 0.00]	•
Total events	0		27				
Heterogeneity. Not ap	plicable						0.01 0.1 1 10 100
Test for overall effect	:Z = 5.04	(P < 0.	00001)			F	avours [experimental] Favours [control]
Risk of bias legend							
(A) Random sequence	e generatio	n (selec	tion bias)			
(B) Allocation conceal	ment (seled	ction bia	s)				
(C) Blinding of particip	pants and	personn	el (perfo	rmance	bias)		
(D) Blinding of outcon	ne assessm	nent (de	tection b	ias)			
(E) Incomplete outcon	ne data (at	trition b	ias)				

(E) incomplete outcome data (attrition (F) Selective reporting (reporting bias) (G) Other bias

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

	Experim	ental	Cont	rol		Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	Events To		Events	Total	Weight	M-H, Random, 95% CI	M–H, Random, 95% CI	ABCDEFG
Kapoor 2016	0	0	0	0		Not estimable		
Ranucci 2010	0	228	10	27	100.0%	0.00 [0.00, 0.06]	←	000000
Total (95% CI)		228		27	100.0%	0.00 [0.00, 0.06]		
Total events	0		10					
Heterogeneity. Not ap	plicable							100
Test for overall effect	: Z = 3.82	(P = 0.	0001)			F	0.01 0.1 1 10 avours [experimental] Favours [control]	100 [°]
Risk of bias legend								
(A) Random sequence	e generatio	n (selec	tion bias)				
(B) Allocation conceal	ment (seled	ction bia	s)					
(C) Blinding of partici	pants and	personn	el (perfo	rmance	bias)			
(D) Blinding of outcon	ne assessm	nent (de	tection b	ias)				
(E) Incomplete outcon	ne data (at	trition b	ias)					
(F) Selective reporting	(reporting	bias)						
(C) Other hind								

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



Supplemental Figure 21: Forest plot of PiCCO and mortality.

	Experim	ental	Cont	rol		Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M–H, Random, 95% CI	M–H, Random, 95% Cl	ABCDEFG
Gil-Anton 2014	0	0	0	0		Not estimable		0000000
Kraft 2013	7	76	13	76	100.0%	0.49 [0.18, 1.31]		•
Total (95% CI)		76		76	100.0%	0.49 [0.18, 1.31]		
Total events	7		13					
Heterogeneity: Not ap	plicable					0.0	01 0 1 1 10 100	
Test for overall effect:	Z = 1.42	(P = 0.	16)				irs [experimental] Favours [control]	
Risk of bias legend								
(A) Random sequence	e generatio	n (selec	tion bias)					
(B) Allocation conceals	ment (seled	ction bia	s)					
(C) Blinding of particip	pants and	personn	el (perfo	rmance	bias)			
(D) Blinding of outcom	ne assessm	nent (de	tection bi	as)				
(E) Incomplete outcom	ne data (at	trition b	ias)					

(F) Selective reporting (reporting bias)

(G) Other bias

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



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



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

dysfunction).

	Experimental		Cont	rol		Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M–H, Random, 95% CI	ABCDEFG
Gaies 2014	0	0	0	0		Not estimable		
Garcia 2016	0	122	5	27	100.0%	0.02 [0.00, 0.31]		
Total (95% CI)		122		27	100.0%	0.02 [0.00, 0.31]		
Total events	0		5					
Heterogeneity: Not ap	plicable						0.01 0.1 1 10 100	l
Test for overall effect:	Z = 2.74	(P = 0.)	006)			F	0.01 0.1 1 10 100 avours [experimental] Favours [control]	
Risk of bias legend								
(A) Random sequence	e generatio	n (selec	tion bias)	ł				
(B) Allocation conceals	ment (selec	tion bia	s)					
(C) Blinding of particip	ants and p	ersonn	el (perfor	mance	bias)			
(D) Blinding of outcom	ne assessm	ent (de	tection bi	as)				
(E) Incomplete outcom	ne data (att	rition b	ias)					
(F) Selective reporting	(reporting	bias)						
(G) Other bias								

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

Study or Subgroup	Experimental p Events Total		Cont Events		Weight	Odds Ratio M-H, Random, 95% CI	Odds Ratio M-H. Random. 95% Cl		Risk of Bias A B C D E F G
Rhodes 2017	0	105	14	34	100.0%	0.01 [0.00, 0.12]	·		
Total (95% CI)		105		34	100.0%	0.01 [0.00, 0.12]			
Total events Heterogeneity: Not ap Test for overall effect		(P = 0.	14 0006)			F	0.01 0.1 1 avours [experimental]	10 100 Favours [control]	
Risk of bias legend		n (salas	tion hins						
 (A) Random sequence (B) Allocation conceal)					
(C) Blinding of particip				rmance	bias)				
(D) Blinding of outcon	ne assessm	ent (de	tection b	ias)					
(E) Incomplete outcom	ne data (at	trition b	ias)						
(F) Selective reporting	(reporting	bias)							
(G) Other bias									

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



Supplemental Figure 27: Forest plot of Venous to arterial carbon dioxide difference and morbidity (organ

dysfunction, acute kidney injury).



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



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



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