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).

<b>(n)</b>			
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± 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± SD or media n [IQR]	7[5-8]	$0.6 \pm 0.0$	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).	
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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%				
Outcomes	Postoperative Mortality and AKI, postoperative increased AKI biomakers, other postoperative adverse outcomes (LOS,LOSICU,L MV, VIS,)	Intraoperative and postoperative AKI	Postoperati ve mortality	Postoperati ve Morbidity= NEC	Mortality, LMV ECMO, cardiac arrest, RRT, neurologic injury, LOSICU, reinterventio ns under CPB	LOS LOSICU, LMV
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
Mortality experimen tal group (n)	1	0	0	NA	9	NA
Organ dysfuncion control group (n)	AKI 3	AKI 28 ( among which 3 had RRT)	NA	ECMO 4	23	NA
Organ dysfuncion experimen tal group (n)	AKI 31	AKI 0 (RRT 0)	NA	ECMO 1	22	NA
Infections control group	NA	NA	NA	NEC 11	NA	NA
Infections experimen tal group (n)	NA	NA	NA	NEC 0	NA	NA
LOS control group in days mean± SD	22 [14-36]	28 [7-76]	NA	NA	NA	16 [4-50]

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 t	trials (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 $5.5\pm 2.6$ mmol/L and lactime to $\leq 5$ mmol/L of $3\pm 6$ hours, lactime to $\leq 2$ mmol/L of $11\pm 9$ 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

	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 $10.7\pm4.9$ mmol/L and $6.3\pm2.4$ mmol/L and lactime to $\leq$ 5mmol/L of $11\pm11h$ and $4\pm4$ hours and lactime to $\leq$ 2mmol/L of $23\pm9$ hours and $16\pm10$ hours	higher initial median and peak median lactate levels		(experiment al group)
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
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
Mortality control	14	7	14	11	11	11
group (n) Mortality experimen tal group	0	0	0	0	0	0
(n) Organ	25 patients with	MOF 11	28	9 ECMO, 7	NA	5 LOS, 1

dysfuncion	Bayley Scales of			RRT		hemorrhagic
control	Infant					shock, 2
group (n)	Development					respiratory
	score (BSID					failure, 3
	score)<70					MOF
	(=neurodevelpme					
	ntal score)					
Organ						
dysfuncion						
experimen	0	MOF 0	0	0	NA	?
tal group						
( <b>n</b> )						
Infections						
control	NA	NA	NA	NA	NA	NA
group (n)						
Infections						
experimen	NA	NA	NA	NA	NA	NA
tal group	1111	1 17 1	1 17 1	1111	1111	1 17 1
(n)						
LOS						
control			$30\pm25$ in non			
group in			survivors;			
days	NA	NA	54±46 in	NA	NA	NA
mean± SD			adverse			
or median			survivors			
experimen						
tal group	NT A	NT A	22   12	NTA	NT A	
in days	NA	NA	22±12	NA	NA	
mean± SD						
or median						
[IQK]						

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				
		34	preoperati					
		children	ve and					
		with	postoperat					
		postoperat	ive	maintenance				
	27 children	ive	cerebral	of optimal				
	(control	(admission	tissue	homodynamic				13 children
	group) with	to PICU)	oxygenati	status using		Maximum		with
	lowest	venous to	on index	vasoactive/ino		postoperat		intraoperati
	central	arterial	(TOI),	tropic agents		ive VIS at		ve
	venous	carbon	postoperat	intraoperativel		24 h and		desaturatio
	oxygen	dioxide	ive			48 h: 122		n rSO2
	saturation	difference	normalize	1-206		adolescent		scores
	ScVO2	(AVCO2)	d tissue	children		s without		(cerebral
	obtained by	of 8.3 (5.6,	hemoglobi	treated using	17 Patients	adverse	postoperative	and somatic
	connecting	14.9)	n index	the	with lactate	outcome	rSO2	NIRS)
	the Pediasat	mmHg	(nTHI),	conventional	levels on	with	desaturation	>3000 %
	CVC to a	with poor	concentrat	method i.e	admission	maximum	scores and	seconds (
	dedicated	postoperat	ion	maintenanace	in PICU of	VIS at	lactate levels:	control
	monitor	ıve	changes in	of optimal	>4.5	24h 5[5-8]	90 patients	group),
	(Vigileo	outcome	oxygenate	cardiac output	mmol/L	and	(experimenta	intraoperati
	Edwards	(control	d	(using markers	(control	maximum	l group) with	ve cerebral
T	Lifesciences	group)/	hemoglobi	of adequate	group)	VIS at 48h	postoperative	rSO2
Intervent	, Irvine, CA) $(S_2 VO2 < 68)$	105 shildron	$n (\Delta HbO2)$	cardiac output:	VERSUS	0 [0-5]	desaturation	desaturatio
ions	(SCVO2<08)	ciliaren	) allu	urine output,	189 patiens	VERSUS	scores	II score
	%) and	witti	tod	serum lactate	(experimen	27	<345%s/62	(=calculate
	blood lactate	ivo	homoglobi	levels and	tal group)	adolescent	patients	u by
	lovols	(admission	n (AHHb)	ScVO2)=	with lactate	s (control	(control	rSO2 < 50%
	(arterial	to PICID	measured	experimental	levels on	group)	group) with	1502<5070
	blood	with	by NIRS	group	admission	with	postoperative	seconds)
	samples)	venous to	(360	VERSUS	in PICU of	adverse	desaturation	VERSUS 9
	during CPB	arterial	children	group 2= 217	<4.5	outcome	scores	chldren
	(>3mmol/L)	carbon	without	children	mmol/L	with	≥345%s	with
	/228	dioxide	major	treated		maximum		intraoperati
	children	difference	morbidity	according to		VIS at 24h		ve
	(experiment	(AVCO2)	(experime	maintenance		7.5[5-		desaturatio
	al group)	of 5.4 (3.0,	ntal	of optimal		10.5 and		n scores
	ScVO2>68	8.4)	group)/27	perfusion		max1mum		<3000% sec
	% with	mmHg	children	pressure (=		VIS at 48h		onds
	blood	without	with major	prossure		5[0-9.2]		(experiment
	lactate levels	poor	morbidity	CVP)- control				al group)
	<3mmol/L	postoperat	and 12	group				
		ive	non	Stoup				
		outcome	survivors (					
		(experime	control					
		nt group)	group)					
	Major	Poor	Postoperat	Mortality,	Mortality,	postoperat	Mortality,	Postoperati
	postoperativ	outcome=1	1ve	Morbidity (=	Morbidity	1ve	Morbidity	Ve Montalita
Outcome	e morbiaity	S (motrop	mortality,	use of ECMO,	(=need for	mortality,	(delayed	Mortality
Outcome	(=mechanica	score) >	major	anu	peritoneal	(resussited	sternal	anu
S	time : ICU	15, ueath,	Cordiac	of poor	dialysis	(resuscitati	ECMO pulm	
	stav	arrest and	arrest	neripheral	PD), LMV,	mechanica	on ary	(-10W
	neurologic	ECMO	events.EC	perfusion	LOSICU	l support.	complication	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	,
	sis,	to PICU;	complicati	enterocolitis,		antibacteri	surgical	
	seizures);	and any	ons,	amputation)),		al therapy,	reinterventio	
	acute renal	unplanned	seizures,br	duration of		acute	ns), LCOS	
	failure (need	surgical	ain	ventilation and		kidney		
	for renal-	re-	infarction,	inotropic		injury or		
	replacement	interventio	sepsis)	treatment		neurologic		
	therapy);	ns during	_			injury)		
	pulmonary	hospital						
	complication	stay;						
	S	Secondary						
	(respiratory	outcomes=						
	distress	LOS,						
	syndrome;	LMV,						
	poor gas	postoperat						
	exchange	ive AKI						
	resulting in a							
	delayed							
	from							
	machanical							
	ventilation							
	pneumonia).							
	gastroenteric							
	complication							
	S							
	(necrotising							
	enterocolitis,							
	mesenteric							
	ischemia,							
	gastric							
	bleeding);							
	need for							
	extracorpore							
	al memorane							
	oxygenation							
	ventricular-							
	assist							
	device: or							
	sepsis (with							
	positive							
	blood							
	cultures))							
	and							
	mortality	III.1 C	III 1 C		III 1 C	11.1.6		
	Uich for	High for	High for		High for	High for	Uigh for	High for
	randomisatio	tion	tion	High for	nanuomisali	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
		nt	nt		nt	nt		t

Mortality control group (n)	10	14	12	3	4	0	15	1
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				
group in				
days				
mean±				
SD or				
median				
[IOR]				

# **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% Cl	ABCDEFG
Cheung 2005	0	43	14	42	11.3%	0.02 [0.00, 0.39]	<b>←</b>	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]		
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]	•	<b>00000<del>9</del>9</b>
Maarslet 2012	4	189	4	17	12.4%	0.07 [0.02, 0.31]	<b>_</b>	
Ranucci 2010	0	228	10	27	11.2%	0.00 [0.00, 0.06]	<b>←</b>	
Schumacher 2014	0	212	11	19	11.2%	0.00 [0.00, 0.03]	←	
Siegel 1996	0	30	7	11	11.1%	0.01 [0.00, 0.20]	·	•••••
Total (95% CI)		1326		364	100.0%	0.01 [0.00, 0.10]		
Total events	19		80					
Heterogeneity: Tau <sup>2</sup> =	14.89; C	hi <sup>2</sup> = 85	5.67, df =	= 8 (P -	< 0.0000	1); $ ^2 = 91\%$		ł
Test for overall effect:	Z = 3.62	(P = 0.)	0003)			F	avours [experimental] Favours [control]	
<u>Risk of bias legend</u> (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 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 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
Cheung 2005	0	0	0	0		Not estimable	
Hatherill 1997	0	0	0	0		Not estimable	
Hosseinpour 2017	0	0	0	0		Not estimable	
Kapoor 2016	0	0	0	0		Not estimable	
Ladha 2016	0	0	0	0		Not estimable	
Maarslet 2012	0	0	0	0		Not estimable	000000
Ranucci 2010	0	228	10	27	100.0%	0.00 [0.00, 0.06]	
Schumacher 2014	0	0	0	0		Not estimable	000000
Siegel 1996	0	0	0	0		Not estimable	000000
Total (95% CI)		228		27	100.0%	0.00 [0.00, 0.06]	
Total events	0		10				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 3.82	(P = 0.1)	0001)			F	avours [experimental] Favours [control]
<u>Risk of bias legend</u> (A) Random sequence (B) Allocation concealn (C) Blinding of particip (D) Blinding of outcom (E) Incomplete outcom	e generatio ment (selec pants and p ne assessm ne data (att	n (selec tion bia personn ent (de trition bi	tion bias s) el (perfo tection b ias)	) rmance ias)	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).

	Experime	ental	Cont	rol		Odds Ratio	Odds R	Ratio	<b>Risk of Bias</b>
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Rando	m, 95% CI	ABCDEFG
Hosseinpour 2017	0	0	0	0		Not estimable			000000
Kapoor 2016	0	0	0	0		Not estimable			
Ranucci 2010	0	228	10	27	100.0%	0.00 [0.00, 0.06]	←		
Total (95% CI)		228		27	100.0%	0.00 [0.00, 0.06]			
Total events	0		10						
Heterogeneity: Not ap	plicable							10 100	
Test for overall effect:	Z = 3.82	(P = 0.)	0001)			F	avours [experimental] F	Favours [control]	
Risk of bias legend									
(A) Random sequence	generatio	n (selec	tion bias)						
(B) Allocation concealm	nent (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)									

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.

Study or Subgroup	Experim Events	ental Total	Cont Events	rol Total	Weight	Odds Ratio M-H, Random, 95% CI	Odds Ratio Risk of Bias 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									
Test for overall effect:	Z = 5.04	(P < 0.)	00001)			F	avours [experimental] Favours [control]			
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)										
(F) Incomplete outcome data (attrition bias)										

(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).

	Experimental		Control		Odds Ratio		Odds	Odds Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Rand	om, 95% Cl	ABCDEFG	
Kapoor 2016	0	0	0	0		Not estimable				
Ranucci 2010	0	228	10	27	100.0%	0.00 [0.00, 0.06]	←			
Total (95% CI)		228		27	100.0%	0.00 [0.00, 0.06]				
Total events	0		10							
Heterogeneity: Not ap	plicable							10 100		
Test for overall effect:	Z = 3.82	(P = 0.)	0001)			F	avours [experimental]	Favours [control]		
<u>Risk of bias legend</u> (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)										

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



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

	Experimental Contro		Control Odds Ratio			Odds Ratio	<b>Risk of Bias</b>			
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									
Test for overall effect:	Z = 1.42	(P = 0.	16)			F	avours [experimental] Favours [control]			
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).



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		Control		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]	<b></b>	
Total (95% CI)		122		27	100.0%	0.02 [0.00, 0.31]		
Total events	0		5					
Heterogeneity: Not ap	plicable							
Test for overall effect:	Z = 2.74	(P = 0.)	006)			F	avours [experimental] Favours [control]	
Risk of bias legend								
(A) Random sequence	e generatio	n (selec	tion bias)	)				
(B) Allocation concealr	ment (seled	tion bia	s)					
(C) Blinding of particip	ants and p	personn	el (perfo	rmance	bias)			
(D) Blinding of outcom	ne assessm	ent (de	tection bi	ias)				
(E) Incomplete outcom	ne data (at	trition b	ias)					
(F) Selective reporting	(reporting	bias)						
(G) Other bias								

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

	Experimental		Control			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		
Rhodes 2017	0	105	14	34	100.0%	0.01 [0.00, 0.12]	←────	000000		
Total (95% CI)		105		34	100.0%	0.01 [0.00, 0.12]				
Total events	0		14							
Heterogeneity: Not ap	plicable							<del></del>		
Test for overall effect: $Z = 3.43$ (P = 0.0006) 0.01 1 10 100										
							arours [experimental] Tarours [control]			
Risk of bias legend										
(A) Random sequence	generation	n (selec	tion bias)							
(B) Allocation concealr	nent (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 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).