Appendix

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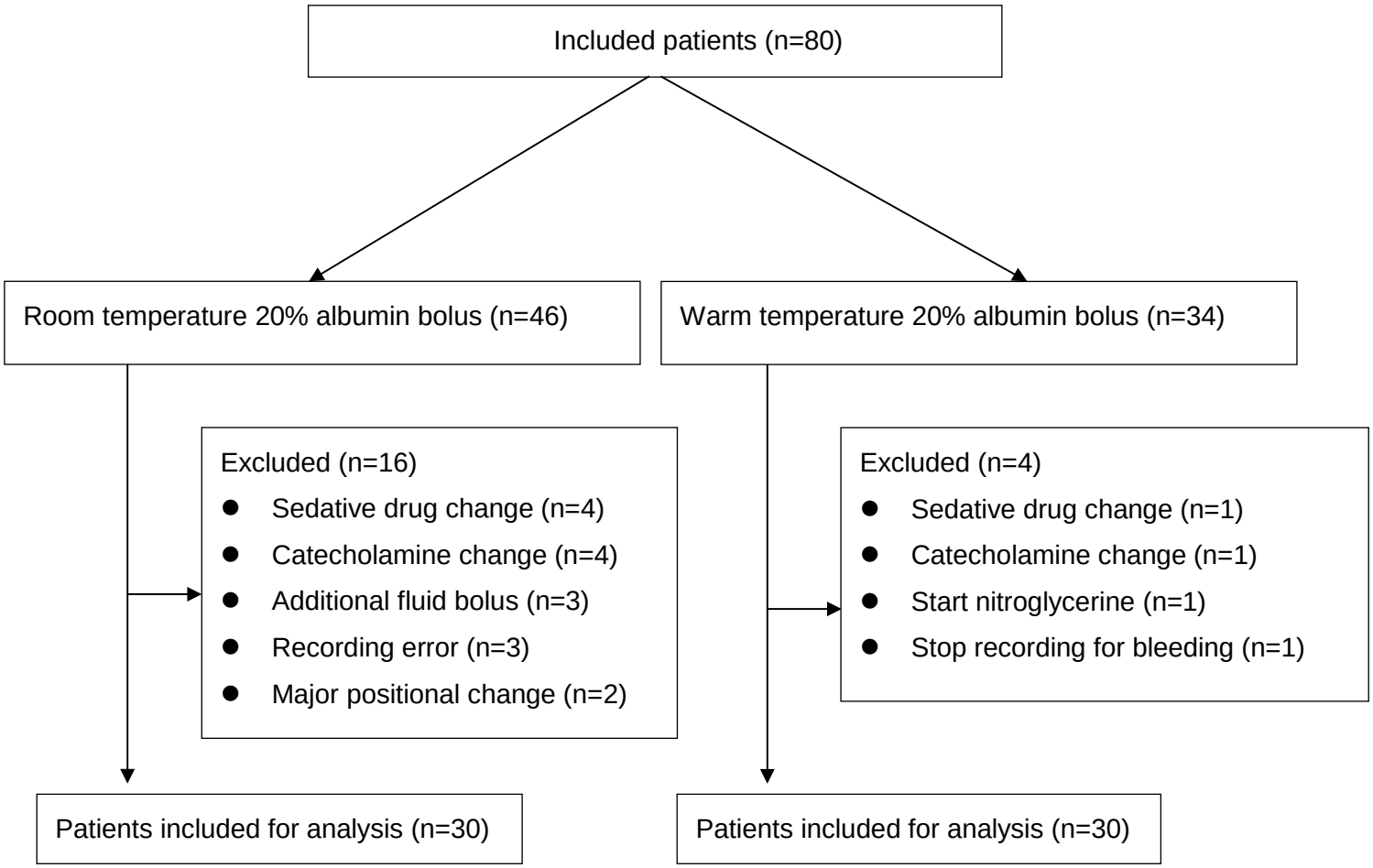
Supplementary Appendix Item 1. Detailed exclusion criteria.

1. Additional bolus: Additional fluid bolus was prescribed during the observation period.
2. Catecholamine: Any change (bolus or continuous infusion) of catecholamine.
3. Sedative drug: Any change (bolus or continuous infusion) of sedative drugs.
4. Muscle relaxant: Any dose of muscle relaxant infusion.
5. Pacing: Any change of pacing setting.
6. Ventilation setting: Any change of ventilator parameters or ventilation setting except for FiO_2.
7. Other: Care givers' intervention that may affect patients' haemodynamic parameters, for example, tracheal suctioning, patients' movement or movement of transducers.

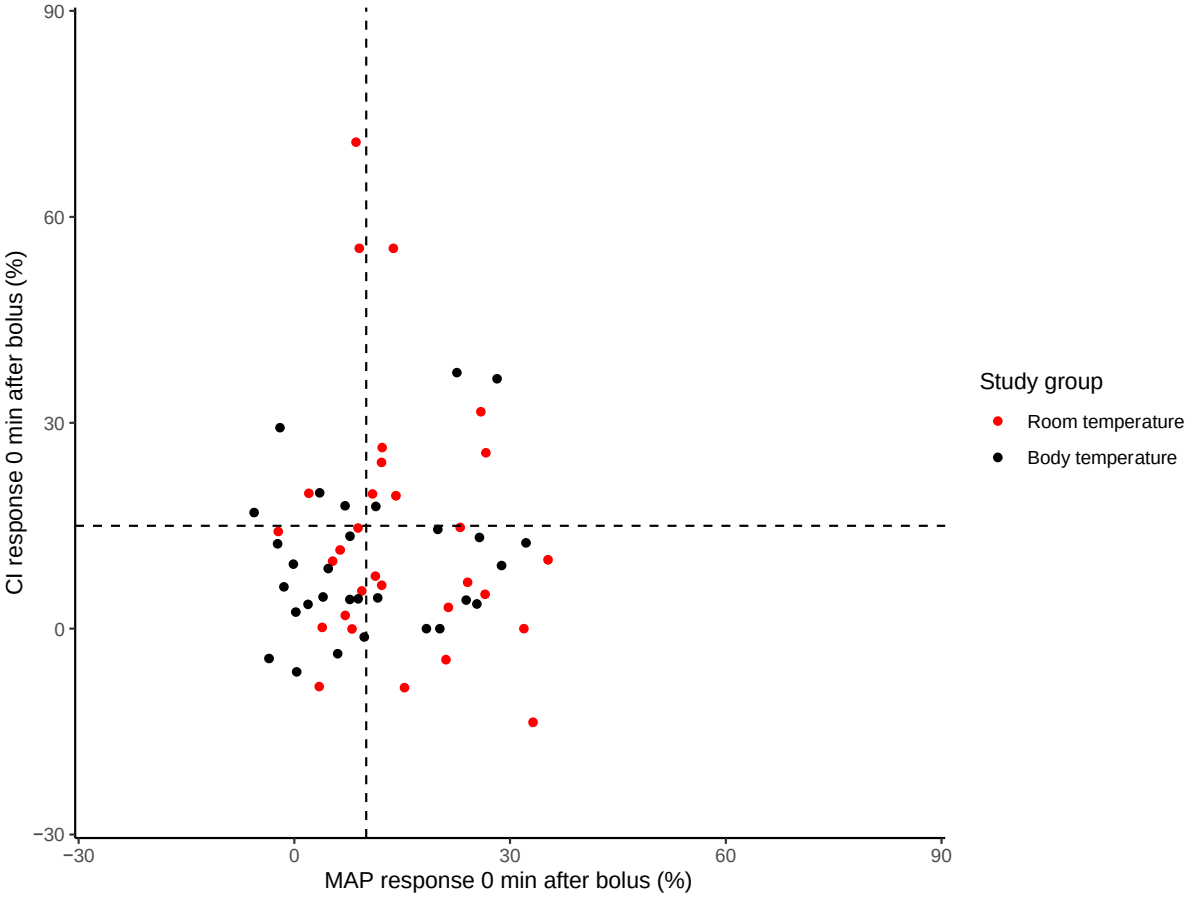
Supplementary Appendix Item 2. Minor confounders in the study patients.

1. Patients awoke during the study periods, but kept stable sedative status without any change of sedative drugs.
2. When patients awoke, bedside nurse talked to patients without touching.

Supplementary Figure 1. Flow chart of study inclusion process

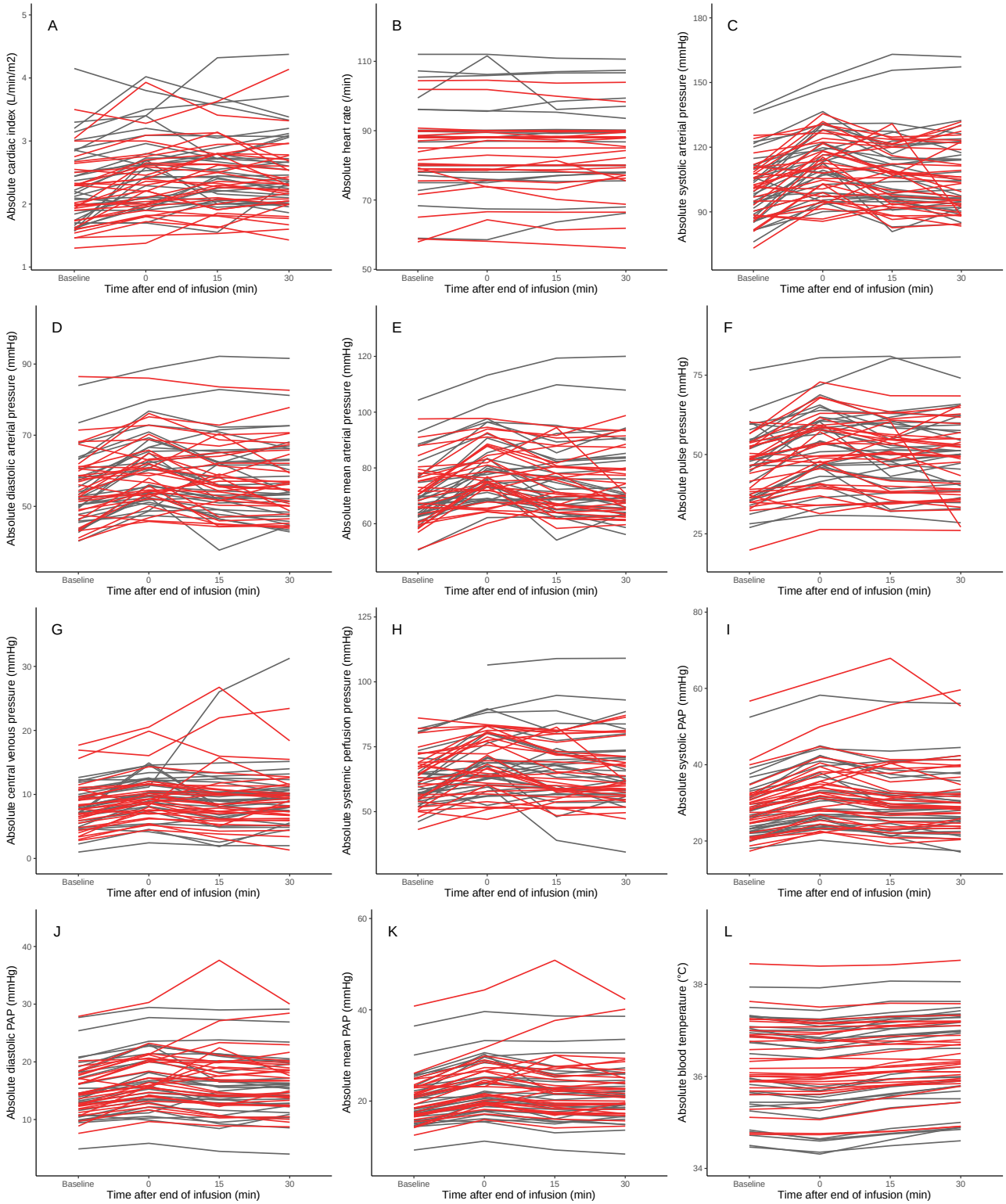


Supplementary Figure 2. CI response and MAP response 0 minute after 20% albumin bolus.



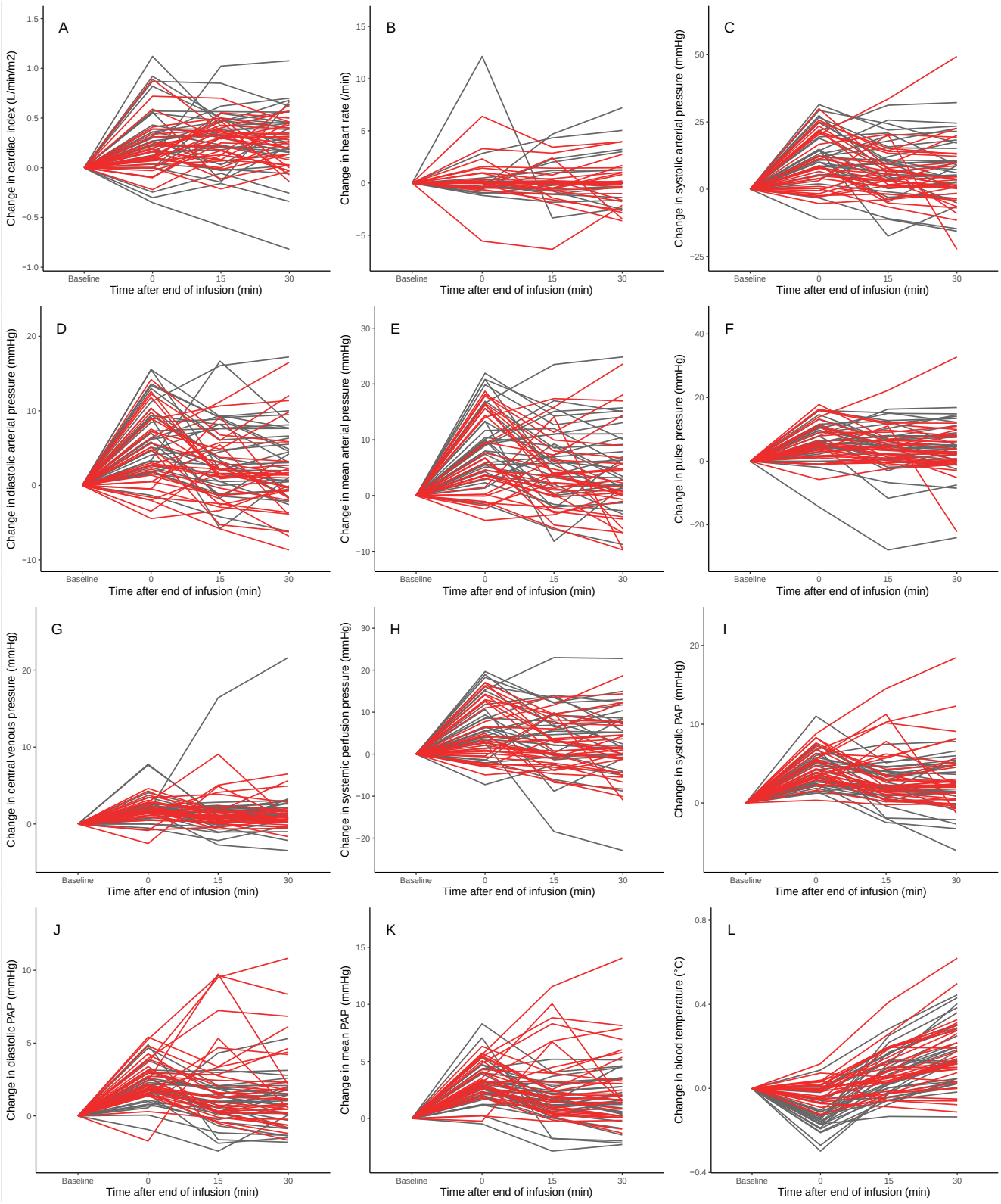
Vertical line shows mean arterial pressure (MAP) response (10%) and horizontal line shows cardiac index (CI) response (15%).

Supplementary Figure 3. Individual haemodynamics and temperature changes (absolute value).



Patients in the room temperature albumin group are represented by a grey line and those in the body temperature albumin group are represented by a red line.

Supplementary Figure 4. Individual haemodynamics and temperature changes (relative change).



Patients in the room temperature albumin group are represented by a grey line and those in the body temperature albumin are represented by a red line.

Supplementary Table 1. Characteristics of study patients at the time of fluid bolus administration

	All patients	Room temperature 20%albumin	Body temperature 20% albumin	
	N = 60	N = 30	N = 30	***P***
Mechanical ventilation mode				0.67
SIMV	54 (90%)	28 (93%)	26 (87%)	-
PSV	6 (10%)	2 (7%)	4 (13%)	-
Mechanical ventilation settings				
Tidal volume (mL/kg PBW)[§]	7.3 [6.4; 8.5]	7.7 [6.9; 8.7]	6.9 [6.2; 7.6]	0.061
PIP (cm H_2O)	19 [17; 21]	19 [17; 21]	18 [16; 21]	0.54
PEEP (cm H_2O)	5 [5; 5]	5 [5; 5]	5 [5; 5]	0.33
FiO_2	0.3 [0.3; 0.5]	0.3 [0.3; 0.5]	0.3 [0.25; 0.4]	0.23
PaO_2/FiO_2 ratio	311 [250; 367]	309 [251; 378]	312 [250; 348]	0.68
SpO_2 (%)	99 [97; 100]	99 [97; 100]	99 [98; 100]	0.61
$EtCO_2$ (mm Hg)	35 [31; 39]	35 [32; 37]	35 [31; 39]	0.75
Body temperature control				
External body active warming	19 (32%)	12 (40%)	7 (23%)	0.17
Haemodynamic status				
Vasopressor support	15 (25%)	8 (27%)	7 (23%)	>0.99
Milrinone administration	6 (10%)	3 (10%)	3 (10%)	>0.99
Heart rhythm				0.44
Paced	33 (55%)	18 (60%)	15 (50%)	-
Sinus rhythm	26 (43%)	11 (37%)	15 (50%)	-
Atrial fibrillation	1 (2%)	1 (3%)	0 (0%)	-
Sedation				
Propofol	54 (90%)	28 (93%)	26 (87%)	0.67
Propofol dose (mg/h)	100 [80; 150]	100 [80; 150]	100 [100; 150]	0.39
Opioids	4 (7%)	0 (0%)	4 (13%)	0.11
*Biochemistry**				
pH	7.4 [7.36; 7.42]	7.41 [7.37; 7.43]	7.39 [7.36; 7.41]	0.14
PaO_2 (mm Hg)	126 [87; 200]	125 [82; 206]	127 [99; 193]	0.61
$PaCO_2$ (mm Hg)	42 [39; 45]	42 [41; 45]	41 [39; 46]	0.80
Bicarbonate (mmol/L)	24 [23; 26]	26 [23; 27]	24 [23; 26]	0.12
Lactate (mmol/L)	1.1 [0.9; 1.5]	1.1 [0.9; 1.5]	1.1 [0.9; 1.6]	0.66
Creatinine (µmol/L)	78 [65; 102]	72 [64; 104]	79 [66; 100]	0.67
Haemoglobin (g/L)	100 [90; 108]	96 [89; 104]	105 [96; 112]	0.017
Blood sugar level (mmol/L)	7.2 [6.5; 8.4]	7.2 [6.3; 8]	7.3 [6.5; 8.8]	0.27

Data is median [interquartile range], or count (percentage).

*: measured on arterial blood gas closest to FBT. [§]: predicted body weight (ARDS Network formula). P values reflect the between-groups comparison.

$EtCO_2$: end-tidal CO_2 partial pressure; FiO_2: fraction of inspiratory oxygen ; $PaCO_2$: arterial partial pressure of CO_2; PaO_2: arterial partial pressure of oxygen; PBW: predicted body weight; PEEP: positive end-expiratory pressure; PIP: peak inspiratory pressure; PSV: pressure support ventilation; SIMV: synchronized intermittent mandatory ventilation; SpO_2: peripheral capillary oxygen saturation.

Supplementary Table 2. Haemodynamic effect of room temperature 20% albumin fluid bolus and body temperature 20% albumin bolus (absolute value).

	Time after FB	All patients	Room temperature 20% albumin	Body temperature 20% albumin
		N = 60	N = 30	N = 30
Mean arterial pressure (mmHg)	Baseline	69 [63; 76]	67 [63; 74]	70 [64; 77]
	0 min	76 [71; 86]	77 [70; 85]	76 [72; 87]
	15 min	74 [67; 82]	74 [67; 82]	73 [67; 81]
	30 min	70 [65; 83]	70 [66; 84]	70 [65; 80]
Systolic arterial pressure (mmHg)	Baseline	100 [89; 110]	98 [89; 111]	101 [89; 108]
	0 min	113 [99; 122]	113 [100; 127]	111 [99; 121]
	15 min	107 [96; 120]	107 [97; 119]	108 [94; 119]
	30 min	104 [93; 120]	104 [95; 121]	103 [92; 117]
Diastolic arterial pressure (mmHg)	Baseline	53 [48; 61]	52 [48; 58]	55 [49; 61]
	0 min	60 [53; 66]	60 [53; 67]	59 [54; 64]
	15 min	56 [51; 64]	56 [51; 64]	56 [52; 64]
	30 min	55 [50; 65]	54 [49; 65]	55 [50; 64]
Pulse pressure (mmHg)	Baseline	47 [36; 53]	47 [36; 54]	46 [37; 51]
	0 min	53 [45; 59]	54 [46; 61]	50 [41; 59]
	15 min	51 [40; 58]	51 [43; 60]	51 [38; 56]
	30 min	50 [39; 57]	51 [41; 59]	49 [38; 55]
Mean PAP (mmHg)	Baseline	19 [17; 23]	19 [16; 23]	19 [17; 23]
	0 min	22 [19; 27]	21 [18; 28]	22 [20; 27]
	15 min	22 [18; 25]	21 [17; 25]	22 [18; 26]
	30 min	21 [18; 25]	21 [18; 24]	21 [18; 25]
Systolic PAP (mmHg)	Baseline	28 [23; 32]	26 [22; 31]	28 [25; 32]
	0 min	31 [26; 38]	29 [26; 38]	33 [28; 37]
	15 min	29 [25; 36]	28 [23; 33]	30 [26; 37]
	30 min	29 [25; 35]	28 [25; 33]	29 [26; 36]
Diastolic PAP (mmHg)	Baseline	14 [12; 17]	14 [11; 18]	14 [12; 17]
	0 min	16 [14; 20]	16 [13; 20]	16 [14; 20]
	15 min	15 [13; 20]	15 [13; 18]	17 [13; 20]
	30 min	15 [12; 19]	15 [12; 19]	17 [13; 19]
Central venous pressure (mmHg)	Baseline	8 [6; 10]	8 [6; 10]	8 [6; 10]
	0 min	10 [8; 12]	10 [8; 12]	9 [7; 11]
	15 min	8 [6; 11]	9 [7; 10]	8 [6; 11]
	30 min	9 [7; 11]	10 [8; 11]	9 [7; 11]
Heart rate (/min)	Baseline	88 [80; 90]	88 [80; 90]	86 [79; 88]
	0 min	88 [80; 90]	88 [80; 90]	88 [79; 88]
	15 min	88 [80; 90]	88 [80; 90]	87 [79; 88]
	30 min	88 [80; 90]	88 [80; 90]	87 [78; 88]

Cardiac index (L/min/m^2)	Baseline	2.1 [1.7; 2.6]	2.2 [1.8; 2.8]	2.0 [1.7; 2.5]
	0 min	2.4 [2.0; 2.7]	2.6 [2.1; 2.9]	2.3 [2.0; 2.6]
	15 min	2.4 [2.0; 2.7]	2.4 [2.1; 2.7]	2.3 [1.9; 2.8]
	30 min	2.4 [2.1; 2.7]	2.4 [2.2; 3.1]	2.3 [2.0; 2.7]
SVRi (dyn.s.cm^{-5}.m^{-2})	Baseline	2198 [1783; 2951]	2099 [1737; 2702]	2507 [1818; 3020]
	0 min	2321 [1791; 2876]	2128 [1847; 2842]	2519 [1772; 2998]
	15 min	2256 [1816; 2674]	2254 [1954; 2572]	2276 [1616; 2748]
	30 min	2208 [1722; 2557]	2208 [1726; 2562]	2197 [1760; 2540]
Systemic perfusion pressure (mmHg)	Baseline	61 [55; 68]	60 [56; 65]	63 [55; 69]
	0 min	68 [60; 78]	68 [63; 76]	68 [60; 78]
	15 min	65 [58; 73]	66 [58; 73]	62 [58; 73]
	30 min	62 [57; 71]	63 [57; 73]	61 [57; 71]
Blood temperature (°C)	Baseline	36.1 [35.6; 37.0]	36.2 [35.4; 37.0]	36.1 [35.9; 36.9]
	0 min	36.1 [35.6; 36.9]	36.1 [35.4; 37.0]	36.1 [35.8; 36.9]
	15 min	36.3 [35.8; 37.1]	36.3 [35.6; 37.1]	36.3 [35.9; 37.0]
	30 min	36.3 [35.9; 37.2]	36.4 [35.7; 37.3]	36.3 [36.0; 37.0]

Data as median [interquartile range].

***:** $p<0.05$: comparison between the room temperature albumin group and the body temperature albumin group at each time point, adjusted for the repetition of measurements in a given patient.

FB: fluid bolus; PAP: pulmonary arterial pressure; SVRi: Systemic vascular resistance index.

Supplementary Table 3. Haemodynamic effect of room temperature 20% albumin bolus vs. body temperature 20% albumin bolus (relative change from baseline).

	Time after FB	All patients	Room temperature 20% albumin	Body temperature 20% albumin
		N = 60	N = 30	N = 30
Mean arterial pressure (mmHg)				
	0 min	8 [4; 14]	9 [6; 13]	5 [1; 14]
	15 min	4 [0; 9]	6 [2; 11]	4 [0; 6]
	30 min	3 [0; 8]	5 [2; 10]	1 [-1; 5]
Systolic arterial pressure (mmHg)				
	0 min	11 [5; 20]	12 [9; 19]	8 [2; 20]
	15 min	7 [1; 14]	10 [1; 16]	4 [1; 9]
	30 min	5 [0; 12]	8 [2; 17]	1 [-1; 10]
Diastolic arterial pressure (mmHg)				
	0 min	5 [2; 9]	6 [3; 9]	3 [0; 9]
	15 min	2 [-1; 6]	4 [1; 8]	2 [-1; 5]
	30 min	2 [-1; 6]	4 [1; 7]	1 [-2; 3]
Pulse pressure (mmHg)				
	0 min	6 [4; 10]	6 [5; 10]	5 [2; 10]
	15 min	4 [1; 8]	5 [2; 8]	4 [1; 6]
	30 min	3 [0; 8]	5 [1; 9]	2 [-1; 7]
Mean PAP (mmHg)				
	0 min	3 [2; 4]	3 [2; 4]	3 [3; 5]
	15 min	2 [1; 3]	2 [1; 2]*	2 [1; 4]*
	30 min	2 [0; 3]	1 [0; 3]	2 [0; 3]
Systolic PAP (mmHg)				
	0 min	4 [3; 6]	4 [2; 5]	5 [3; 6]
	15 min	2 [1; 4]	2 [1; 4]	2 [1; 5]
	30 min	2 [1; 5]	2 [1; 5]	2 [0; 5]
Diastolic PAP (mmHg)				
	0 min	2 [2; 3]	2 [1; 3]	2 [2; 3]
	15 min	1 [0; 2]	1 [0; 2]*	1 [0; 3]*
	30 min	1 [0; 2]	1 [0; 2]*	1 [0; 2]*
Central venous pressure (mmHg)				
	0 min	2 [1; 2]	2 [2; 2]	2 [1; 3]
	15 min	1 [0; 2]	1 [0; 2]	1 [0; 2]
	30 min	1 [0; 2]	1 [0; 3]	1 [0; 1]
Heart rate (/min)				
	0 min	0 [0; 0]	0 [0; 0]	0 [0; 0]
	15 min	0 [0; 0]	0 [0; 0]	0 [-1; 0]
	30 min	0 [0; 0]	0 [0; 0]	0 [-1; 1]
Cardiac index (L/min/m^2)				

	0 min	0.2 [0.1; 0.4]	0.3 [0.1; 0.4]	0.1 [0.1; 0.3]
	15 min	0.3 [0.1; 0.4]	0.3 [0.0; 0.5]	0.3 [0.1; 0.4]
	30 min	0.3 [0.1; 0.4]	0.3 [0.2; 0.5]	0.2 [0.0; 0.4]
SVRi (dyn.s.cm^{-5}.m^{-2})				
	0 min	-32 [-249; 171]	-47 [-212; 190]	-11 [-241; 156]
	15 min	-165 [-431; 162]	61 [-431; 376]	-217 [-419; -71]
	30 min	-125 [-469; 70]	-90 [-483; 120]	-133 [-431; -22]
Systemic perfusion pressure (mmHg)				
	0 min	5 [1; 12]	6 [3; 11]	3 [0; 12]
	15 min	3 [-1; 8]	6 [0; 10]	1 [-2; 5]
	30 min	2 [-1; 8]	5 [0; 8]	1 [-4; 5]
Blood temperature (°C)				
	0 min	-0.1 [-0.1; 0.0]	-0.1 [-0.2; -0.1]*	0.0 [-0.1; 0.0]*
	15 min	0.1 [0.0; 0.1]	0.1 [0.0; 0.1]	0.1 [0.0; 0.1]
	30 min	0.1 [0.0; 0.3]	0.1 [0.0; 0.3]	0.1 [0.0; 0.3]

Data as median [interquartile range].

*****p<0.05 between the room temperature vs. body temperature albumin group at each time point, adjusted for the repeated measures in a given patient.

FB: fluid bolus; PAP: pulmonary arterial pressure; SVRi: Systemic vascular resistance index.

Supplementary Table 4. Dissipation of the haemodynamic response (CI and MAP)

	All patients	Room temperature 20%Albumin	Body temperature 20% albumin	
Early CI responders	N=17	N=10	N=7	
Absence of dissipation at 30 minutes*	14 (82%)	9 (90%)	5 (71%)	0.15
Effect dissipated at 15 minutes[§]	1 (6%)	1 (10%)	0 (0%)	
Effect dissipated at 30 minutes	2 (12%)	0 (0%)	2 (29%)	
Early MAP responders	N=30	N=18	N=12	
Absence of dissipation at 30 minutes[†]	17 (57%)	9 (50%)	8 (67%)	0.47
Effect dissipated	13 (43%)	9 (50%)	4 (33%)	
Time to dissipation (min)	6 [5; 11]	5 [3; 6]	9 [7; 12]	

Data as median [interquartile range], or count (percentage).

*: defined as a CI within 5% of baseline CI

[§]: twelve patients in the room temperature albumin patients were not measured CI at 15 minutes after FBT

†: defined as a MAP within 3 mm Hg of baseline

CI: cardiac index; MAP: mean arterial pressure