



## **Online Appendix**

**This appendix was part of the submitted manuscript and has been peer reviewed.  
It is posted as supplied by the authors.**

Appendix to: Yanase F, Naorungroj T, Cutuli SL, et al. Rapid 500 mL albumin bolus versus rapid 200 mL bolus followed by slower continuous infusion in post-cardiac surgery patients: a pilot before-and-after study. *Crit Care Resusc* 2021; 23: 320-8. <https://doi.org/10.51893/2021.3.OA9>

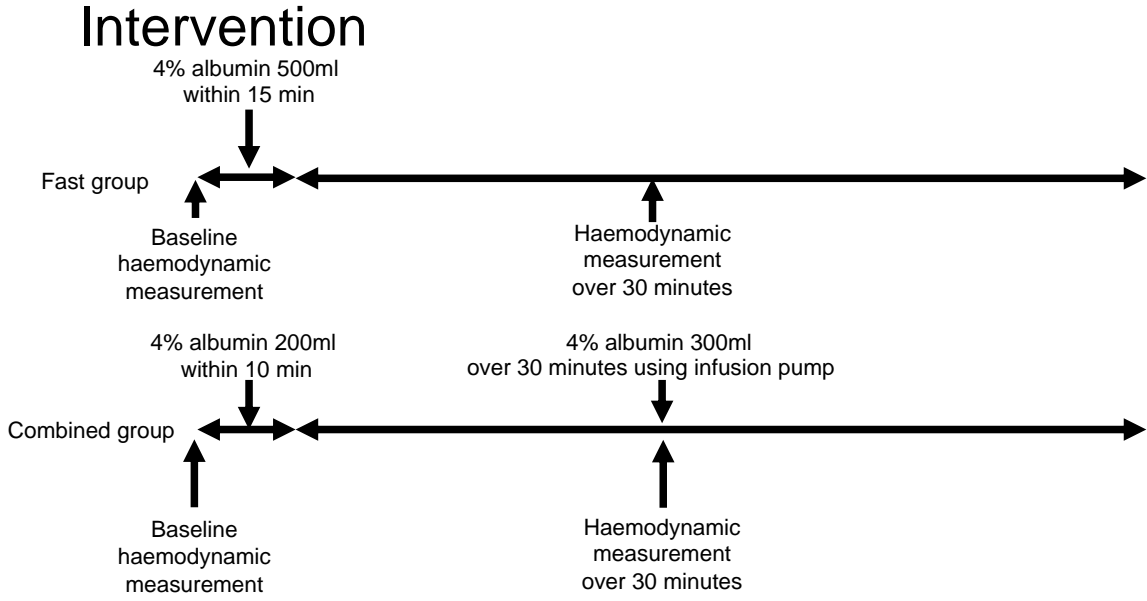
### **Supplementary Appendix 1. Detailed exclusion criteria.**

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<sub>2</sub> setting.
7. Other: Care givers' intervention that may affect patients' haemodynamic parameters, for example, tracheal suctioning, patients' movement or movement of transducers.

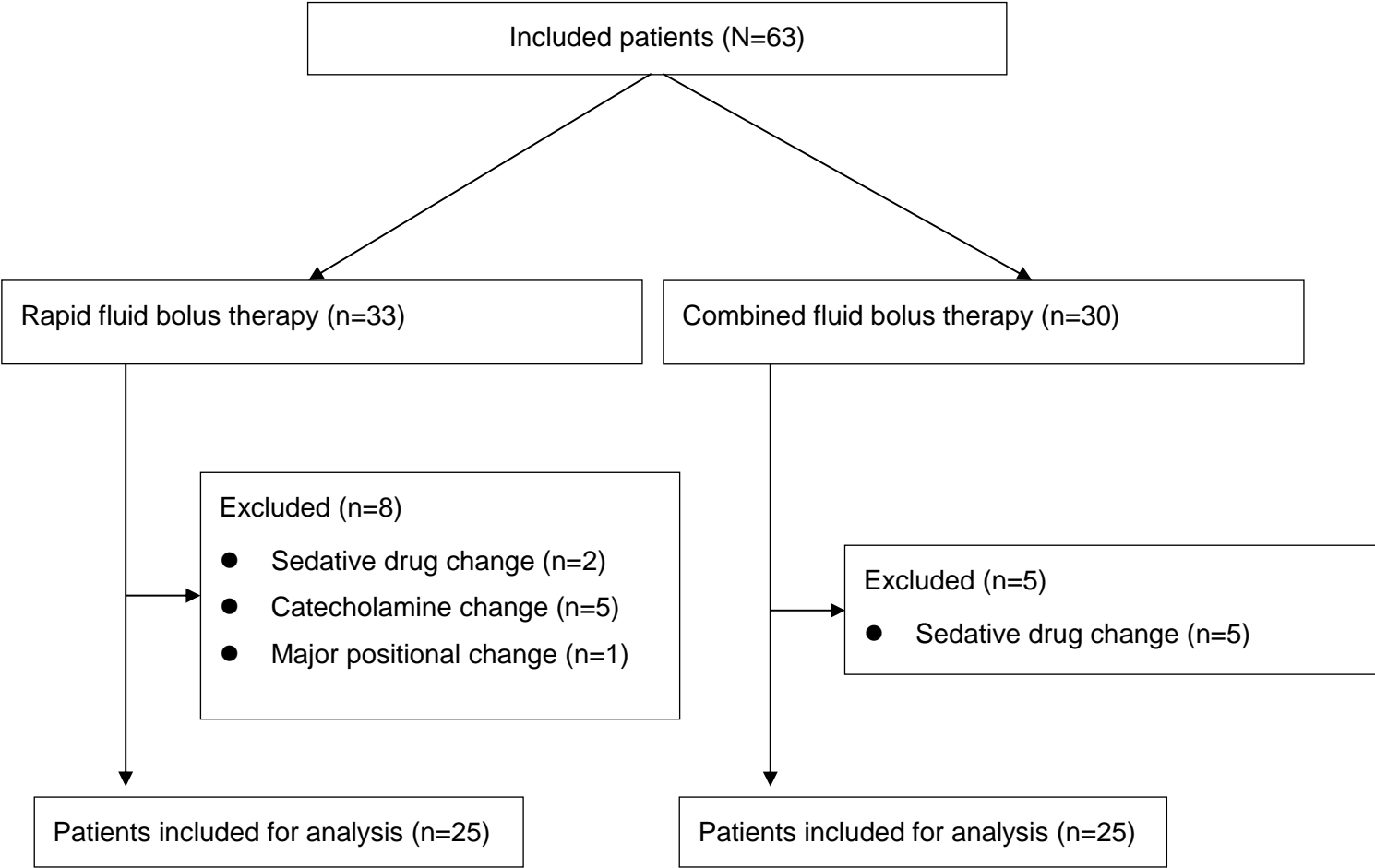
### **Supplementary Appendix 2. Minor confounders in the study patients.**

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

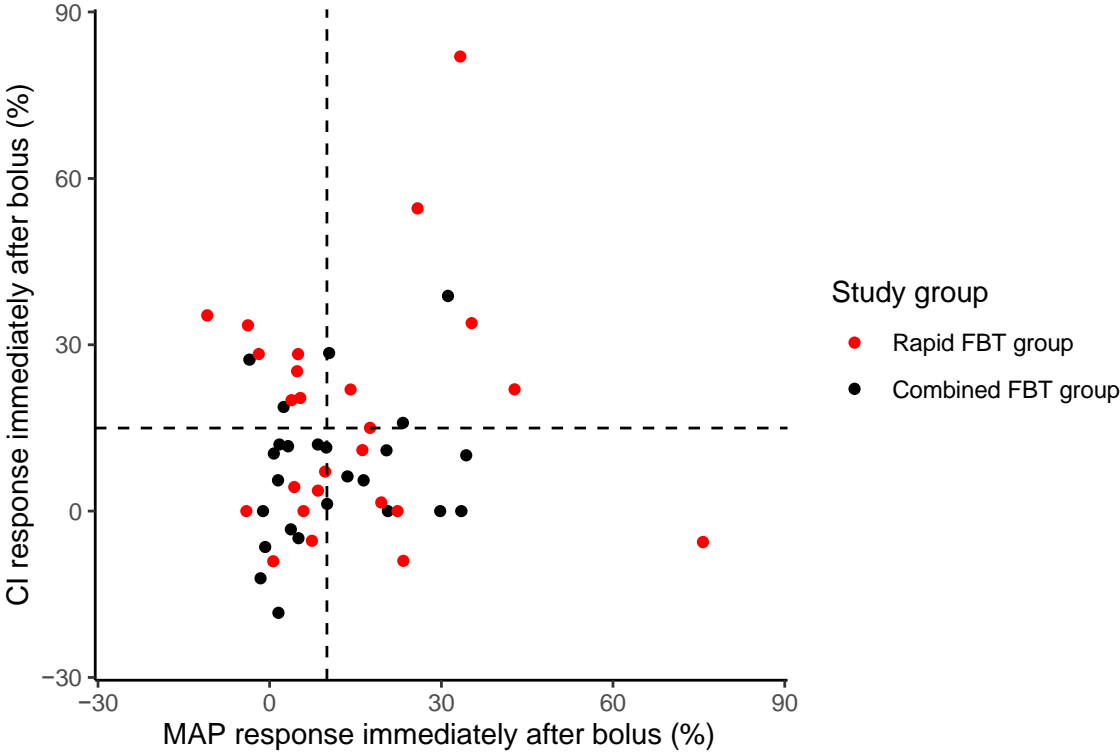
Supplementary Figure 1. Intervention protocol.



Supplementary Figure 2. Flow chart of study inclusion process

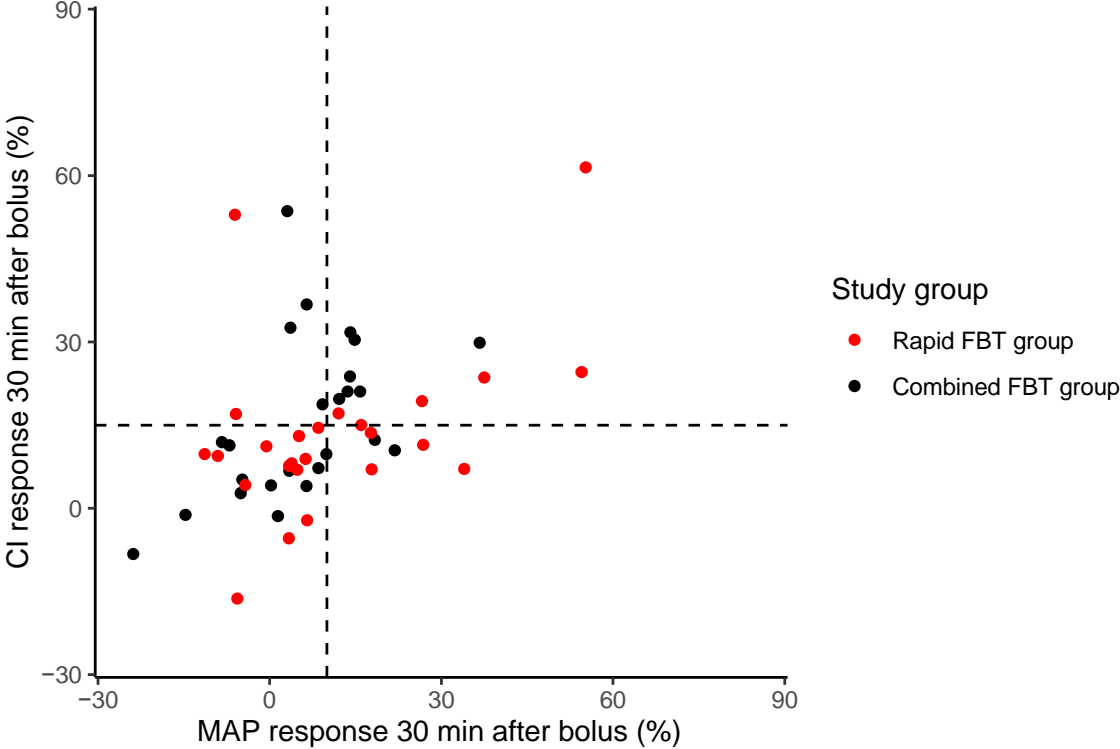


**Supplementary Figure 3.** Scatter plot for %MAP response and %CI response immediately after 4% albumin large bolus (500 ml) bolus and small (200 ml) bolus.



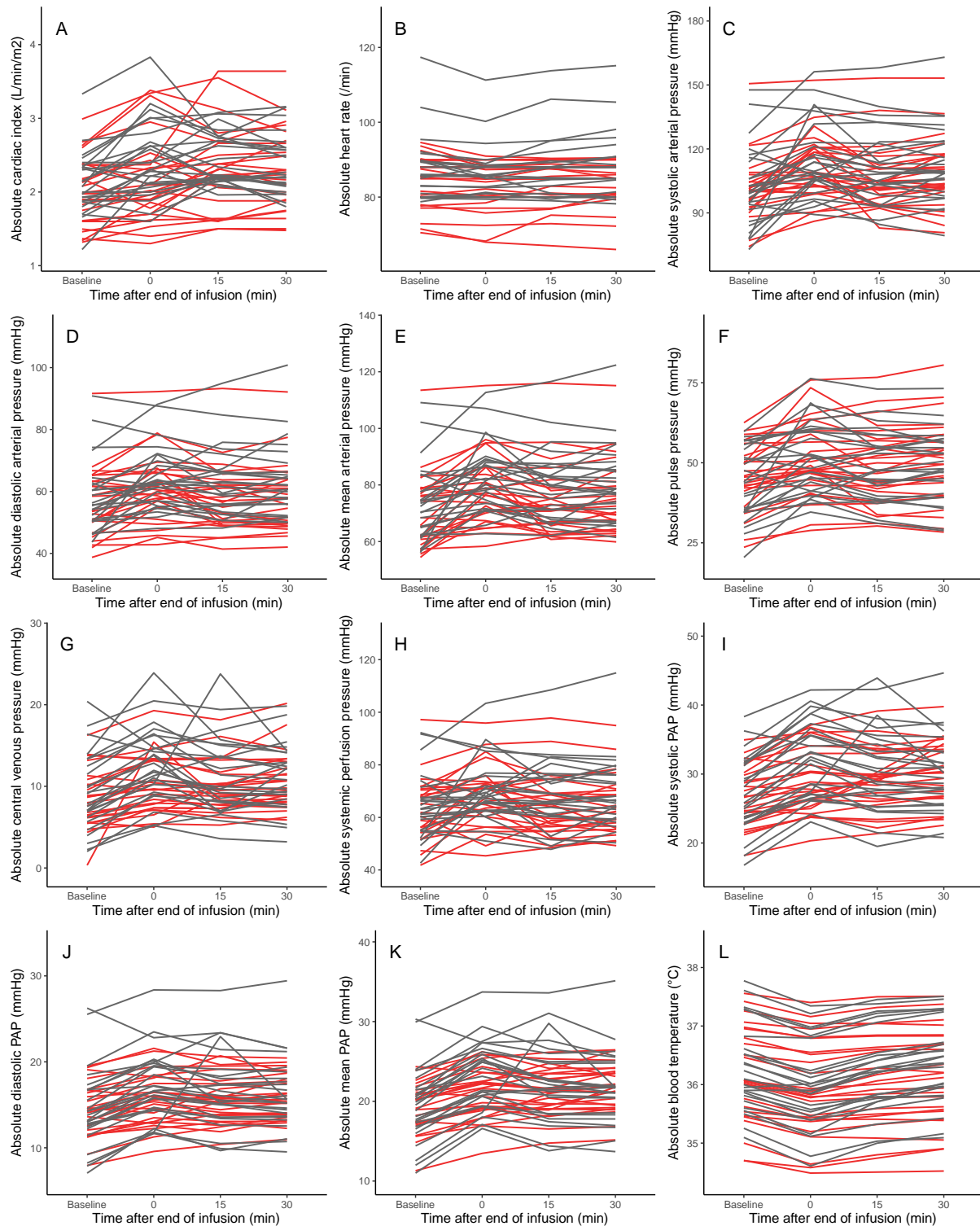
Vertical line shows mean arterial pressure (MAP) response (10%) and horizontal line shows cardiac index (CI) response (15%). Over all rho was 0.09.

**Supplementary Figure 4.** Scatter plot for %MAP response and %CI response 30 minutes after 4% albumin rapid FBT vs 30 minutes after small bolus (end of 500 ml infusion).



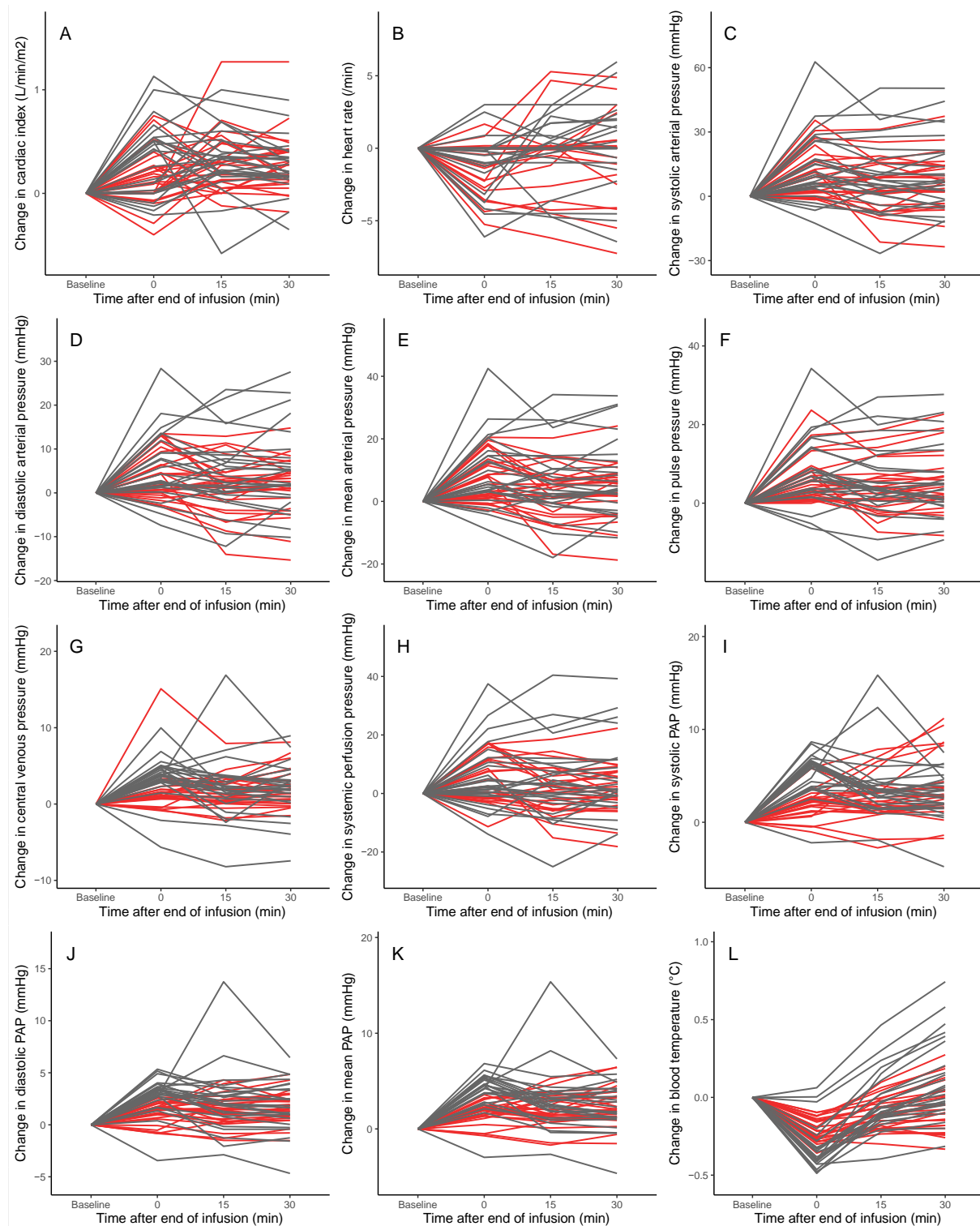
Vertical line shows mean arterial pressure (MAP) response (10%) and horizontal line shows cardiac index (CI) response (15%). Overall rho was 0.47. Rho of the rapid FBT group was 0.38 and that in the combined FBT group was 0.56.

## Supplementary Figure 5. Individual haemodynamics and temperature measurements



Data shown are the absolute value for each patient, at each time point for cardiac index (A), heart rate (B), systolic arterial pressure (C), diastolic arterial pressure (D), mean arterial pressure (E), pulse pressure (F), central venous pressure (G), systemic perfusion pressure (H), systolic pulmonary arterial pressure (I), diastolic pulmonary arterial pressure (J), mean pulmonary arterial pressure (K), and body temperature (L). Patients in the rapid FBT group are represented by a grey line, those in the combined FBT group are represented by a red line.

**Supplementary Figure 6. Relative change from baseline of individual haemodynamics and temperature measurements**



Data shown is the relative value for each patient, at each time point, for cardiac index (A), heart rate (B), systolic arterial pressure (C), diastolic arterial pressure (D), mean arterial pressure (E), pulse pressure (F), central venous pressure (G), systemic perfusion pressure (H), systolic pulmonary arterial pressure (I), diastolic pulmonary arterial pressure (J), mean pulmonary arterial pressure (K), and body temperature (L). Patients in the rapid FBT group are represented by a grey line, those in the combined FBT group are represented by a red line.



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

	All patients	Rapid FBT group	Combined FBT group	P
	N = 50	N = 25	N = 25	
<i>Mechanical ventilation mode</i>				
SIMV	48 (96%)	23 (92%)	25 (100%)	-
PSV	2 (4%)	2 (8%)	0 (0%)	-
<i>Mechanical ventilation settings</i>				
Tidal volume (mL/kg PBW) <sup>§</sup>	7.1 [6.5; 8.0]	7.0 [6.3; 8.1]	7.1 [6.5; 7.7]	0.91
PIP (cm H <sub>2</sub> O)	18 [16; 20]	18 [16; 21]	18 [16; 19]	0.36
PEEP (cm H <sub>2</sub> O)	5 [5; 5]	5 [5; 5]	5 [5; 5]	>0.99
FiO <sub>2</sub>	0.3 [0.3; 0.4]	0.3 [0.3; 0.4]	0.3 [0.3; 0.5]	0.18
PaO <sub>2</sub> /FiO <sub>2</sub> ratio	337 [255; 399]	343 [255; 390]	332 [261; 402]	0.88
SpO <sub>2</sub> (%)	100 [97; 100]	98 [96; 100]	100 [98; 100]	0.10
EtCO <sub>2</sub> (mm Hg)	36 [32; 40]	38 [33; 41]	34 [31; 39]	0.17
<i>Body temperature control</i>				
External body active warming	20 (40%)	11 (44%)	9 (36%)	0.77
<i>Haemodynamic status</i>				
Vasopressor support	8 (16%)	4 (16%)	4 (16%)	>0.99
Milrinone administration	8 (16%)	5 (20%)	3 (12%)	0.70
<i>Heart rhythm</i>				
Paced	26 (52%)	14 (56%)	12 (48%)	-
Sinus rhythm	23 (46%)	10 (40%)	13 (52%)	-
Atrial fibrillation	1 (2%)	1 (4%)	0 (0%)	-
<i>Sedation</i>				
Propofol	47 (94%)	24 (96%)	23 (92%)	>0.99
Propofol dose (mg/h)	120 [100; 150]	100 [100; 150]	150 [100; 150]	0.30
Opioids	4 (8%)	1 (4%)	3 (12%)	0.61
<i>Biochemistry*</i>				
pH	7.38 [7.34; 7.42]	7.38 [7.34; 7.42]	7.37 [7.33; 7.40]	0.72
PaO <sub>2</sub> (mm Hg)	126 [90; 230]	102 [76; 190]	185 [113; 307]	0.065

PaCO <sub>2</sub> (mm Hg)	42 [40; 46]	43 [39; 46]	42 [40; 47]	0.95
Bicarbonate (mmol/L)	25 [23; 26]	24 [23; 26]	25 [24; 26]	0.40
Lactate (mmol/L)	1.1 [0.8; 1.5]	1.2 [0.9; 1.4]	1.1 [0.8; 1.7]	0.79
Creatinine (μmol/L)	71 [61; 78]	71 [60; 76]	71 [61; 81]	0.84
Haemoglobin (g/L)	104 [93; 115]	109 [92; 117]	104 [94; 107]	0.49
Blood sugar level (mmol/L)	6.8 [6.0; 8.0]	6.6 [6.0; 7.8]	7.1 [6.2; 9.1]	0.091

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

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

EtCO<sub>2</sub>: end-tidal CO<sub>2</sub> partial pressure; FiO<sub>2</sub>: fraction of inspiratory oxygen; PaCO<sub>2</sub>: arterial partial pressure of CO<sub>2</sub>; PaO<sub>2</sub>: 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<sub>2</sub>: peripheral capillary oxygen saturation.

**Supplementary Table 2. Haemodynamic effect of 4% albumin rapid FBT, and combined FBT (absolute value).**

	<b>Time after FB</b>	<b>Rapid FBT group</b> N = 25	<b>Combined FBT group</b> N = 25
<i>Mean arterial pressure (mmHg)</i>	Baseline	73 (13)	71 (13)
	0 min	83 (12)	78 (13)
	15 min	80 (13)	74 (13)
	30 min	81 (13)	75 (13)
<i>Systolic arterial pressure (mmHg)</i>	Baseline	102 (19)	102 (15)
	0 min	116 (18)	112 (15)
	15 min	112 (18)	106 (15)
	30 min	113 (18)	108 (16)
<i>Diastolic arterial pressure (mmHg)</i>	Baseline	59 (12)	56 (11)
	0 min	64 (10)	61 (11)
	15 min	63 (11)	58 (11)
	30 min	64 (12)	58 (11)
<i>Pulse pressure (mmHg)</i>	Baseline	43 (11)	45 (10)
	0 min	51 (11)	51 (12)
	15 min	49 (11)	49 (12)
	30 min	49 (11)	50 (13)
<i>Mean PAP (mmHg)</i>	Baseline	19 (5)	19 (3)
	0 min	23 (4)*	21 (3)*
	15 min	22 (5)	21 (3)
	30 min	22 (4)	22 (3)
<i>Systolic PAP (mmHg)</i>	Baseline	27 (6)	27 (4)
	0 min	32 (6)*	29 (5)*
	15 min	31 (6)	29 (4)
	30 min	30 (5)	30 (4)
<i>Diastolic PAP (mmHg)</i>	Baseline	15 (5)	14 (3)
	0 min	17 (4)	16 (3)
	15 min	17 (5)	15 (3)
	30 min	16 (4)	16 (3)
<i>Central venous pressure (mmHg)</i>	Baseline	9 (5)	8 (4)

	0 min	13 (4)*	10 (3)*
	15 min	11 (5)	10 (3)
	30 min	11 (4)	11 (3)
<i>Heart rate (/min)</i>	Baseline	87 (9)	84 (7)
	0 min	86 (7)	83 (7)
	15 min	87 (9)	84 (6)
	30 min	87 (9)	84 (6)
<i>Cardiac index (L/min/m<sup>2</sup>)</i>	Baseline	2.1 (0.4)	2.0 (0.5)
	0 min	2.4 (0.5)	2.1 (0.6)
	15 min	2.5 (0.3)	2.3 (0.6)
	30 min	2.4 (0.4)	2.3 (0.5)
<i>SVRi (dyn.s.cm<sup>-5</sup>.m<sup>-2</sup>)</i>	Baseline	2528 (696)	2643 (747)
	0 min	2428 (836)	2707 (813)
	15 min	2309 (666)	2392 (760)
	30 min	2436 (719)	2362 (688)
<i>Systemic perfusion pressure (mmHg)</i>	Baseline	64 (12)	63 (12)
	0 min	70 (11)	68 (12)
	15 min	69 (13)	64 (12)
	30 min	70 (13)	64 (11)
<i>Blood temperature (°C)</i>	Baseline	36.3 (0.7)	36.1 (0.8)
	0 min	36.0 (0.7)	35.9 (0.8)
	15 min	36.2 (0.7)	36.0 (0.8)
	30 min	36.4 (0.7)	36.1 (0.8)

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Data as mean (standard deviation).

\*: p<0.05: comparison between the bolus group and the slow infusion 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 4% albumin rapid FBT, and combined (relative change from baseline).**

	Time after FB	Rapid FBT group N = 25	Combined FBT group N = 25
<i>Mean arterial pressure (mmHg)</i>			
	0 min	9 (11)	7 (7)
	15 min	7 (12)	3 (8)
	30 min	7 (12)	4 (9)
<i>Systolic arterial pressure (mmHg)</i>			
	0 min	14 (16)	10 (11)
	15 min	10 (17)	5 (12)
	30 min	11 (17)	7 (13)
<i>Diastolic arterial pressure (mmHg)</i>			
	0 min	6 (8)	4 (6)
	15 min	4 (9)	1 (6)
	30 min	5 (9)	2 (6)
<i>Pulse pressure (mmHg)</i>			
	0 min	8 (9)	6 (6)
	15 min	6 (9)	4 (7)
	30 min	6 (9)	5 (7)
<i>Mean PAP (mmHg)</i>			
	0 min	4 (2)*	2 (1)*
	15 min	3 (3)*	2 (2)*
	30 min	2 (2)	2 (2)
<i>Systolic PAP (mmHg)</i>			
	0 min	5 (2)*	2 (2)*
	15 min	4 (4)*	2 (2)*
	30 min	3 (2)	3 (3)
<i>Diastolic PAP (mmHg)</i>			
	0 min	3 (2)*	1 (1)*
	15 min	2 (3)	1 (1)
	30 min	2 (2)	2 (1)
<i>Central venous pressure (mmHg)</i>			
	0 min	4 (3)*	2 (3)*

	15 min	2 (4)	2 (2)
	30 min	2 (3)	2 (2)
<i>Heart rate (/min)</i>			
	0 min	-1 (2)	-1 (2)
	15 min	0 (2)	-1 (2)
	30 min	0 (3)	0 (3)
<i>Cardiac index (L/min/m<sup>2</sup>)</i>			
	0 min	0.3 (0.4)	0.1 (0.3)
	15 min	0.3 (0.3)	0.3 (0.3)
	30 min	0.3 (0.3)	0.3 (0.3)
<i>SVRi (dyn.s.cm<sup>-5</sup>.m<sup>-2</sup>)</i>			
	0 min	-100 (682)	63 (384)
	15 min	-221 (531)	-251 (350)
	30 min	-92 (506)	-281 (294)
<i>Systemic perfusion pressure (mmHg)</i>			
	0 min	6 (12)	5 (8)
	15 min	4 (13)	1 (8)
	30 min	5 (13)	1 (8)
<i>Blood temperature (°C)</i>			
	0 min	-0.3 (0.1)*	-0.2 (0.1)*
	15 min	0.0 (0.2)	-0.1 (0.1)
	30 min	0.1 (0.3)*	-0.1 (0.2)*

Data as mean (standard deviation).

\*:  $p < 0.05$  between the bolus group and the slow infusion 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 4. Dissipation of the haemodynamic response (MAP and CI)**

	<b>Rapid FBT group</b>	<b>Combined FBT group</b>	<b>P</b>
<i>Early MAP responders</i>	N=11	N=11	
Absence of dissipation at 30 minutes*	9 (82%)	9 (82%)	>0.99
Effect dissipated	2 (18%)	2 (18%)	
Time to dissipation (min)	12 [10; 14]	4 [4; 4]	
<i>Early CI responders</i>	N=13	N=5	
Absence of dissipation at 30 minutes <sup>§</sup>	10 (77%)	4 (80%)	>0.99
Effect dissipated at 15 minutes	1 (8%)	1 (20%)	
Effect dissipated at 30 minutes	2 (15%)	0 (0%)	

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

\*: defined as a MAP within 3 mm Hg of baseline

<sup>§</sup>: defined as a CI within 5% of baseline CI

CI: cardiac index; MAP: mean arterial pressure