Temperature and haemodynamic effects of a 100 mL bolus of 20% albumin at room versus body temperature in cardiac surgery patients

Fumitaka Yanase, Salvatore L Cutuli, Thummaporn Naorungroj, Laurent Bitker, Alessandro Belletti, Anthony Wilson, Glenn M Eastwood and Rinaldo Bellomo

ABSTRACT

Objective: To study the temperature and haemodynamic effects of room versus body temperature 20% albumin fluid bolus therapy (FBT).

Design: Single-centre, prospective, before–after trial.

Setting: A tertiary intensive care unit (ICU) in Australia.

Participants: Sixty ventilated post-cardiac surgery patients.

Intervention: Room versus body temperature 100 mL 20% albumin FBT.

Main outcome measures: We recorded haemodynamic data from FBT start to 30 minutes after FBT. The cardiac index (CI) response was defined by a CI increase > 15%, and the mean arterial pressure (MAP) response was defined by a MAP increase > 10%.

Outcomes: Immediately after FBT, median blood temperature decreased by –0.1°C (interquartile range [IQR], –0.1 to 0.0°C) with room temperature albumin versus 0.0°C (IQR, –0.1 to 0.0°C) with body temperature albumin ($P < 0.001$). The CI or MAP responses were similar. There was, however, a time and study group interaction for blood temperature ($P < 0.001$) for absolute and relative changes. In addition, mean pulmonary arterial pressure (PAP) ($P = 0.002$) increased more with body temperature albumin and remained higher for most of the observation period.

Conclusion: Compared with room temperature albumin FBT, body temperature 20% albumin FBT prevents FBT-associated blood temperature fall and increases mean PAP. However, CI and MAP changes were the similar between the two groups, implying that fluid temperature has limited haemodynamic effects in these patients.

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Hypotension, low cardiac index (CI) or both are common after cardiac surgery[1,2] and fluid bolus therapy (FBT) is the usual initial treatment. The aim of FBT is to achieve optimal intravascular volume, CI and mean arterial pressure (MAP).[3,4] However, to achieve such goals, postoperative cardiac surgery patients may receive almost 2 L of crystalloid-based FBT in the first 24 hours.[3] Unfortunately, such therapy contributes to fluid overload.

The fluid overload associated with crystalloid FBT may contribute to organ dysfunction.[5-7] Therefore, the use of colloid FBT is the preferred treatment,[3,8] but regrettably starch-based colloids increase the incidence of acute kidney injury and the risk of bleeding.[9,10] Gelatin- or dextran-based solutions have similar adverse effects.[11,12] However, hyperoncotic (20%) albumin may be a more rational choice because it delivers one-fifth of the volume administered with iso-oncotic albumin solution.[13-15] An additional concern is that FBT fluid is typically given at room temperature. As post-cardiac surgery patients are often hypothermic on intensive care unit (ICU) admission, and hypothermia may contribute to postoperative coagulopathy, the delivery of "cold" FBT may be unhelpful, making fluid warming more rational.[16,17]

In keeping with the above notions, warming fluids from room to body temperature prevented decreases in body temperature and improved cardiac output in volunteers.[18,19] Thus, body temperature 20% albumin FBT may be a physiologically logical choice after cardiac surgery. However, no investigations have assessed the temperature and haemodynamic changes induced by warm versus cold 20% albumin FBT. Accordingly, we assess whether the temperature and haemodynamic changes induced by 20% body temperature albumin FBT would differ from those seen with room temperature 20% albumin FBT.

Methods

Ethics approval

This study was approved by the institutional Ethics Committee (reference number LNR/16/Austin/358, for the body temperature albumin study; and LNR/16/Austin/548, for the room temperature albumin study). The need for consent was waived by the Ethics Committee because of the observational nature of the study and the fact that 20% albumin is frequently used for FBT in the study ICU.

Study design

We conducted a single-centre, prospective, before–after trial from July 2017 to May 2020 of patients prescribed 20% albumin FBT according to clinician preference. The first group of 30 patients received room temperature 20% albumin FBTs as previously described, and in the second group, 30 patients received body temperature 20% albumin. A pilot study of the room temperature albumin group has been previously reported.[20]

We included adult patients (aged ≥ 18 years) who were admitted to the ICU after on-pump cardiac surgery. They all had to be receiving mechanical ventilation and to have a pulmonary artery catheter in place. All patients had to be prescribed 100 mL 20% albumin FBT for a haemodynamic indication by the treating clinical team.

We excluded patients if any intervention with haemodynamic effect was necessary during the 30-minute observation period (Online Appendix, item 1). We excluded pregnant patients or those who required mechanical haemodynamic support (ie, intra-aortic balloon counterpulsation or extracorporeal membrane oxygenation).

Data collection

We have previously described the detailed data collection method.[21] In all patients, we recorded core temperature, systolic arterial pressure, diastolic arterial pressure, MAP, central venous pressure (CVP), systolic pulmonary artery pressure (PAP), diastolic PAP, mean PAP, heart rate and peripheral oxygen saturation (SpO_2) on a second-by-second basis using MediCollector logging software (MediCollector, Boston, MA, USA).

We measured CI by using the continuous or intermittent method depending on the type of pulmonary artery catheter. When patients did not have a continuous cardiac output pulmonary artery catheter, the research team performed intermittent measurements of CI at four time points: before FBT, immediately after FBT, 15 minutes after FBT, and 30 minutes after FBT.

A research team member observed study patients for the full period and recorded all interventions. When the patient unexpectedly needed other interventions that met the exclusion criteria (Online Appendix, item 1), they were removed from the study. However, when they met minor confounders (Online Appendix, item 2), recording continued and the patient was included for analysis.

Fluid bolus therapy

The intervention was the administration of 100 mL of 20% albumin (Albumex 20, CSL Behring, Melbourne, VIC, Australia). FBT was prescribed based on the clinical team's decision. In the room temperature albumin group, patients received 20% albumin stored at room temperature. In contrast, in the body temperature albumin group, during infusion, albumin was warmed to between 37°C and 40°C by a fluid warmer (enFlow [Vital Signs, Totowa, NJ, USA] or HOTLINE [Smiths Medical ASD, Rockland, MA, USA]). After a possible risk of aluminium release from the enFlow fluid warmer was reported, we used the HOTLINE system in all patients.[22] All fluid boluses were infused rapidly using a hand pump infusion system with a compressible reservoir.

Haemodynamic response definitions

We defined the CI response (CI-R) as a CI increase greater than 15% from the baseline and the MAP response (MAP-R) as a MAP increase greater than 10%. We defined the immediate CI-R or immediate MAP-R if the CI-R or MAP-R occurred immediately after FBTs.

We also pre-defined time to dissipation of the CI effect as the time taken for a patient's CI to fall back to within 5% of baseline. We pre-defined time to dissipation of the MAP effect as the time taken for a patient's MAP to fall back to within 3 mmHg of baseline for at least 2 consecutive minutes.

The primary hypothesis was that the core temperature response would differ between body temperature and room temperature 20% albumin groups. The secondary hypothesis was that the CI and MAP response would also differ between the two groups. The exploratory hypothesis was that other haemodynamic variables might respond differently according to study group.

Sample size calculation

Based on data from our previous research, the standard deviation for temperature change by room temperature 20% albumin FBT was known to be 0.13°C after room temperature 20% albumin infusion.[20] We estimated that, with 30 patients in each group, we would have an 80% power (at a two-sided *P* value of 0.05) to detect a difference in temperature change between the two groups equivalent to 73% of the standard deviation (equivalent to a –0.1°C overall body temperature difference).

Data processing before analysis

We applied the same data processing before analysis.[21] We excluded both negative CVP values and values outside three standard deviations for all variables because there were several noisy data; for example, high CVP values during intermittent CI measurement or line flushing. Baseline haemodynamic parameters were calculated by the mean value from 3 minutes before FBT to the start of FBT. For ease of presentation, we illustrated data by 2

minutes basis by calculating its values as the mean value over 120 seconds. We analysed post-bolus data from 0 to 30 minutes after FBT with second-to-second data acquisition.

Statistical analysis

We analysed data using R software, version 3.5.2 (The R Foundation, Vienna, Austria). We reported continuous variables as median with interquartile range (IQR) and categorical variables as count with percentage. We compared all baseline characteristics using Fisher exact test for categorical variables and the Mann–Whitney U test for continuous variables. We applied the Spearman correlation test to evaluate the relationship between CI changes and MAP changes immediately after FBT. We analysed haemodynamic variables using linear mixed effects models, accounting for within subject repeated measures, and treating time as a continuous variable between the room temperature albumin group and the body temperature albumin group. When a study group effect or an interaction between time and the study group was significant, we performed post hoc analysis to examine the significance of the difference at each time point, accounting for the α inflation risk using the Tukey adjustment method. We considered a two-sided *P* value below 0.05 as statistically significant.

Results

We screened 46 patients in the room temperature albumin group and 34 patients in the body temperature albumin group (Online Appendix, supplementary figure 1) to achieve 30 patients in each group. Table 1 and the Online Appendix, supplementary table 1, show the characteristics of the study patients. Both groups were well balanced except for a small difference in haemoglobin value. In particular, core temperature was equivalent in both groups before the intervention (Table 2). All relevant haemodynamic parameters before FBT are shown in Table 2. Such parameters were also well balanced.

Temperature changes after fluid bolus therapy

There was an interaction between time and study group in mean core temperature ($P < 0.001$ for absolute value) (Figure 1) and relative change ($P < 0.001$) (Figure 2). Blood temperature in the room temperature albumin group fell, but there were no changes in the body temperature albumin FBT group.

Cardiac index changes after fluid bolus therapy

There was no time and study group interaction for the changes in CI both in absolute terms (Figure 1) and as relative changes (Figure 2). Immediately after FBT, the median CI increased in a statistically equivalent way in both groups (Online Appendix, supplementary tables 2 and 3). The number of CI responders at each time point was not statistically significant between the two groups (Table 3). Among immediate CI responders, one patient (10%) in the room temperature albumin group and two (29%) in the body temperature albumin group showed CI effect dissipation during the study period ($P = 0.15$) (Online Appendix, supplementary table 4)

Mean arterial pressure changes after fluid bolus therapy

There was no group effect or significant time and study group interaction for the changes in MAP both in absolute terms ($P = 0.22$ and $P = 0.68$) (Figure 1) and as relative changes ($P = 0.08$ and $P = 0.98$) (Figure 2). The median MAP increased by 9 mmHg (IQR, 6–13 mmHg) immediately after FBT in the room temperature albumin group and by 5 mmHg (IQR, 1–14 mmHg) in the body temperature albumin group (Online Appendix, supplementary tables 2 and 3).

The number of MAP responders at each time point was not statistically significant between the two groups (Table 3). Among immediate MAP responders, nine patients (50%) in the room temperature albumin group and four patients (33%) in the body temperature albumin group showed effect dissipation ($P = 0.47$).

Cardiac index and mean arterial pressure correlation

Immediately after the FBT, there was no correlation between changes in CI and change in MAP in the room temperature group ($P = 0.70$) or the body temperature group ($P = 0.52$) (Online Appendix, supplementary figure 2).

Additional haemodynamic changes

There was an interaction between time and study group in mean PAP ($P = 0.002$ in absolute value and relative change). Moreover, mean PAP in the body temperature albumin group returned to baseline more slowly after the initial response and from 8 to 24 minutes after FBT; mean PAP in the body temperature albumin group was significantly higher than in the room temperature albumin group (Figure 2). There were small mean increases (2 mmHg) in each group and we observed almost the same number of CVP responders in each group (Table 3 and Online Appendix, supplementary table 3).

Individual haemodynamic changes are summarised in the Online Appendix, supplementary figures 3 and 4.

Table 1. Baseline characteristics

	All patients	Room temperature 20% albumin	Body temperature 20% albumin	*P**
Total number of patients	60	30	30	
Age (years); median (IQR)	70 (63–77)	70 (65–78)	72 (59–77)	0.62
Sex (male)	48 (80%)	23 (77%)	25 (83%)	0.75
Body mass index (kg/m^2), median (IQR)	27.8 (25.1–30.5)	28.1 (25.1–30.7)	27.7 (25.2–30.1)	0.76
Comorbidities				
Atrial fibrillation	7 (12%)	5 (17%)	2 (7%)	0.24
COPD	1 (2%)	1 (3%)	0 (0%)	0.48
Chronic kidney disease	7 (12%)	3 (10%)	4 (13%)	> 0.99
Diabetes mellitus	17 (28%)	9 (30%)	8 (27%)	> 0.99
Hypertension	42 (70%)	20 (67%)	22 (73%)	> 0.99
Ischaemic heart disease	44 (73%)	20 (67%)	24 (80%)	0.75
APACHE III score, median (IQR)	42 (35–48)	41 (34–45)	45 (37–50)	0.17
EuroSCORE, median (IQR)	5 (4–7)	5 (4–7)	5 (2–7)	0.37
Type of surgery				0.23
On-pump CABG	33 (55%)	13 (43%)	20 (67%)	
Valve	17 (28%)	11 (37%)	6 (20%)	
CABG + valve	7 (12%)	5 (17%)	2 (7%)	
Other	3 (5%)	1 (3%)	2 (7%)	
Urgency of surgery				0.14
Elective	44 (73%)	19 (63%)	25 (83%)	
Non-elective	16 (27%)	11 (37%)	5 (17%)	
CPB duration (min), median (IQR)	114 (91–146)	118 (86–144)	112 (92–148)	0.92
Aorta clamp duration (min), median (IQR)	88 (71–122)	88 (70–120)	88 (74–122)	0.80
Post-CPB TOE assessment				
Left ventricular dysfunction	11 (18%)	8 (30%)	3 (11%)	0.10
Right ventricular dysfunction	5 (8%)	2 (7%)	3 (11%)	> 0.99

APACHE = Acute Physiology and Chronic Health Evaluation; CABG = coronary aortic bypass graft; COPD = chronic obstructive pulmonary disease; CPB = cardiopulmonary bypass; EuroSCORE = European System for Cardiac Operative Risk Evaluation; IQR = interquartile range; TOE = transoesophageal echocardiography. * *P* values reflect the between-groups comparison.

Discussion

Key findings

In a cohort of postoperative cardiac surgery patients, we compared the temperature effect of room temperature versus body temperature 20% albumin 100 mL FBT as well as their differential haemodynamic effects. We observed a significantly different core temperature response both in absolute terms and in relative terms, such that FBT with body temperature 20% albumin prevented the decrease in temperature induced by room temperature 20% albumin. We observed, however, that there was no time and group interaction for changes in CI or MAP and in the number of CI responders or MAP responders. In contrast, there was an interaction for the mean PAP, with a higher mean PAP in the body temperature albumin group.

Relationship with previous studies

To our knowledge, this is the first study to report the differential temperature effects of hyperoncotic albumin FBT in any group of patients or patients after cardiac surgery. Our findings that a decrease in temperature could be prevented are aligned with those of two previous studies in volunteers.[18,19]

Table 2. Baseline haemodynamics

	All patients	Room temperature 20% albumin	Body temperature 20% albumin	*P**
Total number of patients	60	30	30	
Blood temperature (°C)	36.1 (35.6–37.0)	36.2 (35.4–37.0)	36.1 (35.9–36.9)	0.77
Systolic arterial pressure (mmHg)	100 (89–110)	98 (89–111)	101 (89–108)	0.95
Diastolic arterial pressure (mmHg)	53 (48–61)	52 (48–58)	55 (49–61)	0.45
Pulse pressure (mmHg)	47 (36–53)	47 (36–54)	46 (37–51)	0.50
Mean PAP (mmHg)	19 (17–23)	19 (16–23)	19 (17–23)	0.87
Systolic PAP (mmHg)	28 (23–32)	26 (22–31)	28 (25–32)	0.53
Diastolic PAP (mmHg)	14 (12–17)	14 (11–18)	14 (12–17)	0.95
Central venous pressure (mmHg)	8 (6–10)	8 (6–10)	8 (6–10)	0.77
Heart rate (beats/min)	88 (80–90)	88 (80–90)	86 (79–88)	0.36
Cardiac index (L/min/m^2)	2.1 (1.7–2.6)	2.2 (1.8–2.8)	2.0 (1.7–2.5)	0.30
Stroke volume index (mL/m^2)	26 (20–32)	27 (20–33)	26 (21–30)	0.71
SVRi (dyn*s/cm^5*m^2)	2198 (1783–2951)	2099 (1737–2702)	2507 (1818–3020)	0.30
Systemic perfusion pressure (mmHg)	61 (55–68)	60 (56–65)	63 (55–69)	0.60

CI = cardiac index; PAP = pulmonary arterial pressure; SVRi = Systemic Vascular Resistance Index. Data are presented as median (interquartile range). * *P* values reflect the between-groups comparison.

Hyperoncotic albumin solution has some theoretical advantages in patients after cardiac surgery because of a less positive fluid balance and fewer subsequent episodes of FBT.[15] In addition, most 20% albumin preparations are essentially chloride-free, while iso-oncotic albumin preparations may contain up to 128 mmol/L of chloride and all crystalloids contain more than 100 mmol/L. Thus, 20% albumin may attenuate chloride-induced changes in glomerular filtration rate.[14] A controlled trial showed that the supplementary administration of 20% albumin in patients undergoing off-pump coronary aortic bypass graft with a baseline albumin level below 4.0 g/dL reduced the risk of postoperative acute kidney injury,[23] but our short term study could not address these issues.

In this study, there was no difference in CI response. In contrast, warm crystalloid infusion increased CI more than cold crystalloid infusion in healthy volunteers.[18] However, warm FBT increased the heart rate in volunteers which contributed to the increased CI. In contrast, most of our patients were in a paced rhythm and unable to increase their heart rate.

Study implications

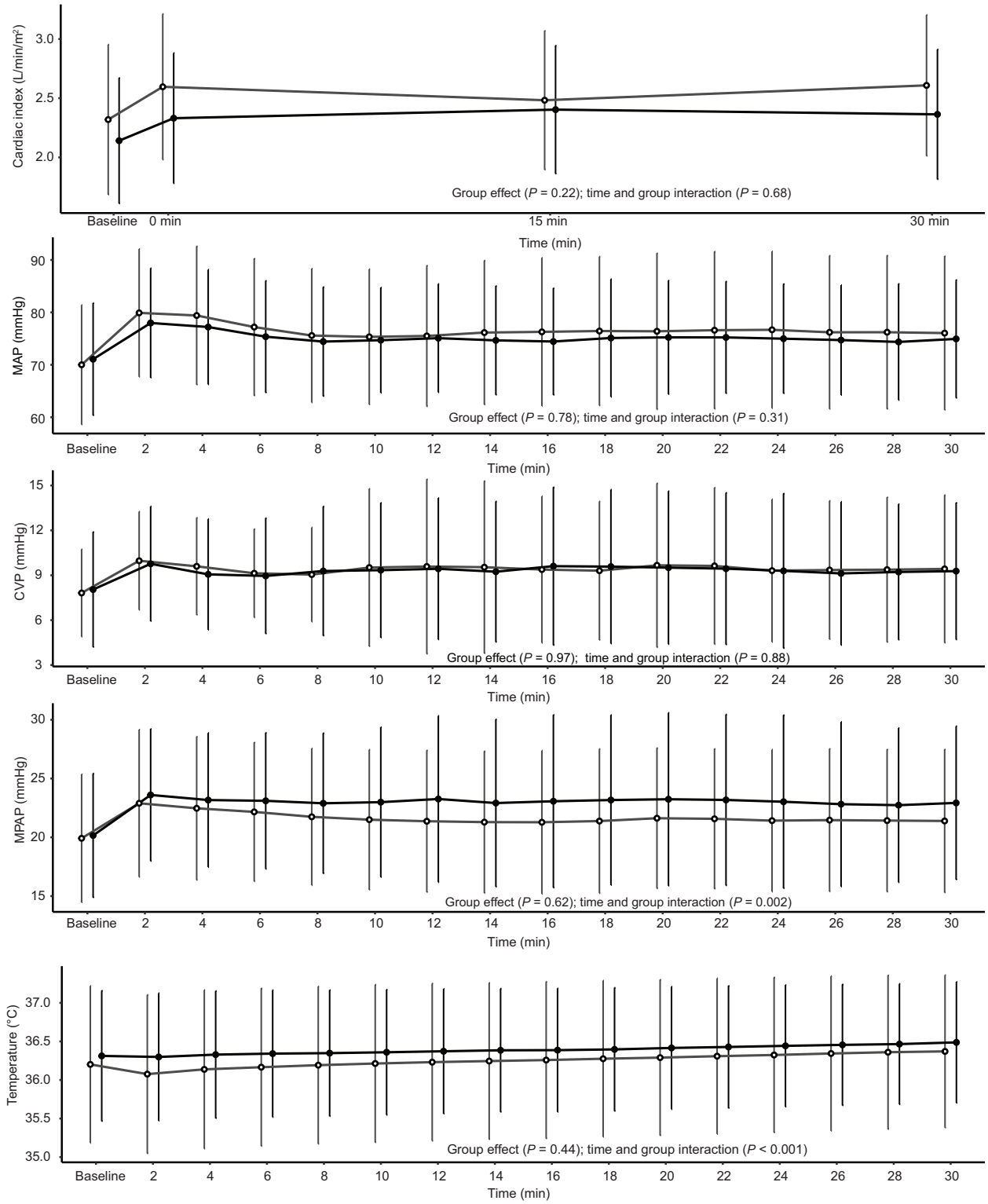
Our findings imply that, in post-cardiac surgery patients, a 100 mL bolus of body temperature 20% albumin prevents the fall in core temperature seen after room temperature FBT. However, they also imply that, when given according to clinical indications, body temperature 20% albumin FBT achieves similar CI effects to room temperature 20% albumin FBT.

Strengths and limitations

To the best of our knowledge, our study is the first to describe the comparison of temperature and haemodynamic changes induced by room temperature or body temperature 20% albumin FBT in patients after cardiac surgery in the absence of major confounders. We recorded such detailed haemodynamic data for all variables except the CI, where measurements every 15 minutes were applied. Finally, at least one researcher observed the patient for the whole study period to exclude haemodynamic confounders.

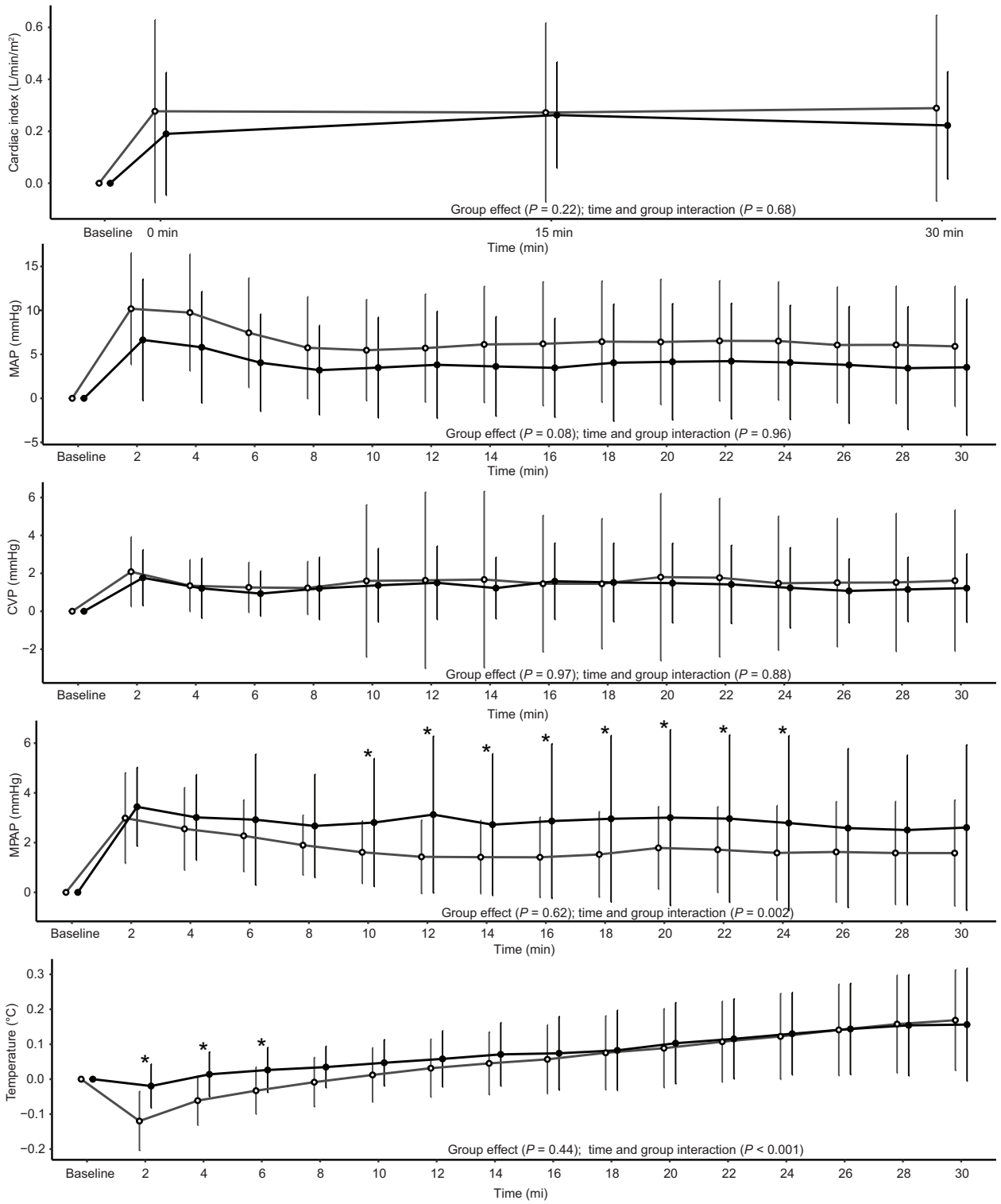
There are several limitations to our study. This was a single-centre study but the physiological effects are unlikely to be centre-dependent. Moreover, it assessed responses in a limited number of patients, which might have affected our ability to detect additional differential effects. However, obtaining second-by-second detailed haemodynamic data in the absence of confounders is difficult. In particular, it requires physical researcher presence at the bedside, which is time-consuming but necessary, as demonstrated by the fact that 20 patients had to be excluded because of major confounders during the study period. We did not record haemodynamic changes beyond 30 minutes. However, changes in sedative drug, vasopressor or inotropic infusion

Figure 1. Haemodynamic response (absolute values) to a room temperature 20% albumin fluid bolus (white) versus a body temperature 20% albumin fluid bolus (black)



MPAP = mean pulmonary arterial pressure. Data are shown as mean with standard error. * Significant difference ($P < 0.05$) between the two groups.

Figure 2. Haemodynamic response (absolute change from baseline) to a room temperature 20% albumin fluid bolus (white) versus a body temperature 20% albumin fluid bolus (black)



MPAP = mean pulmonary arterial pressure. Data are shown as mean with standard error. * Significant difference ($P < 0.05$) between the two groups.

Table 3. Fluid bolus characteristics and hemodynamic response

	All patients	Room temperature 20% albumin	Body temperature 20% albumin	*P**
Total number of patients	60	30	30	
Time from ICU admission to FBT (hour), median (IQR)	1.4 (0.9–2.5)	1.1 (0.9–2.7)	1.6 (0.9–2.4)	0.74
Fluid bolus indication				0.35
Tachycardia	1 (2%)	1 (3%)	0 (0%)	
Low cardiac output	15 (25%)	9 (30%)	6 (20%)	
Low filling pressures	6 (10%)	3 (10%)	3 (10%)	
Hypotension	36 (60%)	15 (50%)	21 (70%)	
Other	2 (3%)	2 (7%)	0 (0%)	
Duration of fluid bolus infusion (min), median (IQR)	3.2 (2.5–4.9)	3.4 (2.5–7.6)	3.0 (2.5–4.0)	0.20
CI response				
At end of bolus administration	17 (28%)	10 (33%)	7 (23%)	0.57
At 15 min of bolus administration	18 (38%)†	7 (39%)†	11 (37%)	> 0.99
At 30 min of bolus administration	25 (42%)	15 (50%)	10 (33%)	0.30
MAP response				
At end of bolus administration	30 (50%)	18 (60%)	12 (40%)	0.20
At 15 min of bolus administration	19 (32%)	13 (43%)	6 (20%)	0.10
At 30 min of bolus administration	20 (33%)	14 (47%)	6 (20%)	0.054
CVP response‡	20 (33%)	9 (30%)	11 (37%)	0.79
Confounding event§				
Minor event	5 (8%)	1 (3%)	4 (13%)	0.35

CI = cardiac index; CVP = central venous pressure; FBT = fluid bolus therapy; ICU = intensive care unit; MAP = mean arterial pressure. * *P* values reflect the between-groups comparison. † Twelve patients in the room temperature albumin group did not have the CI at 15 minutes after FBT. ‡ Defined as +2 mmHg increase in CVP from baseline value, at the end of the bolus. § Refer to the Online Appendix, item 2, for definitions.

are very common in these patients and would have resulted in more than 50% of study patients having to be excluded. In fact, we are not aware of any study in post-cardiac surgery patients that has assessed the haemodynamic response to fluid therapy both beyond 30 minutes and in the absence of such confounders. Of relevance, 40% of patients in the room temperature group used an external warming device during the observation period and this might have attenuated the decrease in body temperature. Nevertheless, passive warming after cardiac surgery is common and we wished to study the impact of fluid temperature in a usual care setting. In addition, a small number of patients woke up during the observation period (minor confounder), which might have affected the results. However, relatively light sedation in the ICU is common, making small episodes of awakening also relatively common.[24]

Conclusion

Body temperature 20% albumin FBT prevented the decrease in core temperature induced by room temperature 20% albumin FBT. Moreover, body temperature 20% albumin was associated with a similar CI effect as room temperature 20% albumin, and the effect of body temperature 20% albumin on mean PAP was significantly greater. These findings can inform the choice of both FBT solution and temperature in the care of post-cardiac surgery patients.

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Competing interests

None declared.

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