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

Fumitaka Yanase, Thummaporn Naorungroj, Salvatore L Cutuli, Glenn M Eastwood and Rinaldo Bellomo

ABSTRACT

Objective: To evaluate the haemodynamic effects of rapid fluid bolus therapy (FBT) (500 mL of 4% albumin over several minutes) versus combined FBT (rapid 200 mL FBT followed by a 300 mL infusion over 30 minutes).
Design: Single centre, prospective, before-and-after trial.
Setting: A tertiary intensive care unit in Australia.
Participants: Fifty mechanically ventilated post-cardiac surgery patients.
Interventions: Rapid 4% albumin FBT versus combined FBT.
Main outcome measures: We recorded haemodynamic parameters from before FBT to 30 minutes after FBT. A mean arterial pressure (MAP) response was defined by a MAP increase > 10%, and a cardiac index (CI) response was defined by a CI increase > 15%.
Results: Immediately after rapid FBT versus combined FBT, there was a CI response in 13 patients (52%) compared with five patients (20%) respectively ($P = 0.038$), and a MAP response in 11 patients (44%) in each group. However, from FBT administration to 30 minutes, there was a time and group interaction such that MAP was higher in the rapid FBT group ($P = 0.003$), as was the case for central venous pressure ($P = 0.002$) and mean pulmonary artery pressure ($P < 0.001$). Body temperature fell immediately and was lower with rapid FBT but became warmer than with combined FBT later ($P < 0.001$). At 30 minutes, a MAP response was seen in ten patients (40%) compared with nine patients (36%) ($P < 0.99$) and a CI response was present in eight patients (32%) compared with 11 patients (44%) ($P = 0.56$) in the rapid versus combined FBT groups respectively.
Conclusion: Rapid FBT was superior to combined FBT in terms of mean MAP levels and immediate CI response. However, the number of MAP responders or CI responders was similar at 30 minutes.

Crit Care Resusc 2021; 23 (3): 320-28

A low mean arterial pressure (MAP) or cardiac index (CI) is common after cardiac surgery[1,2] and typically triggers treatment with fluid bolus therapy (FBT).[3,4] However, insufficient FBT may fail to correct such instability, while excessive FBT may contribute to pulmonary congestion. Therefore, defining the optimal approach to FBT after cardiac surgery is clinically relevant.[5,6]

During haemodynamic instability, FBT is often administered rapidly. However, it may be better to administer the same amount of fluid as a smaller very rapid (3–4 minutes) bolus followed by a continuous infusion of the remaining fluid. This is because rapid FBT increases plasma atrial natriuretic peptide levels, an effect associated with glycocalyx injury, greater fluid extravasation, and intestinal oedema.[7] In contrast, a slow infusion leads to long-lasting plasma volume expanding effects.[8,9]

Slower 4% albumin infusion could achieve more sustained haemodynamic changes after cardiac surgery, but it may fail to correct hypotension or low cardiac output rapidly enough. Logically, a small but very rapid fluid bolus followed by continuous infusion may combine the advantage of a rapid response with those associated with a sustained effect. Despite these physiological considerations and the findings of an international survey that about 30% of intensive care unit (ICU) clinicians define FBT as fluid given in less than 10 minutes while 50% define it as given over 30 minutes,[10] no investigation has compared these two approaches to FBT in post-cardiac surgery patients.

Accordingly, we conducted a prospective before-and-after study of the haemodynamic effect of a rapid complete bolus of 4% albumin compared with a rapid small bolus of 4% albumin followed by a slower continuous infusion over 30 minutes (combined FBT) in post-cardiac surgery patients. We hypothesised that the combined FBT approach would achieve greater MAP effects than rapid FBT during a 30-minute post-FBT observation period.

Methods

We prospectively obtained institutional ethics approval for this study (Reference No. LNR/16/Austin/358). Individual consent was waived, as giving FBT within 30 minutes is common practice in Australia and New Zealand and in our ICU.[10]

Study design

Within an overarching quality improvement program evaluating FBT after cardiac surgery, this single-centre prospective before-and-after study was conducted in a university-affiliated tertiary teaching hospital in Melbourne, Australia, between July 2017 and January 2020.

As with a previous study,[11] we included mechanically ventilated adult patients (aged 18 years or older) admitted to the ICU after on-pump cardiac surgery. All patients had a pulmonary artery catheter in situ and, at the discretion of their treating doctors, were prescribed 500 mL 4% albumin for haemodynamic instability (Albumex 4%, CSL Behring, Melbourne, Australia) within the first 12 hours of ICU admission.

We excluded pregnant women and patients receiving intra-aortic balloon counterpulsation or extracorporeal membrane oxygenation. Patients were also excluded if any major confounding interventions, which could affect haemodynamic parameters, became necessary during the study period (Online Appendix, supplementary appendix 1).

Fluid bolus therapy

The clinicians prescribed 4% albumin FBT based on their clinical judgements. As a part of their FBT quality improvement program, they introduced small bolus FBT followed by continuous infusion (combined FBT). The albumin was stored and given at room temperature. We allocated the first 25 patients to the rapid FBT group and the second 25 patients to the combined FBT group. In the rapid FBT group, 500 mL of albumin was infused rapidly (within 15 minutes) through a central line using a hand pump as previously reported.[11] In the combined FBT group, a small 4% albumin bolus (200 mL) was given rapidly (within 10 minutes) through a central line, and a continuous infusion (300 mL albumin) was given over 30 minutes (Online Appendix, supplementary figure 1).

Data collection

We collected haemodynamic data, including systolic arterial pressure, diastolic arterial pressure, MAP, central venous pressure (CVP), systolic pulmonary arterial pressure (PAP), diastolic PAP, mean PAP, heart rate, CI and peripheral oxygen saturation (SpO_2) on a second-by-second basis using the MediCollector logging software (MediCollector, Boston, MA, USA). We measured CI continuously or intermittently according to the pulmonary artery catheter using the thermodilution technique.

In the rapid FBT group, CI was measured at four time points: before FBT, immediately (0 minutes) after FBT, 15 minutes after FBT, and 30 minutes after FBT. In the combined FBT group, CI was measured immediately after the small fluid bolus, 15 minutes after small fluid bolus, and 30 minutes after the 200 mL FBT. We recorded baseline haemodynamic parameters for a minimum of 3 minutes before the 500 mL FBT or the 200 mL FBT. Ventilator setting and all drug infusions (catecholamine and sedative drugs) at the time of inclusion were recorded and remained unchanged during the study period.

Finally, patients admitted to the ICU only during business hours were recruited because at least one trained researcher was needed to observe study patients and record all interventions, including minor confounders during the study periods. When patients needed unexpected interventions that met the exclusion criteria (Online Appendix, supplementary appendix 1), we stopped data collection and excluded such patients. However, when there were minor confounders (Online Appendix, supplementary appendix 2), we continued the recording and the data were included for analysis.

Haemodynamic response definitions

We defined MAP response (MAP-R) as a MAP increase greater than 10% above the baseline and an immediate MAP-R as an increase immediately after the administration of the 500 mL FBT or the 200 mL FBT. Similarly, we defined a CI response (CI-R) as a CI increase greater than 15% at the same time points. We defined FBT effect dissipation as the time when a patient's MAP was within 3 mmHg of baseline for at least 2 consecutive minutes (MAP dissipation) or a patient's CI was within 5% of baseline (CI dissipation).

Data processing

Negative value of CVP and values outside three standard deviations (SDs) in all variables were excluded as data noise (eg, high CVP when flushing normal saline to measure CI). Baseline haemodynamic parameters were calculated as the mean value from 3 minutes before the 500 mL FBT or the 200 mL FBT. Except for CI, which was measured intermittently, we calculated the mean value over 120 seconds from 0 minutes after the 500 mL FBT or the 200 mL FBT to 30 minutes after the 500 mL FBT or the 200 mL FBT to present every 2-minute data.

Power calculation

The SDs of MAP were estimated at 10 mmHg.[11] We estimated that 25 patients in each group would have an 80% power (two-sided $P = 0.05$) to detect differences between the two groups equivalent to 80% of the SD (equivalent to 8.0 mmHg overall MAP difference), which would be clinically important.

Statistical analysis

We performed our analyses using the R software, version 3.5.2 (The R Foundation for Statistical Computing, Vienna, Austria). We considered two-sided $P < 0.05$ as significant.

We reported categorical data as count (percentage) and continuous data as mean (SD) for haemodynamic variables and median (interquartile range [IQR]) for other variables. We compared all baseline characteristics between the two groups, using Fisher's exact test for categorical variables, Student *t* test for haemodynamic variables, and Mann–Whitney U test for other non-parametric continuous variables. We compared haemodynamic variables collected over the observation period (either absolute values or relative changes from baseline) between the two groups using linear mixed effects modelling, accounting for within-subject repeated measures and treating time as a continuous variable. 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 alpha inflation risk using the Tukey adjustment method. We applied Spearman's correlation to evaluate the relationship between CI change and MAP change immediately after FBT and 30 minutes after FBT.

Results

Patients' characteristics

Of 63 eligible patients, 33 received a 4% albumin rapid FBT and 30 received combined FBT. Of these, 25 patients in each

Table 1. Baseline characteristics of study patients

	All patients	Rapid FBT group	Combined FBT group	*P**
Total number of patients	50	25	25	
Age (years), median (IQR)	68 (62–74)	66 (62–70)	70 (62–75)	0.31
Sex, male	41 (82%)	20 (80%)	21 (84%)	> 0.99
BMI (kg/m²), median (IQR)	27.4 (25.9–30.8)	27.4 (25.9–31.9)	28.1 (25.9–30.1)	0.76
Comorbidities				
Atrial fibrillation	7 (14%)	3 (12%)	4 (16%)	> 0.99
COPD	4 (8%)	2 (8%)	2 (8%)	> 0.99
Chronic kidney disease	3 (6%)	2 (8%)	1 (4%)	> 0.99
Diabetes mellitus	16 (32%)	7 (28%)	9 (36%)	0.76
Hypertension	31 (62%)	16 (64%)	15 (60%)	> 0.99
Ischaemic heart disease	35 (70%)	21 (84%)	17 (68%)	0.16
EuroSCORE, median (IQR)	5 (3–6)	3 (2–6)	5 (4–6)	0.19
Type of surgery				0.20
On-pump CABG	29 (58%)	18 (72%)	11 (44%)	-
Valve	11 (22%)	4 (16%)	7 (28%)	-
CABG + valve	9 (18%)	3 (12%)	6 (24%)	-
Other	1 (2%)	0	1 (4%)	-
CPB duration (min), median (IQR)	118 (100–157)	113 (104–149)	120 (95–160)	0.93
Aorta clamp duration (min), median (IQR)	93 (74–118)	93 (84–118)	93 (70–116)	0.69
Post-CPB TOE assessment				
Left ventricular dysfunction	7 (14%)	5 (20%)	2 (8%)	0.23
Right ventricular dysfunction	1 (2%)	1 (4%)	0	> 0.99

BMI = body mass index; CABG = coronary aortic bypass graft; COPD = chronic obstructive pulmonary disease; CPB = cardiopulmonary bypass; EuroSCORE = European System for Cardiac Operative Risk Evaluation; FBT = fluid bolus therapy; IQR = interquartile range; TOE = transoesophageal echocardiography. * P values reflect the between-groups comparison.

Table 2. Baseline haemodynamics

	All patients	Rapid FBT group	Combined FBT group	*P**
Total number of patients	50	25	25	
Arterial pressure (mmHg), mean (SD)	72 (13)	73 (13)	71 (13)	0.54
Systolic arterial pressure (mmHg), mean (SD)	102 (17)	102 (19)	102 (15)	0.94
Diastolic arterial pressure, (mmHg), mean (SD)	58 (11)	59 (12)	56 (11)	0.52
Pulse pressure (mmHg), mean (SD)	44 (11)	43 (11)	45 (10)	0.63
PAP (mmHg), mean (SD)	19 (4)	19 (5)	19 (3)	0.88
Systolic PAP (mmHg), mean (SD)	27 (5)	27 (6)	27 (4)	0.85
Diastolic PAP (mmHg), mean (SD)	14 (4)	15 (5)	14 (3)	0.87
Central venous pressure (mmHg), mean (SD)	9 (4)	9 (5)	8 (4)	0.53
Heart rate (beats/min), mean (SD)	86 (8)	87 (9)	84 (7)	0.19
Cardiac index (L/min/m²), mean (SD)	2.1 (0.4)	2.1 (0.4)	2.0 (0.5)	0.31
Stroke volume index (mL/m²), mean (SD)	24 (5)	24 (4)	24 (6)	0.79
SVRi (dyn*s/cm^5*m^2), mean (SD)	2586 (717)	2528 (696)	2643 (746)	0.58
Systemic perfusion pressure (mmHg), mean (SD)	64 (12)	64 (12)	63 (12)	0.63
Blood temperature (°C), mean (SD)	36.2 (0.8)	36.3 (0.7)	36.2 (0.8)	0.55

CI = cardiac index; FBT = fluid bolus therapy; PAP = pulmonary arterial pressure; SD = standard deviation; SVRi = systemic vascular resistance index. * P values reflect the between-groups comparison.

group did not have major confounders and were included in the analysis (Online Appendix, supplementary figure 2).

The patients' characteristics are described in Table 1 and in the Online Appendix, supplementary table 1. The median European System for Cardiac Operative Risk Evaluation (EuroSCORE) was similar. Norepinephrine infusion was present in four patients in each group. Finally, half of the patients were in a paced rhythm. There was no difference in baseline haemodynamic parameters (Table 2).

Fluid bolus therapy description

The FBTs were infused over a median time of 6.2 minutes (IQR, 4.4–10.8 minutes) in the rapid FBT group compared with 1.9 minutes (IQR, 1.7–2.3 minutes) in the combined FBT group ($P < 0.001$) (Table 3).

Mean arterial pressure changes

We observed a significant interaction between time and study group. The rapid FBT group achieved a higher immediate MAP increase, which was sustained at higher levels for the full 30 minutes compared with combined FBT ($P = 0.003$ for absolute value and $P = 0.003$ for relative change from baseline) (Figure 1 and Figure 2).

Moreover, mean MAP increased by 9 mmHg (SD, 11 mmHg) immediately after FBT and by 7 mmHg (SD, 12 mmHg) at 30 minutes in the rapid FBT group. It also increased by 7 mmHg (SD, 7 mmHg) immediately after FBT and by 4 mmHg (SD, 9 mmHg) at 30 minutes in the combined FBT group (Online Appendix, supplementary tables 2 and 3).

Eleven patients (44%) in both groups experienced an immediate MAP-R (Table 3), with a similar proportion in the two groups, which remained statistically equivalent at 15 and 30 minutes.

Cardiac index changes

The study group effect or the interaction between time and study group was not significant in both absolute value and relative change from baseline (Figure 1 and Figure 2). Immediately after intervention, mean CI increased by 0.3 L/min/m^2 (SD, 0.4 L/min/m^2) in the rapid FBT group compared with 0.1 L/min/m^2 (SD, 0.3 L/min/m^2) in the combined FBT group. At 30 minutes, the mean CI was 0.3 L/min/m^2 (SD, 0.3 L/min/m^2), greater than the baseline in the rapid FBT group compared with 0.3 L/min/m^2 (SD, 0.3 L/min/m^2) in the combined FBT group (Online Appendix, supplementary tables 2 and 3).

Overall, 13 patients (52%) had an immediate CI-R in the rapid FBT group compared with five patients (20%) in the combined FBT group ($P = 0.038$) (Table 3). Among immediate CI-responders, three patients (23%) experienced CI effect dissipation in the rapid FBT group compared with one patient (20%) in the combined FBT group (Online Appendix, supplementary table 4). After 30 minutes, eight patients

Table 3. Fluid bolus characteristics and haemodynamic response

	All patients	Rapid FBT group	Combined FBT group	P*
Total number of patients	50	25	25	
Time from ICU admission to FBT (h), median (IQR)	1.3 (0.8–2.5)	1.5 (0.8–2.2)	1.3 (0.8–3.1)	0.79
Fluid bolus indication				0.69
Low cardiac output	15 (30%)	7 (28%)	8 (32%)	-
Low filling pressures	4 (8%)	3 (12%)	1 (4%)	-
Hypotension	31 (62%)	15 (60%)	16 (64%)	-
Duration of fluid bolus infusion (min), median (IQR)	4.0 (1.9–6.2)	6.2 (4.4–10.8)	1.9 (1.7–2.3)	< 0.001
Fluid bolus speed (mL/min), median (IQR)	105 (62–118)	81 (46–114)	107 (88–120)	0.054
MAP response†				
At end of bolus administration	22 (44%)	11 (44%)	11 (44%)	> 0.99
At 15 min of bolus administration	17 (34%)	10 (40%)	7 (28%)	0.55
At 30 min of bolus administration	19 (38%)	10 (40%)	9 (36%)	> 0.99
CI response‡				
At end of bolus administration	18 (36%)	13 (52%)	5 (20%)	0.038
At 15 min of bolus administration	21 (42%)	10 (40%)	11 (44%)	>0.99
At 30 min of bolus administration	19 (38%)	8 (32%)	11 (44%)	0.56
CVP increase§	29 (58%)	22 (88%)	7 (28%)	< 0.001
Perfusion pressure response¶	23 (46%)	11 (44%)	12 (48%)	> 0.99
Occurrence of a confounding event**				
Minor event	5 (10%)	4 (16%)	1 (4%)	0.35

CI = cardiac index; CVP = central venous pressure; FBT = fluid bolus therapy; ICU = intensive care unit; IQR = interquartile range; MAP = mean arterial pressure. * P values reflect the between-groups comparison. † Defined as an increase > 10% of baseline value. ‡ Defined as an increase > 15% of baseline value. § Defined as +2 mmHg increase in CVP from baseline value, at the end of the bolus. ¶ Defined as 5% mmHg increase in perfusion pressure from baseline value, at the end of the bolus. ** The definitions are provided in the Online Appendix, supplementary appendix 2.

(32%) had achieved a CI-R in the rapid FBT group compared with 11 patients (44%) in the combined FBT group ($P = 0.56$).

Other haemodynamic effects

There were time and study group interactions for absolute changes and relative changes in CVP ($P = 0.002$) and mean PAP ($P < 0.001$) (Figure 1 and Figure 2). Therefore, mean CVP and mean PAP increased by 4 mmHg (SD, 3 mmHg) and 4 mmHg (SD, 2 mmHg) immediately after rapid FBT and by 2 mmHg (SD, 3 mmHg) and 2 mmHg (SD, 1 mmHg) immediately after combined FBT ($P = 0.023$ and $P < 0.001$ respectively) (Online Appendix, supplementary tables 2 and 3).

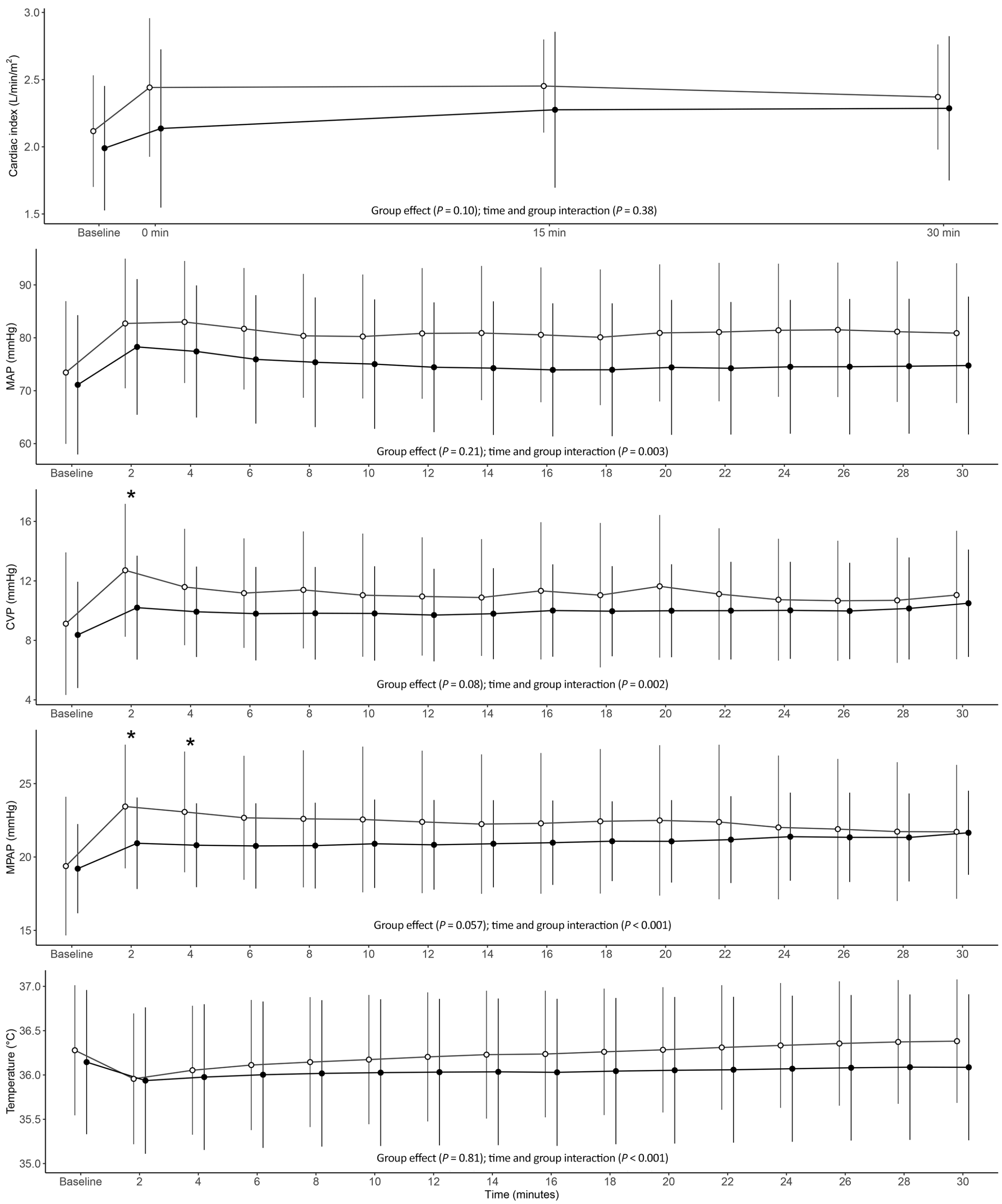
There was also time and study group interaction for both absolute changes and relative changes in blood temperature ($P < 0.001$) (Figure 1 and Figure 2). The mean blood temperature dropped significantly more in the rapid FBT group immediately after FBT (mean, –0.3°C [SD, 0.1°C] *v* –0.2°C [SD, 0.1°C]; $P = 0.007$). However, it rebounded rapidly and was significantly higher in the rapid FBT group 30 minutes after FBT (mean, 0.1°C [SD, 0.3°C] *v* –0.1°C [SD, 0.2°C]; $P < 0.001$) (Figure 1 and Figure 2). The individual haemodynamic and physiological changes are presented in the Online Appendix, supplementary figures 5 and 6.

Relationship between mean arterial pressure change and cardiac index and oxygenation changes

There was no significant correlation between percentage immediate MAP change and percentage immediate CI change from baseline when analysing both groups together ($P = 0.56$) (Online Appendix, supplementary figure 3). In contrast, there was a correlation between percentage MAP and percentage CI change at 30 minutes ($P = 0.001$; $\rho = 0.47$) (Online Appendix, supplementary figure 4), which was stronger after combined FBT ($\rho = 0.56$) than the rapid group ($\rho = 0.38$).

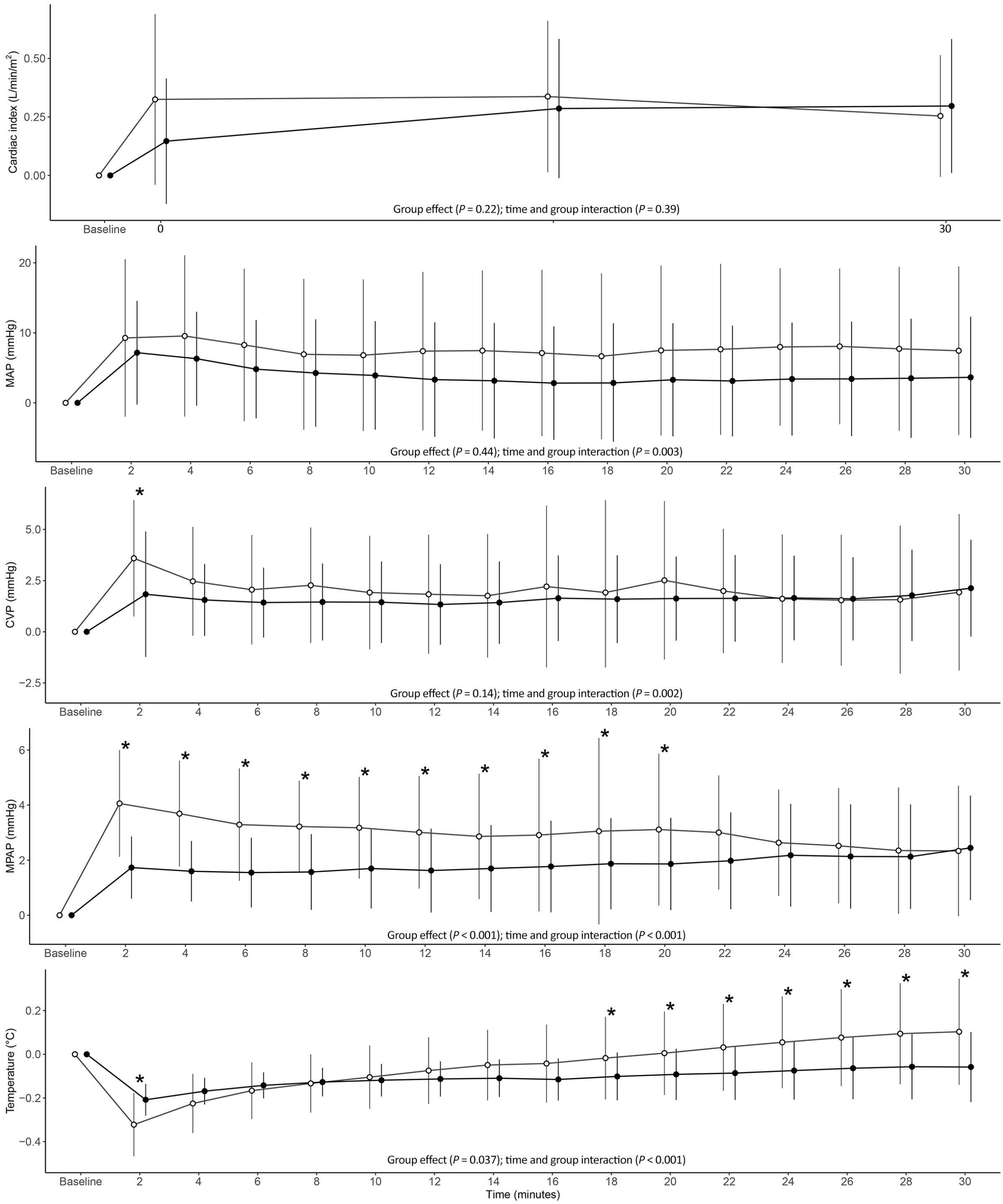
The arterial partial pressure of oxygen to traction of inspired oxygen (PaO_2:FiO_2) ratio after each treatment were not different (median, 312 mmHg [IQR, 273–370 mmHg] in the rapid FBT group *v* 333 mmHg [IQR, 290–390 mmHg] in the combined FBT group; $P = 0.37$).

Figure 1. Comparison of the haemodynamic response (absolute value) to a 500 mL 4% albumin rapid fluid bolus therapy (FBT; white) and to a combined FBT (black)



Data are shown as mean with standard deviation. The asterisk represents a significant difference ($P < 0.05$) at this time point between the two groups adjusted for repeated measurements in a given individual.

Figure 2. Comparison of the haemodynamic response (as absolute change from baseline) to a 500 mL 4% albumin rapid fluid bolus therapy (FBT; white) and to a combined FBT (black)



Data are shown as mean with standard deviation. The asterisk represents a significant difference ($P < 0.05$) at this time point between the two groups adjusted for repeated measurements in a given individual.

Discussion

Key findings

We compared the effect of the rapid FBT with that of the combined FBT in post-cardiac surgery patients. We found a greater number of immediate CI responders in the rapid FBT group but an equal number of immediate MAP responders. However, there were clear time and study group interactions for MAP, CVP, mean PAP, and blood temperature, such that the rapid FBT group showed a greater initial response followed by a slow decline for MAP, CVP and mean PAP for most of the observation period, while temperature immediately fell and then recovered to a higher value. Nevertheless, at the end of the 30 minutes, the number of MAP and CI responders was the same between the two groups. Finally, there was a correlation between MAP changes and CI changes at 30 minutes which was stronger after combined FBT.

Relationship to previous studies

To our knowledge, this is the first study to compare the haemodynamic changes induced by rapid FBT with those by combined FBT. Previous studies have only reported the haemodynamic changes induced by rapid FBT alone and did not report the effect of combined FBT.[12]

In animal models, slower fluid infusion appears to produce less atrial natriuretic peptide release, less glycocalyx injury, and a more sustained intravascular volume effect.[8,9] Few studies, however, have reported the effect of different fluid infusion rates in humans. In patients after abdominal surgery, one study compared different albumin infusion rates (10 mL/kg 5% albumin over 30 minutes *v* 180 minutes) and concluded that both groups achieved similar haemodynamic changes, similar plasma volume expansion, and similar endothelial injury biomarker levels.[13] However, 5% albumin was given over 30 minutes even in the rapid infusion group, a value at the slowest limit of the FBT concept, while the infusion rate in the slow infusion group was well outside the fluid bolus concept.[10]

In keeping with previous studies,[14,15] there was no correlation between percentage CI change and percentage MAP change immediately after FBT. However, at 30 minutes, such a correlation was present and strongest with combined FBT. A previous study also reported a MAP and stroke volume correlation 30 minutes after FBT in patients after cardiac surgery.[16] It is possible that continued extended infusion allows for a more reliable and extended effect on both parameters over time, thus facilitating greater correlation.

Study implications

Our findings imply that, in patients after cardiac surgery, a rapid 500 mL 4% albumin FBT delivers more immediate CI responders and a greater overall increase in MAP, CVP and mean PAP over the following 30 minutes than the combined FBT approach. This observation logically implies that, for the same total amount of fluid, rapid FBT delivers more favourable and pronounced haemodynamic effects than the same amount administered over 30 minutes. Therefore, FBT over a few minutes is a better resuscitation strategy than FBT over 30 minutes, which is a clinically relevant finding.

Strengths and limitations

Our study is the first to compare the haemodynamic changes induced by a rapid 500 mL bolus of 4% albumin with a small 4% albumin bolus followed by a continuous infusion in post-cardiac surgery patients. We recorded secondly haemodynamic data and excluded haemodynamic confounders, with one research staff monitoring the whole data collection. Moreover, iso-oncotic albumin FBT after cardiac surgery is common clinical practice worldwide.[3,17] Finally, our findings clearly indicate the superiority of giving FBT over a few minutes rather than over 30 minutes, a clinically relevant observation.

There are some limitations to our study. Because of the nature of the two different fluid infusion protocols, we had to assess the immediate MAP and CI response when different volumes of 4% albumin were given (500 mL *v* 200 mL) as well as the overall response and the final (at 30 minutes) response, making the comparison complex. But the graphic displays provide clinicians with a clear sense of the haemodynamic events over time. This was a single-centre study including a small number of patients and we could not find a significant difference of MAP at specific time points. However, we identified clear and clinically relevant overall interactions implying adequate power. We only recorded haemodynamic changes over 30 minutes, given that recording haemodynamic parameters without major confounders, such as sedative drug changes, beyond 30 minutes is difficult. Moreover, no previous research has reported the time course of fluid responsiveness beyond 20 minutes after FBT.[18] We did not assess for pulmonary oedema by lung ultrasonography or other test after the FBT. However, the PaO_2:FiO_2 ratio after each treatment was not different between the two groups. We continuously recorded CVP, and did not assess CVP at the end-expiration or at the C wave, but our approach minimised an observer bias. Finally, FBT over 30 minutes might not be a widely accepted approach by some clinicians. However, fluid infusion over 30 minutes is a common practice and was found to be an accepted time frame for FBT in half of the over 3000 survey responses among ICU clinicians.[10]

Conclusion

In conclusion, although the number of MAP responders or CI responders did not change between the two groups at

30 minutes, a rapid FBT of 500 mL 4% albumin achieved a greater number of immediate CI responders, and higher overall MAP, CVP and mean PAP values than a slower combined FBT. Taken together, these findings imply that rapid FBT is haemodynamically superior to combined FBT.

Acknowledgements: Fumitaka Yanase receives funding for PhD studies in Monash University from the Japan Student Services Organization and Endeavour scholarship. The funding agencies had no role in the design and conduct of the study; collection, management, analysis and interpretation of the data; preparation, review or approval of the manuscript; and decision to submit the manuscript for publication.

Competing interests

No relevant disclosures.

Author details

Fumitaka Yanase[1,2]
Thummaporn Naorungroj[1,3]
Salvatore L Cutuli[1,4]
Glenn M Eastwood[1]
Rinaldo Bellomo[1,2,5]

1 Department of Intensive Care, Austin Hospital, Melbourne, Victoria, Australia.
2 Australian and New Zealand Intensive Care Research Centre (ANZIC-RC), School of Public Health and Preventive Medicine, Monash University, Melbourne, Victoria, Australia.
3 Department of Intensive Care, Siriraj Hospital, Mahidol University, Bangkok, Thailand.
4 Dipartimento di Scienze dell'emergenza, anestesiologiche e della Rianimazione, Fondazione Policlinico Universitario A Gemelli IRCCS, Rome, Italy.
5 Centre for Integrated Critical Care, School of Medicine, University of Melbourne, Melbourne, Victoria, Australia.

Correspondence: rinaldo.bellomo@austin.org.au

doi: https://doi.org/10.51893/2021.3.OA9

References

1 Fischer GW, Levin MA. Vasoplegia during cardiac surgery: current concepts and management. *Semin Thorac Cardiovasc Surg* 2010; 22: 140-4.
2 Carrel T, Englberger L, Mohacsi P, et al. Low systemic vascular resistance after cardiopulmonary bypass: incidence, etiology, and clinical importance. *J Card Surg* 2000; 15: 347-53.
3 Parke RL, McGuinness SP, Gilder E, McCarthy LW. Intravenous fluid use after cardiac surgery: a multicentre, prospective, observational study. *Crit Care Resusc* 2014; 16: 164-9.
4 Cecconi M, De Backer D, Antonelli M, et al. Consensus on circulatory shock and hemodynamic monitoring. Task force of the European Society of Intensive Care Medicine. *Intensive Care Med* 2014; 40: 1795-815.
5 Teixeira C, Garzotto F, Piccinni P, et al. Fluid balance and urine volume are independent predictors of mortality in acute kidney injury. *Crit Care* 2013; 17: R14.
6 Garzotto F, Ostermann M, Martín-Langerwerf D, et al. The Dose Response Multicentre Investigation on Fluid Assessment (DoReMIFA) in critically ill patients. *Crit Care* 2016; 20: 196.
7 Chappell D, Bruegger D, Potzel J, et al. Hypervolemia increases release of atrial natriuretic peptide and shedding of the endothelial glycocalyx. *Crit Care* 2014; 18: 538.
8 Bark BP and Grande PO. Infusion rate and plasma volume expansion of dextran and albumin in the septic guinea pig. *Acta Anaesthesiol Scand* 2014; 58: 44-51.
9 Bark BP, Persson J, Grände PO. Importance of the infusion rate for the plasma expanding effect of 5% albumin, 6% HES 130/0.4, 4% gelatin, and 0.9% NaCl in the septic rat. *Crit Care Med* 2013; 41: 857-66.
10 Glassford NJ, Mårtensson J, Eastwood GM, et al. Defining the characteristics and expectations of fluid bolus therapy: a worldwide perspective. *J Crit Care* 2016; 35: 126-32.
11 Yanase F, Bitker L, Lucchetta L, et al. Comparison of the hemodynamic and temperature effects of a 500 mL bolus of 4% albumin at room versus body temperature in cardiac surgery patients. *J Cardiothorac Vasc Anesth* 2021; 35: 499-507.
12 Toscani L, Aya HD, Antonakaki D, et al. What is the impact of the fluid challenge technique on diagnosis of fluid responsiveness? A systematic review and meta-analysis. *Crit Care* 2017; 21: 207.
13 Statkevicius S, Bonnevier J, Fisher J, et al. Albumin infusion rate and plasma volume expansion: a randomized clinical trial in postoperative patients after major surgery. *Crit Care* 2019; 23: 191.
14 Pierrakos C, Velissaris D, Scolletta S, et al. Can changes in arterial pressure be used to detect changes in cardiac index during fluid challenge in patients with septic shock? *Intensive Care Med* 2012; 38: 422-8.
15 Le Manach Y, Hofer CK, Lehot JJ, et al. Can changes in arterial pressure be used to detect changes in cardiac output during volume expansion in the perioperative period? *Anesthesiology* 2012; 117: 1165-74.
16 Smorenberg A, Lust EJ, Beishuizen A, et al. Systolic time intervals vs invasive predictors of fluid responsiveness after coronary artery bypass surgery. *Eur J Cardiothorac Surg* 2013; 44: 891-7.
17 Aronson S, Nisbet P, Bunke M. Fluid resuscitation practices in cardiac surgery patients in the USA: a survey of health care providers. *Perioper Med (Lond)* 2017; 6: 15.
18 Roger C, Zieleskiewicz L, Demattei C, et al. Time course of fluid responsiveness in sepsis: the fluid challenge revisiting (FCREV) study. *Crit Care* 2019; 23: 179.