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Comparison of albumin 4%, gelatine, and ringer lactate as volume expander post-resuscitative phase on cardiac output and lactate serum after Coronary Arterial Bypass Grafting (CABG) on-pump: Single-center randomized prospective study

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ABSTRACT

Background: The use of protein colloid in fluid management post-cardiac surgery is debatable whether it is more beneficial than non-protein colloid or crystalloid. Patients who still need more volume after the resuscitative phase might benefit from optimal fluid management by choosing the most beneficial fluid. This study compared albumin 4% administration to gelatine and ringer lactate as a volume expanders post-resuscitative phase after coronary artery bypass grafting (CABG) on-pump.

Methods: We conducted a single-centered, single-blind, randomized controlled study that assigned 120 patients undergoing elective CABG on-pump. Subjects who met inclusion criteria received 125 ml/hour of either albumin 4%, gelatine colloid, or Ringer's lactate (RL) as the only infusion fluid for 4 hours after the first assessment post-resuscitative phase, after intensive care unit (ICU) admission. After fluid administration, patients were reassessed. The assessment included cardiac output and lactate serum as the primary outcome, while the duration of mechanical ventilation, ICU, and hospital stay were recorded as secondary outcomes.

Results: The mean of cumulative cardiac output improvement differed between the group albumin 4% 1.18 L/min, gelatine 0.88, and RL 0.74 ($p=0.002$). Lactate serum decreased in the albumin 4% group as much as 3.31 gr/dl compared to gelatine 2.13 and RL group 2.37 ($p=0.005$). Duration of mechanical ventilation, length of stay in ICU, and hospital post-operative were shorter in the albumin group than in other groups.

Conclusions: Albumin 4% used as a volume expander in the post-resuscitative phase still improved cardiac output and tissue micro-perfusion than gelatine and ringer lactate.

Keywords: CABG, cardiac output, lactate serum, albumin 4%, gelatine, ringer lactate.

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INTRODUCTION

Fluid administration is considered one of the important first-line therapies in stabilizing the hemodynamics of patients post cardiac surgery. Patients often receive extra intravenous fluid such as crystalloid, colloid, blood products, or combinations. Crystalloid, in the form of ringer lactate (RL), and colloids such as gelatine are commonly used for post-operative fluid in some cardiac institutions. Another alternative is using protein colloid albumin 5% or protein plasma fraction such as plasmanate 5% (containing albumin 4%), preferred for fluid resuscitation and stabilization post-cardiac surgery for a more profound volume expansion effect than crystalloids or non-protein colloids.[1-6]

Coronary artery bypass grafting (CABG) with bypass machine (on pump) induces systemic inflammation responses, leading to capillary leakage. Fluid resuscitation with crystalloid with/or without colloids is conducted to overcome hemodynamic consequences due to capillary leakage and vasodilation caused by the rewarming process and anesthesia. Overload of intravascular fluid in the leakage phase causes fluid accumulation in the interstitial and edema formation. Crystalloid needs a large amount of fluid administration to obtain an optimal hemodynamic response. The use of non-protein colloid is related to complications such as blood coagulation dysfunction and renal disorder. Protein colloids like albumin or protein plasma fraction, with a molecule weights around 66000-69000 Dalton, are considered iso-oncotic fluids have volume expander effects that are more predictable than its other solutions (20-25% solutions). The fluid dose required is lower while preventing a substantial decrease in colloid oncotic pressure. Maintaining colloid oncotic pressure is considered as goal-directed fluid replacement. Albumin can be used as a volume expander and an alternative to avoid unnecessary fluid administration in cardiac surgery.[7–12]

Cost efficiency is the main reason why protein colloids such as albumin 4-5% are not used as first-line fluid therapy. The effectivity in giving protein colloid post-cardiac surgery is well-established, although it is still not given in the first-line fluid therapy. The main objective of this study was to compare the effects between albumin 4%, gelatine colloid and ringer lactate administration post-resuscitative phase after CABG on-pump in improving cardiac output and tissue micro-perfusion represented by decreasing lactate level.[4,5,13]

METHODS

Subjects

This randomized, single-blind, single-center, controlled trial was conducted over 13 months at the post-cardiac surgery intensive care unit (ICU) cardiovascular hospital. The ethical committee of the hospital has approved this study. We included 120 informed and provided written consent before including subjects. Only subjects who fulfilled inclusion criteria after the first assessment (4 hours after ICU admission) were selected as subjects in the study. Inclusion criteria were: patients aged more than 18 years old, post CABG on pump, elective operation, post-operative with decreased cardiac output (<4.0 L/mnt), high lactate level (>4.0 gr/dl) and positive fluid responsiveness on first assessment (4 hours post-operative). Exclusion criteria were: patients with other cardiac diseases (valve problem, aortic disease or congenital heart); surgery combined with valve surgery; patients in another study regimen which could affect fluid resuscitation method; a bleeding problem; and cardiac output decreased with negative fluid responsiveness or patients who refused to participate in the study.

Patients who fulfilled the inclusion criteria were randomized into three groups comprised of 40 patients in each with the following fluid regimens:

Group 1 Control : Ringer Lactate: RL 500 ml given 125 ml/hour for 4 hours

Group 2 Colloid gelatine: GelofusinÒ 500 ml given 125 ml/hour for 4 hours

Group 3 Protein colloid : Albumin 4% or PlasmanateÒ 5% 500 ml given 125 ml/hour for 4 hours

Randomization was based on simple randomization to allocate patients to three groups. The single-blinded method was used for patients and cardiologists/technicians who did the first and second assessments. Fluid administration done by the caregiver (nurse and attending physician) was not blinded, referring to ethical committee recommendation. There were drop out criteria, in case a patient should be dismissed from the study and treated as an indication, drop-out criteria were: unstable hemodynamic post-operative (hypotension with MAP < 50 mmHg; need two inotropic and vasopressor); patient with/need for intra-aortic balloon pump /IABP; experiencing cardiogenic shock; pulmonary hypertension crisis; anaphylactic shock; patient with a maximal fluid dose for a day that had to be replaced with other kinds of fluid; or known/found allergy to albumin or gelatine.

Procedures

After obtaining approval from the hospital's ethical committee for research, the study was conducted with patients who underwent elective coronary bypass surgery with cardiopulmonary bypass machines. All elective surgery patients were informed consent. All patients who agreed to join the research were considered subject candidates. Postoperatively, patients were admitted to the intensive care unit (ICU) and routinely obtained vital signs. Lactate serum was checked initially. All patients received routine post-operative care and initial standard fluid administration was RL or gelatine colloid. Vasopressors and inotropic use were given at the discretion of the attending consultant and not controlled by protocol. The fluid used during the first 4 hours in ICU was given by the instruction of the attending consultant and indication required. The first examination was done during the 4th hour in the ICU, including laboratory tests to check lactate serum and echocardiography examinations to obtain cardiac output and fluid responsiveness. Patients with inadequate cardiac output (<4.0 L/mnt) and elevated lactate serum (>4 gr/dl) with positive fluid responsiveness were, according to inclusion criteria, considered as subjects. Subjects were randomized to be assigned into 3 groups: Group 1 received crystalloid fluid RL, Group 2 received non-protein gelatine colloid, and Group 3 received protein colloid fluid albumin 4% in the form of plasmanateÒ 5%. Fluid administration was done according to protocol. Five hundred cc of each fluid was given in 4 hours duration, and during this period, all other fluid was stopped. After the fluid protocol was finished, cardiac output and lactate serum were performed, labeled as the second examination. During post-operative care, mechanical ventilation duration, ICU, and hospital post-operative length of stay (LOS) were recorded.

Outcome Variables

Primary outcome variables were changes in cardiac output (delta cardiac output in second and first examination) and lactate serum (delta lactate serum in second and first examination) which were examined after the fluid regimen protocol. Cardiac output was examined with echocardiography by a cardiologist or resident who was not aware of the trial. Lactate serum was obtained from an artery blood sample combined with blood gas analysis and examined in the hospital laboratory. Secondary outcome variables were mechanical ventilation duration, ICU, and hospital post-operative LOS.

Statistical analysis

The sample size of this research was counted based on research conducted by a previous study, by consideration $\alpha = 0.05$, $\beta = 0.2$, with power as much as 95%, standard deviation (SD) 0,3, and variable volume expanding potency of 0.7. Consequently, the sample size of 40 patients for each group was required.

Cardiac output improvement was measured as a difference (delta) between cardiac output in the first and second assessments. Data of lactate serum examination for each group was measured as a difference (delta) between lactate serum level in the first and second assessments.

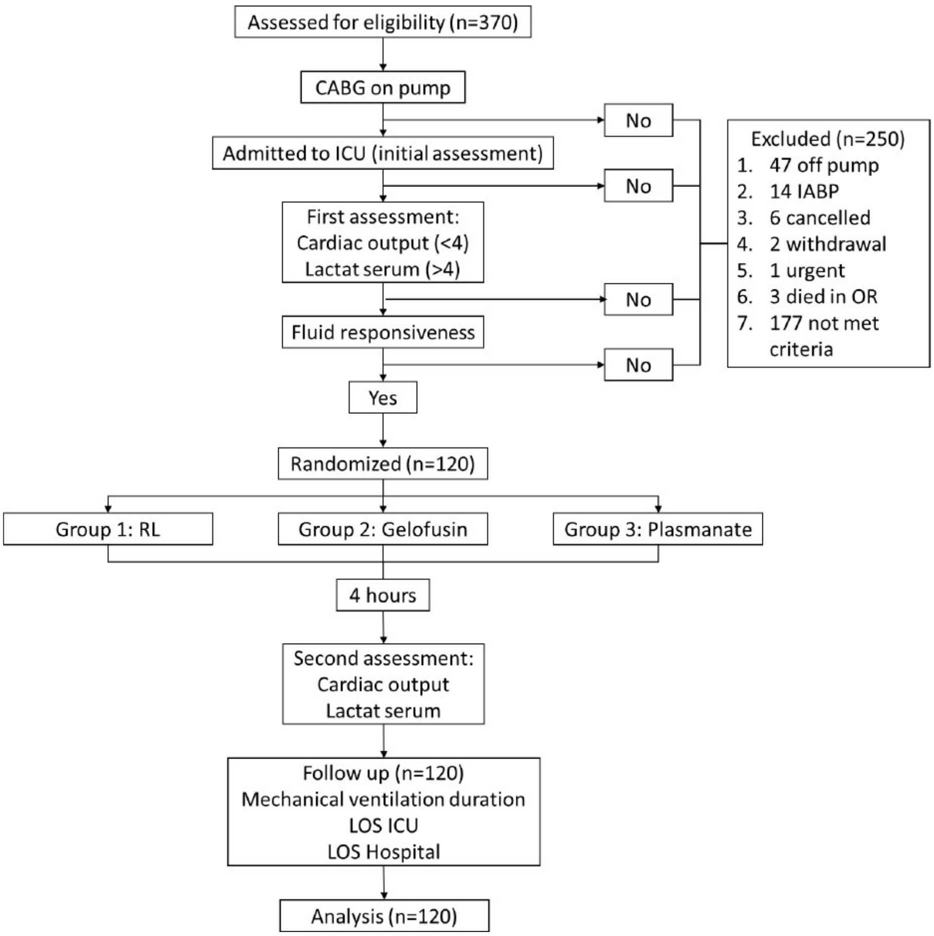

Figure 1. Study patients flow diagram.

Data were analyzed with SPSS Statistic software 22 version and published as mean ± standard deviation (SD). Data distribution was tested with Kolmogorov-Smirnov tests. Non-parametric statistical tests were used for not normally distributed data analysis. Since the distribution test showed data was not normally distributed, the non-parametric Kruskal-Wallis test was used for measuring differences in cardiac output, lactate, mechanical ventilation duration, ICU, and hospital post-operative LOS. All p-values are reported with 95% confidence, and <0.05 were considered statistically significant.

RESULTS

Subjects included 120 patients who met the inclusion criteria from 370 CABG patients willing to join the research. The recruitment process of patients is depicted as part of the study's flow diagram in (Figure 1). No patients in the study group were rejected, and there were no losses to follow up or discontinued intervention.

Characteristics and perioperative data of the three study groups' subjects are shown in Table 1. Characteristics and perioperative subjects' data distribution were considered homogenous, with no

Table 1. Patients' characteristic data.

Characteristics	Ringer Lactate (n=40)	Gelatine colloid (n=40)	Albumin 4% (n=40)	Total	*p value*
Age (yrs)					
≤ 50 yrs	7 (5.8%)	6 (5.0%)	6 (5.0%)	19 (15.8%)	0.939
>50 yrs	33 (27.5%)	34 (28.3%)	34 (28.3%)	101 (84.2%)	
Sex					
Male	35 (29.2%)	33 (27.5%)	35 (29.2%)	103 (85.8%)	0.760
Female	5 (4.2%)	7 (5.8%)	5 (4.2%)	17 (14.2%)	
LVEF (%)					
>50	31 (25.8%)	30 (25.0%)	25 (20.8%)	86 (71.7%)	0.280
20 – 50	9 (7.5%)	10 (8.3%)	15 (12.5%)	34 (28.3%)	
GRAFT number					
1	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	0.664
2	6 (5.0%)	5 (4.2%)	9 (7.5%)	20 (16.7%)	
3	21 (17.5%)	24 (20.0%)	20 (16.7%)	65 (54.2%)	
4	9 (7.5%)	9 (7.5%)	9 (7.5%)	27 (22.5%)	
5	4 (3.3%)	2 (1.7%)	1 (0.8%)	7 (5.9%)	
Use of ACE inhibitor preoperatively					
Yes	20 (16.7%)	26 (11.7%)	16 (20.0%)	58 (48.3%)	0.079
No	20 (16.7%)	14 (21.7%)	24 (13.3%)	62 (51.7%)	
Beta-Blocker					
Yes	38 (31.7%)	35 (29.2%)	33 (27.5%)	106 (88.3%)	0.189
No	2 (1.7%)	5 (4.2%)	7 (5.8%)	14 (11.7%)	

*LVEF: Left Ventricle Ejection Fraction † ACE: Angiotensin-Converting Enzyme

Table 2. Cardiac output (delta) and Lactate serum (delta).

	Mean				*P-value*
Cardiac output*	**1st**	**2nd**	**delta**	**SD**	
Ringer Lactate	3.41	4.15	0.74	0.69	0.002‡
Gelatine	3.51	4.39	0.88	0.29	
Albumin 4%	3.42	4.59	1.18	0.69	
Lactate serum level†					
Ringer Lactate	7.57	5.45	-2.37	-1.17	0.005‡
Gelatine	7.23	5.10	-2.13	-1.27	
Albumin 4%	7.39	4.08	-3.31	-2.04	

The value was presented as the mean delta of cardiac output and lactate examination on the first assessment and second assessment; *Cardiac output mean values were expressed in liter per minute; † Lactate serum level was expressed in mmol/L. ‡P<0,05 ;SD: standard deviation.

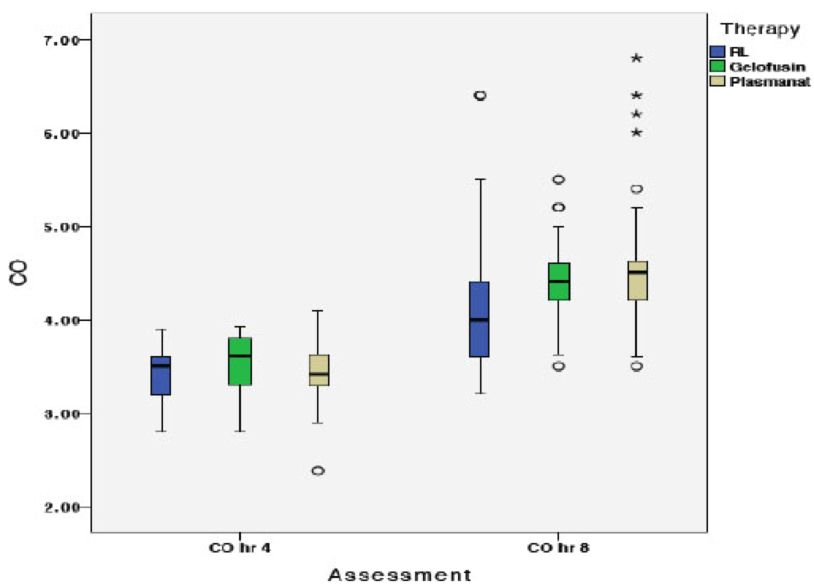

Figure 2. Cardiac output of first and second assessment. *Cardiac output mean values were expressed in liters per minute. *p <0.05.

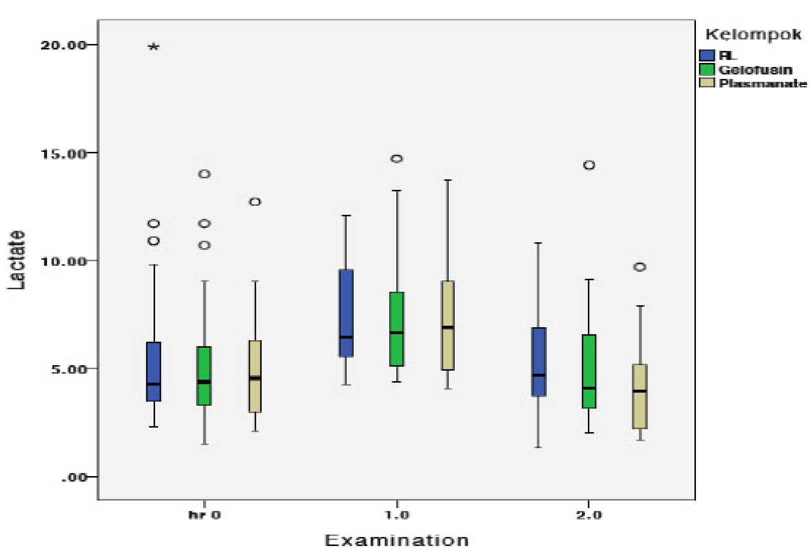

Figure 3. Lactate serum of first and second assessment. *Lactate serum level was expressed in mmol/L. *p<0.05.

significant differences (p-value > 0.05), and eligible for comparison.

Delta means cardiac output showed positive values, which means an increase of cardiac output (CO) value from the first assessment to the second assessment. Cardiac output increase post-fluid administration between 3 groups was different (Figure 2). The highest increase was in the albumin group for 1.18 L min^{-1} (0.69) than the other groups with (p=0.002) (Table 2). Delta means lactate serum level showed negative values, which means there was a decrease of lactate serum level value from the first assessment to the second assessment. Decreased lactate post-fluid administration mostly occurred on albumin group with -3.31 (2.04) followed by the gelatine group with -2.11 (1.29) and RL group -2.37 (1.56) (p=0.004). The p-value concluded a significant difference in lactate decrease in the CABG on-pump patients given RL, gelatine, and albumin 4% (Figure 3).

Effect of fluid management postoperatively can be assessed by the clinical improvements associated with the parameters of mechanical ventilation duration, LOS in ICU and hospital post-operative overall. Time was counted for each parameter since the patient was admitted to ICU. Mechanical ventilation duration was counted in hours, ICU LOS was counted in hours, and post-operative hospital LOS was counted in days.

Effect of treatment variables consisting of mechanical ventilation duration, ICU LOS, and hospital LOS are depicted in Table 3. Mechanical ventilation duration was shorter in albumin 4% regimen subjects, while the longest was in subjects in RL regimen. ICU LOS was shorter

Table 3. Comparison mechanical ventilation duration, ICU length of stay and Hospital post-operative length of stay variables.

Variable	Mean	SD	*P-value*
Mechanical ventilation duration (hour)			
RL	16.10	7.82	<0.001*
Gelatine	12.60	4.24	
Albumin 4%	10.43	2.64	
ICU length of stay (hour)			
RL	31.90	13.02	<0.001*
Gelatine	24.95	6.5	
Albumin 4%	23.95	7.94	
Hospital post-operative length of stay (day)			
RL	8.03	2.56	<0.001*
Gelatine	7.40	1.78	
Albumin 4%	6.20	1.2	

*P<0,05; SD: Standard deviation; ICU: Intensive Care Unit

in subjects in the albumin 4% regimen, while the longest was in the RL regimen. The albumin group's hospital LOS was significantly shorter than subjects in RL and gelatine groups, with p <0.001.

DISCUSSION

Optimal intravenous fluid management post coronary bypass surgery is still challenging for every intensivist working in the post-cardiac intensive care unit. Overload fluid administration can lead to acute heart failure, pulmonary edema, hemodilution, intestinal dysfunction, increased transfusion needs, and prolonged hospital LOS. Complications will increase overall hospital costs. Fluid management has a major role in resuscitation and stabilizing patient's hemodynamic conditions. Intravenous fluid must be prescribed just as medication as consider indications and contraindications for different fluid types. Fluid is only prescribed if it is indicated while calculating the risk from giving too much.[1,2,14–18]

Post coronary bypass patients often received liberal fluid administration. Hemodilution and endothelial dysfunction triggered by a cardiopulmonary bypass machine can lead to blood transfusion requirement and induce fluid extravasation, causing tissue edema, which will deter post-operative improvement by promoting infection and organ dysfunction. In theory, restricting intravenous fluid will be useful to avoid unwanted hemodilution and fluid loading.[18,19]

Patients admitted to ICU are considered still in the resuscitation phase. During this phase, the fluid bolus stabilizes hemodynamics and increases cardiac output. This phase generally lasts from a few minutes up to a few hours. According to the hospital's protocol, the fluid administered usually consists of crystalloid or colloid. If there were no clinical improvements after a few hours, intensivists sometimes are encouraged to add more fluid. Consequently, any overload fluid will extravasate to interstitial and cause edema, which will lead to organ dysfunction and complicate the fluid removal process.[1,15,19–22]

Considering those phenomena, it is critical for intensivists to evaluate what fluid requirement phase are patients in post-cardiac surgery how to administer, target level, and remove. For this purpose, it is very rational not to give fluid as rapid bolus as in the resuscitative phase to avoid a rapid increase in right heart pressure and not interfere with cardiac pumping or filling. The objective of fluid administration in this phase is to maintain tissue perfusion and organ saving. Adequacy of microcirculation perfusion is marked by decreases in lactate serum level, which represents the cellular metabolism endpoint. From a survey among medical practitioners in the USA by Aronson et al. resuscitation fluid for postcardiac surgery patients mostly used crystalloid and albumin 5%.[12,19,20,23]

After fluid administration, we expected an increase in cardiac output in all subjects, indicating the fluid administration was appropriate. Positive fluid responsiveness was assessed initially to provide guidance that fluid administration can still be assigned. This trial result indicated that cardiac output improvement occurred in all study groups, where the most cardiac output improvement was in the albumin group (1.18 L/min) compared to the gelatine and RL group (0.80 L/min and 0.74 L/min, respectively), with significant with p-value of 0.002 (95% confidence level). Cardiac output improvement may restore tissue micro-perfusion, expecting there were lactate levels decrease from the level before the fluid regimen. Lactate serum decreased most significantly shown in the albumin group (3.31) compared to the other groups in second examination. Albumin or protein colloid is not the preferred fluid as the first-line therapy post-operative due to its cost, considering protein colloid cost 5-10 times gelatine or 80 times RL. Some studies resulted in cost-effectivity from protein colloid can be seen by the overall outcome, superseding the morbidity or complication that might occur. One study conducted by Sedrakyan et al., compared non-protein colloid and albumin administration in postcardiac surgery showed less mortality rate in the albumin group.[24–27]

This study revealed the effects of protein colloid by measuring specific variables: mechanical ventilation duration, ICU, and post-operative hospital LOS. The study group with albumin 4% had a shorter mechanical ventilation duration than the other groups. This result might be due to more improvement in cardiac output which will stabilize patients' hemodynamic condition leading to better tissue microcirculatory perfusion, marked by decreased lactate levels. This condition will fulfill the criteria to extubate; therefore mechanical ventilation duration will be shorter compared to the other groups

After being extubated and no longer on mechanical ventilation, stable subjects will be qualified to transfer from the ICU to the next ward, which resulted in the shorter ICU LOS. The mean hospital post-operative LOS in the albumin group was also shorter than the other groups. All variable comparisons measured were significant statistically with p-values <0.05.

Protein colloid administration in the post-resuscitative phase in patients with low or inadequate cardiac output in this study still contributed a significant effect on patients' outcomes. Wigmore et al. showed equivalent cardiovascular optimization between bolus crystalloid and albumin post-cardiac surgery but less fluid accumulation in albumin groups. Several studies also indicated that patients with negative fluid balance for two days consecutively in the first ICU are considered as strong and independent patient survival predictors.[25,28–30]

This study had several limitations. It was conducted as a single-blind, single-center, randomized trial with RL as the control group to measure significant group differences in the efficacy of bolus administration to increase cardiac output and improve tissue micro-perfusion. The ethical committee's consideration for patients' safety and the inability to mask the fluid into the same container made double-blinding not feasible. Additionally, there was no strict protocol to control other confounding factors that can generate bias in the results. For example, previous blood transfusion, inotropic or vasopressor used, and fluid administration during the resuscitation/initial phase (hour 0 – 4) expose the subject to other fluids that might affect data sampling. This study also was not designed to compare complications or side effects.

CONCLUSION

Protein colloid administration, as albumin 4-5%, for post-cardiac surgery which is given in divided dose as intravenous fluid still effective in increasing cardiac output and improving tissue micro-perfusion. Clinical and hemodynamic improvements may lead to shorter mechanical ventilation duration, as well as ICU, and hospital post-operative length of stay.

DISCLOSURE

Author Contribution

PA contributed in all aspect and conduct as guarantor. NLK contributed in concepts, design, intellectual content definitor, literature search, manuscript preparation, manuscript editing, manuscript review. A contributed in all aspect.

Ethical Consideration

The ethic committee of National Cardiovascular Center of Harapan Kita has approved this study with letter number LB.02.01/VII/199/KEP.032/2017.

Conflict of Interest

All authors stated no conflict of interest regarding conducting and publishing this study.

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REFERENCES

1. Stephens RS, Whitman GJR. Postoperative Critical Care of the Adult Cardiac Surgical Patient. Part I. *Crit Care Med*. 2015;43(7):1477–97. Available from: http://dx.doi.org/10.1097/ccm.0000000000001059
2. Parke RL, McGuinness SP, Gilder E, McCarthy LW. Intravenous fluid use after cardiac surgery: a multicentre, prospective, observational study. *Crit Care Resusc*. 2014;16(3):164–9.
3. Hoste EA, Maitland K, Brudney CS, Mehta R, Vincent J-L, Yates D, et al. Four phases of intravenous fluid therapy: a conceptual model. *Br J Anaesth*. 2014/09/09. 2014;113(5):740–7. Available from: https://pubmed.ncbi.nlm.nih.gov/25204700
4. Sedrakyan A, Gondek K, Paltiel D, Elefteriades JA. Volume Expansion With Albumin Decreases Mortality After Coronary Artery Bypass Graft Surgerya. *Chest*. 2003;123(6):1853–7. Available from: http://dx.doi.org/10.1378/chest.123.6.1853
5. Liumbruno G, Bennardello F, Lattanzio A, Piccoli P, Rossettias G. Recommendations for the use of albumin and immunoglobulins. *Blood Transfus*. 2009;7(3):216.
6. Schumacher J, Klotz KF. Fluid therapy in cardiac surgery patients. *Appl Cardiopulm Pathophysiol*. 2009;13(1):138–42.
7. Skhirtladze K, Base EM, Lassnigg A, Kaider A, Linke S, Dworschak M, et al. Comparison of the effects of albumin 5%, hydroxyethyl starch 130/0.4 6%, and Ringer's lactate on blood loss and coagulation after cardiac surgery. *Br J Anaesth*. 2014;112(2):255–64. Available from: http://dx.doi.org/10.1093/bja/aet348
8. Diodato M, Chedrawy EG. Coronary artery bypass graft surgery: the past, present, and future of myocardial revascularisation. *Surg Res Pract*. 2014/01/02. 2014;2014:726158. Available from: https://pubmed.ncbi.nlm.nih.gov/25374960
9. Singh S, Hutton P. Cerebral effects of cardiopulmonary bypass in adults. *BJA CEPD Rev*. 2003;3(4):115–9. Available from: http://dx.doi.org/10.1093/bjacepd/mkg115
10. Hirai S. Systemic inflammatory response syndrome after cardiac surgery under cardiopulmonary bypass. *Ann Thorac Cardiovasc Surg*. 2003;9(6):365–70.
11. Engelman DT, Adams DH, Byrne JG, Aranki SF, Collins JJ, Couper GS, et al. Impact of body mass index and albumin on morbidity and mortality after cardiac surgery. *J Thorac Cardiovasc Surg*. 1999;118(5):866–73. Available from: http://dx.doi.org/10.1016/s0022-5223(99)70056-5
12. Monteiro J, Goraksha S. 'ROSE concept' of fluid management: Relevance in neuroanaesthesia and neurocritical care. *J Neuroanaesth Crit Care*. 2017;04(01):10–6. Available from: http://dx.doi.org/10.4103/2348-0548.197435
13. Shaw A, Raghunathan K. Fluid Management in Cardiac Surgery. *Anesthesiol Clin*. 2013;31(2):269–80. Available from: http://dx.doi.org/10.1016/j.anclin.2012.12.007
14. Dunn J-OC, Grocott MP, Mythen M (Monty) G. The place of goal-directed haemodynamic therapy in the 21st century. *BJA Educ*. 2016;16(6):179–85. Available from: http://dx.doi.org/10.1093/bjaed/mkv039
15. Stephens RS, Whitman GJR. Postoperative Critical Care of the Adult Cardiac Surgical Patient. Part II. *Crit Care Med*. 2015;43(9):1995–2014. Available from: http://dx.doi.org/10.1097/ccm.0000000000001171
16. Thompson R, Aya H. Early goal directed therapy following cardiac surgery. *ICU Manag Pr*. 2014;14(4):4.
17. Aya HD, Cecconi M, Hamilton M, Rhodes A. Goal-directed therapy in cardiac surgery: a systematic review and meta-analysis. *Br J Anaesth*. 2013;110(4):510–7. Available from: http://dx.doi.org/10.1093/bja/aet020
18. van Haren F. Personalised fluid resuscitation in the ICU: still a fluid concept? *Crit Care*. 2017;21(Suppl 3):313. Available from: https://pubmed.ncbi.nlm.nih.gov/29297387
19. Malbrain MLNG, Marik PE, Witters I, Cordemans C, Kirkpatrick AW, Roberts DJ, et al. Fluid overload, de-resuscitation, and outcomes in critically ill or injured patients: a systematic review with suggestions for clinical practice. *Anestezjol Intens Ter*. 2014;46(5):361–80. Available from: http://dx.doi.org/10.5603/ait.2014.0060
20. Malbrain MLNG, Van Regenmortel N, Saugel B, De Tavernier B, Van Gaal P-J, Joannes-Boyau O, et al. Principles of fluid management and stewardship in septic shock: it is time to consider the four D's and the four phases of fluid therapy. *Ann Intensive Care*. 2018;8(1):66. Available from: https://pubmed.ncbi.nlm.nih.gov/29789983
21. Acheampong A, Vincent J-L. A positive fluid balance is an independent prognostic factor in patients with sepsis. *Crit Care*. 2015;19(1):251. Available from: https://pubmed.ncbi.nlm.nih.gov/26073560
22. Morin J-F, Mistry B, Langlois Y, Ma F, Chamoun P, Holcroft C. Fluid Overload after Coronary Artery Bypass Grafting Surgery Increases the Incidence of Post-Operative Complications. *World J Cardiovasc Surg*. 2011;01(02):18–23. Available from: http://dx.doi.org/10.4236/wjcs.2011.12004

23. Aronson S, Nisbet P, Bunke M. Fluid resuscitation practices in cardiac surgery patients in the USA: a survey of health care providers. *Perioper Med (London, England)*. 2017;6:15. Available from: https://pubmed.ncbi.nlm.nih.gov/29075482
24. Jiang Y, Shaw AD. Albumin Supplementation as a Therapeutic Strategy in Cardiac Surgery. *Anesthesiology*. 2016;124(5):983–5. Available from: http://dx.doi.org/10.1097/aln.0000000000001052
25. Maes T, Meuwissen A, Diltoer M, Nguyen DN, La Meir M, Wise R, et al. Impact of maintenance, resuscitation and unintended fluid therapy on global fluid load after elective coronary artery bypass surgery. *J Crit Care*. 2019;49:129–35. Available from: http://dx.doi.org/10.1016/j.jcrc.2018.10.025
26. Runken MC, Khangulov VS, Munson SH, Peyerl FW, Bunke M. Economic Implications Of Increased Utilization Of 5% Albumin For Fluid Resuscitation Post On-Pump Cardiac Procedures In Us Hospitals. *Value Heal*. 2015;18(3):A137. Available from: http://dx.doi.org/10.1016/j.jval.2015.03.799
27. Hoffmann-Petersen J, Leonaviciute D, Jakobsen C-J. Human albumin has greater impact on outcomes after cardiac surgery than hydroxyl-ethyl starches and crystalloids - an epidemiologic study. *J Cardiothorac Vasc Anesth*. 2016;30:S22. Available from: http://dx.doi.org/10.1053/j.jvca.2016.03.067
28. Hosseinzadeh Maleki M, Derakhshan P, Rahmanian Sharifabad A, Amouzeshi A. Comparing the Effects of 5% Albumin and 6% Hydroxyethyl Starch 130/0.4 (Voluven) on Renal Function as Priming Solutions for Cardiopulmonary Bypass: A Randomized Double Blind Clinical Trial. *Anesthesiol pain Med*. 2016;6(1):e30326–e30326. Available from: https://pubmed.ncbi.nlm.nih.gov/27110527
29. Wigmore GJ, Anstey JR, St. John A, Greaney J, Morales-Codina M, Presneill JJ, et al. 20% Human Albumin Solution Fluid Bolus Administration Therapy in Patients After Cardiac Surgery (the HAS FLAIR Study). *J Cardiothorac Vasc Anesth*. 2019;33(11):2920–7. Available from: http://dx.doi.org/10.1053/j.jvca.2019.03.049
30. Parke RL, McGuinness SP, Gilder E, McCarthy LW, Cowdrey K-AL. A Randomised feasibility study to assess a novel strategy to rationalise fluid in patients after cardiac surgery. *Br J Anaesth*. 2015;115(1):45–52. Available from: http://dx.doi.org/10.1093/bja/aev118