



# Priming and replenishment in cardiopulmonary bypass with hydroxyethyl starch 130/0.4 decreases fluid overbalance without renal dysfunction or bleeding in adult valve surgery

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## Abstract

The best priming and replenishment solution in cardiopulmonary bypass remains unknown, and the efficacy and drawbacks of artificial colloid are controversial. We retrospectively compared consecutive patients undergoing elective adult valve surgery in cases wherein cardiopulmonary bypass was primed and replenished with hydroxyethyl starch 130/0.4 ( $n = 12$ ) or crystalloid solution ( $n = 11$ ). The fluid overbalance during cardiopulmonary bypass was much lower in the hydroxyethyl starch 130/0.4 group (mean  $\pm$  standard deviation,  $+95 \pm 1241$  mL) than in the crystalloid solution group ( $+2921 \pm 1984$  mL) ( $P < 0.001$ ). Renal function, intraoperative and postoperative bleeding, and blood products did not deteriorate with the use of hydroxyethyl starch 130/0.4. The postoperative intubation time was shorter in the hydroxyethyl starch 130/0.4 group ( $16.0 \pm 2.6$  h) than in the crystalloid solution group ( $18.7 \pm 2.6$  h) ( $P = 0.018$ ). Although prospective randomized trials are needed to verify our findings, the impact of fluid balance differences requires serious consideration.

**Keywords** Cardiopulmonary bypass · Hydroxyethyl starch · Valve surgery · Renal dysfunction · Bleeding

## Introduction

Hydroxyethyl starch (HES) 130/0.4 is used for priming and replenishment in cardiopulmonary bypass (CPB); however, its safety and efficacy are controversial [1–3]. Because the CRISTAL study [4] showed the clinical superiority of colloid resuscitation over CS for hypovolemic patients without deterioration of renal function, we expect a similar benefit during CPB. In the past, we did not use HES 130/0.4 for priming or replenishment during CPB, and then only used HES for replenishment. Currently, we use HES for priming and replenishment. We compared the use of HES 130/0.4 and CS for priming and replenishment during CPB.

## Materials and methods

Twenty-three adults who underwent elective valve surgery through a conventional sternotomy were retrospectively identified according to priming and replenishment with HES 130/0.4 or a CS (bicarbonate Ringer's solution) between April 2017 and October 2018 at Fujisawa City Hospital. Priming in the HES group involved the use of bicarbonate Ringer's solution (500 mL), HES 130/0.4 (500 mL), and 20% mannitol (200 mL) (Na: 120.4 mEq, Cl: 111.3 mEq, K: 1.7 mEq, Ca: 1.3 mEq, Mg: 0.4 mEq, HCO<sub>3</sub>: 10.4 mEq, citrate: 2.1 mEq), whereas bicarbonate (1000 mL) and 20% mannitol (200 mL) were used in the CS group (Na: 122.7 mEq, Cl: 102.7 mEq, K: 3.6 mEq, Ca: 2.7 mEq, Mg: 0.9 mEq, HCO: 22.7 mEq, citrate: 4.5 mEq). The CS group included 11 consecutive patients [four aortic valve replacement (AVR), seven mitral valve plasty (MVP)], whereas the HES 130/0.4 group included 12 consecutive patients (7 AVR, 5 MVP).

Myocardial protection was performed using antegrade and retrograde intermittent cold blood cardioplegia.

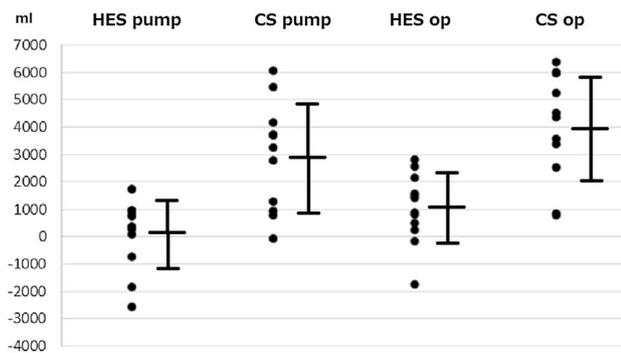
Fluid balance was evaluated during CPB and surgery. The bleeding and transfusion volumes were measured intraoperatively and 24 h postoperatively. Serum creatinine levels

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**Fig. 1** Fluid overbalance during cardiopulmonary bypass (pump balance) and during the operation (op balance). Error bars indicate means  $\pm$  standard deviations. CS crystalloid solution group; HES HES 130/0.4 group

were assessed preoperatively and on postoperative day 3. Postoperative intubation time and hospital stay duration were also investigated. Statistical significance was analyzed using unpaired *t* test in SPSS ver. 23 (SPSS Inc., Chicago, IL, USA).

## Results

There were no intergroup background differences in age [mean  $\pm$  standard deviation, HES:  $74.5 \pm 7.1$  years vs. CS:  $72.7 \pm 7.1$  years, not significant (ns)], sex (female/total, HES: 8/12 vs. CS: 5/11, ns), left ventricular ejection fraction (HES:  $63.9 \pm 8.0\%$  vs. CS:  $60.0 \pm 12.5\%$ , ns), forced expiratory volume-one second (HES:  $1.9 \pm 0.5$  L vs. CS:  $1.6 \pm 0.5$  L, ns), Japan score (calculated 30 days mortality from Japanese database) (HES:  $3.8 \pm 1.8$  vs. CS:  $4.3 \pm 2.0$ , ns), aortic clamp time (HES:  $120 \pm 20$  min vs. CS:  $120 \pm 27$  min, ns), or bypass time (HES:  $165 \pm 30$  min vs. CS:  $168 \pm 30$  min, ns). HES 130/0.4 was used during CPB only in the HES group (HES:  $1840 \pm 396$  mL vs. CS:  $0 \pm 0$  mL,  $P < 0.001$ ) and was used in both groups after bypass during the operation (HES:  $192 \pm 387$  mL vs. CS:  $227 \pm 410$  mL, ns). The degree of fluid overbalance during CPB (HES:  $95 \pm 1241$  mL vs. CS:  $2921 \pm 1984$  mL,  $P < 0.001$ ) and during the operation (HES:  $1042 \pm 1265$  mL vs. CS:  $3967 \pm 1963$  mL,  $P < 0.001$ ) was much lower in the HES group (Fig. 1), where the equal distribution was confirmed by Levene test. There were no intergroup differences in bleeding volume (HES:  $1385 \pm 414$  mL vs. CS:  $1780 \pm 680$  mL, ns) or transfusion volume intraoperatively (HES:  $2471 \pm 1034$  mL vs. CS:  $2378 \pm 1237$  mL, ns) or in transfusion volume postoperatively (HES:  $457 \pm 751$  mL vs. CS:  $538 \pm 591$  mL). There was less postoperative bleeding in the first 24 h in the HES group (HES:  $543 \pm 321$  mL vs. CS:  $913 \pm 483$  mL,  $P = 0.04$ ). No deterioration of serum

creatinine level was observed in either group (postoperative creatinine—preoperative creatinine, HES:  $-0.2 \pm 0.1$  mg/dL vs. CS:  $-0.08 \pm 0.27$  mg/dL, ns). Postoperative intubation time was shorter in the HES group (HES:  $16.0 \pm 2.6$  h vs. CS:  $18.7 \pm 2.6$  h,  $P = 0.018$ ). There was also no intergroup difference in the mean hospital stay duration (HES:  $17.0 \pm 7.5$  days vs. CS:  $19.6 \pm 7.3$  days, ns).

## Discussion

Excessive fluid overbalance after CPB may causes pulmonary impairment and delays recovery. Although colloid osmotic pressure plays an important role in controlling fluid balance, the safety and efficacy of using HES 130/0.4 are controversial [1–4]. Our data suggest the efficacy of HES 130/0.4 in reducing overbalance during CPB and surgery without increasing bleeding or renal dysfunction. It is thought that renal dysfunction may be caused by relative dehydration from HES use. Postoperative care after HES use should aim to prevent dehydration. Use of blood products may be considered, as substitution of HES for a deficit in blood volume depletes coagulation factors. Even with stable volume control using HES, coagulation should be monitored with blood sampling during surgery to avoid overlooking consumption coagulopathy. Although the results of a double-blind randomized prospective pilot study comparing HES 130/0.4 and saline in priming for CPB in France remain awaited [5], the finding of our study—that HES 130/0.4 is beneficial as a priming and replenishment solution during CPB in adult elective valve surgery—should be highlighted for the potential benefit of patients undergoing valve surgery with CPB.

## Compliance with ethical standards

**Conflict of interest** Dr. Masuda received research funding from Senko Medical Instrument Mfg. Co. Ltd. and the Japan Association for Development of Community Medicine. The other authors have no conflicts to disclose.

## References

1. Navickis RJ, Haynes GR, Wilkes MM. Effect of hydroxyethyl starch on bleeding after cardiopulmonary bypass: a meta-analysis of randomized trials. *J Thorac Cardiovasc Surg.* 2012;144:223–30.
2. Myburgh JA, Finfer S, Bellomo R, Billomo R, Cass A, Gattas D, et al. Hydroxyethyl starch or saline for fluid resuscitation in intensive care. *N Engl J Med.* 2012;367:1901–11.
3. Svendsen OS, Farstad M, Mongstad A. Is the use of hydroxyethyl starch as priming solution during cardiac surgery advisable? A randomized, single-center trial. *Perfusion.* 2018;33:483–9.
4. Annane D, Siami S, Jaber S, Martin C, Alatrout S, Declere AD, et al. Effects of fluid resuscitation with colloids vs crystalloids on

mortality in critically ill patients presenting with hypovolemic shock: the CRISTAL randomized trial. *JAMA*. 2013;310:1809–17.

5. ICH GCP/Clinical Trials Registry. Priming of cardiopulmonary bypass with hydroxyethyl starch 130/0.4 or sodium chloride 0.9%: double blind randomized pilot study in adult elective conventional cardiac surgery. Available at: <http://ichgcp.net/clinical-trials-registry/NCT02906514>.

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