Surgery Today (2019) 49:427–434
https://doi.org/10.1007/s00595-018-1752-6

ORIGINAL ARTICLE

Safety and efficacy of hydroxyethyl starch 6% 130/0.4/9 solution versus 5% human serum albumin in thoracic esophagectomy with 3-field lymph nodes dissection

Takeo Fujita[1] · Naoya Okada[1] · Yasumasa Horikiri[1] · Takuji Sato[1] · Hisashi Fujiwara[1] · Shuhei Mayanagi[1] · Jun Kanamori[1] · Hiroyuki Yamamoto[2] · Hiroyuki Daiko[1]

Received: 12 September 2018 / Accepted: 30 November 2018 / Published online: 2 January 2019
© Springer Nature Singapore Pte Ltd. 2019

Abstract

Purpose We investigated the safety and efficacy of administering hydroxyethyl starch 6% 130/0.4/9 (HES130/0.4/9) versus 5% human serum albumin (HSA), perioperatively, to patients undergoing thoracic esophagectomy with 3-field lymph-node dissection for esophageal cancer.

Methods The subjects of this study were 262 patients, scheduled to undergo thoracic esophagectomy for esophageal cancer, who were assigned to one of two groups based on the fluid replacement therapy. We compared the intraoperative and immediate postoperative hemodynamics and incidence of complications in the two groups.

Results Neither group suffered any adverse events. No significant differences were observed in systolic/diastolic blood pressure, heart rate, incidence of postoperative complications, postoperative urine output, or serum creatinine levels, between the groups. A mild postoperative increase (×1.5 increase) in serum creatinine levels was seen in 9.5% and 9.5% of patients in the HSA and HES130/0.4/9 groups, respectively ($p = 0.99$), and a moderate postoperative increase (×2.0 increase) was seen in 4.4% and 3.1%, respectively ($p = 0.84$). Univariate and multivariate analyses revealed that the administration of hydroxyethyl starch was not associated with a postoperative increase in serum creatinine levels.

Conclusion Hydroxyethyl starch 6% 130/0.4/9 was well tolerated and comparable to albumin with respect to its effect on renal function during thoracic esophagectomy with 3-field lymph-node dissection.

Keywords Esophageal cancers · Esophagectomy · Hydroxyethyl starch 6% 130/0.4/9

Introduction

Maintenance of optimal intraoperative fluid balance is of critical importance, especially during traumatic surgical procedures [1, 2]. In fact, the optimal management of volume replacement therapy during anesthesia has helped reduce in-hospital morbidity over the past decades [3]. Thoracic esophagectomy is highly invasive among the cervical/thoracic/abdominal procedures that require precise tissue perfusion and oxygenation. However, mild-to-moderate tissue hypoperfusion and reduced oxygenation during thoracic esophagectomy have been reported occasionally [4, 5]. Although several current guidelines recommend avoiding hypo-tissue perfusion and oxygenation, the safety and efficacy of using hydroxyethyl starch 6% 130/0.4/9 (HES130/0.4/9) during thoracic esophagectomy for esophageal cancer have not been established definitively.

Surgical resection of esophageal cancer has been associated with a high mortality rate [6]. Tissue perfusion is particularly important to optimize blood flow to the gastric conduit because impaired tissue perfusion is a major cause of complications such as anastomotic leak. A multidisciplinary treatment approach, including nutritional support, immunological management, and other preoperative preparations, as

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00595-018-1752-6) contains supplementary material, which is available to authorized users.

✉ Takeo Fujita
takfujit@east.ncc.go.jp

1 Division of Esophageal Surgery, National Cancer Center Hospital East, 6-5-1 Kashiwanoha, Kashiwa, Chiba 277-8577, Japan

2 Division of Anesthesiology, National Cancer Center Hospital East, Kashiwa, Japan

well as modern intraoperative and postoperative care, have improved the immediate postoperative outcomes of esophageal resection remarkably [7]. Maintenance of optimal tissue perfusion and oxygenation is a key determinant of the outcome of thoracic esophagectomy [8, 9]. However, the effect of perioperative HES130/0.4/9 administration during esophageal surgery is not well understood. We conducted the present study to investigate the safety and efficacy of the perioperative administration of HES130/0.4/9 in patients undergoing thoracic esophagectomy for esophageal cancer.

Methods

Patients

Patients who underwent thoracic esophagectomy for esophageal cancer between 2013 and 2014 at the National Cancer Center Hospital East Japan were analyzed prospectively following approval from our institution's investigational review board. Preoperative diagnoses were based on imaging studies, including upper gastrointestinal studies, endoscopy, and conventional cross-sectional imaging (computed tomography). Endoscope-guided biopsy specimens from all patients were examined histologically. Data on the preoperative stage of the disease, histopathological findings, and surgical procedures performed, and outcomes were accessed from the patient medical records.

Thoracic esophagectomy was performed in all patients, under the direction of the regular attending surgeon. For transthoracic esophagectomy, subtotal resection of the esophagus was performed with 3-field regional lymph-node dissection, regardless of the tumor stage. To achieve complete regional lymph-node clearance, we removed the thoracic duct, regardless of the location or type of tumor. In the thoracoscopic approach, principally, the azygos arch is preserved together with the right bronchial artery; however, the azygos arch was transected in all patients who underwent thoracic esophagectomy via the thoracotomy approach. The laparoscopic approach was carried out unless there was bulky lymph node metastasis or a history of laparotomy. The esophagus was usually reconstructed with a gastric tube via the retrosternal route. Right hemi-colic reconstruction was performed via the posterior sternal route if gastrectomy of the remnant stomach was required.

Study design

This was a prospective cohort study. Eligible patients were prospectively assigned to receive either 5% human serum albumin (HSA) solution or HES130/0.4/9 (Voluven®; Otsuka Yakuhin Kogyo, Tokyo, Japan) during surgery. Written informed consent was obtained from all patients. The IRB at the institution approved the study (Approved number #2018-039). A sample size of 260 subjects was required to detect a clinically significant difference in serum creatinine levels (0.5 mg/dL) between the two groups with 80% statistical power at a 2-tailed significance level of 0.05. An increase in serum creatinine by 0.5 mg/dL/day is known to be associated with acute renal dysfunction.

Anesthesia and the administration of hydroxyethyl starch 6% 130/0.4/9 in a balanced electrolyte solution and human serum albumin

The standard institutional anesthetic practice for thoracic esophagectomy was modified to enable the development of intraoperative core hypothermia in this study. No patient was pre-medicated. Briefly, the patient was monitored from when they arrived in the operating room, with electrocardiography, noninvasive blood pressure, pulse oximetry, and capnography. Core temperature was measured in the esophagus every 5 min using a thermistor probe (Mon-a-therm™, Tyco-Mallinckrodt Anesthesiology Product, St. Louis, MO, USA) at room temperature. A 20-gauge catheter was inserted into the forearm vein for fluid and drug administration. Acetate Ringer's solution at room temperature was administered, together with either HSA or HES130/0.4/9 (Voluven®), during the thoracic procedure for esophagectomy. Before the induction of anesthesia, an epidural catheter was inserted in the fifth to sixth thoracic interspace and placed 5 cm beyond the introducing needle tip.

We used 3 mL of epinephrine-containing 1% lidocaine (1:100,000) to detect unintentional intravascular or intrathecal catheter placement, followed by a continuous infusion of 0.375% ropivacaine at 5 mL/h. Anesthesia was induced with 1.5–2.5 mg/kg propofol, 1–2 μg/kg fentanyl, and 0.1 mg/kg vecuronium and maintained with 3% end-tidal sevoflurane in oxygen until tracheal intubation. Anesthesia was then maintained with 2% end-tidal sevoflurane at 40% oxygen (air/oxygen mixture at 4 L/min), supplemented with doses of fentanyl and vecuronium. A heat and moisture-exchanging filter was positioned between the endotracheal tube and the breathing circuit. Patients were covered with a single cotton blanket during the study period. All infusion fluid bags were appropriately warmed before use, regardless of the study arm.

A continuous intravenous infusion of either HSA solution or HES130/0.4/9 (Voluven®) was started using an infusion pump (Terufusor®; TE-312; Terumo, Tokyo, Japan) during the thoracic procedure for esophagectomy. A total of 100 mL of either HAS solution or HES130/0.4/0 (Voluven®) solution was administered during the thoracic procedure, at 150–250 mL/h, dependent on the patient's status and the duration of the thoracic procedure. Simultaneously, patients were warmed intraoperatively with an upper body blanket (Bair Hugger Blanket®; Augustine Medical, Eden Prairie, MN, USA) over a single cotton blanket. The Bair Hugger Model 500 Warming Unit (Augustine Medical) was connected to the blanket at a medium temperature setting (38 °C). After the operation, the endotracheal tube was removed and patients who fulfilled the standard criterion (modified Aldrete score of > 9) were transported from the operating room to the intensive care unit (ICU).

Definition of surgical complications

Surgical site infection (SSI) was diagnosed according to the definition established by the Surgical Wound Infection Task Force 1 and included infections at the incision site or organ/space manipulated during operative intervention. Remote infections were not included in the definition of an SSI, with the exception of bloodstream infections related to an SSI. Symptomatic remote infections were also included in the analysis. Among the remote infections, respiratory infection was defined as the presence of new or progressive infiltrates on chest radiographs, plus at least two of the following signs of respiratory tract infection: temperature > 38 °C, purulent sputum, leukocytosis of $> 1 \times 10^4/\text{mm}^3$ or leukopenia of $< 4 \times 10^3/\text{mm}^3$, and signs of inflammation on auscultation.

Definition of non-infectious surgical complications was judged according to the definition of Clavien–Dindo 2.0 greater than Grade 2. Because there are so many categories of Clavien–Dindo criteria, we analyzed the non-infectious surgical complications based on the responsible organs (such as cardiovascular events or hepatic events) in this study. Diagnostic criteria of postoperative renal dysfunction was based on the RIFLE criteria and AKIN classification.

Perioperative management

Perioperative management was conducted in accordance with the same clinical management pathway (CMP) for all patients, regardless of the type of abdominal approach. All patients received enteral nutrition through a nasal feeding tube until the start of oral intake on postoperative day (POD) 6. None of the patients in this study received total parenteral nutrition in the postoperative period[7)]. Briefly, fluid balance was achieved through a peripheral line, with additional enteral feeding on the first day after surgery. Enteral feeding was administered through a nasoenteral feeding tube (10-Fr), the distal end of which was placed in the jejunum. The rate of enteral feeding was 10 mL/h on the first day after surgery and gradually increased to 120 mL/h by POD 6, in the absence of any problems. Enteral nutrition was discontinued after the absence of anastomotic leakage was confirmed on POD 6. For antibiotic prophylaxis, all patients were given cefmetazole sodium 1 g 30 min before esophagectomy, and every 3 h during the procedure. There were no additional doses given after surgery for prophylaxis in the clinical management pathway.

Perioperative management was performed by the same clinical staff in the same environment, using the ICU and subsequent ward-based facilities. The same principles of care were applied to both groups. CMP was applied in both the ICU on PODs 1 and 2, and in the surgical ward from POD 3 onward. Briefly, the endotracheal tube was removed in the operating room or on arrival in the ICU. Patients remained in the ICU for 1 day after surgery. Bronchial washout with a fiberoptic bronchoscope was not performed routinely. The cervical drain and thoracic drain were removed on POD 1. On POD 6, a radiographic contrast-agent swallow examination was performed to evaluate the anastomosis and any passage problems. If this examination showed no leakage or obstruction, the nasogastric tube was removed and oral intake was initiated according to the postoperative diet program: liquids on the first day of oral intake, semi-solid food on the second and third days, and solid food from the fourth day. In the absence of any complications, the patient was enrolled in the postoperative rehabilitation program and discharged on POD 10-14.

If there were any abnormal clinical findings such as hypoxia, leukocytosis, or abnormal pleural drainage during the course of postoperative CMP, computed tomography, and subsequent radiographic examinations were performed to diagnose and optimally manage the issue as quickly as possible.

Statistical analysis

Between-group differences were analyzed using the Chi-squared test and the Mann–Whitney *U* test. Univariate analysis and multivariate analysis were performed using stepwise regression models to identify clinical and histopathological variables associated with the success or failure of treatment with octreotide. A p value < 0.05 was considered to indicate a significant difference.

Results

Of the 262 patients in this study, 136 received HSA (control group), and 126 received HES130/0.4/9. HES130/0.4/9 was well tolerated and no adverse events specific to its administration were observed. All patients in this study were treated successfully with CMP without any problems. There were no significant differences between the HSA and the HES130/0.4/9 groups in baseline patient characteristics, including age, gender, body mass index, ASA grade, pre-operative treatment, and clinical stage of the disease (Table 1). Table 2 summarizes the operative procedures and parameters during esophagectomy. There were no significant

Table 1 Patients' characteristics

Variables	HSA group ($n=136$)	HES130/0.4/9 group ($n=126$)	p value
Age (mean ± SD)	66.3 ± 8.3	65.3 ± 8.8	0.66
Gender (*M:F*)	114:22	110:16	0.42
Body mass index (mean ± SD)	21.8 ± 2.2	21.3 ± 2.7	0.65
Serum creatinine level (mg/dL; mean ± SD)	0.77 ± 0.14	0.74 ± 0.11	0.56
ASA grade			0.99
Grade 1	46	42	
Grade 2	90	84	
Preoperative treatment			0.37
Chemotherapy	65	68	
Chemo-radiation	13	9	
Clinical stage (UICC 7th)			0.96
Stage I	33	34	
Stage II	41	37	
Stage III	54	48	
Stage IV	8	7	

HAS 5% human serum albumin, *HES130/0.4/9* hydroxyethyl starch 6% 130/0.4/9

Table 2 Operative procedure and parameters during esophagectomy

Variables	HSA group ($n=136$)	HES130/0.4/9 group ($n=126$)	p value
Type of surgical approach			0.03
Thoracoscopic	105	110	
Thoracotomy	31	16	
Type of surgical approach			0.61
Laparoscopic	117	111	
Laparotomy	19	15	
Total time of procedure (min)	378.1	360.5	0.10
Total time of thoracic procedure (min)	190.0	177.2	0.19
Total amount of infusion during surgery (mL)	3621.5	3731.9	0.27
Total amount of blood loss during surgery (mL)	229.8	174.5	0.50

HAS 5% human serum albumin, *HES130/0.4/9* hydroxyethyl starch 6% 130/0.4/9

differences in the abdominal surgical approach, total duration of the procedure, total time of the thoracic phase of the procedure, volume of intraoperative infusion, total urine output during surgery, or blood loss, except for the thoracic surgical approach ($p=0.03$).

Figure 1 shows the intraoperative and early postoperative changes in systolic blood pressure. There were no significant differences between the groups at the baseline ($p=0.65$). No significant differences were observed in the immediate pre- and postoperative systolic blood pressure or diastolic blood pressure before and after esophagectomy between the groups (Fig. 2). Patients in the HES130/0.4/9 group had significantly higher heart rates 2 h and 3 h into the esophagectomy procedure; however, there were no significant differences in heart rates in the immediate postoperative period (Fig. 3).

Table 3 summarizes the short-term outcomes after esophagectomy. There were no significant differences in the incidence of postoperative pneumonia (8.0% in the HSA group versus 7.1% in the HES130/0.4/9 group, $p=0.95$), or in the incidence of anastomotic leakage (surgical site infection; 8.8% versus 6.3%, respectively, $p=0.62$) between the groups. There were no differences in cardiovascular events ($p=0.86$), blood coagulation events ($p=0.93$), or hepatic events ($p=0.96$) between the groups. No significant differences were found in the incidence of infectious surgical complications (12.5% versus 11.1%, respectively, = 0.87). There were no in-hospital deaths in either group. The success rates of CMP were similar in the two groups (75.7% versus 80.9%, respectively; $p=0.38$).

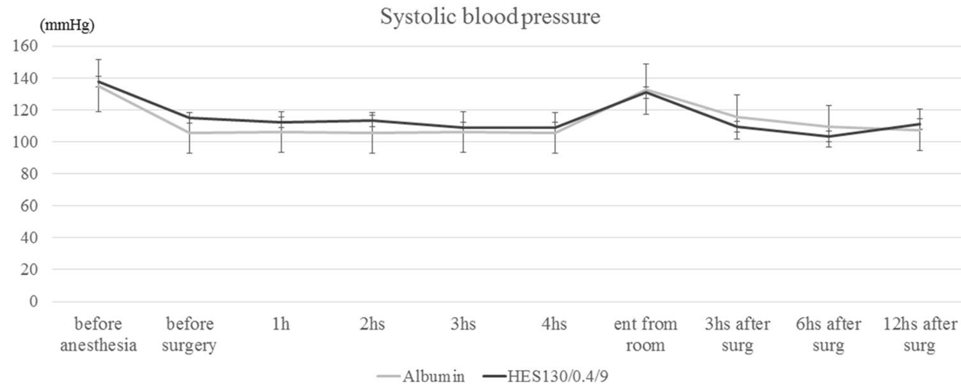

Fig. 1 Systolic blood pressure during esophagectomy. There were no significant differences in systolic blood pressures during esophagectomy between the 5% human serum albumin (HSA) and hydroxyethyl starch 6% 130/0.4/9 (HES130/0.4/9) groups

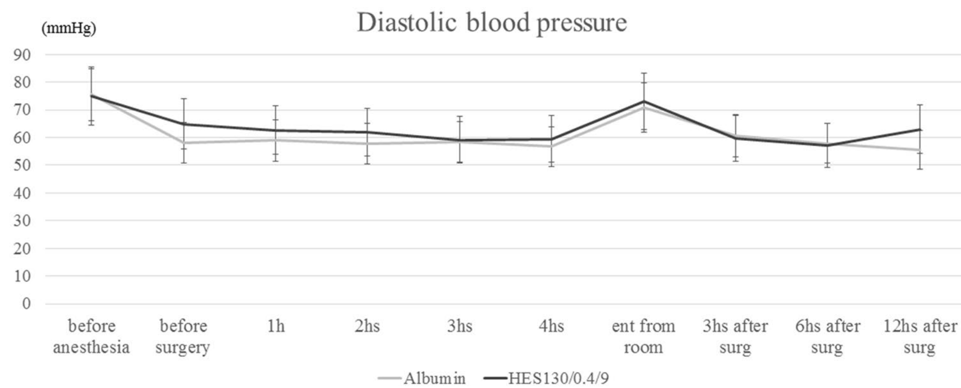

Fig. 2 Diastolic blood pressure during esophagectomy. There were no significant differences in diastolic blood pressures during esophagectomy between the HSA and the HES130/0.4/9 groups

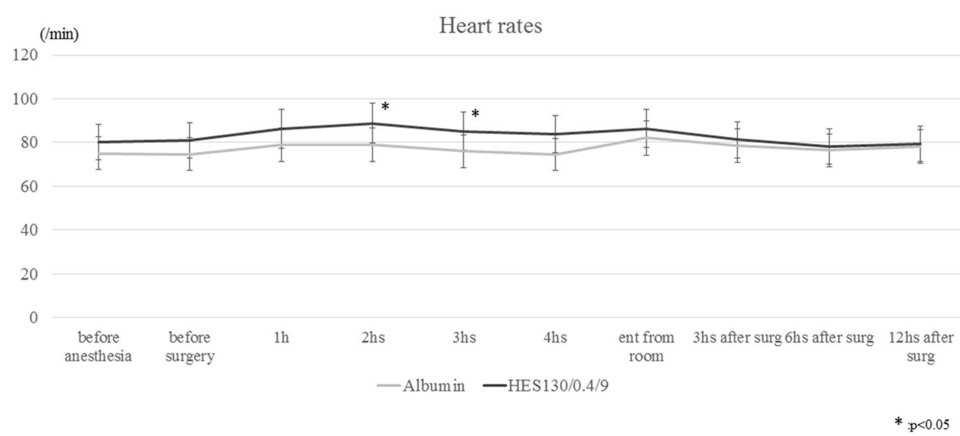

Fig. 3 Heart rates during esophagectomy. No significant difference was observed at most time-points during esophagectomy between the HSA and the HES130/0.4/9 groups

No significant difference was observed in total postoperative urine output (867.2 mL versus 935.7 mL, respectively; $p=0.18$), or total urine output during PODs 0–1 and 1–2 (1005.1 mL versus 920.5 mL; $p=0.44$, and 948.2 mL versus 1152.9 mL; $p=0.21$, respectively) (Fig. 4a). Similarly, there was no significant difference in serum creatinine levels preoperatively ($p=0.31$), or on PODs 0–1 and PODs 1–2 (Fig. 4b).

The use of HES130/0.4/9 as renal-replacement therapy in the intensive care unit was reported previously to be a potential risk factor. As shown in Table 4, there was no significant difference in the elevation of serum creatinine levels between the groups. Most postoperative serum creatinine levels elevated by more than ×1.5 and ×2.0 were detected on the second morning after surgery (POD2). Univariate and multivariate analyses revealed that none of the clinical parameters, including the administration of HES130/0.4/9, were associated with an elevation in the serum creatinine level, except for total blood loss ($p=0.04$) (Table 5).

Table 3 Postoperative surgical complications

Variables	HSA group ($n=136$)	HES130/0.4/9 group ($n=126$)	p value
Pneumonia (%)	11 (8.0%)	9 (7.1%)	0.95
Cardiovascular events (%)	16 (11.7%)	14 (11.1%)	0.86
Coagulation events (%)	2 (1.4%)	3 (2.3%)	0.93
Hepatic events (%)	2 (1.4%)	2 (1.5%)	0.96
Anastomotic leakage (%)	12 (8.8%)	8 (6.3%)	0.62
Surgical site infection (%)	17 (12.5%)	14 (11.1%)	0.87
In hospital death (%)	1 (0.7%)	1 (0.7%)	0.95
Post-operative hospital stay (days, median)	16.5	15.0	0.19
Success rate of CMP (%)	75.7	80.9	0.38

HAS 5% human serum albumin, *CMP* Clinical management pathway, *HES130/0.4/9* hydroxyethyl starch 6% 130/0.4/9

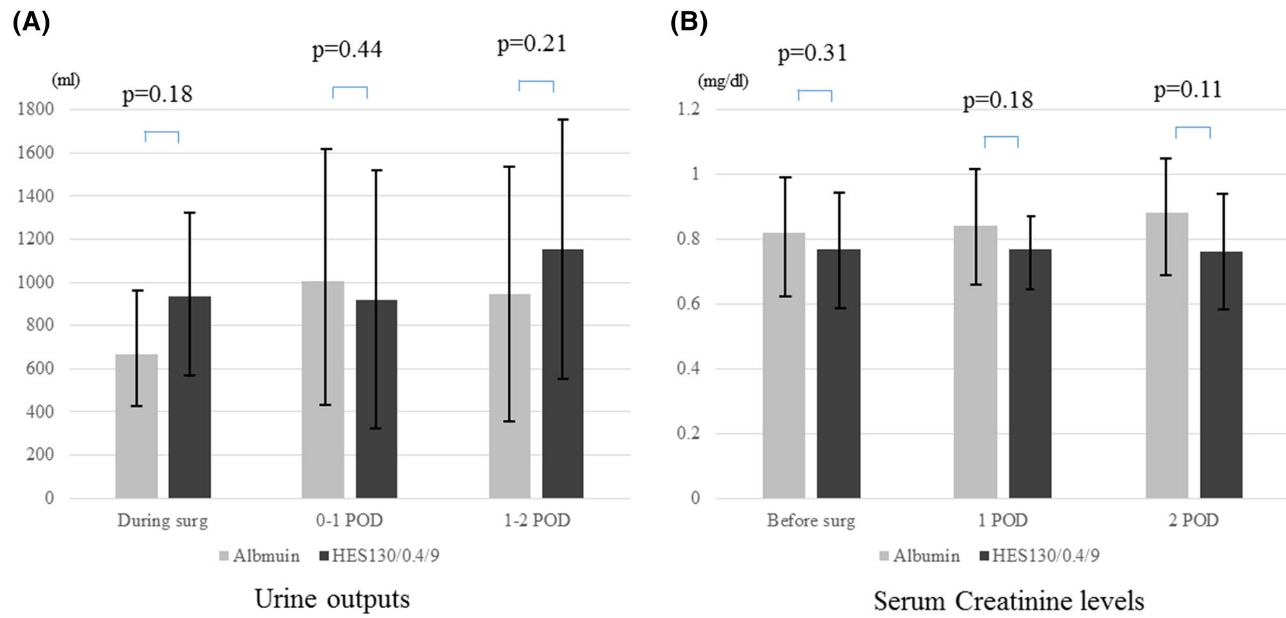

Fig. 4 Intraoperative urine output and serum creatinine levels on postoperative days (PODs) 0–1 and 1–2. No significant differences were observed between the HSA and HES130/0.4/9 groups in urine output or serum creatinine levels at the three time-points

Table 4 Postoperative increase in serum creatinine levels

Variables	HSA group ($n=136$)	HES130/0.4/9 group ($n=126$)	p value
Postoperative renal dysfunction (increase serum Cre[a] × 1.5)	13 (9.5%)	12 (9.5%)	0.99
Postoperative renal dysfunction (increase serum Cre[a] × 2.0)	6 (4.4%)	4 (3.1%)	0.84

HAS 5% human serum albumin, *HES130/0.4/9* hydroxyethyl starch 6% 130/0.4/9

[a]Creatinine

Discussion

With improvements in anesthetic techniques, the surgical field was poised to expand the number of operative procedures that could be performed safely. Among the development of perioperative surgical management factors, optimization of tissue perfusion is considered to be of great importance to the success of surgery. Human albumin is a standard therapy in this setting, in terms of its benefits over crystalloids because of the physiological hypoproteinemia in the acute phase of thoracic esophagectomy. Colloids such as HES are often preferred over pure crystalloid regimens because of their prolonged intravascular

Table 5 Results of univariate and multivariate analyses

	Univariate	Multivariate		
	p value	Odds ratio	95% CI	*p* value
Age (year)	0.43	1.04	0.97–1.21	0.44
Gender	0.31	1.62	0.31–11.41	0.71
Body mass index	0.44	1.19	0.86–1.33	0.89
ASA grade	0.24	1.72	0.71–4.48	0.46
Pre-operative serum creatinine	0.27	1.92	0.35–5.06	0.76
Total amount of infusion	0.28	1.00	0.97–1.11	0.37
Total amount of urine output	0.61	0.99	0.94–1.12	0.24
Total time of operation	0.33	1.01	0.98–1.03	0.13
Time of thoracic procedure	0.07	1.14	0.87–1.20	0.09
Total blood loss	0.06	1.11	1.03–1.12	0.04
Pre-operative treatment	0.79	1.51	0.37–3.63	0.87
HES130/0.4/9	0.33	0.32	0.87–1.25	0.28

HES130/0.4/9 hydroxyethyl starch 6% 130/0.4/9

half-life and enhanced intravascular volume effect to maintain tissue perfusion and oxygenation for surgical, traumatic, and critical care patients.

Six percent hydroxyethyl starch (HES 130/0.4) is an artificial colloid with a plasma-expanding effect superior to that of crystalloids. It is also less allergenic and cheaper than albumin. Although several prospective randomized trials have assessed the safety and efficacy of various surgical procedures [10–12], clinical guidance to maintain tissue perfusion and oxygenation during thoracic esophagectomy is lacking. In the field of esophageal surgery, especially three-field dissection, few studies have investigated the appropriate procedure for maintaining optimal tissue perfusion and oxygenation. Because thoracic esophagectomy with three-field lymph node dissection involves gastroduodenal manipulation for conduit formation and a cervical procedure for lymph node dissection and anastomosis, we must rely on data acquired not only in non-cardiac thoracic surgery, but also in the general surgical techniques applied in abdominal surgical procedures. Moreover, appropriate perfusion of the gastric conduit is crucial to the success of anastomotic procedures. Therefore, the results of the present study are valuable when considering the best practice to maintain appropriate tissue perfusion and oxygenation during thoracic esophagectomy.

To establish appropriate timing of perioperative HES130/0.4/9 in the present study, it was administered mainly during the thoracic procedure for thoracic esophagectomy. Previous studies have focused on the amount and duration of HES130/0.4/9 delivery for several types of surgery, particularly cardiovascular surgery [13, 14]. Linden and colleagues reported comparable efficacy of HES130/0.4/9 and 5% human serum albumin when used for volume replacement in pediatric patients aged 2–12 years old undergoing open-heart surgery [15]. This finding was consistent with that reported by Hung and colleagues in the context of major abdominal surgery [16]. Therefore, given that vasopressor agents are commonly used during thoracic surgical procedures, these findings indicate that HES130/0.4/9 is effective as volume replacement therapy in thoracic esophagectomy, particularly three-field lymph nodes dissection. The results of the present study demonstrate that HES130/0.4/9 maintains tissue perfusion effectively and does not impair postoperative renal function or cause surgical complications.

With respect to renal dysfunction, it is not fully established whether HES130/0.4/9 is associated with postoperative renal dysfunction, particularly in the field of planned surgery. A previous study demonstrated that the administration of HES130/0.4/9 was significantly associated with the elevation of serum creatinine levels in patients in the intensive care unit [17]. However, the risk of renal dysfunction was not fully addressed, particularly for patients undergoing surgery for cancer. In a previous study, elderly patients who received intraoperative HES130/0.4/9 during hepatic tumor resection showed no impairment in renal function or in fibrinolysis and coagulation [18]. The present study also demonstrated that HES130/0.4/9 was not associated with an elevation in serum creatinine levels or surgical complications such as coagulation events in patients undergoing thoracic esophagectomy. A recent study demonstrated that hydroxyethyl starch, but not Ringer's lactate, maintained gastrointestinal recovery time with no impairment of food tolerance in patients undergoing laparoscopic cancer surgery [19]. Furthermore, a certain type of hydroxyethyl starch solution was reported to reduce the metastatic potential of the colon cancer cell line stimulated by activated platelets, by inhibiting platelet activation [20]. Considering these notions, the administration of perioperative HES130/0.4/9 is safe and effective as volume replacement therapy and confers a cost advantage in thoracic esophagectomy.

The present study has several limitations. First, it covered a period of more than 2 years, during which time the thoracic and abdominal surgical devices differed slightly. However, the procedures of anesthesia and perioperative patient management were consistent with the same CMP, which may be considered a strength of the study. Second, the surgical approach used for the thoracic procedure in the control group differed from that used for the HES130/0/4/9 group ($p = 0.03$). Thus, we conducted univariate and logistic multivariate analyses to identify potential clinical parameters other than HES130/0/4/9 administration, that were associated with an elevation of the serum creatinine level. Multivariate analysis revealed that no clinical parameters were associated with an elevation of the serum creatinine level, except for total blood loss (Table 5).

In conclusion, the results of the present study indicate that HES130/0.4/9 administration is effective for the maintenance of tissue perfusion and oxygenation during thoracic esophagectomy with 3-field lymph-node dissection. Further analysis, including investigations on a larger number of patients in a randomized control setting, would provide more detailed results on the potential influence of HES130/0.4/9 in thoracic esophagectomy.

Acknowledgements We thank the members of the Division of Esophageal Surgery for their critical discussion of our manuscript. We also thank the members of the Division of Gastrointestinal Oncology for reviewing and discussing the study.

Author contributions All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated sufficiently in the work to take public responsibility for the content, including participation in the concept, design, analysis, writing, or revision of the manuscript.

Compliance with ethical standards

Conflict of interest There are no financial relationships or support that may pose a conflict of interest.

Disclosure The content has not been published or submitted for publication elsewhere.

References

1. Nishi M, Hiramatsu Y, Hioki K, Kojima Y, Sanada T, Yamanaka H, et al. Risk factors in relation to postoperative complications in patients undergoing esophagectomy or gastrectomy for cancer. Ann Surg. 1988;207:148–54.
2. Böck JC, Barker BC, Clinton AG, Wilson MB, Lewis FR. Post-traumatic changes in, and effect of colloid osmotic pressure on the distribution of body water. Ann Surg. 1989;210:395–403.
3. Kozek-Langenecker SA, Afshari A, Albaladejo P, Santullano CA, De Robertis E, Filipescu DC, et al. Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology. Eur J Anaesthesiol. 2013;30:270–382.
4. Raue W, Haase O, Langelotz C, Neuss H, Müller JM, Schwenk W. Influence of pre-operative fluid infusion on volume status during oesophageal resection—a prospective trial. Acta Anaesthesiol Scand. 2008;52:1218–25.
5. Ishikawa S, Nakazawa K, Makita K. Progressive changes in arterial oxygenation during one-lung anaesthesia are related to the response to compression of the non-dependent lung. Br J Anaesth. 2003;90:21–6.
6. Müller JM, Erasmi H, Stelzner M, Zieren U, Pichlmaier H. Surgical therapy of oesophageal carcinoma. Br J Surg. 1990;77:845–57.
7. Fujita T, Daiko H. Early enteral nutrition reduces the rate of life-threatening complications after thoracic esophagectomy in patients with esophageal cancer. Eur Surg Res. 2012;48:79–84.
8. Boyle NH, Pearce A, Hunter D, Owen WJ, Mason RC. Intraoperative scanning laser Doppler flowmetry in the assessment of gastric tube perfusion during esophageal resection. J Am Coll Surg. 1999;188:498–502.
9. Bludau M, Hölscher AH, Vallböhmer D, Gutschow C, Schröder W. Ischemic conditioning of the gastric conduit prior to esophagectomy improves mucosal oxygen saturation. Ann Thorac Surg. 2010;90:1121–6.
10. Feldheiser A, Pavlova V, Bonomo T, Jones A, Fotopoulou C, Sehouli J, et al. Balanced crystalloid compared with balanced colloid solution using a goal-directed haemodynamic algorithm. Br J Anaesth. 2013;110:231–40.
11. Rasmussen KC, Johansson PI, Højskov M, Kridina I, Kistorp T, Thind P, et al. Hydroxyethyl starch reduces coagulation competence and increase blood loss during major surgery. Results from a randomized controlled trial. Ann Surg. 2014;2:249–54.
12. 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. 2013;112:281–9.
13. Standl T, Lochbuehler H, Galli C, Reich A, Dietrich G, Hagemann H. HES 130/0.4 (Voluven) or human albumin in children younger than 2 year undergoing non-cardiac surgery. A prospective, randomized, open label, multicenter trial. Eur J Aesthesiol. 2008;25:437–45.
14. 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. Anesth Pain Med. 2016;18:Epub.
15. Van der Linden P, De Villé A, Hofer A, Heschl M, Gombotz H. Six percent hydroxyethyl starch 130/0.4 (Voluven®) versus 5% human serum albumin for volume replacement therapy during elective open-heart surgery in pediatric patients. Anesthesiology. 2013;119:1296–309.
16. Hung MH, Zou C, Lin FS, Lin CJ, Chan KC, Chen Y. New 6% hydroxyethyl starch 130/0.4 dose not increase blood loss during major abdominal surgery- a randomized control trial. J Formos Med Assoc. 2014;113:429–35.
17. Myburgh JA, Finfer S, Bellomo R, Billot L, Cass A, Gattas D, et al. Hydroxyethyl starch or saline for fluid resuscitation in intensive care. N Engl J Med. 2012;367:1901–11.
18. Guo JR, Yu J, Jin XJ, Du JM, Guo W, Yuan XH. Effects of acute normovolemic hemodilution on perioperative coagulation and fibrinolysis in elderly patients undergoing hepatic carcnectomy. Chin Med Sci J. 2010;25:146–50.
19. Li Y, He R, Ying X, Hahn RG. Ringer's lactate, but not hydroxyethyl starch,prolongs the food intolerance time after major abdominal surgery; an open-labelled clinical trial. BMC Anesthesiol 2015;72.
20. Liang H, Yang C, Zhang B, Wang H, Liu H, Zhao Z, et al. Hydroxyethyl starch 200/0.5 decrease circulating tumor cells of colorectal cancer patients and reduces metastatic potential of colon cancer cell line through inhibiting platelets activation. Med Oncol J. 2015;32:151.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.