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Original Article

Nephrotoxicity of hydroxyethyl starch 130/0.4 infusion in patients receiving coronary artery bypass surgery: a retrospective study

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Abstract: Background: Hydroxyethyl starch (HES) is helpful to maintain the stable haemodynamics in patients receiving cardiac surgery. However, there are concerns regarding the nephrotoxicity of HES. Objectives: This study was to evaluate the nephrotoxicity of HES 130/0.4 in patients receiving on-pump coronary artery bypass surgery. Methods: Patients receiving on-pump coronary artery bypass surgery in Xinqiao Hospital between September 1, 2012 and December 31, 2014 were retrospectively reviewed. Acute kidney injury (AKI) was defined according to the RIFLE criteria, and the renal injury (sCystatin C) was compared between patients with and without HES 130/0.4 infusion in the first 72 h after surgery. Results: A total of 149 patients were included. The incidence of AKI within 72 h was similar between two groups, and the risk for AKI (95% CI, 0.979-1.139) was not increased by hetastarch, even at a dose of 37 ml/kg. Conclusion: HES 130/0.4 does not increase the risk for AKI when it is used for the volume therapy in patients receiving coronary artery bypass surgery, and may neither enhance tubular injury nor alter the glomerular filtration.

Keywords: Bypass, nephrotoxicity, hydroxyethyl starch

Introduction

The peri-operative use of hydroxyethyl starch (HES) is to improve the hypovolemia and ensure adequate tissue oxygenation while avoiding fluid overload because HES has a better volume-expanding effect than gelatin (4%) and Ringer's solution [1]. However, despite that fluid resuscitation for hypovolemia is the mainstay of medical management strategy for cardiac surgical patients, there is considerable controversy about the effects of HES on the kidney function. In recent years, meta analysis shows that HES at a high dose may increase the risk for renal injury, especially in critically ill patients and those with septicopyemia [2-6], and postoperative acute kidney injury (AKI), which is known to increase the morbidity and mortality, because HES increases the viscosity of blood and urine resulting in osmotic nephrosis and the uptake of HES into proximal tubular epithelial cells [7-9]. Therefore, it is recommended that HES 200/0.5 is avoided following cardiac surgery [10].

Nevertheless, recently, some studies indicate that HES may not increase the incidence of AKI following surgery [11-14], and HES 130/0.4, a new generation HES with less molecular and substitution, has been found to be less nephrotoxic. Heart surgery is a complicated course, and the hemodynamic changes are significantly different in patients receiving different cardiac surgeries. Thus, the nephrotoxicity of HES should be evaluated on the basis of type of surgery.

Although there is evidence showing that infusion of 4 ml/kg HES 200/0.5 at 30 min after anesthesia induction may not increase the incidence of AKI in on-pump coronary artery bypass surgery (CABG) patients [15], the dose of HES is relatively higher in on-pump CABG patients, the risk for AKI is dose-dependent, and the cut-off dose of HES for the prediction of AKI might be up to 14 mL/kg [10]. This study was to evaluate the nephrotoxicity of 6% HES 130/0.4 in on-pump CABG patients, and determine the relationship between HES and renal toxicity.

Materials and methods

Patients

This study was approved by the Institutional Review Board of Xin Qiao Hospital. Patients undergoing on-pump CABG in Xin Qiao Hospital from January 2012 to May 2014 were recruited into present study. Inclusion criteria were as follows: All Patients undergoing isolated on-pump CABG in XinQiao hospital from January 2012 to May 2014 were collected. Exclusion criteria were as follows: The Emergency case, simultaneous valve procedure, repeat cardiac surgery, patients with the history of myocardial infarction, preoperative renal dysfunction, preoperative congestive heart failure or with other serious complications were excluded. Patients admitted into Emergency department, with repeat cardiac surgery, a history of myocardial infarction, preoperative renal dysfunction, preoperative congestive heart failure, other serious complications or concomitant valve procedure were excluded from this study. Finally, 149 patients were included in this study.

The operation under cardiopulmonary bypass (CPB) was performed under mild hypothermia. The circuit was primed with Ringer's solution and sodium chloride the volume of which was determined by body weight and hematocrit, the average flow rate was about 2.3 L/min/m^2, and the mean arterial pressure was controlled between 50 to 70 mmHg. There were no liquid management protocols during surgery, the type of fluid and use of cardioactive drugs were determined by anesthesiologists and physicians on the basis of hemodynamics.

There is evidence showing that the risk for AKI after infusion of pentastarch 10% (250 kDa, 0.45) in cardiac surgery is dose-dependent, the cut-off dose used to predict AKI was 14 mL/kg [10], and a meta analysis including six randomized controlled trails (RCTs) found 6% tetrastarch at 30-43 ml/kg is associated with renal replacement therapy in severe sepsis patients [3]. Thus, in the present study, patients were divided into 4 groups according to the dose of HES: patients in N-HES group did not receive HES infusion; patients in H-HES received infusion of HES at >30 ml/kg; patients in L-HES groups received infusion of HES at <13 ml/kg; patients in M-HES group received infusion of HES at 13-30 ml/kg. HES infusion was conducted within first 72 h after surgery.

Observations

The baseline demographic features, comorbidities, history of myocardial infarction, peripheral vascular disease and left ventricular ejection fraction (LVEF) were recorded before surgery. The number of bypass, duration of CPB and clamping, dose of HES 130/0.4 used, the number of red blood cells and plasma, and liquid management were also recorded during surgery.

The AKI was defined as an increase in serum creatinine (sCr) by 50% or 0.3 mg/dl (26.5 μmol/L) within 48 h and an increase in serum sCystatin C. sCystatin C has been found to reflect the early glomerular filtration, possess a more strong association with urine interleukin 18 and kidney injury molecule 1 in children undergoing cardiac surgery [16], and has been used as a predictor of disease severity in the elderly hypertension and coronary heart disease [17]. sCr and sCystatin C were recorded before surgery and 0, 3 and 7 days after surgery (POD0, POD3 and POD7).

Calculation of sample size

Based on a pilot study on 50 patients, the difference of CystC between N-HES group and HES group was 0.2 mg/L and standard deviation (SD) was 0.4, 32 patients were required to determine the difference in the renal injury when using α of 0.05 and β of 0.8. Doubling the number of patients was necessary to account for other risk factors

Statistical analysis

In a first stage, descriptive analysis of the baseline variable of patients and procedure-related variables was performed, and then the difference between HES groups and N-HES group were compared to determined the homogeneity of these groups, among them, distributed variables were compared using independent samples T test, categorical variables were compared using the Pearson chi-square test. Secondly, univariate analysis was performed to determine the differences in renal function between these groups in terms of the usage of HES. Finally, in order to explore the association between HES and AKI, bivariate logistic regression models were constructed to determine if 6% hetastarch remained an independent predictor of AKI in cardiac operation after control-

Table 1. Patients' characteristics of N-HES group and HES group before surgery

	ALL, n=149		N-HES, n=38		L-HES, n=44		*P* value	M-HES, n=50		*P* value	H-HES, n=17		*P* value
	Mean	SD	Mean	SD	Mean	SD		Mean	SD		Mean	SD	
HES (ml/kg.72 h)	13.27	12.16	0	0	8.32	2.57	0.000	19.61	5.17	0.000	37.12	7.25	0.000
Age	59.36	10.20	60.16	9.38	61.55	8.52	0.485	56.82	11.13	0.140	59.35	12.21	0.790
BMI	24.98	3.19	24.90	3.31	25.77	3.40	0.258	24.95	2.57	0.942	23.38	3.59	0.134
EF (%)	61.24	9.40	59.05	12.11	63.56	7.42	0.134	59.76	9.52	0.838	61.01	11.54	0.688
sCystatin C, mg/L	1.03	0.38	1.16	0.66	1.03	0.33	0.369	1.03	0.40	0.424	0.97	0.16	0.280
sCr, ummol/L	76.74	18.87	72.95	13.94	78.36	21.62	0.501	77.93	19.21	0.488	71.03	10.27	0.705
	N: %		N: %		N: %		P# value	N: %		P# value	N: %		P# value
Male (%)	85.9%		100%		79.5%		0.003	82%		0.006	82.4%		0.008
Diabetes (%)	26.2%		21.1%		31.8%		0.273	28%		0.456	17.6%		0.770
Hypertension (%)	55%		34.2%		75%		0.000	50%		0.139	64.7%		0.035
Valve disease (%)	37.6%		13.2%		43.2%		0.003	48%		0.001	47.1%		0.006

Note: BMI, body mass index; EF, ejection fraction; P, independent samples t-test, compared with N-HES group; P#, chi-square test, vs N-HES group.

Table 2. Patients' characteristics of N-HES group and HES groups during the surgery

	ALL		N-HES		L-HES		P	M-HES		P	H-HES		P
	Mean	SD	Mean	SD	Mean	SD		Mean	SD		Mean	SD	
Number of the graft	3.17	0.63	3.25	1.14	3.10	0.50	0.665	3.20	0.61	0.895	3.18	0.53	0.817
Time of CPB (min)	125.54	27.42	124.45	25.64	127.15	27.41	0.765	119.62[d]	19.99	0.519	137.92[c]	42.6	0.375
Time of aortic cross-clamp (min)	51.27	33.61	76.10	16.91	68.50	21.84	0.313	66.93	12.49	0.076	63.00	20.38	0.128

Note: CPB, cardiopulmonary bypass; P, independent samples t-test, compared with N-HES group; c and d, one-way analysis; c, P<0.05, vs M-HES group; d, P<0.05 vs H-HES group.

ling for the other variables that significant by univariate analysis or thought to be significant affected the renal function. Normally Distributed variables were expressed as mean ± SD and Categorical variables were expressed in percentage.

Data with normal distribution are expressed as mean ± SD and categorical variables are expressed as percentages. Statistical analysis was performed with SPSS version 18.0 for Windows.

Results

Patients' characteristics

A total of 149 patients who underwent isolated on-pump CABG surgery between January 2012 and May 2014 were included into this study. The baseline characteristics are shown in **Table 1**. Most of patients (85.9%) were male, the median age was 59.36 years, the average body mass index (BMI) was 24.98±3.19, 26.2% of patients had diabetes and 55% patients had hypertension. The cardiac function was also determined in these patients: the cardiac function was New York Heart Association (NYHA) class II in 40 (31.5%) patients, and class III in 77 (60.6%) patients. The mean ejection fraction (EF) was 61.24%. Although patients receiving valve surgery were excluded, many patients (37.6%) still had concomitant valve diseases (**Table 1**). In this study, HES was used for volume expansion in 111 (74.5%) patients, and the mean dose of HES in the first 72 h was 17.81±10.83 ml/kg. The all patients were divided into 4 groups (N-HES, L-HES, M-HES, H-HES) according to the dose of HES.

Comparison of N-HES group and HES groups

Table 1 shows there were no significant differences in the age, BMI, diabetes, EF and preoperative kidney function between N-HES group and HES group. When compared with N-HES, the proportion of patients with hypertension was higher in HES group (especially L-HES subgroup), and patients in HES group were more likely to have valve diseases.

All the patients underwent isolated CABG surgery under CPB (**Table 2**), most patients required a median number of 3 coronary bypasses, the mean time of CPB was 125.54±27.42 min, and 51.27±33.61 min for aortic cross-clamping. There were not significant differences in the number of coronary

Table 3. Blood loss and blood transfusion of N-HES group and HES group

Time	Variables (ml)	N-HES		L-HES		P	M-HES		P	H-HES		P
		Mean	SD	Mean	SD		Mean	SD		Mean	SD	
Operation	Bleeding	356.43	140.38	466.54	162.93	0.101	440.77	163.35	0.207	450.91	200.47	0.295
	Blood	733.33	173.21	758.14	331.11	0.829	695.43	366.16	0.764	647.06	320.39	0.462
	Red cell	355.56	218.58	423.26	258.97	0.469	375.87	211.83	0.794	352.94	218.28	0.977
	Plasma	377.78	66.67	334.88	178.46	0.230	319.57	199.58	0.122	294.12	174.89	0.094
POD0-POD3	Blood	977.78	392.99	1000.00	474.09	0.896	1156.30	656.87	0.436	1070.59	360.15	0.550
	Red cell	400.00	264.58	530.23	348.83	0.297	701.96	507.98	0.016	682.35	316.69	0.032
	Plasma	577.78	323.18	469.77	305.14	0.343	454.35	312.49	0.286	388.24	217.61	0.087

Note: P, independent samples t-test, vs N-HES group.

Table 4. Fluid infused urine output and fluid discharged in N-HES group and HES groups

		Operation	POD0	POD1	POD2	POD3
N-HES	Fluid infused	2232.44±541.12^{d}	5567.20±645.81	3053.30 ±599.95	3203.90 ±365.16	3352.56 ±520.96
	Urine output	1349.29±530.77	4301.50±700.52^{c}	2244.00±687.86	2578.00±341.17	2881.50±321.21^{d}
	Fluid discharged	1638.57±514.73	5533.00±1020.19	2586.20±605.84	2841.00±347.08	3224.44±347.56^{b,c,d}
L-HES	Fluid infused	2406.35±758.00^{c,d}	5595.81±1342.06	2697.56±541.10^{d}	2938.93±426.01	2994.08±561.78
	Urine output	1383.08±652.09	4007.09±1068.66^{c}	2244.33±630.82	2403.14±636.40	2426.72±684.25
	Fluid discharged	1880.13±683.47	5273.49±1214.83	2609.09±629.43	2608.81±634.76	2821.79±499.94^{a}
M-HES	Fluid infused	2844.60±938.03^{b}	4909.45±1980.51	2788.71±577.56	3027.92±627.10	3015.45±719.71
	Urine output	1267.22±484.24	3487.69±1263.20^{a,b}	2163.78±476.05	2390.41±521.63	2594.27±626.51
	Fluid discharged	1627.00±611.35	4640.45±1714.99	2563.57±547.55	2628.35±507.07	2832.42±579.80^{a,d}
H-HES	Fluid infused	3052.29±1032.76^{a,b}	5504.71±2041.67	3060.06±692.43^{b}	2962.53±421.13	2877.82±769.32
	Urine output	1302.86±783.56	3568.24±1198.79	2316.59±425.22	2486.76±418.42	2282.08±247.23a^{a}
	Fluid discharged	1672.14±856.52	5127.06±1768.11	2732.00±542.67	2712.94±390.07	2467.73±351.58^{a,c}

Note: The day of surgery refers to POD0; P, independent samples t-test, vs N-HES group; ^{a,b,c,d} one-way analysis of variance, ^{a}P<0.05, vs N-HES group, ^{b}P<0.05, vs L-HES group; ^{c}P<0.05, vs M-HES group; ^{d}P<0.05, vs H-HES group.

bypass and time of CPB between N-HES group and HES group.

The blood loss and blood transfusion were recorded (**Table 3**). As compared to HES group, the blood loss was less in N-HES group although there was no significant difference, and blood loss didn't increase with the increase in the dose of HES in HES groups. The red cell transfusion in HES group was higher than in N-HES group, and the total red cell transfusion in M-HES subgroup and H-HES subgroup was significant higher than in N-HES subgroup. In addition, the plasma infusion was the highest in N-HES group, although there was no significant difference.

The total amounts of fluid infused and discharged on the day of surgery were significantly higher than those at other time points, but quickly dropped on POD1. The volume of fluid infused during operation increased gradually with the increase in HES dose, and the volume of intraoperative H-HES was significantly higher than in N-HES group, but there was no marked difference when the volume of fluid infused in the whole day was taken into account. When compared with HES group, the fluid infused and discharged in N-HES group in POD2 and POD3 was relatively high, and the fluid discharged in N-HES group in POD3 was significantly higher than in L-HES, M-HES and H-HES subgroups (**Table 4**).

Creatinine and CystC were recorded before surgery and POD1, 3 and 7 (**Table 5**), to evaluate the nephrotoxicity of HES. One-way analysis of variance was conducted to explore influence of HES at different doses on the postoperative sCr and sCystatin C (POD1, 3 and 7). There were no significant differences in the baseline sCysC and sCr among groups. A rapid increase in sCr was found after surgery, but it maintained at a high level in POD3 and thereafter reduced in POD7 gradually (**Table 5**). As compared to sCr, sCystatin C didn't increase significantly soon after surgery as in previous studies. The increase in sCystatin C was observed in POD3

Table 5. Serum creatinine and cystine at different time points in N-HES group and HES group

		Pre-operation	POD1	POD3	POD7	P
N-HES	Serum creatinine	72.95±13.94	96.88±19.66	76.68±22.89	74.80±11.88	0.705
	Serum cystine	1.16±0.66	0.92±0.53	1.26±0.46	0.97±0.04	0.280
L-HES	Serum creatinine	78.36±21.62	101.77±30.02	104.15±54.43	96.84±47.57	0.157
	Serum cystine	1.03±0.33	1.22±1.45	1.35±0.64	1.39±0.94	0.492
M-HES	Serum creatinine	77.93±19.21	100.38±34.44	107.64±60.41	92.70±27.47	0.437
	Serum cystine	1.03±0.40	1.02±0.57	1.51±0.71	1.48±1.15	0.581
H-HES	Serum creatinine	71.03±10.27	85.81±18.65	113.93±82.27	107.44±112.34	0.701
	Serum cystine	0.97±0.16	1.07±0.52	1.11±0.32	1.43±1.46	0.679

Note: P, vs N-HES group (independent samples t-test).

Table 6. AKI in POD1 and POD3 in N-HES group and HES group

	N-HES	L-HES	P	M-HES	P	H-HES	P
AKI in POD1, n=111	37.5%	40.5%	0.875	37.8%	0.988	18.8%	0.317
AKI in POD3, n=49	20.0%	31.3%	0.130	25.0%	0.108	25.0%	0.552

and it maintained at a high level in POD7 in all HES groups (**Table 5**). Furthermore, there were no significant differences in both creatinine and sCystatin C between N-HES group and HES group.

In the present study, the overall incidence of AKI was 36% soon after surgery, and then rapidly reduced in POD3 (**Table 6**). In POD1 and POD3, the incidence of AKI in HES subgroups was comparable to that in N-HES group.

Stratified analysis and Binary logistic regression

Because patients were more like to have valve disease in HES group, hierarchical chi-square analysis was performed in valve disease (VD) cohort and non-VD cohort. Stratified analysis showed the χ^2 MH was 0.73 in POD1 and 0.40 in POD3, and HES use was not associated with AKI in both cohorts. Then, risk factors of AKI were investigated by Binary logistic regression (**Table 7**), in addition to the HES dose, baseline demographics, complications and peri-operative variables. Results showed age and BMI were the risk factors for postoperative renal injury, and HES infusion didn't increase the risk for AKI (95% CI, 0.979-1.139), even the dose reached 30 ml/kg.

Conclusion

HES is a complex mixture of amylopectin with various molecular weights and can be metabolized by alpha-amylase into micromolecules which may be cleared by the kidney due to small molecular weight. HES has been the most frequently used non-protein intravascular volume expander, and can ensure adequate tissue oxygenation while avoiding fluid overload. As shown in **Table 3**, more plasma was needed in N-HES group than in HES groups for intravascular volume expansion, and the volume of fluid infused and discharged in N-HES group was higher than in HES subgroups in POD0, POD2 and POD3 (**Table 4**). Despite its important clinical significance, there are always some debates on its safety. One of the major concerns is the renal injury secondary to HES infusion. The U.S. Food and Drug Administration (FDA) has issued a warning [18] about the risk for severe renal injury after use of hydroxyethyl starch based on some meta analyses [2, 6, 19] that show HES at large doses may increase the risk for renal injury.

In fact, the concern about potential nephrotoxicity of HES has been proposed for several decades. The potential mechanism underlying the HES induced AKI includes the decrease in glomerular filtration due to hyperviscosity [20] and tubular nephrosis-like lesions resulting from the stasis of tubular flow and HES uptake in the proximal tubular epithelial cells [21]. Rioux et al. found that HES was an independent predictor of AKI (OR=1.08), the risk for AKI was dose-dependent, and the optimal cut-off volume of HES for the prediction of AKI was 14 mL/kg [10].

Although the study of Lomivorotov et al. showed that HES 200/0.5 at 4 ml/kg infused at 30 min after anesthesia induction failed to increase

Table 7. Binary logistic regression of renal dysfunction

	Binary logistic regression			
	HR	95% CI		P
Age	1.104	1.014	1.202	0.022
Male	0.205	0.022	1.903	0.163
BMI	1.575	1.172	2.118	0.003
DM	0.280	0.052	1.506	0.138
Hypertension	1.636	0.915	2.928	0.097
Dyslipidemia	0.506	0.042	6.105	0.592
Peripheral vascular disease	1.523	0.386	6.006	0.548
NYHA	0.772	0.245	2.428	0.658
LVEF	0.978	0.901	1.063	0.602
Time of CPB	1.025	0.983	1.068	0.246
Time of clamping	0.963	0.907	1.023	0.222
Number of graft	1.795	0.426	7.563	0.425
Pre-Cr	1.034	0.979	1.092	0.228
Pre-CystC	12.360	0.239	638.434	0.212
HES	1.056	0.979	1.139	0.159

Note: BMI, body mass index; DM, diabetes mellitus; NYHA, New York Heart Association; LVEF, left ventricular ejection fraction; CPB, cardiopulmonary bypass; HES, hydroxyethyl starch.

the incidence of AKI in on-pump coronary artery bypass surgery patients [15] and HES didn't show the nephrotoxicity as a prime fluid in CABG under CPB [22], the dose of HES in these studies was significantly lower than that used in clinical practice, the concern about the potential renal adverse reactions associated with HES infusion is still growing. In the present study, the serum Cr, sCystatin C and incidence of AKI were determined before and after surgery to investigate the impact of HES130/0.4 at different doses on the kidney function in patients receiving CABG surgery.

Our results showed that there was a rapid increase in serum Cr after surgery, which maintained at a high level in POD3 and then gradually reduced in POD7. There was no significant difference in the kidney function after infusion of 6% HES130/0.4, even at a mean dose of 37.12±7.25 ml/kg. sCystatin C is a novel indicator of renal injury, and has been found to be more sensitive to and can rapidly reflect the renal injury [23]. The kidney function was similar between N-HES group and HES group. Besides, the incidence of AKI was also comparable among HES subgroups. The logistic regression analysis also revealed that HES failed to increase the risk for AKI in patients receiving CABG surgery.

Although there were more female patients in HES group, and more patients had concomitant valve diseases and hypertension in HES group, the severity of disease might be a potential confounding factor affecting the selection of therapeutic strategies (included HES) and the postoperative outcome, but female gender and hypertension were considered to be potent risk factors of AKI after surgery [3], thus they didn't bias the conclusion of this study, and after taking out the effect of valve disease by Hierarchical chi-square analysis, HES still didn't increase the risk for AKI.

These findings were different from previously reported [19, 24], which may be partially attributed to the difference in study objectives. In our study, patients received the infusion of HES130/0.4 rather than HES of previous generations. HES130/0.4 differs from HES of previous generations in the molecular weight, proportion of hydroxyethyl unit and ratio of substitution at C2 and C6 positions of the glucose ring, which are closely related to the pharmacokinetic and pharmacodynamic properties of HES [25]. HES130/0.4 was considered to be less nephrotoxic because of small molecular weight and substitution. In addition, the total incidence of AKI after coronary artery bypass surgery was 36%, reduced rapidly in POD3. Thus, the discrepancy in the nephrotoxicity of HES may be related to the difference in time point at which nephrotoxicity is evaluated.

Furthermore, the clinical conditions may also affect the safety of HES. HES products may increase the risk for AKI in severe sepsis patients [3], but the use of HES during surgery didn't induce adverse renal effects in surgical patients [11-14]. In patients receiving heart surgery, the hemodynamic changes significantly in patients with different cardiac surgeries. Patients recruited into this study underwent isolated CABG, and the influence of surgery on renal perfusion was various with the other patients, this may partly explain the discrepancy between available studies. On the basis of our findings, HES, even at 37 ml/kg, may not increase the risk for renal injury in patients receiving CABG surgery.

In fact, HES has been used in clinical practice for several decades, and the rapid volume expansion has been confirmed. However, it is undeniable that HES may increase the risk for renal injury in some patients with serious disease, especially those with high risk for AKI due to pre-existing diseases, for many other patients, such as discussed in this study, HES add no risk of AKI to patients. As shown in **Table 3**, although the blood loss in HES was higher than in N-HES group, there was no significant difference between groups. Blood loss didn't increase with the increase in HES dose, and the increased risk for bleeding wasn't found in this study.

There are some limitations in this study. First, the sample size was small for the logistic regression analysis of risk factors of AKI after CABG surgery. Second, data in some patients were missing in N-HES group on the first day after surgery, which was more common in patients with mild disease. This increases the incidence of AKI in N-HES patients. On the other hand, because of the minimal injury after surgery or the recovery of kidney function, data missing in POD3 and POD7 might cause overestimation of the incidence of AKI. Third, the inadequate renal perfusion was a major cause of AKI following cardiac surgery in our study due to the restrictions in measurement of hemodynamics, as Jean-Philippe [10]. Hemodynamic stability was evaluated on the basis of vasopressor, but it was difficult to detect the amount of vasopressor used outside the operation room where the vasopressor was widely applied. Fourth, the uses of fluid and cardiovascular medicine were inconsistent between individuals and usually determined by anesthesiologists and physicians preference based on the hemodynamic parameters. Last, in our study, observations were conducted in POD1, POD3 and POD7, but the influence of HES in proximal tubular epithelial cells may be longer.

In the future, more prospective studies with large sample size are required to investigate the risk factors of AKI after CABG surgery and confirm the influence of HES on the kidney function.

Disclosure of conflict of interest

None.

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