J Surg Med. 2022;6(3):285-288.
DOI: 10.28982/josam.1007641

Research article

Journal of Surgery and Medicine
e-ISSN=2602-2079

Estimated glomerular filtration rate decreased by Hydroxyethyl Starch in isolated coronary artery bypass graft surgery: A retrospective cohort study

Muharrem Koçyiğit, Ozgen Ilgaz Koçyiğit

Acibadem Mehmet Ali Aydınlar University, Vocational School of Health Services, Department of Anesthesiology, Istanbul, Turkey

ORCID ID of the author(s)
MK: 0000-0003-0615-6025
OIK: 0000-0002-0497-5492

Corresponding Author
Muharrem Koçyiğit
Acibadem Mehmet Ali Aydınlar University. Vocational School of Health Services, Department of Anesthesiology, Acibadem Maslak Hospital. Buyukdere cad. No:40 34457 Sariyer, Istanbul, Turkey
E-mail: muharremkocyigit@hotmail.com

Ethics Committee Approval
Ethical approval for this study (ATADEK-2018/18) was provided by the Ethics Committee of Acibadem Mehmet Ali Aydinlar University, on 22 November 2018.
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

Financial Disclosure
The authors declared that this study has received no financial support.

Published
2022 March 22

Abstract

Background/Aim: Hydroxyethyl starches have been widely used to replace the intravascular volume. They increase the risk of renal injury in critically ill patients. In cardiac surgery, patients are at risk for cardiac surgery-associated acute kidney injury. This study aims to analyze the renal functions in coronary surgery with hydroxyethyl starches and crystalloids.

Methods: Patients who underwent isolated on-pump coronary artery bypass graft surgery between January 2017 and June 2019 were included in the study. They were categorized into two groups according to intraoperative volume replacement therapy. The non-HES group consisted of patients who had been given a balanced electrolyte solution; the HES group consisted of patients who were administered a balanced electrolyte solution and 500 ml of hydroxyethyl starch solution. A two-sided *P*-value of <0.05 was considered significant.

Results: There were no significant differences between the two groups in terms of demographic values and preoperative serum urea, creatinine, blood urea nitrogen, and estimated glomerular filtration rate levels (P>0.05). In the HES group, the postoperative value of creatinine was significantly higher and estimated glomerular filtration rate level was significantly lower compared to the preoperative values (P<0.001).

Conclusion: The intraoperative administration of 500 mL hydroxyethyl starch affected renal function in isolated on-pump coronary artery bypass graft surgery patients.

Keywords: Coronary artery bypass graft, Colloids, Hydroxyethyl starch 130-0.4, Glomerular filtration rate

How to cite: Koçyiğit M, Koçyiğit OI. Estimated glomerular filtration rate decreased by Hydroxyethyl Starch in isolated coronary artery bypass graft surgery: A retrospective cohort study. J Surg Med. 2022;6(3):285-288.

Introduction

Colloid hydroxyethyl starches (HESs) have been used fluid resuscitation to replace the intravascular volume for more than 30 years [1, 2]. Despite their efficacy, HES solutions increase the risk of renal injury and the need for renal replacement therapy in critically ill patients [3]. This has made clinicians hesitant to use HESs [4]. Furthermore, patients undergoing cardiac surgery are already at risk for renal injury, as cardiac surgery-associated acute kidney injury (AKI) occurs in 7–54% of patients [5, 6].

This study aimed to analyze the effect of HESs on renal function in isolated coronary artery bypass graft (CABG) surgery patients.

Materials and methods

The ethics approval for this study (ATADEK-2018/18) was obtained from the Ethics Committee of Acibadem Mehmet Ali Aydinlar University, on 22 November 2018. Patient data were retrieved from the electronic medical records in our institution’s database. Written informed consent was waived due to the retrospective nature of the study.

Patients who underwent isolated CABG surgery between January 2017 and June 2019 were included in this study. Patients who had previous cardiac surgery, off-pump cardiac surgery, valve surgery, concomitant surgery, renal failure (dialysis patients), intraoperative ultrafiltration, perioperative or postoperative blood transfusion, and HES infusion in the ICU were excluded.

All operations were performed by the same surgical and anesthesiology team. Patients were premedicated with alprazolam (0.5 mg, orally) the night before surgery and midazolam (0.05 mg/kg, intravenously) half an hour before the surgery. The patients were monitored with a 5-lead electrocardiogram, pulse oximeter, noninvasive blood pressure monitor, and bispectral index and cerebral oximeter. Before the induction of anesthesia, the radial artery was cannulated. Anesthesia was induced with midazolam, propofol, fentanyl, rocuronium and was maintained with a fentanyl infusion and sevoflurane in an O2-air mixture. After endotracheal intubation, transesophageal echocardiography and a central venous line were inserted. The lungs were ventilated with a tidal volume of 5–6 mL/kg and 5 cmH20 positive end-expiratory pressure before and after cardiopulmonary bypass (CPB) to maintain an end-tidal CO2 value of at least 33–35 mmHg and a peripheral capillary oxygen saturation value of at least 96%. Tranexamic acid (25 mg/kg, intravenous) was infused with the induction of anesthesia.

After achieving an activated clotting time of >450 s, aortic and caval cannulation was performed and CPB was initiated. Ringer’s lactate solution was used for CPB priming. The pump flow rate was set at 2.2–2.4 L/min/m2 at 30–32°C. Cold blood cardioplegia was used for cardiac arrest. In all operations, balanced crystalloid solutions (Izolen®, Polifarma, Turkey) were used for infusion during anesthesia induction and maintenance. Balanced crystalloids or 500 mL HES (Voluven®, 6% HES 130/0.4, Fresenius Kabi, Germany) were randomly used during CBP or after coming off the pump. Transesophageal echocardiography was also used for analyzing the hemodynamic status.

At the end of the operation, the patients were transferred to the ICU.

In all patients, hemodynamic monitoring, ventilation, and postoperative analgesia were managed according to a standard clinical protocol. Blood samples were obtained on the first postoperative day in the ICU.

Data on patient demographics, cross-clamping (CC), CPB, and operation duration, as well as laboratory data, including preoperative and postoperative urea, creatinine, blood urea nitrogen (BUN), estimated glomerular filtration rate (eGFR) levels, ICU and hospital stay were reviewed.

Patients' data were categorized into two groups according to intraoperative volume replacement therapy. The non-HES group (n=115) consisted of patients who had been given a balanced electrolyte solution; the HES group (n=45) consisted of patients who were administered a balanced electrolyte solution and 500 mL of HES solution.

Statistical analysis

Statistical analysis was performed using the SPSS version 10 software (SPSS Inc., Chicago, IL, USA). Data were presented in mean, standard deviation (SD) or number and percentage. Student’s t-test, Mann-Whitney U test, and Pearson’s χ^2 test were used as necessary for inter-group comparisons. The Wilcoxon test or t-test was used for related variables comparisons. A two-sided *P*-value of <0.05 was considered significant.

Results

The records of 146 patients were evaluated. Only balanced electrolyte solutions were used during surgery in 111 patients, and 45 patients were managed with both HES and balanced electrolyte solutions.

There were no significant differences in demographic and clinical characteristics between the two groups (Table 1).

The intubation period was significantly longer in the HES group than the non-HES group (6.04 (2.38) hours vs 6.64 (2.15) hours, *P*=0.04). There were no significant differences in ICU stay or hospital discharge times between the two groups (Table 1).

The two groups were similar in terms of preoperative serum urea, creatinine, BUN, and eGFR levels. Postoperative serum creatinine, urea, and BUN values were significantly higher and eGFR level was significantly lower in the HES group than the non-HES group. Additionally, in the HES group, there were significantly differences between preoperative and postoperative values of creatinine and eGFR values [0.99 (0.29) mg/dL vs 1.14 (0.40) mg/dL, *P*<0.001 and 79.56 (18.88) mL/min/1.73m2 vs 71.17 (21.84) mL/min/1.73m2, *P*<0.001, respectively]. There were no differences in the non-HES group in terms of preoperative and postoperative values (Table 2).

No patients required inotropic agent infusion perioperatively.

There were no new-onset strokes, new-onset dialysis, infections, sternal dehiscence, pneumonia, the need for re-exploration for bleeding or renal replacement therapy in any of the patients. There was no mortality at 1 month follow up.

Table 1: Patients' demographic and clinical characteristics

	Non-HES group (n = 111)	HES group (n = 45)	*P*-value
Age (years)	61.57 (8.67)	64.49 (9.05)	0.06
Weight (kg)	81.82 (12.75)	77.94 (10,13)	0.06
Height (cm)	170.13 (8.83)	167.15 (8.95)	0.06
Sex (female/male) (n)	16/95	9/39	0.86
Euroscore logistics (%)	3.78 (3.27)	5.99 (11.45)	0.37
NYHA Class 1 and 2 (%)	88% (n = 98)	93% (n = 42)	0.96
EF (%)	55.79 (9.0)	54.51 (10.61)	0.80
Hypertension (%)	70.3% (n = 78)	75.6% (n = 34)	0.50
Hypercholesterolemia (%)	62.2% (n = 69)	73.3% (n = 33)	0.18
Diabetes Mellitus (%)	43.2% (n = 48)	46.7% (n = 21)	0.69
Thyroid dysfunction	3.6%8n=4)	0	0.19
CVA	1.8% (n=2)	2.2% (n=1)	0.86
Smoking (%)			
Smokers	33.3% (n = 37)	33.3% (n = 15)	0.87
Former smokers	33,3% (n = 37)	35.6% (n = 16)	
Never smoked	33.3% (n = 37)	31.1% (n = 14)	
Medications			
Beta blockers (%)	53.2% (n = 59)	64.4% (n = 29)	0.19
Ca canal blockers (%)	9.0% (n = 10)	11.1% (n = 5)	0.68
ACE inhibitors (%)	31.5% (n = 35)	35.6% (n = 16)	0.62
Anti-lipids (%)	35.1% (n=39)	42.2% (n=19)	0.40
Aspirin (%)	66.7% (n = 74)	64.4% (n = 29)	0.79
Hct	40.77 (4.20)	40.88 (4.68)	0.90
CC time (min)	57.11 (16.98)	63.33 (19.89)	0.07
CPB time (min)	90.23 (23.67)	96.08 (25.43)	0.10
Number of Distal Anastomoses	3.36 (0.8)	3.68 (1.08)	0.10
Intubation time (h)	6.04 (2.38)	6.64 (2.15)	0.04
Chest tube output (mL)	398.15 (216.24)	422.88 (271.15)	0.81
Postoperative Hct	29.58 (4.30)	27.50 (4.07)	0.007
ICU duration (h)	19.55 (10.07)	19.60 (6.70)	0.13
Postoperative AF	11% (n=12)	4.4% (n=2)	0.19
Hospital discharge time(days)	6.36 (4.55)	7.41 (6.75)	0.09

BMI: body mass index, NYHA: New York Heart association, EF: ejection fraction, COPD: chronic obstructive pulmonary disease, ACE: angiotensin-converting enzyme, CC: cross clamp, CPB: cardiopulmonary bypass, ICU: intensive care unit, AF: atrial fibrillation

Table 2: Preoperative and postoperative renal values

	Non-HES group (n = 111)	HES group (n = 45)	*P*-value
Urea preoperative (mg/dL)	36.81 (13.02)	38.77 (14.48)*	0.42
Urea postoperative (mg/dL)	37.62 (14.23)	42.68 (12.83)*	0.01
BUN preoperative (mg/dL)	17.17 (6.07)	18.11 (6.79)*	0.40
BUN postoperative (mg/dL)	17.53 (6.70)	19.93 (5.99)*	0.01
Creatinine preoperative(mg/dL)	0.97 (0.24)	0.99 (0.29)#	0.67
Creatinine postoperative (mg/dL)	0.99 (0.27)	1.14 (0.40)#	0.02
eGFR preoperative (mL/min/1.73m^2)	81.69 (18.12)	79.56 (18.88)#	0,52
eGFR postoperative (mL/min/1.73m^2)	80.76 (19.22)	71.17 (21.84)#	0,01

BUN: Blood urea nitrogen, eGFR: estimated glomerular filtration rate, # $P<0.001$, * $P=0.056$: These *P*-values indicate the preoperative and postoperative differences in the HES group.

Discussion

This study shows that the intraoperative administration of 500 mL HES can increase serum urea, creatinine, BUN levels and decrease eGFR levels after isolated on-pump coronary artery bypass surgery.

Hüter et al. [7] stated that HES is used for perioperative fluid therapy and pump-priming in cardiac surgery. HES increases the intravascular volume due to osmotic pressure because of its molecular weight. The molecular weight of HES can affect glomerular filtration and cause interstitial inflammatory changes in the kidneys, leading to kidney injury [7]. HES types with a higher molecular weight and higher hydroxyethylation ratios can accumulate in the interstitial space, leading to nephrotoxicity. Those with a lower molecular weight and lower hydroxyethylation ratios are less likely to lead to nephrotoxicity [5]. On the other hand, it has been reported that HES 130/0.4 attenuates the glycocalyx response to injury and sustains vascular barrier function [8].

In three meta-analyses of randomized studies on cardiac and non-cardiac patients, HES 130/0.40 was compared with crystalloids and found to have no significant association with AKI in cardiac and non-cardiac surgical patients [1, 4, 9]. In our study, in the HES group, the postoperative values of sCr were significantly increased and eGFR was significantly decreased than the corresponding preoperative values and significantly different from the non-HES group.

Tobey et al. [4] mentioned that in cardiac surgery, the incidence of major cardiac and cerebral events is higher with a low-volume HES infusion because the need for higher amounts of crystalloids in these patients can cause edema. Momeni et al. [10] reported that a low-volume (<30 mL/kg) or high-volume (>30 mL/kg) HES infusion did not affect the incidence of renal replacement therapy and mortality, but that low-volume HES infusions can reduce the incidence of AKI. Conversely, in Bayer et al.'s [2] study including 6,478 patients who underwent cardiac surgery with CPB, treatment with 6% HES 130/0.4 was associated with a higher risk of renal failure and a greater use of renal replacement therapy than crystalloids.

Preoperative poor left ventricular function, diabetes mellitus, hypertension, previous cardiac surgery, chronic kidney disease, and prolonged CPB duration are predictive risk factors for postoperative AKI [5, 6, 11]. In our study, there were no significant differences between the groups in terms of left ventricular function, diabetes mellitus, hypertension, CC, and CPB duration.

An intraoperative blood transfusion during cardiac surgery increases the incidence of AKI [12]. Each unit of blood transfused increases the risk of AKI by 10–20 % after cardiac surgery with CPB [13]. Therefore, we excluded patients who received blood transfusions during the intraoperative and postoperative ICU periods.

Limitations

The limitations of the study included the lack of blindness due to its retrospective nature. We evaluated the biochemical renal function parameters we used in daily follow-up. Other renal biomarkers can be used in randomized controlled trials in the future. This was a single-center study which focused on isolated CABG surgery to lessen the burden of confounding variables.

Conclusion

This study suggested that intraoperative administration of as low as 500 mL of HES reduced the level of estimated glomerular filtration rate in cardiac patients.

References

1. Gillies MA, Habicher M, Jhanji S, Sander M, Mythen M, Hamilton M, Pearse RM. Incidence of postoperative death and acute kidney injury associated with i.v. 6% hydroxyethyl starch use: systematic review and meta-analysis. Br J Anaesth. 2014 Jan;112(1):25-34. doi: 10.1093/bja/aet303.
2. Bayer O, Schwarzkopf D, Doenst T, Cook D, Kabisch B, Schelenz C, et al. Perioperative fluid therapy with tetrastarch and gelatin in cardiac surgery--a prospective sequential analysis. Crit Care Med. 2013 Nov;41(11):2532-42. doi: 10.1097/CCM.0b013e3182978fb6.
3. Reinhart K, Perner A, Sprung CL, Jaeschke R, Schortgen F, Groeneveld BJ, et al. European Society of Intensive Care Medicine. Consensus statement of the ESICM task force on colloid volume therapy in critically ill patients. Intensive Care Med. 2012 Mar;38(3):368-83. doi: 10.1007/s00134-012-2472-9.
4. Martin C, Jacob M, Vicaut E, Guidet B, Van Aken H, Kurz A. Effect of waxy maize-derived hydroxyethyl starch 130/0.4 on renal function in surgical patients. Anesthesiology. 2013 Feb;118(2):387-94. doi: 10.1097/ALN.0b013e31827e5569.
5. Tobey R, Cheng H, Gao M, Li Z, Young N, Boyd D, et al. Postoperative Acute Kidney Injury and Blood Product Transfusion After Synthetic Colloid Use During Cardiac Surgery. J Cardiothorac Vasc Anesth. 2017 Jun;31(3):853-862. doi: 10.1053/j.jvca.2016.12.024.
6. Chew STH, Hwang NC. Acute Kidney Injury After Cardiac Surgery: A Narrative Review of the Literature. J Cardiothorac Vasc Anesth. 2019 Apr;33(4):1122-1138. doi: 10.1053/j.jvca.2018.08.003.
7. Hüter L, Simon TP, Weinmann L, Schuerholz T, Reinhart K, Wolf G, et al. Hydroxyethylstarch impairs renal function and induces interstitial proliferation, macrophage infiltration and tubular damage in an isolated renal perfusion model. Crit Care. 2009;13(1):R23. doi: 10.1186/cc7726.
8. Strunden MS, Bornscheuer A, Schuster A, Kiefmann R, Goetz AE, Heckel K. Glycocalyx degradation causes microvascular perfusion failure in the ex vivo perfused mouse lung: hydroxyethyl starch 130/0.4 pretreatment attenuates this response. Shock. 2012 Nov;38(5):559-66. doi: 10.1097/SHK.0b013e31826f2583.
9. Van Der Linden P, James M, Mythen M, Weiskopf RB. Safety of modern starches used during surgery. Anesth Analg. 2013 Jan;116(1):35-48. doi: 10.1213/ANE.0b013e31827175da.
10. Momeni M, Nkoy Ena L, Van Dyck M, Matta A, Kahn D, Thiry D, et al. The dose of hydroxyethyl starch 6% 130/0.4 for fluid therapy and the incidence of acute kidney injury after cardiac surgery: A

retrospective matched study. PLoS One. 2017 Oct 18;12(10):e0186403. doi: 10.1371/journal.pone.0186403.

11. Coleman MD, Shaefi S, Sladen RN. Preventing acute kidney injury after cardiac surgery. Curr Opin Anaesthesiol. 2011 Feb;24(1):70-6. doi: 10.1097/ACO.0b013e3283422ebc.
12. Kindzelski BA, Corcoran P, Siegenthaler MP, Horvath KA. Postoperative acute kidney injury following intraoperative blood product transfusions during cardiac surgery. Perfusion. 2018 Jan;33(1):62-70. doi: 10.1177/0267659117712405.
13. Karkouti K. Transfusion and risk of acute kidney injury in cardiac surgery. Br J Anaesth. 2012 Dec;109 Suppl 1:i29-i38. doi: 10.1093/bja/aes422.

This paper has been checked for language accuracy by JOSAM editors.

The National Library of Medicine (NLM) citation style guide has been used in this paper.