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Acute normovolemic hemodilution and acute kidney injury after open abdominal cancer surgery

Acute normovolemic hemodilution (ANH) is considered a useful method to reduce the risk of perioperative allogeneic blood transfusion [1,2]. We have determined whether ANH could be a risk factor for acute kidney injury (AKI) in patients undergoing open abdominal cancer surgery.

Our retrospective study protocol was approved by our hospital's Ethics Committee and was publicized on our hospital's internet homepage (2018–1038). The requirement of patients' written informed consent was waived by the Ethics Committee because the study was retrospective. The patients' characteristics and perioperative data were collected from electronic anesthesia and medical records of adult cancer patients (≥18 years old) who underwent open abdominal surgery at Hirosaki University Hospital during the period from April 1, 2016 to March 31, 2018. Patients with end-stage kidney disease who require intermittent hemodialysis and those who underwent a total or partial nephrectomy were excluded from this study.

The primary outcome was the development of AKI based on the Kidney Disease: Improving Global Outcomes serum creatinine (Cre) criteria. We compared the baseline characteristics of the patients who received ANH (the ANH group) and those who did not (the non-ANH group). We performed a propensity score-adjusted multivariate logistic regression analysis to determine whether ANH is a risk factor for postoperative AKI and to calculate the adjusted odds ratios (aORs) and 95% confidence intervals (95% CIs) after controlling simultaneously for potential confounders.

Of the 547 patients, 186 patients (34%) were in the ANH group. Overall, 38 patients developed postoperative AKI (6.9%). The incidence of AKI was not significantly different between the non-ANH (8.0%) and ANH (4.8%) groups ($p = 0.201$). Among the 114 patients with underlying CKD stage 3 or 4, the incidence of AKI and the changes in serum Cre were not significantly different between the patients who received ANH ($n = 16$) and those who did not ($n = 98$). Table 1 shows a comparison of pre- and intra-operative data between the patients with and without postoperative AKI. The propensity score-adjusted multivariate logistic regression analysis showed that the use of ANH was not independently associated with postoperative AKI (aOR 0.682, 95% CI: 0.270–1.720, $p = 0.419$). Four perioperative factors were revealed as independent associated factors for postoperative AKI: CKD stage ≥3 (aOR 2.700, 95% CI: 1.310–5.580, $p = 0.007$), urine out < 0.5 mL/kg/h (aOR 4.490, 95% CI: 2.050–9.850, $p < 0.001$), duration of surgery ≥5 h (aOR 3.850, 95% CI: 1.860–7.990, $p < 0.001$), and urgent/emergency surgery (aOR 3.190, 95% CI: 1.170–8.720, $p = 0.024$). The area under the receiver operating curve was 0.803 (95% CI: 0.735–0.871).

Our findings revealed that ANH did not increase the risk of AKI even though ANH increased the rates of anemia (intraoperative Hb < 9.0 g/dL), hyperchloridemia (Cl > 114 mEq/L and changes in Cl > 5 mEq/L), and metabolic acidosis (BE < −2 mEq/L) during surgery. In addition, even though patients with CKD stage ≥3 are considered to be at high risk of developing postoperative AKI [3,4], the incidence of AKI and changes in serum Cre were not different between the ANH and non-ANH groups in the present study. These results suggest that ANH can be conducted safely without increasing the risk of AKI if the ANH is well indicated for the patient. However, since the number of patients with

Table 1
Patient characteristics and pre- and post-operative data in patients with or without AKI.

	Non-AKI $n = 509$	AKI $n = 38$	p-Value
Male, n (%)	249 (48.9)	28 (73.7)	0.004
Age ≥ 65 yrs, n (%)	304 (59.7)	31 (81.6)	0.009
BMI ≥22 kg/m^2, n (%)	283 (55.6)	26 (68.4)	0.131
ASA-PS ≥3, n (%)	119 (23.4)	17 (44.7)	0.006
CKD stage ≥3, n (%)	99 (19.4)	15 (39.5)	0.006
RCRI ≥2, n (%)	92 (18.1)	12 (31.6)	0.052
Anticoagulant/antiplatelet, n (%)	89 (17.5)	6 (15.8)	1.000
Types of surgery			
Upper abdominal surgery, n (%)	285 (56.0)	22 (57.9)	0.867
Urgent/emergency, n (%)	35 (6.9)	6 (15.8)	0.055
Laboratory data			
Hb ≤12 g/dL, n (%)	300 (58.9)	29 (76.3)	0.039
Plt ≤15 × 10^4/μL, n (%)	88 (17.3)	16 (42.1)	0.001
Cre ≥1.0 mg/dL, n (%)	62 (12.2)	13 (34.2)	0.001
Na ≥137 mEq/L, n (%)	369 (72.5)	31 (81.6)	0.259
Cl ≥110 mEq/L, n (%)	160 (31.4)	12 (31.6)	1.000
BE ≤1.0 mEq/L, n (%)	239 (47.1)	23 (60.5)	0.13
Surgery and fluid balance			
Duration of surgery ≥5 h, n (%)	84 (16.5)	15 (39.5)	0.001
Duration of anesthesia ≥6 h, n (%)	98 (19.3)	16 (42.1)	0.004
Crystalloid ≥15 mL/kg/h, n (%)	45 (8.8)	3 (7.9)	1.000
Hydroxyethyl starch ≥20 mL/kg, n (%)	146 (28.7)	13 (34.2)	0.463
Estimated blood loss ≥10 g/kg, n (%)	210 (41.3)	21 (55.3)	0.124
Urine output < 0.5 mL/kg/h, n (%)	52 (10.2)	12 (31.6)	0.001
Intraoperative transfusion			
ANH, n (%)	177 (34.8)	9 (23.7)	0.214
RBC, n (%)	70 (13.8)	7 (18.4)	0.466
FFP, n (%)	25 (4.9)	4 (10.5)	0.134
PC, n (%)	5 (1.0)	2 (5.3)	0.079
Intraoperative laboratory data			
Hb nadir < 9.0 g/dL, n (%)	271 (54.4)	27 (71.1)	0.061
Hb postop < 9.0 g/dL, n (%)	176 (35.3)	19 (50.0)	0.080
Cl peak ≥114 mEq/L, n (%)	172 (34.2)	8 (21.1)	0.110
Cl increase > 5 mEq/L, n (%)	174 (34.6)	13 (34.2)	1.000
BE nadir < −2 mEq/L, n (%)	185 (36.9)	18 (47.4)	0.225
BE decrease ≥4 mEq/L, n (%)	55 (11.0)	10 (26.3)	0.016

ANH: acute normovolemic hemodilution, ASA-PS: American Society of Anesthesiologist-physical status, BE: base excess, BMI: body mass index, CKD stage: chronic kidney disease grade, Cre: Creatinine, Hb: hemoglobin, Plt: platelet count, RCRI: Revised Cardiac Risk Index. BE decrease: BE preoperative − BE nadir, Cl delta: Cl peak-Cl preop, Cl: chloride, FFP: fresh frozen plasma, PC: platelet concentration, RBC: red blood cells.

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underlying CKD stage 3 or 4 in this study was small (n = 114), further studies with large numbers of patients are required to assess the safety of ANH for patients with CKD stage 3 or 4.

In conclusion, the results of this retrospective analysis indicate that ANH conducted safely does not increase the risk of postoperative AKI.

Author contributions

N.M. collected data and drafted the manuscript. **J.S.** designed the study, collected data, performed the statistical analysis and drafted the manuscript. **T.O.** collected data and evaluated the data. **M.K.** collected data and evaluated the data. **S.N.** designed the study and evaluated the data. **M.K.** evaluated the data and extensively revised the manuscript **K.H.** designed the study, evaluated the data and extensively revised the manuscript.

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IRB contact information

This study protocol was approved by Hirosaki University's Ethics Committee (2018-1038).

Declaration of competing interest

All authors declare no conflict of interest. All authors read and approved the final manuscript and attest to the integrity of the original data and the analysis reported in this manuscript.

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