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Association between the preoperative N-terminal pro-B-type natriuretic peptide and acute kidney injury in gastrointestinal surgery patients managed with enhanced recovery strategy: a retrospective cohort study

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Abstract

Importance Previous evidence has indicated that N-terminal pro-B-type natriuretic peptide (NT-proBNP) is associated with postoperative acute kidney injury (AKI). However, the association between preoperative NT-proBNP level and postoperative AKI in surgeries managed with enhanced recovery after surgery (ERAS) strategy requires further clarification.

Objective To explore the association between preoperative NT-proBNP and the incidence of postoperative AKI in patients who underwent gastrointestinal surgeries and managed with ERAS strategy.

Design A retrospective cohort study.

Setting A review of documented cases of elective gastrointestinal surgeries managed with ERAS strategy occurred at Xijing Hospital from 01 May 2017 to 30 June 2022.

Participants A total of 629 patients aged 18 years or older who were scheduled for elective gastrointestinal surgeries and subjected to the ERAS strategy with preoperative NT-proBNP and creatinine measurements were included in the analysis.

Exposure Preoperative serum concentrations of NT-proBNP.

Main outcomes and measures The primary outcome was the incidence of postoperative AKI. Preoperative NT-proBNP was divided into high- or low-level groups based on the median (165 pg/ml). Logistic regression was used to explore the association between increased preoperative NT-proBNP level and risk of AKI.

Results After screening 1932 case records, 629 cases were included in the final analyses. The average age was 63.5 (15.3) years old and 197 (31.3%) of them were female. Among them, 112 (17.8%) developed postoperative AKI. The incidence of AKI was 21% in the high NT-proBNP group, and 14.6% in the low NT-proBNP group. Patients with higher preoperative NT-proBNP levels (≥ 165 pg/mL) have significant higher risk of postoperative AKI as compared to those in the lower group (adjusted OR 1.75; 95% CI 1.12 to 2.73).

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Conclusions and relevance Increased preoperative NT-proBNP is associated with an elevated risk of postoperative AKI in patients who underwent gastrointestinal surgery and managed with ERAS strategy.

Trial registry number Clinical trial registry number: NCT06145347

Key points

NT-proBNP is associated with postoperative AKI.

The implementation of ERAS may be associated with increased risk of postoperative AKI.

In this cohort analysis of 629 patients, 17.8% developed postoperative AKI.

Increased total volume infusion significantly mediated 15.5% of NT-proBNP-associated elevated AKI risk in this study.

Increased preoperative NT-proBNP is associated with an elevated risk of postoperative AKI in patients who underwent gastrointestinal surgery and managed with ERAS strategy.

Keywords Preoperative NT-proBNP, Postoperative AKI, ERAS, Gastrointestinal surgery

Introduction

Acute kidney injury (AKI) is a common postoperative complication, which refers to a rapid decrease in glomerular filtration rate within 7 days following surgery (Ojo and Campbell 2022; Kellum et al. 2021). The reported incidence of postoperative AKI ranges from 2% to 39% and reaches 13.4% in abdominal surgery (O'Connor et al. 2016). Postoperative AKI is associated with poor prognosis, such as chronic kidney disease, prolonged hospitalization, increased medical costs and death (Hobson et al. 2015; Grams et al. 2016).

N-terminal pro B-type natriuretic peptide (NT-proBNP) is produced by B-type natriuretic peptide precursor when myocardial cells are subjected to pressure or stretching, which represents the severity of left ventricular dysfunction, reflects potential intravascular volume status (Cao et al. 2019; Friese et al. 2007; Berri et al. 2012; Nongnuch et al. 2014), and therefore can be used as perioperative risk predictor (Choi et al. 2010; Yang et al. 2012). Recent studies have shown that NT-proBNP is associated with renal function (Weber and Hamm 2006; Mair et al. 2008; Nojiri et al. 2015), as associations between preoperative NT-proBNP and postoperative AKI or renal failure were observed both in cardiac and non-cardiac surgery (Zhao et al. 2021; Wang et al. 2021; Elíasdóttir et al. 2008; Grass et al. 2019; Lone et al. 2022). Preoperative NT-proBNP outperformed the euroSCORE or ejection fraction in predicting postoperative AKI (Elíasdóttir et al. 2008; Roques et al. 1999). The elevated preoperative NT-proBNP levels indicated the presence of preexisting intravascular volume overload and cardiac dysfunction. These coupled with a liberal perioperative fluid management predispose patients to the development of postoperative AKI (Vernooij et al. 2021; Tobin et al. 2018).

ERAS (enhanced recovery after surgery) refers to a series of evidence-based and multimodal perioperative optimization measures aimed at reducing the occurrence of complications, promoting recovery, controlling inflammation, and reducing stress reaction (Ban et al. 2019; Thacker et al. 2016). Previous evidence indicated that despite the potential in improving prognosis, the implementation of ERAS may associated with increased risk of postoperative AKI (Myles et al. 2018; Marcotte et al. 2018). This may be attributed to the excessive fluid restriction (Huepenbecker et al. 2021). Then, the potential risk of postoperative AKI associated with preexisting fluid overload, as evidenced by elevated preoperative NT-proBNP levels, compounded by subsequent restrictive perioperative fluid management in the ERAS pathway, requires further clarification.

Given that ERAS strategy is widely used in gastrointestinal surgeries, and the prevalence of postoperative AKI is relatively high among patients undergoing gastrointestinal surgeries, it is important to explore an early detection mechanism of AKI (Hoste et al. 2018; Brusasco et al. 2024). In this retrospective cohort study, we aimed to investigate the association between preoperative NT-proBNP level and postoperative AKI in gastrointestinal surgical patients managed with ERAS management.

Methods

Study design and data sources

This study was based on data from the "Real World Study of Enhanced Recovery After Surgery Program" of a tertiary teaching hospital and used consecutive data of patients from 01 May 2017 to 30 June 2022 (Nie et al. 2022). The use of patient records in this study was approved by institutional ethic committee of Xijing Hospital (KY- 20232265-F- 1, Chairperson Prof Yanyan Jia) with waived consent on 29 January 2024. Data were

obtained from both electronic health records (EHR) and anesthesia information management system (AIMS). For patients subjected to multiple procedures during the study period, the first one was included in the final analyses. The study was reported in line with the STROBE Statement and STROCSS criteria (Agha et al. 2019; Elm et al. 2007). The study was registered at ClinicalTrials.gov (Identifier NCT06145347).

Study population

Patients who were over 18 years old scheduled for elective gastrointestinal surgeries between 01 May 2017 and 30 June 2022 and had preoperative NT-proBNP and creatinine measurements within 7 days prior to surgery were included in the final analyses. The data from patients who were on chronic peritoneal or hemodialysis, with preoperative serum creatinine levels > 4.5 mg/dL (400 μmol/L), had diagnosed with end-stage renal disease patient (defined as glomerular filtration rate < 15 ml min^{-1} 1.73 m^{-2}), or with a history of kidney transplantation; who were schedule for organ transplantation surgery; were pregnant; or with surgical duration less than 1 h were excluded from the analyses.

Exposure

Preoperative serum NT-proBNP concentrations were extracted from the EHR. If multiple measurements were available, the most recent value to the index surgery was recorded. In particular, serum NT-proBNP concentrations were measured with Roche Elecsys NT-proBNP assay (Roche Diagnostics, Shanghai, China) or Cobas e601 or the Cobas e411 system in the Central Laboratory of Xijing Hospital, with a normal range being 5 to 35,000 pg ml^{-1} and an intra-assay coefficients of variation of 1.2%–4.2%, and interassay coefficients of variation of 1.6%–4.6%.

Outcomes

The primary outcome was incidence of postoperative AKI defined according to the creatinine criteria of the KDIGO guidelines (increase in serum creatinine of ≥ 26.5 μmol/L within 48 h or ≥ 1.5 times baseline within 7 days after surgery) (Vickers et al. 2011). The most recent serum creatinine value to the index surgery was used as the baseline. The secondary outcome was stage 2 or 3 AKI (increases in serum creatinine to ≥ 2 times baseline or ≥ 353.6 μmol/L or initiation of renal replacement therapy per KIDIGO criteria).

Covariates

Covariates included age, sex, medical histories (yes/no) of diabetes, hypertension, heart failure, coronary artery disease, abnormal liver function, preoperative laboratory findings of creatinine, hemoglobin, serum albumin, operation information of surgery duration, preoperative blood pressure, and estimated blood loss, urine output. These data were extracted from EHR or AIMS.

Statistical analysis

Normality was checked via Shapiro–Wilk or Kolmogorov–Smirnov tests. Continuous variables with normal distribution were expressed as mean (standard deviation, SD) and analyzed with independent sample t tests. Skewed continuous variables were presented as median (interquartile range, IQR) and compared using the Mann–Whitney U test. Categorical variables were presented as count and percentage and compared using the χ^2 or the Fisher's exact test.

Natural logarithmic (log) transformation was performed for NT-proBNP concentrations due to their skewed distribution. A restricted cubic spline (RCS) model was conducted to explore the possible non-linearity in the relationship between log (NT-proBNP) and AKI incidence. The NT-proBNP concentrations were then divided into high (≥ 165 pg/mL) or low (< 165 pg/mL) level group based on the median of the preoperative NT-proBNP concentrations.

The primary analysis aimed to investigate whether preoperative NT-proBNP was associated with postoperative AKI. Odds ratios (ORs) and 95% confidence intervals (CIs) were presented using a univariable logistic regression model. Variance inflation factors (VIFs) were calculated to examine the possible multi-collinearity.

The secondary analysis was conducted following the similar rationale, where AKI stage 1, 2, or 3 was used as an endpoint. Multivariable logistic regressions were used to obtain ORs and 95% CIs.

Sensitivity analysis

Several sensitivity analyses were carried out to test the robustness of the findings. First, NT-pro BNP was converted into quartiles. Second, participants with missing data were excluded from the analyses. Last, we excluded patients who did not have incomplete adherence to the ERAS strategy using the same statistical approach to avoiding possible biases. (Detailed ERAS strategy was shown in Table S1.)

This study examined the proportion of mediation through total volume infusion in the association of NT-pro BNP levels and AKI risk using the mediation method (Muñoz et al. 2021).

Subgroup analyses

We performed subgroup analyses to examine the modification effects of age (≥ 50 years vs < 50 years), sex, procedure type (endoscopic surgery vs open surgery),

intraoperative fluid balance (> 0 ml vs ≤0 ml), use of NSAIDS after surgery (yes vs no), ASA (I-II vs III-IV), and eGFR (≥ 90 ml/min/1.73 m^2 vs < 90 ml/min/1.73 m^2) on the association between blood NT-proBNP concentrations and postoperative AKI.

Throughout the study, multiple imputation with chained equations was used for the missingness in covariates, with 18 data sets being imputed, averaging predictions and taking into account uncertainty owing to imputation (Azur et al. 2011). Statistical analyses were performed using the R statistical software version 4.3.2 (R Foundation for Statistical Computing, Vienna, Austria). All statistical tests were two-tailed, and a two-side 0.05 was treated as statistical significance.

Results

Enrollment of the study population

The data included in the final analyses is shown in Fig. 1. Between May 2017 and June 2022, 1932 patient records were identified and screened. Of these, 249 records were excluded due to preoperative renal insufficiency; 13 records were excluded due to a history of organ transplantation; 3 were excluded due to pregnant; and the left 1034 were excluded as the surgery duration less than 1 h. Finally, 629 records were included in the final analyses.

Among the included cases, 197 (31.3%) were female, and the average age was 63.5 (15.3) years old. 17.8% (112 of 629) developed postoperative AKI within 1 week after surgery, with stage 1 AKI (62 of 112, 55.4%) the predominant. The median (IQR) preoperative NT-proBNP was 165 (62.3 to 428.5) pg ml^{-1}. Characteristics of the overall study cohort and high or low preoperative NT-proBNP groups are shown in Table 1.

A linear regression model combining all these clinical variables yielded a R^2 of 0.1. Figure 2 depicts the multivariable-adjusted OR from the restricted cubic spline models for postoperative AKI by preoperative log (NT-proBNP) in the cohort. In the RCS model, a non-linear relationship of log (NT-proBNP) with the OR of AKI risk was established (p-non-linearity = 0.01, knot = 3, cut off: 5.1 pg/ml). Associations between log (NT-proBNP) and AKI was J-shaped; it can be observed that the OR of AKI risk was relatively flat until 5.1 pg/ml of log (NT-proBNP), and then started to increase rapidly afterwards.

Association of NT-proBNP and risk of AKI

The association between NT-proBNP and AKI risk is shown in Table 2. NT-pro BNP levels were categorized into high or low levels, using with the low level (< 165.0 pg/mL, the log165.0 was 5.1, which was equal to the cut off value output from the RCS model) as reference. As demonstrated in the Table 2, patients with preoperative NT-pro BNP levels in the high group (≥ 165.0 pg/mL) has significant higher risk of postoperative AKI as compared to those in low-level group (unadjusted OR 1.56; 95% CI 1.03 to 2.36). After adjusting for age, sex, and BMI, increased preoperative NT-pro BNP levels was associated with increased risk of postoperative AKI (adjusted OR 1.75; 95% CI 1.13 to 2.73). However, further adjusting potential confoundings showed increased preoperative NT-pro BNP levels were not associated with significant increased AKI risk as demonstrated in models 3–5 (Table 2), and this might due to the presence of a nonlinear association between the newly added covariates and AKI, which violates the linearity assumption of logistic regression.

The associations between NT-proBNP and different AKI stages are shown in Table 3. Increased preoperative NT-pro BNP levels were not significantly associated with separated different AKI stages. These might attributed to the limited sample size in separated AKI stage strata.

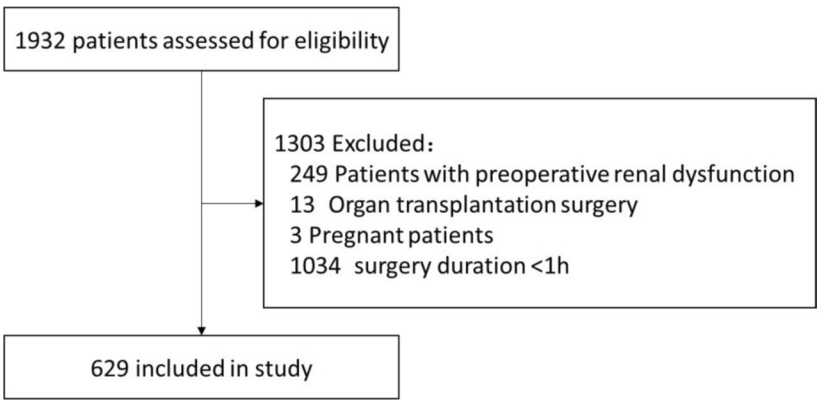

Fig. 1 Flowchart of the study

Table 1 Baseline characteristics of the study

Variables	Overall	NT-proBNP (pg/mL)	
		Low level (< 165)	High level (≥ 165)
n	629	314	315
Age, mean (SD), y	63.5 ± 15.3	58.5 ± 14.9	68.5 ± 14.1
Male (%)	432 (68.7)	207 (65.9)	225 (71.4)
BMI, mean (SD)	23.2 ± 5.1	23.0 ± 4.0	23.3 ± 5.9
Medical history			
Hypertension (%)	590 (93.8)	297 (94.6)	293 (93.0)
Diabetes mellitus (%)	564 (89.7)	282 (89.8)	282 (89.5)
Coronary artery disease (%)	129 (20.5)	43 (13.7)	66 (21.0)
Abnormal liver function (%)	2 (0.3)	1 (0.3)	1 (0.3)
Heart failure (%)	2 (0.3)	0	2 (0.6)
Endoscopic surgery (%)	161 (25.6)	95 (30.3)	66 (21.0)
Pre-operative laboratory findings			
Hemoglobin, median (IQR), g/L	119 (96 to 139)	124 (102 to 143)	113 (91 to 132)
Urea, median (IQR), mmol/L	5.9 (4.7 to 8.0)	6.0 (5.0, 7.0)	6.0 (5.0, 9.0)
Creatinine, median (IQR), μmol/L	72.0 (62.0, 87.0)	71.0 (61.0 to 84.3)	76.0 (63.0 to 93.0)
NT-proBNP, median (IQR), pg/ml	165.0 (62.3 to 428.5)	62.3 (35.1 to 106.0)	428.1 (256.7 to 730.3)
Serum albumin, median (IQR), g/L	38.0 (32.8 to 41.8)	39.7 (34.9 to 43.1)	35.8 (31.4 to 40.2)
Intraoperative information			
ASA physical status score			
I (%)	5 (0.8)	4 (1.3)	1 (0.3)
II (%)	276 (43.9)	183 (58.3)	93 (29.5)
III (%)	336 (53.4)	124 (39.5)	212 (67.3)
IV (%)	12 (1.9)	3 (1.0)	9 (2.9)
Duration of surgery, median (IQR), hour	2.8 (2.0 to 3.9)	2.9 (2.0 to 3.8)	2.8 (1.9 to 4.0)
Preoperative systolic blood pressure, median (IQR), mmHg	123 (110 to 138)	121 (109 to 134)	125 (112 to 140)
Preoperative diastolic blood pressure, median (IQR), mmHg	70 (62 to 78)	71 (63 to 78)	70 (62 to 78)
Diuretics (%)	3 (0.5)	3 (1.0)	0
NSAIDs (%)	614 (97.6)	303 (96.5)	311 (98.7)
Antibiotics (%)	627 (99.7)	314 (100.0)	313 (99.4)
Total volume infusion, median (IQR), ml	2800 (2100 to 3650)	2700 (2075 to 3600)	2800 (2100 to 3700)
Estimated blood loss, median (IQR), ml	50 (20 to 100)	50 (20 to 100)	50 (20 to 100)
Urine output, median (IQR), mL	400 (200 to 700)	300 (200 to 700)	400 (200 to 700)
Postoperative information			
Postoperative NSAIDS (%)	439 (69.8)	228 (72.6)	211 (67.0)
Postoperative infections			
AKI (%)	112 (17.8)	46 (14.6)	66 (21.0)

Abbreviations: *SD* standard deviation, *BMI* body mass index, *NT-proBNP* N-terminal pro-B-type natriuretic peptide, *CI* confidence interval, *IQR* interquartile range, *ASA* American Society of Anesthesiologists, *NSAIDS* non-steroidal anti-inflammatory drugs

Sensitivity analyses

The association between NT-proBNP (quartiles) and AKI risk is shown in Table S3; NT-pro BNP levels were categorized into quartiles with the lowest quartile (Q1, NT-pro BNP levels < 61.6 pg/ml) being the reference. As demonstrated in the Table S4, patients with preoperative NT-pro BNP levels in the highest quartile (> 402.7 pg/ml) has significant higher risk of postoperative AKI as compared to those in Q1 (unadjusted OR 1.91; 95% CI 1.06 to 3.41). After adjusting the potential confoundings, preoperative NT-pro BNP levels in Q4 was associated with increased risk of postoperative AKI as compared to those in Q1 (adjusted OR of model 2, 2.36; 95% CI 1.26 to 4.42; adjusted OR of model 3, 2.01; 95% CI 1.03 to 3.91). However, preoperative NT-pro BNP levels in Q2 or Q3 was not associated with significant increased AKI risks as compared to Q1. Among patients with complete data ($n = 611$, Table S5), and complete adherence to the ERAS

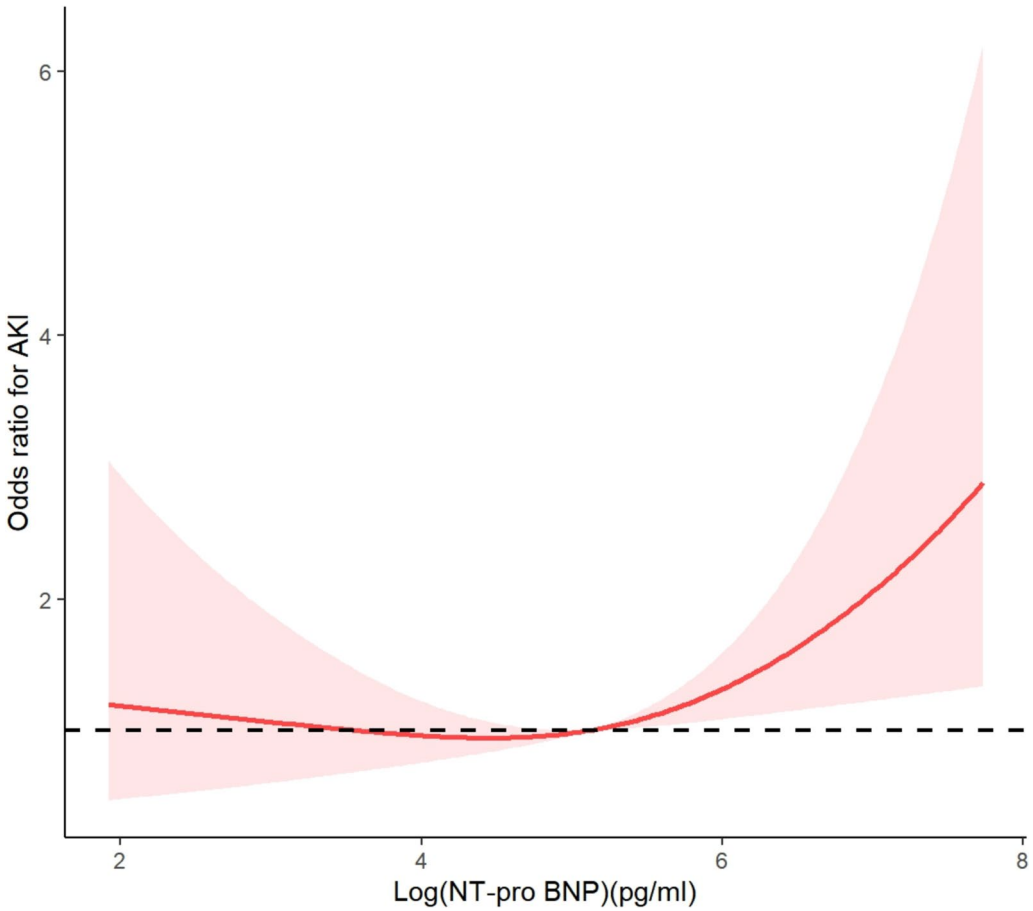

Fig. 2 The adjusted OR of AKI as a function of preoperative log (NT-proBNP) concentrations. The shadow area indicates 95% CIs. Three knots were used, located at the 5 th, 50 th, and 95 th percentiles of the log (NT-proBNP)

strategy (n = 595, Table S6), the association between increased preoperative NT-pro BNP levels and risk of AKI persisted.

Association of total volume infusion and risk of AKI

This study observed a positive association between total volume infusion and AKI. As shown in Table S7, increased risk of AKI was observed in patients with the lowest quartile of total volume infusion levels (< 2100 ml) compared with those with the highest quartile (Q4 > 3600 ml) (OR 2.02; 95% CI 1.13 to 3.61). Univariate logistic regression model adjusted for age, sex, and BMI.

Mediation analyses

As shown in Table 3, significant mediated effects by total volume infusion were observed on the relationships between NT-proBNP levels and AKI (P = 0.040). Increased total volume infusion significantly mediated 15.5% of NT-proBNP-associated elevated AKI risk.

Subgroup analyses

We found that in subgroups of age ≥ 50 (OR 1.68; 95% CI 1.05 to 2.69), female (OR 3.33; 95% CI 1.49 to 7.45), open surgery (OR 1.70; 95% CI 1.05 to 2.74), use of NSAIDS after surgery (OR 1.72; 95% CI 1.04 to 2.85), intraoperative fluid balance > 0 ml (OR 1.84; 95% CI 1.20 to 2.83), ASA I-II (OR 2.71; 95% CI 1.42 to 5.19), and eGFR ≥ 90 ml/min/1.73 m^2 (OR 2.05; 95% CI 1.13 to 3.70), high level of NT-proBNP was significantly related to increased risk of AKI. The effect modification or interactions were detected in sex, ASA physical status score, and eGFR subgroups, with stronger association between preoperative NT-proBNP levels and the risks of AKI in female (P for interaction, 0.024), ASA I-II (P for interaction, 0.017), and eGFR ≥ 90 ml/min/1.73 m^2 subgroups (Fig. 3).

Discussion

In this retrospective cohort study, we found increased preoperative NT-proBNP levels were associated with higher risk of AKI among patients undergoing elective gastrointestinal surgeries and managed with enhanced

Table 2 Univariate and multivariate logistic regression models for the association between NT-proBNP and AKI risk

NT-proBNP (pg/mL)					
	Low level (< 165.0) (*N* = 314)	**High level (≥ 165.0) (*N* = 315)**		**Low level (< 165.0) (*N* = 314)**	**High level (≥ 165.0) (*N* = 315)**
Median (IQR)	62.0 (35.3 to 106.1)	428.6 (260.1 to 372.4)		62.0 (35.3 to 106.1)	428.6 (260.1 to 372.4)
Model 1[a]	Ref	1.56 (1.03 to 2.36)	Stage 1	Ref	0.74 (0.44 to 1.26)
			Stage 2	Ref	1.10 (0.52 to 2.29)
			Stage 3	Ref	0.64 (0.26 to 1.59)
Model 2[b]	Ref	1.75 (1.13 to 2.73)	Stage 1	Ref	0.75 (0.42, 1.35)
			Stage 2	Ref	1.24 (0.56, 2.74)
			Stage 3	Ref	0.51 (0.19, 1.35)
Model 3[c]	Ref	1.57 (0.98 to 2.52)	Stage 1	Ref	0.66 (0.36, 1.22)
			Stage 2	Ref	1.24 (0.55, 2.84)
			Stage 3	Ref	0.51 (0.18, 1.41)
Model 4[d]	Ref	1.49 (0.92 to 2.40)	Stage 1	Ref	0.66 (0.36 to 1.22)
			Stage 2	Ref	1.29 (0.56 to 3.00)
			Stage 3	Ref	0.53 (0.19 to 1.49)
Model 5[e]	Ref	1.43 (0.87 to 2.34)	Stage 1	Ref	0.65 (0.35 to 1.20)
			Stage 2	Ref	1.28 (0.55 to 3.00)
			Stage 3	Ref	0.59 (0.21 to 1.68)

Abbreviations: *NT-proBNP* N-terminal pro-B-type natriuretic peptide, *AKI* acute kidney injury. [a]Non-adjusted model adjusted for none. [b]Model 2 adjusted for age, sex and BMI. [c]Model 3 adjusted for hemoglobin, creatinine, serum albumin, and covariates included in model 2. [d]Model 4 adjusted for and estimated blood loss, duration of surgery, urine output, intraoperative diuretics, intraoperative NSAIDs, intraoperative antibiotics, postoperative infections, and covariates included in model 3. [e]Fully adjusted model adjusted for all covariates. Stage 1 means patients who were diagnosed as stage 1 AKI according to KDIGO 2021 guideline. Stage 2 means patients who were diagnosed as stage 2 AKI according to KDIGO 2021 guideline. Stage 3 means patients who were diagnosed as stage 3 AKI according to KDIGO 2021 guideline. *KDIGO*, Kidney Disease: Improving Global Outcomes

Table 3 Mediated effects by total volume infused on the associations of NT-proBNP levels with AKI (*n* = 629)

Categories	**Quartiles of NT-proBNP levels and AKI**	***P***
Mediation: Total volume infused		
Total effects (95% CI)	3.22×10^{-5} (9.62×10^{-6} to5.43×10^{-5})	0.004
Direct effects (95% CI)	2.71×10^{-5} (6.14×10^{-6} to 4.87×10^{-5})	0.010
Mediated effects (95% CI)	5.13×10^{-6} (2.53×10^{-7} to 1.10×10^{-5})	0.040
Proportion mediated by total volume infused 15.5%		

Abbreviations: *NT-proBNP* N-terminal pro-B-type natriuretic peptide, *CI* confidence interval, *AKI* acute kidney injury. Mediation analyses were conducted using the R statistical software version 4.3.2

recovery after surgery (ERAS) strategy. NT-proBNP-associated AKI risk may be partially mediated by total volume infusion. This study suggests that serum NT-proBNP could be a promising biomarker for the prediction of AKI, providing more scientific basis for the prevention of AKI.

NT-proBNP has been shown to be able to predict adverse renal outcomes in several settings, including acute coronary syndromes, critical illness, and cardiac or non-cardiac surgery (Jarai et al. 2012; Cardinale et al. 2018; Espriella et al. 2022). However, the association between NT-proBNP levels and the occurrence of postoperative AKI could be influenced by the implementation of ERAS protocols (Drakeford et al. 2022; Koerner et al. 2019). Previous studies have explored the association of ERAS and postoperative AKI, but the findings were inconsistent. A meta-analysis of 19 cohort studies showed that ERAS protocols had no promoting effect on the incidence of postoperative AKI (Shen et al. 2021), while some reseachers suggested ERAS protocols should be optimized to prevent postoperative AKI (Drakeford et al. 2022; Koerner et al. 2019). The inappropriately positive perioperative fluid balance might be the explanation of higher AKI incidence in the ERAS cohort (Huepenbecker et al. 2021; Zorrilla-Vaca et al. 2021). In a retrospective review of investigating AKI and colorectal

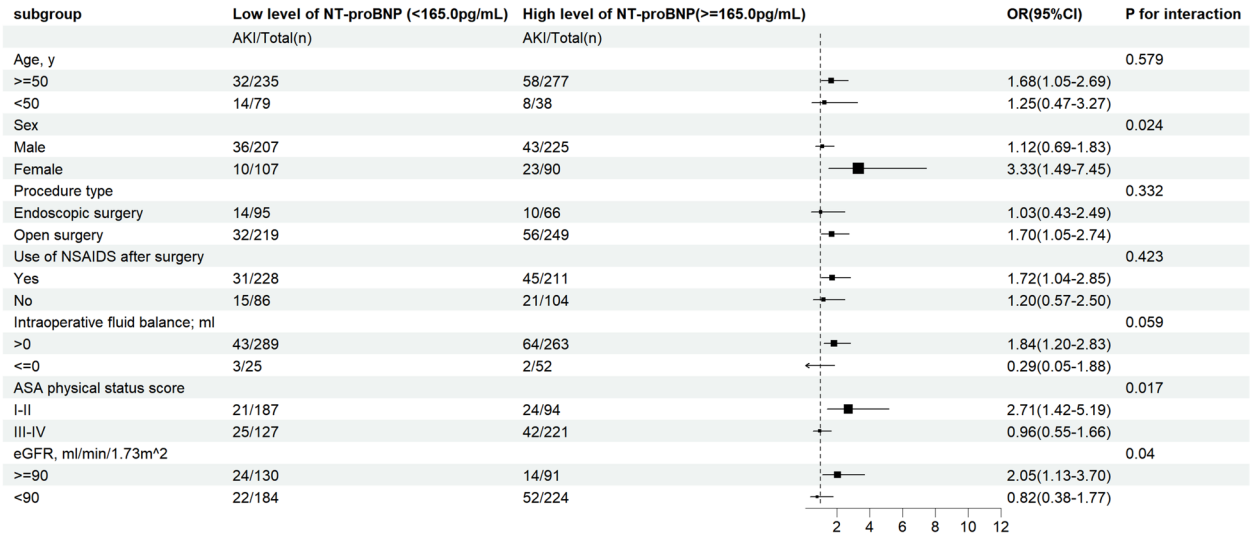

Fig. 3 Subgroup analysis of the trial. Abbreviations: AKI acute kidney injury, NSAIDS nonsteroidal anti-inflammatory drugs, ASA American society of Anesthesiologists, eGFR estimated glomerular filtration rate. Intraoperative fluid balance = Total volume infused-urine output-estimated blood loss − physiological requirement. Physiological requirement = body weight × 3 ml/kg/h × duration of surgery. eGFR for male = [(140 − age) × weight × 1.23]/serum creatinine, eGFR for female = [(140 − age) × weight × 1.04]/serum creatinine

surgery managed with ERAS, no significant difference in intraoperative total fluid (3760 vs 3468 ml, $P = 0.233$) was detected between the ERAS and standard care cohorts, and ERAS was not associated with postoperative AKI (Horres et al. 2017). Larissa et al. reported that the incidence of postoperative AKI after open gynecologic surgery was higher in ERAS cohort as compared to the counterpart cohort (13.1% vs 5.8%, $P < 0.001$), and net fluid balance was 1535 ml in the ERAS vs 1261 mL in the counterpart cohort ($P < 0.001$). Given that either inadequate renal perfusion or renal hyperperfusion would lead to AKI, the contradict situation might attribute to the different preoperative fluid load (Andreucci et al. 2001). Thus, the relationship between preexisting fluid load status, as evidenced by preoperative NT-proBNP levels, and ERAS strategy, and AKI requires further clarification. In an encapsulated organ such as the kidney, tissue edema from fluid overload can contribute to the progression of AKI as the kidney lacks the capacity to accommodate additional volume without an increase in interstitial pressure and compromised organ blood flow (Kambhampati et al. 2012). NT-proBNP reflected potential intravascular volume status well, which prompted the researchers to explore the relationship between NT-proBNP and AKI under a preoperatively sufficient volume circumstance caused by ERAS strategy.

The key point of our research is whether increased preoperative NT-proBNP leads to AKI under ERAS strategy. Mechanistically, excessive fluid infusion may theoretically increase the risk of AKI in elevated preoperative NT-proBNP of patients who were not tolerable to excessive fluid due to intraoperative pre-existing intravascular volume overload and cardiac dysfunction. The excessive intraoperative fluid infusion taxed the kidneys, thus resulting in postoperative AKI; this was confirmed by our subgroup analyses. Positive fluid balance is associated with increased incidence of AKI after major surgery, because large amounts of fluid intraoperatively were given in response to hypotension and significant blood loss, both independent factor for AKI (Kambhampati et al. 2012). For these patients, intraoperative fluid administration could consult guideline for enhanced recovery after colon and rectal surgery and guideline for the management of heart failure, which recommended tailored infusion to avoid volume overload (Carmichael et al. 2017).

Limitations of our study include the single center and retrospective design with relative small sample size, primarily due to limited availability of subjects. We plan to expand the sample size through multicenter collaboration in future research to further validate our initial finding. Second, the diagnosis of AKI relied on serum creatinine increase solely, and urine output was not considered; hence, actual AKI prevalence might be underestimated and underreported. Third, we did not include covariates that were not available in the registry database (such as novel markers of kidney injury, the use of diuretic), resulting in residual confoundings. Besides, the incidence of severe postoperative AKI

(KDIGO Stages 2 or 3) in this cohort was low, making our analyses for these outcomes less reliable.

Conclusions

In this retrospective cohort study, we found that increased level of preoperative NT-proBNP was associated with higher risk of postoperative AKI in patients who underwent gastrointestinal surgery and managed with ERAS strategy. Further studies with large sample size are needed to verify the association and to elucidate the optimal fluid management in this patient population with increased preoperative NT-proBNP levels.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13741-025-00528-6.

Additional file 1.

Authors' contributions

Hailong Dong, and Chong Lei conceptualized and designed the study. Chong Lei and Zefei Zhang drafted the manuscript. Hang Nie and Zefei Zhang performed data collection. Zefei Zhang and Ziyu Zheng performed database maintenance and data analysis. All authors interpreted the data. The authors readed and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This study was approved by KY- 20232265-F- 1 from Approval Form I E C of our hospital. The need for written informed consent was waived, because of the study's retrospective nature.

Consent for publication

All authors approved the final manuscript and the submission to this journal.

Competing interests

The authors declare no competing interests.

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References

Agha R, Abdall-Razak A, Crossley E, et al. STROCSS 2019 guideline: strengthening the reporting of cohort studies in surgery. Int J Surg. 2019;72:156–65.
Andreucci M, Federico S, Andreucci VE. Edema and acute renal failure. Semin Nephrol. 2001;21(3):251–6.
Azur MJ, Stuart EA, Frangakis C, Leaf PJ. Multiple imputation by chained equations: what is it and how does it work? Int J Methods Psychiatr Res. 2011;20(1):40–9.
Ban KA, Berian JR, Ko CY. Does implementation of enhanced recovery after surgery (ERAS) protocols in colorectal surgery improve patient outcomes? Clin Colon Rectal Surg. 2019;32(2):109–13.
Berri RN, Sahai SK, Durand JB, et al. Serum brain naturietic peptide measurements reflect fluid balance after pancreatectomy. J Am Coll Surg. 2012;214(5):778–87.
Brusasco C, Cucciolini G, Barberis A, et al. Improving patient outcomes in abdominal surgery. J Clin Med. 2024;13(7):1993.
Cao Z, Jia Y, Zhu B. BNP and NT-proBNP as diagnostic biomarkers for cardiac dysfunction in both clinical and forensic medicine. Int J Mol Sci. 2019;20(8):1820.
Cardinale D, Cosentino N, Moltrasio M, et al. Acute kidney injury after lung cancer surgery: incidence and clinical relevance, predictors, and role of N-terminal pro B-type natriuretic peptide. Lung Cancer. 2018;123:155–9.
Carmichael JC, Keller DS, Baldini G, et al. Clinical practice guidelines for enhanced recovery after colon and rectal surgery from the American Society of Colon and Rectal Surgeons and Society of American Gastrointestinal and Endoscopic Surgeons. Dis Colon Rectum. 2017;60(8):761–84.
Choi JH, Cho DK, Song YB, et al. Preoperative NT-proBNP and CRP predict perioperative major cardiovascular events in non-cardiac surgery. Heart. 2010;96(1):56–62.
Drakeford PA, Tham SQ, Kwek JL, et al. Acute kidney injury within an enhanced recovery after surgery (ERAS) program for colorectal surgery. World J Surg. 2022;46(1):19–33.
Elíasdóttir SB, Klemenzson G, Torfason B, Valsson F. Brain natriuretic peptide is a good predictor for outcome in cardiac surgery. Acta Anaesthesiol Scand. 2008;52(2):182–7.
von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet. 2007;370(9596):1453–7.
de la Espriella R, Bayés-Genís A, Llàcer P, et al. Prognostic value of NT-proBNP and CA125 across glomerular filtration rate categories in acute heart failure. Eur J Intern Med. 2022;95:67–73.
Friese RS, Dineen S, Jennings A, et al. Serum B-type natriuretic peptide: a marker of fluid resuscitation after injury? J Trauma. 2007;62(6):1346–50; discussion 50-1.
Grams ME, Sang Y, Coresh J, et al. Acute kidney injury after major surgery: a retrospective analysis of Veterans Health Administration data. Am J Kidney Dis. 2016;67(6):872–80.
Grass F, Lovely JK, Crippa J, et al. Early acute kidney injury within an established enhanced recovery pathway: uncommon and transitory. World J Surg. 2019;43(5):1207–15.
Hobson C, Ozrazgat-Baslanti T, Kuxhausen A, et al. Cost and mortality associated with postoperative acute kidney injury. Ann Surg. 2015;261(6):1207–14.
Horres CR, Adam MA, Sun Z, et al. Enhanced recovery protocols for colorectal surgery and postoperative renal function: a retrospective review. Perioper Med (Lond). 2017;6:13.
Hoste EAJ, Kellum JA, Selby NM, et al. Global epidemiology and outcomes of acute kidney injury. Nat Rev Nephrol. 2018;14(10):607–25.
Huepenbecker SP, Iniesta MD, Zorrilla-Vaca A, et al. Incidence of acute kidney injury after open gynecologic surgery in an enhanced recovery after surgery pathway. Gynecol Oncol. 2021;163(1):191–8.
Jarai R, Dangas G, Huber K, et al. B-type natriuretic peptide and risk of contrast-induced acute kidney injury in acute ST-segment-elevation myocardial infarction: a substudy from the HORIZONS-AMI trial. Circ Cardiovasc Interv. 2012;5(6):813–20.
Kambhampati G, Ross EA, Alsabbagh MM, et al. Perioperative fluid balance and acute kidney injury. Clin Exp Nephrol. 2012;16(5):730–8.
Kellum JA, Romagnani P, Ashuntantang G, et al. Acute kidney injury. Nat Rev Dis Primers. 2021;7(1):52.
Koerner CP, Lopez-Aguiar AG, Zaidi M, et al. Caution: increased acute kidney injury in enhanced recovery after surgery (ERAS) protocols. Am Surg. 2019;85(2):156–61.
Lone Z, Zhang A, Benidir T, et al. The role of enhanced recovery after surgery protocols in the development of acute kidney injury following radical cystectomy. Urol Oncol. 2022;40(10):453.e1-.e7.

Mair J, Gerda F, Renate H, et al. Head-to-head comparison of B-type natriuretic peptide (BNP) and NT-proBNP in daily clinical practice. Int J Cardiol. 2008;124(2):244–6.
Marcotte JH, Patel K, Desai R, et al. Acute kidney injury following implementation of an enhanced recovery after surgery (ERAS) protocol in colorectal surgery. Int J Colorectal Dis. 2018;33(9):1259–67.
Muñoz Aguilera E, Leira Y, Miró Catalina Q, et al. Is systemic inflammation a missing link between periodontitis and hypertension? Results from two large population-based surveys. J Intern Med. 2021;289(4):532–46.
Myles PS, Bellomo R, Corcoran T, et al. Restrictive versus liberal fluid therapy for major abdominal surgery. N Engl J Med. 2018;378(24):2263–74.
Nie H, Hao Y, Feng X, et al. Postoperative short-term use of the nonsteroidal anti-inflammatory drug flurbiprofen did not increase the anastomotic leakage rate in patients undergoing elective gastrointestinal surgery-a retrospective cohort study. Perioper Med (Lond). 2022;11(1):38.
Nojiri T, Inoue M, Shintani Y, et al. B-type natriuretic peptide-guided risk assessment for postoperative complications in lung cancer surgery. World J Surg. 2015;39(5):1092–8.
Nongnuch A, Panorchan K, Davenport A. Predialysis NTproBNP predicts magnitude of extracellular volume overload in haemodialysis patients. Am J Nephrol. 2014;40(3):251–7.
O'Connor ME, Kirwan CJ, Pearse RM, Prowle JR. Incidence and associations of acute kidney injury after major abdominal surgery. Intensive Care Med. 2016;42(4):521–30.
Ojo B, Campbell CH. Perioperative acute kidney injury: impact and recent update. Curr Opin Anaesthesiol. 2022;35(2):215–23.
Roques F, Nashef SA, Michel P, et al. Risk factors and outcome in European cardiac surgery: analysis of the EuroSCORE multinational database of 19030 patients. Eur J Cardiothorac Surg. 1999;15(6):816–22; discussion 22-3.
Shen W, Wu Z, Wang Y, Sun Y, Wu A. Impact of Enhanced Recovery After Surgery (ERAS) protocol versus standard of care on postoperative acute kidney injury (AKI): a meta-analysis. PLoS One. 2021;16(5): e0251476.
Thacker JK, Mountford WK, Ernst FR, Krukas MR, Mythen MM. Perioperative fluid utilization variability and association with outcomes: considerations for enhanced recovery efforts in sample US surgical populations. Ann Surg. 2016;263(3):502–10.
Tobin G, Chacko AG, Simon R. Evaluation of NT-ProBNP as a marker of the volume status of neurosurgical patients developing hyponatremia and natriuresis: a pilot study. Neurol India. 2018;66(5):1383–8.
Vernooij LM, van Klei WA, Moons KG, et al. The comparative and added prognostic value of biomarkers to the revised cardiac risk index for preoperative prediction of major adverse cardiac events and all-cause mortality in patients who undergo noncardiac surgery. Cochrane Database Syst Rev. 2021;12(12):Cd013139.
Vickers AJ, Cronin AM, Begg CB. One statistical test is sufficient for assessing new predictive markers. BMC Med Res Methodol. 2011;11: 13.
Wang C, Gao Y, Tian Y, et al. Prediction of acute kidney injury after cardiac surgery from preoperative N-terminal pro-B-type natriuretic peptide. Br J Anaesth. 2021;127(6):862–70.
Weber M, Hamm C. Role of B-type natriuretic peptide (BNP) and NT-proBNP in clinical routine. Heart. 2006;92(6):843–9.
Yang JH, Choi JH, Ki YW, et al. Plasma N-terminal pro-B-type natriuretic peptide is predictive of perioperative cardiac events in patients undergoing vascular surgery. Korean J Intern Med. 2012;27(3):301–10.
Zhao BC, Zhuang PP, Lei SH, et al. Pre-operative N-terminal pro-B-type natriuretic peptide for prediction of acute kidney injury after noncardiac surgery: a retrospective cohort study. Eur J Anaesthesiol. 2021;38(6):591–9.
Zorrilla-Vaca A, Mena GE, Cata J, Healy R, Grant MC. Enhanced recovery programs for colorectal surgery and postoperative acute kidney injury: results from a systematic review and meta-analysis of observational studies. Am Surg. 2021;87(9):1444–51.

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