Incidence, risk factors and outcomes of postoperative acute kidney injury in elderly patients undergoing abdominal surgery

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Abstract

Objectives To investigate the incidence, risk factors and outcomes of acute kidney injury (AKI) in elderly patients undergoing abdominal surgery.

Methods A retrospective study exploring the incidence of AKI in patients older than 75 years within 48 hours after abdominal surgery was conducted. Patients' preoperative characteristics, intraoperative management including medication and outcomes were evaluated for associations with AKI using a logistic regression model.

Results During the 2.5-year period, a total of 409 abdominal surgeries were performed. Both pre- and post-operative SCr measurements were available for 329 (80.4%) cases. 26 patients (7.9%) developed AKI, of whom 25 (7.6%) and 1 (0.3%) reached the AKI stages 1 and 2 respectively. Older age (83.0 vs 80.4 years; p=0.002), preoperative liver function damage represented by AST (47.5 vs 21.0 IU/L; p=0.023), intraoperative combined administration of hydroxyethyl starch(HES) and furosemide (15.38% vs 1.65%; p=0.003) were independent risk factors for the development of postoperative AKI. Furthermore, AKI patients had significantly longer ICU stay (3 vs 0 days; p<0.001) and higher in-hospital mortality (23.08% vs 2.31%; p<0.001)

Conclusion Intraoperative combined administration of HES and furosemide is an independent factor which can be controlled by anesthesiologists and surgeons for AKI. This provides important recommendations for reducing the incidence of postoperative AKI.

Introduction

Acute kidney injury (AKI) is a complex clinical syndrome commonly seen in hospital patients. Several studies had reported that the prevalence of AKI after abdominal surgery was 0.8–22.4% [1–4]. Patients with AKI possess higher risks of chronic kidney disease (CKD) and end-stage renal failure, ultimately leading to in-hospital death and economic burden [5, 6]. Amelioration of AKI could offer survival benefit [7]. Identification of risk factors is the fundamental step to develop underlying preventative and therapeutic strategies for AKI. therefore, investigation of clinical characteristics of patients with postoperative AKI has been a hot topic.

Previous studies have reported several risk factors for developing AKI after abdominal surgery, such as older age, high body mass index (BMI), male gender, morbidities of type 2 diabetes, hypertension and ischemic heart disease [3, 4, 8]. Besides, many nephrotoxic drugs including furosemide, hydroxyethyl starch (HES), nonsteroidal anti-inflammatory drugs (NSAID) and contrast agent, could have negative influence in perioperative renal function and were considered as possible risk factors for postoperative AKI. Although great attention is focused on AKI, risk factors for AKI of elderly patients after abdominal surgery were not well investigated. We hypothesized that clinical characteristics, chronic comorbidities and intraoperative single usage of nephrotoxic drugs have deleterious effect on renal function, and designed this retrospective cohort study focus on patients ≥ 75 years old age, aimed to identify the incidence and risk factors of postoperative AKI in elderly patients. In particular, some factors that could be modified, such as medicine factors.

Materials And Methods

Patient and study design

From January 2016 to June 2018, patients (≥ 75years old age) who planned to undergo abdominal surgery (colon surgery and rectal surgery) were eligible for the study. Patients who sustained severe chronic kidney diseases(CKD) in need of renal transplantation or dialysis, and lacked of either pre- or post-operative measurement of serum creatinine (SCr) were excluded. In patients with more than one surgery, only the first procedure was considered.

All variables were collected from electronic clinical records, including intraoperative data recorded by the anesthesiologist.

The analyzed variables included demographic characteristics (age, gender and weight), preoperative clinical characteristics {comorbidities (hypertension, diabetes mellitus, hyperlipemia and ischemic heart diseases), preoperative serum albumin (Alb), hemoglobin (HGB), alanine aminotransferase (ALT), aspartic aminotransferase (AST) and Scr}, procedure-related variables {type of surgery (laparoscopy or laparotomy), duration of anesthesia and surgery, intraoperative occurrence of hypotension, blood loss, usage of vasoactive drugs and nephrotoxic drugs (HES, NSAIDs and furosemide)}, in-hospital therapeutic needs (ICU admission) and long-term outcomes (readmission and in-hospital mortality).

Definitions

Kidney Disease: Improving Global Outcomes (KDIGO) criteria was used to estimate the incidence and severity of AKI [9]. In order to evaluate the correlation of AKI with surgical procedure and preoperative clinical characteristics, potential influence of other factors arising in the postoperative period should be eliminated. So we focused on AKI occurred within 48 hours after operation to avoid the influences of postoperative infection and application of nephrotoxic drugs. To diagnosis AKI, we set preoperative SCr within 7 days as baseline, and compared to the postoperative Scr in the first and second postoperative day. According to changes in SCr, AKI was classified into stage 1 (SCr ≥26.5μmol/L above baseline or 1.5~1.9 times baseline), stage 2 (SCr 2.0~2.9 times baseline), or stage 3 (SCr ≥3 times baseline or postoperative SCr of ≥354μmol/L with at least 26.5 μmol/L elevation from baseline)[10].

The preoperative baseline SCr, weight, gender and age were used to calculate preoperative estimated glomerular filtration rate (eGFR). For further analysis of the cohort according to preexisting kidney function, patients were classified into 2 groups: eGFR ≤60, and >60 mL/min/1.73m2. CKD group was defined as eGFR <60 mL/min/1.73m^2 [9].

Intraoperative systolic and diastolic blood pressure (SBP and DBP, resp.) were recorded every 5 minutes and mean arterial pressure (MAP) was calculated as (2/3DBP + 1/3SBP). When blood pressure was measured both invasively and noninvasively, invasive measurements were used for analysis. Intraoperative hypotension (IOH) was defined as MAP <65mmHg [11].

Statistical Analysis

Continuous variables are expressed as mean (standard deviation) and categorical variables as percentage of number of cases. Comparisons between patients with and without AKI were performed by the Student's t-test or the Mann-Whitney U test for numerical data, and $\chi 2$ test or Fisher's exact test for categorical data. Logistic regression method was used to determine independent predictors of AKI. Risk factors for AKI were initially assessed with univariate analysis, and variables that were statistically significant (P < 0.05) in the univariate analysis were then included in the multivariate analysis with forward conditional elimination of data. Data are presented as odds ratios (ORs) with 95% confidence intervals (CIs). A two-tailed P value <0.05 was considered significant. Analysis was performed with the statistical software package SPSS 23.0 for Windows

Results

A total of 409 patients underwent abdominal surgery, 80 (19.6%) cases were excluded for lacking of pre- or post-operative SCr measurements, and 329 patients were enrolled finally. Of these, 26 patients (7.9%) complicated AKI, of whom 25 (7.6%), and 1 (0.3%) were classified as AKI stages 1 and 2. There were 128 laparoscopic surgeries and 201 laparotomic surgeries, and the incidence of AKI was 14 (10.94%) and 12 (5.97%), respectively (Table 1). Of the 26 AKI patients, 18 out of 26 patients (69.2%) recovered preoperative levels within a week, 2 patients (7.69%) required dialysis to prevent deteriorating renal function, and 6 patients (23.08%) died.

Table 1

Characteristics of patient-, medication- and procedure-related factors in patients with and without AKI after abdominal surgery

Factors	**AKI (n = 26;7.9%)**	**non-AKI (n = 303;92.1%)**	**P**
Demographic characteristics			
sex (male)	19(73.08%)	147(48.5%)	0.016
Age (years)	83.00 ± 4.707	80.40 ± 4.094	0.002
Weight (kg)	65.19 ± 13.88	62.01 ± 11.99	0.201
Comorbidities			
Hypertension (%)	14(53.85%)	196(64.69%)	0.270
Diabetes mellitus (%)	4(15.38%)	61(20.13%)	0.560
Hyperlipemia (%)	0(0)	26(8.58%)	0.239
Ischemic heart diseases (%)	7(26.92%)	70(23.10%)	0.659
Preoperative laboratory indexes			
HGB (g/L)	123 (113.5,134.5)	118.57(109,132.5)	0.593
ALB (g/L)	35.76(28.63,35.8)	35.80(32.45, 39.2)	0.013
ALT (IU/L)	29.5(13.5,135.5)	14.5(10.0, 22.0)	0.003
AST (IU/L)	47.5(18.8,136.0)	21.0(17.0, 28.0)	0.001
Baseline creatinine			
eGFR□60 (mL/min/1.73 m^2)	15(57.69%)	145(47.85%)	0.335
Procedure- related variables			
Hypotension (%)	15(57.69%)	66(21.78%)	0.000
The use of pressor agent (%)	21(80.77%)	255(84.16%)	0.863
duration of surgery (min)	120(76.8, 174.3)	113(63, 191)	0.977
duration of anesthesia (min)	185(144.8, 227.3)	170(110.5, 255.5)	0.614

HGB = hemoglobin; ALB = albumin; ALT = alanine aminotransferase; AST = aspartic aminotransferase; eGFR = estimated glomerular filtration rate; HES = hydroxyethyl starch; NSAIDs = nonsteroidal anti-inflammatory drugs.

Data were presented as median (interquartile range) for continuous variables or number(percentage) for categorical variables.

Factors	AKI (n = 26;7.9%)	non-AKI (n = 303;92.1%)	P
Blood loss (ml)	20 (10, 85)	20(10, 50)	0.993
Intraoperative usage of nephrotoxic drugs			
HES (%)	6(23.08%)	117(38.61%)	0.116
NSAID (%)	5(19.23%)	40(13.20%)	0.391
HES + NSAID (%)	5(19.23%)	45(14.85%)	0.551
HES + furosemide (%)	4(15.38%)	5(1.65%)	0.000
Type of surgery			
Laparoscopic (%)	14(53.85%)	114(37.62%)	0.103

HGB = hemoglobin; ALB = albumin; ALT = alanine aminotransferase; AST = aspartic aminotransferase; eGFR = estimated glomerular filtration rate; HES = hydroxyethyl starch; NSAIDs = nonsteroidal anti-inflammatory drugs.

Data were presented as median (interquartile range) for continuous variables or number(percentage) for categorical variables.

In Table 1, Demographic characteristics, comorbidities and perioperative factors between patients with or without AKI were compared. AKI Patients were older (83 vs 80 years, P = 0.005) and male ratio was also significantly higher (73.08% vs 48.5%, P = 0.016). We didn’t find that significant differences in comorbidities, including hypertension, diabetes mellitus, hyperlipemia and ischemic heart diseases. Among the preoperative laboratory variables, we found significant difference in ALB, ALT and AST between the AKI and non-AKI groups(P = 0.013, P = 0.003, P = 0.001). In addition, intraoperative hypotension, combination therapy with HES and Furosemide were inferred as risk factors for postoperative AKI ($P < 0.001$).

We performed multivariate logistic regression analysis to determine the pre- and intra-operative risk factors for the development of AKI. The variables included were as follows: age, sex, preoperative ALB and AST, intraoperative hypotension and combined therapy of HES and furosemide. We identified that age (AOR = 1.115; 95% CI, 1.022–1.216), preoperative AST (AOR = 1.004; 95% CI, 1.001–1.007) and intraoperative combined therapy of HES and furosemide (AOR = 9.612; 95% CI, 2.197–42.404) were independent predictors for the development postoperative AKI (Table 2).

Table 2
Risk factors for postoperative AKI after abdominal surgery(Multivariable analysis)

Variable	AOR	95% CI	P
Age (per year)	1.115	1.022, 1.216	0.014
Preoperative AST (IU/L)	1.004	1.001, 1.007	0.023
HES + Furosemide	9.612	2.197,42.404	0.003
AST = aspartic aminotransferase; HES = hydroxyethyl starch; AOR = adjusted odds ratio; CI = confidence interval.			

In Table 3, patients who developed AKI had a longer ICU stay (3 vs 0 day; P < 0.001) and higher in-hospital mortality (23.08% vs 2.31%; P < 0.001). AKI was also associated with a longer postoperative hospital stay and showed marginal significant different (14.5 vs 10 days; P = 0.053).

Table 3
Outcomes measures in patients with and without AKI after abdominal surgery

Outcomes	AKI (n = 26;7.9%;n[%])	non-AKI (n = 303;92.1%; n[%])	P
Postoperative hospital stay (day)	14.5(7, 224.5)	10(7, 14)	0.053
ICU stay after operation (day)	3(0, 12)	0(0, 2)	0.000
Readmission (n/%)	2(7.69%)	15(5.00%)	0.544
In-hospital mortality (n/%)	6(23.08%)	7(2.31%)	0.000
ICU = Intensive Care Unit.			
Data were presented as median (interquartile range) for continuous variables or number (percentage) for categorical variables.			

Discussion

In this retrospective study, we determined the incidence, predictive factors, and outcomes for early AKI (within 48 hours), defined according to the KDIGO guidelines, occurring after abdominal surgery in elderly patients(≥ 75y). The incidence of AKI was 7.9% and that 0.61% required renal replacement therapy. After controlling for confounding variables, old age, preoperative hepatic dysfunction and intraoperative combined administration of HES and furosemide were identified as independent predictors for AKI. Furthermore, ICU stay and in-hospital mortality increased with occurrence of AKI.

Postoperative AKI remains a leading cause of mortality, prolonged hospital stay, and increased hospital cost. Kim M et al. [1] and Kheterpal S et al.[12]reported a rate of 1.1% and 1.0% after intraabdominal surgery. Causey MW et al. [13] reported an incidence of 11.8% in patients submitted to colorectal surgery. Teixeira et al. [3] found an AKI incidence of 22.4% after abdominal surgery. However, direct comparison of these studies is difficult, as the judgment criteria of AKI and age restrictions were inconsistent. But we strictly control these factors in the inclusion criteria in this study.

Previous studies had reported many risk factors for AKI after abdominal surgery such as old age, male gender, liver disease, higher BMI, CKD, Hydroxyethyl starch, use of diuretics and vasopressors [2, 3, 7, 14–16]. Age is a well-known risk factor for renal function impairment in many studies[2, 8], since the capacity of the kidney to adapt to hemodynamic changes declines with age, even minor injury can produce function impairment due to this natural phenomenon. There were also many studies report that postoperative AKI is associated with preoperative liver function damage[2, 17]. These were all consistent with our findings.

Large multicenter non-blinded randomized control trials (RCTs) and meta-analyses have raised concerns about the safety of HES solutions in terms of adverse renal events and mortality [18–20]. After assessing the data submitted by the companies and scientific literatures, the European Medicines Agency’s Pharmacovigilance Risk Assessment Committee (PRAC) suggested that patients treated with HES were at greater risks of kidney injury when compared with crystalloids[21]. Many studies reported that diuretics can also increase the risk of AKI[2, 18, 22, 23], especially loop diuretics[24], and the degree of renal injury was believed to be positively correlated to the dose of diuretic[25–28]. Research has shown that combination of diuretics and other nephrotoxic agents could lead to renal dysfunction more than diuretics alone[29], Therefore, the recent KDIGO guidelines do not recommend the use of loop diuretics for prevention or treatment of AKI[10]. In present study, although HES administration alone in operation has no statistical difference between subgroups of patients with and without AKI, incidence of postoperative AKI was considerably increased in patients with combined administration of HES and diuretics. It was consistent with Landoni G’s study [30].We infer that HES and diuretics might increase the risk of postoperative AKI when combined administration in surgeries. This discovery was of great value to anesthesiologists in managing intraoperative medications. They should avoid the combination HES with furosemide to reduce the risk of postoperative AKI for elder patients.

Studies have confirmed that male sex[23], preoperative lower ALB[17, 20, 23] and intraoperative hypotension[31, 32] are risk factors for postoperative AKI. In our study, although these factors were significantly associated with postoperative AKI in univariate analysis, they were independent risk factors after adjusting for age and intraoperative nephrotoxicity in multivariate analysis. It may be related to the small sample size we collected.

In our study, postoperative AKI after abdominal surgery significantly increased the lengths of ICU stay after operation, medical costs and in-hospital mortality. This finding was consistent with various previous studies[3, 6, 8, 20, 23, 33, 34].

A major innovation of this study was that, for the first time, all patients were at age of 75 years and above. Meanwhile, despite its retrospective design, many covariates with impacts on AKI development and outcome were analyzed. Furthermore, mortality data were collected completely for all patients. However, there were several limitations in this study. First, the single-center nature of the study largely limited its generalizability. Second, we did not have reliable information on urine output for the patient cohort. Using urine output data in addition of SCr might define more AKI cases in the patients.

Conclusion

AKI after abdominal surgery is a frequent occurrence for elderly. Although the overall postoperative mortality is low, AKI is associated with increased ICU stay, medication costs and in-hospital mortality. Age, Preoperative AST and intraoperative usage of HES + furosemide were independent predictors for AKI after abdominal surgeries. According with this result, we could provide valuable guidance for surgeons and anesthesiologists, that avoidance of combined administration of these medicines to prevent postoperative AKI.

Declarations

Ethics statement and consent to participate

The study protocol was approved by the ethics committee of Xuanwu Hospital of Capital Medical University Approval (□□□No. 086), This study is a retrospective observational study using existing data from electronic medical records. IRB waived the requirement for informed consent from the patients according to the ethical guidelines for medical and health research involving human subjects in China.

Authors' contributions

Jianghua Shen participated in the definition, acquisition, analysis and interpretation of data, and provided intellectual content of critical importance to the work, and approved final version to be submitted. Simiao Zhao, Denglei Ma and Minghui Chen participated in the analysis and interpretation of data, and approved final version to be submitted. Suying Yan participated in the conception, analysis and interpretation of data, and revised the article, and provided intellectual content of critical importance to the work, and approved final version to be submitted. All authors read and approved the final manuscript.

Conflict of interest

The authors have declared that no conflict of interest exists.

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