Correlation between perioperative parecoxib and postoperative acute kidney injury in patients undergoing non-cardiac surgery: a retrospective cohort analysis

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Research article

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Abstract

Background: The association of nonsteroidal anti-inflammatory drugs with postoperative acute kidney injury is controversial. However, there are few studies focusing on the association between parecoxib and postoperative acute kidney injury.

Methods: We retrospectively reviewed the electronic medical records and laboratory results of 9,246 adult patients (18–60 years) undergoing non-cardiac surgery at Third Xiangya Hospital of Central South University from January 1, 2012 to August 31, 2017. Study groups were either treated with or without parecoxib. Univariable analysis identified demographic, preoperative laboratory, and intraoperative factors associated with acute kidney injury. Logistic stepwise regression was used to calculate the adjusted odds ratio of parecoxib and acute kidney injury association.

Results: The incidence of postoperative acute kidney injury was 6.06% and parecoxib was used in 0.105% of patients. The mortality was 4.64% in the acute kidney injury group. The incidence of acute kidney injury was lower in the parecoxib-administered group (4%) than in the without parecoxib-administered group (6.3%, p = 0.005). Postoperative acute kidney injury risk reduced by 33.40% in the parecoxib-administered group after adjusting for interference factors.

Conclusions: Intraoperative single-dose parecoxib (40 mg or 80 mg) might reduce postoperative acute kidney injury risk in adult patients undergoing non-cardiac surgery.

Background

Acute kidney injury (AKI), a long-recognized complication of surgery with a high incidence of morbidity and mortality, increases health care costs and length of hospital stay [1–3]. Even in patients undergoing non-cardiac surgery with low-grade American Society of Anesthesiologists (ASA) physical status such as ASA I–II, the incidence of postoperative AKI can reach 6% [4]. Mild kidney injury, such as a small increase in postoperative serum creatinine, is associated with renal dysfunction for as long as 1 to 2 years after surgery [5].

Nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly used perioperative anesthetic adjuvants, with anti-inflammatory and analgesic effects. The main mechanism of action of NSAIDs is the inhibition of cyclooxygenase (COX) enzymes, which can ultimately result in the reduction of prostanoids and thromboxane [6]. COX exists in two forms: COX-1, which is present in most body tissues body including the stomach and intestines and COX-2, which is primarily found at sites of inflammation [7]. Accumulating evidence suggests that traditional NSAIDs, such as aspirin and ibuprofen, are associated with acute and chronic gastrointestinal bleeding and kidney disease [8, 9]. These NSAIDs are nonselective COX (COX-1 and COX-2) inhibitors and their side effects are mostly COX-1 related.

Parecoxib is a parenteral specific COX-2 inhibitor, which enhances its therapeutic gain with minimal adverse effects [6, 10]. Parecoxib is used as a perioperative analgesia in over 80 countries, however,

clinical data about parecoxib on postoperative AKI are scarce. Therefore, it is important to establish its safety during the perioperative period. The aim of this study was to assess the correlation between the perioperative use of parecoxib and postoperative AKI in patients undergoing non-cardiac surgery.

Methods

Design and selection criteria

This retrospective study was performed at the Third Xiangya Hospital of Central South University from January 1, 2012, to August 31, 2017. The inclusion criteria were patients aged 18–60 years who underwent non-cardiac surgery. The exclusion criteria were ASA grade VI, administration of local anesthesia, liver transplantation, cardiac surgery, urological surgery (including kidney transplantation), lack of serum creatinine or covariate data, and preoperative combined CKD, defined as estimate glomerular filtration rate (eGFR) < 60 $mL \cdot min^{-1} \cdot 1.73\ m^{(2)\ -1}$, ≥ 3 months). Parecoxib doses larger than 80 mg were not included because the routine dose is not more than 80 mg/day. The study was approved by the Ethics Committee under approval number 2020S264 that waived the need for informed consent because of the observational nature of the study.

Data collection

The following information was collected: 1) epidemiological data including age, sex, and BMI; 2) individual history including preoperative complications and medication history; 3) laboratory data including serum creatinine and eGFR calculated using the Chronic Kidney Disease epidemiology collaboration (CKD-EPI) formula; 4) intraoperative data including the emergency, surgical grade, operative time, anesthesia method, ASA grade, in and out fluid amounts, intraoperative erythrocyte transfusion volume, and hemorrhage volume; and 5) postoperative outcomes such as the occurrence of AKI, admission to ICU, and mortality. All clinical data of the 9,246 patients who underwent non-cardiac surgery were obtained by a retrospective review of the computerized patient record system of our hospital.

Definitions

Postoperative AKI was defined according to the Kidney Disease: Improving Global Outcomes (KDIGO) 2012 creatinine criteria [11], as one of the following: an increase in serum creatinine by ≥ 0.3 mg/dL within 48 h or a ≥ 1.5-times increase in serum creatinine from baseline within 7 postoperative days. The baseline serum creatinine level was calculated using the lowest level at preoperative day 7. The primary outcome was the impact of parecoxib on AKI, defined as AKI occurring within 7 postoperative days. Parecoxib administration was defined during the operative time. Surgical grade was classified using the surgical classification catalog constituted by the Chinese Ministry of Health, published in 2018.

Statistical analysis

All statistical analyses were performed using SAS version 9.4 software (SAS Institute, Inc., Cary, NC, USA) and CRAN R (v3.4.3). The continuous results are expressed as mean(SD), whereas categorical variables are expressed as numbers with percentages. The Kruskal-Wallis rank sum test was used to compare continuous variables between groups, whereas the chi-square ($\chi 2$) test or Fisher's exact probability method was used for categorical variables. Univariable logistic regression analysis was used to identify epidemiological, preoperative laboratory, and intraoperative factors that were significantly associated with AKI development. The data were adjusted for potential confounders. The results of the classification variable are expressed as OR or Beta and 95% CI and all p-values < 0.05 were considered significant.

Results

Of the 108,198 records identified, those of 9,246 patients were included in the analysis (Fig. 1). Reasons for excluding patients were age < 18 or > 60 years (n = 4,783), ASA grade VI (n = 13), exposure to local anesthesia (n = 12,054), cardiac surgery (n = 387), urological surgery including kidney transplantation (n = 3,589), liver transplantation (n = 107), no recorded preoperative or postoperative creatinine data (n = 73,093), no recorded covariate data such as routine blood panel or infusion volume (n = 4,114), preoperative chronic kidney disease (CKD) (n = 472), and administration of parecoxib doses > 80 mg (n = 340).

AKI

The incidence of postoperative AKI was 6.06% (560/9,246). In the AKI group, the probability of admission to the intensive care unit (ICU) and mortality were 10.18% and 4.64%, respectively (Table 1). There was no difference in age, body mass index (BMI), and angiotensin receptor blockers (ARB) use among patients with and without AKI (Table 1). Significant differences between patients with AKI and without AKI are shown in Table 1 (all p < 0.05).

Table 1
Baseline characteristics of patients aged 18–60 years with and without acute kidney injury (AKI)

Clinical features	without AKI (n = 8686)	With AKI (n = 560)	p-value
Age (years)	44.25 ± 10.43	45.06 ± 10.18	0.074
BMI	22.93 ± 4.93	22.54 ± 3.83	0.07
eGFR	101.98 ± 16.38	94.41 ± 19.78	< 0.001
Male	4267 (49.13%)	300 (53.57%)	0.041
Smoking	1213 (13.97%)	105 (18.75%)	0.002
Alcohol consumption	822 (9.46%)	74 (13.21%)	0.004
Anemia	1538 (17.71%)	161 (28.75%)	< 0.001
Hypertension	1884 (21.69%)	211 (37.68%)	< 0.001
Diabetes mellitus	509 (5.86%)	52 (9.29%)	< 0.001
ACEI	189 (2.18%)	21 (3.75%)	0.015
ARB	116 (1.34%)	13 (2.32%)	0.054
CCB	1125 (12.95%)	119 (21.25%)	< 0.001
Diuretics	77 (0.89%)	19 (3.39%)	< 0.001
ASA grade			< 0.001
I–II	6633 (76.36%)	317 (56.61%)	
III–V	2053 (23.64%)	243 (43.39%)	
Anesthesia method			< 0.001
General anesthesia	7735 (89.05%)	531 (94.82%)	
No general anesthesia	951 (10.95%)	29 (5.18%)	

AKI: acute kidney injury, BMI: body mass index, eGFR: estimated glomerular filtration rate, ACEI: angiotensin-converting enzyme inhibitors, ARB: angiotensin receptor blockers, CCB: calcium-channel blockers, ASA: American Society of Anesthesiologists, ICU, intensive care unit. Data are expressed as number of patients (%) or mean ± standard deviation (SD).

Clinical features	without AKI (n = 8686)	With AKI (n = 560)	p-value
Emergency	1395 (16.06%)	130 (23.21%)	< 0.001
Surgical Grade			< 0.001
1	245 (2.82%)	14 (2.50%)	
2	2746 (31.61%)	118 (21.07%)	
3	5349 (61.58%)	386 (68.93%)	
4	346 (3.98%)	42 (7.50%)	
Operative time (min)			< 0.001
≤ 60	1338 (15.4%)	63 (11.25%)	
61–120	2176 (25.05%)	111 (19.82%)	
121–180	2032 (23.39%)	135 (24.11%)	
> 180	3140 (36.15%)	251 (44.82%)	
Intraoperative erythrocyte Transfusion, mL (%)			< 0.001
< 100	6735 (77.54)	339 (60.54)	
100–600	868 (9.99)	82 (14.64)	
601–1000	508 (5.85)	42 (7.50)	
> 1000	575 (6.62)	97 (17.32)	
Intraoperative Hemorrhage, mL (%)			< 0.001
< 100	2623 (30.20)	131 (23.39)	
100–600	4771 (54.93)	292 (52.14)	
601–1000	670 (7.71)	60 (10.71)	
> 1000	622 (7.16)	77 (13.75)	
In fluid amount (10 mL/24 h)	916.67 (625.00–1432.29)	1125.00 (703.12–1604.17)	< 0.001

AKI: acute kidney injury, BMI: body mass index, eGFR: estimated glomerular filtration rate, ACEI: angiotensin-converting enzyme inhibitors, ARB: angiotensin receptor blockers, CCB: calcium-channel blockers, ASA: American Society of Anesthesiologists, ICU, intensive care unit. Data are expressed as number of patients (%) or mean ± standard deviation (SD).

Clinical features	without AKI (n = 8686)	With AKI (n = 560)	p-value
Out fluids amount (10 mL/24 h)	333.33 (145.83–541.67)	375.00 (208.33–687.50)	< 0.001
Parecoxib	934 (10.75%)	39 (6.96%)	0.005
Admission to ICU	376 (4.33%)	57 (10.18%)	< 0.001
Death	32 (0.37%)	26 (4.64%)	< 0.001

AKI: acute kidney injury, BMI: body mass index, eGFR: estimated glomerular filtration rate, ACEI: angiotensin-converting enzyme inhibitors, ARB: angiotensin receptor blockers, CCB: calcium-channel blockers, ASA: American Society of Anesthesiologists, ICU, intensive care unit. Data are expressed as number of patients (%) or mean ± standard deviation (SD).

Parecoxib

Parecoxib was used in 0.105% (973/9,246) of patients (Table 2). The incidence of acute kidney injury was lower in the parecoxib-administered group (4%) than in the without parecoxib-administered group (6.3%, p = 0.005). There was no difference in age; BMI; estimated glomerular filtration rate (eGFR); sex; smoking; alcohol consumption; presence of diabetes mellitus; use of angiotensin-converting enzyme inhibitors (ACEI), ARB, or diuretics; ASA grade; and intraoperative erythrocyte transfusion between patients treated with and without parecoxib (Table 2). Significant differences between patients treated with and without parecoxib are shown in Table 2 (all $p < 0.05$).

Table 2
Baseline characteristics of patients aged 18–60 years treated with and without parecoxib

Clinical features	Without parecoxib (n = 8273)	With parecoxib (n = 973)	p-value
Age (year)	44.23 ± 10.46	44.89 ± 10.04	0.06
BMI	22.89 ± 4.99	23.03 ± 3.76	0.409
eGFR	101.66 ± 16.66	101.56 ± 16.23	0.858
Male	4062 (49.1%)	508 (52.2%)	0.063
Smoking	1175 (14.2%)	146 (15%)	0.479
Alcohol consumption	811 (9.8%)	89 (9.1%)	0.544
Anemia	1547 (18.7%)	152 (15.6%)	0.019
Hypertension	1903 (23%)	189(19.4%)	0.011
Diabetes mellitus	505 (6.1%)	56 (5.8%)	0.666
ACEI	199 (2.4%)	14 (1.4%)	0.065
ARB	116 (1.4%)	14 (1.4%)	0.902
CCB	1142 (13.8%)	103 (10.6%)	0.006
Diuretics	91 (1.1%)	8 (0.8%)	0.482
ASA grade			0.09
I–II	6196 (74.9%)	753 (77.4%)	
III–V	2077 (25.1%)	220 (22.6%)	
Anesthesia method			< 0.001
General anesthesia	7363 (89%)	907 (93.2%)	
No general anesthesia	910 (11%)	66 (6.8%)	
Emergency	1406 (17%)	119 (12.2%)	< 0.001
Surgical grade			< 0.001
1	240 (2.9%)	19 (2%)	
2	2623 (31.7%)	243 (25%)	

BMI: body mass index, eGFR: estimated glomerular filtration rate, ACEI: angiotensin-converting enzyme inhibitors, ARB: angiotensin receptor blockers, CCB: calcium-channel blockers, ASA: American Society of Anesthesiologists, AKI: acute kidney injury. Data are expressed as number of patients (%) or mean ± standard deviation (SD).

Clinical features	Without parecoxib (n = 8273)	With parecoxib (n = 973)	p-value
3	5080 (61.4%)	656 (67.4%)	
4	330 (4%)	55 (5.7%)	
Operative time (min)			< 0.001
≤ 60	1315 (15.9%)	88 (9%)	
61–120	2085 (25.2%)	204 (21%)	
121–180	1919 (23.2%)	246 (25.3%)	
> 180	2954 (35.7%)	435 (44.7%)	
Intraoperative erythrocyte Transfusion, mL (%)			0.94
< 100	6329 (76.5%)	744 (76.5%)	
100–600	852 (10.3%)	98 (10.1%)	
601–1000	496 (6%)	56 (5.8%)	
> 1000	596 (7.2%)	75 (7.7%)	
Intraoperative hemorrhage, mL (%)			0.003
< 100	2507 (30.3%)	251 (25.8%)	
100–600	4500 (4.4%)	559 (57.5%)	
601–1000	662 (8%)	70 (7.2%)	
> 1000	604 (7.3%)	93 (9.6%)	
In fluid amount (10 mL/24 h)	1037.07 ± 565.54	1159.31 ± 579.85	< 0.001
Out fluid amount (10 mL/24 h)	410.17 ± 374.16	373.74 ± 334.53	0.004
AKI	521 (6.3%)	39 (4%)	0.005

BMI: body mass index, eGFR: estimated glomerular filtration rate, ACEI: angiotensin-converting enzyme inhibitors, ARB: angiotensin receptor blockers, CCB: calcium-channel blockers, ASA: American Society of Anesthesiologists, AKI: acute kidney injury. Data are expressed as number of patients (%) or mean ± standard deviation (SD).

Univariable analysis

The factors shown by the univariable analysis to influence AKI development in patients aged 18–60 who underwent non-cardiac surgery are listed in Table 3. In the univariable analysis, male sex, smoking, alcohol consumption, anemia, hypertension, diabetes mellitus, ACEI use, CCB use, diuretic use, ASA grade

III–V, emergency, surgical grade 4, duration of the operation, transfusion, and hemorrhage were independently associated with an increased risk of postoperative AKI (Table 3).

Table 3
Univariable analysis of acute kidney injury (AKI)

Variable	Statistics	Univariable
		OR (95% CI) p-value
Parecoxib	0.11 ± 0.31	0.62 (0.45, 0.87) 0.0050
Age (year)	44.30 ± 10.42	1.01 (1.00, 1.02) 0.0737
Male	4567 (49.39%)	1.19 (1.01, 1.42) 0.0416
BMI	22.90 ± 4.87	0.98 (0.95, 1.00) 0.0396
Smoking	1318 (14.25%)	1.42 (1.14, 1.77) 0.0018
Alcohol consumption	896 (9.69%)	1.46 (1.13, 1.88) 0.0038
Anemia	1699 (18.38%)	1.88 (1.55, 2.27) <0.0001
Hypertension	2095 (22.66%)	2.18 (1.83, 2.61) <0.0001
Diabetes mellitus	561 (6.07%)	1.64 (1.22, 2.22) 0.0011
ACEI	210 (2.27%)	1.75 (1.11, 2.77) 0.0167
ARB	129 (1.40%)	1.76 (0.98, 3.14) 0.0570
CCB	1244 (13.45%)	1.81 (1.47, 2.24) <0.0001
Diuretics	96 (1.04%)	3.93 (2.36, 6.54) <0.0001
eGFR	97.94 ± 22.36	0.96 (0.96, 0.97) <0.0001
ASA grade III–V	2296 (24.83%)	2.48 (2.08, 2.95) <0.0001
No general anesthesia	980 (10.60%)	0.44 (0.30, 0.65) <0.0001
Emergency	1525 (16.49%)	1.58 (1.29, 1.94) <0.0001
Surgical grade 4	388 (4.20%)	2.12 (1.14, 3.98) 0.0184
Operative time (min)		
≤ 60	1401 (15.15%)	1
61–120	2287 (24.74%)	1.08 (0.79, 1.49) 0.6200
121–180	2167 (23.44%)	1.41 (1.04, 1.92) 0.0279
> 180	3391 (36.68%)	1.70 (1.28, 2.25) 0.0003
Intraoperative erythrocyte transfusion, mL (%)		

OR: odds ratio, BMI: body mass index, ACEI: angiotensin-converting enzyme inhibitors, ARB: angiotensin receptor blockers, CCB: calcium-channel blockers, ASA: American Society of Anesthesiologists.

Variable	Statistics	Univariable
		OR (95% CI) p-value
< 100	7074 (76.51%)	1
100–600	950 (10.27%)	1.88 (1.46, 2.41) <0.0001
601–1000	550 (5.95%)	1.64 (1.18, 2.29) 0.0035
> 1000	672 (7.27%)	3.35 (2.63, 4.27) <0.0001
Intraoperative hemorrhage, mL (%)		
< 100	2754 (29.79%)	1
100–600	5063 (54.76%)	1.23 (0.99, 1.51) 0.0596
601–1000	730 (7.9%)	1.79 (1.31, 2.46) 0.0003
> 1000	699 (7.56%)	2.48 (1.85, 3.33) <0.0001
OR: odds ratio, BMI: body mass index, ACEI: angiotensin-converting enzyme inhibitors, ARB: angiotensin receptor blockers, CCB: calcium-channel blockers, ASA: American Society of Anesthesiologists.		

Parecoxib (OR, 0.62; 95%CI, 0.45–0.87, p = 0.005), eGFR (OR 0.96, 95%CI 0.96–0.97, p < 0.0001), and no general anesthesia (OR, 0.44; 95%CI, 0.30–0.65, p < 0.0001) were independently associated with a decreased risk of postoperative AKI (Table 3). Age (OR, 1.01; 95%CI, 1.00–1.02, p = 0.0737), BMI (OR, 0.98; 95%CI, 0.95–1.00, p = 0.0396), and ARB use (OR, 1.76; 95%CI, 0.98–3.14, p = 0.0570) were not correlated with AKI (Table 3).

Multivariable regression analysis

The occurrence of postoperative AKI was regarded as a dependent variable and the administration of parecoxib was an independent variable when we performed the stepwise regression analysis (Table 4). The risk adjustment models were constructed using logistic stepwise regression.

Table 4
Odds ratio of postoperative acute kidney injury (AKI) associated with parecoxib

	Non-adjusted: Model 1	Adjusted I: Model 2	Adjusted II: Model 3
OR (95% CI) p-value	0.62 (0.45, 0.87) 0.0050	0.64 (0.46, 0.90) 0.0096	0.63 (0.44, 0.89) 0.0095
Model 1: Non-adjusted.			
Model 2: Adjusted for age, sex, BMI, smoking, alcohol consumption, anemia, hypertension, diabetes mellitus, ACEI, CCB, diuretics, ASA, anesthesia method, emergency, surgical grade, in fluids, out fluids, transfusion, and hemorrhage.			
Model 3: Adjusted for age, sex, BMI, smoking, alcohol consumption, anemia, hypertension, diabetes mellitus, ACEI, ARB, CCB, diuretics, eGFR, ASA, anesthesia method, emergency, surgical grade, operative time, in fluids, out fluids, transfusion, and hemorrhage.			

Model 1 was non-adjusted, whereas model 2 and model 3 were adjusted for age, sex, BMI, smoking, alcohol consumption, anemia, hypertension, diabetes mellitus, ACEI use, CCB use, diuretic use, ASA, anesthesia method, emergency, surgical grade, fluids in and out, transfusion, and hemorrhage. Model 3 was also adjusted for ARB use, eGFR, and duration of the operation. After adjusting for these interference factors, parecoxib was still independently associated with postoperative AKI (OR, 0.63; 95% CI, 0.44–0.89, model 3 in Table 4).

Sensitivity analysis

Table 5 shows the sensitivity analysis of postoperative AKI associated with parecoxib. For patients with an eGFR < 90 $mL \cdot min^{-1} \cdot 1.73\ m^{(2)\ -1}$ or who were non-smokers, single-dose parecoxib (40 mg or 80 mg) reduced the incidence of postoperative AKI. We divided the outcome of postoperative AKI into three groups: stage 0, no AKI; stage 1, AKI grade 1; and stage 2, AKI grade 2 and 3. The multivariable logistic regression showed that parecoxib reduced the incidence of postoperative AKI in differently ranked AKIs.

Table 5
Sensitivity analysis of association between postoperative acute kidney injury (AKI) and parecoxib

		Model 1	Model 2	Model 3
	Without parecoxib	Parecoxib (40 or 80 mg)		
eGFR < 90	1	0.49 (0.31, 0.79) 0.0032	0.54 (0.33, 0.87) 0.0119	0.50 (0.30, 0.84) 0.0084
Non-smoker	1	0.57 (0.39, 0.84) 0.0040	0.56 (0.37, 0.84) 0.0046	0.56 (0.38, 0.84) 0.0052
AKI RANK	0	-0.03 (-0.05, -0.00) 0.0176	-0.02 (-0.05, -0.00) 0.0283	-0.02 (-0.04, -0.00) 0.0254
AKI RANK (outcome of postoperative AKI was divided into three groups: stage 0, no AKI; stage 1, AKI grade 1; stage 2, AKI grade 2 and 3)				
Model 1: Non-adjusted.				
Model 2: Adjusted for age, sex, BMI, smoking, alcohol consumption, anemia, hypertension, diabetes mellitus, ACEI, CCB, diuretics, ASA, anesthesia method, emergency, surgical grade, in fluids, out fluids, transfusion, and hemorrhage.				
Model 3: Adjusted for age, sex, BMI, smoking, alcohol consumption, anemia, hypertension, diabetes mellitus, ACEI, ARB, CCB, diuretics, eGFR, ASA, anesthesia method, emergency, surgical grade, operative time, in fluids, out fluids, transfusion, and hemorrhage.				

Discussion

According to the surgery type and AKI diagnostic criteria, the incidence of postoperative AKI ranges from 1.0 to 31% [12–14], and our study revealed an incidence of 6.06% in our study population of patients aged 18–60 years who underwent non-cardiac surgery. The incidence was similar to that recently published in data by Nishimoto [15] (6%, non-cardiac surgery; mean age, 63 years). In our study, the univariable analysis identified male sex, smoking, alcohol consumption, anemia, hypertension, diabetes mellitus, ACEI use, CCB use, diuretic use, eGFR, ASA grade III–V, no general anesthesia, emergency, surgical grade 4, duration of the operation (> 120 min), transfusion (> 100 mL), and hemorrhage (> 600 mL) to be associated with AKI, which are similar to previously published data [16, 17].

However, age and BMI did not correlate with AKI in our study, which is inconsistent with the findings of previous studies [18]. This discrepancy can be explained by the difference in mean age and BMI between

the studies, which were both lower at 44.30 ± 10.42 years and 22.90 ± 4.87 kg/m^2, respectively, than those in our study population. The results of the sensitivity analysis suggested that single-dose (40 mg or 80 mg) parecoxib may reduce the risk of postoperative AKI in differentially ranked AKI and in patients with an eGFR < 90 mL·min^{-1}·1.73 $m^{(2)\ -1}$ and who are non-smokers.

Numerous studies have investigated the association between NSAIDs and AKI [9, 19]. An updated Cochrane systematic review and meta-analysis published in 2018 indicated that NSAIDs have uncertain effects on the rate of AKI and may slightly increase serum creatinine in patients with normal kidney function following surgery [19]. In another meta-analysis, a significant risk of AKI was observed with most traditional NSAIDs but not with two COX-2 specific inhibitors (rofecoxib and celecoxib) [9]. A pooled analysis of 28 randomized clinical trials investigating the safety of parecoxib for the management of postoperative pain showed its associated risk of renal failure and impairment was 1%, similar to that with the placebo (0.9%) [20].

However, our study indicated that intraoperative single-dose parecoxib (40 mg or 80 mg) significantly decreased the risk of postoperative AKI in patients aged 18–60 years who underwent non-cardiac surgery. Moreover, this is not the first time a renoprotective effect has been postulated for parecoxib. For example, a study also showed that a single-dose of parecoxib (20 mg/kg) reduced tubular renal injury and serum inflammatory cytokines level (interleukin (IL)-1α, IL-β, IL6, and tumor necrosis factor (TNF)-α) in an ischemic rat model [21]. Moreover, a number of animal studies have suggested that pretreatment with COX-2 inhibitors improved outcomes in function and histology not only in the kidney but also in other organs after ischemia [21, 22, 24]. To the best of our knowledge, this is the first clinical report to suggest that parecoxib may be renoprotective in patients aged 18–60 years who underwent non-cardiac surgery.

The mechanism by which parecoxib decreases the risk of postoperative AKI is unknown. However, one possible underlying mechanism is likely related to inflammation. A previous study showed that inflammation is a predictor of postoperative AKI and a mediator of increased mortality after AKI in non-cardiac surgery [25]. However, perioperative parecoxib reduced local and systemic inflammatory cytokines postoperatively [26, 27]. Another possible mechanism is associated with hemodynamic change. COX-1 contributes to controlling renal GFR, whereas COX-2 is involved in sodium and water excretion [28]. COX-2 inhibitors are associated with mild hypertension owing to modest sodium retention in the first days of therapy [29]. The renoprotective mechanism of parecoxib may be related to its anti-inflammatory effects and sodium regulation.

Our study had some limitations that are worth mentioning. First, this was a retrospective single-center observational study; thus, it may have had some selection bias. Second, the timing of the serum creatinine measurement was based on clinical discretion; thus, it may vary with different doctors. Third, our study population (aged 18–60 years with non-cardiac surgery) might have been a selective population with relatively low risk for AKI. Therefore, our result should be extrapolated cautiously.

Conclusions

In conclusion, in non-cardiac surgery patients, a single dose of parecoxib (40 mg or 80 mg) might decrease the risk of postoperative AKI in those aged 18–60 years. However, these short-term effects may not represent the benefit of this drug in the long term. Furthermore, more comprehensive studies are needed to confirm the effects of parecoxib on the risk of postoperative AKI. Based on our study, we recommend the single-use of parecoxib for patients at risk of AKI, excluding other risks.

Abbreviations

AKI: Acute kidney injury; ASA: American Society of Anesthesiologists; eGFR: estimate glomerular filtration rate; NSAIDs: Nonsteroidal anti-inflammatory drugs; ICU: intensive care unit; BMI: body mass index; ARB: angiotensin receptor blockers; ACEI: angiotensin-converting enzyme inhibitors

Declarations

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Author's Contributions

Yongzhong Tang helped in designing the study, analyzing and interpreting the data, and drafting and revising the manuscript. Pingping Zeng and Yan Liao helped in collecting, analyzing and interpreting the data, and drafting and revising the manuscript. Zheng Qin, Hao Zhang and Bo Li helped in analyzing and interpreting the data. Wen Ouyang helped in Supervising, Funding acquisition and drafting and revising the manuscript. Dan Li helped in designing the study, analyzing and interpreting the data, and drafting and revising the manuscript.

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Ethics declarations

Ethics approval and consent to participate: This study was approved by the ethics committee of the third Xiangya hospital of Central South University (2020S264). Because of the observational nature of the study, informed consent was waived.

Consent for publication Not applicable.

Competing interests: The authors declare they have no competing interests.

Availability of data and materials The data used and analyzed in this study are available from the corresponding author on reasonable request.

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Figures

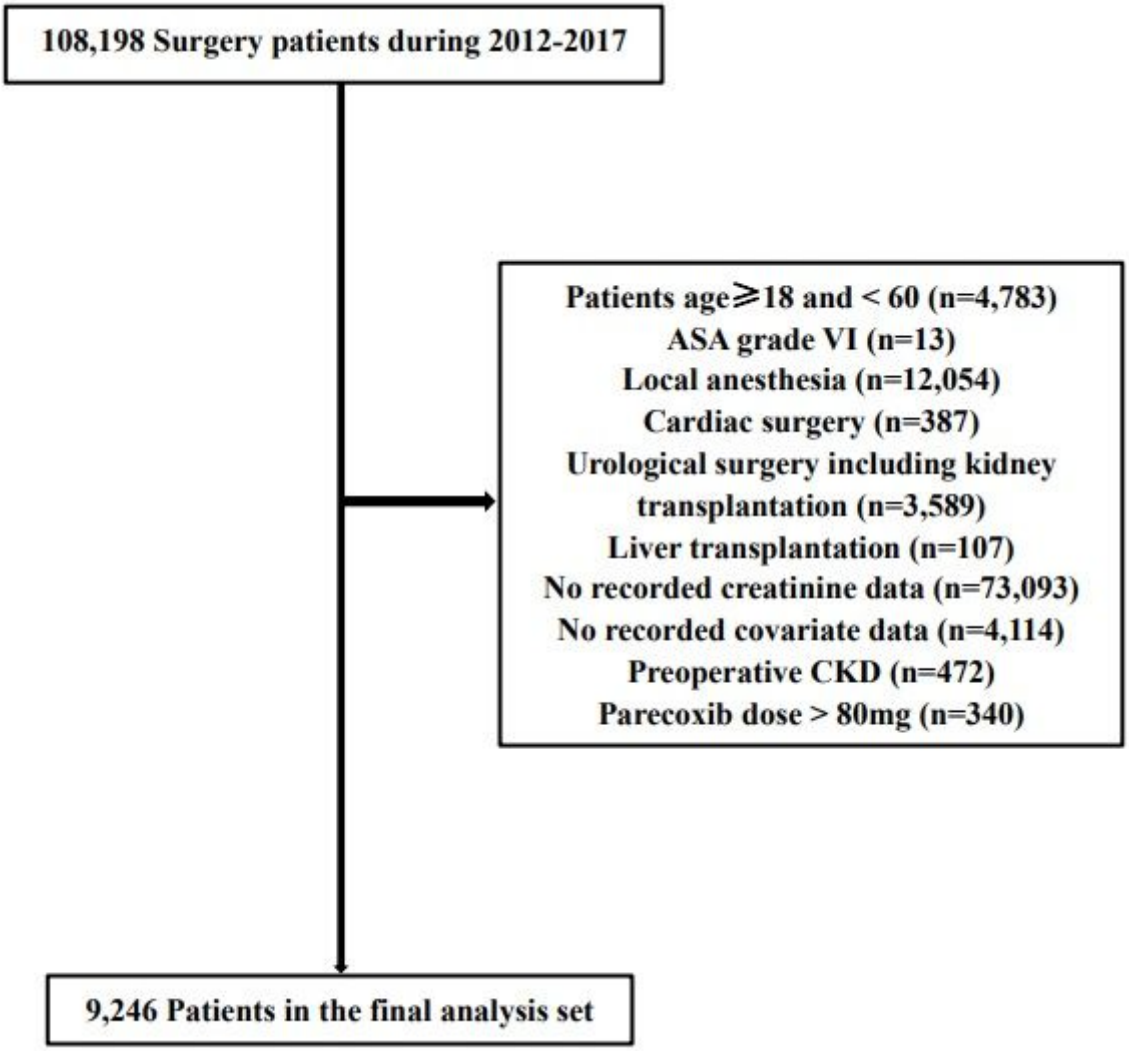

Figure 1

Enrollment of patients undergoing non-cardiac surgery.