BJA

British Journal of Anaesthesia, 126 (4): 799–807 (2021)

doi: 10.1016/j.bja.2020.11.018
Advance Access Publication Date: 17 December 2020
Clinical Practice

CLINICAL PRACTICE

Assessment of prognostic value of intraoperative oliguria for postoperative acute kidney injury: a retrospective cohort study

Bing-Cheng Zhao, Shao-Hui Lei, Xiao Yang, Ya Zhang, Shi-Da Qiu, Wei-Feng Liu, Cai Li and Ke-Xuan Liu*

Department of Anaesthesiology, Nanfang Hospital, Southern Medical University, Guangzhou, China

*Corresponding author. E-mail: liukexuan705@163.com

Abstract

Background: Oliguria is often viewed as a sign of renal hypoperfusion and an indicator for volume expansion during surgery. However, the prognostic association and the predictive utility of intraoperative oliguria for postoperative acute kidney injury (AKI) are unclear.

Methods: We conducted a retrospective cohort study on patients undergoing major thoracic surgery in an academic hospital to assess the association of intraoperative oliguria with postoperative AKI and its predictive value. To contextualise our findings, we included our results in a meta-analysis of observational studies on the importance of oliguria during noncardiac surgery.

Results: In our cohort study, 3862 patients were included; 205 (5.3%) developed AKI after surgery. Intraoperative urine output of 0.3 ml kg^{-1} h^{-1} was the optimal threshold for oliguria in multivariable analysis. Patients with oliguria had an increased risk of AKI (adjusted odds ratio: 2.60; 95% confidence interval: 1.24–5.05). However, intraoperative oliguria had a sensitivity of 5.9%, specificity of 98%, positive likelihood ratio of 2.74, and negative likelihood ratio of 0.96, suggesting poor predictive ability. Moreover, it did not improve upon the predictive performance of a multivariable model, based on discrimination and reclassification indices. Our findings were generally consistent with the results of a systematic review and meta-analysis, including six additional studies.

Conclusions: Intraoperative oliguria has moderate association with, but poor predictive ability for, postoperative AKI. It remains of clinical interest as a risk factor potentially modifiable to interventions.

Keywords: acute kidney injury; anaesthesia; oliguria; postoperative outcome; risk prediction; thoracic surgery; systematic review and meta-analysis

Editor's key points

- The importance of oliguria during surgery and its relationship with postoperative acute kidney injury are unclear.
- Efforts to promote urine flow may not reduce the risk of acute kidney injury.
- The authors identified a weak relationship between oliguria and acute kidney injury, but the occurrence of oliguria did not meaningfully add to its likelihood.
- These findings suggest against using oliguria as an isolated predictor for the development of postoperative acute kidney injury.

Acute kidney injury (AKI) occurs in 13% of patients undergoing major surgery and is associated with increased hospital length of stay, cost, and mortality.[1,2] No robust risk prediction model for AKI is widely used in noncardiac surgical practice, and there is an interest in identifying reliable early markers of

Received: 17 March 2020; **Accepted:** 15 November 2020

renal injury,[3] with the hope of initiating interventions to prevent postoperative AKI.

The kidneys are particularly susceptible to changes in volume status. Inadequate intravascular volume may cause renal hypoperfusion and increase the risk of postoperative AKI.[4] Oliguria is a protective compensatory response to acute hypovolaemia, and thus, it is traditionally viewed as a sign of potentially inadequate fluid volume. Despite that the proposed link between intraoperative urine output and postoperative renal failure is not supported by earlier observational and trial data,[5–8] urine output is still one of the most frequently used indicators for volume expansion amongst anaesthesiologists around the world.[9–11] Recently, several studies using contemporary consensus definition for AKI found significant associations between intraoperative oliguria and AKI after noncardiac surgery.[12–14] However, these studies conflict on the optimal urine output threshold for oliguria and on whether intraoperative oliguria is a useful predictor for postoperative AKI.

Hypovolaemic state and AKI occur frequently in patients undergoing major thoracic surgery because of the practice of perioperative fluid restriction.[15] These surgeries are underrepresented in recent studies on the importance of intraoperative oliguria. Knowing the relationship between oliguria and AKI is of particular interest for patients undergoing thoracic surgery, because volume expansion targeting a higher urine output may lead to fluid overload, which markedly increases the risk of postoperative pulmonary complications.[16]

We hypothesised that intraoperative oliguria would be associated with AKI after major thoracic surgery. We conducted a retrospective cohort study to test this hypothesis and to evaluate the predictive utility of intraoperative oliguria for postoperative AKI. To place our results in context, we conducted a systematic review and meta-analysis of studies reporting on the prognostic association and predictive performance of intraoperative oliguria for AKI after a broader range of noncardiac surgery.

Methods

The retrospective cohort study was conducted in Southern Medical University Nanfang Hospital, a tertiary academic hospital in southern China. The institutional review board approved the study and waived the informed consent. The reporting of the cohort study adheres to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines (checklist in Supplementary Table S1).[17] The systematic review and meta-analysis was conducted according to the Checklist for Critical Appraisal and Data Extraction for Systematic Reviews of Prediction Modelling Studies for reviews of prognostic factors guidelines,[18] and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (checklist in Supplementary Table S2).[19]

Cohort study: study population

All adult (age ≥18 yr) patients admitted to the hospital and undergoing elective lung resection or oesophagectomy between February 2008 and May 2018 were identified. The International Classification of Diseases, Ninth Revision, Clinical Modification procedure codes used for identification of surgical types are described in Supplementary Table S3. Patients were excluded if they (i) did not have serum creatinine measurements before and after surgery; (ii) underwent surgery involving any concurrent cardiovascular, abdominal, or urological procedures; (iii) had end-stage renal disease (defined as having a history of renal replacement therapy or kidney transplantation, or an estimated glomerular filtration rate <15 ml min^{-1} [1.73 m]$^{-2}$ based on the Chinese Modification of Diet in Renal Disease equation[20]) or evidence of AKI before surgery; (iv) received diuretic medications (furosemide, mannitol, etc.) during surgery; or (v) did not have intraoperative urine output recordings. For patients who had more than one thoracic surgery during the study period, only the first surgery was included.

Cohort study: variables and outcomes

Variables that may have an association with postoperative AKI were selected based on literature review. These included patient characteristics (age, sex, and BMI), ASA physical status, medical history (hypertension, diabetes mellitus, cardiovascular diseases, chronic use of renin–angiotensin–aldosterone system inhibitors, and perioperative use of NSAIDs and aminoglycosides), preoperative laboratory tests (haemoglobin, serum albumin, and serum creatinine), and surgical characteristics (type and duration of surgery, intraoperative lowest MAP, i.v. fluid, blood loss, and urine output). For each patient, the average intraoperative urine output was calculated by dividing the total intraoperative urine volume by the duration of surgery (from anaesthesia induction to the end of wound closure) and by the most recent body weight measured before surgery.

The primary outcome was postoperative AKI, defined according to the creatinine criteria of the Kidney Disease: Improving Global Outcomes (KDIGO) 2012 guidelines,[21] namely, an increase in serum creatinine of ≥26.5 μmol L^{-1} within 48 h after surgery or ≥1.5 times baseline within 7 postoperative days. The most recent serum creatinine available before surgery was used as the baseline value.

Cohort study: statistical analyses

A statistical analysis plan was prespecified and published before analyses were done (http://www.nfyy.com/ks/zk/mzttk/lcsy). Continuous variables are presented as median and inter-quartile range, and were compared using Mann–Whitney *U*-test. Categorical variables are presented as count and percentage of the total, and were compared using χ^2 or Fisher's exact test, as appropriate. We assessed the association between intraoperative oliguria and postoperative AKI on the basis of categorising intraoperative urine output at iterative thresholds to objectively identify an optimal cut-off to define oliguria. First, we used univariable logistic regression with restricted cubic splines to examine the potential non-linear association between intraoperative urine output and odds of postoperative AKI. Then, we applied the approach proposed by Mazumdar and colleagues[22] to identify a single statistically optimal threshold of intraoperative urine output to define oliguria. This is an iterative process that evaluates every possible threshold of urine output at intervals of 0.1 ml

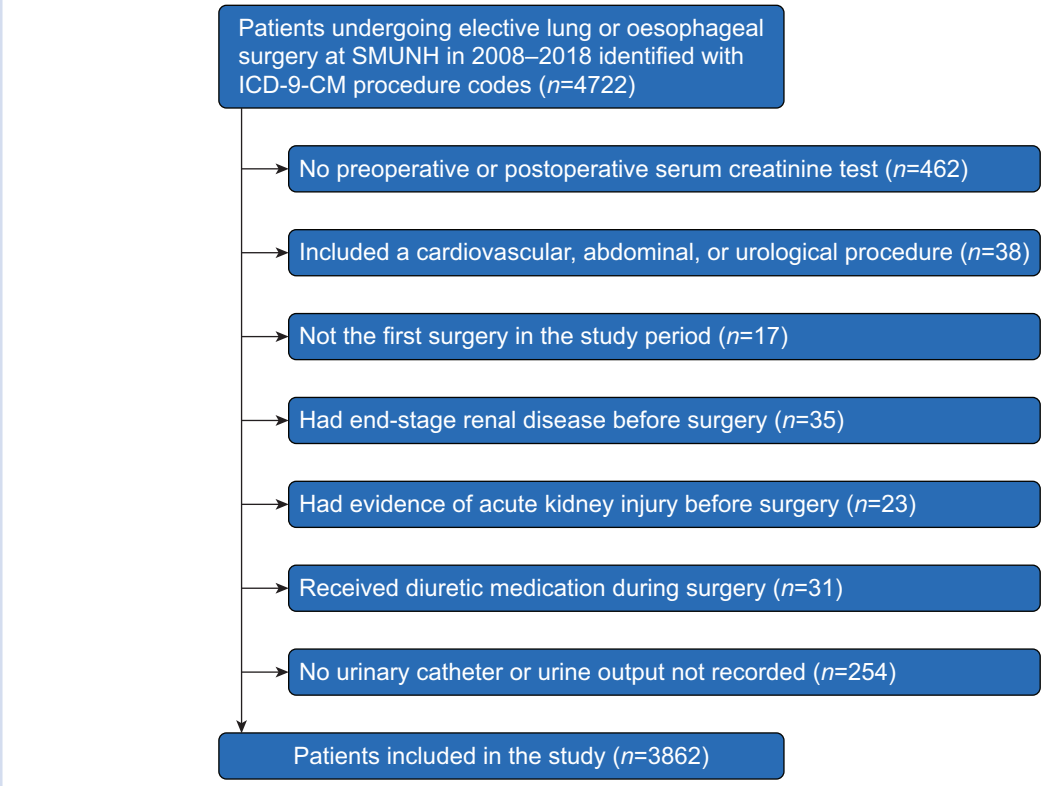

Fig 1. Flow chart for patient selection for the cohort study. ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; SMUNH, Southern Medical University Nanfang Hospital.

kg^{-1} h^{-1} in a multivariable logistic regression model, and the urine output that yields the smallest statistically significant *P*-value from a χ^2 test based on the log-likelihood of the multivariable model with and without intraoperative oliguria was selected as the optimal threshold. In the multivariable analysis, we adjusted all aforementioned *a priori* selected variables. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated for the association between intraoperative oliguria and postoperative AKI. Sensitivity, specificity, and positive and negative likelihood ratios were calculated for predictive ability. In addition, discrimination of the prediction models with and without intraoperative oliguria was assessed by the area under the receiver operating characteristic curve (AUROC). Calibration of the models was assessed using calibration curves and the Hosmer–Lemeshow goodness-of-fit test. The category-free net reclassification improvement (NRI), representing the ability of intraoperative oliguria to correctly reclassify patients at certain predicted risks based on a previous model, was calculated for AKI and no AKI cases, respectively.

Formal sample size calculation was not conducted; we planned to include all eligible patients from our database to maximise the statistical power, and caution was taken that more than 10 events per variable in the multivariable model are required to avoid overfitting. In the multivariable logistic regression analysis, missing data were handled via multiple imputation with chained equations. Pre-planned sensitivity analyses were performed by conducting a complete case analysis (excluding patients with missing data) and by using the traditional threshold for oliguria (urine output <0.5 ml kg^{-1} h^{-1}). Analyses were performed using R version 3.5.2 (R Foundation for Statistical Computing, Vienna, Austria). All statistical tests were two-tailed.

Systematic review and meta-analysis

We conducted a systematic review and meta-analysis of the current evidence on the predictive value of intraoperative oliguria for postoperative AKI, to contextualise the results of our cohort study. The protocol was not prospectively registered. We searched the electronic databases PubMed, Embase, and Web of Science using text keywords (urine OR oliguria) AND (acute kidney injury OR AKI) AND (surgery OR intraoperative OR postoperative) for the years 2004–2020. The references of relevant studies were screened for additional suitable publications. We included observational studies that reported the association of intraoperative oliguria with postoperative AKI in adult patients undergoing noncardiac surgery. Studies on transplant surgery or nephrectomy and studies that did not use the consensus definition for AKI were excluded. We assessed risk of bias of included studies using the Quality in Prognosis Studies tool.[23] The assessment for study eligibility, data extraction, and risk-of-bias assessment were performed by two researchers independently and in duplicate, with any

Table 1 Patient characteristics according to the occurrence of postoperative AKI. Values are count (percentage) or median (interquartile range). ACEI, angiotensin-converting enzyme inhibitor; AKI, acute kidney injury; ARB, angiotensin receptor blocker; ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease. *A total of 229 (5.9%) patients had missing data for one or more variables. †History of coronary heart disease, stroke, or congestive heart failure. ‡From anaesthesia induction to the end of wound closure. ¶Interval between surgery and discharge or death.

Characteristics	Overall, *n*=3862	No AKI, *n*=3657	AKI (any stage), *n*=205	P-value	Missing data (%)*
Age (yr)	59 (51; 65)	58 (51; 65)	63 (56; 69)	<0.001	0
Sex (male)	2624 (68)	2463 (67)	161 (79)	0.001	0
BMI (kg m^{-2})	22.0 (19.9; 24.2)	22.0 (20.0; 24.2)	21.8 (19.5; 24.4)	0.56	3.2
ASA physical status				<0.001	1.9
1	577 (15)	558 (15)	19 (10)		
2	2929 (76)	2782 (76)	147 (72)		
3	280 (7)	247 (7)	33 (16)		
4	4 (<1)	3 (<1)	1 (<1)		
Hypertension	920 (24)	826 (23)	94 (46)	<0.001	0
Diabetes mellitus	434 (11)	387 (11)	47 (23)	<0.001	0
Cardiovascular diseases†	198 (5)	171 (5)	27 (13)	<0.001	0
COPD	332 (9)	317 (9)	15 (7)	0.587	0
Chronic use of ACEI/ARB	233 (6)	197 (5)	36 (18)	<0.001	0
Perioperative use of NSAIDs	1329 (34)	1267 (35)	62 (30)	0.22	0
Perioperative use of aminoglycosides	97 (3)	88 (2)	9 (4)	0.12	0
Preoperative haemoglobin (g L^{-1})	132 (121; 143)	133 (122; 143)	128 (115; 140)	<0.001	0.1
Preoperative serum albumin (g L^{-1})	39.5 (36.9; 42.2)	39.6 (37.0; 42.3)	37.7 (34.8; 40.7)	<0.001	0.2
Preoperative serum creatinine (μmol L^{-1})	70 (60; 82)	70 (60; 82)	75 (62; 90)	0.001	0
Type of surgery				<0.001	0
Wedge resection/segmentectomy	748 (19)	722 (20)	26 (13)		
Lobectomy	1691 (44)	1629 (45)	62 (30)		
Pneumonectomy	75 (2)	68 (2)	7 (3)		
Oesophagectomy	1348 (35)	1238 (34)	110 (51)		
Minimally invasive surgery	2228 (58)	2146 (59)	82 (40)	<0.001	0
Duration of surgery‡ (h)	3.50 (2.75; 4.33)	3.48 (2.73; 4.30)	3.96 (3.20; 5.07)	<0.001	0
Fluid administration‡ (ml kg^{-1})	31.9 (22.7; 44.0)	31.3 (22.5; 43.3)	40.3 (28.0; 52.5)	<0.001	0.8
Blood loss‡ (ml kg^{-1})	1.82 (0.94; 3.36)	1.82 (0.91; 3.33)	2.94 (1.69; 4.47)	<0.001	0.8
Urine output‡ (ml kg^{-1} h^{-1})	1.42 (0.88; 2.25)	1.42 (0.89; 2.25)	1.35 (0.76; 2.23)	0.44	0
Lowest MAP‡ (mm Hg)	69 (62; 76)	69 (62; 76)	65 (58; 74)	<0.001	0
Hospital stay¶ (days)	10.8 (8.7; 13.8)	10.7 (8.7; 13.7)	13.2 (10.9; 20.7)	<0.001	0

discrepancy resolved by consensus or through discussion with a third author.

We planned to perform meta-analysis when three or more studies reported on the association of intraoperative oliguria (any definition) with postoperative AKI. The strength of association was estimated primarily by pooling unadjusted data using an inverse-variance weighted random-effects model, and reported as OR with 95% CI. Potential publication bias was assessed by the funnel plot and, when ≥10 studies were included, by Egger's test. Between-study heterogeneity was assessed using the I^2 statistic, with I^2 ≥50% representing substantial heterogeneity. In a sensitivity analysis, we pooled the most fully adjusted estimates for the association between intraoperative oliguria and AKI in each study. As there is a concern that pooling *post hoc* identified study-specific prognostic marker thresholds tends to overestimate the predictive power of the marker,[24] another sensitivity analysis was performed by only pooling the results of studies that used urine output <0.5 ml kg^{-1} h^{-1} as the threshold for oliguria. The discriminatory performance was summarised using hierarchical summary receiver operating characteristic (HSROC) curve.[25] The predictive utility was also evaluated by the sensitivity, specificity, and likelihood ratios of the HSROC-derived hypothetical summary point. Statistical analyses were performed using Stata® version 12.0 (StataCorp, College Station, TX, USA).

Results

Of 4722 patients undergoing major thoracic surgery identified in our database, 3862 were eligible (Fig. 1). The included patients had a median age of 59 yr and 68% were men. Some 65% patients underwent lung resection and 35% oesophagectomy. Acute kidney injury occurred in 205 (5.3%) patients within 7 days after surgery, including 172 (4.5%) KDIGO Stage 1, 21 (0.5%) Stage 2, and 12 (0.3%) Stage 3 AKI. No patient required renal replacement therapy. The characteristics of patients with and without AKI are presented in Table 1.

Prognostic association of intraoperative oliguria

A univariable restricted cubic spine regression plot suggested a non-linear relationship between intraoperative urine output and postoperative AKI (Supplementary Fig. S1). Odds for AKI increased for decreasing urine output at low levels, but no association between urine output and AKI was observed at high urine output levels. Using a minimum *P*-value approach, the multivariable analysis demonstrated that urine output of 0.3 ml kg^{-1} h^{-1} was the optimal threshold. Intraoperative oliguria, defined by urine output <0.3 ml kg^{-1} h^{-1}, occurred in 2.3% (*n*=90) of patients. The incidence of AKI was 13.3% and 5.1% for patients with and without oliguria, respectively. In the multivariable analysis, intraoperative oliguria was a

Table 2 Multivariable logistic regression models for postoperative acute kidney injury. ACEI, angiotensin-converting enzyme inhibitor; aOR, adjusted odds ratio; ARB, angiotensin receptor blocker; ASA, American society of Anesthesiologists; AUROC, area under the receiver operating characteristic curve; CI, confidence interval; COPD, chronic obstructive pulmonary disease; HL, Hosmer–Lemeshow. *History of coronary heart disease, stroke, or congestive heart failure. †From anaesthesia induction to the end of wound closure. ‡Natural logarithmic transformation.

	Base model		Base model plus intraoperative oliguria	
	aOR (95% CI)	*P*-value	aOR (95% CI)	*P*-value
Variables in the model				
Age (yr)	1.02 (1.00; 1.04)	0.014	1.02 (1.00; 1.04)	0.011
Sex (male)	1.31 (0.89; 1.95)	0.181	1.35 (0.91; 2.02)	0.14
BMI (kg m^{-2})	1.02 (0.97; 1.07)	0.508	1.01 (0.96; 1.07)	0.64
ASA physical status				
1–2	1 (reference)		1 (reference)	
3–4	1.15 (0.72; 1.77)	0.546	1.14 (0.72; 1.76)	0.574
Hypertension	2.07 (1.43; 2.96)	<0.001	2.10 (1.45; 3.00)	<0.001
Diabetes mellitus	1.72 (1.17; 2.50)	0.005	1.69 (1.14; 2.46)	0.007
Cardiovascular diseases*	1.67 (1.00; 2.69)	0.042	1.67 (1.00; 2.69)	0.042
COPD	0.70 (0.38; 1.21)	0.230	0.68 (0.37; 1.18)	0.20
Chronic use of ACEI/ARB	1.80 (1.09; 2.91)	0.019	1.75 (1.07; 2.85)	0.025
Perioperative use of NSAIDs	1.04 (0.75; 1.43)	0.797	1.06 (0.76; 1.45)	0.74
Perioperative use of aminoglycosides	1.04 (0.45; 2.12)	0.928	1.07 (0.46; 2.19)	0.87
Preoperative haemoglobin (g L^{-1})	1.00 (0.99; 1.01)	0.728	1.00 (0.99; 1.01)	0.71
Preoperative serum albumin (g L^{-1})	0.93 (0.89; 0.97)	<0.001	0.93 (0.89; 0.97)	<0.001
Preoperative serum creatinine (μmol L^{-1})	1.01 (1.01; 1.02)	<0.001	1.01 (1.01; 1.02)	<0.001
Type of surgery				
Wedge resection/segmentectomy/lobectomy	1 (reference)		1 (reference)	
Pneumonectomy/oesophagectomy	1.37 (0.91; 2.10)	0.137	1.38 (0.91; 2.10)	0.14
Minimally invasive surgery	0.75 (0.50; 1.13)	0.167	0.76 (0.51; 1.14)	0.19
Duration of surgery† (h)	1.12 (0.99; 1.26)	0.058	1.12 (0.99; 1.26)	0.059
Fluid administration† (ml kg^{-1})	1.01 (0.99; 1.02)	0.322	1.01 (0.99; 1.02)	0.30
Blood loss†‡ (ml kg^{-1})	1.25 (1.03; 1.52)	0.027	1.24 (1.02; 1.51)	0.031
Lowest MAP† (mm Hg)	0.99 (0.97; 1.00)	0.052	0.99 (0.97; 1.00)	0.070
Urine output† (ml kg^{-1} h^{-1})				
>0.3			1 (reference)	
<0.3			2.60 (1.24; 5.05)	0.007
Performance of the model				
Discrimination (AUROC)	0.770 (0.737; 0.802)		0.772 (0.739; 0.805)	
Calibration (HL test χ^2)	10.81	0.213	8.61	0.38

significant risk factor for postoperative AKI (adjusted OR: 2.60; 95% CI: 1.24–5.05; Table 2).

To supplement the aforementioned analyses, we undertook tests of interaction to determine if intraoperative fluid administration and blood pressure modified the association between oliguria and AKI. The interaction terms between i.v. fluid and oliguria and between lowest MAP and oliguria were not significant (P=0.73 and 0.45, respectively), suggesting no effect modifications by these factors. In a sensitivity analysis that excluded patients with missing data, intraoperative urine output <0.3 ml kg^{-1} h^{-1} was again identified as the optimal threshold for oliguria and was significantly associated with postoperative AKI (Supplementary Table S4). In another sensitivity analysis, oliguria defined as urine output <0.5 ml kg^{-1} h^{-1} occurred in 7.9% (n=304) of patients. Acute kidney injury occurred in 7.9% and 5.1% of patients with urine output <0.5 and ≥0.5 ml kg^{-1} h^{-1}, respectively. Intraoperative urine output <0.5 ml kg^{-1} h^{-1} was not associated with postoperative AKI (adjusted OR: 1.48; 95% CI: 0.89–2.35).

Predictive ability of intraoperative oliguria

Applying intraoperative oliguria <0.3 ml kg^{-1} h^{-1} to predict postoperative AKI revealed a low sensitivity of 5.9% and a specificity of 98%. The positive and negative likelihood ratios were 2.74 and 0.96, respectively (Table 3). The AUROC was 0.52 (95% CI: 0.50–0.54). Multivariable models with and without intraoperative oliguria were similar in discriminative ability, and both had good calibration (Table 2; Supplementary Fig. S2). Reclassification analysis showed that overall NRI was 0.12 (95% CI: 0.02–0.23), event NRI was −0.65 (95% CI: −0.75 to −0.55), and non-event NRI was 0.77 (95% CI: 0.75–0.79) (Supplementary Table S5). This indicates improved overall risk classification, but decreased correct risk classification for patients who developed postoperative AKI.

Systematic review and meta-analysis

A total of 1832 unique records were identified by the literature search, and seven studies (including the current one) were selected for inclusion (Supplementary Fig. S3).[12–14,26–28] A summary of the study characteristics is provided in Table 4, and the assessment for risk of bias is detailed in Supplementary Table S6. According to the definitions of intraoperative oliguria used by the individual studies, some 469/2465 (19.0%) of patients who experienced oliguria developed postoperative AKI compared with 1029/14 157 (7.3%) of patients who did not. Meta-analysis of unadjusted data

Table 3 Contingency table of intraoperative oliguria and postoperative AKI. AKI, acute kidney injury; LR−, negative likelihood ratio; LR+, positive likelihood ratio; NPV, negative predictive value; PPV, positive predictive value.

	AKI	No AKI	Total	
Oliguria	12	78	90	PPV=13%
No oliguria	193	3579	3772	NPV=95%
Total	205	3657	3862	LR+=2.74
	Sensitivity=5.9%	Specificity=98%	Incidence of AKI=5.3%	LR−=0.96

showed significant association between intraoperative oliguria and AKI (OR: 2.20; 95% CI: 1.63–2.96; I^2=72.5%; Fig. 2a). The funnel plot did not suggest publication bias (Supplementary Fig. S4); the Egger test was not performed because of the small number of studies. The association remained significant in sensitivity analyses pooling adjusted data (adjusted OR: 2.05; 95% CI: 1.63–2.59; Supplementary Fig. S5) and when only studies using urine output <0.5 ml kg^{-1} h^{-1} as threshold for oliguria were pooled (unadjusted OR: 2.08; 95% CI: 1.38–3.13; and adjusted OR: 1.75; 95% CI 1.48–2.07; Supplementary Fig. S6).

With regard to predictive ability, the criteria for oliguria used by the included studies had acceptable specificity but low sensitivity (<0.5) for AKI prediction, with a higher sensitivity generally associated with a lower specificity (Fig. 2b). The summary sensitivity was 0.21 (95% CI: 0.11–0.56) and specificity was 0.90 (95% CI: 0.79–0.96). The summary positive likelihood ratio was 2.04 (95% CI: 1.51–2.77) and negative likelihood ratio was 0.88 (95% CI: 0.82–0.95). Hierarchical analysis resulted in an area under the HSROC curve of 0.58 (95% CI: 0.54–0.62).

Only one study besides ours explored the incremental predictive value of oliguria beyond a base model for postoperative AKI.[12] Similar to our result, no clinically significant increase in AUROC was found (from 0.782 to 0.791) and the overall risk classification was better (overall NRI: 0.16; 95% CI: 0.05–0.27), but the classification for patients who developed AKI was significantly worse (event NRI: −0.56; 95% CI: −0.62 to −0.49).[12]

Discussion

We conducted a retrospective cohort study to assess the prognostic association and predictive utility of intraoperative oliguria for postoperative AKI in patients undergoing major thoracic surgery, and complemented this with a systematic review and meta-analysis of studies on variable types of noncardiac surgery. We report two main findings.

First, in our cohort study of patients undergoing thoracic surgery, intraoperative oliguria <0.3 ml kg^{-1} h^{-1} was associated with postoperative AKI. This finding is different from those of older studies showing no relationship between

Table 4 Main characteristics of studies included in the systematic review and meta-analysis. AKI, acute kidney injury; AKIN, Acute Kidney Injury Network; KDIGO, Kidney Disease: Improving Global Outcomes; RIFLE, risk, injury, failure, loss, end-stage kidney disease; UO, urine output.

Study	Country	Study design	Patients			Types of surgery	Criteria for oliguria	Criteria for AKI	Overall incidence of AKI (%)
			No.	Male (%)	Age (yr)				
Slankamenac and colleagues[26] (2013)	Switzerland	Single centre, retrospective cohort	549	55	59	Hepatectomy	Average UO <400 ml $(24\ h)^{-1}$	RIFLE Stages R, I, F	14.9
Goren and colleagues[27] (2017)	Israel	Single centre, retrospective cohort	153	47	64	Pancreatic surgery	Average UO <0.5 ml kg^{-1} h^{-1}	AKIN Stages 1–3	9.8
Mizota and colleagues[12] (2017)	Japan	Single centre, retrospective cohort	3560	61	66	Major abdominal surgery	Average UO <0.3 ml kg^{-1} h^{-1}	KDIGO Stages 1–3	6.3
Shiba and colleagues[13] (2018)	Japan	Single centre, retrospective cohort	5894	48	62	Noncardiac surgery	UO <0.5 ml kg^{-1} h^{-1} for ≥120 min	RIFLE Stages R, I, F	7.3
Myles and colleagues[14] (2019)	International (seven countries)	Secondary analysis of a multicentre RCT	2444	53	67	Major abdominal surgery	UO <0.5 ml kg^{-1} h^{-1} for ≥60 min	KDIGO Stages 1–3	21.0
Shim and colleagues[28] (2020)	Korea	Single centre, retrospective matched cohort	453	52	64	Colorectal surgery	Average UO <0.5 ml kg^{-1} h^{-1}	KDIGO Stages 1–3	17.4
Present study (2020)	China	Single centre, retrospective cohort	3862	68	59	Major thoracic surgery	Average UO <0.3 ml kg^{-1} h^{-1}	KDIGO Stages 1–3	5.3

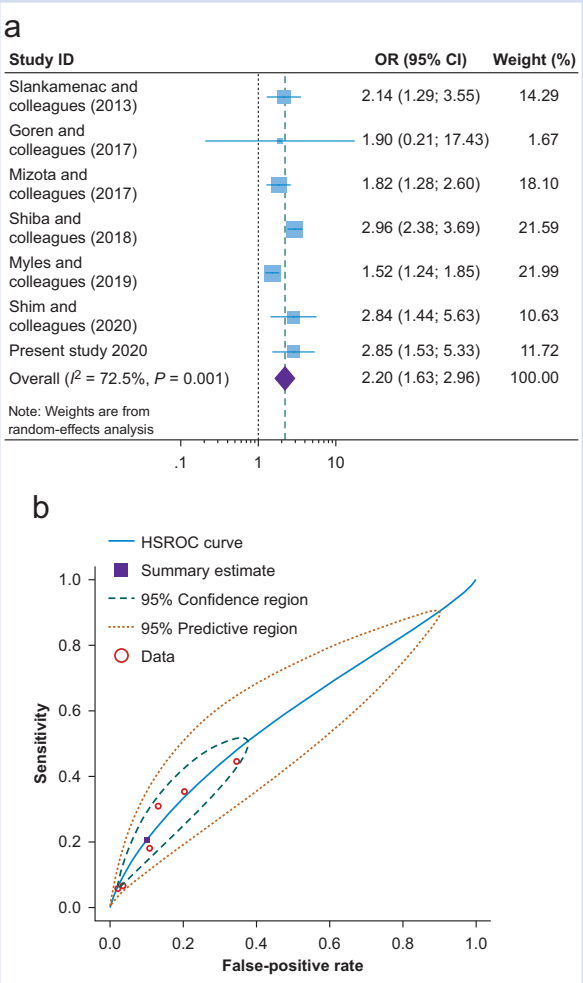

Fig 2. Prognostic association and predictive performance of intraoperative oliguria for postoperative acute kidney injury. (a) Forest plot representing the summary odds ratios (ORs) with 95% confidence interval (CI) for the unadjusted association between intraoperative oliguria (as defined in each study) and postoperative acute kidney injury. (b) The blue square represents the summary operating point of the hierarchical summary receiver operating characteristic (HSROC) curve, a hypothetical point that summarises the predictive value of oliguria as defined in each study (sensitivity: 0.21, 95% CI: 0.11–0.56; specificity: 0.90, 95% CI: 0.79–0.96; positive likelihood ratio: 2.04, 95% CI: 1.51–2.77; negative likelihood ratio: 0.88, 95% CI: 0.82–0.95). The area under the HSROC curve was 0.58 (95% CI: 0.54–0.62).

intraoperative oliguria and postoperative renal failure.[5–7] Most of those studies had a small sample size and considered only advanced and severe renal dysfunction. Thus, they could have missed the association of intraoperative oliguria with mild postoperative renal injury, which accounts for the vast majority of AKI after noncardiac surgery and is predictive of perioperative and long-term adverse outcomes.[1,2,29] On the contrary, our result is generally consistent with recent studies in noncardiac surgeries that used a consensus definition for AKI.[12–14] Our meta-analysis confirmed the prognostic association of intraoperative oliguria with AKI. However, the OR reported in individual studies and the pooled OR suggested that the strength of this association is, at best, moderate.

Second, we showed that intraoperative oliguria does not appear to be able to accurately predict postoperative AKI for individual patients, either by itself or as an additive factor to a multivariable prediction model. Despite the significant association with postoperative AKI, the predictive ability of intraoperative oliguria was poor with very low sensitivity, acceptable specificity, modest positive likelihood ratio, and negative likelihood ratio close to 1. This can be interpreted as a modest increase in risk (odds) of AKI for those with intraoperative oliguria, but for those without oliguria, there is minimal change in predicted risk. Using only intraoperative oliguria to predict risk would miss the majority of postoperative AKI events. The discriminative ability of intraoperative oliguria was low, as shown by the small AUROC of oliguria as a single predictor and the unchanged AUROC when oliguria was added to a multivariable prediction model. Moreover, when incorporated into a multivariable model, the presence or absence of intraoperative oliguria improved risk reclassification overall, but worsened the prediction of patients who developed postoperative AKI by assigning many of them a lower risk. This would have negative clinical impact and suggests that the absence of oliguria should not be viewed as a sign for low AKI risk.

The limited predictive ability of intraoperative oliguria might be explained by the complex physiology of urine production during surgery and the multifaceted aetiology of surgery-associated AKI. Besides volume status, intraoperative urine output is also subject to sympathetic tone and neurohormonal regulation. Several perioperative factors, such as pain, surgical stress, and some medications, can increase the secretion of stress hormones, such as antidiuretic hormone, and cause oliguria.[30,31] Thus, oliguria does not necessarily reflect renal hypoperfusion. However, hypoperfusion-induced renal injury is just one of many causes of surgery-associated AKI. Other factors, such as systematic inflammation, congestive heart failure, hyperglycaemia, and nephrotoxins, are also common and important causes of postoperative AKI.[7]

Although not accurate for individual risk prediction, intraoperative oliguria remains of clinical interest as a potentially preventable and modifiable risk factor for postoperative AKI. Traditionally, for patients undergoing thoracic surgery, a restrictive i.v. fluid regimen of 1–2 ml kg^{-1} h^{-1} during and up to 24 h after surgery, with a positive fluid balance of <1500 ml, has been recommended.[15,32] However, these recommendations were based mainly on observational studies showing associations between excessive fluid administration and postoperative pulmonary complications (Level III evidence). No high-quality randomised trial has been conducted to support the benefit of a very restrictive fluid regimen in terms of reduced overall morbidity or improved patient-centred outcomes after thoracic surgery. Recent studies have suggested that very restrictive fluid regimens may result in oliguria, which is associated with an increased risk of postoperative AKI.[8,33] Thus, further studies need to explore the optimal amount of fluid that is enough to avoid renal hypoperfusion and injury, and not too much to increase the risk of pulmonary complications after general thoracic surgery.

When oliguria occurs, whether interventions, such as fluid expansion and vasopressor infusion, could restore urine

output and avoid kidney injury is unclear. No randomised trial has directly compared intraoperative fluid protocols with and without oliguria reversal as a target for preventing postoperative AKI.[8] Considering that oliguria does not always point to hypovolaemia and renal hypoperfusion, it should not be used in isolation to trigger specific haemodynamic interventions. A careful integration of the patient's information on antecedent fluid infusions and losses, signs of hypovolaemia or fluid overload, systemic haemodynamics, fluid responsiveness, and duration of oliguria may help in deciding the appropriate renal protection strategies.[34,35] Finally, whether close monitoring of intraoperative urine output (hourly or real-time measurement) and personalised haemodynamic interventions targeting oliguria reversal are effective in decreasing the incidence of postoperative AKI should be tested by randomised trials.

This work has several limitations. First, we used a retrospective cohort of patients undergoing general thoracic surgery in a single centre. Although the results are similar with previous studies on abdominal surgery, more external data on thoracic surgery are needed to confirm our findings because different sites of operation and body positioning may impact urine output dynamics.[36] Second, in our study, oliguria was defined as urine output averaged over the entire length of surgery below the threshold. Because we do not have hour-by-hour or more granular data on intraoperative urine output, we could not assess the effects of duration of oliguria on AKI. Third, more than one threshold might exist in the relationship between intraoperative urine output and postoperative AKI. Some studies have shown an already increased risk of AKI at intraoperative urine output levels much higher than the traditional criteria for oliguria.[37,38] We did not investigate other possible thresholds in this study with relatively small sample size and low event incidence. The systematic review and meta-analysis also have limitations. It was undertaken in a short time frame to contextualise the results of our cohort study; thus, we did not register the review in the International Prospective Register of Systematic Reviews or publish the protocol before conduct. The included studies are heterogeneous in surgery types, baseline risk of AKI, and definitions and criteria for intraoperative oliguria. Because of the small number of studies included, we could not perform statistical analysis to explore the sources of heterogeneity and to test for potential publication bias.

In summary, there is moderate association between intraoperative oliguria and postoperative AKI. However, the predictive ability of intraoperative oliguria for AKI is poor. Intraoperative oliguria remains interesting as a potentially modifiable risk factor. Further studies need to examine whether close monitoring of intraoperative urine output and appropriate use of fluid, vasopressor, or other interventions in patients who experience oliguria could reduce the risk of postoperative AKI.

Authors' contributions

Study conception/design: B-CZ, S-HL, K-XL
Data acquisition/analysis/interpretation: B-CZ, S-HL, XY, YZ, S-DQ
Writing of first draft of the paper: B-CZ, S-HL
Critical revision of the paper: W-FL, CL, K-XL
Final approval of the version to be published: all authors

Acknowledgements

This study was coordinated by the Department of Anaesthesiology and Department of Information, Southern Medical University Nanfang Hospital, Guangzhou, China, and the Department of Information Technology and Department of Medical Statistics, Lejiu Healthcare Technology Co., Ltd, Shanghai, China. This study was funded by China Postdoctoral Science Foundation, grant ID 2019M662976

Declarations of interest

The authors declare that they have no conflict of interest.

Funding

China Postdoctoral Science Fund (2019M662976) to B-CZ.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2020.11.018.

References

1. 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**: 521–30
2. O'Connor ME, Hewson RW, Kirwan CJ, Ackland GL, Pearse RM, Prowle JR. Acute kidney injury and mortality 1 year after major noncardiac surgery. *Br J Surg* 2017; **104**: 868–76
3. Devarajan P. Biomarkers for the early detection of acute kidney injury. *Curr Opin Pediatr* 2011; **23**: 194–200
4. Prowle JR, Kirwan CJ, Bellomo R. Fluid management for the prevention and attenuation of acute kidney injury. *Nat Rev Nephrol* 2014; **10**: 37–47
5. Alpert RA, Roizen MF, Hamilton WK, et al. Intraoperative urinary output does not predict postoperative renal function in patients undergoing abdominal aortic revascularization. *Surgery* 1984; **95**: 707–11
6. Kheterpal S, Tremper KK, Englesbe MJ, et al. Predictors of postoperative acute renal failure after noncardiac surgery in patients with previously normal renal function. *Anesthesiology* 2007; **107**: 892–902
7. Zarbock A, Koyner JL, Hoste EAJ, Kellum JA. Update on perioperative acute kidney injury. *Anesth Analg* 2018; **127**: 1236–45
8. Egal M, de Geus HR, van Bommel J, Groeneveld AB. Targeting oliguria reversal in perioperative restrictive fluid management does not influence the occurrence of renal dysfunction: a systematic review and meta-analysis. *Eur J Anaesthesiol* 2016; **33**: 425–35
9. Cannesson M, Pestel G, Ricks C, Hoeft A, Perel A. Hemodynamic monitoring and management in patients undergoing high risk surgery: a survey among North American and European anesthesiologists. *Crit Care* 2011; **15**: R197
10. Kim SH, Kim MJ, Lee JH, Cho SH, Chae WS, Cannesson M. Current practice in hemodynamic monitoring and management in high-risk surgery patients: a national survey of Korean anesthesiologists. *Korean J Anesthesiol* 2013; **65**: 19–32

11. Suehiro K, Tanaka K, Mukai A, et al. Hemodynamic monitoring and management in high-risk surgery: a survey among Japanese anesthesiologists. *J Anesth* 2016; **30**: 526–9
12. Mizota T, Yamamoto Y, Hamada M, Matsukawa S, Shimizu S, Kai S. Intraoperative oliguria predicts acute kidney injury after major abdominal surgery. *Br J Anaesth* 2017; **119**: 1127–34
13. Shiba A, Uchino S, Fujii T, Takinami M, Uezono S. Association between intraoperative oliguria and acute kidney injury after major noncardiac surgery. *Anesth Analg* 2018; **127**: 1229–35
14. Myles PS, McIlroy DR, Bellomo R, Wallace S. Importance of intraoperative oliguria during major abdominal surgery: findings of the restrictive versus liberal fluid therapy in major abdominal surgery trial. *Br J Anaesth* 2019; **122**: 726–33
15. Assaad S, Popescu W, Perrino A. Fluid management in thoracic surgery. *Curr Opin Anaesthesiol* 2013; **26**: 31–9
16. Wu Y, Yang R, Xu J, Rusidanmu A, Zhang X, Hu J. Effects of intraoperative fluid management on postoperative outcomes after lobectomy. *Ann Thorac Surg* 2019; **107**: 1663–9
17. Vandenbroucke JP, von Elm E, Altman DG, et al. Strengthening the reporting of observational studies in epidemiology (STROBE): explanation and elaboration. *Int J Surg* 2014; **12**: 1500–24
18. Riley RD, Moons KGM, Snell KIE, et al. A guide to systematic review and meta-analysis of prognostic factor studies. *BMJ* 2019; **364**: k4597
19. Moher D, Liberati A, Tetzlaff J, et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: the PRISMA statement. *PLoS Med* 2009; **6**, e1000097
20. Ma YC, Zuo L, Chen JH, et al. Modified glomerular filtration rate estimating equation for Chinese patients with chronic kidney disease. *J Am Soc Nephrol* 2006; **17**: 2937–44
21. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO clinical practice guideline for acute kidney injury. *Kidney Int Suppl* 2012; **2**: 1–138
22. Mazumdar M, Smith A, Bacik J. Methods for categorizing a prognostic variable in a multivariable setting. *Stat Med* 2003; **22**: 559–71
23. Hayden JA, van der Windt DA, Cartwright JL, Côté P, Bombardier C. Assessing bias in studies of prognostic factors. *Ann Intern Med* 2013; **158**: 280–6
24. Potgieter D, Simmers D, Ryan L, et al. N-terminal pro-B-type natriuretic peptides' prognostic utility is overestimated in meta-analyses using study-specific optimal diagnostic thresholds. *Anesthesiology* 2015; **123**: 264–71
25. Lee J, Kim KW, Choi SH, Huh J, Park SH. Systematic review and meta-analysis of studies evaluating diagnostic test accuracy: a practical review for clinical researchers—part II: statistical methods of meta-analysis. *Korean J Radiol* 2015; **16**: 1188–96
26. Slankamenac K, Beck-Schimmer B, Breitenstein S, Puhan MA, Clavien PA. Novel prediction score including pre- and intraoperative parameters best predicts acute kidney injury after liver surgery. *World J Surg* 2013; **37**: 2618–28
27. Goren O, Levy A, Cattan A, Lahat G, Matot I. Acute kidney injury in pancreatic surgery; association with urine output and intraoperative fluid administration. *Am J Surg* 2017; **214**: 246–50
28. Shim JW, Kim KR, Jung Y, et al. Role of intraoperative oliguria in risk stratification for postoperative acute kidney injury in patients undergoing colorectal surgery with an enhanced recovery protocol: a propensity score matching analysis. *PLoS One* 2020; **15**, e0231447
29. Turan A, Cohen B, Adegboye J, et al. Mild acute kidney injury after noncardiac surgery is associated with long-term renal dysfunction: a retrospective cohort study. *Anesthesiology* 2020; **132**: 1053–61
30. Klein SJ, Lehner GF, Forni LG, Joannidis M. Oliguria in critically ill patients: a narrative review. *J Nephrol* 2018; **31**: 855–62
31. du Toit L, Biccard BM. The relationship between intraoperative oliguria and acute kidney injury. *Br J Anaesth* 2019; **122**: 707–10
32. Evans RG, Naidu B. Does a conservative fluid management strategy in the perioperative management of lung resection patients reduce the risk of acute lung injury? *Interact Cardiovasc Thorac Surg* 2012; **15**: 498–504
33. Myles PS, Bellomo R, Corcoran T, et al. Restrictive versus liberal fluid therapy for major abdominal surgery. *N Engl J Med* 2018; **378**: 2263–74
34. Schortgen F, Schetz M. Does this critically ill patient with oliguria need more fluids, a vasopressor, or neither? *Intensive Care Med* 2017; **43**: 907–10
35. Perner A, Prowle J, Joannidis M, Young P, Hjortrup PB, Pettilä V. Fluid management in acute kidney injury. *Intensive Care Med* 2017; **43**: 807–15
36. Pump B, Talleruphuus U, Christensen NJ, Warberg J, Norsk P. Effects of supine, prone, and lateral positions on cardiovascular and renal variables in humans. *Am J Physiol Regul Integr Comp Physiol* 2002; **283**: R174–80
37. Hori D, Katz NM, Fine DM, et al. Defining oliguria during cardiopulmonary bypass and its relationship with cardiac surgery-associated acute kidney injury. *Br J Anaesth* 2016; **117**: 733–40
38. Hur M, Park SK, Yoo S, et al. The association between intraoperative urine output and postoperative acute kidney injury differs between partial and radical nephrectomy. *Sci Rep* 2019; **9**: 760

Handling editor: Paul Myles