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Intraoperative oliguria predicts acute kidney injury after major abdominal surgery

T. Mizota[1,*], Y. Yamamoto[2], M. Hamada[1], S. Matsukawa[1], S. Shimizu[1] and S. Kai[1]

[1]Department of Anaesthesia, Kyoto University Hospital, 54 Shogoin-Kawahara-cho, Sakyo-ku, Kyoto 606-8507, Japan and [2]Department of Healthcare Epidemiology, School of Public Health in the Graduate School of Medicine, Kyoto University, Yoshida Konoemachi, Sakyo-ku, Kyoto 606-8501, Japan

*Corresponding author. E-mail: mizota@kuhp.kyoto-u.ac.jp

Abstract

Background. The threshold of intraoperative urine output below which the risk of acute kidney injury (AKI) increases is unclear. The aim of this retrospective cohort study was to investigate the relationship between intraoperative urine output during major abdominal surgery and the development of postoperative AKI and to identify an optimal threshold for predicting the differential risk of AKI.

Methods. Perioperative data were collected retrospectively on 3560 patients undergoing major abdominal surgery (liver, colorectal, gastric, pancreatic, or oesophageal resection) at Kyoto University Hospital. We evaluated the relationship between intraoperative urine output and the development of postoperative AKI as defined by recent guidelines. Logistic regression analysis was performed to adjust for patient and operative variables, and the minimum *P*-value approach was used to determine the threshold of intraoperative urine output that independently altered the risk of AKI.

Results. The overall incidence of AKI in the study population was 6.3%. Using the minimum *P*-value approach, a threshold of 0.3 ml kg^{-1} h^{-1} was identified, below which there was an increased risk of AKI (adjusted odds ratio, 2.65; 95% confidence interval, 1.77–3.97; $P<0.001$). The addition of oliguria <0.3 ml kg^{-1} h^{-1} to a model with conventional risk factors significantly improved risk stratification for AKI (net reclassification improvement, 0.159; 95% confidence interval, 0.049–0.270; $P=0.005$).

Conclusions. Among patients undergoing major abdominal surgery, intraoperative oliguria <0.3 ml kg^{-1} h^{-1} was significantly associated with increased risk of postoperative AKI.

Key words: acute kidney injury; general surgery; monitoring, intraoperative; oliguria

Oliguria is widely viewed as an early marker of decreased kidney perfusion and impending acute kidney injury (AKI). The use of urine output (UO) to guide fluid therapy is often recommended by textbooks and guidelines[1–3] and is the standard practice in perioperative or critical care settings.[4 5]

Although oliguria is usually defined as a UO <0.5 ml kg^{-1} h^{-1} in medical and surgical practice,[1 2] this threshold of UO is not supported by clinical evidence. The most recent update of the Surviving Sepsis Campaign guidelines does not mention a target value of UO;[3] in contrast, the previous version recommended that initial resuscitation goals should include UO ≥ 0.5 ml kg^{-1} h^{-1}.[6] Although serum creatinine (SCr) roughly represents the glomerular filtration rate,[7] UO is influenced by many factors, including haemodynamics, sympathetic tone, and aldosterone and antidiuretic hormone concentrations. Therefore, thresholds of clinically significant oliguria, indicating renal hypoperfusion or

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Editor's key points

- The risks of excessive fluid administration and the benefits of restrictive fluid therapy in some patient groups are well recognized.
- However, oliguria, traditionally defined as a urine output <0.5 ml kg^{-1} h^{-1}, is considered a risk factor for acute kidney injury (AKI) despite conflicting data.
- This large retrospective study examined different thresholds of urine output associated with risk of AKI after major abdominal surgery.
- Intraoperative urine output <0.3 ml kg^{-1} h^{-1} was independently associated with a significant risk of AKI, but urine outputs of 0.3–0.5 ml kg^{-1} h^{-1} were not.
- These results cast doubt on the risks of perioperative oliguria as conventionally defined.

impending AKI, may vary depending on clinical settings or patient conditions.

Fluid replacement targeting a higher UO tends to lead to increased fluid loading, which may be harmful; recent randomized trials have demonstrated that perioperative fluid overloading markedly increases postoperative morbidity and length of hospital stay.[8–11] Conversely, allowing a lower UO may cause renal hypoperfusion and associated kidney damage. Therefore, identification of the optimal threshold for clinically significant oliguria might help to optimize fluid management. However, to our knowledge, no study has attempted to identify an optimal threshold of intraoperative UO in surgical patients associated with increased risk of postoperative AKI.

The authors hypothesized that there is a threshold of intraoperative UO below which the risk of postoperative AKI increases. The aims of this large-scale retrospective study were as follows: (i) to investigate the relationship between intraoperative UO during major abdominal surgery and the development of postoperative AKI; and (ii) to identify an optimal threshold that predicts the differential risk of AKI.

Methods

Study design, setting, and population

This single-centre retrospective cohort study was conducted in Kyoto University Hospital, which is a teaching hospital in Japan with 1121 beds. The institutional review board approved the study protocol (approval number: R0672, July 26, 2016) and waived the requirement for informed consent.

We included patients aged 18 yr or older who underwent major abdominal surgery under general anaesthesia at Kyoto University Hospital from March 2008 to April 2015 (i.e. from the inception of an electronic database of surgical patients at our centre to the conception of this study). Major abdominal surgery included liver, colorectal, gastric, pancreatic, or oesophageal resection by either laparotomy or a laparoscopic approach. For patients who had more than one surgery meeting the inclusion criteria during the study period, only the index procedure was included. Exclusion criteria were concurrent cardiac or urological procedures and patients with end-stage renal disease (i.e. estimated glomerular filtration rate of <15 ml min^{-1} 1.73 m^{-2}, as determined using a formula validated in Japan,[12] or receipt of haemodialysis). In addition, patients who received diuretics (furosemide, human atrial natriuretic peptide, or mannitol) during surgery were also excluded to eliminate their confounding effects.

Data collection

Data on study participants were collected from the electronic database and the electronic medical record system. To prevent variability in data collection, we collected data according to uniform criteria, especially regarding definitions of the medical conditions. Definitions of variables are listed in Supplementary Table S1. Procedure names recorded in the electronic database were used to identify and group major abdominal surgeries. The type of surgery was categorized into six groups (liver, colorectal, gastric, pancreatic, oesophageal, and complex) and also divided into laparoscopic or non-laparoscopic surgery. 'Complex' means concomitant resection of two or more organs listed above. For each patient, we calculated the average intraoperative UO per hour based on body weight by dividing the total intraoperative UO by the duration of operating room stay and by the measured body weight.

Outcome

The primary outcome was AKI as determined by change in SCr according to the Kidney Disease: Improving Global Outcomes (KDIGO) definition[13] (increase in SCr of $\geq$26.5 μmol litre^{-1} within 48 h or $\geq$1.5 times baseline within 7 days after surgery). The most recent SCr measured before the surgery was used as the baseline value.

Statistical analyses

The analyses of the relationship between intraoperative UO and AKI were planned before data evaluation. We examined the unadjusted relationship between intraoperative UO and the risk of AKI using a cubic spline function to identify any inflection point that could be used to dichotomize intraoperative UO into categories in a clinically meaningful way. If we observed an area of inflation, the optimal threshold for intraoperative UO was determined using the minimum *P*-value approach. This approach evaluated every possible threshold of intraoperative UO at intervals of 0.1 ml kg^{-1} h^{-1} in the multivariable logistic regression model, and the intraoperative UO that demonstrated the smallest statistically significant *P*-value was selected as the optimal threshold to dichotomize intraoperative UO. In the multivariable model, the AKI risk index[14] was used to adjust for the preoperative risk of AKI. This is a previously developed and validated risk index for predicting postoperative AKI in patients undergoing general surgery and includes age, sex, emergency surgery, intraperitoneal surgery, diabetes mellitus, active congestive heart failure, ascites, hypertension, and preoperative renal insufficiency. In addition, type of surgery, intraoperative blood loss (per kilogram body weight), and intraoperative continuous infusion of vasopressors were included in the model to adjust for the type and invasiveness of surgery. The linearity of the association between intraoperative blood loss and the log-odds of AKI was assessed using a cubic spline function and categorized if significant non-linearity ($P<0.05$) was found. Multicollinearity among variables was assessed by the variance inflation factor, with a reference value of 10. Discrimination and calibration of the multivariable model was assessed based on the c-index and the Hosmer–Lemeshow goodness-of-fit test, respectively. We assessed whether the addition of intraoperative UO to the model that included only AKI risk index and

operative variables can improve the predictive ability for AKI by calculating the category-free net reclassification improvement (NRI) and the integrated discrimination improvement (IDI).

We expected that the relationship between intraoperative UO and AKI would vary depending on patient or operative characteristics. Accordingly, we assessed this potential heterogeneity by subgroup analyses. We used the same model in the following subgroups: (i) AKI risk index (class 1/class 2/class 3–5); (ii) type of surgery (liver/colorectal/gastric/others); (iii) blood loss ($<10/\geq 10$ ml kg^{-1}); and (iv) laparoscopic surgery (yes/no). We calculated the adjusted odds ratio for AKI in each subgroup and then tested the interaction between subgroups and intraoperative UO.

We assessed the robustness of our findings using sensitivity analyses. Sensitivity models were constructed as a logistic regression identical to the primary model above, except: (i) with the primary outcome AKI redefined on the basis of SCr concentrations only up to 2 days after surgery; (ii) using severe AKI (stage 2–3 AKI according to KDIGO guidelines) as the outcome; (iii) adjusting for the duration of the surgery; (iv) using ideal body weight (determined with the body mass index method)[15 16] to calculate UO per body weight; (v) excluding patients who received intraoperative vasopressor infusion; (vi) excluding patients who received diuretics before surgery; and (vii) excluding emergency surgeries.

The sample size was determined by including all eligible patients in the electronic database to maximize the power. Previous studies have suggested that at least 8–10 events per variable are required for reliable multivariable logistic regression analysis.[17 18] We assumed ~500 eligible surgeries per year and predicted the prevalence of AKI to be 6% on the basis of published reports.[19–21] We therefore estimated that we can conduct multivariable logistic regression with ~24 variables using our data set. As for missing values, we planned to conduct a complete patient analysis if the missing values were <5% because such an analysis might have been feasible in that case.[22]

All statistical tests were two tailed, and a *P*-value of <0.05 was considered to be statistically significant. All statistical analyses were performed using the statistical program R (http://cran.r-project.org (accessed 1 March 2017)).

Results

Figure 1 shows the flow diagram of this study. A total of 3804 index major abdominal surgeries were identified in the electronic database spanning a period of ~7 yr from March 2008 to April 2015. After excluding patients with end-stage renal disease (*n*=39) and those who received diuretics during the surgery (*n*=201), 3564 patients met the inclusion criteria of this study. Among these patients, data on intraoperative UO were missing in three patients and data on intraoperative blood loss were missing in one patient. Overall, there were four (0.1%) patients with any missing predictor; therefore, we conducted complete patient analysis, leaving 3560 patients for further evaluation.

Study participants were aged 19–94 yr, and 38.7% were women. The most common surgeries were liver resection (31.9%) and colorectal resection (29.6%). The median intraoperative UO for the study population was 0.81 ml kg^{-1} h^{-1}.

Of the 3560 patients included in this study, 226 patients [6.3%; 95% confidence interval) CI, 5.6–7.2%] developed AKI; patients with AKI had a significant increase in in-hospital mortality (6.6 *vs* 0.8%; *P*<0.001) and prolonged hospital stay (median, 26 *vs* 15 days; *P*<0.001). Table 1 shows patient characteristics

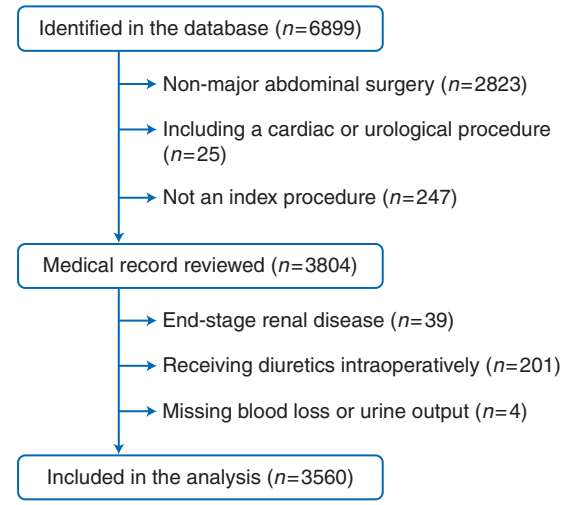

Fig 1 Flow diagram of the study population. We first identified adult patients undergoing major abdominal surgery under general anaesthesia from those undergoing surgery in the Departments of Gastrointestinal Surgery, Hepatobiliary Pancreatic Surgery and Transplantation, and Pediatric Surgery of Kyoto University Hospital using patient age, procedure name, and anaesthetic technique as recorded in the electronic database. Then, we performed medical record review for further assessment for eligibility.

and operative variables stratified by the AKI status. Patients who developed AKI had a higher AKI risk index, had more blood loss, and were more likely to receive intraoperative vasopressor infusion. Intraoperative UO in patients with AKI was lower than in those without. The cubic spline relating intraoperative UO to AKI was negatively sloped, with an inflection point at approximately 0.3–0.4 ml kg^{-1} h^{-1}, after which the probability of AKI almost plateaued (Fig. 2). Based on this result, the range from 0.1 to 1.0 ml kg^{-1} h^{-1} was selected for determining the optimal threshold for intraoperative UO, and possible thresholds at intervals of 0.1 ml kg^{-1} h^{-1} were considered. Using the minimum *P*-value approach, multivariable analysis demonstrated that the ideal threshold of intraoperative UO was 0.3 ml kg^{-1} h^{-1} (Supplementary Table S2). An intraoperative UO of <0.3 ml kg^{-1} h^{-1} occurred in 11.3% of patients. These patients had a higher AKI risk index, were more likely to undergo laparoscopic surgery, and had less blood loss and lower net fluid balance (Supplementary Table S3). The incidences of AKI were 10.2 and 5.9% in patients with an intraoperative UO of <0.3 and ≥0.3 ml kg^{-1} h^{-1}, respectively.

Multivariable analysis demonstrated that an intraoperative UO of <0.3 ml kg^{-1} h^{-1} was independently associated with the development of AKI (adjusted odds ratio, 2.65; 95% CI, 1.77–3.97; *P*<0.001; Table 2). In this multivariable analysis, intraoperative blood loss was categorized into three groups (<10, 10–<20, and ≥20 ml kg^{-1}) based on the result of cubic spline function analysis (Supplementary Fig. S1). Each variable included in the models demonstrated a variance inflation factor of <10, suggesting no multicollinearity. Both multivariable models without or with intraoperative UO demonstrated good discrimination [c-indices, 0.782 (95% CI, 0.751–0.813) and 0.791 (95% CI, 0.760–0.821),

Table 1 Patient characteristics and operative variables of 3560 eligible patients. Data are presented as median (IQR) or numbers (percentages). AKI, acute kidney injury; ASA-PS, American Society of Anesthesiologists physical status; eGFR, estimated glomerular filtration rate; IQR, interquartile range; SCr, serum creatinine; UO, urine output

Parameter	All patients (*n*=3560)	No AKI (*n*=3334)	AKI (*n*=226)	*P*-value
Age [yr; median (IQR)]	66 (56–73)	66 (56–73)	66 (60–73)	0.062
Male gender [*n* (%)]	2182 (61.3)	2001 (60.0)	181 (80.1)	<0.001
Hypertension [*n* (%)]	1078 (30.3)	961 (28.8)	117 (51.8)	<0.001
Diabetes mellitus [*n* (%)]	566 (15.9)	508 (15.2)	58 (25.7)	<0.001
Active congestive heart failure [*n* (%)]	57 (1.6)	50 (1.5)	7 (3.1)	0.09
Ascites [*n* (%)]	294 (8.3)	269 (8.1)	25 (11.1)	0.132
ASA-PS (I/II/III/IV/missing; *n*)	991/2297/231/3/38	975/2116/206/2/35	16/181/25/1/3	<0.001
Preoperative SCr [μmol litre^{-1}; median (IQR)]	62.8 (53.0–78.7)	61.9 (53.0–77.8)	70.7 (61.9–84.9)	<0.001
Preoperative eGFR [ml min^{-1} 1.73 m^{-2}; median (IQR)]	75.4 (64.1–87.9)	75.4 (64.5–88.0)	72.9 (58.8–86.0)	0.004
AKI risk index [*n* (%)]				<0.001
Class 1	1278 (35.9)	1248 (37.4)	30 (13.3)	
Class 2	1174 (33.0)	1106 (33.2)	68 (30.1)	
Class 3	750 (21.1)	672 (20.2)	78 (34.5)	
Class 4	283 (7.9)	244 (7.3)	39 (17.3)	
Class 5	75 (2.1)	64 (1.9)	11 (4.9)	
Type of surgery [*n* (%)]				<0.001
Liver	1135 (31.9)	1034 (31.0)	101 (44.7)	
Colorectal	1054 (29.6)	1012 (30.4)	42 (18.6)	
Gastric	627 (17.6)	593 (17.8)	34 (15.0)	
Pancreatic	525 (14.7)	486 (14.6)	39 (17.3)	
Oesophageal	189 (5.3)	183 (5.5)	6 (2.7)	
Complex	30 (0.8)	26 (0.8)	4 (1.8)	
Laparoscopic surgery	1860 (52.2)	1800 (54.0)	60 (26.5)	<0.001
Emergency surgery	46 (1.3)	41 (1.2)	5 (2.2)	0.212
Epidural anaesthesia	1721 (48.3)	1589 (47.7)	132 (58.4)	0.002
Duration of surgery [min; median (IQR)]	352 (257–468)	345 (254–461)	439 (329–591)	<0.001
Intraoperative fluid administration [ml kg^{-1}; median (IQR)]				
Crystalloid	51.2 (36.8–71.8)	50.5 (36.5–71.2)	59.5 (44.2–81.9)	<0.001
Colloid	0.0 (0.0–8.5)	0.0 (0.0–8.3)	7.8 (0.0–14.2)	<0.001
Intraoperative blood loss [*n* (%)]				<0.001
<10 ml kg^{-1}	2770 (77.8)	2669 (80.1)	101 (44.7)	
10–<20 ml kg^{-1}	453 (12.7)	403 (12.1)	50 (22.1)	
≥20 ml kg^{-1}	337 (9.5)	262 (7.9)	75 (33.2)	
Intraoperative red blood cell transfusion [*n* (%)]	298 (8.4)	231 (6.9)	67 (29.6)	<0.001
Intraoperative UO [ml kg^{-1} h^{-1}; median (IQR)]	0.81 (0.47–1.40)	0.82 (0.47–1.41)	0.69 (0.41–1.26)	0.009
Net fluid balance during surgery [ml kg^{-1}; median (IQR)]	43.2 (31.4–59.9)	42.8 (31.1–59.4)	50.8 (36.0–68.8)	<0.001
Intraoperative vasopressor infusion [*n* (%)]	324 (9.1)	273 (8.2)	51 (22.6)	<0.001

respectively] and calibration (*P*-values for Hosmer–Lemeshow goodness-of-fit test, 0.414 and 0.164, respectively).

We found that the category-free NRI for the addition of intraoperative UO to the model that included only AKI risk index and operative variables was 0.159 (95% CI, 0.049–0.270; *P*=0.005; Table 3). The IDI for the addition of intraoperative UO was 0.009 (95% CI, 0.003–0.015; *P*=0.003).

As oliguria is usually defined as diuresis of <0.5 ml kg^{-1} h^{-1}, we carried out additional analysis calculating the risk of AKI associated with milder oliguria (intraoperative UO of 0.3–<0.5 ml kg^{-1} h^{-1}) while excluding patients with intraoperative UO of <0.3 ml kg^{-1} h^{-1}. There was not a statistically significant risk of AKI for intraoperative UO of 0.3–<0.5 ml kg^{-1} h^{-1} (adjusted odds ratio, 1.37; 95% CI, 0.88–2.13; *P*=0.160).

Subgroup analyses based on the AKI risk index, type of surgery, blood loss, and laparoscopic surgery yielded wider confidence intervals but did not substantially affect the point estimates for the impact of intraoperative UO of <0.3 ml kg^{-1} h^{-1} on AKI, suggesting that there was no interaction between these variables and intraoperative UO (Fig. 3). The relationship between intraoperative UO and AKI was qualitatively preserved across sensitivity analyses (Supplementary Table S4).

Discussion

In this cohort study of 3560 patients undergoing major abdominal surgery, we found that an intraoperative UO of <0.3 ml kg^{-1} h^{-1} was independently associated with postoperative AKI; 11.3% of patients had an intraoperative UO of <0.3 ml kg^{-1} h^{-1}, and the risk for AKI increased by ~2.7 times in these patients. The NRI analysis demonstrated that an intraoperative UO of <0.3 ml kg^{-1} h^{-1} significantly improved risk stratification for AKI compared with assessment limited to the AKI risk index and operative variables. In contrast, an intraoperative UO of 0.3–<0.5 ml kg^{-1} h^{-1} was not significantly associated with an increased risk of AKI.

Previous studies in perioperative settings failed to demonstrate a significant association between intraoperative UO and AKI,[23 24] and a recent review suggested that intraoperative UO is

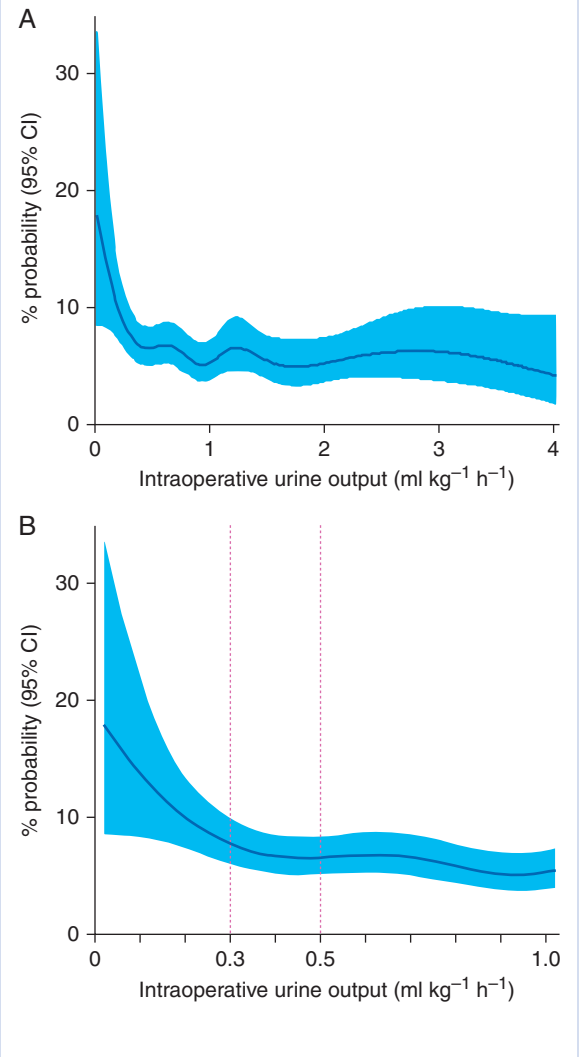

Fig 2 Cubic spline function curves of the unadjusted relationship between intraoperative urine output and the probability of AKI. Shaded areas represent 95% confidence intervals. (A) Range of intraoperative urine output from 0 to 4 ml kg^{-1} h^{-1}. (B) Range of intraoperative urine output from 0 to 1 ml kg^{-1} h^{-1}.

not related to perioperative renal function.[25] Alpert and colleagues[23] reported that there was no significant correlation between intraoperative UO and postoperative renal function in patients undergoing abdominal aortic reconstruction. However, their study included only 137 patients and was therefore too underpowered to draw a conclusion regarding the predictive value of intraoperative UO for postoperative AKI. Moreover, it included only patients undergoing abdominal aortic reconstruction, which limits generalizability. A large retrospective study that evaluated risk factors for AKI in non-cardiac surgical patients did not find intraoperative oliguria to be predictive of postoperative AKI.[24] However, that study examined only a single threshold of low UO (<0.5 ml kg^{-1} h^{-1}). This approach might miss the association between intraoperative UO and AKI even if patients with severe oliguria had a high incidence of AKI because of dilution by the larger patient population with UO immediately below the predetermined threshold with few AKI events. Furthermore, diuretics were used during surgery for some of the participants, which might have biased the results.

Our study was designed to overcome some of the limitations of these studies. First, it involved a large cohort of patients undergoing a broad spectrum of intra-abdominal procedures, which enabled a robust evaluation of relationships between exposure and outcome with sufficient statistical power. Second, we excluded patients receiving diuretics during surgery, which enabled us to analyse the relationship between intraoperative UO and AKI eliminating the effect of diuretics. Third, rather than evaluating predetermined values, we statistically identified the clinically relevant threshold of UO. This approach allowed us to relate the severity of intraoperative UO and AKI better. To our knowledge, this is the first study to attempt to identify an optimal threshold of intraoperative UO associated with a differential risk of AKI.

In view of the results of recent randomized trials showing that perioperative fluid overloading is associated with poor postoperative outcomes,[8–11] intraoperative fluid restriction has been incorporated into various 'enhanced recovery after surgery' protocols.[26–28] However, intraoperative fluid restriction might cause hypoperfusion of vital organs because of hypovolaemia. Therefore, monitoring of organ hypoperfusion during the surgery is of increasing importance. As UO is usually monitored routinely in patients undergoing major abdominal surgery, our results suggest that an intraoperative UO of <0.3 ml kg^{-1} h^{-1} might serve as an early and easily available indicator of renal hypoperfusion or impending AKI. A urine flow rate of <0.3 ml kg^{-1} h^{-1} is similar to the classical definition of oliguria (i.e. UO of <400 ml day^{-1}), which is determined based on the minimal UO required to eliminate 300 mOsm day^{-1} in a maximal urine concentration of 1200 mOsm kg^{-1}.[29]

Patients with an intraoperative UO of <0.3 ml kg^{-1} h^{-1} were more likely to undergo laparoscopic surgery. This finding is in line with previous studies that reported reduced diuresis during laparoscopic surgeries.[30 31] Possible mechanisms include a direct pressure effect of pneumoperitoneum on the renal vasculature resulting in reduced renal blood flow and the intraoperative release of stress hormones.[31] Therefore, there is a possibility that the threshold of clinically significant oliguria might be different between laparoscopic and non-laparoscopic patients. However, in our subgroup analysis, an intraoperative UO of <0.3 ml kg^{-1} h^{-1} was significantly associated with AKI in both laparoscopic and non-laparoscopic patients.

We could not find a statistically significant association between an intraoperative UO of 0.3–<0.5 ml kg^{-1} h^{-1} and AKI. The point estimate of the odds ratio for an intraoperative UO of 0.3–<0.5 ml kg^{-1} h^{-1} was 1.37, which is substantially smaller than that for an intraoperative UO of <0.3 ml kg^{-1} h^{-1}. This finding suggests that the impact of an intraoperative UO of 0.3–<0.5 ml kg^{-1} h^{-1} on AKI, if it exists, is small compared with that of an intraoperative UO of <0.3 ml kg^{-1} h^{-1}. The widely used definition of intraoperative oliguria (<0.5 ml kg^{-1} h^{-1}) should be reconsidered, because fluid replacement using a higher target of UO tends to increase the amount of fluid administered and may cause harm.[8–11]

Our study has several strengths. We found that our results remained robust after stratifying our analysis by various patient and operative variables. This suggests that the relationship between intraoperative UO and AKI does not change significantly depending on patient characteristics or the type of surgery. We also confirmed the robustness of our findings through

Table 2 Models to predict postoperative acute kidney injury. AKI, acute kidney injury; aOR, adjusted odds ratio; CI, confidence interval; UO, urine output

	Patient/operative variables only		Patient/operative variables and Intraoperative UO	
	aOR (95% CI)	P-value	aOR (95% CI)	P-value
AKI risk index				
Class 1	1 (reference)		1 (reference)	
Class 2	2.31 (1.48–3.62)	<0.001	2.26 (1.44–3.54)	<0.001
Class 3	3.82 (2.44–5.97)	<0.001	3.69 (2.36–5.78)	<0.001
Class 4	5.91 (3.53–9.89)	<0.001	5.43 (3.23–9.12)	<0.001
Class 5	7.39 (3.42–15.90)	<0.001	7.35 (3.38–16.00)	<0.001
Type of surgery				
Liver	1 (reference)		1 (reference)	
Colorectal	0.73 (0.47–1.13)	0.155	0.66 (0.42–1.02)	0.062
Gastric	1.06 (0.66–1.69)	0.805	0.87 (0.54–1.41)	0.576
Pancreatic	0.55 (0.37–0.83)	0.004	0.57 (0.38–0.86)	0.008
Oesophageal	0.55 (0.23–1.31)	0.177	0.58 (0.24–1.39)	0.224
Complex	1.17 (0.38–3.66)	0.785	1.20 (0.39–3.74)	0.754
Intraoperative blood loss				
<10 ml kg^{-1}	1 (reference)		1 (reference)	
10–<20 ml kg^{-1}	3.03 (2.00–4.59)	<0.001	3.22 (2.12–4.91)	<0.001
≥ 20 ml kg^{-1}	5.58 (3.71–8.40)	<0.001	6.03 (3.97–9.14)	<0.001
Intraoperative vasopressor infusion	1.64 (1.12–2.39)	0.010	1.67 (1.15–2.44)	0.008
Intraoperative UO				
≥ 0.3 ml kg^{-1} h^{-1}	–	–	1 (reference)	
<0.3 ml kg^{-1} h^{-1}	–	–	2.65 (1.77–3.97)	<0.001

Table 3 Reclassification table comparing models with and without intraoperative urine output as a predictor of acute kidney injury. AKI, acute kidney injury; CI, confidence interval

	Number of patients			Net reclassification improvement (95% CI)
	Total	Reclassified up	Reclassified down	
AKI present	226	50	176	−0.558 (−0.623 to −0.490)
AKI absent	3334	472	2862	0.717 (0.701–0.732)
Total	3560	522	3038	0.159 (0.049–0.270)

extensive sensitivity analyses. We had complete data on independent variables and the primary outcome in 99.9% of participants.

Our study has many limitations that should be considered when interpreting the results. Information on clinical risk factors of AKI was not prospectively collected; instead, it was retrieved from the electronic database and the electronic medical record system. Thus, the effects of certain risk factors might have been biased. The findings of this observational study are merely an association and cannot imply causation; thus, we are unable to ascertain whether intraoperative management targeting the urine flow rate at ≥ 0.3 ml kg^{-1} h^{-1} will reduce the risk of AKI. Future randomized trials are needed to address this hypothesis. We could not clearly determine the duration of oliguria, because our database contained only total UO and not hourly UO during the surgery. However, most patients with oliguria were assumed to have a continuous reduction of UO for 3–4 h, considering that the duration of surgery was ≥ 3 h in 93.0% patients and ≥ 4 h in 79.5% patients. The single-centre design might limit the generalizability, and external validation is warranted to corroborate our findings. However, the incidence of AKI observed in our study was similar to that in recent large-scale studies reporting the incidence of AKI according to KDIGO criteria after intra-abdominal surgeries[19] or non-cardiac surgeries.[20 21] Our study included patients undergoing major abdominal surgery, so it is unclear whether our findings can be extrapolated to patients undergoing other surgeries. For example, Hori and colleagues[32] reported an independent association between a urine flow rate of <1.5 ml kg^{-1} h^{-1} during cardiac surgery and AKI. Further studies are required to determine optimal thresholds of UO in various clinical settings.

In conclusion, among patients undergoing major abdominal surgery, intraoperative oliguria <0.3 ml kg^{-1} h^{-1} was independently associated with postoperative AKI. Further research is required to determine whether intraoperative management targeting the urine flow rate at ≥ 0.3 ml kg^{-1} h^{-1} will reduce the risk of AKI.

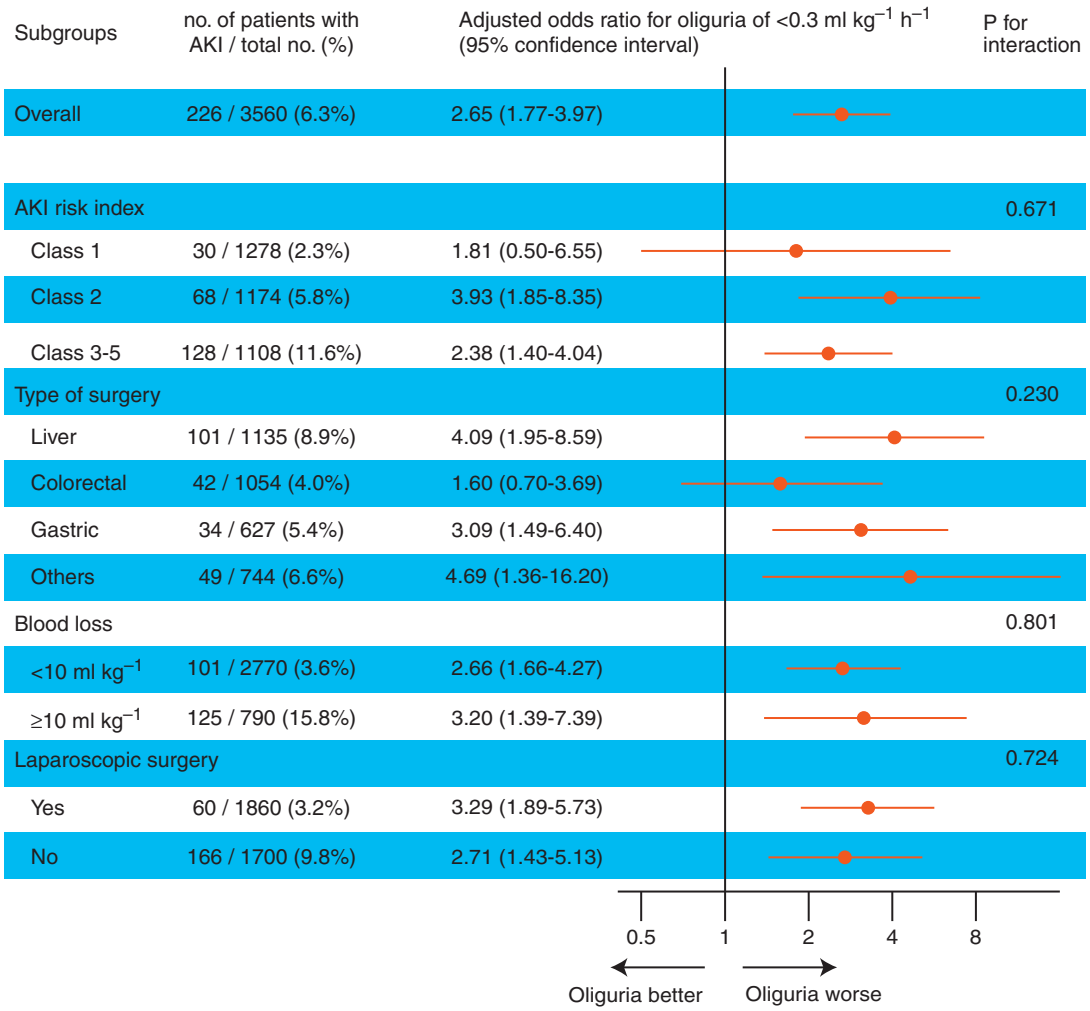

Fig 3 Subgroup analyses stratified by patient and operative variables. AKI, acute kidney injury.

Authors' contributions

Conception of the study: T.M.
Study design: T.M., S.M.
Data collection: T.M., M.H., S.M., S.S.
Data analysis: T.M., Y.Y., M.H., S.M., S.S., S.K.
Drafting the manuscript: T.M.
Editing and approval of the manuscript: T.M., Y.Y., M.H., S.M., S.S., S.K.

Supplementary material

Supplementary material is available at *British Journal of Anaesthesia* online.

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Declaration of interest

None declared.

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