ORIGINAL ARTICLE

Epidemiology and Long-term Outcomes of Acute Kidney Injury in Adult Patients with Perforation Peritonitis Undergoing Emergency Laparotomy

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Abstract

Background: Reported incidence of acute kidney injury (AKI) is around 5.0–7.5% of all hospitalized patients, and 40% of them are postoperative patients. Major abdominal surgeries account for 3.1–35% of cases of postoperative AKI in various series. The aim of the study was to identify the incidence and risk factors of AKI in peritonitis patients undergoing emergency laparotomy.

Materials and methods: Adult patients aged 18–65 years undergoing emergency laparotomy for perforation peritonitis were included in this prospective observational study. Baseline clinical and laboratory data, intraoperative details and postoperative outcome data (AKI at day 7, length of intensive care unit and hospital stay, and mortality) were recorded. Logistic regression model was constructed to predict AKI at day 7.

Results: $N = 140$ patients were included in this study and 69 patients (49.3%) developed AKI within day 7. Larger volume of crystalloid [OR (95% CI) 1.00 (1.00–1.00); $p = 0.012$], intraoperative vasopressor use (OR 7.42 (2.41–22.83); $p < 0.001$), intraoperative blood loss [OR 1.004(1.00–1.01); $p = 0.003$] and the presence of chronic liver disease (CLD) [OR 22.44 (1.68–299.26); $p = 0.019$] were risk factors for the development of AKI. Acute kidney injury patients had increased mortality at day 90 (24.6% vs 1.4%; $p < 0.001$), length of ICU stay (3 days vs 0 days, $p < 0.001$), and length of hospital stay (11 days vs 7 days; $p < 0.001$).

Conclusion: In peritonitis patients undergoing emergency laparotomy, as many as 49% of patients develop AKI within 1 week. The presence of CLD, intraoperative blood loss, and the use of crystalloids and vasopressor increase the odds of developing AKI.

Keywords: Acute kidney injury, Major surgery, Postoperative, Sepsis.

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Highlights

Acute kidney injury (AKI) is common in patients undergoing emergency laparotomy for perforation peritonitis and adversely affects clinical outcomes. The presence of CLD, intraoperative blood loss, and the use of crystalloids and vasopressor increase the odds of developing AKI.

Introduction

Acute kidney injury is observed in 5.0–7.5% of all hospitalized patients and 40% of them are postsurgical. Major intraperitoneal surgeries contribute to around one-third cases of postoperative AKI in several published literature.[1–4] Postoperative AKI has been studied extensively in the setting of cardiovascular surgery with an incidence of about 30% following cardiac surgery.[5] The development of AKI increases cost and length of hospital stay and mortality.[6]

Literature on AKI in elective major abdominal surgeries has observed that older age, higher body mass index (BMI), preexisting kidney dysfunction, hypoalbuminemia, use of angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers, higher modified end-stage liver disease (MELD) score, higher revised cardiac risk index (RCRI) score, and higher SAPS II score as major risk factors.[7]

There is an increased risk of developing AKI in secondary peritonitis patients undergoing emergent/urgent surgery and probably contributed by hypotension, volume depletion, sepsis, and use of nephrotoxic drugs. Reported mortality in this cohort is high and around 15–17%.[8] However, epidemiological data on these patients are lacking. Moreover, these patients may be at risk of long-term kidney dysfunction because of the frequent association of sepsis. Hence, we planned to conduct a prospective cohort study to identify the incidence, risk factors, and long-term adverse renal outcomes of patients undergoing emergency laparotomy.

The primary objective of this study was to know the incidence of AKI on the third postoperative day and secondary objectives were (1) incidence of AKI on the 7th postoperative day, (2) risk factors of

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AKI, (3) hospital mortality, (4) length of hospital stay, (5) need for renal replacement therapy (RRT), and (6) long-term adverse renal outcome at 3 months in those developing postoperative AKI.

Materials and Methods

This cohort study was conducted at All India Institute of Medical Sciences, New Delhi, India from January 2021 to August 2022.

Study Population

This study was approved by the Institute Ethics Committee and registered in the national clinical trial registry (CTRI/2021/02/031198, www.ctri.nic.in) before recruitment of the first patient. One hundred and forty adult patients, aged between 18 and 65 years, scheduled for emergency laparotomy for perforation peritonitis were recruited in this research. Before being included in the study, written informed consent was obtained from each patient or their legally authorized representative. Any patient with previous history of CKD or AKI or patients on RRT, were excluded.

Study Protocol

Preoperative

Preoperative data collection included demographic and clinical parameters (age, sex, height, weight, BMI, and comorbid illness) and laboratory parameters [hemogram, renal function test, electrolytes, arterial blood gas (ABG), Acute Physiology and Chronic Health Evaluation Score (APACHE II), and RCRI score]. Estimated glomerular filtration rate (eGFR) was calculated as per standard formula [Modification of Diet in Renal Disease (MDRD) formula-4 Variables; eGFR = 175 × standardized $Scr^{-1.154}$ × $age^{-0.203}$ × 1.212 (if black) × 0.742 (if female)].[9]

Intraoperative

Perioperative anesthetic management was provided as per standard institutional protocol. Balanced general anesthesia with endotracheal intubation was used in all patients. Analgesia was provided by intermittent boluses of fentanyl 0.5–1 µg/kg. Ringer's lactate was the intravenous fluid and noradrenaline was the vasopressor of choice. Intraoperative monitoring consisted of 3-lead/5-lead electrocardiogram (ECG), SpO_2, capnography ($EtCO_2$), noninvasive blood pressure (NIBP). The central venous catheter (CVC) and radial artery cannula were inserted in the patients who required fluid boluses for volume resuscitation or vasopressor/inotrope infusion to maintain the mean arterial pressure (MAP) more than 65 mm Hg or as per the clinical decision of the concerned anesthesiologist.

The following data were collected: site of perforation, Manheim's peritonitis index (MPI), duration of anesthesia (min), duration of surgery, number of intraoperative hypotensive episodes, type and amount of crystalloids used, type and amount of colloids used, blood or blood product transfused, vasopressors used and dose.

Postoperative

Patients requiring organ support were shifted to the intensive care unit (ICU) or high dependency unit for postoperative management. Vasopressor and/or inotropes support was provided as necessary to maintain MAP >65 mm Hg. They were subsequently managed as per the standard ICU protocol of the institute. The following clinical parameters were recorded: postoperative ABG, renal function test, serum electrolytes, cumulative fluid balance by day 3 and day 7, any surgical complications (hemorrhage, anastomotic leak, re-exploration, surgical site infection, abdominal compartment syndrome, abdomen closure-primary or secondary, drain placement) or medical complications (sepsis, vasopressor requirement, and need of mechanical ventilation), admission to ICU, need for RRT, length of ICU stay, and hospital stay. All the patients were followed up in the outpatient department or telephonically at 3 months from the date of surgery. Renal function test was noted and eGFR was calculated at the time of follow-up. Any requirement of RRT was also noted.

Kidney Disease Improving Global Outcomes (KDIGO) criteria were used for defining AKI.[4] Long-term adverse renal outcome was defined as any requirement of RRT or 25% decline in eGFR from the baseline preoperative value.[10]

Sample Size Calculation and Statistical Analysis

Anticipated frequency of postoperative AKI following emergency laparotomy is around 7–20%. With a conservative estimate of 10% incidence, and 5% confidence limit, $N = 139$ patients were required.

All clinical and laboratory data were collected in a predefined case record form and data were presented in a spreadsheet, and statistical analysis was performed in Jamovi software for Mac OS (a R-based open access analysis platform). Data were reported as median and interquartile range (IQR) for continuous parameters and as absolute numbers (percentages) for categorical parameters. Nonparametric and categorical variables were compared between AKI and No-AKI groups by Mann–Whitney *U* test and Fisher exact test, respectively. Binary regression model was constructed to identify risk factors of AKI. Parameters that were associated with AKI in univariable analysis were included in the multivariable model.

Results

One hundred and forty patients were included and $n = 69$ patients developed AKI by day 7. Baseline demographic, clinical and laboratory data were reported in Table 1. Patients who developed AKI had lower hemoglobin, higher INR, higher APACHE II score, higher incidence of CLD, lower serum sodium, higher intraoperative blood loss, higher intraoperative hypotension, more use of crystalloids, colloids and vasopressors, and increased duration of anesthesia (Table 1).

On postoperative day 3 (POD 3), according to urine output criteria, 47 (34.3%) patients and as per serum creatinine criteria, 55 (40.1%) patients developed AKI. Out of the patients who developed AKI on POD 3, 41 patients had AKI KDIGO stage I (29.9%), 16 patients (11.7%) had stage II and 4 (2.9%) had stage III. On postoperative day 7, based on urine output (UO), a further 22 patients (16.1%) developed AKI and as per serum creatinine criteria [10 patients (19.1%)]. Out of the patients who developed AKI 18 (13.1%) had AKI KDIGO stage I, 7 patients (5.1%) had stage II and 4 patients (2.9%) had stage III (Fig. 1).

Variables associated with AKI in univariate analysis were initially chosen for inclusion in binary regression model (Table 2). Binary regression model yielded that larger volume of crystalloid [OR (95% CI) 1.00 (1.00–1.00; $p = 0.012$], intraoperative vasopressor use [OR (95% CI) 7.42 (2.41–22.83); $p < 0.001$], intraoperative blood loss [OR (95% CI) 1.004 (1.00–1.01); $p = 0.003$] and presence of CLD [OR (95% CI) 22.4 (1.7–299.3); $p = 0.019$] were independently associated with AKI.

In this cohort, day 90 eGFR was significantly lower than baseline eGFR [median (IQR) 110 (84–141) at baseline vs 101 (75–118) at day 90; $p < 0.001$]. Baseline eGFR was similar in patients who had AKI and

Table 1: Baseline and demographic data

Variables	*Total (n = 140)*	*AKI (n = 69)*	*No-AKI (n = 71)*	*p-value*
Age (years)	40 (24.8–50)	40 (24–50)	40 (26.5–51)	0.801
Gender (male/female)	71/69	36/33	35/36	0.733
BMI (kg/m^2)	20.5 (18.3–23.7)	20.5 (18.1–23.5)	20.5 (18.4–23.8)	0.841
eGFR (mL/min/1.73 m^2)	109 (84.3–141)	106 (70.3–143)	112.2 (94.7–134)	0.219
Hb (mg/dL)	10.9 (8.97–13.0)	10.1 (8.10–12.3)	11.7 (9.45–13.3)	0.013
Serum sodium (mmol/L)	137 (135–140)	137 (134–138)	138 (136–140)	0.004
K (mmol/L)	4.28 (3.98–4.68)	4.2 (4.0–4.7)	4.2 (3.9–4.5)	0.595
Creatinine (mg/dL)	0.799 (0.60–0.90)	0.70 (0.60–1.10)	0.70 (0.59–0.80)	0.157
Platelet (10^3/µL)	230 (177–316)	219 (162–310)	240 (191–322)	0.280
INR	1.20 (1.06–1.37)	1.23 (1.10–1.40)	1.14 (1.01–1.31)	0.009
APACHE II	6.5 (4–9)	8 (6–10)	5 (3–8)	<0.001
pH	7.38 (7.33–7.40)	7.37 (7.31–7.39)	7.38 (7.35–7.41)	0.085
pCO_2 (mm Hg)	36.3 (33.0–39.5)	36.4 (33.7–41.0)	34.8 (31.5–38.5)	0.010
HCO_3 (mEq/L)	21 (19.3–22.8)	21.1 (19.0–23.9)	20.8 (19.4–22.3)	0.050
Lactate (mmol/L)	1.27 (0.70–1.40)	1.05 (0.80–2.0)	0.90 (0.60–1.20)	0.799
Diabetes mellitus (Yes/No)	10/130	6/63	4/67	0.482
Hypertension (Yes/No)	13/127	7/62	6/65	0.730
Malignancy (Yes/No)	36/104	22/47	14/57	0.100
Chronic liver disease (Yes/No)	9/131	8/61	1/70	0.014
Vasopressor use (Yes/No)	72/68	52/17	20/51	<0.001
Abdominal closure (Yes/No)	127/13	58/11	69/2	0.007
Intraoperative hypotension (Yes/No)	74/65	55/14	19/51	<0.001
Crystalloids (mL)	2000 (1500–2525)	2500 (1700–3000)	1800 (1000–2100)	<0.001
Colloid (mL)	0 (0–500)	500 (0–500)	0 (0–500)	<0.001
Blood loss (mL)	300 (200–500)	400 (200–600)	200 (150–325)	<0.001
Duration of anesthesia (minutes)	213 (155–280)	245 (180–350)	195 (140–240)	<0.001

Data are presented as mean± standard deviation (SD), median and interquartile range IQR) or proportion as applicable

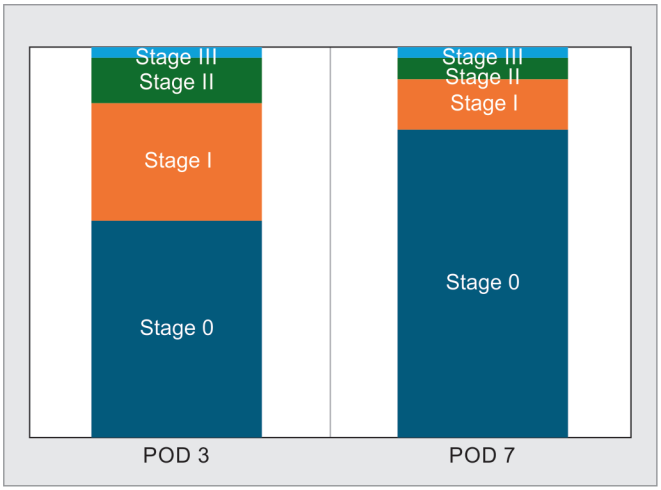

Fig. 1: Bar diagram showing acute kidney injury stage as per KDIGO criteria on postoperative day 3 and day 7.

Table 2: Logistic regression model to predict AKI of any stage within 7 postoperative day

Variables	*Odds ratio (95% CI)*	*p-value*
Hemoglobin	0.857 (0.68–1.07)	0.182
Sodium	0.930 (0.82–1.05)	0.242
Creatinine	2.815 (0.47–16.74)	0.076
APACHE II	1.163 (0.977–1.38)	0.069
pO_2	0.997 (0.989–1.00)	0.424
pCO_2	1.109 (0.994–1.24)	0.073
Crystalloid	1.00 (1.00–1.00)	0.012
Vasopressor	7.424 (2.414–22.83)	<0.001
Abdomen closure	0.0745 (0.005–1.06)	0.081
Blood loss	1.004 (1.00–1.01)	0.003
INR	2.258 (0.399–12.76)	0.356
CLD	22.442 (1.683–299.26)	0.019

Model performance AUC = 0.92; AIC = 128; R^2 = 0.475; AIC, akaike information criteria; AUC, area under the curve

who didn't have [median (IQR) 106 (70–143) in AKI group and 112 (95–134) in non-AKI group; $p = 0.22$]. At postoperative day 90, eGFR was significantly lower in patients who had AKI and who did not have [median (IQR) 80.5 (69–107) in AKI group and 106 (84–123) in non-AKI group; $p < 0.001$]. Repeated measure of ANOVA reported that there was a significant interaction between eGFR and age ($p = 0.004$) and between eGFR and baseline APACHE II score ($p = 0.022$).

Table 3: Clinical outcomes of AKI and non-AKI patients on 90-days follow-up

Outcome	*All (n = 140)*	*AKI (n = 69)*	*No-AKI (n = 71)*	*p-value*
Mortality (Yes/No)	18/122	17/52	1/70	<0.001
LOS-Hospital	6 (8.5–15)	11 (7–20)	7 (5–10)	<0.001
LOS–ICU	0 (0–4)	3 (0–6)	0 (0–0)	<0.001
eGFR at day 90	101 (75.3–118)	80.5 (69–107)	106 (84–123)	<0.001

LOS-Hospital, hospital length of stay; LOS-ICU, intensive care unit length of stay

Within the study period of 90 days, 18 patients (12.86%) died. Follow-up outcome data are provided in Table 3. Median (IQR) postoperative hospital stay for patients without AKI was 7 (5–10) days and with AKI was 11 (7–20). Median (IQR) postoperative ICU stay for patients with no-AKI was 0 (0–0) and with AKI was 3 (0–6) (Table 3).

Discussion

We have found that nearly one-third and 16% of patients fulfilled the criteria of AKI at postoperative day 3 and day 7, respectively. Larger volume of crystalloid use, intraoperative vasopressor, intraoperative blood loss, and presence of CLD were independent risk factors for postoperative AKI. Patients with postoperative AKI had longer hospital stays and higher postoperative mortality. Follow-up data reported that eGFR declined from baseline to postoperative day 90 and it was associated with both patients' age and baseline APACHE II score.

Mikkelsen et al. reported that 17.4% of patients developed AKI as per KDIGO criteria, following emergency laparotomy by day POD 7, and around 11% of all AKI was stage III.[11] A higher incidence of AKI reported in our study was probably due to the fact that relatively less sick patients were included in the aforementioned study. Though the authors did not report baseline disease severity, only 9% of patients included in that study had a qSOFA >1. The pathophysiology of postoperative AKI is probably multifactorial. We observed that risk factors for postoperative AKI were higher use of crystalloid, intraoperative vasopressor use, intraoperative blood loss, and the presence of CLD. Though, the baseline severity of illness measured by APACHE II score was not an independent predictor in our study, a trend of association was observed.

A retrospective study conducted by Mikkelsen et al. reported that risk factors for postoperative AKI were old age, smoking status, higher quick sequential organ failure assessment (qSOFA), lower performance score at admission, higher ASA class and Charlson Comorbidity Index (CCI). Furthermore, patients who developed AKI had hypertension and diabetes mellitus. Intraoperative peritoneal contamination was also found to be associated with the development of AKI.[11] In the previous studies performed in elective surgeries, risk factors associated with AKI were older age, higher non-renal RCRI and SAPS, intraoperative transfusions, comorbid conditions, lower baseline eGFR, longer and complex surgical procedures.[10,12,13] In a prospective observational study conducted by Kheterpal et al., liver disease was an independent preoperative predictor of AKI in their cohort.[14] A recent study from India reported a univariate association between sepsis and AKI in peritonitis patients, which is intuitive.[15] Risk factors of AKI in Indian patients after hepatic resection were reported previously.[16]

We observed a decline in eGFR at postoperative day 90; though the eGFR was lower in patients with AKI, it was probably contributed by the older age and higher APACHE II score of the patients also.

Our study has several limitations. First, this was a single-center study and included only a limited number of patients. Second, our follow-up period was restricted to 90 days only, hence, further decline (or recovery) of renal function could not be determined. Third, we used eGFR for renal function monitoring instead of the "24-hour creatinine clearance," which is considered to be the "gold standard."

Conclusion

We have found that in patients who are undergoing emergency laparotomy for perforation peritonitis, larger volume of crystalloid use, intraoperative vasopressor use, and blood loss were associated with postoperative AKI. There was a decline in eGFR at postoperative day 90 which was probably contributed by the patients' age and higher disease severity. Postoperative AKI adversely affected clinical outcome in these patients.

Ethical Approval

Permission from the Institute Ethics Committee (IECPG-650/25.11.2020) obtained and registered in the National Clinical Trial Registry of India (CTRI/2021/02/031198, www.ctri.nic.in).

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