ORIGINAL RESEARCH

Incidence and Predictors of Acute Kidney Injury in Patients Undergoing Elective Hepatic Resection for Malignant Tumors: A 3-year Prospective Observational Study

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Abstract

Background: Acute kidney injury (AKI) is common in patients undergoing major surgeries, and leads to the need for renal replacement therapy and increased morbidity, intensive care unit (ICU) and hospital length of stay (LOS), cost, and mortality. We evaluated the incidence and predictors of postoperative AKI in patients undergoing hepatic resections and their short-term outcomes.

Materials and methods: This prospective observational study was conducted over a 3-year period in 180 patients undergoing elective hepatic resections for a variety of indications. We used the Acute Kidney Injury Network criteria to determine the incidence of AKI at 72 hours. Perioperative variables contributing to the development of AKI and the short-term postoperative outcomes of patients were evaluated.

Results: Postoperative AKI occurred in 29.4% of patients. Persistent renal dysfunction was seen in five patients. Development of AKI was associated with hepatic failure (18.5 vs 5.5%, $p < 0.005$), prolonged ICU (2 vs 1 days, $p < 0.001$) and hospital LOS (11 vs 8 days, $p < 0.004$), and increased ICU and hospital mortality (9.6 vs 1.4%, $p < 0.02$). Age [OR (odds ratio) 1.033, 95% CI (confidence interval) 1.003–1.065, $p = 0.03$], BMI (body mass index) (OR 1.131, 95% CI 1.043–1.227, $p = 0.003$), and need for postoperative ventilation (OR 3.456, 95% CI 1.593–7.495, $p = 0.002$) were independent predictors of AKI.

Conclusion: AKI after elective hepatic resection occurred in nearly one-third of our patients. Persistent renal dysfunction was seen in five patients. Age, BMI, and need for postoperative ventilation were independent predictors of postoperative AKI. (CTRI reg. No.: CTRI/2016/06/007044).

Keywords: Acute kidney injury, Hepatic resection, Obesity, Postoperative mechanical ventilation, Postoperative morbidity, Postoperative mortality, Predictors of outcome.

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Introduction

Acute kidney injury (AKI) commonly occurs in postsurgical patients and leads to increased morbidity and intensive care unit (ICU) and hospital length of stay (LOS), cost, and mortality.[1] In a multicenter study from 30 Chinese ICUs, 44.8% of postsurgical patients developed AKI. The incidence was highest after cardiac surgery (42.1%), followed by in those who had undergone abdominal surgery (36.2%).[2] In the United States, 17-million-hospitalized patients developed AKI, adding $10-billion extra costs to the healthcare system.[3] In a study by the Alberta Kidney Disease Network of nearly 240,000 adults, Colister et al. found that even mild forms of AKI increased the hospital LOS and costs by 1.2 to 1.3 times more than those without AKI.[4] The costs increased with increasing severity and the costs remained higher even a year after admission. Of the global 13.3-million cases per year of AKI, an estimated 85% are in the developing countries.[5] AKI is associated with a 12-fold increase in the crude risk of death after surgery in the postoperative period.[6,7]

In patients undergoing partial liver resections, Bredt and Peres reported that postsurgical AKI occurred in 80 of 446 patients (17.9%).[8] The commonest etiology of AKI in these patients is hypovolemia and hypotension, causing renal hypoperfusion and ischemic renal tubular necrosis due to hemorrhage in the intraoperative period.[9] This could be contributed due to the previous practice of keeping "the central venous pressure (CVP) low to prevent hepatic venous bleeding." There are several other risk factors, which may be nonmodifiable, i.e., old age, presence of comorbidities, such as cardiovascular and renal diseases and high body mass index.[10]

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We conducted this prospective observational study to determine the incidence of AKI and the predictors of AKI in patients undergoing hepatic resection. We also analyzed the short-term outcomes in these patients.

Materials and Methods

This prospective observational study was carried out in a tertiary cancer institute over 3 years after institutional ethics committee approval and obtaining informed consent from all patients.

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We included all consecutive adult patients undergoing elective hepatic resection. We excluded pediatric patients, those undergoing emergency hepatectomy, and those who were dialysis dependent.

We collected patients' demographic data, American Society of Anesthesiologists (ASA) physical status, and comorbid conditions [chronic kidney disease (CKD) (estimated GFR [glomerular filtration rate] < 60 mL/min/1.73 m^2, not on dialysis)] hypertension, ischemic heart disease, cerebrovascular disease, diabetes mellitus, chronic obstructive pulmonary disease, cirrhosis of the liver (confirmed by history or preoperative imaging endoscopy, or intraoperative examination of the liver), and peripheral vascular disease. Prior history of chemotherapy and previous surgeries (particularly prior nephrectomy) was also recorded. Preoperative use of nephrotoxic medications (nonsteroidal anti-inflammatory drugs (NSAIDs), angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARB), statins, diuretics, and use of contrast for imaging prior to surgery was noted. The most recent preoperative laboratory values were noted from patients' electronic medical record, complete blood count, and renal and liver function tests. The preoperative estimated GFR calculated using Modification of Diet in Renal Disease equation, Child–Pugh score, and Model for End-stage Liver disease (MELD) score were also recorded. The future liver remnant was calculated and the cutoff for resection was 40% (cirrhotic patients) and 25–30% (patients without cirrhosis).

All surgical details including surgical approach (open or minimally invasive surgery), the extent of resections (major vs minor), and the duration of surgery were noted. The patients were classified as having undergone major resections (>three Couinaud segments) and minor resections. Epidural analgesia and inhalational agent use were recorded. The epidural infusions consisted of 0.1% Bupivacaine with 2 µg/mL fentanyl in all patients who had an epidural catheter inserted, as per our institutional protocol.

All patients received maintenance fluids as per our institutional protocol (enhanced recovery after surgery protocol). Intraoperative fluid therapy (volume and type of fluids), intraoperative blood loss, and replacement were recorded. Intraoperative hemodynamic instability [decrease in mean arterial pressure (MAP) >20% from baseline], need for vasopressors, oliguria (urine output <0.5 mL/kg/hour for >6 hours), and need for postoperative ventilation were also noted.

We used the Acute Kidney Injury Network (AKIN) classification for the diagnosis of AKI, and the patients were divided into three stages. Late renal dysfunction was defined by a persistent increase in the creatinine level (>0.3 mg/dL or 1.5–1.9 times increase in serum creatinine from baseline) at 30 days after surgery. The indications for the use of renal replacement therapy (RRT) were oliguria (urine output <500 mL/day), hyperkalemia, metabolic acidosis, uremia, and/or fluid overload. We did not measure any AKI biomarkers during preoperative, intraoperative, or postoperative periods.

The primary outcome was AKI at 72 hours postoperatively. The secondary outcomes were the need for RRT, ICU and hospital LOS, need for ICU readmission, postoperative ventilation, and Clavien–Dindo class 3 and 4 surgical complications, liver failure [as per International Study Group of Liver Surgery criteria], and ICU mortality and hospital or 30-day outcome, whichever was earlier.

Statistical Analysis

The continuous variables are presented as mean [±SD (standard deviation)] or median [interquartile range (IQR)] depending on the normality of the distribution. The categorical variables are presented as frequencies with percentages. Continuous variables were compared using Student's *t*-test and Mann–Whitney *U* test. Univariate analysis of categorical variables was compared by Pearson's X^2 test or Fisher's exact test. Logistic regression was applied to identify independent predictors; variables with significance <0.2 in univariate analyses were included in multivariate analyses. All analyses were two-sided, and significance was set at a *p*-value of 0.05. Statistical analyses were performed using IBM® SPSS® Statistics v 24.

Sample Size Calculation

As per previous records, we estimated the incidence of postoperative AKI to be 30%. With this, 162 patients needed to be recruited to detect the incidence (30%), with a two-sided precision of 15% and a confidence level of 95%. Allowing for a 10% attrition rate, we recruited 180 patients.

Results

We included 180 patients, who had hepatic resection over 34 months. The median age of patients was 55 (45–63) years, 67.2% were males and nearly 50% had ASA II physical status (Table 1). Thirty-seven patients had cirrhosis of the liver and 92 had undergone previous surgeries related to cancer (Table 2). The baseline investigations were within normal limits (Table 3). Most surgeries were performed using an open approach and most lasted upto 300 minutes (Table 4). Thoracic epidural catheters were inserted in 89.4% of patients. The commonest indications for partial hepatic resection were either metastasis from colorectal primary tumors (45.6%) or hepatocellular carcinomas (38.9%). One hundred seventeen (65%) patients had major liver resections (Table 5).

Postoperative complications (Clavien–Dindo 3 and 4) occurred in 44 (24.4%) patients and AKI occurred in 53 (29.4%) patients. Late renal dysfunction was seen in four patients, two of these patients had developed AKI by 72 hours, while two others had AKI after readmission to the ICU after the development of complications (Table 6). The hospital LOS was significantly longer [8 (6–12) vs 11 (8–14) days, $p = 0.004$] in patients who developed AKI. Postoperative AKI was also associated with increased ICU and 30-day mortality [5 (9.4%) vs 2 (1.6%), $p < 0.02$].

On univariate analysis, age and BMI, presence of cirrhosis, postoperative ventilation, and postoperative use of more than one

Table 1: Demographics and ASA status

Variables	*All patients (n = 180)*	*No-AKI (n = 127)*	*Pts with AKI (n = 53)*	*p*
Age, years	55 (43–63)	53 (43–62)	59 (48–66)	0.017*
Females	59 (32.8)	45 (35.4)	14 (26.4)	0.24
Males	121 (67.2)	82 (64.6)	39 (73.6)	0.24
Weight, kg	58 (52–66)	57 (49–64)	63 (56–72)	0.000*
Height, m	162 (156–168)	161 (156–168)	163 (157–167.0]	0.267
BMI, kg/m^2 median (IQR)	22.4 (19.9–25.6)	22.1 (19.1–24.4)	24 (21.2–28.9)	0.002*
ASA I, *n* (%)	73 (40.6)	58 (45.7)	15 (28.3)	0.031*
ASA II, *n* (%)	92 (51.1)	59 (46.5)	33 (62.3)	0.053*
ASA III, *n* (%)	15 (08.3)	10 (07.9)	5 (09.4)	0.73

Data presented as median (IQR) and *n* (%); *Significant difference

Table 2: Comorbidities and previous treatment

Variables n (%)	*All patients (n = 180)*	*No-AKI (n = 127)*	*Pts with AKI (n = 53)*	*p*
Cirrhosis of liver	37 (20.6)	21 (16.5)	16 (30.2)	0.04
CKD (e-GFR ≤60 mL/min/1.73 m^2)	20 (11.1)	11 (8.7)	9 (17.0)	0.11
Hypertension	6 (3.3)	5 (3.9)	1 (1.9)	0.098
DM	39 (21.7)	25 (19.7)	14 (26.4)	0.32
Hyperlipidemia	1 (0.6)	0 (0.0)	1 (1.9)	0.29
COPD	23 (12.8)	15 (11.8)	8 (15.1)	0.55
IHD	6 (3.3)	5 (3.9)	1 (1.9)	0.67
Previous. chemotherapy	30 (16.7)	18 (14.2)	12 (22.6)	0.73
Nephrotoxic drugs*	9 (5.0)	6 (4.7)	3 (5.7)	0.85
Previous surgery, other	92 (51.1)	65 (51.2)	27 (50.9)	0.98
Previous nephrectomy	2 (1.1)	1 (0.8)	1 (1.9)	0.5
MELD score, median (IQR)	8 (7–9)	8 (7–9)	8 (6 – 10)	0.92

*Nephrotoxic drugs: NSAIDs, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), diuretics, statins CKD, e-GFR <60 mL/min/1.73 m^2; DM, diabetes mellitus; IHD, ischemic heart disease; COPD, chronic obstructive airway disease; MELD score, Model for End-stage Liver Disease score

Table 3: Preoperative investigations

Baseline values	*Total (n = 18)*	*Non-AKI (n = 127)*	*Patients with AKI (n = 53)*	*p value*
Hemoglobin (g/dL)	12.3 (11.2–13.3)	12.3 (11.3–13.4)	12.1 (11.2–13.2)	0.6
S. albumin (g/dL)	4.0 (3.7–4.3)	4.0 (3.7–4.3)	4.0 (3.7–4.2)	0.6
S. creatinine (mg/dL)	0.9 (0.7–1.0)	0.9 (0.7–1.0)	0.9 (0.8–1.1)	0.25
e-GFR (mL/min/1.73 m^2)	88.4 (70.0–108.7)	90.3 (70.4–109.9)	81.9 (68.7–102.5)	0.29
S. bilirubin (mg/dL)	0.6 (0.5–0.9)	0.6 (0.5–0.9)	0.6 (0.5–0.9)	0.9
AST (IU/L)	33.52 (4.0–47.0)	34.0 (24.0–45.5)	33.0 (25.0–50.0)	0.95
ALT (IU/L)	26.5 (19.0–44.8)	25.0 (19.0–44.0)	28.0 (17.0–45.0)	0.79
Alkaline phosphatase (IU/L)	120 (92–176)	128 (90.5–179.0)	110 (93–155)	0.63

All data expressed as median (IQR); AST: aspartate aminotransferase, previously known as SGOT: serum glutamic-oxaloacetic transaminase; ALT: alanine transaminase, previously known as SGPT: serum glutamic-pyruvic transaminase; IU/L: international units/liter

Table 4: Details of surgery and anesthesia

Variables	*Total (n = 180)*	*Non-AKI (n = 127)*	*AKI (n = 53)*	*p value*
Surgical details				
Duration of surgery (mins)	310 (245–390)	315 (240–390)	315 (229–386)	0.94
Major surgery	117 (65.0)	80 (63.0)	37 (69.8)	0.38
Minor surgery	63 (35.0)	47 (37.0)	16 (30.2)	1
Open surgery	175 (97.2)	123 (96.8)	52 (98.1)	1
Minimally invasive surgery	5 (2.7)	4 (3.1)	1 (1.8)	1
Synchronous surgery*	31 (17.2)	24 (18.9)	7 (13.2)	0.36
Indications for surgery				
Liver metastasis	82 (45.6)	56 (44.1)	26 (49.1)	0.39
Hepatocellular carcinoma	70 (38.9)	47 (37.0)	23 (43.4)	0.53
Cholangiocarcinoma	19 (10.6)	16 (12.6)	3 (5.7)	0.20
Carcinoma gallbladder	3 (1.7)	3 (2.4)	0 (0.0)	0.56
Biliary cystadenocarcinoma	2 (1.1)	1 (0.8)	1 (1.9)	0.50
Neuroendocrine tumor	4 (2.2)	4 (3.1)	0 (0.0)	0.32
Extent of resection				
Major resections	117 (65)	80 (63.0)	37 (69.8)	0.38
Minor resections	63 (35)	47 (37.0)	16 (30.2)	0.38
Anesthesia details				
Isoflurane	34 (18.9)	21 (16.5)	13 (24.5)	0.2
Sevoflurane	146 (81.1)	106 (83.5)	40 (75.5)	0.2
Epidural analgesia	161 (89.4)	114 (89.8)	47 (88.7)	1

*Synchronous surgery: Hepatectomy with resection of primary tumor; @ Major resection: >three couinaud segments resected

Table 5: Intraoperative blood loss, blood products transfused, fluid therapy, and need for postoperative ventilation

Variables	*Total (n = 180)*	*Non-AKI (n = 127)*	*AKI (n = 53)*	*p-value*
Blood loss (mL)	1800 (938–2725)	1700 (900–2700)	2000 (1200–3500)	0.14
Crystalloids (mL)	2000 (1500–2500)	2000 (1500–2500)	2000 (1500–3000)	0.08
PRBCs transfused median no. of units (IQR)	3 (2–4)	3 (2–3)	3 (1–4)	0.95
No of patients who received blood transfusion (%)	111 (61.7)	73 (57.5)	38 (71.7)	0.07
RDPs transfused median no. of units (IQR)	6 (3.3)	4 (3.1)	2 (3.8)	1
FFP units, median no. of units (IQR)	4 (3–6)	4 (3–5)	4 (3.2–5.5)	0.93
No of patients who received FFP (%)	37 (20.6)	23 (18.1)	14 (26.4)	0.19
Gelatin, mL (IQR)	1000 (500–1500)	1000 (500–1500)	1000 (900–1500)	0.29
Albumin, mL (IQR)	1000 (500–1500)	1000 (500–1500)	1000 (500–1000)	0.85
Hemodynamic instability *n*, (%)	174 (96.7)	122 (96.1)	52 (98.1)	0.67
Urine output (<0.5 mL/kg/hr) n (%)	1 (0.6)	0 (0.0)	1 (1.9)	0.29
Need for vasopressor infusion *n* (%)	65 (36.1)	47 (37.0)	18 (34.0)	0.69
Need for postop ventilation *n* (%)	40 (22.2)	19 (15.0)	21 (39.6)	<0.001

Hemodynamic instability: fall in mean arterial pressure >20 mm Hg from baseline

Table 6: Postoperative outcomes at 30 days

Outcome variables	*Total (n = 180)*	*No-AKI (n = 127)*	*Patients with AKI (n = 53)*	*p value*
Postoperative complications,* *n* (%)	44 (24.4)	27 (21.3)	17 (32.1)	0.12
ICU readmissions, *n* (%)	20 (11.1)	12 (9.4)	8 (15.1)	0.27
Postop reintubations, *n* (%)	17 (9.4)	9 (7.1)	8 (15.1)	0.09
Patients with renal failure				
AKIN stage 1, *n* (%)	46 (39.13)	0	46 (86.7)	–
AKIN stage 2, *n* (%)	4 (2.2)	0	4 (7.5)	–
AKIN stage 3, *n* (%)	3 (1.67)	0	3 (5.6)	–
Late AKI (after 72 hrs)[@]	4 (2.2)	0	4 (7.3)	–
Sr. creatinine at discharge	0.8 (0.6–1.0)	0.8 (0.6–1.0)	0.9 (0.7–1.1)	0.003
Sr. creatinine at 30 days	0.9 (0.7–1.0)	0.8 (0.7–1.0)	0.9 (0.8–1.0)	0.14
RRT within 30 days, *n* (%)	6 (3.3)	0	6 (9.4)	0.009
Postop RRT, *n* (%)	9 (5.0)	0	9 (11.3)	0.02
Persistent renal dysfunction	5 (2.5)	0	5 (9.4)	–
Liver failure, *n* (%)	17 (9.4)	7 (5.5)	10 (18.9)	0.005
ICU LOS days, median (IQR)	1 (1–3)	1 (1–2)	2 (1–4)	0.001
Hospital LOS days, median (IQR)	10 (7–14)	8 (6–12)	11 (8–14)	0.004
ICU mortality, *n* (%)	7 (3.9)	2 (1.6)	5 (9.4)	0.02
Hospital mortality, *n* (%)	7 (3.9)	2 (1.6)	5 (9.4)	0.02

*Clavian–Dindo class 3 and 4 postsurgical complications; [@]All needed RRT; Data are expressed as median (IQR), unless specified otherwise; RRT, renal replacement therapy; LOS, length of stay; AKIN, Acute Kidney Injury Network

Table 7: Predictors of postoperative AKI on multivariate analysis

		95% CI		
Variables	*Odds ratio*	*Lower*	*Upper*	*p*
Age	1.033	1.003	1.065	0.032
BMI	1.131	1.043	1.227	0.003
Postoperative ventilation	3.456	1.593	7.495	0.002

nephrotoxic drug were predictors of postoperative AKI. However, on multivariate analysis, only age, BMI, and the need for postoperative ventilation were independent predictors (Table 7).

Discussion

In our cohort of patients undergoing hepatic resections, we analyzed the incidence of postoperative AKI and other complications and factors predicting the development of AKI. Nearly 30% of patients developed AKI. Persistent renal dysfunction was seen in five patients (9.4%).

This is much higher than previously reported. In a historical cohort study of 642 patients after liver resection over a 7-year period, Tomozawa et al. reported an incidence of 12.1% using AKIN criteria.[11] Patients who developed AKI were older and had lower estimated glomerular filtration rate (eGFR), serum albumin, hemoglobin concentration, and higher ASA class and serum creatinine preoperatively. Lim et al., in a single-center retrospective study of 457 patients over a 25-year period, reported AKI in 15.1% of patients.[12] In another study of 446 partial hepatic resections in 405 patients over 8 years, postoperative AKI occurred in 17.9% of patients.[8] Garnier et al. reported a 21.6% incidence of AKI after major hepatic resections, of which five patients had stage 3 AKI.[13] The incidence of postoperative AKI was 15.1% in a study of 569 patients by Slankamenac et al.[14]

The higher rate of AKI in our study may have been because of a higher percentage of patients undergoing major liver resections, as compared to previous studies (65% vs 36% and 57%, respectively).[11,14]

In our cohort, higher age [odds ratio (OR) –1.033, 95% confidence interval (CI): 1.003–1.065, $p = 0.03$] and body mass index (BMI) (OR –1.131, 95% CI: 1.043–1.227, $p = 0.003$) and the need for postoperative ventilation (OR –3.456, 95% CI: 1.593–7.495, $p = 0.002$) were independent predictors of development of AKI. Cho et al. prospectively enrolled 117 patients undergoing hepatobiliary surgery. They found age to be an independent predictor for the development of postoperative AKI (OR 1.040, 95% CI 1.005–1.076, $p < 0.024$).[15] In a retrospective study involving 457 patients undergoing hepatic resections, Lim et al. also found age (OR 1.030, 95% CI 1.001–1.050, $p = 0.040$) was an independent predictor of the development of AKI.[12] In contrast to this, Dedinská et al. compared the incidence of overall complications in patients undergoing hepatic resections and patients younger and older than 65 years of age, who had a normal preoperative renal function.[7] The mean (± SD) age of patients included in the study was 58.7 (± 11.7) years. The incidence of overall complications was higher in patients older than 65 years (27.6 vs 23.3%, $p = 0.0496$). However, the incidence of AKI was similar in both groups.

Sixteen patients in our cohort had BMI >30 kg/m^2 (two patients had BMI >35 kg/m^2) and BMI was an independent predictor of AKI. The literature suggests that underweight, overweight, and obese patients are more likely to develop AKI after liver resection and other surgeries. Mathur et al. evaluated postoperative complications in 3,960 patients undergoing hepatic resections. The incidence of postoperative complications was higher in obese patients as compared to others. The OR of having progressive renal dysfunction varied according to BMI and was higher in those who were underweight (1.02) and obese (1.59), as compared to patients who were overweight (0.52) or had normal (0.63) BMI ($p < 0.020$).[16] A Chinese retrospective study in cardiac surgery patients evaluated the association of BMI with the development of postoperative AKI.[17] The 8,455 patients were divided into four categories depending on their weight: underweight, normal, overweight, and obese. The incidence of AKI in the four groups was 29.9, 31.0, 36.5, and 46.0% ($p < 0.001$). They suggested that the best AKI-related outcomes were seen, when the BMI was between 24 and 28 kg/m^2. In a matched case–control cohort, a part of Obesity and Surgical Outcomes Study database, Kelz et al. found that elderly obese patients undergoing major surgeries had increased likelihood of development of AKI within 30 days, even after adjustment for other risk factors (OR 1.68, 95% CI: 1.11–2.52, $p < 0.01$).[18]

Studies in critically ill patients also show an association between obesity and the occurrence of AKI. Danziger et al. found that in a cohort of 14,986 critically ill patients, AKI developed in 21.1% of patients. They reported that with every 5-kg/m^2 increase in patients' body mass index, the adjusted risk of AKI increased (OR 1.10, 95% CI 1.06–1.24; $p < 0.00$). Obesity was also inversely associated with both short- and long-term survival.[19] Soto et al. studied the incidence of AKI in a cohort of acute respiratory distress syndrome (ARDS) patients.[20] They found that the incidence of AKI increased progressively as the BMI increased as compared to those with a normal BMI. Underweight patients also had a higher incidence of AKI in this cohort. The incidence of any AKI was as follows: underweight 58%, normal BMI 57%, overweight 60%, obese 69%, and severely obese 67%. They concluded that higher BMI was associated with decreased ARDS-related mortality. However, even after adjustment for obesity, AKI remained associated with increased mortality.

While the exact mechanism of obesity-related AKI remains unknown, the likely mechanisms have been extensively discussed.[21,22] The obese patients develop structural and hemodynamic changes which together are termed obesity-related glomerulopathy.[23] Activation of renin–angiotensin–aldosterone system (RAAS) leads to vasoconstriction of afferent and efferent arterioles. This results from an imbalance between afferent and efferent arterial vasomotor tones, leading to increased renal blood flow, GFR, filtration fraction, and excretion of albumin. This is accompanied by podocyte injury, glomerular enlargement, and mesangial expansion. If the patient has hypertension or diabetes, these changes are amplified. Apart from this, obesity leads to increased oxidative stress, endothelial dysfunction, and inflammation, which manifests as an increase in systemic markers, such as F2-isoprostanes, interleukin-6, and plasminogen activator inhibitor-1. Obese patients are also at an increased risk of vital organ hypoperfusion due to underestimation of intraoperative volume requirements.

Assessing volume status in obese patients may be difficult as typical signs of volume overload, such as distended neck veins and peripheral edema, are difficult to appreciate due to redundant fatty tissues. Obesity is also associated with multiple independent risk factors, such as metabolic syndrome, CKD, diabetes, and heart failure, which may contribute to postoperative AKI.

In our cohort, patients who needed postoperative ventilation had an increased incidence of AKI (OR 3.456, 95% CI 1.593–7.495, $p = 0.002$). In a retrospective study in 186 patients undergoing coronary artery bypass graft (CABG), mechanical ventilation (MV) >24 hours ($p = 0.006$) was found to be associated with postoperative AKI.[24] Heringlake et al., while assessing the effect of time to extubation after cardiac surgery in 586 elective CABG patients, reported that patients requiring MV for >16 hours had an increased incidence of AKI 53.8 vs 17.4%, $p < 0.001$).[25] In a systematic review of 31 studies in critically ill patients, van den Akker et al. found that invasive MV led to AKI (pooled OR 3.16, 95% CI: 2.32–4.28, $p < 0.001$). Since the effect of MV was seen across all subgroups, including those with different settings of tidal volume and positive end-expiratory pressure, the authors concluded that the renal dysfunction caused by MV was due to its effects on hemodynamic parameters.[26] The proposed pathophysiological mechanisms for ventilator-induced kidney injury are detailed elsewhere.[27] Positive pressure ventilation (PPV) reduces the cardiac output through multiple effects on the cardiovascular system, particularly in volume-depleted patients, leading to renal hypoperfusion, resulting in AKI. PPV also affects neurohormonal milieu, causing vasopressin release, stimulation of RAAS, and atrial natriuretic peptide production. As a consequence, there is decreased renal blood flow, diversion of blood flow from cortex to the medulla, decreased GFR, salt and water retention, and decreased urine output.

A thoracic epidural catheter was inserted in 146 (81.1%) patients and was used for intraoperative and postoperative analgesia, as per our institutional protocol. The surgical teams often demand limiting fluid infusions to keep "the CVP low" to minimize intraoperative blood loss during hepatic resections. This combined with the use of epidural analgesia with a sympathetic blockade can lead to hypotension, leading to renal hypoperfusion and AKI. Kambakamba et al. found that intraoperative use of epidural analgesia during hepatic resection was associated with a significant increase in

AKI (13.8 vs 5.0%, $p = 0.025$) and that it was an independent predictor for AKI development.[28] Ham et al. compared patient-controlled analgesia (148 patients) and epidural analgesia (168 patents) in living donors, undergoing hepatic resection as part of a liver transplantation procedure.[29] The incidence of AKI was similar (8.1 vs 7.1%; $p = 0.747$) in both groups of patients and epidural analgesia was not found to be a predictor of AKI on either univariate or multivariate analysis.

We found that patients who developed AKI after liver resection had an increased incidence of liver failure ($p = 0.005$), need for RRT ($p = 0.009$), ICU ($p = 0.001$) and hospital LOS ($p = 0.004$), and ICU and hospital mortality ($p = 0.02$). Though we did not perform cost analysis, this will obviously translate into increased costs.

We did not study long-term outcomes of patients who developed AKI after hepatic resections, but studies have described persistently increased risk of end-stage renal disease and mortality.[30,31]

The strength of our study is the prospective nature of data collection. However, it is limited due to the small sample size. We also cannot rule out the effects of unmeasured confounders, which could influence the results, but are part of the problem of any observational studies.

Conclusion

In this study of patients undergoing hepatic resections, nearly 30% of patients developed AKI. Development of AKI was associated with prolonged ICU and hospital LOS and led to increased mortality. Age, BMI, and need for postoperative MV after surgery were independent predictors of postoperative AKI.

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