



## ORIGINAL ARTICLE

# Acute kidney injury, long-term renal function and mortality in patients undergoing major abdominal surgery: a cohort analysis

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## Abstract

**Background:** Acute kidney injury (AKI) is frequent during hospitalization and may contribute to adverse consequences. We aimed to evaluate long-term adverse renal function and mortality after postoperative AKI in a cohort of patients undergoing major abdominal surgery.

**Methods:** We performed a retrospective analysis of adult patients who underwent major non-vascular abdominal surgery between January 2010 and February 2011 at the Department of Surgery II of Hospital de Santa Maria–Centro Hospitalar Lisboa Norte, Portugal. Exclusion criteria were as follows: chronic kidney disease on renal replacement therapy, undergoing renal replacement therapy the week before surgery, death before discharge and loss to follow-up through January 2014. Patients were categorized according to the development of postoperative AKI in the first 48 h after surgery using the Kidney Disease: Improving Global Outcomes classification. AKI was defined by an increase in absolute serum creatinine (SCr)  $\geq 0.3$  mg/dL or by a percentage increase in SCr  $\geq 50\%$  and/or by a decrease in urine output to  $< 0.5$  mL/kg/h for  $> 6$  h. Adverse renal outcomes (need for long-term dialysis and/or a 25% decrease in estimated glomerular filtration rate after hospital discharge) and mortality after discharge were evaluated. Cumulative mortality was analysed with the Kaplan–Meier method and log-rank test and outcome predictive factors with the Cox regression. Significance was set at  $P < 0.05$ .

**Results:** Of 390 selected patients, 72 (18.5%) developed postoperative AKI. The median follow-up was 38 months. Adverse renal outcomes and death after hospital discharge were more frequent among AKI patients (47.2 versus 22.0%,  $P < 0.0001$ ; and 47.2 versus 20.5%,  $P < 0.0001$ , respectively). The 4 year cumulative probability of death was 44.4% for AKI patients, while it was 19.8% for patients with no AKI (log-rank test,  $P < 0.0001$ ). In multivariate analysis, AKI was a risk factor for adverse renal outcomes (adjusted hazard ratio 1.6,  $P = 0.046$ ) and mortality (adjusted hazard ratio 1.4,  $P = 0.043$ ).

**Conclusions:** AKI after major abdominal surgery was independently associated with the risk of long-term need for dialysis and/or renal function decline and with the risk of death after hospital discharge.

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**Key words:** acute kidney injury, chronic kidney insufficiency, general surgery, mortality

## Introduction

Acute kidney injury (AKI), defined as an increase in baseline serum creatinine (SCr) or a decrease in urine output over a 48-h period [1], occurs in ~20% of hospitalizations [2], and is more frequent in patients admitted to intensive care units (ICUs) and after cardiac surgery [2].

Similar to the consequences of AKI in critically ill patients, postoperative AKI has been associated with longer lengths of ICU and hospital stay [3–8], higher risk for developing chronic kidney disease (CKD) [9, 10] and increased early [4–8, 11–17] and long-term mortality [3, 8, 11, 13–21].

Previous studies on long-term outcomes of postoperative AKI have focussed mainly on vascular, cardiothoracic and mixed settings [3, 8–11, 13–21]. In this study, we evaluated long-term adverse renal function and mortality after postoperative AKI in a cohort of patients undergoing major abdominal surgery.

## Materials and methods

The STROBE statement was followed for reporting of this study [22].

### Study design

This study is a retrospective analysis of clinical data from patients who underwent elective or urgent major non-vascular abdominal surgery at the Department of Surgery II of Hospital de Santa Maria—Centro Hospitalar Lisboa Norte from January 2010 to February 2011.

Due to the non-interventional design of the study, ethical approval was waived by the Ethical Committee at Centro Hospitalar Lisboa Norte in accordance with institutional guidelines.

### Setting

Centro Hospitalar Lisboa Norte is an academic and referral centre for 3 000 000 inhabitants. The Department of Surgery II is one of the general surgery departments at Centro Hospitalar Lisboa Norte and is located within its major hospital, Hospital de Santa Maria.

All patients undergoing major abdominal surgery in the Department of Surgery II are admitted in the postoperative period into the post-anaesthesia care unit (PACU), an eight-bed surgical unit coordinated by a full-time senior intensivist, functioning at level II according to the European Society of Intensive Care Medicine [23]. The PACU is run in a flexible manner with beds for simple surgical recovery, high dependency/intermediate care and full intensive care as needed, with a nurse:patient ratio of 1:2.

For the present study, relevant clinical data of all patients who underwent urgent or elective major abdominal surgery at the Department of Surgery II from January 2010 to February 2011 were reviewed. Data collection was performed in January 2014.

### Participants

Selection of potentially eligible patients was conducted based on the PACU patient admission register. All adult patients ( $\geq 18$  years of age) who underwent urgent or elective major non-vascular abdominal surgery and were afterwards admitted to the PACU were selected if the procedure involved (i) an intraperitoneal

approach, (ii) general anaesthesia and (iii) a predictable length of hospital stay of at least 2 days [24, 25].

Exclusion criteria included (i) CKD patients already on renal replacement therapy, (ii) patients who underwent renal replacement therapy the week before surgery, (iii) patients who had less than two determinations of SCr during their hospital stay, (iv) patients who were discharged from the hospital <2 days after the procedure, (v) patients who died in the hospital and (vi) patients lost to follow-up.

In patients with more than one surgery, only the first procedure was considered. In patients with multiple hospital admissions, only the first one was considered.

Selected participants were further divided into two groups according to the development of AKI in the first 48 h after surgery.

### Variables and data sources

All variables were collected from electronic and handwritten patient clinical records, including intraoperative data recorded by the anaesthesiologist. All scores and formulas were calculated based on raw clinical data.

The analysed variables included demographic characteristics [age, gender and ethnicity (Caucasian or other ethnicities)], preoperative clinical characteristics [comorbidities, physical status according to the American Society of Anesthesiologists (ASA) score [26], preoperative serum haemoglobin and SCr], procedure-related variables [risk of postoperative complications according to the Revised Cardiac Risk Index (RCRI) score [25], nature of the procedure (elective or urgent), type of surgery (laparoscopy, laparotomy or laparoscopy converted to laparotomy), operative site, duration of anaesthesia, intraoperative blood pressure, use of fluids (colloids—hydroxyethyl starch, gelatin and albumin 5%; crystalloids—sodium chloride 0.9%, Ringer's lactate and poly-electrolyte solution), blood transfusions and vasoactive drugs] and postoperative variables [illness severity according to the Simplified Acute Physiologic Score (SAPS) II [27] using the worst variables recorded during the first 24 h, postoperative fluid balance during the first 48 h, postoperative complications (AKI, haemorrhage, anastomotic leak, surgical site infection and need of mechanical ventilation), in-hospital therapeutic needs (renal replacement therapy and ICU admission) and long-term outcomes (long-term adverse renal outcomes and time and cause of death)]. Regarding preoperative clinical characteristics, the comorbidities registered were diabetes mellitus (diagnosed according to the American Diabetes Association criteria [28]), hypertension (diagnosed according to the seventh report of the Joint National Committee [29]), cardiovascular disease (including chronic heart failure, cardiac ischaemic disease and history of transient ischaemic attack or stroke), chronic obstructive pulmonary disease (COPD; including emphysema and chronic bronchitis) and malignancy. For cardiovascular disease and COPD, an indication on clinical records of a previous diagnosis was considered sufficient. The estimated glomerular filtration rate (eGFR) was determined with the four-variable Modification of Diet in Renal Disease formula [30].

All surgeries were intraperitoneal and therefore were considered high risk according to the RCRI score [25].

Pertaining to the intraoperative variables, systolic and diastolic blood pressure (SBP and DBP, respectively) were recorded automatically every 5 min and intraoperative mean arterial pressure

(MAP) was calculated as  $[(2 \times \text{DBP}) + \text{SBP}]/3$ . When available, invasive measurements were preferred to non-invasive ones. Intraoperative hypotension (IOH) was defined as intraoperative MAP  $<65$  mmHg, and the number of episodes of IOH was registered. Blood transfusions were done at the physician's discretion in patients with active bleeding or haemodynamically unstable or when the serum haemoglobin level was  $<7$ – $8$  g/dL [31] or, in older patients and in patients with coronary artery disease,  $<10$  g/dL.

The development of AKI during the first 48 h after surgery was diagnosed and staged using the Kidney Disease: Improving Global Outcomes classification [1] into Stage 1 (an increase in SCr  $\geq 0.3$  mg/dL or an increase in SCr 1.5–1.9 times the baseline value and/or urine output  $<0.5$  mL/kg/h for 6–12 h), Stage 2 (an SCr increase between 2 and 2.9 times the baseline value and/or urine output decreased to  $<0.5$  mL/kg/h for  $\geq 12$  h) and Stage 3 (an increase in SCr equal to or greater than three times the baseline value or  $\geq 4$  mg/dL or initiation of renal replacement therapy and/or urine output  $<0.3$  mL/kg/h for  $>24$  h or anuria for  $\geq 12$  h). Preoperative SCr was considered baseline SCr. Renal function recovery was considered if at hospital discharge SCr was 1.5 times lower than the baseline SCr and/or  $<0.3$  mg/dL and there was no dialysis requirement at hospital discharge.

Long-term adverse renal outcomes were defined as the need for long-term dialysis and/or a 25% decrease in eGFR after hospital discharge, as previously applied [32].

### Statistical methods

Continuous variables were presented as the mean  $\pm$  SD and categorical variables as the total number and percentage of cases for each category. After grouping participants according to the development of postoperative AKI, the variables of both groups were compared using Student's *t*-test for normally distributed continuous variables, Mann–Whitney *U*-test for non-normally distributed continuous variables and  $\chi^2$  test for categorical variables. A univariate analysis comparing adverse renal outcomes and mortality in AKI patients classified by SCr or urine output (UO) criteria was made using the  $\chi^2$  test. The Kaplan–Meier method was used to determine cumulative mortality curves, which were compared using the log-rank test. Patients were censored at the last follow-up date (January 2014) if alive. Patients lost to follow-up were excluded from all analyses.

Univariate analysis was used to determine statistically significant factors that may have contributed to long-term adverse renal outcomes and death. These factors were then analysed using the Cox regression method. Given that RCRI and SAPS II scores take into account renal function, non-renal RCRI and non-renal SAPS II were chosen as covariates. Data were expressed as hazard ratios (HRs) with 95% confidence intervals (CIs). No sensitivity analyses were carried out.

Statistical significance was defined as  $P < 0.05$ . Analyses were performed with the statistical software package SPSS 21.0 for Windows.

## Results

### Participants

After analysis of the PACU patient admission register, 479 patients were selected as potentially eligible. Of these, 89 were excluded: 10 had CKD on renal replacement therapy (all haemodialysis), 32 were hospitalized for  $<48$  h or had less than two SCr determinations, 29 died during hospitalization and 18 were lost to follow-up. None required renal replacement therapy in the week preceding surgery. Consequently, we focussed on a cohort of 390 patients.

Demographic, preoperative, intraoperative and postoperative patient variables and long-term outcomes, including comparisons between the AKI and no-AKI groups, are described in Tables 1–3. We registered no missing data.

Concerning all patients, the mean age was 62 years, with a male:female ratio of  $\sim 1 : 1$ . Most patients were Caucasian ( $n = 374$ ; 95.9%) and had a mean baseline eGFR of 79 mL/min/1.73 m<sup>2</sup>. Regarding comorbidities, 19.2% ( $n = 75$ ) had diabetes mellitus, nearly half ( $n = 198$ ; 50.8%) had hypertension, 25.5% ( $n = 81$ ) had cardiovascular disease, 4.9% ( $n = 19$ ) had COPD and 44.4% ( $n = 173$ ) had a previous diagnosis of malignancy; 43% of the patients ( $n = 168$ ) underwent a surgery for their malignancy or a related complication. Most patients underwent elective procedures ( $n = 316$ ; 81.1%) with laparotomy ( $n = 333$ ; 85.4%), with a mean anaesthesia time of 225 min. The most frequent operative site was colorectal (49.2%), followed by gastric surgery ( $n = 77$ ; 19.7%).

Seventy-two survivors (18.5%) developed AKI: 57 (79.2%) were at Stage 1, 12 (16.7%) were at Stage 2 and 3 (4.1%) were at Stage 3. Fifty-four patients (75%) met SCr criteria, nine patients (12.5%) met UO criteria and nine patients (12.5%) met both SCr and UO criteria for AKI diagnosis. Two patients with Stage 3 AKI received

**Table 1.** Demographics and preoperative clinical characteristics

	All patients ( $n = 390$ )	No AKI ( $n = 318$ )	AKI ( $n = 72$ )	P-value
Age (years)	62.0 $\pm$ 15.5	60.1 $\pm$ 15.7	70.0 $\pm$ 11.6	$<0.0001$
Male	196 (50.3%)	152 (47.8%)	44 (61.1%)	0.041
Caucasian	374 (95.9%)	305 (95.9%)	69 (95.8%)	0.976
Diabetes mellitus	75 (19.2%)	59 (18.6%)	16 (22.2%)	0.476
Arterial hypertension	198 (50.8%)	155 (48.7%)	43 (59.7%)	0.092
Cardiovascular disease	81 (25.5%)	53 (16.7%)	28 (38.9%)	$<0.0001$
COPD	19 (4.9%)	11 (3.5%)	8 (11.1%)	0.006
Malignancy	173 (44.4%)	129 (40.6%)	44 (61.1%)	0.002
ASA score IV/V	22 (5.6%)	16 (5.0%)	6 (8.3%)	0.273
Serum haemoglobin (g/dL)	10.9 $\pm$ 1.6	11.2 $\pm$ 1.8	10.6 $\pm$ 1.6	$<0.0001$
Baseline eGFR (mL/min/1.73 m <sup>2</sup> )	79.2 $\pm$ 25.4	79.0 $\pm$ 25.0	80.0 $\pm$ 28.0	0.770
SCr at hospital discharge (mg/dL)	0.9 $\pm$ 0.4	0.8 $\pm$ 0.2	1.1 $\pm$ 0.7	$<0.0001$

AKI, acute kidney injury; COPD, chronic obstructive pulmonary disease; ASA, American Society of Anesthesiologists score; eGFR, estimated glomerular filtration rate; SCr, serum creatinine.

Table 2. Procedure-related variables

	All patients (n = 390)	No AKI (n = 318)	AKI (n = 72)	P-value
RCRI score	1.3 ± 0.5	1.2 ± 0.5	1.5 ± 0.7	<0.0001
Urgent surgery	74 (18.9%)	67 (21.0%)	7 (9.7%)	0.027
Surgical approach				
Laparoscopy	52 (13.3%)	44 (13.8%)	8 (11.1%)	0.539
Laparoscopy converted to laparotomy	5 (1.3%)	5 (1.6%)	0 (0%)	0.284
Laparotomy	333 (85.4%)	269 (84.6%)	64 (88.9%)	0.351
Operative site				
Colorectal	192 (49.2%)	144 (45.3%)	48 (66.7%)	0.001
Gastric	77 (19.7%)	68 (21.4%)	9 (12.5%)	0.087
Hepato-biliary-pancreatic	60 (15.4%)	51 (16.0%)	9 (12.5%)	0.452
Small bowel	14 (3.6%)	12 (3.8%)	2 (4.2%)	0.682
Oesophageal	8 (2.0%)	7 (2.2%)	1 (1.4%)	0.661
Other	39 (10.0%)	36 (11.3%)	3 (4.2%)	0.068
Intraoperative characteristics				
Anaesthesia time (min)	225 ± 101	218 ± 92	257 ± 32	0.003
Number of IOH episodes	0.9 ± 1.7	0.9 ± 1.7	1.0 ± 1.4	0.664
Use of crystalloids only	164 (42.1%)	146 (45.9%)	18 (25.0%)	0.001
Amount of crystalloid use (L)	2.3 ± 1.2	2.3 ± 1.2	2.3 ± 1.2	0.447
Use of both crystalloids and colloids	226 (57.9%)	172 (54.1%)	54 (75.0%)	0.001
Amount of crystalloids use (L)	2.2 ± 1.3	2.2 ± 1.1	2.3 ± 1.5	0.527
Amount of colloids use (L)	0.4 ± 0.3	0.4 ± 0.3	0.7 ± 0.5	<0.0001
Blood transfusions (units)	0.4 ± 0.7	0.3 ± 0.5	0.8 ± 1.0	<0.0001
Use of vasoactive drugs	60 (15.3%)	48 (15.1%)	12 (16.7%)	0.738

AKI, acute kidney injury; RCRI, Revised Cardiac Risk Index; IOH, intraoperative hypotension.

Table 3. Postoperative variables and long-term outcomes

	All patients (n = 390)	No AKI (n = 318)	AKI (n = 72)	P-value
Postoperative variables				
SAPS II	19.2 ± 10.3	18.7 ± 10.0	26.9 ± 12.7	<0.0001
Fluid balance (L)	2.6 ± 2.6	2.6 ± 2.6	2.6 ± 2.8	0.548
Complications				
Haemorrhage	32 (8.2%)	20 (6.3%)	12 (16.7%)	0.004
Anastomotic leak	15 (3.8%)	10 (3.1%)	5 (6.9%)	0.130
Surgical site infection	59 (15.1%)	47 (14.8%)	12 (16.7%)	0.687
Need of MV	5 (1.3%)	4 (1.3%)	1 (1.4%)	0.929
Admission to ICU	8 (2.0%)	4 (1.3%)	4 (5.6%)	0.02
Length of stay				
PACU (days)	3.5 ± 6.1	3.3 ± 4.8	5.6 ± 9.6	0.001
Hospital (days)	11.6 ± 11.4	10.7 ± 10.5	15.6 ± 14.3	0.001
Long-term outcomes				
Adverse renal outcome	104 (26.7%)	70 (22.0%)	34 (47.2%)	<0.0001
Death	97 (24.8%)	63 (19.8%)	34 (47.2%)	<0.0001

AKI, acute kidney injury; SAPS II, Simplified Acute Physiology Score, version II; MV, mechanical ventilation; ICU, intensive care unit; PACU, post-anaesthesia care unit.

renal replacement therapy (in both cases, intermittent haemodialysis) during hospitalization. AKI patients were significantly more likely to be older and male, to have cardiovascular disease, COPD and malignancy and to have a lower preoperative serum haemoglobin level (Table 1). They also had significantly higher RCRI scores and underwent more elective and colorectal surgeries, with longer anaesthesia times. Intraoperatively, patients who developed AKI were more likely to receive fluids—either only crystalloids or both crystalloids and colloids—and blood transfusions (Table 2). Postoperatively, AKI patients scored significantly higher on SAPS II, suffered more from bleeding and were more likely to be admitted to the ICU and to have longer PACU and hospital stays (Table 3).

The median follow-up time was 38 months (minimum: 1 month; maximum: 48 months). A little over one-quarter of all patients developed an adverse renal outcome (n = 104; 26.7%) and one-quarter died (n = 97; 24.8%) during follow-up (Table 3). Two patients required renal replacement therapy (chronic haemodialysis) during follow-up.

### Long-term outcomes

Patients with adverse renal outcomes were more likely to be older and to have preoperative diabetes mellitus, arterial hypertension, cardiovascular disease, malignancy and lower baseline eGFR. Additionally, those patients also had significantly higher

ASA, non-renal RCRI and non-renal SAPS II scores and had higher positive fluid balance and SCr at hospital discharge. Regarding long-term mortality, patients who died during follow-up were more likely to be older and to have preoperative cardiovascular disease, malignancy and lower baseline eGFR. Furthermore, those patients also were more likely to undergo laparotomy, had significantly higher non-renal RCRI and non-renal SAPS II scores, received more erythrocyte transfusions, had higher positive fluid balance and SCr at hospital discharge and were more likely to have surgical site infection (Table 4).

Adverse renal outcomes and mortality after hospital discharge were more frequent among AKI patients (47.2 versus 22.0%,  $P < 0.0001$ ; and 47.2 versus 19.8%,  $P < 0.0001$ , respectively). The 4 year cumulative probability of death was 44.4% for AKI patients, while it was 19.8% for patients with no AKI (log-rank test,  $P < 0.0001$ ) (Figure 1). The incidence of adverse renal outcomes

was 47.3% for AKI Stage 1 ( $n = 27$ ), 33.3% for AKI Stage 2 ( $n = 4$ ) and 100% for AKI Stage 3 ( $n = 3$ ) ( $P = 0.118$ ). Furthermore, 49.1% of patients with AKI Stage 1 ( $n = 28$ ), 33.3% of patients with AKI Stage 2 ( $n = 4$ ) and 66.6% of patients with AKI Stage 3 ( $n = 2$ ) ( $P = 0.480$ ) died during follow-up.

In multivariate analysis, AKI was independently associated with long-term adverse renal outcomes [adjusted HR 1.60 (95% CI 1.01–2.50),  $P = 0.046$ ] and with mortality [adjusted HR 1.40; (95% CI 1.10–2.00),  $P = 0.043$ ] (Table 5).

Other factors were also associated with long-term adverse renal outcomes, such as age [adjusted HR 1.04 (95% CI 1.02–1.10),  $P = < 0.0001$ ] and non-renal SAPS II score [adjusted HR 1.03, (95% CI 1.02–1.100),  $P = 0.001$ ] (Table 5).

Age [adjusted HR 1.04 (95% CI 1.02–1.06),  $P = 0.001$ ], malignancy [adjusted HR 2.50 (95% CI 1.60–4.10),  $P = < 0.0001$ ], non-renal SAPS II score [adjusted HR 1.04 (95% CI 1.01–1.07),  $P = 0.007$ ]

**Table 4.** Characteristics of patients according to adverse renal outcomes and mortality

	No adverse RO ( $n = 286$ )	Adverse RO ( $n = 104$ )	P-value	Alive ( $n = 293$ )	Dead ( $n = 97$ )	P-value
<b>Demographics</b>						
Age (years)	59 (15)	69 (13)	<0.0001	59 (15)	71 (11)	<0.0001
Male	141 (71.9%)	55 (28.1%)	0.531	140 (71.4%)	56 (28.6%)	0.089
Caucasian	272 (72.7%)	102 (27.3%)	0.191	280 (74.9%)	94 (25.1%)	0.563
<b>Preoperative clinical characteristics</b>						
Diabetes mellitus	46 (61.3%)	29 (38.7%)	0.009	59 (78.7%)	16 (21.3%)	0.430
Arterial hypertension	130 (76.9%)	68 (23.1%)	<0.0001	141 (71.2%)	57 (28.8%)	0.069
Cardiovascular disease	45 (55.5%)	36 (44.5%)	<0.0001	48 (59.3%)	33 (40.7%)	<0.0001
COPD	11 (57.9%)	8 (42.1%)	0.119	12 (63.2%)	7 (36.8%)	0.216
Malignancy	117 (67.6%)	56 (32.4%)	0.023	105 (60.7%)	68 (39.3%)	<0.0001
ASA score IV/V	12 (54.5%)	10 (45.5%)	0.04	14 (63.6%)	8 (36.4%)	0.199
Serum haemoglobin (g/dL)	10.9 (1.4)	11 (1.7)	0.467	10.9 (1.3)	11.1 (1.7)	0.235
eGFR (mL/min/1.73 m <sup>2</sup> )	75 (24)	90 (23)	<0.0001	79 (26)	77 (23)	<0.0001
<b>Procedure-related variables</b>						
Non-renal RCRI score	1.2 (0.4)	1.4 (0.6)	<0.0001	1.2 (0.4)	1.4 (0.6)	<0.0001
Urgent surgery	51 (68.9%)	23 (31.1%)	0.340	54 (72.9%)	20 (27.1%)	0.634
Laparotomy	245 (73.6%)	88 (26.4%)	0.795	240 (72%)	93 (28%)	0.001
<b>Operative site</b>						
Colorectal	141 (73.4%)	51 (26.6%)	0.963	139 (72.3%)	53 (27.7%)	0.219
Gastric	61 (79.2%)	16 (20.8%)	0.192	61 (79.2%)	16 (20.8%)	0.354
Hepato-biliary-pancreatic	39 (65%)	21 (35%)	0.113	46 (76.7%)	14 (23.3%)	0.764
Small bowel	10 (71.4%)	4 (28.6%)	0.870	10 (71.4%)	4 (28.6%)	0.744
Oesophageal	7 (87.5%)	1 (12.5%)	0.360	6 (75%)	2 (25%)	0.933
Other	28 (71.8%)	11 (28.2%)	0.819	31 (79.5%)	8 (20.5%)	0.507
<b>Intraoperative characteristics</b>						
Anaesthesia time (minutes)	228 (99)	215 (109)	0.256	227 (102)	219 (100)	0.541
IOH (episodes)	0.9 (1.7)	0.9 (1.3)	0.491	0.9 (1.7)	1 (1.5)	0.599
Colloid use (L)	0.4 (0.3)	0.4 (0.3)	0.843	0.4 (0.3)	0.4 (0.3)	0.917
Erythrocyte transfusion (units)	0.5 (0.5)	0.5 (0.5)	0.807	0.5 (0.5)	0.7 (0.5)	0.005
Use of vasoactive drugs	42 (70%)	18 (30%)	0.526	45 (75)	15 (25%)	0.980
<b>Postoperative variables</b>						
Non-renal SAPS II	16 (9)	22 (10)	<0.0001	16 (9)	24 (10)	<0.0001
Fluid balance (L)	1.3 (1.3)	1.6 (1.4)	0.043	1.2 (1.3)	1.8 (1.4)	<0.0001
<b>Complications</b>						
Haemorrhage	20 (62.5%)	12 (37.5%)	0.148	22 (68.8%)	10 (31.2%)	0.384
Anastomotic leak	9 (60%)	6 (40%)	0.234	11 (73.3%)	4 (26.7%)	0.870
Surgical site infection	44 (74.6%)	15 (25.4%)	0.815	36 (61%)	23 (39%)	0.006
Need of MV	4 (80%)	1 (20%)	0.734	4 (80%)	1 (20%)	0.800
Admission to ICU	6 (75%)	2 (25%)	0.924	5 (62.5%)	3 (37.5%)	0.395
SCr at hospital discharge (mg/dL)	0.8 (0.2)	1.1 (0.9)	<0.0001	0.9 (0.3)	1 (0.6)	0.008
AKI	38 (52.8%)	34 (47.2%)	<0.0001	38 (52.8%)	34 (47.2%)	<0.0001

RO, renal outcome; COPD, chronic obstructive pulmonary disease; ASA, American Society of Anesthesiologists score; eGFR, estimated glomerular filtration rate; RCRI, Revised Cardiac Risk Index; IOH, intraoperative hypotension; SAPS II, Simplified Acute Physiology Score, version II; MV, mechanical ventilation; ICU, intensive care unit; SCr, serum creatinine; AKI, acute kidney injury.



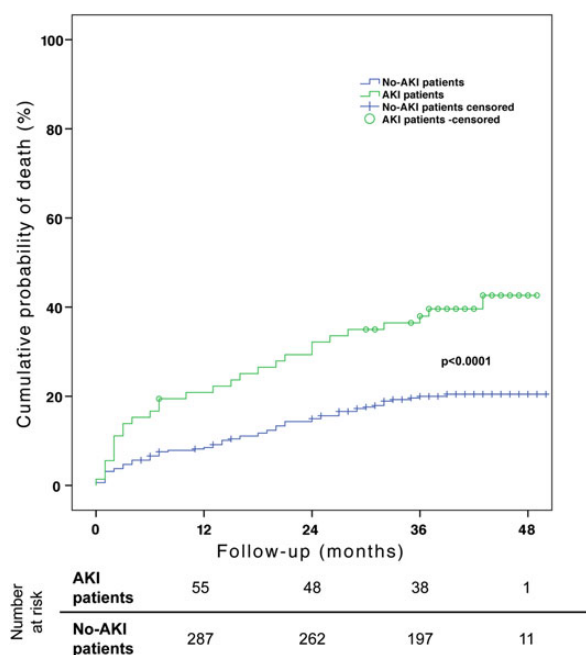


Fig. 1. Comparison of cumulative mortality curves according to the development of postoperative AKI. AKI, acute kidney injury. Log-rank test  $P < 0.0001$ .

and surgical site infection [adjusted HR 1.80 (95% CI 1.10–2.90),  $P = 0.016$ ] were also factors that independently contributed to death after hospitalization (Table 5).

Twenty-eight of the 54 patients with AKI (51.9%) who met SCr criteria, 1 of the 9 patients with AKI (11.1%) who met UO criteria ( $P = 0.023$ ) and 5 of the 9 patients with AKI (55.6%) who met both SCr and UO criteria had adverse renal outcomes. In addition, 27 of the 54 patients with AKI (50%) who met SCr criteria, 2 of the 9 patients with AKI (22.2%) who met UO criteria ( $P = 0.122$ ) and 5 of the 9 patients with AKI (55.6%) who met both SCr and UO criteria died during follow-up.

Sixty-two patients with AKI (86.1%) had renal function recovery at hospital discharge, while 10 patients (13.9%) with AKI did not. Twenty-nine of the 62 patients with AKI (46.8%) who recovered renal function and 5 of the 10 patients with AKI (50%) who did not recover renal function had adverse renal outcomes ( $P = 0.850$ ); 30 of the 62 patients with AKI (48.3%) who recovered renal function and 4 of the 10 patients with AKI (40%) who did not recover renal function died during follow-up ( $P = 0.622$ ).

Of interest, patients with postoperative AKI with adverse long-term renal outcomes had significantly higher mortality than those without poor renal outcomes (62 versus 27.9%;  $P = 0.012$ ).

Malignancy, sepsis and cardiovascular disease were the main causes of death. The registered mortality causes were, respectively, for AKI and no-AKI patients: 52.9% ( $n = 38$ ) and 76.2% ( $n = 242$ ) for malignancy ( $P = 0.019$ ), 14.7% ( $n = 11$ ) and 7.9% ( $n = 25$ ) for sepsis ( $P = 0.296$ ), 8.8% ( $n = 6$ ) and 4.8% ( $n = 15$ ) for cardiovascular disease ( $P = 0.428$ ) and 2.9% ( $n = 2$ ) and 3.2% ( $n = 10$ ) for other causes ( $P = 0.949$ ). The cause of death was unknown in 20.6% ( $n = 15$ ) of AKI patients and 7.9% ( $n = 26$ ) of no-AKI patients.

## Discussion

In this retrospective study of a cohort of 390 patients who underwent major non-vascular abdominal surgery, postoperative

AKI was independently associated with the risk of developing long-term adverse renal outcomes and of death after hospital discharge. We found that AKI in the postoperative period was associated with poor long-term renal function and long-term mortality: patients with AKI had a 1.6-fold higher risk of long-term dialysis or 25% decrease in eGFR and a 1.4-fold higher risk of death than patients with no postoperative AKI. These findings expand on results from previous studies that showed an increased risk of short-term mortality associated with AKI after major non-cardiac surgery [6, 11, 18].

In a previous study [6], we analysed 450 patients who underwent major non-vascular abdominal surgery between January 2010 and February 2011 at the Department of Surgery II—Centro Hospitalar Lisboa Norte, Portugal. The reported incidence of postoperative AKI in the first 48 h after surgery was 22.4%, and AKI was independently associated with increased in-hospital mortality [adjusted odds ratio 3.7 (95% CI 1.2–11.7)  $P = 0.024$ ]. In the current analysis, we studied adverse renal outcomes (need of long-term dialysis and/or a 25% decrease in eGFR after hospital discharge) and mortality of those patients of the same cohort who were discharged alive after surgery.

Previous publications had already accounted for increased long-term mortality after postoperative AKI in other settings, namely after hepato-biliary-pancreatic, vascular, cardiothoracic and mixed types of surgery [3, 8, 11, 13–21]. Additionally, it has been shown that even small decreases in eGFR increase the long-term risk of death in hospitalized AKI patients [33]. In accordance, although our study included mostly patients with Stage 1 AKI (79.2%), the same association was found for patients undergoing major abdominal surgery. These findings reinforce the notion that postoperative AKI leads to poor long-term outcomes, even in patients with mild elevations of SCr.

Previous studies [34, 35] demonstrated a greater impact of AKI defined by SCr on short-term mortality than AKI defined by UO. In the present study, AKI defined exclusively by SCr was associated with worse renal outcomes than AKI defined solely by UO. However, although long-term mortality was higher among patients with AKI defined exclusively by SCr when compared with those patients with AKI defined solely by UO, this difference did not reach statistical significance. Therefore, the exact impact of AKI diagnosed by SCr and/or UO on long-term outcomes should be better determined in larger and prospective studies.

To our knowledge, the association between postoperative AKI and the development of long-term need of dialysis and/or sustained decline in renal function had only been previously reported for hepato-biliary-pancreatic and cardiac surgery [9, 10]. In AKI, it is believed that the initiating mechanism and the subsequent maladaptive response to injury may contribute to a reduced ability to restore baseline renal structure and function [34, 35], increasing the probability of the development of or more rapid progression of CKD. In our study, we show that this may be true also for AKI after major abdominal surgery.

The post-AKI development of CKD may contribute to the burden of cardiovascular disease and mortality [36], and in our study, we also found that patients with adverse long-term renal outcomes after postoperative AKI were more likely to die after hospital discharge.

In the present study, some limitations have to be noted. First, the single-centre and retrospective nature with a small cohort of patients may compromise, at least in part, the results of our study. Second, we did not evaluate AKI developing after the first postoperative 48 h, which could help to explain the higher than expected percentage of patients in the no-AKI group that had long-term renal function decline (22%). Third, data on

Table 5. Univariate and multivariate analysis of factors predictive of outcomes

	Long-term adverse renal outcomes				Mortality			
	Unadjusted HR (95% CI)	P-value	Adjusted HR (95% CI)	P-value	Unadjusted HR (95% CI)	P-value	Adjusted HR (95% CI)	P-value
<b>Demographics</b>								
Age (years)	1.05 (1.04–1.07)	<0.0001	1.04 (1.02–1.10)	<0.0001	1.06 (1.04–1.07)	<0.0001	1.04 (1.02–1.06)	0.001
Male	1.20 (0.80–1.70)	0.472			1.40 (0.90–2.10)	0.131		
Caucasian	2.20 (0.50–9.00)	0.262			0.90 (0.30–2.60)	0.947		
<b>Preoperative clinical characteristics</b>								
Diabetes mellitus	1.80 (1.20–2.80)	0.006	0.90 (0.60–1.50)	0.887	0.90 (0.50–1.50)	0.692		
Arterial hypertension	1.90 (1.30–2.90)	0.002	1.40 (0.90–2.20)	0.112	1.30 (0.90–2.00)	0.152		
Cardiovascular disease	2.40 (1.60–3.60)	<0.0001	0.50 (0.20–1.20)	0.140	2.20 (1.50–3.40)	<0.0001	0.80 (0.30–2.00)	0.642
COPD	1.50 (0.70–3.10)	0.291			1.50 (0.70–3.50)	0.302		
Malignancy	1.90 (1.30–2.90)	0.001	1.20 (0.80–1.80)	0.416	3.10 (2.00–4.80)	<0.0001	2.50 (1.60–4.10)	<0.0001
ASA score IV/V	2.00 (1.10–3.90)	0.035	1.60 (0.80–3.20)	0.227	1.90 (0.90–3.90)	0.09		
Serum haemoglobin (per g/dL decrease)	1.30 (0.70–2.70)	0.591			1.30 (0.70–2.50)	0.327		
eGFR (per mL/min/1.73 m <sup>2</sup> decrease)	1.02 (1.01–1.02)	<0.0001	1.02 (1.01–1.10)	<0.0001	0.90 (0.90–1.01)	0.655		
<b>Procedure-related variables</b>								
Non-renal RCRI score (per point)	2.10 (1.50–2.80)	<0.0001	1.90 (1.00–3.60)	0.05	1.90 (1.40–2.70)	<0.0001	1.70 (0.80–3.40)	0.141
Urgent surgery	1.10 (0.70–1.80)	0.559			1.10 (0.70–1.90)	0.610		
Laparotomy	1.10 (0.70–1.90)	0.626			5.70 (1.80–18.20)	0.003	2.90 (0.90–9.60)	0.072
<b>Operative site</b>								
Colorectal	0.90 (0.60–1.40)	0.788			1.20 (0.80–1.90)	0.295		
Gastric	0.80 (0.40–1.30)	0.297			0.70 (0.40–1.30)	0.277		
Hepato-biliary-pancreatic	1.50 (0.90–2.40)	0.125			1.03 (0.60–1.80)	0.931		
Small bowel	1.50 (0.60–4.10)	0.414			1.40 (0.50–3.90)	0.475		
Oesophageal	0.40 (0.10–2.60)	0.314			0.50 (0.10–3.30)	0.446		
Other	1.03 (0.60–1.90)	0.910			0.90 (0.40–1.80)	0.694		
<b>Intraoperative characteristics</b>								
Anaesthesia time (min)	0.90 (0.90–1.01)	0.158			0.90 (0.80–1.10)	0.324		
IOH (per episode)	0.90 (0.80–1.10)	0.686			1.10 (0.90–1.20)	0.574		
Colloid use (per L)	1.01 (0.90–1.02)	0.151			0.90 (0.90–1.01)	0.241		
Erythrocyte transfusion (per unit)	0.90 (0.60–1.30)	0.426			1.70 (1.10–2.70)	0.011	1.30 (0.80–2.00)	0.275
Use of vasoactive drugs	1.04 (0.60–1.70)	0.894			1.10 (0.60–1.80)	0.891		
<b>Postoperative variables</b>								
Non-renal SAPS II (per point)	1.05 (1.04–1.07)	<0.0001	1.03 (1.02–1.10)	0.001	1.07 (1.05–1.10)	<0.0001	1.04 (1.01–1.06)	0.007
Fluid balance (L)	1.00 (1.00–1.00)	0.002	0.99 (0.99–1.00)	0.06	1.00 (1.00–1.00)	<0.0001	0.99 (0.98–1.01)	0.064
<b>Complications</b>								
Haemorrhage	1.90 (1.01–3.40)	0.044	1.40 (0.70–2.60)	0.344	1.60 (0.80–3.10)	0.169		
Anastomotic leak	1.70 (0.70–3.80)	0.222			1.20 (0.40–3.40)	0.679		
Surgical site infection	1.10 (0.60–1.90)	0.746			2.00 (1.30–3.30)	0.002	1.80 (1.10–2.90)	0.016
Need of MV	0.70 (0.10–5.30)	0.764			0.80 (0.10–5.50)	0.798		
Admission to ICU	1.10 (0.30–4.60)	0.858			2.10 (0.60–6.40)	0.228		
AKI	3.00 (1.90–4.50)	<0.0001	1.60 (1.01–2.50)	0.046	2.80 (1.80–4.20)	<0.0001	1.40 (1.10–2.00)	0.043

HR, hazard ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease; ASA, American Society of Anesthesiologists score; eGFR, estimated glomerular filtration rate; RCRI, Revised Cardiac Risk Index; IOH, intraoperative hypotension; SAPS II, Simplified Acute Physiology Score, version II; MV, mechanical ventilation; ICU, intensive care unit; AKI, acute kidney injury.

intra-abdominal pressure were not available for all patients and, as such, it was not analysed. Fourth, we did not evaluate patients' rehospitalizations after hospital discharge. In fact, patients with postoperative AKI had a significantly higher rate of cardiovascular disease, COPD and malignancies, and, as such, would be more likely to need rehospitalization. Therefore, those patients would be more prone to develop sepsis and dehydration or to receive nephrotoxics (antibiotics, diuretics, angiotensin-converting enzyme inhibitors, angiotensin II receptor antagonists and chemotherapy), which could exacerbate renal function deterioration and increase mortality. Fifth, we did not register if patients developed proteinuria or cardiovascular disease during follow-up, both factors that could influence long-term mortality. Finally, we were unable to determine differences in long-term outcomes according to AKI severity, possibly maybe largely due to the limited sample size.

## Conclusions

In this retrospective study, we showed that AKI after major non-vascular abdominal surgery is independently associated with the risk of long-term need of dialysis and/or renal function decline and with the risk of death after hospital discharge. Taking preventive measures to minimize the occurrence of postoperative AKI, or to reduce its severity, could potentially contribute to improved long-term outcomes.

## Conflict of interest statement

The authors declare no conflicts of interest.

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