Postoperative acute kidney injury in high-risk patients undergoing major abdominal surgery☆

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ABSTRACT

Purpose: Acute kidney injury (AKI) is a frequent complication in high-risk patients undergoing major surgery and is associated with longer hospital stay, increased risk for nosocomial infection and significantly higher costs.
Materials and methods: A prospective observational study exploring the incidence of AKI (AKIN classification at any stage) in high-risk patients within 48 hours after major abdominal surgery was conducted. Patients' preoperative characteristics, intraoperative management, and outcome were evaluated for associations with AKI using a logistic regression model.
Results: Data from 258 patients were analyzed. Thirty-one patients (12%) developed AKI, reaching the AKIN stage 1. No patient reached an AKIN stage higher than 1. AKI patients were older (75.2 vs 70.2 years; P = 0.0113) and had a higher body mass index (26.5 vs 25.1 kg/m^2). In addition, AKI patients had a significantly longer ICU length of stay (3.4 vs 2.4 days; $P=$ .0017). Creatinine levels of AKI patients increased significantly compared to the preoperative levels at 24 ($P=$ .0486), 48 ($P=$ .0011) and 72 hours ($P=$ .0055), while after 72 hours it showed a downwards trend. At ICU discharge, 28 out of 31 patients (90.3%) recovered preoperative levels.
Multivariate analysis identified age (OR 1.088; $P=$ .002) and BMI (OR 1.124; $P=$ .022) as risk factors for AKI development. Moreover, AKI development was an independent risk factor for ICU stays longer than 48 hours (OR 2.561; $P=$ .019).
Conclusions: Mild AKI is a not rare complication in high-risk patients undergoing major abdominal surgery. Although in almost the totality of cases, the indicators of renal function recovered to preoperative levels, postoperative AKI represents a primary risk factor for a prolonged ICU stay.

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1. Introduction

Acute kidney injury (AKI) is a frequent postoperative complication after major surgery [1,2]. A recent international cross-sectional study (AKI-EPI) [3], with the aim to analyze the epidemiology of AKI in patients admitted to intensive care unit (ICU), showed that 48.1% of AKI patients had surgery before ICU admission, confirming its high prevalence in post-surgical population. AKI is associated with longer hospital stays, increased risk for nosocomial infections, and significant burden on costs [4–6]. Its importance as a risk factor for a worse prognosis in non-cardiac, non-thoracic, and non-vascular patients has been emphasized [7,8]. Over the last 10 years, the diffusion and application of guidelines and recommendations on diagnosis and management of kidney dysfunction has alerted physicians regarding this previously overlooked issue, leading to a significant increase in diagnostic capability and epidemiologic research of patients with AKI [9–12]. Although great attention is focused on kidney function, to date, many aspects of postoperative AKI remain uncertain, and the relationship between perioperative care and renal dysfunction has not been fully addressed [7,13].

The aim of the present study was to evaluate the incidence and predisposing factors of AKI in high-risk patients undergoing major abdominal surgery.

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2. Methods

2.1. Setting and study population.

All high-risk patients (less than 6 metabolic equivalent (MET) [14], and/or a Revised Cardiac Risk Index for Pre-Operative Risk (RCRI) ≥3 [15] scheduled for major abdominal surgery (colectomy, hepatic resection, pancreatic surgery, esophageal resection, gastric surgery [16]), were electively admitted to the ICU [17–20] and included in the study group. The AKI group included all those patients who met the AKIN criteria during the 48 hours following surgery (any stage) [10]. In order to specifically address the potential impact of surgical and anaesthesiology approaches on renal function, and limit the possibility of mid/long term confounding factors (eg, sepsis, hemodynamic impairments, or other complications), according to AKI definitions [11] and based on recent literature observations [21], patients included were those who developed AKI within 48 hours after surgery. The following perioperative data were recorded: age, body mass index (BMI), comorbidities (arteriopathy, diabetes, arterial hypertension, ischemic heart disease, chronic obstructive pulmonary disease), surgical technique (open laparotomy, videolaparoscopic, robotic-assisted), surgical time, ICU length of stay (LoS), basal (pre-operative) and daily serum creatinine, urinary output, and fluid balance. The Institutional Ethics Committee approved the study. Informed consent was obtained from all the participants.

2.2. Intraoperative management

Intraoperative fluid therapy was set at 5 mL/kg per hour of crystalloid solutions (lactate's Ringer or Acetate Ringer) [22] in both open and minimally invasive techniques performed with pneumoperitoneum (no carbon dioxide re-uptake and warming was used). During surgery, the attending anesthetist was free to administer additional fluid boluses. Anesthesia was delivered according to personal preference of the attending anaesthesiologists (total intra-venous or balanced) and adapted to entropy-based neuromonitoring (Entropy, GE Healthcare, Milwaukee, WI). Arterial blood pressure was monitored with radial catheter (20 gauge). Fluid administration was based on pulse pressure variation (PPV [%] = (PPmax − PPmin) / [(PPmax + PPmin)/2] * 100; GE Healthcare; Milwaukee, USA), keeping it under 10% [23]. Mean blood pressure was maintained above 65 mmHg. Central body temperature was monitored with a nasopharyngeal probe and kept at 36.5-37 °C. Neuromuscular block was monitored with the Train of Four ratio (E-NMT Module, GE Healthcare, Milwaukee, U.S.A).

2.3. Statistical analysis

The SPSS 21 (SPSS Inc, Chicago, IL) was used for statistical analysis. Continuous variables were analyzed with the two-tailed Mann-Whitney *U* test. Categorical variables were studied using Fisher exact test. A 2-sided *P* < .05 was considered to be statistically significant. Continuous variables are expressed as mean (SD). In order to define the possible clinical factors associated with the development of AKI, a multivariable logistic regression model (backward selection) was adopted (covariates were retained in the model if the *P* value was <.1). The odds ratio (OR) and 95% confidence interval (CI) were computed. The ICU LoS was dichotomized at 48 hours in consideration that patients included were admitted in ICU for postoperative management and monitoring (thus foreseeing a LoS ≤48 h).

Expecting proportion of AKI patient in our population was 7.5% [1], we estimated to enroll at least 192 patients to guarantee a margin of error, equal or less than 5% (5%-15%) using a 95% confidence level.

3. Results

During a 9-month study period, a total of 899 patients underwent general surgery: among them, 258 met the inclusion criteria and were enrolled in the study (Fig. 1). Baseline and clinical characteristics of the patients are summarized in Table 1. Overall, 31 patients (12%) developed AKI, reaching AKIN stage 1 during the first 48 hours. Two patients developed AKI after the first 48 hours and, according to study protocol, were excluded: one patient reached AKIN 1 stage at postoperative day 5 and the second one reached AKIN 1 stage on day 7.

The mean age of AKI patients resulted significantly higher than the NO-AKI group (75.2 (8.9) vs 70.2 (11.2) years; *P*= .0113), as well as BMI (26.5(3.4) vs 25.1(4.4) Kg/m^2; *P*= .0067). Surgical approaches are summarized in Fig. 1, including a group with both videolaparoscopic and robotic-assisted techniques (both performed with pneumoperitoneum). AKI patients had significantly longer ICU LoS than NO-AKI group (3.4 (1.9) vs 2.4 (1.7) days; *P*= .0017) (Table 1).

Fig. 2 shows the serum creatinine level trends: whereas the preoperative mean creatinine levels were similar between the two groups, AKI patients showed significantly higher levels during the study period than NO-AKI patients (Mann-Whitney test, *P*< .001). Increase in creatinine was statistically significant at 24 hours (*P*= .0486), at 48 hours (*P*= .0011), and at 72 hours (*P*= .0055). After 72 hours the creatinine levels showed a downward trend, and, at the end of monitoring (day 5 after surgery), 28 out of 31 patients (90.3%) recovered preoperative levels of creatinine. In order to evaluate difference in creatinine trend from the third day onwards a generalized estimating equation linear regression model was used. The difference in slope between AKI and NO-AKI groups was not statistically significant (*P*= .2929). Three patients did not recover baseline creatinine after the first 5 postoperative days but were eventually discharged from the hospital with a creatinine level insignificantly different to the preoperative one. Among groups, neither fluid balance (Fig. 3) nor urinary output (Fig. 4) differed significantly during the study period.

Table 2 summarizes multiple logistic regression analyses, which included age, gender, BMI, surgical technique and duration, and comorbidities. Age (OR 1.088, 95% CI 1.032-1.146, *P*= .002) and BMI (OR 1.124, 95% CI 1.017-1.242, *P*= .022) were independent risk factors for early postoperative AKI development, whereas videolaparoscopic surgical technique resulted an independent protective factor for AKI (OR 0.264, 95% CI 0.093-0.746, *P*= .012).

Based on the observation that AKI patients showed a significantly longer ICU LoS, a multivariate analysis was also performed to verify if AKI could be an independent risk factor for a longer ICU stay. The model included age, gender, BMI, surgical technique, operation duration, comorbidities: AKI was associated with a significant increased risk to have an ICU stay longer than 48 hours (OR 2.561, 95% CI 1.169-5.068; *P*= .019).

4. Discussion

The main finding of this study was that a consistent incidence of early AKI (within 48 hours) after major abdominal surgery in high-risk patients (12%) occurs. Interestingly, in this cohort only 2 patients had delayed AKI (later than 48 hours post-operatively), showing that, in the context of uncomplicated high risk surgery, delayed AKI is a rare occurrence. Despite the fact that in this population early AKI severity never exceeded stage 1, and most of them (90.3%) recovered before ICU discharge, this study clearly shows that AKI is a strong predisposing factor for prolonged ICU stay (OR 2.561). This result is even more interesting considering that we designed the study excluding many potential confounding factors (eg, need of transfusion) to focus the attention on surgical population without factors known to increase AKI incidence.

A recent large retrospective study on about 160,000 patients undergoing major surgery (about 45,000 of them underwent general surgery) [24] showed an incidence of stage 1 AKI of 9.4%, similar to the