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Original article

Incidence and perioperative risk factors for early acute kidney injury after radical cystectomy and urinary diversion

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Abstract

Background: Early postoperative acute kidney injury (AKI) is associated with increased morbidity and mortality following major surgery. Only few reports exist on postoperative AKI and specifically its risk factors after radical cystectomy (RC) and urinary diversion (UD). We aimed to identify risk factors for AKI in patients undergoing RC and UD.

Methods: In an observational single-center cohort study, 912 consecutive bladder cancer patients undergoing RC and UD from 2000 to 2016 were evaluated for risk factors for AKI. Multiple logistic regression analysis was performed to model the association between variables and AKI.

Results: Early postoperative AKI occurred in 100/912 patients (11%). An increased risk was seen in patients with surgery lasting $>$ 400 minutes, male and obese patients ($>$ 25 kg/m²). Independent predictors were duration of surgery ($P = 0.020$), intraoperative blood loss ($P = 0.049$), preoperative serum creatinine values ($P = 0.004$), intraoperative administration of crystalloids ($P = 0.032$), body mass index ($P = 0.031$), and fluid balance ($P = 0.006$). Patients with AKI had a longer hospitalization time (18d vs 17d, $P = 0.040$). Limitations include the potential bias due to the design as a case series with prospectively collected data with some missing values.

Conclusions: An increased risk for AKI was seen in patients with an operative time $>$ 400 minutes. Hence, in this group of patients the role of postoperative fluid management for preserving renal function should be considered. Further independent predictors of postoperative AKI were male sex, obesity, intraoperative blood loss, and a low preoperative plasma creatinine. So specially in male and obese patients, optimized perioperative nephroprotective strategies are of importance.

Keywords: Acute kidney injury; Body mass index; Cystectomy; Duration of surgery

1. Introduction

Radical cystectomy (RC) with pelvic lymph node dissection (PLND) and urinary diversion (UD) is still the gold standard treatment for patients with invasive bladder cancer. This major surgery is associated with a high postoperative complication rate of up to 60%. In addition, patient comorbidities, preoperative postrenal obstruction due to tumor localization and potentially nephrotoxic preoperative medication (antibiotics and chemotherapy) can impair renal function preoperatively. Postoperative acute kidney injury (AKI) is associated with increased morbidity, mortality, and length of hospital stay (LOS) following many types of major cardiac and noncardiac surgeries [1–7]. AKI has many different causes ranging from prerenal factors to ischemic or toxic injuries and may involve multiple pathways including hemodynamic injury, systemic inflammation, and toxic injury. Type of surgery, pre-existing renal dysfunction and comorbidities are additional possible risk factors. However, little has been published on postoperative AKI after RC and UD [8]. More specifically, little is known about the effects of duration of surgery and body mass

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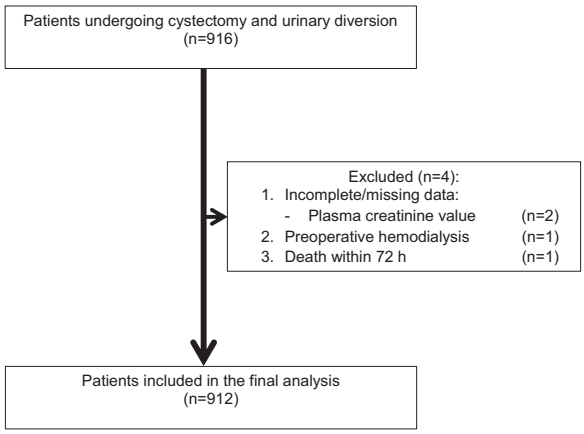

Fig. 1. Flow chart with inclusion and exclusion criteria used in the analysis.

index (BMI) on the risk of developing AKI and no information is available on preoperative risk factors for AKI.

In this study we attempted to identify risk factors for postoperative AKI in patients undergoing open RC, PLND, and UD for bladder cancer.

2. Patients and methods

In an observational single tertiary center study, we reviewed 916 consecutive patients who underwent open RC, PLND, and UD for bladder cancer at our institution between January 2000 and June 2016. Patients with insufficient follow-up, preoperative hemodialysis and death within 24 hours after surgery were excluded from the analysis, leaving 912 (data missing: 0.4%) patients for the study (Fig. 1). The study was conducted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement and approved by the Ethics Committee of Canton Bern, Switzerland (KEKBE 2016–00660).

Data on patients and procedures were extracted from a prospectively maintained cystectomy database and retrospectively gathered from the patients' paper charts. The data included patient age, sex, BMI, American Society of Anesthesiologists (ASA) physical status, history of hypertension, diabetes mellitus, preoperative anemia (defined according to the WHO criteria: hemoglobin <130 g/l for men and <120 g/l for women), chronic kidney disease, use of antihypertensives or betablockers, and neoadjuvant chemotherapy (usually 4 cycles cisplatin-based or in case of lower estimated glomerular filtration rate [eGFR] [<60 ml/min] carboplatin-based). Surgical factors recorded included type of UD, duration of surgery, intraoperative blood loss, and the total volume of fluid administered including blood transfusion; the intraoperative fluid balance was calculated according to the latter 2 factors.

A similar standardized surgical technique for open RC, PLND, and UD (ileal orthotopic bladder substitute, cutaneous catheterizable ileal reservoir, ileal conduit, or ureterocutaneostomy) has been applied for the last 15 years at our center and has been described previously. All patients undergoing this procedure were followed prospectively according to a standardized institutional follow-up protocol [9,10].

Fluids administered perioperatively were balanced physiological Ringer's solution (crystalloids) and 6% hydroxyethyl starch or 4% gelatin (colloids). Restrictive hydration using preemptive continuous administration of norepinephrine combined with fluid maintenance of around 1 to 3 ml/kg bodyweight (BW)/hour of crystalloids has been systematically applied from 2007 onwards. Intraoperative blood loss was primarily replaced with crystalloids, in some cases with colloids at the discretion of the anesthesiologist in charge; patients were transfused if hemoglobin values decreased to <80 g/l or to <100 g/l in patients with ischemic disease.

Postoperative hydration consisted primarily of 1,500 ml of crystalloids per day until resumption of normal food intake [11]. Postoperative hypotension was treated with additional boluses of Ringer's solution. Postoperatively, patients were allowed to drink clear fluids immediately. A liquid diet was started on postoperative day (POD) 1, as was active mobilization [12].

Plasma creatinine values were determined preoperatively and daily during the first 7 days postoperatively and on POD 12 according to our in-house protocol.

AKI was defined according to the Acute Kidney Injury Network (AKIN) classification based on changes in plasma creatinine levels. We defined a clinically relevant decrease in renal function (AKI) as a 50% (stage 1), 100% (stage 2), or >200% (stage 3) increase in plasma creatinine values compared to preoperative baseline within 72 hours postoperatively [13]. We favored the AKIN classification because of its superior sensitivity compared to the RIFLE criteria and because early postoperative (within 72 h) assessment is better at identifying the potential influence of perioperative factors (preoperative patient variables and surgical parameters) on the occurrence of AKI [14]. Following UD, ureteral stents were always left in place for >6 days, thus reducing the risk of bias in term of postrenal components. Data on urine output were not used for diagnosis of AKI because it was inconsistently charted. The eGFR was calculated based on the Chronic Kidney Disease Epidemiology Collaboration equation [15–17].

The primary endpoint was the incidence of AKI within 72 hours postoperatively. In addition, we sought to identify independent risk factors for AKI.

2.1. Statistical analysis

Baseline, intraoperative and postoperative variables between patients who developed AKI and patients who did not were compared for categorical data using the Fisher exact or the chi-square test, and continuous data using the Mann-Whitney-*U* test. Data were expressed in medians