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Original Article

Intra-abdominal hypertension does not predict renal recovery or in-hospital mortality in critically ill patients with acute kidney injury

Hyo Jeong Chang, Jihyun Yang, Sun Chul Kim, Myung-Gyu Kim, Sang-Kyung Jo, Won-Yong Cho*, Hyoung-Kyu Kim

Division of Nephrology, Department of Internal Medicine, Korea University Anam Hospital, Seoul, Korea

Abstract

Background: Although emerging evidence suggests that intra-abdominal hypertension (IAH) is a predictor of the development of acute kidney injury (AKI), it remains unclear whether the presence of IAH is a predictor of prognosis in patients with AKI. The purpose of this study was to assess whether the presence of IAH could predict prognosis in critically ill patients with AKI. The prognostic value of urinary biomarkers was also determined.

Methods: In this prospective observational study, we enrolled 57 patients with established AKI, who were admitted to the intensive care unit between February 2012 and June 2014. IAH was defined as a sustained elevation in intra-abdominal pressure of ≥ 12 mmHg, in three consecutive measurements performed daily on the first 3 days. Urinary neutrophil gelatinase-associated lipocalin (NGAL), liver-type fatty acid-binding protein, and simplified acute physiology score II score at the time of admission were also examined.

Results: IAH was observed in 78.9% of patients. The in-hospital mortality was 21.1%, and renal recovery during hospitalization was achieved in 40.4% of patients. Although high urinary NGAL [odds ratio (OR), 1.015] and liver-type fatty acid-binding protein (OR, 1.003) were found to be independent predictors of renal recovery, IAH was not. High urinary NGAL (OR, 1.003) and a high simplified acute physiology score II score (OR, 1.102) were independent predictors of in-hospital mortality, while IAH or urinary liver-type fatty acid-binding protein was not.

Conclusion: Although IAH is prevalent in critically ill patients with AKI, it did not predict AKI prognosis. However, urinary NGAL was found to be a useful predictor of both renal recovery and in-hospital mortality.

Introduction

Elevated intra-abdominal pressure (IAP) has long been known to be associated with altered renal function. Bradley and Bradley [1], more than 60 years ago, found that intra-abdominal hypertension (IAH) induced by abdominal

* Corresponding author. Department of Internal Medicine, Korea University Medical College, Korea University Anam Hospital, 73 Incho-ro, Seongbuk-gu, Seoul 136-705, Korea.
E-mail address: wonyong@korea.ac.kr (W-Y Cho).

compression resulted in reduced renal plasma and urine flow in humans, and suggested that an increase in renal venous pressure accounted for this change in renal function.

IAH, defined as a pathological increase in IAP, is commonly found in critically ill patients admitted to intensive care units (ICUs), and recently has been implicated as a possible cause of acute kidney injury (AKI). Although several epidemiological studies indicated that IAH is a useful predictor for AKI development [2–5], the predictive value of IAH for renal recovery or mortality remains unclear.

The purpose of this study was to determine the prevalence of IAH and to examine whether the presence of IAH during hospitalization could predict short-term renal recovery or in-hospital mortality in critically ill patients with established AKI. The prognostic value of urinary biomarkers, including neutrophil gelatinase-associated lipocalin (NGAL) and liver-type fatty acid-binding protein (L-FABP), in renal recovery or in-hospital mortality was also investigated.

Methods

Patients

This was a single-center, prospective observational study conducted between February 2012 and June 2014. This study included 57 consecutive patients who were at least 18 years old and admitted with a diagnosis of AKI to the medical ICU of the Korea University Medical Center, Seoul, Korea. Exclusion criteria were patients with end-stage renal failure who were receiving maintenance dialysis or had contraindications to the insertion of a urinary catheter for intravesical pressure measurement, such as patients with pelvic fracture or urethral injury. The study protocol was approved by the institutional review board of this center, and written informed consent was obtained.

Data collection

Data on age, sex, predisposing condition for increased IAP, length of ICU and hospital stay, and in-hospital mortality were collected. Patients were followed up until death or discharge from hospital. The calculation of the Simplified Acute Physiology Score II (SAPS II) [6] was based on the worst values recorded on the day of ICU admission. The primary endpoint was renal recovery from AKI on Day 7, and the secondary endpoint was in-hospital mortality.

Measurement of IAP

IAP was measured intravesically once a day for the first 3 days via a Foley catheter, according to the U-tube manometer technique [7,8], and the mean value was calculated. The sterile saline instillation volume was no more than 25 mL, according to the World Society of the Abdominal Compartment Syndrome consensus [9]. IAP was measured in the supine position at the end of expiration after ensuring that abdominal muscle contractions were absent. The symphysis pubis was considered the reference line, and the pressure was expressed in mmHg (1 mmHg = 1.36 cmH$_2$O) [7–9].

Measurement of urinary NGAL and L-FABP

Urine samples were collected on ICU admission and centrifuged at 2,500 rpm at 4°C for 5 minutes. The supernatants were frozen at -80°C until further biomarker analysis. Urinary NGAL and L-FABP were measured using the NGAL ELISA (BioPorto, Gentofte, Denmark), and human L-FABP Assay kits (CMIC Co. Ltd, Tokyo, Japan), respectively, according to the manufacturer's instructions.

Case definition

IAH was defined as a sustained pathological elevation in IAP of ≥ 12 mmHg, in three consecutive measurements performed daily on the first 3 days, according to the World Society of the Abdominal Compartment Syndrome consensus [9]. We defined the following risk factors of IAH [10–13]:

(1) Mechanical ventilation, defined as the use of invasive positive pressure ventilation through an endotracheal tube or a tracheostomy tube
(2) Liver dysfunction, defined as decompensated or compensated cirrhosis or other liver failure with ascites
(3) Positive fluid balance, defined as >1.5 L of total input–output in the initial 72 hours
(4) Ileus, defined as abdominal distension or failure of enteral feeding evidenced by gastric dilatation or gastroparesis with gastric residual $>1,000$ mL in 24 hours
(5) Acidosis, defined as an arterial pH of <7.2
(6) Hypothermia, defined as a core temperature of <33°C
(7) Polytransfusion, defined as the transfusion of >6 units of packed red cells in 24 hours
(8) Coagulopathy, defined as a platelet count of $<55,000/$mm^3 or an activated partial thromboplastin time more than two times normal or a prothrombin time of $>50\%$ or an international standardized ratio of >1.5
(9) Sepsis, defined according to the American–European consensus conference definitions
(10) Shock, defined as a cardiovascular Sequential Organ Failure Assessment (SOFA) subscore of >3, i.e., hypotension requiring dopamine >5 μg/kg/min, or norepinephrine and/or epinephrine <0.1 μg/kg/min.

According to the types of changes in IAP during admission, we categorized these IAP changes into downtrend or uptrend and fluctuation. Downtrend of IAP was defined as a continuous decrease in IAP during initial 3 days. AKI was diagnosed and staged on the day of admission according to the risk–injury–failure–loss–end-stage kidney disease (RIFLE) criteria. Renal recovery during hospitalization was defined as a serum creatinine level of <0.45 mg/dL or within 20% above the baseline value, and without a requirement for dialysis [14] on Day 7 postadmission.

Statistical analysis

All statistical analyses were performed using SPSS version 20.0 (IBM Corp, Armonk, NY, USA). Continuous variables, including IAP and SAPS II score, were expressed as mean $\pm$ standard deviation, calculated using the Student t test. Skewed data, including urinary NGAL and L-FABP levels, were expressed as median and interquartile ranges, and comparisons were assessed using the Mann–Whitney U test. Categorical variables were expressed as proportions, and the chi-square test was used for comparisons. Univariate and multivariate logistic regression analyses were