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Acute intestinal damage following severe burn correlates with the development of multiple organ dysfunction syndrome: A prospective cohort study

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ABSTRACT

Background: Severely burned patients occasionally suffer intestinal ischemia leading to a fatal outcome, and the gut is considered a "motor" driving the development of multiple organ failure. However, in clinical settings, it has been difficult to assess acute intestinal damage following burn and its consequence to patient outcome. Intestinal fatty acid binding protein (I-FABP) is a known biomarker for diagnosing intestinal ischemia/damage. This study aimed to assess the extent of intestinal damage using serial I-FABP measurements following severe burn and to clarify the association between intestinal damage and the development of organ dysfunctions.

Methods: Patients aged >15 years old who suffered burn over 20% total body surface area (TBSA) were enrolled in this prospective cohort study. Patients with cardiac arrest on admission or who were transferred >24 h after injury were excluded. Patients with chemical burn were also excluded. Burn size and Acute Physiology and Chronic Health Evaluation II (APACHE II) score were recorded at the time of patient enrollment. I-FABP was measured on admission and at 1, 4, 7, 14, and 30 days following injury. Other biomarkers such as lactate, lactate dehydrogenase (LDH), creatine kinase (CK), aspartate aminotransferase (AST), alanine aminotransferase, amylase, and creatinine (Cre) were also measured at the same time points as I-FABP. We also evaluated the serial change in Sequential Organ Failure Assessment (SOFA) score.

Results: The study included 32 patients. Serum I-FABP level on the day of admission was significantly increased in the patients compared with healthy controls. Increased I-FABP levels were normalized at 4 days after injury. The serum level of I-FABP on the day of admission correlated with %TBSA (III) and APACHE II score. A high I-FABP level on admission was associated with the subsequent development of multiple organ dysfunction. The increase in I-FABP level also correlated with increases of AST, LDH, and CK levels.

Abbreviations: ALT, alanine aminotransferase; AMY, amylase; APACHE, Acute Physiology and Chronic Health Evaluation; AST, aspartate aminotransferase; CK, creatine kinase; Cre, creatinine; Hct, hematocrit; I-FABP, intestinal fatty acid binding protein; LDH, lactate dehydrogenase; MODS, multiple organ dysfunction syndrome; SOFA, Sequential Organ Failure Assessment; TBSA, total body surface area.

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Conclusions: Serum level of I-FABP on admission day does not correlate with burn size, but with the deep burn area. The gut might be a crucial target organ following severe burn, and gut damage could have an important role in the development of multiple organ dysfunction.

1. Background

Intestinal fatty acid binding protein (I-FABP) is a specific biomarker for damage of differentiated enterocytes used to diagnose intestinal ischemia [1–5]. More recently, I-FABP has been shown to predict outcomes of critically ill patients or those with cardiac arrest [6–8]. In burn patients, the rate of intra-abdominal complications including abdominal compartment syndrome and bowel ischemia was reported to be 2.8%, the mortality rate of these patients was 78%, and the incidence of ischemic bowel complications undergoing operative intervention was 1.7% [9]. Other researchers conducted autopsies of patients who died tragically from burn and found that more than half of them had pathologic findings of intestinal ischemia [10]. These findings somehow explain that the gut can be a "motor" driving the development of multiple organ failure [11]. Although the importance of intestinal damage in burn patients is recognized, no clear evidence has been presented of an association between the extent of intestinal damage and burn severity. We hypothesized that intestinal damage would occur with burn and would worsen the patients' prognosis. Therefore, the aim of this study was to clarify the association between burn severity and serum I-FABP level and to highlight the practical importance of intestinal damage following burn.

2. Methods

This study was approved by the Institutional Review Board of the Japan Community Healthcare Organization Chukyo Hospital. The patients and their families were informed about the study because participation in this study did not in any way affect routine treatment, and no invasive procedures were done (blood samples for the study were taken from the remaining serum drawn during routine blood tests).

2.1. Study population

Patients aged >15 years old consequently admitted between November 2014 and July 2016 to the burn center of the Japan Community Healthcare Organization Chukyo Hospital were considered eligible. Exclusion criteria were patients who were in cardiopulmonary arrest on admission or who were transferred to the hospital more than 24 h after injury. Patients with chemical burns or intestinal disease were also excluded.

2.2. Data collection

After enrollment, the following items were recorded for each patient: age, gender, %TBSA (total body surface area) burned including 2nd degree burns (II) and 3rd degree or deeper burns (III), presence or absence of inhalation injury, and Acute Physiology and Chronic Health Evaluation II (APACHE II) score. I-FABP concentrations were measured at 6 time points from each patient: the day of admission (D0), 1 day after injury (D1), 3–5 days after injury (D4), and around one week (7–10 days: D7), two weeks (13–16 days: D14), and one month (28–33 days: D30) after injury. We also recorded routine biomarkers: lactate (as a marker of tissue ischemia); non-specific intestinal enzymes: lactate dehydrogenase (LDH) and creatine kinase (CK); and surrounding organ enzymes: aspartate aminotransferase (AST) and alanine aminotransferase (ALT) for liver, amylase (AMY) for pancreas, and creatinine (Cre) for kidney. To assess the influence of hemoconcentration, we also measured the patients' hematocrit (Hct). We computed Sequential Organ Failure Assessment (SOFA) scores and divided the patients into two groups according to the development of multiple organ dysfunction syndrome (MODS): the MODS (+) group, comprising patients with a SOFA score for at least two organs of ≥ 2, and the MODS (−) group, comprising patients with all other SOFA scores. All patients were treated according to the usual practices of the center without interference by the research team. Abdominal compartment syndrome was diagnosed on the basis of a combination of high peak airway pressures, oliguria despite adequate filling pressures, and intra-abdominal pressures of >30 cm H_2O [12].

2.3. I-FABP measurement

Serum samples for I-FABP were stored at −20 °C until analysis. Serum levels of I-FABP were measured using synthetic regional peptides and a recombinant I-FABP assay at Dainippon Sumitomo Pharma Biomedical Center in Osaka, Japan.

2.4. Statistical analysis

Differences in the daily changes of serum I-FABP levels were compared with normal controls using the Mann–Whitney test. Different time points of SOFA scores were compared with the SOFA scores of day 0 using Wilcoxon Signed Rank Sum tests. Because of the nature of I-FABP, the distribution of serum levels of I-FABP is not normal; thus, correlations between serum levels of I-FABP and other biomarkers were investigated using scatter plots and Spearman's rank-order correlation coefficient rho (ρ). A value of $p < 0.05$ was considered to indicate statistical significance. Statistical analyses were performed with Prism 6.07 for Windows (GraphPad Software, Inc., San Diego, CA).

3. Results

3.1. Patient characteristics

This study comprised 32 patients with major burns (>20%TBSA burned). %TBSA burned (II+III) and %TBSA burned (III) were