Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.JournalofSurgicalResearch.com

Intestinal fatty acid–binding protein levels in patients with chronic renal failure

Kyoko Okada, MD,[a,b] *Motohiro Sekino, MD, PhD,*[c,*] *Hiroyuki Funaoka, PhD,*[d] *Shuntaro Sato, MS,*[e] *Taiga Ichinomiya, MD, PhD,*[b] *Hiroaki Murata, MD, PhD,*[b] *Takuji Maekawa, MD, PhD,*[a] *Masaharu Nishikido, MD, PhD,*[f] *Kiyoyuki Eishi, MD, PhD,*[g] *and Tetsuya Hara, MD, PhD*[b]

[a] *Department of Anesthesiology, Nagasaki University Hospital, Nagasaki, Japan*
[b] *Department of Anesthesiology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan*
[c] *Division of Intensive Care, Nagasaki University Hospital, Nagasaki, Japan*
[d] *DS Pharma Biomedical Co, Ltd, Osaka, Japan*
[e] *Clinical Research Center, Nagasaki University Hospital, Nagasaki, Japan*
[f] *Department of Urology, National Hospital Organization Nagasaki Medical Center, Nagasaki, Japan*
[g] *Department of Cardiovascular Surgery, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan*

ARTICLE INFO

Article history:
Received 8 February 2018
Received in revised form
30 March 2018
Accepted 24 April 2018
Available online xxx

Keywords:
Biomarker
Critically ill patients
Enterocyte
Glomerular filtration rate
Intestinal ischemia
Renal insufficiency

ABSTRACT

Background: Intestinal fatty acid–binding protein (I-FABP), a biomarker of enterocyte injury, has been reported to be a diagnostic marker of intestinal ischemia and a prognostic marker in critically ill patients. However, the kinetics of I-FABP in renal failure patients is unknown. We sought to identify I-FABP levels in patients with chronic kidney disease (CKD) and end-stage kidney disease (ESKD) on hemodialysis (HD) and to identify the manner in which the I-FABP levels change.

Materials and methods: Adult patients who were admitted for elective cardiac surgery with either normal renal function (NRF), CKD, or ESKD on HD were enrolled. Serum I-FABP levels in NRF and CKD patients and in ESKD patients before and after HD were determined.

Results: A total of 124 patients were evaluated: 47 NRF, 53 CKD, and 24 ESKD. The I-FABP levels of the CKD patients and pre-HD ESKD patients were significantly higher than those of the NRF patients ($P = 0.018$ and $P < 0.001$, respectively). I-FABP levels were significantly negatively correlated with the estimated glomerular filtration rate in NRF and CKD patients (Spearman's $\rho = -0.313$, $P = 0.002$). In addition, I-FABP levels in ESKD patients were significantly lower after HD than those before HD ($P < 0.001$).

Conclusions: I-FABP levels in CKD and pre-HD ESKD patients were significantly higher than those in NRF patients. In addition, I-FABP was significantly eliminated by HD in patients with ESKD. Clinicians and researchers should consider this aspect of I-FABP when using it as a diagnostic and prognostic marker in patients with renal insufficiency.

* *Corresponding author*. Division of Intensive Care, Nagasaki University Hospital, 1-7-1 Sakamoto, Nagasaki 852-8501, Japan. Tel.: +81 95 819 7370; fax: +81 95 819 7373.
E-mail address: m-sekino@nagasaki-u.ac.jp (M. Sekino).

0022-4804/$ – see front matter © 2018 Elsevier Inc. All rights reserved.
https://doi.org/10.1016/j.jss.2018.04.057

Introduction

Intestinal fatty acid–binding protein (I-FABP) is a low–molecular weight (14-15 kDa) cytosolic, water-soluble protein specifically expressed by enterocytes from the duodenum to the ileum.[1] I-FABP is rapidly released into systemic circulation on enterocyte injury and is thus reported as a useful biomarker for diagnosing acute intestinal ischemia, including nonocclusive mesenteric ischemia (NOMI),[2,3] and necrotizing enterocolitis.[4] Recently, it was reported that an elevated I-FABP level was associated with states of shock and 28-day mortality in general ICU patients.[5] Relevant studies have been conducted to investigate I-FABP levels, related factors, and the clinical course of critically ill patients, including septic shock,[6,7] trauma,[8] cardiac arrest,[9] acute heart failure,[10] and cardiovascular surgery with cardiopulmonary bypass.[11]

I-FABP is thought to be rapidly cleared by the kidneys (half-time of approximately 11 min) similar to other members of the FABP multigene family.[12,13] I-FABP levels in patients with renal insufficiency are predicted to be elevated, although it can be removed by renal replacement therapy. However, these aspects of I-FABP are not fully elucidated. It is important to study I-FABP levels in renal failure patients, as most patients suffering from critical illnesses also suffer from renal problems,[14] and these problems likely alter I-FABP levels. Therefore, clinicians and researchers who use I-FABP as a diagnostic and prognostic marker should be aware of the typical concentration and kinetics of I-FABP in patients with renal problems.

The purpose of this pilot study was to elucidate the association between the I-FABP level and renal function in patients with chronic kidney disease (CKD) and end-stage kidney disease (ESKD) undergoing hemodialysis (HD) and to determine whether I-FABP is eliminated by HD in patients with ESKD.

Materials and methods

Study design and oversight

We conducted a single-center, prospective, preliminary, observational study in a dialysis unit and operation room at Nagasaki University Hospital from July 2014 to March 2017. The study was approved by the Institutional Review Board of Nagasaki University Hospital (No.14032491), and written informed consent was obtained from the patients.

Study population

Adult (≥18 y of age) patients with normal renal function (NRF), CKD, and ESKD undergoing conventional HD, who were admitted to our hospital for elective cardiac surgery, were randomly enrolled. Exclusion criteria were as follows: history of small intestine resection or recent abdominal complication, recent admission to the hospital for acute cardiac failure, cardiogenic pulmonary edema, and renal failure.

Data collection

Data on age, sex, body mass index, admitting diagnosis, comorbidities, and left ventricular ejection fraction were collected for all patients at baseline.

Blood samples for I-FABP in NRF and CKD patients were collected at the time of anesthetic induction for the elective cardiac surgery. The blood samples were taken through the arterial line. Estimated glomerular filtration rates (eGFRs) of patients with NRF and CKD were calculated using serum creatinine (Cr) measured at admission. eGFR was used as a measure of renal function and was calculated using the following equation for Japanese patients: eGFR (mL/min/1.73 m^2) = $194 \times Cr^{-1.094} \times age^{-0.287}$ (if female × 0.739).[15]

Blood samples for I-FABP and Cr for ESKD patients on HD were collected just before (pre) and just after (post) conventional HD, and before the elective cardiac surgery. The blood samples were taken through the arterial line of their vascular access. The HD protocols were as follows: 150-320 mL/min blood flow, 500 mL/min dialyzate, and 4 h of treatment. Blood flow, amount of water removal, and the dialyzers were decided by the attending physician in the dialysis unit. Dialysis time, the amount of water removal, and dialysis vintage of the patients were collected.

Serum Cr was measured by enzymatic methods using a commercial kit (Mizuho Medy CO, Ltd Saga, Japan) at Nagasaki University Hospital.

Serum I-FABP measurement

Samples for I-FABP analysis were separated by a centrifugal separator and the serum was frozen at −20°C until assayed. All measurements were performed in a blinded fashion at a laboratory (DS Pharma Biomedical Co, Ltd Osaka, Japan) according to manufacturer's instructions, using an enzyme-linked immunosorbent assay highly specific for human I-FABP (DS Pharma Biomedical Co, Ltd Osaka, Japan).[16]

Statistical analysis

Baseline characteristics were compared among NRF patients, CKD patients, and ESKD patients on HD. For this pilot study, NRF was defined as eGFR ≥60 mL/min/1.73 m^2; CKD was defined as eGFR <60 mL/min/1.73 m^2;[17] and ESKD patients on HD were those who needed maintenance HD for ESKD. We could not subdivide the patient groups because of the small number of participants. Categorical variables are presented as frequencies and percentages, and quantitative variables as medians and interquartile ranges (IQRs). Differences between groups were assessed using the Kruskal–Wallis test and Fisher's exact test.

I-FABP levels of CKD patients and pre- and post-HD ESKD patients were compared with the levels for NRF patients using Wilcoxon's rank-sum test. The correlation of I-FABP levels and eGFRs in patients with NRF and CKD was evaluated using Spearman's rank correlation coefficient, ρ. The association of I-FABP levels and Cr levels before and after HD in ESKD patients was calculated by repeated measures ANOVA.