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Diagnostic value of intestinal fatty acid-binding protein for pneumatosis intestinalis

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Abstract

BACKGROUND: Pneumatosis intestinalis (PI) is known as a sign of a life-threatening bowel ischemia. We aimed to evaluate the utility of intestinal fatty acid-binding protein (I-FABP) in the diagnosis of pathologic PI.

METHODS: All consecutive patients who presented to our emergency department with PI were prospectively enrolled. The diagnostic performance of I-FABP for pathologic PI was compared with that of other traditional biomarkers and various parameters.

RESULTS: Seventy patients with PI were enrolled. Pathologic PI was diagnosed in 27 patients (39%). The levels of most biomarkers were significantly higher in patients with pathologic PI than those with nonpathologic PI ($P < .05$). Receiver operator characteristic analysis revealed that the area under the curve (AUC) was highest for I-FABP (area under the curve = .82) in the diagnosis of pathologic PI.

CONCLUSIONS: High I-FABP value, in combination with other parameters, might be clinically useful for pathologic PI.

Pneumatosis intestinalis (PI) is a physical or radiographic finding suggesting that gas exists in the bowel wall; PI is considered a sign of a life-threatening bowel ischemia.[1,2] With the popularization of computed tomography (CT) scans, nonischemic causes of PI have also been reported. The pathogenesis of PI is poorly understood—it is not a disease and is considered to result from several factors, such as injuries to the intestinal mucosa, elevations of intraintestinal pressure, disseminated gas from pulmonary disease, and bacterial causes.[3,4] Pathologic PI, which is associated with bowel necrosis, is a severe gastrointestinal disorder with high mortality and morbidity.[5,6] Delayed diagnosis and treatment can result in multiple organ failure and poor outcome. Almost half of patients with PI, however, can be treated nonoperatively.[7–11] Exploratory laparotomy may also cause serious complications.

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The authors declare no conflicts of interest.

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Therefore, surgery is very important but difficult to justify because of the often vague and nonspecific clinical findings. CT scan findings are considered useful as an objective tool,[6,10,12,13] but they require significant expertise. In this context, a simple and effective diagnostic method is needed.

Some circulating biomarkers of pathologic PI have been evaluated in a clinical setting, and the usefulness of lactate has been reported.[5,7–9,11] Other investigators have noted that blood urea nitrogen (BUN), amylase (AMY), and lactate dehydrogenase (LDH) may be useful in the diagnosis and outcome.[2,14] Since the early 1990s, intestinal fatty acid-binding protein (I-FABP) has attracted considerable attention as a new biomarker for use in the diagnosis of acute intestinal disease. However, since the results have been inconsistent, I-FABP has not yet been applied in a clinical setting. I-FABP is a small (14 to 15 kDa), cytosolic, water-soluble protein that constitutes up to 2% of the cytoplasmic protein content of a mature enterocyte and is abundant in the mucosa of the stomach, small intestine, and bowel. If the intestinal mucosal tissue is injured, I-FABP is rapidly released into the bloodstream. Some authors have reported that the serum I-FABP level is elevated in patients with intestinal ischemia.[15–19] However, no studies have reported the diagnostic value of I-FABP for pathologic PI that is associated with intestinal ischemia. We hypothesize that I-FABP responds differently to pathologic PI or nonpathologic PI. In this study, therefore, we examined the value of several biomarkers, including I-FABP, and various parameters sampled at the time of admission to hospital in the early diagnosis of pathologic PI.

Methods

The study was approved by the local ethics committee of Saiseikai Yokohamashi Tobu Hospital. This prospective, noninterventional study was conducted in the Emergency and Trauma Center of Saiseikai Yokohamashi Tobu Hospital, a tertiary-care hospital in Yokohama, Japan, from January 2009 to December 2014. All consecutive patients aged 18 years or older who presented to our emergency department with PI identified by an attending acute care surgeon or an experienced faculty emergency radiologist via CT scans were prospectively enrolled. Later, the presence of PI, which was identified by an attending acute care surgeon, was confirmed by a radiologist. Exclusion criteria were age less than 18 years, trauma, findings of PI that were refuted by the radiologist, and preexisting intestinal damage due to intestinal surgery within the previous 7 days.

Study design and sample collection

After enrollment, the following data points were recorded for each patient: age, sex, medical history, clinical findings (vital signs, physical peritoneal signs), radiologic findings, and routine laboratory test results. After the initial assessment, blood samples were taken to investigate both I-FABP and traditional biomarkers. The diagnostic performance of I-FABP for pathologic PI was compared with that of other traditional biomarkers and various parameters.

All patients were treated according to the usual practice of the center, without interference by the research team. The attending Japanese board-certified surgeon determined the operative indication in a comprehensive manner, taking the CT findings, physical examination results, and laboratory results into consideration. Diagnostic laparoscopy was considered a viable operative exploration to define pathologic PI. According to the clinical, surgical, and pathologic results, the diagnosis of each patient was retrospectively classified as either pathologic PI or nonpathologic PI. Pathologic PI was defined as bowel ischemia in need of emergency intervention, regardless of the underlying pathophysiological processes.

CT imaging and evaluation

All CT scans were performed with 64 multidetector CT scanners (Aquilion CT scanner; Toshiba, Tokyo, Japan). Intravenous contrast media (iohexol, Omnipaque 300; Daiichi Sankyo, Tokyo, Japan) was used in all patients unless contraindicated. Acute kidney injury (AKI) after administering intravenous contrast media was considered to have developed if there was a .5 mg/dL absolute increase in serum creatinine within 72 hours of admission. CT images were reviewed retrospectively in consensus by an attending radiologist and an experienced faculty emergency radiologist. The following CT features were assessed: segment of bowel involved, presence of portal venous gas (PVG), ascites, thickening (>.3 cm), stranding, free air, and bowel dilation (>3.0-cm small bowel, >6.0-cm large bowel).

Laboratory analysis

An I-FABP assay is currently in clinical development and has not yet been applied in a clinical setting. For the I-FABP assay, samples were stored at −20°C until analysis. I-FABP was measured at the DS Pharma Biomedical Center in Osaka, Japan. Serum levels of I-FABP were quantified using synthetic regional peptides and a recombinant I-FABP assay (Dainippon Sumitomo Pharma; Osaka, Japan). The serum I-FABP level in the healthy volunteers was 1.1 ± .9 ng/mL, ranging from .1 to 2.0 ng/mL.[20] Other traditional biomarkers were as follows: (1) inflammation markers (white blood cell count [WBC] and C-reactive protein [CRP]); (2) tissue ischemic markers (base deficits [BD] and lactate); (3) nonspecific bowel enzymes (AMY, LDH, aspartateaminotranferase [AST], and creatine kinase [CK]); (4) coagulation activity marker (D-dimer); and (5) renal function markers (BUN and creatinin [Cr]). All other biomarkers were measured immediately in serum using commercially available assays at Saiseikai Yokohamashi