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The importance of presepsin value in detection of gastrointestinal anastomotic leak: a pilot study

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ABSTRACT

Background: Early diagnosis of anastomotic leakage is the most important factor in reducing its morbidity and mortality. Anastomotic integrity monitoring of the leukocyte count (WBC), C-reactive protein (CRP), and neutrophil-lymphocyte ratio (NLR) are commonly used laboratory parameters. The availability of follow-up presepsin anastomotic integrity was investigated in this study.

Materials and methods: This study included patients who had gastrointestinal anastomosis due to major abdominal surgery between January 2016 and February 2017. Blood samples were collected to determine the WBC, CRP, NLR, and presepsin values before the anastomosis was performed and then taken on postoperative days 1, 3, and 5.

Results: This is a prospective nonrandomized study with 100 consecutive patients enrolled in the anastomosis group (male/female, 42:58). WBC, CRP, NLR, and presepsin values are based on certain days in the complication group, and the complication group increased with statistical significance. Presepsin had a specificity of 98.63% in determining anastomotic leak.

Conclusions: Presepsin can be used as a supplemental marker with CRP and NLR for anastomotic integrity.

Introduction

Studies have shown that the rate of negative patient conditions or inadequate surgical technique that induced gastrointestinal anastomotic leak was 1%-40% and the mortality rate due to these effects was 4%-15%.[1-3]

Despite developing surgical and staple techniques, anastomotic leaks continue to be a serious problem for surgeons.[4,5] Factors that risk the integrity of the anastomosis include male sex, old age, advanced-stage cancer, neoadjuvant treatment, malnutrition, anastomosis made under emergency conditions, proximity to the anal canal anastomosis, anastomoses in tension, obstructions at the distal part of anastomosis, and local sepsis conditions.[6-8]

Late diagnosis, local recurrence, sepsis, and long-term hospital stay are associated with increased costs and high mortality rate.[9,10]

Yaegashi *et al.*[11] in 2005 used soluble cluster of differentiation 14 (CD14) subtype to pinpoint the presepsin. CD14 is localized as a multifunctional glycoprotein mainly on the

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membrane surface of monocytes/macrophages. CD14 can be found on the cell surface of neutrophils as membrane by a glycosylphosphatidylinositol tail, and this works as a specific receptor complex for lipopolysaccharides (LPSs) or LPS-binding proteins (LBPs). The LPS-LBP-CD14 complex has an effect on circulation by shedding CD14 on the cell membrane, efficient soluble CD14 (sCD14), which is released from hepatocytes.[12,13]

During inflammation, plasma protease activity generates (sCD14) fragments. The 64-amino-acid N-terminal fragments create the sCD14 subtype, which has a new name, presepsin.[14]

In recent years, several authors discussed the role of presepsin as a biomarker. Based on these studies, it was determined that presepsin has a more important role as a biomarker than more well-known biomarkers such as C-reactive protein (CRP) and procalcitonin because it is more sensitive and has a specific role during inflammation.[15-19]

Early diagnosis is the most important factor for decreasing mortality and morbidity of anastomotic leakage.[20,21] Although the most used parameters were CRP and WBC values at follow-up, there is no single parameter. The aim of this study was to determine the role of presepsin against CRP, WBC, or neutrophil lymphocyte ratio (NLR) in anastomotic integrity.

Materials and methods

Patients

One hundred patients who underwent elective anastomosis because of benign or malignant underlying gastrointestinal etiologies between January 2016 and February 2017 were included in the study. Ethical approval was received from our hospital in December 2015.

The ratio of men to women in the group who underwent anastomosis was 42:58. The average age was 49 y (range, 18-85 y).

No patients had preoperative bowel preparation, and operation was performed appropriate to mesocolic-mesorectal resection rules in all patients. The mean number of lymph nodes was 21 (19 $\pm$ 32) and 16 (11 $\pm$ 24) in patients who were operated on for colon and rectum tumors, respectively. The blood flow of the anastomotic bowel segments was assessed macroscopically, and no indicator was used.

Left hemicolectomy for left colon and rectosigmoid colon carcinoma in 60 patients (60%), low anterior resection (LAR) + deflector ileostomy due to rectal cancer in 19 patients (19%), right hemicolectomy due to right colon cancer in 14 patients (14%), and ileostomy closure operation in seven patients (7%) were performed. Long-term neoadjuvant chemoradiotherapy was administered to 12 of 19 patients who were operated on because of rectum tumor. According to TNM classification, 16 patients were stage II, 59 patients were stage III, and 18 patients were stage IV.

In 27 patients (27%), anastomotic leak developed. Anastomosis developed in 13 patients who had LAR, nine patients who had left hemicolectomy, three patients who had right hemicolectomy, and two patients who had ileostomy.

The use of carbohydrate-rich drink was started 12 h postoperative; when hourly urine output was sufficient, Foley catheter is withdrawn and early mobilization was achieved. No perioperative patients were drained. The standard diverting ileostomy was performed in patients with LAR. Percutaneous drainage was performed in 13 patients, nine patients were treated with the EndoVac system, and permanent stoma was opened in four patients with leak according to LAR. In 14 patients with leak who were operated on for colon tumors, nine of them were treated with percutaneous drainage and stoma was created in five of them. Patients with normal vital values, clinical findings, laboratory parameters, adequate oral intake, and patients who were able to meet their daily needs were discharged. There was no readmission due to morbidity-mortality within 30 d postoperatively.

In the anastomotic leak group after radiologic and surgical treatment, eight patients were categorized as grade IIIa, four patients as grade IIIb, six patients as grade IVa, two patients as grade IVb, and seven patients as grade V according to Clavien-Dindo classification. At 3-mo follow-up of an anastomotic esophagus group, there were no findings in favor of anastomosis, intra-abdominal collection, or intra-abdominal abscess.

Methods

Written informed consent was obtained from all patients. According to results of blood samples obtained 12 h before surgery and postoperative days 1, 3, and 5, preoperative examinations, patients who had not undergone any preoperative medical treatment, no local or systemic infection, and who have an American Society of Anesthesiologists score between I-III were evaluated. In the anastomotic leak group, only patients who underwent reoperation or underwent percutaneous drainage were evaluated. Preoperatively, enoxaparin (0.4 mL, subcutaneous 1 $\times$ 1) and ceftriaxone (1 g, 1 $\times$ 1, intravenous [i.v.]) were administered. Postoperatively, i.v. hydration, ranitidine hydrochloride (1 $\times$ 1, i.v.), tenoxicam (3 $\times$ 1, i.v.), and enoxaparin (0.4 mL, subcutaneous, 1 $\times$ 1) were administered to the patients. The patients who underwent surgery because of anastomotic leaks were administered ceftriaxone (1 g, 2 $\times$ 1, i.v.) and metronidazole (2 $\times$ 1, i.v.), postoperatively. Anastomotic leaks were detected based on evaluations of the patients' clinical findings, laboratory values, rectosigmoidoscopy, and oral/i.v. rectal contrast-enhanced computerized tomography. Oral-IV-rectal contrast-enhanced computerized tomography scan was performed in patients who have increased inflammatory parameters (Leukocyte and CRP), tachycardia, increased respiratory rate, postoperative ileus (>4 d), fever, and abdominal pain distension. Relaparotomy was performed in patients with extravasation, abdominal sepsis, necrosis, free intra-abdominal air. Patients with no collection around the anastomosis, minimal free air, sign of peritonitis, and abdominal sepsis were treated with antibiotic therapy accompanied with percutaneous drainage or EndoVac system treatment.[22]

Although normal value range in a healthy population is described as 60.1-365 pg/mL, a normal value at the international level has not been determined.[23] The normal CRP (0.01-0.5 mg/dL) and WBC (4-11 m) values were based on the reference values used in our hospital laboratories.

Blood samples were obtained by venipuncture into ethylenediaminetetraacetic acid blood collection tubes without additives and immediately centrifuged at 2500 rpm for 10 min. The plasma was collected after centrifugation and stored at