Intraoperative acidosis is a new predictor for postoperative pancreatic fistula after pancreaticoduodenectomy

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BACKGROUND: Early diagnosis of postoperative pancreatic fistula (POPF) is important for proper interventions. The preoperative, intraoperative and early postoperative biochemical markers have predictive value of POPF. The present study was to evaluate several simple biochemical parameters in the prediction of POPF.

METHODS: Patients who underwent pancreaticoduodenectomy in our center between 2006 and 2015 were reviewed retrospectively. Preoperative and early postoperative biochemical parameters were evaluated. Additionally, the relationship between POPF and pH and lactate level at the end of surgery were analyzed, and neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and red cell distribution width-to-platelet ratio (RPR) were calculated for postoperative days (PODs) 1 and 3. Diagnosis and grading of POPF were performed according to the standards of the International Study Group on Pancreatic Fistula. The patients were divided into two groups: Group 1 with no fistula or grade-A fistula; group 2 with grade-B or -C fistula. These simple biochemical markers were then compared between the two groups.

RESULTS: Serum amylase level was significantly higher at POD3, and pH level was significantly lower at the end of operation in group 2 compared with those in group 1. However, the serum amylase was below the upper limit of normal serum level and therefore, the difference was not significant in clinical practice. Receiver operating charecteristic curve analysis showed that pH level was a reliable predictor of POPF (area under the curve: 0.713; 95% CI: 0.573-0.853).

CONCLUSIONS: A low pH level at the end of pancreaticoduodenectomy was a risk factor of POPF. NLR, PLR, and RPR had no predictive value of POPF after pancreaticoduodenectomy.

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KEY WORDS: acidosis; fistula; intraoperative; predictor; pancreaticoduodenectomy

Introduction

Pancreaticoduodenectomy (PD) is a major abdominal operation with relatively high in-hospital mortality (up to 3%).[1, 2] Postoperative pancreatic fistula (POPF) and accompanying abdominal sepsis are potential causes of mortality after pancreatic surgery.[1-3] Prediction or early diagnosis of POPF is crucial to obviate mortality in the management of this complication. Postoperative drain fluid analysis,[4-7] serum biochemical markers,[8, 9] area of pancreatic cut surface, diameter of pancreatic canal, and texture of pancreatic remnant[10, 11] are all related to POPF.

PD has a relatively long operation time, blood loss and potential risk of hypothermia, which are the causes of intraoperative acidosis as found in patients with major trauma.[1, 2, 12] Low serum pH level is related to an increase in morbidity and mortality in trauma or major operations.[12, 13]

Classically, neutrophilia and lymphocytopenia are expected cellular responses in systemic inflammation.[14] Based on these data, the neutrophil-to-lymphocyte ratio (NLR) has long been used as an easy marker for inflammatory response in malignancies, chronic inflammatory diseases, and postoperative complications.[14-16] Recently,

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platelet-to-lymphocyte ratio (PLR) and red cell distribution width-to-platelet ratio (RPR) have also been considered as simple inflammatory biomarkers in malignancies and inflammatory diseases for prediction of disease activity and even survival.[17-19]

In this study, we aimed to evaluate intraoperative and early postoperative serum biochemical markers to predict the risk of POPF. In addition to routine biochemical parameters, intraoperative acidosis, NLR, PLR, and RPR were also evaluated.

Methods

The medical records of all patients who underwent standard or pylorus-preserving PD with or without total pancreatectomy at the authors' institution between June 2006 and January 2015 were retrospectively reviewed using a computer-based data management system. Data reviewed included demographics, body mass index (BMI), hospital stay, intraoperative transfusions, intraoperative blood loss, operation time, the American Society of Anesthesiologists (ASA) scores, comorbities, use of prophylactic octreotid, preoperative endoscopic retrograde cholangio-pancreatography (ERCP), preoperative placement of biliary stent, preoperative endoscopic biopsies, postoperative laboratory findings, complications, and findings in physical examination. Chronic obstructive lung disease, ischemic heart disease, diabetes mellitus, hypertension, and previous major surgery were considered as comorbidities.

Laboratory parameters evaluated the first three days after surgery included aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), total bilirubin, amylase, albumin, calcium, hemoglobin, white blood cell (WBC), platelet, international normalized ratio (INR), and red cell distribution width (RDW). All of these parameters were measured at postoperative days 1 and 3. Corrected calcium (coCa) level was calculated according to the following formula:

coCa=0.8×[normal albumin (4 mg/dL)−patient's albumin]+serum Ca

To indicate intraoperative acidosis, pH and lactate levels at the end of surgery were measured. Additionally, NLR, PLR, and RPR were calculated. In our case series, surgeons generally prefered to examine the C-reactive protein (CRP) level after postoperative day 3. CRP levels on postoperative day 1 or 3 were measured in only 10% of the cases. Therefore, CRP was excluded from further analysis.

The amylase content of drain fluids was firstly measured at postoperative day 1 and then at postoperative days 3, 5 and 7. The drainage of any measurable volume of amylase-rich fluid (3×normal serum amylase level, which was 120 U/L for our laboratory) from abdominal drains on or after postoperative day 3 was considered as an indication of POPF and was graded according to the International Study Group on Pancreatic Fistula (ISGPF).[3] Biochemically detected leak without peripancreatic fluid collection and clinical findings of systemic inflammation was considered as a grade-A fistula. The patients with grade-A fistula do not have clinical significance. A leak with clinical findings and changes in management was considered as a grade-B fistula. A leak that required percutaneous drainage of fluid collection, reoperation, and intensive care management was considered as a grade-C fistula. The patients with grade-B or -C fistula were faced with a clinically relevant complication. According to this definition, two groups were designated: Group 1: patients with no fistula or grade-A fistula; and group 2: patients with clinically relevant POPF (grade-B or -C fistula). All of the parameters mentioned above were compared between these two groups. The measured serum levels of AST, ALT, ALP, GGT and bilirubin in the last three days preoperatively were considered as the preoperative values regardless of whether preoperative biliary drainage was applied or not. These preoperative values were also compared between the two groups because of close relationship with pathologies of the biliary system. To identify the appropriate cut-off values of significant parameters, analysis of receiver operating charecteristic (ROC) curves was performed.

To eliminate the effect of postoperative inflammatory processes other than POPF on the inflammatory markers, including WBC count, NLR, PLR, and RPR, the patients with an inflammatory complications other than POPF, including wound infection, pneumonia or atelectasis, were excluded. Additionally, the patients who underwent total pancreatectomy along with PD were also excluded due to the lack of pancreaticojejunostomy (PJ).

Surgical procedure

Pylorus-preserving PD was carried out as a routine operation and standard PD was performed in patients with the anatomic distortion of the pylorus or those with the tumor infiltration of the distal part of the stomach. End-to-side PJ or end-to-end dunking PJ was carried out by using 4/0 interrupted sutures with polypropylene or polyglactine according to the surgeons' preferences. End-to-side hepaticojejunostomy (HJ) was performed 7 to 10 cm distally to PJ with 4/0 propylene or polydioxanone interrupted sutures. Finally, end-to-side double-layer duodenojejunostomy was performed 40 cm distally to HJ. In standard PD, gastrojejunostomy was performed 50 cm distally to HJ, and a Braun anastomosis was added. Two