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Pancreatic perfusion data and post-pancreaticoduodenectomy outcomes

Motokazu Sugimoto, MD, PhD,[a,b] *Shinichiro Takahashi, MD, PhD,*[a,*] *Tatsushi Kobayashi, MD,*[c] *Motohiro Kojima, MD, PhD,*[b] *Naoto Gotohda, MD, PhD,*[a] *Mitsuo Satake, MD,*[c] *Atsushi Ochiai, MD, PhD,*[b] *and Masaru Konishi, MD*[a]

[a] *Department of Hepatobiliary-Pancreatic Surgery, National Cancer Center Hospital East, Kashiwa, Chiba, Japan*
[b] *Division of Pathology, Research Center for Innovative Oncology, National Cancer Center Hospital East, Kashiwa, Chiba, Japan*
[c] *Department of Radiology, National Cancer Center Hospital East, Kashiwa, Chiba, Japan*

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ABSTRACT

Background: Precise risk assessment for postoperative pancreatic fistula (POPF) after pancreaticoduodenectomy (PD) may be facilitated using imaging modalities. Computed tomography perfusion (CTP) of the pancreas may represent histologic findings. This study aimed to evaluate the utility of CTP data for the risk of POPF after PD, in relation to histologic findings.

Methods: Twenty patients who underwent preoperative pancreatic CTP measurement using 320-detector row CT before PD were investigated. Clinicopathologic findings, including CTP data, were analyzed to assess the occurrence of POPF. In addition, the correlation between CTP data and histologic findings was evaluated.

Results: POPF occurred in 11 cases (grade A, 6; grade B, 5; and grade C, 0). In CTP data, both high arterial flow (AF) and short mean transit time (MTT) were related to POPF occurrence ($P = 0.001$, $P = 0.001$). AF was negatively correlated with fibrosis in the pancreatic parenchyma ($r = -0.680$), whereas MTT was positively correlated with fibrosis ($r = 0.725$). AF >80 mL/min/100 mL and MTT <16 s showed high sensitivity, specificity, positive predictive value, and negative predictive value (80.0%, 100.0%, 100.0%, and 83.3%, respectively) for the occurrence of POPF.

Conclusions: CTP data for the pancreas were found to be correlated with the occurrence of POPF after PD. Alterations in the blood flow to the remnant pancreas may reflect histological changes, including fibrosis in the pancreatic stump, and influence the outcome after PD. CTP may thus facilitate objective and quantitative risk assessment of POPF after PD.

1. Introduction

Soft pancreatic consistency has traditionally been regarded as a definite risk factor for postoperative pancreatic fistula (POPF) after pancreaticoduodenectomy (PD); however, the consistency is assessed intraoperatively in a subjective and qualitative manner [1–3]. On the other hand, objective and quantitative assessment of POPF risk using preoperative imaging modalities, such as computed tomography (CT) or magnetic resonance imaging (MRI), have been increasingly reported [4–8].

* *Corresponding author*. Department of Hepatobiliary-Pancreatic Surgery, National Cancer Center Hospital East, 6-5-1 Kashiwa-no-ha, Kashiwa, Chiba 277 8577, Japan. Tel.: +81 4 7133 1111; fax: +81 4 7131 4724.
E-mail address: shtakaha@east.ncc.go.jp (S. Takahashi).
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Computed tomography perfusion (CTP) is a functional imaging technique that is used to assess hemodynamic changes in an organ, and its utility in the diagnosis of cerebrovascular and coronary artery disease has been widely reported [9,10]. In 1995, Miles *et al.* [11] demonstrated the feasibility of absolute quantification to assess blood perfusion in the pancreas for the first time. Subsequently, circulatory alterations were reported in patients with acute or chronic pancreatitis [12–14]. A new generation of CT systems with 320-detector rows offers significant advantages over conventional multidetector CT. Using 320-detector row CT, volumetric acquisition over a range of 16 cm can be achieved with single-rotation scanning, with acceptable image quality and relatively low radiation exposure [15–18]. Therefore, this technique makes it possible to obtain perfusion data of the entire pancreas by performing only one dynamic volume scan with the administration of a single contrast material bolus.

A few studies have reported the clinical utility of CTP of the pancreas using 320-detector row CT. Kandel *et al.* [15] have stated that the perfusion of pancreatic carcinomas is significantly lower than that of normal pancreatic tissue. In hepatic CTP imaging, parameters obtained using CTP have been reported to be correlated with fibrotic changes in liver biopsy specimens [19,20]. Therefore, CTP data may reflect the histologic findings for the specific organ. However, to our knowledge, no such comparison of CTP data with histologic findings has been reported for the pancreas. The aims of the present study were to evaluate the correlations between preoperative CTP data and the incidence of POPF after PD as well as with histologic findings.

2. Material and methods

2.1. Patients and clinical data collection

Between March 2012 and February 2013, 20 patients who were scheduled to undergo PD were prospectively recruited for preoperative CTP examination at the National Cancer Center Hospital East, Japan. All patients were examined by preoperative contrast-enhanced multidetector row CT focusing on the lesion, as part of the diagnostic workup; subsequently, PD was indicated for suspected malignancy. CTP was then performed in patients from whom written consent was obtained. Clinicopathologic data were reviewed from medical records. This study was approved by the Institutional Review Board of the National Cancer Center.

2.2. Surgical techniques and preoperative management

Details of the surgical maneuvers and preoperative management have been mentioned in our previous article [21]. Subtotal stomach-preserving PD [22] and modified Child reconstruction were performed in all cases. End-to-side pancreaticojejunostomy with the placement of a 6Fr internal short stent through the main pancreatic duct (MPD) was performed as a two-layered anastomosis using interrupted duct-to-mucosa sutures, with coverage of the entire cut surface of the pancreas by the seromuscular layer of the jejunum. Pancreatic consistency was evaluated subjectively as soft or hard by the surgeon during the operation. The definition of POPF was based on the classification of the International Study Group on Pancreatic Fistula [23].

2.3. Acquisition and interpretation of CTP data

Patients were examined using a 320-detector row CT (Aquilion ONE; Toshiba Medical Systems Corporation, Ohtawara, Japan). Slices for CTP were selected from precontrast abdominopelvic helical scans and included images as large as an entire pancreas. For CTP, 60 mL of a nonionic contrast material (Iohexol, Ioverin 350; Teva Pharma Japan Inc, Nagoya, Japan) was administered at a rate of 3.5 mL/s with a power injector (Dual Shot GX; Nemoto Kyorindo, Tokyo, Japan), followed by a 40-mL saline bolus. All dynamic CTP images were acquired with the following parameters: 0.5 mm slice thickness, 320 slices, 512 × 512 matrix, 100 kV, 60 mA, and 0.5 s gantry rotation time. The scans were performed 23 times during 6–180 s after injection of the contrast material under quiet breathing. The effective radiation dose for this protocol was 9.72 mSv. Misregistrations due to respiration and automatism were compensated automatically by the Body Registration software (Toshiba Medical Systems) on the console. Regions of interest (ROIs) were placed on the abdominal aorta at the level of the celiac axis, liver, and pancreas to generate time-density curves. Three different ROIs were then placed in the remnant pancreas (body and tail) on both axial and coronal CTP slices, and arterial flow (AF) (mL/min/100 mL) and mean transit time (MTT) (s) were measured at each ROI using the compartment model [24,25] using the Body Perfusion software (Toshiba Medical Systems). ROIs in the pancreas were made as large as possible while avoiding large vessels. Intermediate values for AF and MTT using the median of three ROIs in the axial and coronal slices were analyzed as the CTP data. Examples of two representative cases are shown in Figure 1A–D,E–H. All radiological analyses were performed by an experienced radiologist (T.K.), who was blinded to the operative outcomes and other clinicopathologic findings.

2.4. Histologic evaluation

Histological evaluation was performed as described in our previous article [26]. Formalin-fixed, paraffin-embedded specimens obtained from a pancreatic stump were cut into 3-μm thick serial sections. The sections were stained with hematoxylin and eosin (HE) to assess the area of the entire cut surface and MPD; azan-Mallory (azan) stain, to assess the degree of fibrosis; and anti-CD31 antibodies, to assess vessel number and density. Anti-CD31 immunohistochemical staining was performed automatically using a Ventana BenchMark ULTRA (Ventana Medical Systems, Tucson, AZ). Monoclonal anti-human CD31 antibody (Dako, Glostrup, Denmark) was used at a dilution of 1:200, and the conditions for antigen retrieval and primary antibody incubation were set at 95°C for 8 min and 35°C for 60 min, respectively. The slides were photographed using a NanoZoomer Digital Pathology virtual slide viewer (Hamamatsu Photonics, Hamamatsu, Japan) and subjected to morphometric analysis. Histologic analysis of the two cases for which CTP images are presented in Figure 1 A–D,E–H are shown in Figures 2 and 3. Morphometric analysis was performed as described in our previous article [26], and the details of the procedure are outlined in the