Predictive Significance of Tumor Grade Using 256-Slice CT Whole-Tumor Perfusion Imaging in Colorectal Adenocarcinoma

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Rationale and Objectives: The preoperative assessment of tumor grade has important clinical implications for the treatment and prognosis of patients with colorectal adenocarcinomas. The purpose of this study is to investigate the predictive significance of colorectal adenocarcinoma grade using 256-slice whole-tumor computed tomography (CT) perfusion.

Materials and Methods: Fifty-three patients with proven colorectal adenocarcinomas were enrolled. All of them underwent 256-slice whole-tumor CT perfusion. They were divided into two different subgroups according to postoperative pathological results: low grade and high grade. The Kruskal–Wallis test or one-way analysis of variance was used for comparison of CT perfusion parameters between different tumor grades. Multivariant correlation between pathologic tumor stage, histologic tumor differentiation, and whole-tumor CT perfusion parameters was evaluated by Spearman rank correlation coefficient. According to receiver operating characteristic (ROC) curves, perfusion parameters including blood flow (BF), peak enhancement index (PEI), blood volume (BV), and time to peak (TTP) of 53 patients were analyzed, and the sensitivity, specificity, and accuracy of these parameters in predicting tumor grade were calculated.

Results: There were significant differences in BF and TTP between low-grade and high-grade tumors. According to the ROC curve, BF and TTP were of diagnostic significance, with the area under the curve values of 0.828 and 0.736, respectively. The diagnostic threshold of BF was 32.12 mL/min/100 g and that of TTP was 18.10 seconds.

Conclusions: The CT perfusion parameters (BF, TTP) of first-pass 256-slice whole-tumor CT perfusion imaging can reflect tumor grade in colorectal adenocarcinoma.

Key Words: Colorectal adenocarcinoma; Tomography; X-ray; Perfusion imaging.

INTRODUCTION

Colorectal adenocarcinoma is one of malignant tumors with the highest morbidity and mortality all over the world (1,2). The 5-year survival rate of patients with colorectal adenocarcinoma is closely related to tumor stage and grade, and higher stage and higher grade tumors result in poorer prognosis (3). Clinical studies have confirmed that neoadjuvant chemoradiotherapy is superior to other adjuvant means in decreasing local relapse rate and lowering tumor stages in patients with high-stage and high-grade tumors. Sauer et al. (4) compared the efficacy of preoperative chemoradiotherapy to that of postoperative chemoradiotherapy in a 5-year randomized controlled trial and concluded that preoperative chemoradiotherapy, as compared to postoperative chemoradiotherapy, significantly decreased the 5-year cumulative incidence of local relapse (6% vs. 13%, $P = 0.006$), lowered tumor grades and stages, and significantly increased the rate of sphincter preservation (39% vs. 19%, $P = 0.004$). Therefore, early diagnosis and preoperative tumor grade evaluation are clinically important for patients with colorectal adenocarcinoma (4,5). Endoscopic colorectal biopsy can be used for pathological diagnosis of colorectal adenocarcinoma by harvesting a sufficient amount of tissue preoperatively, but it is limited because of partial sample harvesting and nonuniformity of tumor growth, which result in difficulties in obtaining a precise determination of the degree of tumor grade. Therefore, a preoperative precise determination of the degree of tumor grade by functional imaging is clinically important.

Computed tomography (CT) perfusion imaging is a newly emerging imaging modality that can quantitatively measure

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the degree of vascular enhancement, provide real-time tracking, calculate different CT perfusion parameters using different mathematical models, and thereby reflect the information of tumor microenvironment. There is evidence that CT perfusion parameters are correlated with tumor angiogenesis, reflecting the features of tumor angiogenesis to some extent (6–9). Several studies have demonstrated that tumor grade and prognosis are correlated with CT perfusion parameters (8,10–14). Few studies have reported on preoperative CT perfusion imaging for precise evaluation of the grade of colorectal adenocarcinoma (13). Owing to the limitations of the scanning equipment, most CT perfusion studies are confined to one or several levels of tumors, with poor repeatability; moreover, one level of perfusion information cannot represent the whole-volume perfusion information because of the nonuniformity of tumor angiogenesis. This study performed 256-slice whole-tumor CT perfusion imaging in colorectal adenocarcinoma and compared perfusion imaging findings to postoperative pathological outcomes to analyze the diagnostic value of whole-tumor CT perfusion parameters for tumor grades.

MATERIALS AND METHODS

Clinical Data

The Institute of Clinical Medical Science, China-Japan Friendship Hospital approved this research. Each patient provided written consent after being informed of the possible risks and contraindications. Fifty-nine patients who received preoperative fibercolonoscopy in the department of gastrointestinal surgery and were pathologically confirmed to have colorectal adenocarcinoma between August 2010 and April 2013 underwent 256-slice spiral CT whole-tumor perfusion imaging. Patients who met any of the following criteria were excluded: (1) preoperative neoadjuvant chemoradiotherapy ($n = 3$); (2) contrast agent-induced allergic reaction ($n = 0$); (3) severe heart, liver, and kidney diseases ($n = 0$); (4) presence of obvious peristaltic motion artifacts on CT perfusion images of the ascending colon, transverse colon, and descending colon ($n = 3$). Fifty-three patients, 33 males and 20 females, aged 58.9 ± 14.8 (range 20–85) years were included in the final analysis. The tumors examined were located in the rectum ($n = 34$), sigmoid colon ($n = 7$), descending colon ($n = 3$), transverse colon ($n = 1$), ascending colon ($n = 3$), and cecum ($n = 5$).

Pre-examination Preparation

Each patient provided written consent after being informed of the possible risks and contraindications. The patients were asked to fast for the examination. At 15 minutes before examination, 10 mg of anisodamine hydrochloride was intramuscularly injected to reduce intestinal peristalsis, and 1000–1500 mL of warm normal saline was injected via the anus using a Foley catheter to engorge the intestinal canal as far as possible. Injection was immediately terminated if patients felt uncomfortable. After the examination, patients were asked to breathe smoothly and abdominal breathing was inhibited by the use of abdominal bandage.

CT Perfusion Examination

CT perfusion imaging was performed using a 256-slice CT scanner (Brilliance iCT; Philips Medical Systems, The Netherlands). First, CT scanning (3-mm section thickness and 3-mm section interval) of the abdominopelvic cavity was performed without intravenous contrast medium to localize the tumor, and the whole-tumor sections were selected at the level of the tumor for "Jog Mode" scan (total z-axis coverage 10–12 cm). A bolus of 50 mL of contrast medium iopromide (Ultravist 370, Bayer Schering Pharma AG, Berlin, Germany) was intravenously injected at a flow rate of 5 mL/s into the median cubital vein. A dynamic scan of the selected region was triggered with a Jog Mode of 7.6 seconds after iopromide administration. The following parameters were used: duration of data acquisition 60.8 seconds, tube voltage 100 kV, tube current 80 mA, matrix 512 × 512, field of view 500, reconstructed section thickness 3 mm, and section interval 3 mm.

Image Analysis

The perfusion data were transferred to an image processing workstation (Extended Brilliant Workshop 4.52; Philips Medical Systems) and then analyzed separately by two experienced radiologists using CT perfusion software (Philips Medical Systems). The artery (abdominal aorta, ipsilateral iliac artery, or femoral artery) that was best displayed at the target plane was used as the input artery and a region of interest (ROI) of 2 mm^2 was designated; thus a time–density curve of the artery was automatically generated by the software. After reading of CT plain and perfusion images, tumor shape and size were determined. The ROI was drawn manually along the peripheral boundary of the visible tumor (15) (Fig 1). Care was taken to exclude visible vessel shadow, tumor necrosis area, intraluminal gas, and pericolonic fat.

Perfusion parameters including blood flow (BF; measured in mL/min/100 g; reflect tumor angiogenesis), blood volume (BV; measured in mL/100 g; reflect functionalized vascular structure), time to peak (TTP; measured in seconds; reflect tissue perfusion pressure), and peak enhancement index (PEI; measured in Hounsfield units and reflects the volume of blood in the tissue) were calculated using the slope method. Perfusion images and color-coded maps for BF, BV, and TTP were generated (Fig 1). Corresponding CT perfusion parameters were obtained. A global value representing the perfusion of the entire tumor was calculated by taking the mean value of all individual sections involved.

Pathological Diagnosis

Postoperative samples were pathologically diagnosed with colorectal adenocarcinoma by two experienced pathologists