European Journal of Radiology 80 (2011) 279–283

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Quantitative assessment of perirectal tumor infiltration with dynamic contrast-enhanced multi-detector row CT in rectal cancer

Can-Hui Sun[a,1], Shi-Ting Feng[a,1], Ping Xiao[b], Zhen-Peng Peng[a], Margaret H. Pui[c], Xue-Hua Li[a], Zi-Ping Li[a,*], Quan-Fei Meng[a]

[a] Department of Radiology, The First Affiliated Hospital, Sun Yat-Sen University, 58th, The Second Zhongshan Road, Guangzhou, China
[b] Department of Pathology, The First Affiliated Hospital, Sun Yat-Sen University, China
[c] Department of Radiology, ParkwayHealth Medical Centers, 4th Floor, 389 Nanjing Xi Road, Shanghai, China

ARTICLE INFO

Article history:
Received 18 March 2010
Received in revised form 26 June 2010
Accepted 30 June 2010

Keywords:
Rectal neoplasms
Neoplasm invasiveness
Dynamic contrast enhancement
Tomography
Spiral computed
Discriminant function analysis

ABSTRACT

Objective: To evaluate the efficacy of discriminant function analysis of perirectal tumor infiltration with dynamic contrast-enhanced 64-detector row CT in rectal cancer.
Materials and methods: Forty-nine patients with rectal cancer underwent dynamic contrast-enhanced CT. A total of 96 axial CT slices containing the tumors were evaluated. The 96 images were separated into two groups with or without perirectal tumor infiltration based on pathological findings. The discriminant function was set-up using CT density differences between the mass and the adjacent perirectal tissue within 5 mm from the mass at 20 and 40 s as independent variables. The results of the discriminant function analysis were compared to those of CT morphology and pathology.
Results: CT morphological diagnosis was accurate on 71.9% (69/96) of the slices with 82.5% sensitivity and 64.3% specificity. Discriminant function analysis correctly identified 88.5% (85/96) of the slices with 85.0% sensitivity and 91.1% specificity. Overstaging occurred significantly more ($P < 0.05$) on morphological analysis (20.8%, 20/96) than discriminant function analysis (5.2%, 5/96) of the CT slices.
Conclusions: Discriminant function analysis of dynamic contrast-enhanced CT improves the diagnostic accuracy and specificity of perirectal tumor infiltration in rectal cancer.

1. Introduction

Rectal cancer is a common alimentary tract malignancy with high mortality rate for local recurrence and distant metastasis [1]. When the tumor penetrates through the bowel wall into the pericolic region, regional lymph node and distant metastases increase significantly [2]. Therefore, the risk of recurrence and overall survival depend largely on the extent of local infiltration of rectal cancer. The depth of local invasion has a great impact on the choice of treatment [3]. Morphological imaging methods including computed tomography (CT), magnetic resonance imaging (MRI) and endorectal ultrasonography (EUS) often overestimate the pericolic infiltration of colorectal cancer because it is difficult to distinguish peritumoral inflammation or fibroplasia from tumor infiltration [3–8]. With improved spatial and temporal resolution of 64-detector row CT, dynamic contrast-enhanced imaging and measurement of the CT values of the pericolic tissues may differentiate tumor infiltration from inflammation or fibroplasia. The objectives of our study were to determine the efficacy of CT density analysis for assessing perirectal tumor infiltration and to establish a discriminant function that may improve the diagnostic accuracy and specificity of perirectal tumor infiltration in rectal cancer.

2. Materials and methods

2.1. Study population

Prior to 2009, patients did not routinely receive neoadjuvant therapy for rectal cancer at our institution. To avoid the confounding influence of chemotherapy or radiation treatment, 49 consecutive patients (22 men, 27 women; age range, 18–73 years; mean age, 56.3 years) with histologically confirmed and untreated rectal cancer measuring 2.3–15.0 cm in diameter were enrolled in the study from June 2007 to December 2008. Informed consent was obtained from all patients and the study was approved by the institutional research ethics board.

2.2. Scanning technique

Before the CT examination, patients were instructed and practiced breath-holding to produce the same degree of respi-

* Corresponding author. Tel.: +86 20 87755766x8471; fax: +86 20 87615805.
E-mail address: liziping163@tom.com (Z.-P. Li).
[1] Both authors contributed equally to this study.

0720-048X/$ – see front matter © 2010 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.ejrad.2010.06.048

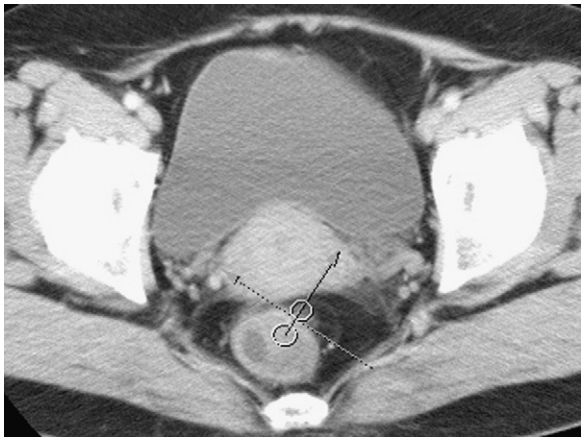

Fig. 1. Determination of tumor and perirectal CT densities. A 30–75 mm^2 circular region of interest (ROI) is placed in the center of the tumor and a straight line (thick arrow) is drawn through the center of the ROI perpendicular to the tangent of the exterior bowel wall (thin arrow). A second circular perirectal ROI of 5 mm in diameter is placed along this line (thick arrow) outside the bowel. Blood vessels and cystic areas are not included in the ROI. The mean CT densities of the tumor ROI and perirectal ROI are recorded.

ration for scanning. Bowel cleansing was performed the night before and immediately prior to CT using 1–1.5 L of warm saline enema.

Dynamic contrast-enhanced CT was performed using a 64-detector row scanner (Aquillion; Toshiba, Tokyo, Japan) 2–10 days (mean 5.7 days) before surgery. The slice with the maximal diameter of the tumor mass was located on routine unenhanced scans. Dynamic contrast-enhanced CT was then acquired with 0 pitch, 1 Hz tube rotation, 120 kVp and 150 mA to obtain four 5 mm thick axial sections of the tumor at the rate of 1 section/s. Nine seconds after intravenous injection of 40 mL of iopromide (Ultravist 300, Schering, Berlin, Germany) antecubitally at 4 mL/s, 14 sets of four axial images were obtained at 5 s intervals from 10 to 75 s.

2.3. Image and data analysis

The images were transferred to a workstation (HP workstation XW8200, Vitrea2, version 3.7) and displayed with window width of 250–400 Hounsfield units (HU) and window level of −15 to −35 HU for analysis. One hundred images that did not include the tumor were excluded from analysis because of partial volume effect or improper scan level resulting from variable degree of respiration. A total of 96 slices containing the tumors were analysed. The mean CT densities of the tumor and perirectal tissues within 5 mm of tumors were recorded at different time points (Fig. 1). Two gastrointestinal radiologists (C.H.S. and Z.P.L. with 9 and 16 years of experience in gastrointestinal radiology, respectively) reviewed the CT images preoperatively by consensus. The 96 CT slices were classified as non-perirectal tumor infiltration if the tumors appeared to be confined within the bowel walls with smooth, well-defined outer margins. When the serosa appeared blurred with perirectal fat stranding or nodules, perirectal tumor infiltration was suspected [9,10]. The surgically removed tumor masses were sectioned and one paraffin block was prepared for each tumor section corresponding to the axial CT slices. The 96 CT slices were separated by histology into perirectal or non-perirectal tumor infiltration group.

2.4. Statistical analysis

CT densities of perirectal tissues within 5 mm of the tumors at different time points were measured after dynamic contrast enhancement and compared with the masses themselves to obtain CT density differences. Fourteen CT density differences at 14 contrast enhancement time points for the perirectal and non-perirectal tumor infiltration groups were obtained and compared using analysis of variance with significance defined at $P < 0.05$. A stepwise discriminant analysis was performed to identify the CT density differences that were most useful in separating the perirectal tumor infiltration from non-perirectal infiltration groups. A discriminant function was generated by setting the differences of CT densities at various contrast enhancement time points as independent variables in the SAS 8.0 DISCRIM analysis (SAS8.0, SAS Institute, Cary, NC, USA). A discriminating CT density difference at one time point was initially selected. All remaining CT density differences at other time points were then tested. The second CT density difference at a time point that improved the discriminant function was then chosen. Subsequent CT density differences at other time points were selected according to their contributions to the discriminant function. At each step, the previously selected discriminating CT density difference was re-examined. If a CT density difference reduced the discriminant function when combined with the subsequently selected CT density differences, it was eliminated and additional CT density differences were included until those remaining no longer contributed to the discriminant function [11]. A non-parametric method was applied to the discriminant analysis. The discriminant function was assessed with Wilks′ Lambda test. The effectiveness of the discriminant function was evaluated by the backward substitution method. Using discriminant function analysis, the CT images were re-categorized for perirectal or non-perirectal tumor infiltration and compared with the results of morphological analysis.

3. Results

Of the 96 paraffin sections obtained from the resected tumors, 40 (41.7%) showed perirectal tumor infiltration and 60 (62.5%) showed varying degrees of perirectal inflammation and fibroplasia (Fig. 2). In the perirectal tumor infiltration group, 77.5% (31/40) of the paraffin sections showed tumor infiltration within 2 mm of the tumor margin (Fig. 3). Distinct perirectal soft tissue nodules were identified on 9 paraffin sections.

Fourteen CT density differences at 14 time points for the perirectal tumor infiltration group and the non-perirectal tumor infiltration group were obtained, respectively (Fig. 4). The mean CT density differences ranged from 43.65 ± 27.77 to 52.33 ± 30.80 HU in the perirectal tumor infiltration group, and ranged from 100.37 ± 20.31 to 116.18 ± 21.40 HU in the non-perirectal infiltration group. The mean values of CT density differences in the perirectal tumor infiltration group were significantly lower than those in the non-perirectal tumor infiltration group at various contrast enhancement time points ($F = 6.278$, $P < 0.001$).

By stepwise discriminant analysis, only the CT density differences at 20 s and 40 s after contrast injection in the perirectal and non-perirectal tumor infiltration groups showed significant discriminant function ($\chi^2 = 105.320$, $P < 0.001$). The discriminant function (D) was calculated using the equation:

$$D = -3.450 + 0.023X_1 + 0.017X_2 - 0.001X_1^2 - 0.001X_2^2 + 0.002X_I \times X_2$$

where X_1 was the CT density difference at 20 s and X_2 was the CT density difference at 40 s. The center of gravity (CG) values of perirectal and non-perirectal tumor infiltration groups were −1.721 and 1.230 respectively. If D was closer to the CG value of −1.721, the CT slice was categorized as perirectal tumor infiltration. Otherwise, it would be categorized as non-perirectal tumor infiltration. 88.5% of the samples were classified correctly using