Original Article

High perirenal fat thickness predicts a poor progression-free survival in patients with localized clear cell renal cell carcinoma

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Abstract

Objectives: The aim of the study was to assess the association between the progression-free survival (PFS) and perirenal fat thickness (PFT) in a population of histopathologically confirmed, localized clear cell renal cell carcinoma (ccRCC) patients.

Methods: We retrospectively enrolled 174 patients with localized ccRCC at our center between December 2009 and December 2015. The preoperative visceral fat area (VFA), PFT, and subcutaneous fat area (SFA) were evaluated. Kaplan-Meier curves were used to assess the differences in PFS between the high and the low PFT groups within sexes. Potential independent prognostic factors of PFS were identified by univariable and multivariable Cox analyses.

Results: During the follow-up period (median, 38 months), 27 patients (21 with high PFT and 6 with low PFT) experienced tumor progression. Kaplan-Meier curves revealed that high PFT was associated with a worse PFS than low PFT ($P = 0.005$). In the univariable Cox analyses, high VFA, high PFT, T stage, and the presence of sarcomatoid differentiation were significantly associated with a poor PFS. Moreover, both high PFT and VFA retained significance in the multivariable analysis.

Conclusion: We first report the evidence that high PFT presents as an independent risk factor of tumor progression in localized ccRCC. We suggest that this noninvasive and readily available preoperative parameter may help in the risk stratification of ccRCC patients before surgery. © 2018 Elsevier Inc. All rights reserved.

Keywords: Perirenal fat thickness; Progression; Survival; Clear cell; Renal cell carcinoma

1. Introduction

Renal cell carcinoma (RCC), which is the most common solid lesion within the kidney and accounts for approximately 90% of all kidney malignancies, represents 2 to 3% of all cancers [1]. RCC is composed of several histopathological subtypes, among which clear cell RCC (ccRCC) is the most common subtype [2]. Though the exact etiology of RCC remains unclear, the association of obesity with the development of RCC has been reported by several previous studies [3–5]. Visceral fat accumulation, which can be quantitatively measured from a routine computed tomography (CT) image, has recently been studied for its contribution to the survival of RCC patients, and results have suggested that visceral fat accumulation be included in the risk stratification. However, controversial results were reported from studies on different ethnicities of patients and on different tumor stages [6–12]. In the investigations of Okhunov et al. [13,14], renal neoplasms with high perirenal fat thickness (PFT) were more likely to be identified as ccRCC than those with low PFT. In addition, they demonstrated the ability of perineoplasm perirenal fat to promote the migration of ccRCC cells, which suggests a potential mechanism for the involvement of perirenal fat in ccRCC pathogenesis. Nevertheless, to the best of our knowledge, there is no available study regarding the association of PFT and the progression-free survival

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(PFS) of ccRCC patients. Therefore, we conducted the present study, which enrolled 174 histopathologically confirmed, localized ccRCC patients, to address the relationships between the PFS and the value of the visceral fat area (VFA) and PFT.

2. Methods

2.1. Patients and data collection

A total of 174 patients with histologically confirmed, localized ccRCC who were treated with partial or radical nephrectomy in our center between December 2009 and December 2015 were retrospectively enrolled into the present study. In the current study, patients who had no available preoperative CT images for further analysis, patients who had operations elsewhere or patients with a tumor location that may have affected the measurement of PFT (posteriorly at the level of renal hilum) were excluded. Clinicopathological parameters were collected from the medical records, including age at initial diagnosis (less than 60 years vs. 60 years or older), sex, tumor location (right vs. left kidney), Fuhrman grade, T stage based on the American Joint Committee on Cancer (AJCC; T1 vs. T2), the values of subcutaneous fat area (SFA), VFA, and PFT, and the presence of histological necrosis, sarcomatoid component, hypertension, and diabetes. Given the small number of patients with Fuhrman grade 4 (4 subjects), patients with Fuhrman grades 3 and 4 were combined into 1 group for further analysis. Cancer progression was defined as the presence of distant metastasis or local recurrence after nephrectomy. All the surgical procedures were mainly performed by 1 surgeon (JCX). This study was conducted with the approval from the institutional ethics committee of The First Affiliated Hospital of Xiamen University. Patient records/information were anonymized and de-identified prior to analysis. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from each individual participant included in the study.

2.2. The measurement of VFA, SFA, and PFT

Routine abdominal CT scans (Somaris/7 CT 2012B, Siemens AG, Germany) were performed preoperatively for all the enrolled patients. The evaluation of SFA and VFA (Fig. 1) was in accordance with the measurements reported by a previous study [10]. In brief, the visceral compartment was separated from the subcutaneous compartment by manually outlining the contour of the abdominal muscular wall at the level of umbilicus. Thereafter, an image display window width from −195 to −45 Hounsfield units was used to identify pixels containing fat, and the values of VFA and SFA were then calculated automatically using the software analysis program (Syngo MultiModality Workplace, version VE31A, Siemens AG, Germany).

Likewise, PFT was also evaluated in accordance with a previous study [13]. In brief, it was defined as distance between the kidney's posterior surface and the external margin of iliopsoas at the level of the renal hilum in the CT images and measured using the ruler function of the software (Fig. 2). All the preoperative CT images were reviewed by a radiologist (CS) who was blinded to the clinical and pathological data before the evaluation.

To date, no available ideal cutoff value has been identified to distinguish high SFA and VFA values from low values, but several previous studies used the sex-specific median values to dichotomize their cohorts. Therefore, in the current study, the sex-specific median values were used to distinguish high SFA (greater than 127.64 cm^2 for males and 190.48 cm^2 for females) and high VFA (greater than 111.64 cm^2 for males and 81.84 cm^2 for females) from low values. In addition, the sex-specific
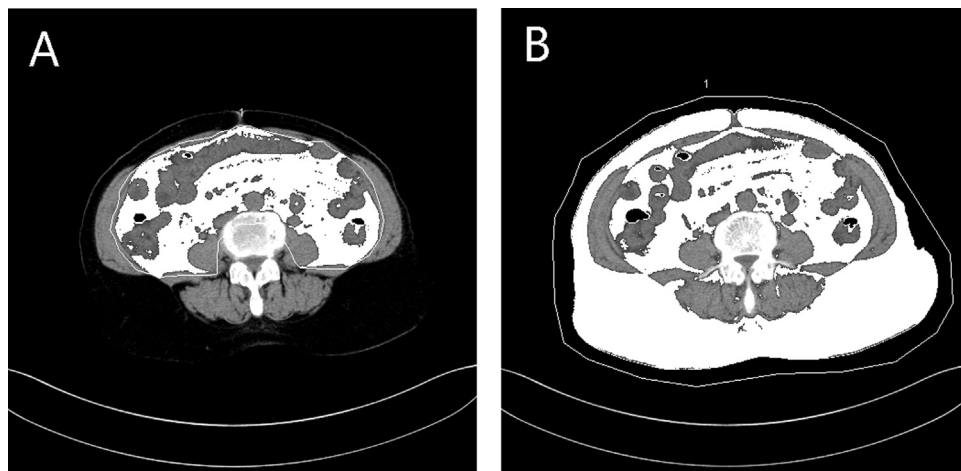

Fig. 1. Axial CT images at the level of umbilicus used for evaluating the visceral fat area (A), subcutaneous fat area plus visceral fat area (B).