Visceral Obesity in Predicting Oncologic Outcomes of Localized Renal Cell Carcinoma

Yong Hyun Park, Jeong Keun Lee, Kwang Mo Kim, Ha Rim Kook, Hansol Lee, Ki Bum Kim, Sangchul Lee, Seok-Soo Byun and Sang Eun Lee*

From the Department of Urology, Seoul National University Bundang Hospital, Seongnam and College of Medicine, Seoul National University, Seoul, Korea

Purpose: We investigate the clinicopathological features and prognostic significance of visceral obesity in patients with localized renal cell carcinoma.

Materials and Methods: This study included 706 patients with localized renal cell carcinoma who had undergone curative surgery between January 2003 and April 2012. Visceral, subcutaneous and total adipose tissue were measured based on preoperative computerized tomography of the umbilical region. Visceral adipose tissue percent was calculated using the formula, VAT% = [visceral adipose tissue/total adipose tissue] × 100. The association between clinicopathological factors and visceral obesity was examined.

Results: A higher VAT% at diagnosis was associated with older age at diagnosis, higher prevalence of diabetes and higher prevalence of former or current smoking status. The distribution of histological subtypes differed significantly among VAT% quartiles. The proportion of high grade tumors increased as VAT% increased (OR 1.023, 95% CI 1.000−1.126, p = 0.037). A U-shaped association between VAT% quartiles and the risk of disease recurrence was observed for all patients. Disease recurrence was significantly increased in the lowest (HR 3.198, 95% CI 1.765−10.040, p = 0.036) and highest (HR 4.760, 95% CI 2.937−13.210, p = 0.010) VAT% quartiles.

Conclusions: Relative visceral obesity as assessed by VAT% was associated with clinicopathological characteristics of localized renal cell carcinoma. A U-shaped association between VAT% quartiles and risk of disease recurrence was observed among patients with localized renal cell carcinoma.

Key Words: carcinoma, renal cell; intra-abdominal fat; adipose tissue; prognosis

Abbreviations and Acronyms

BMI = body mass index

CT = computerized tomography

ECOG = Eastern Cooperative Oncology Group

RCC = renal cell carcinoma

SAT = subcutaneous adipose tissue

TAT = total adipose tissue

VAT = visceral adipose tissue

Accepted for publication March 25, 2014.

Study received institutional review board approval.

* Correspondence: Department of Urology, Seoul National University Bundang Hospital, 82, Gumi-ro 173 Beon-gil, Bundang-gu, Seongnam, Gyeonggi-do, 463-707, Republic of Korea (telephone: +82-31-787-7341; FAX: +82-31-787-4057; e-mail: selee@snubh.org).

See Editorial on page 1015.

For another article on a related topic see page 1229.

Obesity has become a major public health problem of epidemic proportions, with approximately 1.6 billion overweight adults and at least 400 million obese individuals as of 2005. These figures are expected to reach 2.3 billion and 700 million, respectively, by 2015.[1] There is strong evidence that obesity is a modifiable risk factor for cancer. Approximately 20% of all cancers are associated with excess weight.[2] Additionally, obesity is associated with increased treatment related side effects, poor quality of life, and an increased risk of cancer recurrence and mortality in several cancers.[3–5] Prior studies have largely suggested that the risk of renal cell carcinoma increases as body weight increases.[6–8] However, in contrast to those with other cancers, overweight and obese patients with RCC might

0022-5347/14/1924-1043/0
THE JOURNAL OF UROLOGY®

http://dx.doi.org/10.1016/j.juro.2014.03.107
Vol. 192, 1043-1049, October 2014
Printed in U.S.A.

have more favorable pathological features and a better prognosis than normal or underweight patients.[9–12] To date, these paradoxical findings have not been fully elucidated.

Furthermore, most prior studies used body mass index, which measures excess weight rather than excess fat, as a measure of obesity. BMI does not distinguish between excess fat, muscle or bone mass, nor does it provide any information regarding the distribution of fat among individuals. Given these limitations of BMI, studies that use direct measurements of body fat may yield a more accurate estimate of the association between adiposity and the risk of cancer. Additionally, cancers that are more closely associated with visceral obesity than with BMI have been shown to predominantly involve the colon, breast and endometrium.[13–15] Therefore, to fully understand the relationship between increased obesity and the clinicopathological features of RCC, body fat content and distribution need to be determined. To date, little information is available on the association between visceral obesity and the oncologic outcomes of patients with RCC. Thus, we investigated the clinicopathological features and prognostic significance of visceral obesity in patients with localized RCC.

MATERIALS AND METHODS

Patients

The present study included 706 patients with RCC who had undergone curative surgery between January 2003 and April 2012, and met the criteria of 1) localized RCC, 2) information available on preoperative height and weight, 3) available preoperative CT, and 4) followup of more than 1 year. After receiving approval by the institutional review board at Seoul National University Bundang Hospital, clinical information, preoperative imaging findings and final pathological data of the eligible patients were reviewed.

TNM staging was based on the 7th TNM classification of the UICC (Union for International Cancer Control) and the AJCC (American Joint Committee on Cancer) guidelines,[16] and histological subtypes were determined according to the UICC/AJCC and Heidelberg recommendations.[17] Cancer specific death was defined as evidence of cancer progression before death determined by reviewing patient medical records and/or the ICD 10th revision determined by reviewing the Korea National Statistical Office database.

Adiposity Measurement

Visceral, subcutaneous and total adipose tissue were measured on preoperative CT of the umbilical region using imaging software (Rapidia 3D 2.8 software, Infinitt, Seoul, Korea). The CT attenuation level was set between −250 and −50 Hounsfield units, regions of adipose tissue were manually delineated, and areas of VAT, SAT and TAT were calculated (fig. 1). VAT% was calculated using the formula, VAT% = [VAT/TAT] × 100. Patient height and body weight recorded before surgery were used to calculate BMI, and patients were categorized according to BMI on the basis of the Asia-Pacific criteria for obesity as underweight (less than 18.5 kg/m^2), normal (18.5 to 22.9 kg/m^2), overweight (23 to 24.9 kg/m^2) and obese (25 kg/m^2 or greater).[18]

Outcome Measurements and Statistical Analysis

Continuous variables are presented as mean (±SD) or median (IQR) and categorical variables are presented as proportions. The correlation between BMI and visceral adiposity was assessed using the Pearson correlation coefficient (r). Demographic, clinical and pathological data were compared using Student's t-test or 1-way analysis of variance for continuous variables and the chi-square test for categorical variables. The association between variables and adverse pathological outcomes was evaluated using logistic regression analysis. Survival analysis for recurrence was performed using the Kaplan-Meier method and the differences between groups were determined using the log rank test. Cox proportional hazard regression with forward stepwise regression was performed to identify independent prognostic factors for recurrence. Variables included in the multivariate analysis were age, gender, symptoms at initial diagnosis, BMI, ECOG performance status, Charlson comorbidity index, preoperative laboratory data, T stage, histological

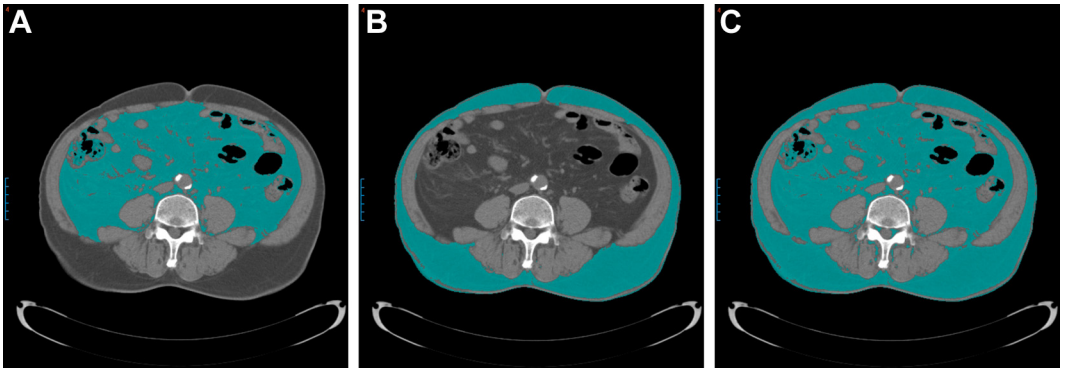

Figure 1. Radiological measurement of visceral and subcutaneous adipose tissue. Measurement of VAT (*A*), SAT (*B*) and TAT (*C*) by CT analysis software for representative patient.