Original article

Body mass index and the clinicopathological characteristics of clinically localized renal masses—An international retrospective review

Efrat Tsivian, M.D.[a,*], Matvey Tsivian, M.D.[a], Kae Jack Tay, M.D.[a], Thomas Longo, M.D.[a],
Ziv Zukerman, M.D.[b], Giuseppe Martorana, M.D.[b], Riccardo Schiavina, M.D.[b],
Eugenio Brunocilla, M.D.[b], Thomas J. Polascik, M.D.[a]

[a] *Division of Urology, Department of Surgery, Duke University Medical Center, Durham, NC*
[b] *Department of Urology, University of Bologna, S. Orsola-Malpighi Hospital, Bologna, Italy*

Abstract

Objectives: To investigate the potential association between body mass index (BMI) and clinicopathological features of clinically localized renal masses.

Materials and methods: An international, multi-institutional retrospective review of patients who underwent surgery for clinically localized renal masses between 2000 and 2010 was undertaken after an institutional review board approval. Patients were divided into 4 absolute BMI groups based on the entire cohort's percentiles and 4 relative BMI groups based on their respective population (American or Italian). Renal mass pathological diagnosis, renal cell carcinoma (RCC) subtype, Fuhrman grade (low and high), and clinical stage were compared among groups using Fisher's exact test, Kruskal-Wallis test, and the Cochran-Armitage trend test. A multivariate logistic analysis was performed to evaluate independent association between tumor and patient characteristics with tumor pathology (Fuhrman grade).

Results: A total of 1,748 patients having a median BMI of 28 (interquartile range 25–32) were evaluated. Benign masses and RCC cases had similar proportion across BMI groups ($P = 0.4$). The most common RCC subtype was clear cell followed by papillary carcinoma, chromophobe, and other subtypes. Their distribution was comparable across BMI groups ($P = 0.7$). Similarly, clinical stage distribution was comparable with the overall cohort. The distribution of Fuhrman grade in RCC, however, demonstrated an increased proportions of low grade with increasing BMI ($P < 0.05$). This trend was maintained in subgroups according to gender, stage and age ($P < 0.05$ in all subgroup analysis). In a multivariable model that included potential confounders (i.e., age, sex, and tumor size) higher BMI groups had lower odds of presenting a high Fuhrman grade.

Conclusion: In this study, higher BMI was associated with lower grade of RCC in clinically localized renal masses. This may, in part, explain better survival rates in patients with higher BMI and may correlate with a possible link between adipose tissue and RCC biology. © 2017 Elsevier Inc. All rights reserved.

Keywords: BMI; Renal mass; Fuhrman grade; RCC

1. Introduction

The incidence of renal masses has been increasing steadily in recent years, at least in part owing to the widespread use of cross-sectional imaging. Interestingly, the prevalence of obesity is on the rise as well as [1] suggesting a potential link between the 2 trends, especially considering that obesity represents a well-established risk factor for renal cell carcinoma (RCC) [2].

A large contemporary study has shown that obesity represents a risk factor for RCC-specific mortality [3]. This finding has been challenged by surgical cohorts showing better cancer-specific survival in patients with obesity [4,5]. This discrepancy in the literature may be due to different study designs, geographic and socio-economic factors, or confounding factors that were not previously explored.

* Corresponding author. Tel.: +1-919-684-4314; fax: +1-919-684-5220.
E-mail address: efrat.tsivian@dm.duke.edu (E. Tsivian).

Most of the research available has focused on either "kidney cancer" including all subtypes of malignancy groups evaluated as a single entity, or the most frequent histotype of RCC (clear cell) [4]. In reality, a variable proportion (up to 40%) of patients treated for a renal mass harbor benign tumors, and histotypes other than clear cell may represent up to 30% of renal cell malignancies [6]. Furthermore, although the effect of sex, tumor size, and age on localized renal mass pathology has been documented [7] little is known of the association between other RCC pathological characteristics and body mass index (BMI).

In this study, therefore, we perform a detailed analysis of the potential associations between BMI and the clinicopathological features of clinically localized renal masses in a large international cohort.

2. Materials and methods

2.1. Cohort

After approval from the institutional review board, we reviewed the records of patients who underwent surgery for a clinically localized renal mass between the years 2000 and 2010 at Duke University Medical Center, Durham NC, USA and S. Orsola-Malpighi Hospital, Bologna, Italy. Only patients who underwent partial nephrectomy, radical nephrectomy, or renal mass enucleation were included in the study. Patients with incomplete data (missing BMI, renal mass pathologic diagnosis, radiological size, or Fuhrman grade for RCC) or those who underwent ablative therapy were excluded from the analysis. The entire cohort was divided into 4 BMI groups based on the entire cohort (American and Italian combined) BMI percentiles (absolute BMI). The groups included group A (BMI < 25), B (BMI 25–27.9), C (BMI 28–31.9), and D (BMI ≥ 32). Moreover, we also divided the cohort into 4 relative BMI groups based on the BMI percentiles of each population (Italian and American) to account for the different BMI distributions. The relative BMI groups were as follows: A (Duke BMI < 26 and Bologna BMI < 24), B (Duke BMI 26–28.99 and Bologna BMI 24–25.9), C (Duke BMI 29–33.9 and Bologna BMI 26–28.9), and D (Duke BMI ≥ 34 and Bologna BMI ≥ 29). Variables that were compared among the groups included renal mass pathology (benign vs. malignant), tumor size, RCC subtype, Fuhrman grade, and clinical stage. Fuhrman grade was divided into 2 categories, namely, low (1–2) and high (3–4) to account for possible interobserver variation [8].

2.2. Statistical analysis

Variables retrieved included patient demographics, clinical stage, and rates of benign vs. malignant, tumor size, RCC subtypes, and Fuhrman grade. These were compared between the American and Italian cohort using Student's

t-test for normal distributed continuous variables, Wilcoxon rank sum test for abnormal continuous variables, and Fisher's test for categorical variables. The data are reported as median (IQR) or number (%). Furthermore, Fisher's test, Kruskal-Wallis test, and the Cochran-Armitage trend test were used to assess differences in the variables between the different absolute BMI and relative BMI groups.

A multivariate logistic analysis was performed to evaluate independent association between tumor and patient characteristics with tumor pathology (Fuhrman grade).

All tests were 2-tailed and $P < 0.05$ was considered statistically significant. Analyses were performed using R v3.1.2 (the R Foundation for Statistical Computing Platform, Vienna, Austria) using "gmodels" and "Hmisc" libraries.

3. Results

Of the 2,235 available records, 1,748 met the criteria and were reviewed after institutional review board approval. Of those 1,117 (64%) underwent surgery at Duke University Medical Center and 631 (36%) were treated at S. Orsola-Malpighi Hospital. Radical nephrectomies constituted 57% of cases, whereas partial nephrectomies were performed in 43% of patients. Patient and renal mass characteristics are detailed in Table 1. Most patients were males (64%) and the median age was 62 years (52–70). The median BMI of the entire cohort was 28 (25–32). The median BMI was significantly different ($P < 0.01$) between the American (median: 29, IQR: 26–34) and the Italian cohort (median: 26, IQR: 24–29). Renal mass pathology was malignant in 83% of patients and was comparable among the different BMI groups ($P = 0.4$). The most common subtype was clear cell (76%) followed by papillary carcinoma, chromophobe, and other subtypes (18%, 3%, and 3%, respectively). Their distribution was also comparable across BMI groups ($P = 0.7$). Similarly, clinical stage distribution was comparable with the overall cohort with T1a, T1b, T2a, and T2b accounting for 50%, 29%, 13%, and 8%, respectively. Furthermore, no association was found between radiological size and BMI group for both overall and malignant masses ($P = 0.5$ and $P = 0.2$). However, there was a significant difference in the distribution of Fuhrman grade across the absolute BMI and relative BMI groups ($P < 0.01$ in both cases) (Table 2). Low Fuhrman grade had a higher rate among the groups with higher BMI and the rate of high Fuhrman grade increased in the lower BMI groups (Fig.). This trend was maintained in subgroup analysis that was performed based on sex ($P = 0.005$), clinical stage ($P < 0.05$), and for clear cell RCC (<0.01).

In a multivariable model that included potential confounders (i.e., age, sex, and tumor size) higher BMI groups had lower odds of presenting a high Fuhrman grade (Table 3). In fact, the highest BMI group was 50% less likely to present with a high Fuhrman grade.