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Renal cell carcinoma: Associations between tumor imaging features and epidemiological risk factors

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Abstract: PURPOSE To investigate associations between imaging features of tumors and age, gender and body mass index (BMI) in patients with renal cell carcinoma. METHOD This IRB-approved, HIPAA-compliant study included 1348 patients with histopathologically confirmed renal cell carcinoma of the clear cell subtype (ccRCC, n = 904) or non-clear cell subtype (n = 444), who underwent pre-treatment CT imaging less than 180 days before nephrectomy between 1999 and 2011. Two radiologists independently, retrospectively analyzed all imaging studies and identified features (necrosis, renal vein invasion, contact with renal sinus fat, multicystic appearance and nodular enhancement), which were then correlated with patient age, gender and BMI at time of surgery. RESULTS Inter-reader agreement on imaging features ranged from substantial to excellent (kappa: 0.688 to 0.982). In the ccRCC group, multicystic tumor appearance was significantly associated with lower patient age (p < 0.05) and lower BMI (p < 0.05); the presence of renal vein invasion was significantly associated with lower BMI in males (p < 0.05); and both tumor contact with the renal sinus and nodular enhancement were significantly associated with greater patient age (p < 0.05). In the non-clear cell RCC group, necrosis was associated with lower BMI for females (p < 0.05). CONCLUSIONS This study demonstrated significant associations between imaging features of RCC and patient age and BMI, hinting an influence of these factors on tumor biology and genomic make-up. These findings could aid future studies in selecting patients while investigating genomic, molecular and metabolic variables in RCC and might potentially impact on future stratification and therapy of patients.

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ABSTRACT

Purpose: To investigate associations between imaging features of tumors and age, gender and body mass index (BMI) in patients with renal cell carcinoma.

Method: This IRB-approved, HIPAA-compliant study included 1348 patients with histopathologically confirmed renal cell carcinoma of the clear cell subtype (ccRCC, $n = 904$) or non-clear cell subtype ($n = 444$), who underwent pre-treatment CT imaging less than 180 days before nephrectomy between 1999 and 2011. Two radiologists independently, retrospectively analyzed all imaging studies and identified features (necrosis, renal vein invasion, contact with renal sinus fat, multicystic appearance and nodular enhancement), which were then correlated with patient age, gender and BMI at time of surgery.

Results: Inter-reader agreement on imaging features ranged from substantial to excellent (kappa: 0.688 to 0.982). In the ccRCC group, multicystic tumor appearance was significantly associated with lower patient age ($p < 0.05$) and lower BMI ($p < 0.05$); the presence of renal vein invasion was significantly associated with lower BMI in males ($p < 0.05$); and both tumor contact with the renal sinus and nodular enhancement were significantly associated with greater patient age ($p < 0.05$). In the non-clear cell RCC group, necrosis was associated with lower BMI for females ($p < 0.05$).

Conclusions: This study demonstrated significant associations between imaging features of RCC and patient age and BMI, hinting an influence of these factors on tumor biology and genomic make-up. These findings could aid future studies in selecting patients while investigating genomic, molecular and metabolic variables in RCC and might potentially impact on future stratification and therapy of patients.

1. Introduction

Several risk factors have been identified that are potentially responsible for the increasing number of newly-diagnosed renal cell carcinomas [1], among them smoking [2], hypertension [3], age [4], male gender [5] and, especially with regard to the clear cell histopathologic subtype, obesity [6–10]. Though an elevated BMI is considered a major risk factor for the development of kidney cancer and is thought to be the cause of up to 27–40% of all RCCs in the United States [11,12], several independent reports have indicated that outcomes are better in obese patients than in patients of normal weight [13–16]. However, recent studies [17,18] indicate that the protective effect of obesity extended only to men and not to women. The causes of the paradoxical nature of obesity as both a risk factor and a protective characteristic in men are still unknown but may lie in the genomic make-up of the tumor [19,9].

This underscores that even within individual RCC subtypes, prognosis and clinical behavior vary strongly, and imaging features are similarly diverse: Whereas some tumors show extensive necrosis, cystic components or strong peripheral enhancement, others have a rather homogeneous enhancement pattern and appear solid on imaging. To our knowledge, no studies have yet investigated whether these 'imaging phenotypes' are also associated with specific risk factors (i.e., age, gender and BMI) that could themselves influence tumor biology and

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