Letter to Editor

Body Composition Imaging, Clinicopathological Status, and Genetic Profile in Clear Cell Renal Cell Carcinoma

Dear Editor,

We commend Dr Sekar and colleagues for their *Nigerian Journal of Clinical Practice* article entitled "Clinicopathological Comparison of VHL Expression as a Prognostic Tumor Marker in Renal Cell Carcinoma: A Single Center Experience" which was published online in April 2021.[1] The authors analyzed, by immunohistochemistry, 30 specimens of renal cell carcinoma (RCC), 28 of which were clear cell RCC (ccRCC) and 2 chromophobe RCC. These samples were divided into two groups: loss of von Hippel – Lindau (VHL) expression (n = 23) and VHL expression retained (n = 7).[1] The authors found statistically significant correlation between solid lesions and loss of VHL expression (p < 0.0009), absence of necrosis within the lesion together with loss of VHL expression (p = 0.0001) and renal vein involvement in combination with retained VHL expression (p = 0.0307).[1] It is interesting to point out that these data are in keeping with the radiogenomics analysis conducted by Karlo *et al.*[2] These authors evaluated the associations between ccRCC computed tomography (CT) features and VHL, polybromo 1 (PBRM1), SET domain containing 2 (SETD2), lysine (K)-specific demethylase 5C (KDM5C), and BRCA1- associated protein 1 (ubiquitin carboxy-terminal hydrolase) (BAP1) gene mutations. The study showed a correlation between solid RCC phenotype and VHL (p = 0.016) and PBRM1 (p = 0.017) mutations, while KDM5C and BAP1 gene mutations were significantly correlated with evidence of renal vein invasion (p = 0.022 and 0.046, respectively). Conversely, no correlation was found between absence or presence of necrosis within the lesions according to loss or retained VHL expression.[2] Sekar *et al.*[1] reported no significant difference in BMI between the two groups. However, BMI does not provide information on the body composition, for example it does not provide data on quantity of adipose tissue, nor on the abdominal compartmental distribution [i.e., visceral adipose tissue (VAT) and subcutaneous adipose tissue].[3] Computed tomography and magnetic resonance imaging are fundamental imaging techniques allowing for noninvasive tissue characterization and quantification.[3-5]

The excessive amount of adipose tissue, in particular VAT, plays an active role in ccRCC development. In fact, increased VAT was found in ccRCC patients.[3] In addition, a different amount of total abdominal adipose tissue, especially VAT, has been demonstrated among ccRCC patients with KDM5C gene mutations compared with patients with VHL gene mutations.[5] In morbidly obese patients, VAT secretes high levels of Hypoxia-inducible factor 1α (HIF-1α). HIF-1 is associated with angiogenesis, tumor metastasis and tumor resistance to therapy.[5] The VHL protein contributes to HIF degradation, hence, with loss of VHL expression the lack of degradation of HIF determines angiogenesis and cell growth.[5]

Moreover, HIF determines an increased KDM5C activity, which acts as a tumor suppressor, activating a negative feedback loop on tumor growth.[5] The excessive amount of VAT found in ccRCC patients with KDM5C gene mutation compared to patients with VHL gene mutation could depend upon the inactivity of the KDM5C gene which, despite the excessive secretion of HIF-1α, cannot act as tumor suppressor.[5]

Considering the relationship among abdominal adipose tissue, especially VAT, and genetic mutations in ccRCC, it would be interesting to analyze clinicopathological comparison of gene expression by considering body composition and different genetic mutations profile of ccRCC.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

F Greco, B Beomonte Zobel[1,2], CA Mallio[1,2]

U.O.C. Diagnostica per Immagini Territoriale Aziendale, Cittadella della Salute Azienda Sanitaria Locale di Lecce, Piazza Filippo Bottazzi, Lecce, [1]Department of Medicine and Surgery, Università Campus Bio-Medico di Roma, Via Alvaro del Portillo, [2]Operative Research Unit of Diagnostic Imaging, Fondazione Policlinico Universitario Campus Bio-Medico, Via Alvaro del Portillo, Roma, Italy

Address for correspondence: Dr. F Greco, U.O.C. Diagnostica per Immagini Territoriale Aziendale, Cittadella della Salute Azienda Sanitaria Locale di Lecce, Piazza Filippo Bottazzi, 73100, Lecce, Italy.
E-mail: federicogreco@outlook.com

Received: 30-Jan-2022; **Accepted:** 27-Oct-2022; **Published:** 20-Dec-2022

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Quick Response Code:

Website: www.njcponline.com

DOI: 10.4103/njcp.njcp_80_22

How to cite this article: Greco F, Zobel BB, Mallio CA. Body composition imaging, clinicopathological status, and genetic profile in clear cell renal cell carcinoma. Niger J Clin Pract 2022;25:2081-2.