Editorial Commentary

Nephrometry score correlated with tumor proliferative activity inT1 clear cell renal cell carcinoma—the tiger in the tall grasses versus the cat in plain sight

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The authors Kikuchi *et al.* (1) aimed to correlate radiological risk stratification with the Ki-67 biomarker. In this article, the authors evaluated 145 pathological T1 clear cell renal cell carcinomas (RCC) and compared their renal nephrometry score (RNS) with tumor proliferative activity, as assessed by the Ki67 index and microvessel density.

Ki-67 is a marker of cell proliferation and performs a central role in cell division. It is expressed during all stages of the cell cycle except G0, and has been found to be co-expressed with other recognised proliferation markers (2). Studies have reported the association of Ki67 with poorer prognosis in various types of cancer. Dudderidge *et al.* performed immunohistochemical staining on 176 radical nephrectomy specimens with Ki67 antibodies and found that a labelling index of more than 12% heralded poorer prognosis for the patients with localised RCC (3). Xie *et al.*'s meta-analysis also correlated Ki67 expression with poorer prognosis and advanced clinicopathological features (2). It would be of great utility if we were able to determine the correlation between tumour pathology and Ki67 expression.

The RNS provides radiological description of renal masses from cross-sectional computed tomography (CT) imaging or magnetic resonance imaging (MRI) (4). The score is based on tumour characteristics, including size, depth and location. It has been extensively validated in numerous studies to compare treatment approach outcomes (5), and the likelihood of surgical complications (6). Kikuchi's study potentially provides the link between the complexity of the tumour, as represented by the RNS, and its malignant potential as measured by the levels of Ki67 expression.

While this is an interesting revelation on the relationship between tumour anatomy and proliferative potential, the authors could have studied the individual components of the RNS and correlated it to the Ki67, as opposed to merely examining the score as a whole. It is difficult to postulate from available data, but it appears that tumour complexity was more dependent on the location relative to polar lines, exophytic/endophytic properties and proximity to the collecting system as compared to radius or anatomic plane of the mass. It is logical that Ki-67, which is a known cell proliferation biomarker in many tumours, may correlate with pathological grading and staging. A more interesting question would be why a central (endophytic) tumour would have a higher Ki-67 index (2).

In addition, it would also be useful to study the expression of other relevant molecular markers besides Ki-67. In particular, the Hypoxia-Inducible Pathway, dysregulated signalling pathways involving the vascular endothelial growth factor, vascular endothelial growth factor and the mammalian target of rapamycin, have been found to be instrumental in the pathogenesis and progression of clear cell carcinoma. Hence, it would be ideal to correlate other relevant markers of interest with the RNS as well.

The author's study adds to the recently published body

of knowledge regarding association of kidney cancer anatomical features with cancer pathology or biology, by demonstrating the correlation of a high RNS score with greater tumour proliferative potential, with expectations of a more rapid growth rate. The RNS has also been shown to correlate with functional grade (7), risk of upstaging of a clinical T1 renal mass (8) and malignancy (9). We may opt for surveillance at higher frequencies, offer interventions at lower thresholds or offer surgery over ablative procedures for such patients.

In conclusion, the small exophytic tumour lying on the periphery is akin to a lower grade renal cell carcinoma with lower aggressive potential. It is easy to capture a cat in plain sight. However, the greater importance lies in eliminating the tiger lurking in the tall grass, the complex tumours with high RNS scores. Kikuchi *et al.*'s study suggest that image characteristics reflect molecular biological differences between the cat and the tiger and more work should be done to elucidate radiological and pathological predictors for tumour growth rate.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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