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We thank the editor(s) for their comment on our study, in which we examine the performance of the Mayo Clinic risk stratification score (or Leibovich score)[1] in UK patients with localised clear cell renal cell carcinoma (RCC). Outcomes by metastasis-free survival (MFS) amongst intermediate- or high-risk patients, according to the model, have improved over time. The implications of this for the clinic are important and readily apparent, since the model is widely employed to counsel patients, guide intensity of follow-up and for the design and powering of adjuvant trials. Our results mirror those of those of other recently reported data amongst US patients.[2]

The reasons behind this alteration in performance are likely multi-factorial. As highlighted, progress in imaging, surgical technique and pathological review that have taken place over the past several decades must be considered. A further, often overlooked, explanation may come from the fact that even our best current prognostic markers (in this case tumor size, stage, grade, presence or absence of necrosis) are still relatively poor at determining outcome at an individual patient level. The Mayo Clinic risk stratification score, amongst our contemporary cohort of patients, accounted for just 22% of the observed variance in MFS. In other words, the majority of the observed variance remains unexplained by the model alone.

The molecular complexity and heterogeneity that characterises RCC, as alluded to by the editor(s), remains unaccounted for in prognostic nomograms limited to gross pathology alone. If the goal of delivering truly personalised care to patients is to be met, robust biomarkers that can add value to and further refine existing risk-stratification tools must be identified. We acknowledge the challenges in achieving this, but assays such as the 16-gene recurrence score,[3,4] for example, provide sufficient promise to suggest these challenges are surmountable.

Successful translation of biomarkers to the clinic has been hampered both by a lack of a clearly defined evaluative infrastructure as well as limited availability of high quality, clinically annotated, biobanks of sufficient size to allow meaningful late-stage assessment of biomarker performance, as we have recently highlighted.[5] Underpinning the current study, samples of serum, plasma and urine were collected

by strict standard operating procedures prior to surgery in all patients, including healthy controls, and in a subset of RCC patients (n=200) longitudinally for up to 2 years. An archival tissue block was also collected. This multicentre UK RCC research tissue bank represents an important resource for prognostic and diagnostic biomarker validation studies in this disease and collaborative access is welcomed.

The use of prognostic models to individualise our approach to patient care remains integral to oncological practice. Model performance is, however, susceptible to alteration over time and periodic re-evaluation is necessary. Advances in -omic technologies are set to give us much more information to improve our ability to predict outcome, but at present we have to be very careful not to overestimate the accuracy and stability of prognostic indices.

References

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