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Re: Presence of Tumor Necrosis is Not a Significant Predictor of Survival in Clear Cell Renal Cell Carcinoma: Higher Prognostic Accuracy of Extent Based Rather Than Presence/Absence Classification

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To the Editor: We congratulate Klatte et al on their work and recent article. However, their conclusion that the presence of tumor necrosis does not provide independent prognostic information for patients with clear cell renal cell carcinoma (ccRCC) is concerning. This interpretation of their nonstatistically significant result is misleading and potentially harmful if read by clinicians unfamiliar with existing evidence.

Incorrect interpretation of statistically nonsignificant findings in urology is problematic, since nonsignificant results are often a reflection of inadequate power and not necessarily an absence of association.¹ To highlight this issue, we refer to the statistics that formed the basis of the study conclusions (table 2 in article). In the multivariable model the risk of death from ccRCC associated with the presence of necrosis was not statistically significant (HR 1.8, 95% CI 0.59 to 5.45). However, tumor stage (HR 1.42, 95% CI 0.95 to 2.13) and grade (HR 1.37, 95% CI 0.89 to 2.13) similarly were not statistically significant. Given the lack of statistical significance, should we conclude that tumor stage and grade are also of no importance? Clearly the probability of type II error is a concern in this analysis. Based on these data, authoritative statements about the futility of established prognostic factors are unsubstantiated and likely erroneous.

Application of the stage, size, grade and necrosis (SSIGN) score,² which incorporates the presence of coagulative tumor necrosis, gives credence to the independent usefulness of this feature.³ Coagulative tumor necrosis is a well-defined microscopic pathological feature, and must be separated from the more common degenerative features of fibrosis and fibrin deposition found in ccRCC. Large data sets consistently reveal that the presence of coagulative tumor necrosis carries important prognostic information that can be used for patient counseling and postoperative surveillance.^{4–7} The observation that the extent of necrosis may further stratify patient risk adds to our understanding, although it will be important (as the authors note) to validate these results externally in larger data sets.

We suspect that coagulative tumor necrosis is underreported by pathologists and underused by urologists despite the value of this information. Given the current evidence, and pending adequately powered contradictory data, the presence of coagulative tumor necrosis should be considered a strong adverse prognostic feature of ccRCC.

Respectfully,

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