Letter to the Editor

Below safety limits, every unit of glomerular filtration rate counts—reply letter

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Response to: Mistretta FA, Mazzone E, Knipper S, et al. Benefit of nephron sparing surgery translates into lower cancer specific mortality in patients with localized renal cell carcinoma. Ann Transl Med 2018;6:S104.

Veccia A, Autorino R. Is there a relation between preserved renal function and oncological outcomes in patients undergoing partial nephrectomy for renal cell carcinoma? Ann Transl Med 2018;6:S88

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We value the editorials by Mistretta *et al.* (1) and Veccia *et al.* (2) on our recently published paper "*Below safety limits, every unit of glomerular filtration rate counts: assessing the relationship between renal function and cancer-specific mortality in renal cell carcinoma*" (3).

The authors (2) noted that our results seemed to be paradoxically in contrast with previous papers that showed that partial nephrectomy in the imperative setting was associated with higher recurrence, as well as higher cancer-specific mortality (CSM), even though it provided better preservation of renal function (4). Additionally, as reported by the authors, a previous study showed that patients with preoperatively impaired renal function tended to recover it after radical nephrectomy, more likely among patients with lower preoperative estimated glomerular filtration rate (eGFR) (5). Unfortunately, we were not able to specifically investigate the subset of patients, who were treated with partial nephrectomy due to an imperative indication. Nevertheless, sub-analyses according to type of surgery were performed. Specifically, a linear and inverse relationship between postoperative eGFR and CSM was found only below the breakpoint of 65 mL/min for both partial and radical nephrectomy groups. It may be postulated that in patients for whom postoperative eGFR could be secured above this threshold, the role of surgery may be less determinant.

We also agree with the authors that the retrospective nature of our database may represent an important weakness of our study. Additionally, the multicenter source of data entailed a certain degree of heterogeneity in surgical techniques, peri-operative management, pathological assessment and follow-up schedules. Nonetheless, we attempted to overcome at least part of these issues by using multiple statistical approaches to assess the potential relationship between eGFR and CSM. All our models were adjusted for several confounders and all invariably supported our hypothesis. Nonetheless, we acknowledge that our results should be cautiously interpreted. Indeed, a multifaceted interplay exists among renal function, host and cancer (6), so that causal associations should not be attempted through a retrospective trial.

Finally, we agree with Mistretta *et al.* (1), as well as Veccia *et al.* (2), that additional studies are warranted to better elucidate the potential relationship between eGFR and CSM. Nonetheless, the results of our paper further highlight that preservation of renal function should be among priorities when planning surgery per kidney cancer.

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Footnote

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

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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