12-1-2021

AUTHOR REPLY

Marcus Jamil
Henry Ford Health, mjamil1@hfhs.org

Patrick Etta
Henry Ford Health, petta1@hfhs.org

Firas Abdollah
Henry Ford Health, FABDOLL1@hfhs.org

Recommended Citation
Jamil M, Etta P, and Abdollah F. AUTHOR REPLY. Urology 2021; 158:115-116.

11. Su C, Peng C, Agbodza E, et al. Publication trend, resource utilization, and impact of the US National Cancer Database: a systematic review. *Med (Baltimore)*. 2018;97:e9823.
12. Brenner DJ, Hall EJ. Computed tomography — an increasing source of radiation exposure. *N Engl J Med*. 2007;357:2277–2284.
13. Ingimarsson JP, Sigurdsson MI, Hardarson S, et al. The impact of tumour size on the probability of synchronous metastasis and survival in renal cell carcinoma patients: a population-based study. *BMC Urol*. 2014;14:72.
14. Pierorazio PM, Johnson MH, Ball MW, et al. Five-year analysis of a multi-institutional prospective clinical trial of delayed intervention and surveillance for small renal masses: the DISSRM registry. *Eur Urol*. 2015;68:408–415.
15. Patel HD, Nichols PE, Su ZT, et al. Renal mass biopsy is associated with reduction in surgery for early-stage kidney cancer. *Urology*. 2020;135:76–81.
16. Frank I, Blute ML, Cheville JC, et al. Solid renal tumors: an analysis of pathological features related to tumor size. *J Urol*. 2003;170 (6 Pt 1):2217–2220.

EDITORIAL COMMENT

The increased use of cross-sectional imaging has led to significant stage migration in renal cell carcinoma (RCC). As more computed tomography (CT) and magnetic resonance imaging scans are performed for unrelated conditions, more RCCs have been detected − particularly small, asymptomatic lesions. For larger RCCs, obtaining chest imaging to rule out synchronous lung metastasis (sLM) remains an important clinical principle, supported by current guidelines. However, regarding chest imaging, guidelines do not necessarily reflect the stage migration in RCC over the past decade.[1] As smaller, more indolent, RCCs are detected the optimal role of chest imaging with initial RCC diagnosis remains unclear.

The authors of this well-presented manuscript investigated the rate of sLM in RCC, stratifying patients by tumor size. While prior studies have demonstrated a correlation between increasing tumor size and synchronous metastasis, the strength and slope of this relationship remain unclear in contemporary patients. By examining this statistical relationship, clinicians may better understand sLM rates for a newly diagnosed RCC and offer chest imaging when most appropriate.

The authors utilized the National Cancer Database, evaluating 253,838 patients with RCC between 2010 and 2016. Of these patients, 5.7% (14,524) had a sLM. Patients were stratified by RCC size and the rate of sLM was calculated at 10-millimeter (mm) intervals. For tumors under 40 mm, only 0.9% had an sLM. Conversely, for tumors 90 mm and above, the sLM rate was roughly 20%. Figure 1 illustrates this graphically as the sLM versus RCC size plot produces a linear-quadratic function. Multivariable logistic regression also demonstrated that RCC size remained an important predictor of sLM, particularly for those greater than 40 mm (Table 2).

The above study offers important insights regarding the incidence of sLMs in patients with newly diagnosed RCC. Of note, approximately 8% (1,135/14,525) of patients with a sLM had a RCC <40 mm. Avoiding low-yield imaging for lower risk lesions could influence healthcare costs, radiation exposure, and patient counseling.[2] However, the treatment paradigms for patients with metastatic RCC differ vastly from those for localized disease, including the clinical trial options available.[3] Patients with oligometastatic disease often require systemic therapy, cytoreductive nephrectomy, and/or metastasectomy.[4] While sLMs in cT1a RCC are rare, missing these cases may have a profound effect on treatment decisions and survival outcomes. Thus, implementing a risk-adapted chest imaging protocol requires careful patient counseling. One must not only incorporate rates of sLM into the discussion, but also the impact of not capturing sLM at the time of diagnosis, and its potential implications for survival.

Arnav Srivastava, Brian Shinder, Eric A. Singer,
Rutgers Cancer Institute of New Jersey, Section of Urologic Oncology

References

1. Campbell S, Uzzo RG, Allaf ME. et al. Renal mass and localized renal cancer: AUA Guideline. *J Urol*. 2017;198:520–529. [cited 10/1/2020].
2. Farber NJ, Kim CJ, Modi PK, Hon JD, Sadimin ET, Singer EA. Renal cell carcinoma: the search for a reliable biomarker. *Transl Cancer Res*. 2017;6:620–632. https://doi.org/10.21037/tcr.2017.05.19.
3. Patel HV, Shinder B, Srinivasan R, Singer EA. Challenges and opportunities in the management of metastatic renal cell carcinoma: combination therapy and the role of cytoreductive surgery. *Curr Opin Oncol*. 2020;32:240–249. https://doi.org/10.1097/CCO.0000000000000621.
4. Schmidt AL, Tabakin AL, Singer EA, Choueiri TK, McKay RR. Next steps: sequencing therapies in metastatic kidney cancer in the contemporary era. *Am Soc Clin Oncol Educ Book*. 2021;41:1–11. https://doi.org/10.1200/EDBK—320785. MarPMID:33793313.

https://doi.org/10.1016/j.urology.2021.04.076
UROLOGY 158: 115, 2021.

AUTHOR REPLY

We thank Dr. Singer and colleagues for their thoughtful comments on our investigation of synchronous lung metastasis (sLM) in patients with newly identified renal masses (RMs). As stated in our original investigation and by the editors, we assessed a large cohort of 253,818 patients. Of these patients, 120,386 (47%) had a RM size <40 mm. Furthermore, only 0.9% of patients with a RM size <40 mm displayed sLM. When examining only patients with confirmed sLM we found that only 8% (1,135/14,524) had a RM <40 mm.

It is paramount to consider the malignant and metastatic potential of small renal masses (SRM) when interpreting our data. Previous investigations have shown that 20%-40% of SRMs are in fact benign.[1] All RMs in our investigation had histopathological confirmation of malignancy, therefore, our results likely over inflated the true metastatic potential of SRMs one would identify in the general population, again putting into question the true utility of staging chest imaging for RM <40 mm. It is also noteworthy that the presence of *positive* chest imaging does not automatically conclude the presence of metastatic disease. Interestingly, examining a population of patients with SRMs managed with surveillance, Kassiri et al reported that among patients with lung findings which were deemed actionable, 0% were found to be metastatic lesions.[2] This further highlights that the radiative, emotional, and cost burden of potentially unnecessary workup may not always halt with initial

chest screening but can be prolonged in pursuit of ultimately negative diagnostic tests and procedures.

Lastly, the author's agree with the editor's comment regarding the potentially devastating effect of missing sLM. That said, cut-offs in medicine are generally based on a delicate balance of benefit versus cost. For example, it has been shown that a small percentage of patients with a PSA < 4.00 ng/mL harbor high-risk prostate cancer, yet contemporary guidelines recommendation against biopsy in these individuals because of the very limited benefit and yield.[3,4] Ultimately, the authors emphasize the importance of a shared and well-informed decision between a patient and provider in the initial staging of SRMs.

Acknowledgements. None

Marcus Jamil, Patrick Etta, Firas Abdollah, Vattikuti Urology Institute Center for Outcomes Research, Analytics and Evaluation (VCORE), Vattikuti Urology Institute, Henry Ford Health System, Detroit, MI

References

1. Pierorazio PM, et al. Five-year analysis of a multi-institutional prospective clinical trial of delayed intervention and surveillance for small renal masses: the DISSRM registry. *Eur Urol*. 2015;68:408–415.
2. Kassiri B, Cheaib JG, Pierorazio PM. Patients with small renal masses undergoing active surveillance-is yearly chest imaging necessary? *J Urol*. 2019;201:1061–1063.
3. Mahal BA, et al. Association of very low prostate-specific antigen levels with increased cancer-specific death in men with high-grade prostate cancer. *Cancer*. 2016;122:78–83.
4. Mahal BA, et al. Clinical and genomic characterization of low-prostate-specific antigen, high-grade prostate cancer. *Eur Urol*. 2018;74:146–154.

https://doi.org/10.1016/j.urology.2021.04.077
UROLOGY 158: 115–116, 2021.