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LETTER TO THE EDITOR

"Novel" nomogram and algorithm do not aid in the distinction of primary vs. metastatic mucinous carcinoma of the ovary: letter to the Editor

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To the Editor,

Classifying mucinous adenocarcinomas of the ovary as primary or metastatic continues to bedevil the practicing pathologist, and yet, for management and prognosis, this is a critical distinction. Recently, Simons et al. undertook this formidable task and published an 11-year retrospective review of 1753 primary ovarian (MOC) and metastatic to the ovary (mMC) mucinous carcinomas [1]. Briefly, of their cohort, the majority (58%) were mMC, of which almost half (49.9%) involved the adnexa bilaterally, and carcinomas demonstrating signet ring morphology were almost exclusively metastatic (98.4%). In comparison, MOC patients were significantly younger (54.6 vs. 59.6 years; $p < 0.01$) and had larger tumors (19.0 vs. 12.0 cm, $p < 0.001$) which were more often unilateral (90.1%). Simons et al. state that larger unilateral tumors in younger patients tend to be of primary ovarian origin [1]. Using these variables, Simons et al. have suggested an algorithm and a "novel" nomogram with "higher sensitivity but lower specificity compared to earlier algorithms" which aid in indicating tumor origin [1].

In our single institution's experience and retrospective review of mucinous carcinomas of the ovary over 15 years (as yet unpublished data), we identified 24 MOC and 20 mMC and came to somewhat different conclusions. A slight majority of tumors (55%) were of primary ovarian origin, and 45% were mMC. Interestingly, mMC showed bilateral ovarian involvement in only 38.9% of our patients. Our cohort of patients was older, and as it pertains to MOC vs. mMC, patient age differences were not statistically significant (60 vs. 64.4 years; $p > 0.05$). Tumor size varied widely (0.8–30 cm) in both categories but similar to the Simons' data, on average MOC were larger (12.1 vs. 6.9 cm). Overall, the left ovary was involved more often than the right (71% vs. 54%).

Differences between the two data analyses could be explained by population bias, cohort size, and variability in methods of extracting data and assigning final designation of primary vs. metastatic. However, we struggle in understanding the rationale of the proposed nomogram. It denotes patients with a $\text{Score}_{(\text{size+age})} < 6.1$ are the only patients meeting criteria for metastatic disease, and to obtain such a low score, one must be either extremely young (< 20 years) or with a rather small tumor (< 7 cm). Most pathologists would have a high level of certainty assessing a small unilateral tumor in a young patient, which, conversely to the nomogram's illustration, is the clinical scenario most compatible with a primary ovarian tumor. At the same time, older patients or those with a larger adnexal mass may be considered to have a primary ovarian origin tumor because the age and/or size will incur a $\text{Score}_{(\text{size+age})} \geq 6.1$. Lastly, this crucial point, namely 6.1, is not even illustrated on the graph, and one must "guesstimate" its location. While this visual tool describes an easy to follow algorithm, we believe it is not more reliable in replacing established principles [2, 3].

In our opinion, and as illustrated by our data and in part by Simons' data, age of presentation, tumor size, and unilateral vs. bilateral ovarian involvement serve as general guidelines. We agree with Simons that signet ring morphology should prompt evaluation for metastatic disease [1]; we also agree that immunohistochemical discernment is not entirely conclusive. We concur wholeheartedly that only "multidisciplinary communication" can adequately establish primary vs. metastatic disease in patients with this unfortunate malignancy [1]. However, the nomogram is not the solution.

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Contributions Dr. Komforti was responsible for the concept and design of the manuscript, the data collection on mucinous carcinomas, and manuscript preparation. Dr. Thomas was responsible for the analysis of the data and manuscript preparation and revisions.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

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Dr. Komforti performed the data collection and analysis while employed by Northwell Health.