Editorial

The timing of radical cystectomy following neoadjuvant chemotherapy

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Low-morbidity therapies such as intravesical chemo- and immunotherapies and transurethral resection of bladder tumor (TURBT) are effective options for patients with localized, non-invasive bladder cancer. However, muscle-invasive bladder cancer (MIBC) typically requires more definitive management that is often associated with a higher morbidity and a higher rate of perioperative complications, and radical cystectomy (RC) is regarded as the standard of care for patients with advanced disease (1). The literature is replete with evidence supporting the use of chemotherapy in conjunction with RC, and more recent efforts have elucidated a survival benefit with neoadjuvant chemotherapy (NAC) delivered prior to RC versus adjuvant chemotherapy (AC) shortly after the time of surgery (2).

Mmeje and colleagues have conducted a timely and highly relevant retrospective study concerning the perioperative profile of patients receiving NAC prior to RC (3). With a focus on the recovery window (RW; the time between NAC administration and RC), they generated two hypotheses: (I) patients can undergo RC at earlier timepoints after receiving NAC without increasing the risk of perioperative morbidity, and (II) an increased RW between NAC and RC corresponds with an increased risk of lymph node (LN) metastasis. Expectedly, patients with the longest RWs were more likely to have extravesical disease and LN metastasis at the time of RC, though what is less clear is precisely what rationale was used to define the various RW cohorts (21d intervals) at the start of the study.

Globally, Mmeje and colleagues present findings that also align with the experiences at our institution. More importantly, the study raises even more questions that would be amenable to further analysis. For example, the authors state that both age and operative time were factors associated with increased complication rates. We would be interested in the authors' discussion of matched age groups across the various RW cohorts and valuation of whether two patients of the same age in different cohorts varied in their complication rates. Second, matching patients by ethnicity and degree of exposure to known bladder carcinogens, for instance, would also provide surgeons with a broader, more nuanced understanding of the bladder cancer patient landscape in the context of MIBC treatment. Third, the authors have pointed out that they retrospectively analyzed multiple chemotherapy regimens. While it would be interesting to assess the incidence nodal metastases, complications, and RW as a function of the specific regimen, the retrospective nature of the analysis would likely have made statistical power difficult to achieve with their existing patient database.

Fourth, a very recent study in *The Lancet* demonstrated the non-inferiority of robotic cystectomy versus open surgery (4). Both approaches were similar with respect to adversities such as urinary tract infections and postoperative ileus. As robotic approaches gain prevalence, efforts should also be undertaken to assess their role in the multimodal approach to MIBC management, specifically in the context of NAC versus AC administration.

Lastly, there are a variety of social factors that act as

certain confounders in the treatment of MIBC. While this particular study assesses tangible, quantifiable factors such as age, operative time, estimated blood loss (EBL), readmission rate, etc., it is more difficult to systematically evaluate or predict factors such as patient preference, tolerance of NAC, overall care philosophy, healthcare literacy, physician bias, and likelihood for intermittent loss to follow-up. Regarding the latter, the authors allude to the likely significant differences in the rate of follow-up and adherence to structured care plans (critical to the care of patients with complex disease) between the major academic centers and the community and private hospitals through which, presumably, the vast majority of urologic care is delivered. Expanded analysis of all of these factors combined with the recent breakthroughs in genomic analysis will yield tools to further refine the personalization of MIBC treatment strategies, durations, and aggression. This study is an essential step in that direction.

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Footnote

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

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