Perioperative chemotherapy for muscle-invasive bladder cancer: Closing the gap between evidence and practice

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See related article on page 25.

Cite as: *Can Urol Assoc J* 2016;10(1-2):31-2. http://dx.doi.org/10.5489/cuaj.3600
Published online February 8, 2016.

Practice guidelines recommend neoadjuvant chemotherapy (NAC) for muscle-invasive bladder cancer (MIBC) on the basis of meta-analysis showing an improvement in long-term survival of approximately 5%.[1-4] Due to the absence of level 1 evidence, existing guidelines do not strongly support the use of adjuvant chemotherapy (AC). However, emerging evidence provides growing support for use of AC[5-7] and it is likely that future guidelines will advocate that patients receive either NAC or AC.

Despite practice guidelines, international studies show a disconnect between evidence and practice. We have previously described real world practice patterns in Ontario.[8] Between 1994 and 2008, NAC was used in only 4% of patients, while AC was delivered to 18%. There was no significant uptake of NAC over time. Similar trends have been found in several other population-based studies of bladder cancer.[9-11] Potential reasons for underuse of NAC are not well-understood, but may relate to clinicians prioritizing local treatment, medical contraindications to chemotherapy, and patient preferences.[12] More recent data suggest use of perioperative chemotherapy may be increasing. Using the National Cancer Database in the U.S., Reardon et al found that use of any perioperative chemotherapy (i.e., NAC or AC) increased from 30% to 40% ($p<0.001$); most of this increase was driven by uptake of NAC, which increased from 10% to 21% ($p=0.005$).[13] Our group at Queen's University is currently updating our Ontario data set to evaluate whether chemotherapy use has changed from 2009–2013.

While the literature is replete with reports describing low use of NAC for bladder cancer, relatively few studies have sought to change clinical practice. Nayan et al are to be congratulated for their elegant study reported in this issue of *Canadian Urological Association Journal* (*CUAJ*). In this study they describe use of NAC/AC at University Health Network (UHN) from 2000–2013. The group at UHN implemented a multidisciplinary bladder cancer clinic (MDBCC) in 2008 and used time series analysis to evaluate the extent to which this clinic may have changed practice. The very description of the MDBCC itself is a useful addition to the literature, as this model of care has the potential to impact overall quality of care for bladder cancer beyond chemotherapy alone. Use of NAC increased significantly over time (8% to 48%, $p=0.036$) and time series analysis suggests this increase was due, at least in part, to the advent of the MDBCC. The paper would have been even stronger if details had been provided regarding which patients did (and did not) attend the MDBCC; this would allow readers to better understand the external validity of the results. It is also notable that overall use of any perioperative chemotherapy (i.e., NAC or AC) did not change over the study period (42% [70/168] in 2000–2007 period and 42% [46/110] in 2008–2012 period). Accordingly, the data suggest that rather than increasing use of chemotherapy, during the study period patients became more likely to have NAC instead of AC. The extent to which this will lead to improved outcomes is not known. Finally, Nayan et al raise an important point by acknowledging that optimal utilization rate of chemotherapy in this setting is not known. Given that up to half of patients with MIBC are not eligible for cisplatin-based therapy,[14,15] practice within UHN may be approaching the optimal chemotherapy utilization rate.

The MDBCC described by Nayan et al represent an important step in improving care of patients with bladder cancer, but much work remains. The MDBCC may serve as a model of care for other jurisdictions to consider as we try to close other known gaps related to provider volume,[16,17] lymph node harvest,[18] and low use of bladder sparing protocols[19] in Ontario. However, as we work to improve health system performance and quality of care, we must be mindful of the fact that even with optimal delivery of our current

gold standard, a substantial proportion of our patients will ultimately relapse and die. This speaks to the importance of clinical trials and health services research working in parallel to identify novel therapies to improve patient outcomes and using real world data to understand how to optimally deploy them in practice.

Competing interests: The author declares no competing financial or personal interests. Dr. Booth is supported as the Canada Research Chair in Population Cancer Care

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