

Optimizing care and outcomes of patients with muscle-invasive bladder cancer

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Cite as: *Can Urol Assoc J* 2013;7(9-10):e625-7. <http://dx.doi.org/10.5489/cuaj.1698>
Published online October 9, 2013.

“**A**chieving the achievable” for patients with cancer requires that health providers and systems optimally use the best knowledge we already have.¹ Fundamental questions that drive any quality improvement initiative include:

- **Adoption:** Are we treating the right patients? If not, why not?
- **Quality of care:** Are we treating patients the right way? If not, why not?
- **Outcomes:** Are we achieving the expected patient outcomes? (**Effectiveness**).
 - If not, is the efficacy-effectiveness gap explained by sub-optimal adoption, quality of care and/or other factors? (**Processes of Care**)

Answers to these questions will identify remediable problems in the delivery of care, which in turn will inform future **Knowledge Translation** to improve the patient outcomes.² The Canadian Association of Genitourinary Medical Oncologists (CAGMO) Consensus Statement regarding the use of neoadjuvant chemotherapy (NACT) for muscle-invasive bladder cancer (MIBC) is an important step towards improving the care of patients with this disease.³

What does the current evidence tell us about optimal management of MIBC?

Definitive management of MIBC involves cystectomy or radical radiotherapy (RT). There is a surprising lack of good comparative data evaluating whether one modality is superior to the other; it is, therefore, not surprising that variations in practice exist worldwide. This is reflected in the substantial discordance of international guidelines for the definitive management of MIBC; some guidelines strongly recommend

cystectomy over RT, while other guidelines endorse both treatment options.⁴⁻⁸ The evidence and guidelines are much clearer for NACT. Efficacy of NACT has been clearly defined in a series of well-designed clinical trials and subsequent meta-analyses.⁹⁻¹³ The efficacy of adjuvant chemotherapy (ACT) is less clear, although the limited available evidence does suggest it might benefit patients with an effect size comparable to NACT.¹⁴⁻¹⁷ Based on this evidence, international guidelines recommend NACT for patients with MIBC, but do not endorse ACT.¹⁸⁻²⁰

What do we know about treatment in routine clinical practice?

Unlike in some parts of Europe and Asia where RT is the preferred definitive treatment option for MIBC, North America has shown marked shifts in practice away from RT towards cystectomy. In many North American jurisdictions, the use of radical RT for MIBC is largely restricted to patients of advanced age and/or comorbidity.²¹⁻²⁴ While differences in utilization of cystectomy or RT may be understood on the basis of a lack of comparative evidence, the use of perioperative chemotherapy in routine practice is not consistent with evidence of guidelines.

Multiple population-based reports in the United States^{22,25,26} and Canada^{17,27} have reported dismally low rates of NACT utilization. Paradoxically, most studies report higher rates of ACT. This latter finding is particularly striking and suggests that patient and physician preferences need to be carefully considered in light of any program designed to improve the quality of care.

CAGMO Consensus Statement

On this background, Seah and colleagues should be congratulated for their thoughtful and comprehensive review of

the evidence for NACT in MIBC and the streamlined process of care they propose.³ The consensus statement provides clear direction for practitioners regarding referral patterns, relevant investigations, timelines for care, and treatment recommendations. In addition to their careful review and well-constructed consensus statement, the CAGMO group also plans to study future NACT practices in Canada to see whether there is any improvement over time. It would have been helpful for the group to have done a baseline quantitative analysis of practice before publication and dissemination of the document. This would have allowed for a more insightful follow-up analysis. Despite this limitation, the authors have addressed an important issue and are making efforts to improve care in a very real way.

Further efforts are required to better understand the barriers to use of NACT. Although not the focus of their article, the potential underlying reasons for underutilization of NACT were discussed by Seah and colleagues. Patient preference and shared decision-making have not been well-described in MIBC. Findings from other studies suggest that there is considerable variability among patients regarding what factors influence their treatment preferences.^{28,29} Based on my own clinical experience, I believe that the absolute survival benefit of 5% is considered by many clinicians and patients to be modest in magnitude. The CAGMO authors believe the effect size of NACT for bladder cancer is comparable to the benefit of ACT for breast and colon cancer – on this point I would disagree. The relevant overviews in breast³⁰ and colon cancer³¹ suggest the effect size of ACT is slightly greater than 5% for all patients, and substantially greater than 5% among those patients with node positive disease. Future work is needed to understand how we might be able to use molecular tools to identify patients with MIBC who are likely to derive the greatest benefit from NACT. Indeed, treatment in the preoperative setting provides an ideal research model to identify biomarkers that could influence how we treat patients with this disease.³² Other aspects of quality care that require attention include the oft-forgotten role of curative intent RT for MIBC and the known association between cystectomy surgical volume and patient outcomes.³³

While we wait for new treatments and molecular tools, we need to do a better job of using the best available knowledge to provide the best available treatment to our patients with MIBC. The consensus statement and the model of care proposed by Seah and colleagues is an important step in this direction.

Competing interests: None declared.

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