

Finding treatment success in patients unfit for radical cystectomy

Michael Leveridge, MD, FRCSC

Department of Urology, Department of Oncology, Kingston General Hospital/Queen's University, Kingston, ON, Canada

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Bladder cancer is a disease of the elderly, whose incidence continues to rise along with age at rate of up to 296 per 100 000 men and 74 per 100 000 women aged 85 and above.¹ Applying our standard treatment decisions to the elderly is fraught due to their rise in comorbidities, which obviate or dramatically increase the risks of treatment. McPherson et al from Western University have studied these highest-risk patients and found that trimodal therapy that avoids cystectomy can provide very reasonable outcomes with modest toxicity.²

Urologists are typically the first point of contact in diagnosing muscle-invasive bladder cancer (MIBC) and act as *de facto* quarterbacks for subsequent referral and care. Our weapon of choice has always been cystectomy; it is the standard for curative management, controls local disease, and decreases the complexity of followup. The authors point out though that morbidity and mortality rise from the already significant baseline in octogenarians. More recent population data from Ontario, in fact, show that 30- and 90-day mortality after radical cystectomy in octogenarians is 6% and 15%, respectively.³ Three-year overall and disease-free survival in this age group was about 35% and 40%, respectively (after cystectomy). The current study cohort, explicitly in worse medical condition than selected-for-cystectomy patients nonetheless fared better. It is heartening to see therapeutic options that seem to carry less early risk to the patient.

This study is also notable for the contortions undertaken to ensure that patients received chemotherapy in some form, even if the standard cisplatin was contraindicated. A weakness here is that we don't know the denominator of all elderly patients at this centre (from those fit for surgery through those whose comorbidities leapfrog the study cohort, too ill for chemoradiation), but it is clear that an effort to treat medically tenuous patients (25% Eastern Cooperative Oncology

Group [ECOG] 2+, only 12.5% ECOG 0) was made. Prior studies have shown decreased medical oncology referral and use of chemotherapy in older patients.³⁻⁵ Dash et al showed that over 40% of bladder cancer patients over age 70 were cisplatin-ineligible, while Gupta et al showed lower use of cisplatin in chemotherapy-treated MIBC patients in a Surveillance, Epidemiology, and End Results (SEER)-Medicare analysis (53% for patients <75 years vs. 30% for those 80+ years).^{6,7} The presence of hydronephrosis in one-third of McPherson et al's cohort suggests a similar level of risk.

Numbers are too low to confirm that a conventional treatment course of radiotherapy should be applied over a lower-dose protocol, but the toxicity data and trends here suggest that an effort to maximize local therapy may benefit survival without Grade 3–4 toxicity. In a phase 3 study of radiotherapy vs. chemoradiotherapy (as the authors here discuss), a 62Gy/32 fraction protocol was not significantly different from a 55Gy/20 fraction course (hazard ratio favouring chemotherapy 0.63 [95% confidence interval 0.41–0.98] vs. 0.77 [0.43–1.36]).⁸

Finally, while these encouraging results are seen in the setting of a multidisciplinary, tertiary cancer centre (and in comparison to population data lend support to such centralization of complex care), it is notable that only 31 patients (78%) appear to have had a surveillance cystoscopy and followup imaging was left to the "discretion of the clinical team."² Rigorous adherence to a followup schedule may eke out a small additional benefit to the outcomes noted.

We are limited somewhat by the unknown selection criteria and small numbers, but this study does reveal that acceptable survival and local control outcomes, historically comparable to radical cystectomy, can be achieved in unwell, older patients. Patients with impaired performance status or some renal dysfunction clearly should not be discounted from receiving chemotherapy. Importantly, these data do not suggest that cystectomy is unwise or unacceptably risky in healthy octogenarians, but it is a powerful tool that comes at a cost that may be untenable in the old or infirm. Knowing that safe and effective treatment may still

be afforded these patients, however, may make urologists feel less compelled to offer high-risk surgery to the patients at highest risk of harm.

Competing interests: The author reports no competing personal or financial interests.

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Correspondence: Dr. Michael Leveridge, Department of Urology, Department of Oncology, Kingston General Hospital/Queen's University, Kingston, ON, Canada; leveridm@kgh.kari.net; twitter: @_TheUrologist_

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Fizazi et al. study²

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