

## Preventable Cancer Deaths Associated with Bladder Preservation for Muscle Invasive Bladder Cancer



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This commentary introduces the concept of preventable cancer death associated with bladder preservation for muscle-invasive bladder cancer (MIBC). Neoadjuvant chemotherapy (NAC) and radical cystectomy (RC) is the standard of care for most MIBC. Another approach is bladder preservation. Trimodal therapy (complete transurethral resection [TUR] and chemo-radiation<sup>1</sup> or NAC and bladder-sparing surgery (BSS),<sup>2</sup> offer survival rates similar with cystectomy in properly selected cases. Tumor recurrence in the bladder is common after bladder sparing, however the impact of local recurrence on mortality is neither well defined nor emphasized in bladder preservation studies. This study determines the risk of dying of bladder cancer in a mature cohort of patients who deferred a post-NAC RC in favor of treatment by NAC and BSS (NAC and TUR alone is not considered a standard of care).

From 1994 to 2015, 159 patients who had solitary, small (<5cm), organ-confined invasive bladder cancer opted for BSS (radical TUR alone and surveillance (100 patients) or open partial cystectomy (59 patients) after they achieved a complete clinical response to NAC. Complete clinical response was defined as no residual disease (cT0) on post-NAC radical TUR of the primary tumor site and negative CT/MRI scans. Patients were followed every 6 months for 5 years, annually thereafter, with cystoscopy and radiologic imaging.

The median age was 75 years (18-96 years), and 75% were males. With median follow-up of 77 months (range, 24-120 months), the overall and cancer specific survival was 75% and 93%, respectively, and 137 patients (86%) retained the bladder. Of the 159 patients, 12 (7.5%) have died of bladder cancer. Bladder relapse occurred in 57 patients (36%). **Figure 1** shows survival among patients who did or did not recur in the bladder. Bladder cancer-free

survival was 96% in patients who had no recurrence in the bladder v 86% of those who relapsed in the bladder ( $P = .02$ , log rank). Forty-five patients (78%) recurred with noninvasive tumors and 12 (22%) had muscle-invasive cancers. **Figure 2** shows bladder cancer-free survival by stage of recurrence in the bladder. There was no difference in survival between patients who had no (96%) or noninvasive bladder tumors (93%). Of 12 patients who had recurrent MIBC, only 7 (58%) were salvaged by delayed RC, and 5 (42%) died of metastatic bladder cancer ( $P = .001$ , log rank). The median time to noninvasive or MIBC local relapse was 16 months and 19 months, respectively, and median time to metastases was 34 and 16 months after detection of local recurrence. Four patients who did not recur in the bladder have died of systemic disease.

### COMMENTARY

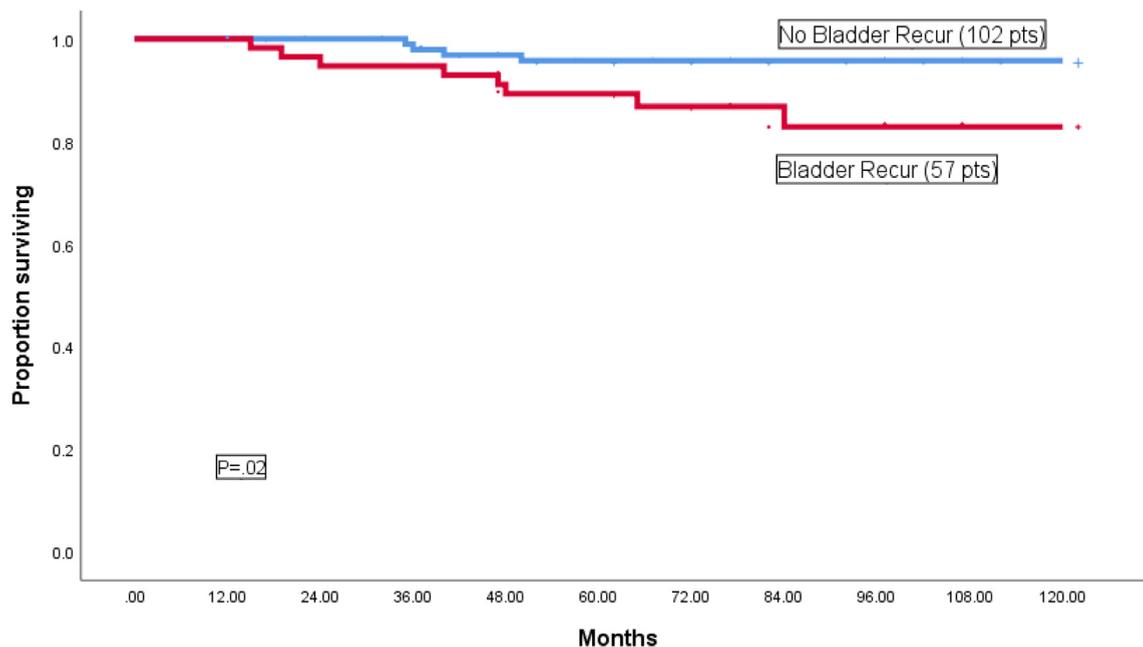
This report introduces the concept of preventable cancer deaths associated with local tumor recurrence after successful bladder preservation that may not have occurred with immediate cystectomy. Tumor recurrence in the bladder after complete response to bladder sparing strategies occurs in at least a third of patients. Most can be treated successfully by TUR and intravesical therapy or salvage RC. Some cannot, leading to local and systemic spread ultimately causing a cancer death. Assuming all 8 patients who failed in the bladder and died would have survived had they undergone NAC and RC, places the excess mortality risk in this bladder preservation study at 5%, although there is no guarantee earlier RC would have saved all these patients. In another robust study (median follow-up, 9 years), 125 (36%) of 342 complete responders to trimodal therapy recurred in the bladder.<sup>3,4</sup> Thirty-five of these patients eventually died of disease (derived from figures in papers) despite salvage RC, for an excess mortality rate of 9%. Thus, in these 2 mature bladder preservation studies, potentially preventable cancer deaths occurred in 5%-9%. For some patients, that may be an acceptable risk to save the bladder; for others, it may be too high.

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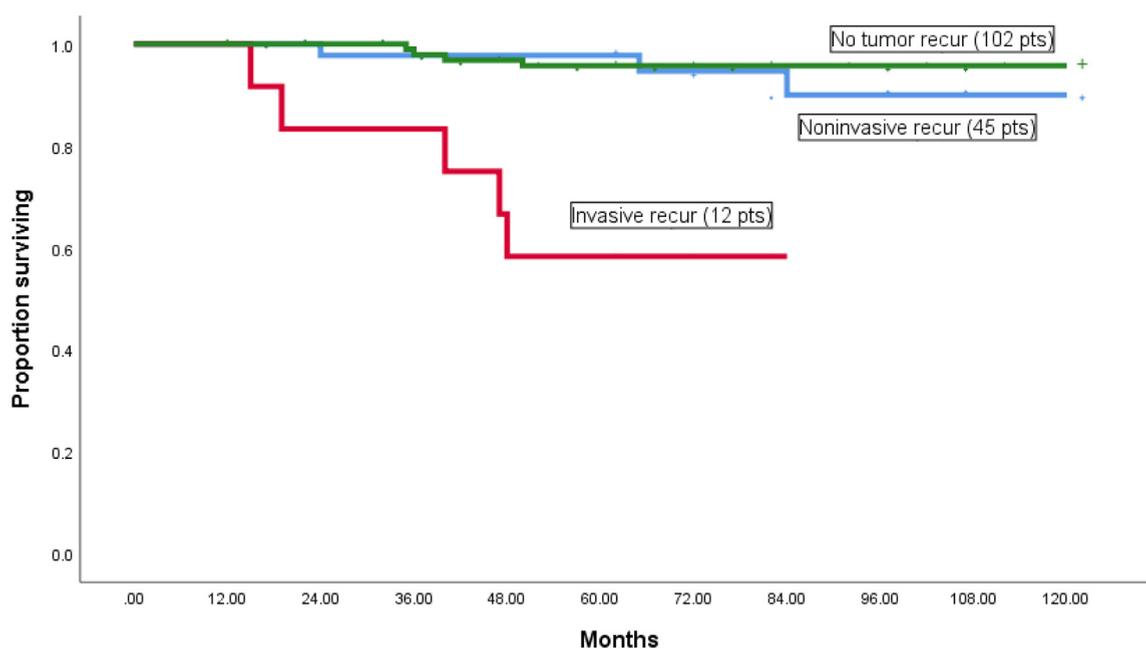
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**Figure 1.** Bladder cancer-free survival by tumor recurrence in the bladder. (Color version available online.)



**Figure 2.** Bladder cancer-free survival by stage of tumor relapse in the bladder (no tumor recurrence in bladder, 102 pts, 4 died; noninvasive tumor recurrence, 45 pts, 3 died; muscle-invasive tumor recurrence, 12 pts, 5 died). (Color version available online.)

## References

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