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Re: Long-Term Outcomes in Patients with Muscle-Invasive Bladder Cancer after Selective Bladder-Preserving Combined-Modality Therapy: A Pooled Analysis of Radiation Therapy Oncology Group Protocols 8802, 8903, 9506, 9706, 9906, and 0233

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Editorial Comment

For this widely reported study 6 different RTOG (Radiation Therapy Oncology Group) trials (5 phase II and 1 phase III) were pooled to examine 468 patients with muscle invasive bladder cancer who underwent bladder preserving, combined modality therapy. This therapy includes maximal transurethral resection, radiation and concurrent chemotherapy, and importantly prompt salvage radical cystectomy for those who do not respond.

In this group 69% of patients had a complete response, defined as no masses on examination while under anesthesia, no cystoscopic visualization of tumor, negative biopsy at previous tumor site and negative cytology. Importantly 100 patients (21%) underwent cystectomy, with the majority (62) undergoing immediate cystectomy due to incomplete response and 36 undergoing salvage cystectomy. In those who underwent cystectomy the 5-year overall survival rate was 45% and 10-year survival was 18%. Despite chemotherapy, 27% of the immediate cystectomy group had node positive disease at cystectomy.

This pooling of data results in a variety of eligible patients, exclusion criteria, and radiation treatment fields and dosing. Nevertheless, with a median followup of 4.3 years (7.8 years among survivors) the overall 5-year survival rate was 57% and 10-year survival was 36%. The 5 and 10-year disease specific survival rates were 61% and 65%, respectively.

Unfortunately any trial that randomizes surgery vs radiation therapy probably cannot currently be undertaken, and recent failures that support this notion include the United Kingdom SPARE (Selective bladder Preservation Against Radical Excision) trial (cystectomy vs bladder preservation)¹ and the American College of Surgeons SPIRIT (Surgical Prostatectomy vs Interstitial Radiotherapy Intervention Trial) cohort, ACOSOG-Z0070 (prostatectomy vs brachytherapy).² The current situation makes accurate and fair comparisons between different treatments difficult. Although pooling multiple studies with

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various entrance criteria, varying treatments and different time periods may weaken some conclusions, the authors have compiled a significant number of patients with long-term followup and offer some important takeaway points.

First, this study again reveals our inability to accurately stage muscle invasive cancer, since a significant number of patients had metastatic nodal disease at cystectomy. Also in carefully selected patients a bladder sparing approach can result in cure, although importantly this approach requires diligent and lifelong cystoscopic evaluation of the bladder, since up to a third of patients ultimately have disease recurrence within the bladder. In addition, the optimal combination of chemotherapy and radiation therapy has not been achieved, as treatment agents and forms of radiation therapy continue to evolve. Unfortunately no quality of life data are available, which are integral in determining the optimal combination. Finally, as with radical cystectomy, we need to continue to improve our selection criteria and prognostic abilities to determine the optimal treatment for this heterogeneous population of patients.

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