

Conclusions: Dose escalation with HIMRT does not appear to increase the risk for a decline in SF compared to CIMRT. SF at baseline was the most important factor for predicting a decline in SF at 2 years.

Author Disclosure: M.K. Buyyounouski, None; T. Li, None; D. Watkins-Bruner, None; E.M. Horwitz, None; A. Pollack, None.

14 Late Pelvic Toxicity Following Bladder-Sparing Therapy in Patients With Invasive Bladder Cancer: Analysis of RTOG 89-03, 95-06, 97-06, 99-06

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Purpose/Objectives: In selected patients with muscle-invasive bladder cancer, bladder-sparing approaches using combined-modality therapy (transurethral resection of bladder tumor (TURBT), radiation therapy (RT), chemotherapy) can achieve high rates of complete tumor response and survival rates similar to radical cystectomy. To evaluate long-term effects of chemoradiation to pelvic organs, we investigated late toxicity profiles of a large group of patients treated on prospective protocols who retained their bladders.

Materials/Methods: 157 patients with muscle-invasive bladder cancer enrolled on one of 4 prospective protocols (RTOG 8903, 9506, 9706, 9906; Table 1) who underwent combined-modality therapy, survived ≥ 2 years from start of treatment with their bladder intact. Rates of late genitourinary (GU) and gastrointestinal (GI) pelvic toxicity using the RTOG Late Radiation Morbidity Schema were studied, with worst toxicity grade (scale 0–5) occurring ≥ 180 days after start of consolidation therapy reported for each patient. Persistence of toxicity was defined as grade 3+ toxicity that did not decrease by at least one grade. Univariate and multivariate logistic and Cox regression analyses were performed to evaluate relationship between clinical characteristics and frequency and time to late grade 3+ pelvic toxicity. Covariates included age, gender, stage, presence of carcinoma-in-situ (CIS), completeness of TURBT, and protocol.

Results: Median age was 65 (range 34–90) years, 82% were male, 95% had transitional cell histology, 71% had T2 disease, 15% had associated CIS, and 83% underwent a visibly complete TURBT. Median follow-up was 5.4 (range 2.0–13.2) years. 5-year overall survival was 79%. Of the 157 patients, 11 (7.0%) experienced late grade 3+ pelvic toxicity: 9 (5.7%) GU and 3 (1.9%) GI. In only 1 patient did grade 3+ toxicity persist. Notably there was only one grade 4 late GU toxicity and no treatment-related deaths. None of the clinical variables studied predicted for late grade 3+ pelvic toxicity.

Conclusions: Rates of significant late pelvic toxicity for patients completing combined-modality bladder-sparing therapy for invasive bladder cancer and retaining their native bladder are low. Bladder-sparing approaches remain an effective treatment alternative to radical cystectomy.

Supported by NCI grants U10 CA21661, U10 CA37422, U10 CA32115.

Author Disclosure: W.U. Shipley, None; K. Bae, None; J.A. Efstathiou, None; D.S. Kaufman, None; M.P. Hagan, None; H.M. Sandler, None.

15 Fit of a Generalized Lyman Normal-Tissue Complication Probability (NTCP) Model to Grade ≥ 2 Late Rectal Toxicity Data From Patients Treated on Protocol RTOG 94-06

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Purpose/Objective(s): RTOG 94-06 was a multi-institutional dose-escalation trial designed to determine the maximum tolerated dose for 3D conformal radiotherapy (3D-CRT) of prostate cancer. The purpose of the present study was to estimate the parameters of the Lyman NTCP model using censored time-to-toxicity data for the grade ≥ 2 rectal toxicity endpoint among patients treated on RTOG 94-06.

Materials/Methods: Since the standard Lyman NTCP model is designed for the analysis of binary (yes/no) toxicity data, we first generalized the Lyman model to take into account censored time-to-event data. The generalized model assumed a lognormal distribution of event times and was combined with the Kutcher-Burman method for reduction of the rectal dose-volume histograms (DVHs). The generalized Lyman model was fitted to data representing the time to grade ≥ 2 late rectal toxicity, defined as toxicity starting or persisting > 120 days after start of therapy. Patients not experiencing the endpoint were censored at last follow-up. The parameters estimated from the fit of the model were the three Lyman model parameters (TD50, n, and m) and two parameters (μ and σ) representing the mean and standard deviation of the distribution of logarithms of event times. Confidence intervals for the parameter estimates were obtained by a bootstrap analysis with 1000 replicates.

Results: Of the 1084 patients enrolled on protocol RTOG 94-06, 1023 had rectal toxicity and DVH data available for this secondary analysis and had treatment breaks < 2 weeks. The parameter estimates (with 95% bootstrap confidence intervals) obtained from fitting the generalized Lyman model to the rectal toxicity data were: TD50 = 78 Gy (72,84); m = 0.14 (0.10, 0.25); n = 0.08 (0.04, 0.26); $\mu = 0.45 \ln(\text{yr})$ (0.30, 0.62); and $\sigma = 0.75 \ln(\text{yr})$ (0.66, 0.84). The NTCP was calculated for each patient from the model fit, and ranged from $\sim 0\%$ to 42% (median 14%). Fig. 1 illustrates the fit of the model by showing freedom from grade ≥ 2 rectal toxicity in cohorts of patients defined by their estimated NTCP values.

Conclusions: The generalized Lyman model successfully identified subsets of this study cohort with significantly different rates of late rectal toxicity. The large size of this patient group, together with the considerable variation in rectal DVHs resulting from the different 3D-CRT techniques used by participating institutions, resulted in relatively narrow confidence intervals for the model parameters. However, the model fit requires validation on an independent sample.

Supported by NIH grants R01 CA104342, U24 CA81647, U10 CA21661, U10 CA37422 and U10 CA32115.