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Impact of Bladder Cancer on Health Related Quality of Life in 1,476 Older Americans: A Cross-Sectional Study

Chunkit Fung*, Chintan Pandya, Elizabeth Guancial, Katia Noyes, Deepak M. Sahasrabudhe, Edward M. Messing, and Supriya G. Mohile

Division of Medical Oncology (CF, EG, DMS, SGM) and Departments of Surgery (KN) and Urology (EMM), University of Rochester Medical Center and Department of Public Health Sciences, University of Rochester School of Medicine and Dentistry (CP), Rochester, New York

Abstract

Purpose—The impact of bladder cancer diagnosis on health related quality of life is poorly understood. We compared health related quality of life measures in patients before and after bladder cancer diagnosis.

Materials and Methods—We performed a cross-sectional study in 1,476 patients 65 years old or older with bladder cancer in the SEER-MHOS linkage database between 1998 and 2007 to assess differences in physical and mental component summary scores in 620 and 856 who completed a survey before and after bladder cancer diagnosis, respectively. To determine differences in physical and mental scores in the prediagnosis and post-diagnosis cohorts, we used ANOVA adjusting for baseline covariates.

Results—There were statistically significant differences in physical and mental component summary scores between the prediagnosis and post-diagnosis groups (–2.7, 95% CI –3.8, –1.7 vs –1.4, 95% CI –2.6, –0.3). In patients with non-muscle invasive bladder cancer the physical and mental score differences were –1.9 ($p < 0.01$) and –1.4 ($p = 0.01$), respectively. In those with muscle invasive bladder cancer there was a statistically and clinically significant difference in the physical but not the mental score (–5.3, $p < 0.01$ vs –2.7, $p = 0.07$). This difference in the physical domain persisted up to 10 years after the diagnosis of muscle invasive bladder cancer. Patients with bladder cancer who had 4 or more comorbid medical conditions and 1 or more deficits in daily living activity were most at risk for low physical component summary scores.

Conclusions—Future research into interventions to improve health related quality of life and methods to incorporate health related quality of life into decision making models are critical to improve outcomes in older patients with bladder cancer.

Keywords

urinary bladder neoplasms; aged; quality of life; questionnaires; quality improvement

*Correspondence: Division of Medical Oncology, University of Rochester Medical Center, James P. Wilmot Cancer Center, 601 Elmwood Ave., Box 704, Rochester, New York 14642 (telephone: 585-273-5573; FAX: 585-276-0350; chunkit_fung@urmc.rochester.edu).

BLADDER cancer is common in the United States with approximately 73,510 new cases and 14,880 deaths in 2012.¹ NMIBC and MIBC account for approximately 75% and 25% of all BC cases, respectively.² In patients diagnosed with and treated for BC disease treatment specific effects may have a substantial impact on HRQOL.

Our knowledge about the long-term burden of BC and its treatment on HRQOL is currently limited. Most studies of HRQOL in survivors of BC have been small with 259 to 525 patients.^{3–5} Furthermore, most research has focused on the impact of radical cystectomy with various urinary diversions on HRQOL in patients with MIBC while those with NMIBC have rarely been studied.^{6,7} To our knowledge no study has quantified the nature and extent of HRQOL differences from before to after BC diagnosis.

The main objective of the current cross-sectional study was to examine the impact of BC diagnosis on HRQOL by comparing HRQOL in patients 65 years old or older with BC who completed surveys before or after BC diagnosis between 1998 and 2007 using the SEER-MHOS data set. We also analyzed the association of demographics, general health and BC specific characteristics with HRQOL in patients with BC.

MATERIALS AND METHODS

Data Source

We used cross-sectional data from the SEER-MHOS data set, which linked survey data from CMS (Centers for Medicare and Medicaid Services) MHOS in 2007 with data from SEER cancer registries.⁸ MHOS is a yearly survey administered to a random sample of 1,000 Medicare beneficiaries in participating Medicare managed care plans beginning in 1998. Each participant was selected from a random drawing and requested to complete a baseline survey on HRQOL and subsequent 2-year followup surveys if the patient was still enrolled in the same plan at followup. The response rate ranged from 64.1% to 84.9%.⁸

Due to inadequate statistical power as only 179 patients who completed surveys before and after BC diagnosis were included in analysis, we used a cross-sectional design to include any patient with BC who completed a survey before or after diagnosis. To ensure the independence of error terms on regression analysis^{9,10} only post-diagnosis surveys were included in analysis for these 179 patients. The SEER program collects information on all newly diagnosed cancer cases in populations in defined geographic areas in the United States. SEER-MHOS linkage data were previously described in detail.⁸ This study was granted exempt status by the University of Rochester institutional review board.

Study Sample

We initially identified 3,826 patients with SEER confirmed BC during 1998 to 2007 in the SEER-MHOS data set. We excluded 1,376 patients based on certain criteria, including 1) age less than 65 years at the time of survey completion, 2) incomplete BC staging data and 3) no survey completed more than 1 year previously (selected as a comparator group) or at any time after BC diagnosis. We further excluded 974 patients with missing covariates, resulting in a final sample of 1,476 (fig. 1). Baseline characteristics of patients included in study were similar to those excluded based on the Wilcoxon 2-sample test ($p = 0.46$).

Variables

Dependent—HRQOL was measured by PCS and MCS scores of SF-36®, version 1¹¹ or VR-12,¹² which are validated measures of self-reported HRQOL.¹¹ PCS assesses physical functioning, role-physical, bodily pain and general health domains, and MCS assesses vitality, social functioning, role-emotional and mental health domains. MHOS began using VR-12 instead of SF-36 in 2006, affecting the surveys from 2006 to 2007 in our study. Because SF-36 and VR-12 PCS and MCS were rescored using a published algorithm,¹³ the scores are equivalent. PCS and MCS scores are normalized to the general population of the United States on a scale of 0 to 100 (mean $\pm$ SD score 50 ± 10). Higher scores reflect better HRQOL and a change of 5 points or greater is considered clinically meaningful (supplementary table 1, <http://jurology.com/>).¹⁴

Independent—The main independent variable was BC diagnosis. We examined other cancer specific variables, including age at diagnosis, BC stage, histology and initial treatment. To adjust for the effects of socioeconomic and general health related variables on HRQOL we included race, gender, marital status, education level, household income, smoking status, medical comorbidity and ADL.

Statistical Analysis

We summarized the baseline characteristics of our study cohort using the mean $\pm$ SD for continuous variables and proportions for categorical variables. To compare baseline characteristics between patients who completed surveys before and after BC diagnosis, we used the chi-square test. To determine differences in PCS and MCS scores in the prediagnosis vs post-diagnosis cohorts, including at various intervals after diagnosis, we used ANOVA adjusting for baseline covariates such as cancer stage, race, gender, age at BC diagnosis, marital status, education level, household income, smoking status, comorbidity scores and ADL. To assess the association of baseline characteristics with PCS and MCS scores before and after BC diagnosis, we used multivariable regression models adjusting for the mentioned baseline covariates used on ANOVA. PCS and MCS scores of the multivariable regression models are shown as the least squares mean $\pm$ SD. Statistical significance was considered at $p \leq 0.05$. All statistical analysis was done with SAS® 9.3.

RESULTS

Patient Characteristics

Of 1,476 eligible patients with BC HRQOL data were available on 620 and 856 before and after BC diagnosis, respectively (supplementary table 2, <http://jurology.com/>). White patients and men accounted for most patients in the prediagnosis vs post-diagnosis groups (85.8% and 80.6% vs 86.7% and 77.2%, respectively). Most patients had NMIBC in the prediagnosis and post-diagnosis groups (77.4% and 88.0%, respectively), and in each cohort papillary transitional cell carcinoma was the predominant histology (greater than 96%). Baseline socioeconomic characteristics, including marital status, education level and household income, were similar in the 2 groups. Mean age at diagnosis was higher in patients surveyed after vs before diagnosis (76.4 vs 73.9 years, $p < 0.01$). After BC diagnosis

patients had more medical comorbidities (4 or more in 18.7% vs 14%, $p < 0.01$) and more ADL deficits (1 or more in 45.4% vs 31.9%, each $p < 0.01$) than before diagnosis.

HRQOL Before and After Diagnosis

In patients surveyed before diagnosis the baseline PCS score (mean 40.1) was approximately 1 SD lower than in the general population of the United States while the MCS score (mean 51.1) was comparable to the national average (supplementary table 1, <http://jurology.com/>). After adjusting PCS and MCS scores for baseline covariates we found statistically significant differences in the scores (-2.7 , $p < 0.01$ and -1.4 , $p = 0.02$, respectively) between the prediagnosis and post-diagnosis cohorts. In patients with NMIBC the difference in PCS and MCS scores was -1.9 ($p < 0.01$) and -1.4 ($p < 0.01$), respectively. In those with MIBC there was a significant difference in the PCS score but not the MCS score (-5.3 , $p < 0.01$ vs -2.7 , $p = 0.07$).

In all 1,476 patients with BC the PCS and MCS scores during the 0 to 1 and 1 to 3-year intervals after BC diagnosis differed significantly from those before diagnosis. However, by year 5 these differences were not statistically significant (fig. 2). In patients with NMIBC the PCS scores for all intervals after diagnosis significantly differed from those before diagnosis but the difference in the MCS score was statistically significant only during the first 5 years after diagnosis (fig. 3). In patients with MIBC the PCS scores at 0 to 1, 1 to 3 and 5 to 10 years after diagnosis significantly differed from those before diagnosis (each difference 5 points or greater). However, no significant difference in MCS score was noted for any interval (fig. 4).

Baseline Characteristic Associations with HRQOL

Education level, comorbid medical condition and impaired ADL were significantly associated with differences in PCS and MCS scores in patients surveyed before vs after BC diagnosis ($p < 0.05$, supplementary table 3, <http://jurology.com/>). In patients with 4 or more comorbid medical conditions PCS and MCS scores after diagnosis differed by 4.5 and 0.5 points, respectively, compared to those before diagnosis. In patients with 1 or more ADL impairments PCS and MCS scores after diagnosis differed by 5.1 and 3.1 points, respectively. More advanced BC, older age at diagnosis and lower household income were significantly associated with differences in adjusted PCS scores in patients before and after diagnosis ($p < 0.05$).

DISCUSSION

Currently little is known about the long-term effect of BC and the impacts of BC therapy on HRQOL.^{6,15} To our knowledge this is the first and largest cross-sectional study of differences in HRQOL in patients surveyed before and after BC diagnosis. There were statistically significant differences in PCS and MCS scores in all patients with BC. In those with NMIBC the PCS and MCS scores significantly differed but not in a clinically meaningful way since the differences were less than 5 points.¹⁴ In contrast, in patients with MIBC the 5.3-point difference in PCS score was clinically and statistically significant, and it persisted for all times after MIBC diagnosis. Patients with BC who had 4 or more comorbid

medical conditions and 1 or more ADL deficits were most at risk for this clinically meaningful difference in the PCS domain.

In 2 prior studies Reeve et al examined the effects of cancer diagnosis on HRQOL using data from the SEER-MHOS data set.^{16,17} In the first study they compared prospective changes in HRQOL in 1,432 patients diagnosed with cancer at a total of 9 sites, including 89 with BC, to HRQOL changes in matched controls.¹⁶ Baseline mean PCS and MCS scores (43.2 and 52.3 points) in the prediagnosis group were similar to the means in our study (40.1 and 51.1, respectively). Reeve et al also observed notable decreases in HRQOL after a cancer diagnosis across most cancer sites. In patients with BC the mean PCS score decreased significantly by 4.3 points (95% CI -2.5, -6.1) while the decrease in MCS score was not significant. We similarly reported significant differences in PCS scores in the NMIBC and MIBC prediagnosis vs post-diagnosis cohorts. However, the difference in MCS scores in our study was statistically significant, most likely due to our larger sample size of 1,476 patients. In the other study Reeve et al reported that HRQOL in men after localized prostate cancer diagnosis showed significant decrements in physical, mental and social aspects of life relative to controls.¹⁷

Disease recurrence, cancer progression and adverse effects related to MIBC treatment may account for the clinically significant difference in PCS scores in our study. In patients with localized MIBC after radical cystectomy overall 5-year recurrence-free survival was only 68%² while median progression-free survival in patients with metastatic BC was 7.4 months.¹⁸ In patients with MIBC radical cystectomy with urinary tract reconstruction is associated with decreased HRQOL, particularly in the sexual^{3,4,6} and urinary^{3,6} domains. Patients with an ileal conduit frequently report decreased body image, increased self-consciousness and decreased travel and activity levels⁶ while patients with a continent diversion complain of urinary symptoms related to catheter use.⁶ Even patients with a neobladder report nighttime urinary leakage, which negatively impacts HRQOL.⁶ A recent study demonstrated that urinary incontinence was highly prevalent in BC cases (59.6%) and associated with lower PCS scores (-1.12, $p = 0.0009$) and MCS scores (-0.59, $p = 0.1$).¹⁹ However, current data revealed no significant difference in HRQOL among various urinary diversion approaches.^{3,6} Decreased HRQOL after MIBC diagnosis may also be attributable to the adverse effects of chemotherapy¹⁸ and radiotherapy.²⁰ At a median followup of 5.4 years 7% of patients experienced late pelvic toxicity after combined trimodal therapy for MIBC, including urinary urgency and frequency, hematuria, sigmoid obstruction and proctitis.²⁰

BC is a common malignancy in older adults²¹ who have significant comorbidities and disability. Since the competing risk of noncancer mortality is high in this population,^{22,23} HRQOL should be a key consideration when assessing the benefits and risks of alternative therapy options, especially in those with incurable MIBC. Incorporating age, comorbidity and functional status into the treatment decision making process may be warranted because these factors were associated with significant HRQOL differences in our study. HRQOL may also have a significant influence on treatment acceptance and tolerance by patients with MIBC. This may be a reason why fewer elderly patients undergo radical treatment for potentially curable BC compared to their younger counterparts.²²⁻²⁴ This under treatment may partially explain the negative effect of age on overall²² and BC specific^{23,24} survival.

Future studies of interventions that improve the tolerability of treatments and maintain HRQOL in older patients with MIBC are imperative. For example, implementing an exercise program⁵ or geriatric assessment²⁵ before treatment is initiated may improve HRQOL in patients with BC.

Strengths of our study include the large number of patients (1,476), the population based setting and the use of validated questionnaires (SF-36 and VR-12)¹¹ to measure HRQOL. Limitations are those inherent to the SEER-MHOS program, including the lack of data on chemotherapy and absent information on subsequent treatment courses. An inherent limitation of the cross-sectional design is potential differences in baseline characteristics of the prediagnosis and post-diagnosis groups. To minimize the potential confounding effects of baseline covariates on HRQOL, we performed multivariable regression models including covariates that could be associated with HRQOL, although we could not adjust for unmeasured factors. The SEER-MHOS data set also does not include patients who died before completing the followup survey. Although we could not estimate the effect of this response bias, it most likely underestimated the negative impact of BC diagnosis on HRQOL since patients close to death would have had worse HRQOL. Therefore, this potential response bias should not have affected our conclusion. Finally, interval subgroup analysis was exploratory and sensitive to chance findings and limited power.

Future prospective studies of the impact of various management options on HRQOL are critical since BC is one of the most expensive malignancies from diagnosis to death.²⁶ Identifying potentially modifiable factors that may improve HRQOL in this elderly population is critical to optimize health care resource utilization. In the interim, health care providers should be aware of the effects of BC diagnosis on HRQOL and of future research to determine optimal ways to communicate this information to patients who have multiple treatment options. Assessing and managing BC treatment related side effects and/or symptoms related to disease progression should be consistently performed and prospectively studied to determine the resulting impact on HRQOL.

CONCLUSIONS

Older patients with BC are a vulnerable population with significant medical comorbidity and ADL deficits. PCS and MCS scores of patients after BC diagnosis are significantly different than those before diagnosis. Future research evaluating interventions to improve HRQOL and standardize methods of measuring and incorporating HRQOL into decision making models for older patients with BC is critical to improve outcomes.

Abbreviations and Acronyms

ADL	daily living activity
BC	bladder cancer
HRQOL	health related quality of life
MCS	mental component summary

MHOS	Medicare Health Outcomes Survey
MIBC	muscle invasive BC
NMIBC	nonmuscle invasive BC
PCS	physical component summary
SEER	Surveillance, Epidemiology and End Results
VR-12	Veterans RAND 12-Item Health Survey

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Figure 1.

Study design. Study included patients with BC who completed SF-36 or VR-12 more than 1 year before and/or any time after diagnosis. To accurately capture diagnosis effects on HRQOL we excluded patients who completed baseline SF-36 or VR-12 within 1 year of diagnosis in comparator group. Of surveys completed by 179 patients before and after diagnosis only those completed after diagnosis were included to ensure independence of error terms on regression analysis. Of surveys completed by patients who completed more than 1 after diagnosis only those completed closest to diagnosis were included. Covariates included race, gender, age at diagnosis, marital status, education, household income, smoking, comorbidity score and ADL.

Figure 2.

Cross-sectional analysis of PCS (blue bars) and MCS (red bars) HRQOL scores of all 1,476 patients with BC by time since diagnosis adjusted for baseline covariates, including cancer stage, race, gender, age at diagnosis, marital status, education, household income, smoking, comorbidity score and ADL. Total scores were normalized to general American population on scale of 0 to 100 (mean $\pm$ SD 50 ± 10). Asterisk indicates PCS and MCS at each time after diagnosis vs those greater than 1 year before diagnosis (ANOVA $p < 0.05$).

Figure 3.

Cross-sectional analysis of PCS (blue bars) and MCS (red bars) HRQOL scores of 1,234 patients with NMIBC by time since diagnosis unadjusted for baseline covariates. Total scores were normalized to general American population on scale of 0 to 100 (mean $\pm$ SD 50 $\pm$ 10). Asterisk indicates PCS and MCS at each time after diagnosis vs those greater than 1 year before diagnosis (bivariate $p < 0.05$).

Figure 4.

Cross-sectional analysis of PCS (blue bars) and MCS (red bars) HRQOL scores of 242 patients with MIBC by time since diagnosis unadjusted for baseline covariates. Total scores were normalized to general American population on scale of 0 to 100 (mean $\pm$ SD 50 ± 10). No comparison was made after 10 years due to only 1 MIBC case. Asterisk indicates PCS and MCS at each time after diagnosis vs those greater than 1 year before diagnosis (bivariate $p < 0.05$).