Nonmuscle Invasive Bladder Cancer Influences Physical Health Related Quality of Life and Urinary Incontinence

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OBJECTIVE To evaluate the effects of nonmuscle invasive bladder cancer (NMIBC) on health-related quality of life (HRQOL) and urinary function within patients diagnosed with NMIBC as compared to the general population.

METHODS Using the Surveillance, Epidemiology, and End Results-Medicare Health Outcome Survey (SEER-MHOS) database (1998-2013), 325 patients diagnosed with NMIBC with baseline and postdiagnosis MHOS surveys were propensity-matched 1:5 to noncancer controls (NCC). Multivariate linear regression analysis compared NMIBC patients with matched NCC in terms of physical component summary (PCS), mental component summary (MCS), and health domain scales. Changes in urinary function were assessed using χ^2 testing.

RESULTS Patients diagnosed with NMIBC experienced significant decline in PCS vs NCC (−3.0, 95% confidence interval [CI −4.1, −2.0] vs −1.5, 95%CI [−2.0, −1.0], $P = .01$), while the observed decline in MCS was not significantly different ($P = .09$) between groups. On sub-analysis, the significant decline in PCS was confined to patients with high-risk NMIBC ($P = .01$). NMIBC patients had significantly greater decline in role physical ($P = .04$), general health ($P = .04$) and role emotional ($P < 0.01$) health domain scales. NMIBC patients were more likely to report worsened urinary leakage, require physician intervention, and receive new treatment for urinary leakage (P values all $< .01$).

CONCLUSION NMIBC diagnosis was associated with significant decreases in physical HRQOL and urinary function compared with NCC. Further study focused on NMIBC patients, and the inherent HRQOL factors to this diagnosis is needed to assess where improvements can be made in treating this patient population. UROLOGY 125: 146−153, 2019. © 2018 Elsevier Inc.

In 2018, an estimated 81,190 patients will be diagnosed with bladder cancer, representing 4.7% of new cancer cases within the United States.[1] Of these patients, 70% will have nonmuscle invasive bladder cancer (NMIBC) at the time of presentation.[2] These patients require long-term surveillance with cystoscopy to evaluate for recurrent disease[3] and may need intravesical therapies to reduce the high risk of recurrence.[4,5] As a result, patients who develop NMIBC are likely to suffer significant changes in health-related quality of life (HRQOL).[6]

Despite the higher prevalence of NMIBC, most efforts evaluating HRQOL in bladder cancer have focused on muscle-invasive disease and the impact of radical cystectomy.[7-9] Prior population-based studies evaluating patients with bladder cancer, irrespective of stage, found a statistically, and clinically significant decline in physical related health quality of life.[10-12] However, due to lack of stage stratification, limited insight can be gleaned from these series concerning NMIBC. Consequently, there remains a clinical need for improved understanding of NMIBC effects on HRQOL.

The Medicare Health Outcomes Survey (MHOS) provides HRQOL data from beneficiaries of Medicare Advantage plans. Patients are then linked to the National Cancer Institute's Surveillance Epidemiology and End Results (SEER) database. This allows for assessment of HRQOL changes associated with bladder cancer diagnoses, stratified by stage. We utilized the MHOS-SEER database to investigate the impact on HRQOL brought on by the diagnosis and treatment of NMIBC.

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METHODS

Data Source

We utilized the SEER-MHOS database which provides HRQOL data from Medicare Advantage plan beneficiaries by surveying random beneficiaries (N = 1000-1200 per plan) at 2-year intervals.[13] Follow-up surveys are distributed 2 years later to the same beneficiary, allowing for longitudinal assessment of HRQOL. SEER linkage provides identification of stage-specific cancer diagnosis within the period from baseline to follow-up survey administration.[14] MHOS survey questions include self-reported education, age, race, ethnicity, smoking status, marital status, and baseline comorbid disease. Additionally, surveys include symptom-specific questions related to major disease states including questions which evaluate the incidence, severity, and treatment for urinary incontinence. Within the MHOS database HRQOL is determined using a combination of the Short Form − 36 questionnaire (SF-36) and the Veterans RAND − 12 questionnaire (VR-12) which has previously been described.[14] HRQOL scores are calculated and reported as a physical component summary (PCS) and mental component summary (MCS) which are normalized to the general US population, with mean of 50, and standard deviation of 10.[15] Additionally, both surveys have physical and mental health domain scores evaluating specific categories of HRQOL including physical functioning, role physical, bodily pain, general health, vitality, social functioning, mental health, and role emotional.[14] Health domain scores differ in their weighting and validation methods and are not directly additive to give the PCS and MCS.[16] MHOS data qualify as a limited data set; thus individual respondents are not required to provide informed consent.[11]

Study Cohort

Patients with a diagnosis of NMIBC (Ta, T1, and Tis) were identified in the 1998-2013 MHOS cohorts (initial surveys 1998-2011, follow-up surveys 2000-2013) with SEER linkage in 2011, using the TNM stage variables. All NMIBC patients had both baseline MHOS data (pre-NMIBC diagnosis) and follow-up survey (postdiagnosis) data. Exclusion criteria included patients with another cancer diagnosis before or during the study interval, bladder cancer stage T2 or higher, evidence of nodal or metastatic disease at the time of diagnosis, treatment with radical cystectomy, greater than one follow-up surveys or those with greater than 2 years between initial and follow-up surveys. A cohort of noncancer controls was created by propensity matching NMIBC patients (1:5 ratio) to a random sample of MHOS respondents on gender, age (≥75 vs <75), ethnicity, marital status, tobacco use, education, year of survey, and self-reported comorbidities (hypertension, angina, congestive heart failure, myocardial infarction, other cardiac [coronary artery disease], stroke, chronic obstructive pulmonary disease, diabetes, other gastrointestinal [Crohn's disease, inflammatory bowel disease, ulcerative colitis], hip arthritis, hand arthritis, and sciatica).[15] Student's *t* test and χ^2 tests were performed where appropriate to assess the adequacy of our propensity matching on demographic variables for NMIBC patients and noncancer controls.

HRQOL Assessment

Mental and Physical Summary Scoring. Overall changes from baseline (prediagnosis) in PCS and MCS were compared between NMIBC patients and noncancer controls with multivariate linear regression analysis, controlled for gender, age, race, smoking status, education status and comorbidities. Since treatment of NMIBC, in the form of intravesical therapy, is determined by risk stratification and likely influences HRQOL, we further evaluated changes in PCS and MCS stratified by NMIBC risk stratification (high risk vs nonhigh risk) according to contemporary EAU risk stratification criteria (high risk = all high grade (HG), T1, or CIS).[17] To better understand the impact of NMIBC on MCS and PCS over time, patients were stratified by 6-month blocks (0-6 months, 7-12 months, 13-18 months, and 19-24 months) from NMIBC diagnosis to completion of their follow-up survey. Differences in mean PCS and MCS for each period were evaluated with Student's *t* test. Minimum clinically significant changes in PCS and MCS have been previously determined to be 2 points.[11,18,19]

Health Domain Scores. We assessed further granularity within PCS and MCS scores by evaluating MHOS health domain scores. Physical health domain scores included general health, physical functioning, role-physical, and bodily pain. Mental health domain scores included: role-emotional, vitality, mental health, and social functioning.[16] These are considered clinically significant if altered by at least 3 points.[11,19,20]

Urinary Function Assessment. The MHOS questionnaire includes four questions assessing urinary incontinence distributed with the standardized health survey questions. These include (1) *"Many people experience problems with urinary incontinence, the leakage of urine. In the past six months, have you accidentally leaked urine?"*, (2) *"How much of a problem, if any, was the urine leakage for you?"*, (3) *"Have you talked with your current doctor or other health provider about your urine leakage problem?"*, and (4) *"There are many ways to treat urinary incontinence including bladder training, exercises, medications, and surgery. Have you received these or any other treatments for your current urine leakage problem?"*.[15] Based on responses to these questions we evaluated the number of respondents changing their answer for urinary continence between baseline and follow-up surveys in both cohorts and compared them utilizing the χ^2 test.

All statistical analyses were performed utilizing the SAS statistical software package (version 9.4; SAS Institute Inc., Cary, NC). Statistical significance was set at $P < .05$ for all analyses.

RESULTS

We propensity matched 325 NMIBC patients with 1625 noncancer controls (Table 1). Propensity matching was appropriate in all parameters with the exception of age, where NMIBC patients were significantly older than noncancer controls (75.6 ± 6.6 vs 73.8 ± 9.0 years, $P < .01$). The NMIBC population consisted of the following stage proportions at diagnosis: Ta (n = 211, 64.9%), T1 (n = 88, 27.1 %), and CIS (n = 26, 8.0%).

NMIBC and noncancer controls had similar baseline mean PCS (40.1 ± 9.2 vs 39.5 ± 9.6, $P = .39$) and MCS (52.2 ± 9.0 vs 52.0 ± 10.2, $P = .60$). On follow-up surveys, mean PCS decreased significantly more in NMIBC patients than noncancer controls (−3.0, 95% CI [−4.1, −2.0] vs −1.5 points, 95% CI [−2.0, −1.0], $P = .01$) (Table 2). When stratified by NMIBC risk status, PCS significantly decreased in patients with high-risk NMIBC (−3.4 points, 95% CI [−4.9, −1.9] vs noncancer controls (−1.4 points, 95% CI [−2.0, −0.7], $P = .01$), but not in patients who had nonhigh risk disease (−2.6 points, 95% CI [−4.2, −1.0] vs −1.7 points, 95% CI [−2.5, −0.9], respectively, $P = .37$). With respect to mental health, we observed a

Table 1. Patient demographics for patients with nonmuscle invasive bladder cancer (NMIBC) and propensity-matched noncancer controls.

	NMIBC 325		Noncancer Controls 1625		*P* Value
Age Mean (SD)	75.6 (6.6)		73.8 (9.0)		**<.01**
	N	%	N	%	
Gender					.92
Male	235	72.3	1179	72.6	
Female	90	27.7	446	27.5	
Ethnicity					.45
Caucasian	271	83.4	1304	80.3	
African-American	16	4.9	65	4.0	
Hispanic	17	5.2	123	7.6	
Other	21	6.4	133	8.2	
Marital Status					.88
Married	202	62.2	995	61.2	
Divorced	35	10.8	186	11.5	
Widowed	65	20.0	324	19.9	
Other	23	7.1	120	7.4	
Active Smoking					.75
Yes	45	13.9	236	14.5	
No	280	86.2	1389	85.5	
Education					.25
High school Graduate	139	42.8	640	39.4	
Comorbidities					
Hypertension	182	56.0	928	57.1	.71
Angina	67	20.6	319	19.6	.68
Congestive Heart failure	24	7.4	148	9.1	.31
Myocardial infarction	41	12.6	222	13.7	.61
Other Cardiac	78	24.0	374	23.0	.7
stroke	29	8.9	167	10.3	.45
Chronic Obstructive pulmonary disease	48	14.8	236	14.5	.91
Diabetes	65	20.0	389	23.3	.21
Gastrointestinal	15	4.6	88	5.4	.55
Hip arthritis	135	41.5	668	41.1	.88
Hand arthritis	114	35.1	568	35.0	.96
Sciatica	78	24.0	419	25.8	.5
Stage					
Ta	211	64.9	NA	NA	NA
T1	88	27.1	NA	NA	NA
CIS	26	8.0	NA	NA	NA

P values were considered statistically significant at $P < .05$. NMIBC: Nonmuscle invasive bladder cancer.

nonsignificant decrease in NMIBC patient MCS (−1.8 points, 95% CI [−2.8, −0.8]) vs noncancer controls (−0.7 points, 95% CI [−1.2, 0.2], $P = .09$). Similarly, there were no significant differences in MCS when stratifying by NMIBC risk-status. We then stratified mean PCS and MCS changes among NMIBC patients in 6-month periods, revealing PCS was significantly lower compared to baseline at all-time points, while MCS were significantly lower at only the 7−12 and >12−18-month time points (Fig. 1).

Health Domain Scales

With respect to physical health domains, NMIBC patients had significantly greater decline in role physical (−11.4, 95% CI [−7.0, −16.2], vs −6.0, 95% CI [−4.0, −8.1], $P = .04$), and general health (−7.6, 95% CI [−5.5, −9.6], vs −2.7, 95% CI [−1.7, −3.6], $P = .04$) compared to noncancer controls. With respect to mental health domains, NMIBC patients had significantly greater decline in role emotional compared to noncancer controls (−7.1, 95% CI [−2.6, −11.6], vs −5.0, 95% CI [−3.0, −6.9], respectively, $P < .01$), (Table 2). There were no other statistically significant differences in physical or mental health domains between groups.

Urinary Function Assessment

With respect to urinary function, 63.7% and 71.9% NMIBC patients and noncancer controls, responded to the urinary function questions respectively. Nonresponders tended to have a more substantial decline in the MCS ($P = .04$) and were more likely to be smokers, married, and white. Between baseline and follow-up surveys, NMIBC patients and noncancer controls both reported changes in urinary function, however, NMIBC patients fared worse (Table 3). Specifically, NMIBC patients trended towards significantly more *de novo* urinary incontinence vs noncancer controls (15.0% vs 11.2%, $P = .09$) and were significantly more likely to report increased severity of urinary incontinence from baseline (20.0% vs 11.4%, $P < .01$). Additionally, NMIBC patients were significantly more likely to discuss their incontinence with a physician (20.3% vs 7.4%, $P < .01$) and to receive a new treatment for urinary incontinence (17.5% vs 5.0%, $P < .01$) compared to noncancer controls.

Table 2. Mean change in physical and mental health related quality of life measures.

	NMIBC		Noncancer Controls		
	ΔMean	95% CI	ΔMean	95%CI	*P* Value
	Physical component score				
High risk	−3.4	[−4.9,−1.9]	−1.4	[−2.0, −0.7]	**0.01**
Nonhigh risk	−2.6	[−4.2,−1.0]	−1.7	[−2.5, −0.9]	0.37
All	−3.0	[−4.1, −2.0]	−1.5	[−2.0, −1.0]	**0.01**
Physical functioning	−6.1	[−3.7, −8.5]	−4.1	[−2.7, −5.4]	0.3
Role physical	−11.6	[−7.0, −16.2]	−6.0	[−4.0, −8.1]	**0.04**
Bodily pain	−4.0	[−1.7, −6.3]	−1.9	[−0.6, −3.1]	0.49
General health	−7.6	[−5.5, −9.6]	−2.7	[−1.7, −3.6]	**0.04**
	Mental component score				
High risk	−2.0	[−3.4, −0.7]	−0.7	[−1.4,0.0]	0.22
Nonhigh risk	−1.8	[−4.0, −0.1]	−0.7	[−1.4,0.1]	0.22
All	−2.0	[−2.8, −0.8]	−0.7	[−1.2, 0.2]	0.09
Vitality	−4.7	[−2.5, −6.9]	−2.6	[−1.4, −3.6]	0.13
Social functioning	−7.1	[−4.1, −10.2]	−3.4	[−1.9, −4.6]	0.13
Mental health	−2.5	[−0.8, −4.3]	−0.8	[0.2, −1.8]	0.16
Role emotional	−7.1	[−2.6, −11.6]	−5.0	[−3.0, −6.9]	**< 0.01**

Changes in physical and mental component summaries are presented in the greyed lines. Changes in health domain scores are presented in in white lines. Minimally important difference is considered to be 2 and 3 points for physical and mental component summaries and health domain changes respectively. *P* values were considered statistically significant at $P < .05$.
NMIBC: Nonmuscle invasive bladder cancer.
High Risk: Tumor stage and grade within SEER-MHOS met at least one of the following: T1, High Grade, or CIS*.
Nonhigh Risk: Tumor stage and grade within SEER-MHOS did not meet any of the following: T1, High Grade, or CIS*.
*EAU risk stratification for NMIBC (Babjuk et al 2016).

DISCUSSION

Despite the high prevalence of NMIBC, our understanding of its impact on patient HRQOL remains limited. In this population-based study of the SEER-MHOS database, we observed clinically significant declines in overall physical HRQOL (PCS) and domains of physical health (general health and role-physical functioning) and mental health (role emotional) among patients diagnosed with NMIBC compared with noncancer controls. On subanalysis, declines in PCS were limited to those patients with high-risk NMIBC. Additionally, patients with NMIBC were significantly more likely to report urinary incontinence as a worse problem, to discuss their incontinence with a physician and to receive treatment for incontinence vs noncancer controls. These findings shed light on the deleterious impact of NMIBC on patient HRQOL and are in line with trends reported by other investigators in institutional,[6,21] and population-based studies.[11,12,22,23]

Until recently, there has been little in the published literature examining HRQOL in patients with NMIBC, with most studies focusing on patients undergoing cystectomy.[24] However, in the last several years a handful of population based[12,23] and institutional based[6,21] studies examining HRQOL in NMIBC patients have been published. Using the SEER-MHOS database with cohorts from 1998 to 2007, Fung et al reported on HRQOL in a cohort of 1476 NMIBC patients. In this population, NMIBC patients reported significantly worse PCS and MCS compared to those with pre-diagnosis surveys.[12] However, a limitation of this cross-sectional study was potential confounding through comparison of two distinct cohorts (those with prediagnosis surveys and those with postdiagnosis surveys). A more contemporary evaluation, by Smith et al, reported HRQOL outcomes on 535 patients, including N = 458 with NMIBC, in the SEER-MHOS database (1999-2013) with both pre- and post-bladder cancer diagnosis surveys available. Among patients with NMIBC, similar to our findings, they observed a significant decline in PCS, but not MCS compared to propensity-matched noncancer controls. On evaluation of 6-month time periods both analyses found PCS significantly decreased over all time points, however we found MCS significantly lower at the two mid-time points where they did not.[20] With respect to the health domain scores, they observed significant declines in "role physical" and "general health" among NMBIC patients vs noncancer controls. However, unlike our findings, they observed significant differences in bodily pain, social functioning, and vitality, but not role emotional which was present in our analysis. While this study is based on the same MHOS cohorts and methodologically similar to ours, there is a key difference that may account for these discrepancies: unlike Smith et al which demonstrate baseline alterations in PCS and MCS seen with multiple other cancer types,[10,11] we excluded patients with any prior or new cancer diagnosis (besides NMIBC) during the study period. This is highlighted by the higher baseline PCS and MCS for both NMIBC and noncancer controls in our study compared to Smith et al Additionally, unlike Smith et al we further evaluated changes in HRQOL stratified by disease risk-status as well as the association between NMIBC diagnosis and changes in urinary function questions contained within MHOS.

Contemporary management of NMIBC is based on disease risk strata with both international guidelines calling for induction intravesical BCG followed by prolonged

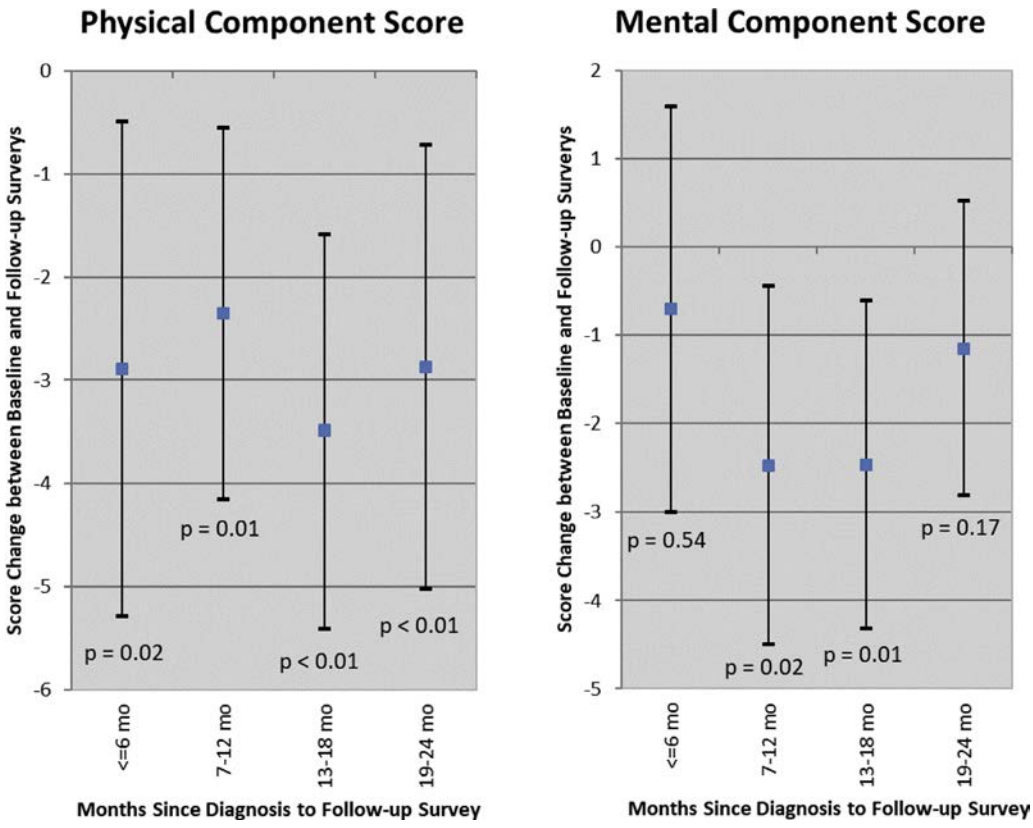

Figure 1. Changes in adjusted health related quality of life among patients with nonmuscle invasive bladder cancer stratified by time from diagnosis to follow-up MHOS questionnaire.

maintenance BCG in patients with high-risk disease.[17,25] Conversely, contemporary guideline-based management of patients with low-risk disease is limited to a single immediately postoperative intravesical chemotherapy instillation, without induction or maintenance intravesical therapy. As a result of these differences, the higher intensity of treatment of patients with high-risk disease, combined with their higher risk of recurrence, has the potential to impact HRQOL more than those without high-risk disease. Thus, we evaluated changes in HRQOL according to NMIBC risk status, observing that only patients with high-risk disease (defined as any HG disease, T1, or CIS) had a significant decline in PCS vs noncancer controls. SEER-MHOS does not provide data on receipt of BCG and other intravesical agents preventing examination of the association between intravesical therapy and HRQOL. However, the significant side effects of intravesical BCG are well described, and head to head comparisons have repeatedly shown greater side effects of intravesical BCG vs intravesical chemotherapy.[25-27] As a result, one possible explanation for the significant decline in PCS in high-risk NMIBC patients but not non–high-risk patients is their likely greater receipt of induction and maintenance intravesical therapies. Conversely, it is possible that high-risk NMIBC intrinsicly produces symptoms leading to declines in PCS.

Recently, a systematic review of bladder cancer patient experiences identified the urinary domain as an area of significant change and patient discomfort.[28] As a result, we evaluated patient responses to the urinary incontinence questions contained within MHOS, which to date has not been reported. NMIBC patients were significantly more likely to report worsened urinary incontinence (20.0% vs 11.4%), to discuss their incontinence with a provider for the first time (20.3% vs 7.4%), and to receive a new treatment for urinary incontinence (17.5% vs 5.0%) compared with noncancer controls. This worsening of urinary function appears similar to a recent multi-institutional analysis in Spain (244 patients) by Schmidt et al in which 16% of patients without urinary problems and 9% with "moderate" (at least 1 small or moderate bother question positive) urinary difficulties at baseline reported worsened urinary function at 12 months post-NMIBC diagnosis as characterized by the Bladder Cancer Index Urinary Domain Score. Interestingly, the overall urinary function was improved 12 months after NMIBC diagnosis in the Schmidt et al cohort but appeared to only deteriorate in the MHOS data.[21] Because MHOS is a general HRQOL instrument, and not a means to evaluate specific urinary function parameters we can only infer what leads to this discordance. One possible explanation is that, according to our data, NMIBC patients were more likely to receive a new treatment for incontinence vs noncancer controls and thus long-term may have had improved

Table 3. NMIBC patient reported changes in urinary function from baseline on the MHOS questionnaire.

	NMIBC	Noncancer Control	*P* Value
Patients answering atleast one urinary incontinence question on baseline and follow up surveys.	N 207 % 63.7	N 1169 % 71.9	**.01**
Urinary Incontinence in the last 6 months			.09
Unchanged, dry	49.5	57.8	
Unchanged, incontinent	24.3	22.9	
Progressed to incontinence	15.0	11.2	
Regressed to continent, dry	11.2	8.1	
How much of a problem is urinary incontinence			**<.01**
Unchanged, not a problem	66.3	78.1	
Unchanged, stay small/ big problem	4.4	2.0	
Problem worsened	20.0	11.4	
Problem improved	9.3	8.6	
Discussed urinary incontinence with a physician			**<.01**
Never discussed	62.5	76.4	
Discussed at baseline and follow-up	10.4	9.3	
Newly discussed at follow-up	20.3	7.4	
Discussed at baseline but not follow-up	6.8	6.9	
Received treatment for urinary incontinence			**<.01**
Never treated	72.5	85.0	
Treated at baseline and follow-up	6.9	5.3	
New treatment at follow-up	17.5	5.0	
Treatment at baseline but not follow-up	3.2	4.7	

P values were considered statistically significant at $P < .05$. Results presented as % to protect the identities of patients with cell size with N <11.
NMIBC: nonmuscle invasive bladder cancer.

urinary function overall. An additional possibility is that there are differences between these regions of the world in the use, and duration of maintenance intravesical therapy.

The SEER-MHOS database has several strengths, including its prospective design allowing for longitudinal assessment, the inclusion of healthy controls for baseline comparison, and the utilization of commonly implemented HRQOL surveys (SF-36 and VR-12) allowing generalizability and comparison between diseases. Limitations of the SEER-MHOS, population-based data set include the lack of granularity making it difficult to examine relationships between specific patient factors, treatments, and HRQOL. For example, data on interventions such cystoscopy, transurethral resection of bladder tumors or intravesical therapy is absent. Second, by design MHOS assesses changes in HRQOL over 2 years in time, as such It is impossible to determine if the observed changes in HRQOL are uniform beyond 2 years. Additionally, recurrence, and progression is not available within the SEER data, and it is likely that recurrence affects HRQOL.[6] Third, MHOS is specific to beneficiaries of Medicare Advantage Organizations; thus the NMIBC specific findings may not be directly relatable to other patient populations.[6,21] Fourth, despite attempting to minimize the risk of unmeasured confounding between groups using propensity matching, there may be other unmeasured covariates in the MHOS which may have contributed to our findings.[11] Finally, the MHOS survey is a general HRQOL instrument which may not adequately address the primary drivers of HRQOL for patients with NMIBC. We attempted to address this potential limitation by evaluating the urinary function specific questions available in MHOS, however, at least some of the observed differences may be due to improved access to urologic care. Urinary incontinence is considered by the MHOS authors to constitute a major disease state and thus it is contained within the general survey. Additionally, these urinary specific questions focus on incontinence and fail to capture other aspects of urinary function such as urgency, frequency, and strength of stream, which could also contribute to HRQOL, however, urgency incontinence would be captured, and is arguable the most bothersome symptom.[29] Understanding the difference in urinary incontinence between NMIBC patients and noncancer controls within MHOS is meaningful for comparison to studies using specific instruments such as the Bladder Cancer Index and future evaluations of the MHOS cohorts.

CONCLUSION

MHOS patients diagnosed with NMIBC experience significantly decreased physical HRQOL and altered urinary function compared to propensity-matched, noncancer controls. The burden of declined physical HRQOL is disproportionally experienced by patients with high-risk NMIBC compared to those with non−high-risk NMIBC. Further prospective evaluation in NMIBC patients with bladder cancer-specific instruments is needed to better understand the influences on HRQOL, the duration of these changes, and areas for improving treatment outcomes.

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EDITORIAL COMMENT

In the study "Nonmuscle Invasive Bladder Cancer Influences Physical Health Related Quality of Life and Urinary Incontinence, Wayne G. Brisbane and colleagues examine patient-reported quality of life (QOL) and urinary incontinence outcomes associated with the diagnosis and management of non-muscle invasive bladder cancer. The study is based on SEER cancer registry data linked to patient-reported outcomes (PROs) data collected as part of the Medical Health Outcomes Survey (SEER-MHOS), which allowed the authors to not only evaluate patient-reported outcomes in a representative sample of bladder cancer patients managed with endoscopic and intravesical treatments, but also benchmark those outcomes to surveys taken from noncancer controls who participated in MHOS as part of their Medicare Advantage plan. Though changes in patient-reported QOL and urinary function were apparent in both groups, declines in PRO scores were more pronounced among NMIBC patients than in noncancer controls. For example, SF-36 physical component summary (PCS) scores decreased by 3.0 points among bladder cancer patients from before diagnosis to after treatment (assessments were performed at 2 year intervals according to MHOS assessment frames) but only 1.5 in the control group ($P = .01$). Similarly, problems with urinary incontinence were more commonly reported by patients than controls; 15.2% of NMIBC patient respondents endorsed new urinary incontinence compared to 11.2% of controls ($P = .09$), and 20.0% of patients reported increased severity of incontinence compared to 11.4% of controls ($P < .01$). Notably, significant deficits in physical health and QOL were driven primarily by low scores in high-risk NMIBC cases (high-grade Ta disease, CIS, and T1 disease), implicating a close association between frequent interventions, such as repeated cystoscopy, biopsy, resection and intravesical therapies, and poorer patient-reported

outcomes. Although these results may not be surprising and likely confirm the observations of practicing urologists who often manage bladder cancer, they provide empirical evidence that quantifies the burdens associated with the diagnosis and treatment of NMIBC. Moreover, these data have several palpable implications in my opinion. First, they represent a step forward and knowledge gained; they pencil in previously undescribed details about patient-reported symptoms and QOL outcomes within the outlines of a relatively understudied area. Second, they underscore the importance of PROs and QOL assessments among bladder cancer patients managed with endoscopic and intravesical therapies, which is particularly relevant given the exploding number of clinical trials evaluating emerging NMIBC therapies that are currently underway.[1] Patient-report outcome and QOL measures should be compulsory components in these trials. Finally, they foreshadow a not-distant future in which PROs will enter routine clinical care. The salutary effects of using PRO measures to inform and guide clinical care have come into focus in recent years, and increasingly health systems are steering toward them.[2]

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AUTHOR REPLY

We would like to thank Scott M. Gilbert for [his] thoughtful examination of this manuscript. As outlined, a major finding of this work is that patients with high-risk nonmuscle invasive bladder cancer (NMIBC) as defined by the European Urological Association and American Urological Association [ref] had significantly worse patient reported outcomes compared to those with nonhigh-risk disease. The survey tools utilized for the Medicare Health Outcomes Survey (MHOS) are not cancer specific instruments, yet still demonstrated statistically and clinically significant decreases in physical and mental health-related quality of life.[1] As noted by Dr. Gilbert, there are multiple factors at work including treatment side effects and oncologic burden. Further work will be needed to delineate if there are adjustments in clinical practice that can decrease the treatment and disease related burden experienced by patients. While MHOS is able to demonstrate general trends, specific causes remain obscure and want of clarification. Investigation of such topics is a priority among funding organizations such as the Patient-Centered Outcomes research Institute (PCORI) and will require further exploration amidst the changing landscape of treatment options for high-risk NMIBC. We agree that patient reported outcomes will become a compulsory component of research and will increasingly be interwoven into clinical care. To make meaningful contributions survey questions will need to balance inclusivity with specific disease process-oriented questions. Next steps will likely include engaging patients and their advocates with disease specific questions to prioritize research and clinical objectives.[2]

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