

# Measuring Health-Related Quality of Life Outcomes in Bladder Cancer Patients Using the Bladder Cancer Index (BCI)

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**BACKGROUND.** Health-related quality of life (HRQOL) has not been adequately measured in bladder cancer. A recently developed reliable and disease-specific quality of life instrument (Bladder Cancer Index, BCI) was used to measure urinary, sexual, and bowel function and bother domains in patients with bladder cancer managed with several different interventions, including cystectomy and endoscopic-based procedures.

**METHODS.** Patients with bladder cancer were identified from a prospective bladder cancer outcomes database and contacted as part of an Institutional Review Board-approved study to assess treatment impact on HRQOL. HRQOL was measured using the BCI across stratified treatment groups. Bivariate and multivariable analyses adjusted for age, gender, income, education, relationship status, and follow-up time were performed to compare urinary, bowel, and sexual domains between treatment groups.

**RESULTS.** In all, 315 bladder cancer patients treated at the University of Michigan completed the BCI in 2004. Significant differences were seen in mean BCI function and bother scores between cystectomy and native bladder treatment groups. In addition, urinary function scores were significantly lower among cystectomy patients treated with continent neobladder compared with those treated with ileal conduit (all pairwise  $P < .05$ ).

**CONCLUSIONS.** The BCI is responsive to functional and bother differences in patients with bladder cancer treated with different surgical approaches. Significant differences between therapy groups in each of the urinary, bowel, and sexual domains exist. Among patients treated with orthotopic continent urinary diversion, functional impairments related to urinary incontinence and lack of urinary control account for the low observed urinary function scores. *Cancer* 2007;109:1756-62. © 2007 American Cancer Society.

**KEYWORDS:** bladder cancer, health-related quality of life assessment, cancer outcomes.

**F**or patients diagnosed and treated for bladder cancer, disease- and treatment-specific effects can have a substantial impact on functional outcomes and health-related quality of life (HRQOL). In patients treated with radical cystectomy and urinary diversion, these concerns are particularly relevant given the long-term effects on urinary, gastrointestinal, and sexual functioning, as well as potential changes in body image. As a result, there has been considerable effort directed toward limiting the functional and HRQOL impairments associated with cystectomy and urinary diversion, primarily through surgical advances such as continent urinary diversion.<sup>1,2</sup>

Despite the long-recognized need for HRQOL assessment among this group of patients, a lack of reliable and sensitive measures has limited research in this area. Furthermore, the focus of this work has largely

excluded the majority of patients with bladder cancer whose disease is not managed with cystectomy. As there are few validated HRQOL measures that are specific for bladder cancer,<sup>3</sup> and those that do exist are limited to patients treated with cystectomy,<sup>4</sup> little is known regarding the burden of disease and treatment among this prevalent group. Consequently, the full extent of disease and treatment effects has not been adequately measured among the overall bladder cancer population.

Given these limitations, we developed and validated a reliable and disease-specific instrument known as the Bladder Cancer Index (BCI) to evaluate HRQOL in a wide range of patients with bladder cancer.<sup>5</sup> The objective of this study was to assess the ability of the BCI to detect disease-specific HRQOL differences among a diverse group of bladder cancer patients managed with different standard treatments across the continuum of bladder cancer care.

## MATERIALS AND METHODS

### Study Sample

After Institutional Review Board approval, patients with bladder cancer were identified from a prospective institutional bladder cancer database and contacted regarding study participation. Study participants included patients diagnosed and treated for bladder cancer at the University of Michigan between 1995 and 2004. The study sample was not limited by age, gender, disease stage, or previous treatments, and included patients managed with various treatment modalities, including cystoscopy alone, cystoscopy with intravesical therapy, radical cystectomy with ileal conduit diversion, and radical cystectomy with neobladder diversion. Because orthotopic diversions are the preferred method of continent urinary diversion at the University of Michigan, nonorthotopic continent urinary diversions were not commonly performed during the study period and were therefore not included in the analysis. The BCI questionnaire, consent form, and instructions were mailed to study participants for completion and then returned to the University of Michigan Medical Center for questionnaire scoring and data collection.

### HRQOL Assessment

The BCI is a reliable, disease-specific HRQOL instrument developed using standard psychometric methodology and has been evaluated with test-retest validity, internal consistency, and divergent/convergent validity in multiple performance phases.<sup>5</sup> The index consists of 34 items within 3 primary domains measuring urinary, bowel, and sexual health, and 2 subdomains (function and bother) for each primary domain. For patients managed with an ileal conduit urinary diversion, BCI urinary

items assess stoma and appliance function, and are designed to measure symptoms such as urinary leakage and skin irritation that may result from suboptimal stomal placement, retraction, and appliance fit. Item responses are based on Likert scales, with domain and subdomain scores standardized to a 0–100 point scale where higher scores correspond to better health states.

### Outcome Measures

HRQOL assessments were performed at a single time after bladder cancer treatment using the BCI. The primary outcome measures included function and bother scores for each BCI domain (urinary, bowel, and sexual).

### Statistical Analysis

Cases were stratified into 4 groups according to treatment type: 1) native bladder, no treatment with intravesical therapy; 2) native bladder, treatment with intravesical therapy; 3) cystectomy with ileal conduit urinary diversion; and 4) cystectomy with neobladder urinary diversion. Urinary, bowel, and sexual function and bother scores were compared between treatment groups in 2 ways: bivariate comparisons were performed using analysis of variance (ANOVA); and multivariable comparisons, adjusted for demographic (age, gender), socioeconomic (income, education level, relationship status), and clinical (treatment type, follow-up time) parameters were performed using analysis of covariance (ANCOVA). Final models were constructed using a backwards selection method. Tukey multiple comparison adjustment was used to preserve the overall error in pairwise assessments. All statistical tests were 2-tailed and performed at the 5% significance level. Analyses were performed using the SAS System (Cary, NC).

## RESULTS

A total of 315 bladder cancer patients treated at the University of Michigan completed the BCI in 2004. Initially, 693 patients were contacted to participate in the study; of those, 29 were deceased, 36 had no available contact information, and 313 refused participation, resulting in a response rate of 45%. The median age was 69 years (range, 41–89), and the median follow-up period was 2.9 years (range, 0.2–9.8). Complete demographic and clinical information stratified according to treatment group are presented in Tables 1 and 2, respectively. Patients treated with cystectomy and neobladder tended to be younger than other groups; however, age differences were not significant between groups. Significant differences did exist for gender, income level, grade, stage, and presence of carcinoma in situ (CIS). As expected, the cystectomy groups consisted of significantly higher

**TABLE 1**  
Demographic Characteristics

	Native bladder		Cystectomy		Total no. (%)
	No intravesical Tx no. (%)	Intravesical Tx no. (%)	Ileal conduit no. (%)	Neobladder no. (%)	
n	52 (16.5)	75 (23.8)	66 (21.0)	122 (38.7)	315
Median age, y	72.7	72.5	73.6	64.9	
Sex*					
Men	36 (69.2)	69 (92.0)	60 (90.9)	93 (76.2)	258 (81.9)
Women	16 (30.8)	6 (8.0)	6 (9.1)	29 (23.8)	57 (18.1)
Race					
White	48 (92.3)	69 (93.2)	62 (95.4)	111 (91.0)	290 (92.6)
Black	3 (5.8)	3 (4.1)	2 (3.1)	1 (0.8)	9 (2.9)
Other	1 (1.9)	2 (2.7)	1 (1.5)	10 (8.2)	14 (4.5)
Income level*					
≥30K	35 (70.0)	47 (66.2)	34 (53.1)	88 (76.5)	204 (68.0)
<30K	15 (30.0)	24 (33.8)	30 (46.9)	27 (23.5)	96 (32.0)
Education					
College	21 (41.2)	28 (37.3)	20 (30.3)	47 (38.5)	116 (36.9)
High school	24 (47.1)	41 (54.7)	37 (56.1)	68 (55.7)	170 (54.1)
<High school	6 (11.8)	6 (8.0)	9 (13.6)	7 (5.7)	28 (8.9)
Living status					
Married/partner	39 (78.0)	63 (84.0)	53 (81.5)	99 (81.2)	254 (81.4)
Single	11 (22.0)	12 (16.0)	12 (18.5)	23 (18.8)	58 (18.6)

Tx indicates transection.

\* Significant differences within category between the 4 treatment groups ( $P \leq .05$ ).**TABLE 2**  
Clinical and Pathologic Characteristics

	Native bladder		Cystectomy		Total no. (%)
	No intravesical Tx no. (%)	Intravesical Tx no. (%)	Ileal conduit no. (%)	Neobladder no. (%)	
n	52 (16.5)	75 (23.8)	66 (21.0)	122 (38.7)	315
Stage*					
Ta	13 (37.1)	31 (43.7)	3 (5.0)	5 (4.2)	52 (16.5)
T1/Tis	8 (22.9)	37 (52.1)	20 (33.3)	49 (41.2)	114 (36.2)
T2	10 (28.6)	3 (4.2)	31 (51.7)	57 (47.9)	101 (32.1)
T3	3 (8.6)	0 (0)	5 (8.3)	7 (5.9)	15 (4.8)
T4	1 (2.8)	0 (0)	1 (1.7)	1 (0.8)	3 (0.9)
Unknown					30 (9.5)
CIS present*	6 (11.5)	37 (49.3)	35 (53.0)	68 (55.7)	145 (46.4)
Grade*					
Low	22 (42.3)	18 (24.0)	3 (4.6)	6 (5.0)	49 (15.6)
High	22 (42.3)	48 (64.0)	51 (78.5)	102 (84.3)	223 (70.8)
Unknown	8 (15.4)	9 (12.0)	11 (16.9)	13 (10.7)	43 (13.6)
Histology					
TCC	51 (98.1)	74 (98.7)	62 (93.9)	119 (97.5)	306 (97.1)
Other	1 (1.9)	1 (1.3)	4 (6.1)	3 (2.5)	9 (2.9)

Tx indicates transection; CIS, carcinoma in situ; TCC, transitional cell carcinoma.

\* Significant differences within category between treatment groups ( $P \leq .05$ ).

**TABLE 3**  
Adjusted Mean BCI Domain Scores

BCI Score	Native bladder		Cystectomy	
	No intravesical Tx n = 52	Intravesical Tx n = 75	Ileal conduit n = 66	Neobladder n = 122
Urinary domain				
Function	90.7 <sup>†</sup>	89.2 <sup>‡</sup>	86.5*	49.8 <sup>*‡†</sup>
Bother	95.4*	93.4 <sup>‡</sup>	88.4	86.3 <sup>*‡</sup>
Bowel domain				
Function	82.0	88.6 <sup>*‡</sup>	77.6*	76.6 <sup>‡</sup>
Bother	93.0 <sup>*†</sup>	92.3 <sup>‡§</sup>	80.8 <sup>*‡</sup>	85.7 <sup>†§</sup>
Sexual domain				
Function	45.7 <sup>*†</sup>	42.2 <sup>‡§</sup>	20.0 <sup>*‡</sup>	25.5 <sup>†§</sup>
Bother	67.4 <sup>*†</sup>	71.7 <sup>‡§</sup>	50.3 <sup>*‡</sup>	49.9 <sup>†§</sup>

BCI indicates Bladder Cancer Index; Tx, transection.

Same symbol in the same row indicates a statistically significant pairwise difference of mean scores between treatment groups (multiple-comparison adjusted  $P \leq .05$ ).

Scores adjusted for age, gender, income, education, relationship status, and follow-up time.

stage and grade disease compared with the native bladder groups.

Mean BCI scores varied by treatment type as illustrated in Table 3. In general, the cystectomy groups displayed relatively lower scores compared with native bladder groups in all of the function and bother subdomains. Significant differences were seen between the urinary function scores for the cystectomy/neobladder group compared with the other 3 treatment groups (all pairwise  $P < .001$ ). Notably, the mean score for this domain was more than 30 points lower among patients treated with cystectomy and orthotopic continent urinary diversion relative to the other groups, exceeding the one-half standard error convention used to determine clinically significant differences. There were also significant differences in mean urinary bother scores between the cystectomy/neobladder group and the 2 native bladder groups (both  $P < .01$ ). Both cystectomy groups displayed significantly lower bother scores in the bowel domain compared with the native bladder groups (all pairwise  $P < .05$ ), and for the sexual domain there were significantly lower scores among the 2 cystectomy groups relative to the native bladder groups in both the function (SF) and bother (SB) subdomains (all pairwise SF  $P < .001$ ; all pairwise SB  $P < .03$ ). Complete pairwise comparisons for adjusted mean domain scores are shown in Table 3. Adjusting for covariates did not change the estimated mean scores (unadjusted scores not shown).

A subanalysis of the response distribution for urinary function items was performed according to treatment group given the unexpected but significant differences observed between cystectomy groups. Figures 1 and 2 illustrate the responses for daytime and nighttime urinary function questions, respectively. In general, the neobladder

group more commonly reported frequent urinary leakage and occasional urinary dribbling compared with the other groups, including the ileal conduit group. The responses for nighttime urinary leakage and lack of control worsened dramatically in the neobladder group (Fig. 2); greater than 54% reported urinary leakage every night and approximately 48% reported no urinary control or frequent dribbling at night. The proportion of ileal conduit patients with these levels of impairment in urinary function were considerably less (6.7% leakage every night and 10.2% no urinary control or frequent dribbling at night). Because orthotopic urinary diversion is often employed to minimize the impact of treatment on both urinary function and body image, we also analyzed a single body image question. The response distribution for this item was not significantly different between the cystectomy groups (Mantel-Haenszel chi-square  $P = .40$ ).

## DISCUSSION

Using the BCI, we have shown differences in disease-specific HRQOL among bladder cancer patients with various levels of disease severity and managed with standard treatments ranging from cystoscopy to radical cystectomy. HRQOL differences between native bladder groups and cystectomy groups were observed in urinary, bowel, and sexual function and bother domains. Interestingly, urinary function scores were significantly lower among cystectomy patients treated with a neobladder urinary diversion compared with those in other treatment groups, including the cystectomy/ileal conduit group. Although bother scores were also lower in the cystectomy/neobladder group compared with the native bladder groups, there was no difference in urinary bother

### Daytime Urinary Items

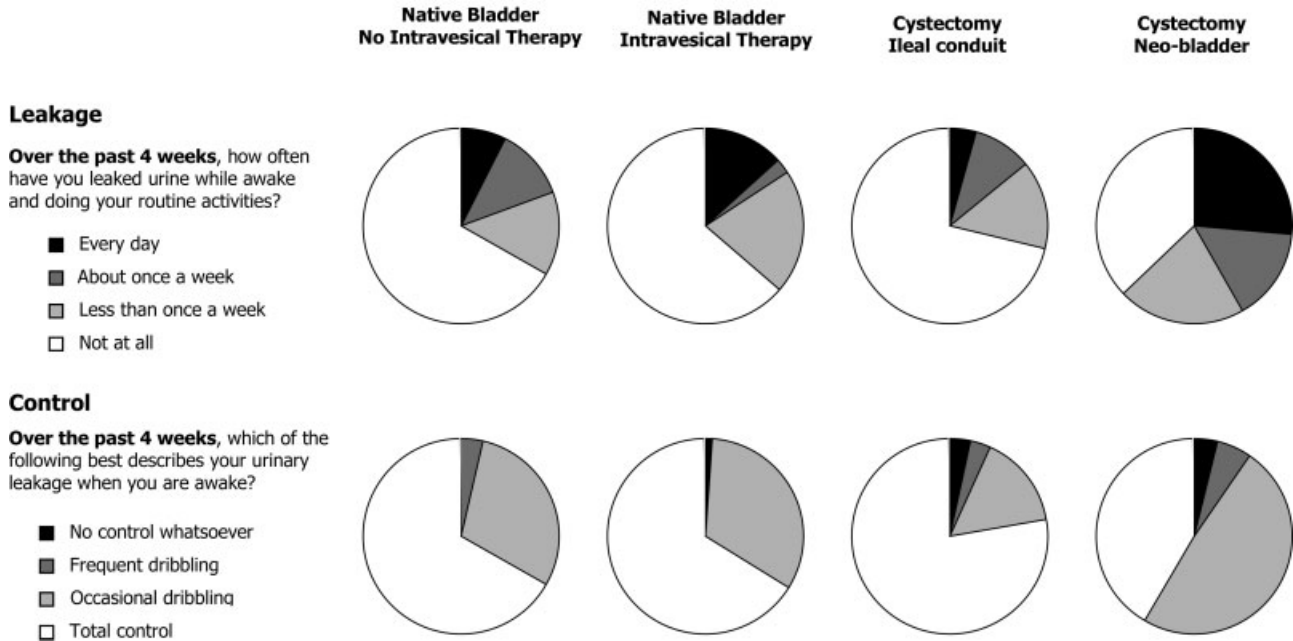


FIGURE 1. Differences in daytime urinary leakage and control between treatment groups.

### Nighttime Urinary Items

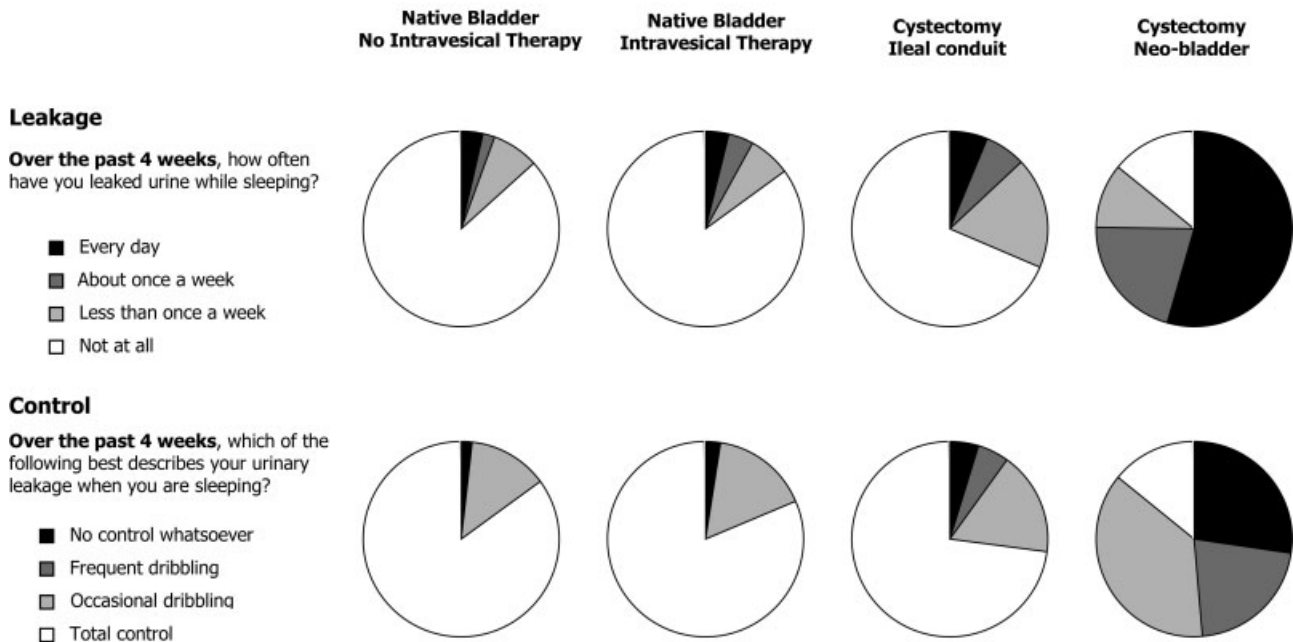


FIGURE 2. Differences in nighttime urinary leakage and control between treatment groups.

between the cystectomy groups. Similar differences favoring the native bladder groups were seen in both the bowel and sexual domains, indicating that the BCI is sensitive in detecting a range of disease-specific HRQOL differences between cystectomy and native bladder groups. Although urinary, bowel, and sexual scores did vary between the native bladder groups, the differences were not significant. Further evaluation will be necessary to determine if small differences between native bladder groups are detectable with the BCI. These preliminary data indicate that the BCI is a sensitive instrument capable of detecting therapy effects across the spectrum of treatment modalities in bladder cancer patients with both urinary diversions and intact bladders.

In the context of the current state of knowledge regarding disease-specific HRQOL in bladder cancer, our results are important. Although there has been longstanding interest regarding the HRQOL impact of cystectomy and urinary diversion,<sup>6</sup> previous research in this area has been limited by a lack of reliable, responsive, and disease-specific HRQOL measures.<sup>7,8</sup> The need to address the limitations in this area of research has been outlined by several recent reviews.<sup>3,9-11</sup> The effort to measure HRQOL among bladder cancer patients has also been limited to the cystectomy population<sup>4</sup>; however, there is a substantial need to broaden the scope of HRQOL assessment to include the majority of patients with bladder cancer who are managed with less invasive treatments.<sup>12</sup> Currently, the burden of disease and the impact of treatment are unknown for the noncystectomy bladder cancer population. The BCI addresses this gap and is the first disease-specific, responsive, and reliable HRQOL assessment measure that can be used in all bladder cancer patients, regardless of disease severity or primary treatment modality.

The finding that urinary function was lower in the cystectomy/neobladder group compared with the cystectomy/ileal conduit group is in contrast to the commonly held belief that continent urinary diversion offers improved HRQOL outcomes compared with incontinent urinary diversion.<sup>2</sup> Although the urologic community has adopted continent diversion as a means to preserve urinary function and body image, there is limited empirical evidence indicating that there is an HRQOL benefit favoring continent diversion.<sup>3,9-11</sup> As previously indicated, much of the uncertainty regarding a definitive benefit of continent urinary diversion is related to limitations of HRQOL assessment used in previous studies.<sup>3,9-11</sup> Our results indicate that known complications related to continent urinary diversion, such as incontinence and lack of urinary control, particularly at night, contribute significantly to the relatively low urinary function scores observed among cystectomy/neobladder

patients. Interestingly, although function scores differed significantly, there was no difference in urinary bother between the cystectomy groups, indicating that neobladder patients adapt to functional impairments. It is possible that additional unmeasured factors, such as patient expectation, preference, and compromise between preserving anatomic urinary function (urinating per urethra) in exchange for physiology function (full urinary control), influence overall HRQOL. Nevertheless, these results indicate that functional issues related to daytime and nighttime urinary incontinence are areas that may be targeted to improve HRQOL among cystectomy patients treated with neobladder.

Although we have shown that the BCI can discriminate HRQOL outcomes according to different treatments for a broad range of bladder cancer patients, the results concerning differences between the cystectomy/ileal conduit and cystectomy/neobladder groups should be interpreted cautiously. Limitations of the cross-sectional design obviate our ability to adjust for baseline quality of life and selection bias may have also impacted our findings. Response bias may also have been present, given the survey component of the study. This limitation will be addressed in a prospective study where all subjects will be approached regarding participation in HRQOL assessment before treatment. In addition, a larger number of subjects and a defined time interval between treatment and HRQOL assessment will reduce the chance of a type II error and may reveal significant differences that we were unable to detect.

Other study limitations were present. A lack of longitudinal follow-up assessment did not allow us to determine the stability of HRQOL scores over time. In addition, a lack of detailed clinical information prevented adjustment for unmeasured covariates, and the level to which factors such as the number and setting of intravesical treatments, agent used, and exposure to other therapies such as radiation and chemotherapy could not be determined in this study. Furthermore, the study did not include nonorthotopic continent urinary diversions, and interpretation of the results should be limited to orthotopic continent urinary diversion. Finally, our assessment of body image was based on a single item, and was likely not sensitive to all important aspects of body image among bladder cancer patients. To address this, we plan to administer a 10-item body image scale with the BCI<sup>13</sup> and will assess this change in future projects.

Although measurable functional differences were apparent using the BCI, the overall quality of life of patients treated with continent and incontinent urinary

diversion may not differ significantly. Whereas some may argue that our results suggest that HRQOL is worse in patients treated with neobladder compared with those managed with ileal conduit, the fact that urinary bother scores were not significantly different should limit this interpretation. Other important motivating factors that were not apparent from our results, such as patient preferences, attempt to preserve body image and anatomic voiding, and acceptance of known urinary dysfunction may ultimately affect HRQOL outcomes in important ways. Further evaluation and prospective study using the BCI will improve our understanding of disease-specific HRQOL in both cystectomy and non-cystectomy bladder cancer patients.

### Conclusions

The BCI is a disease-specific, reliable, and responsive HRQOL assessment tool that can detect HRQOL outcome differences between different disease stages and treatment modalities in bladder cancer patients. It is the first instrument developed for bladder cancer HRQOL assessment using standard psychometric methods that is both disease-specific and inclusive of all bladder cancer patients. As indicated by differences in urinary, bowel, and sexual domain scores, the HRQOL impact of bladder cancer management varies according to treatment modality. Observed differences in urinary function between neobladder and ileal conduit urinary diversions indicate that patients with orthotopic continent urinary diversion experience greater leakage and lack of control, particularly at night; however, this group does not appear to be more bothered by this relative impairment in function. The results of this study indicate that efforts to address urinary leakage and control may result in improved HRQOL scores among patients treated with orthotopic continent urinary diversion. Future prospective studies using the BCI will further elucidate HRQOL outcomes and the impact of treatment among bladder cancer patients managed with endoscopic and intra-

vesical therapies, as well as those treated with cystectomy and urinary diversion.

### REFERENCES

- Hautmann RE, de Petriconi R, Gottfried HW, Kleinschmidt K, Mattes R, Paiss T. The ileal neobladder: complications and functional results in 363 patients after 11 years of follow-up. *J Urol.* 1999;61:427-428.
- Hautmann RE. Urinary diversion: ileal conduit to neobladder. *J Urol.* 2003;69:834-842.
- Gerharz EW, Mansson A, Hunt S, Skinner EC, Mansson W. Quality of life after cystectomy and urinary diversion: an evidence based analysis. *J Urol.* 2005;74:1729-1736.
- Cookson MS, Dutta SC, Chang SS, Clark T, Smith JA, Wells N. Health related quality of life in patients treated with radical cystectomy and urinary diversion for urothelial carcinoma of the bladder: development and validation of a new disease specific questionnaire. *J Urol.* 2003;70:1926-1930.
- Wei JT, Dunn RL, Gilbert SM, Montie JE, Wood DP. Development and validation of the bladder cancer index (BCI): a disease specific measure of quality of life. Abstract 35. American Urological Association Annual Meeting, Atlanta, GA, May 2006.
- Hautmann RE, de Petriconi R, Gottfried HW, Kleinschmidt K, Mattes R, Paiss T. The ileal neobladder: complications and functional results in 363 patients after 11 years of followup. *J Urol.* 1999;61:422-427.
- Cella DF, Tulsky DS, Gray G, et al. The Functional Assessment of Cancer Therapy scale: development and validation of the general measure. *J Clin Oncol.* 1993;1:570-579.
- Allareddy V, Kennedy J, West MM, Konety BR. Quality of life in long-term survivors of bladder cancer. *Cancer.* 2006;06:2355-2362.
- Porter MP, Wei JT, Penson DF. Quality of life issues in bladder cancer patients following cystectomy and urinary diversion. *Urol Clin North Am.* 2005;2:207-216.
- Porter MP, Penson DF. Health related quality of life after radical cystectomy and urinary diversion for bladder cancer: a systematic review and critical analysis of the literature. *J Urol.* 2005;73:1318-1322.
- Gerharz EW, Mansson A, Mansson W. Quality of life in patients with bladder cancer. *Urol Oncol.* 2005;3:201-207.
- Botteman MF, Pashos CL, Hauser RS, Laskin BL, Redaelli A. Quality of life aspects of bladder cancer: a review of the literature. *Qual Life Res.* 2003;2:675-688.
- Hopwood P, Fletcher I, Lee A, Al Ghazal S. A body image scale for use with cancer patients. *Eur J Cancer.* 2001;7:189-197.