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Preoperative Patient Reported Mental Health is Associated with High Grade Complications after Radical Cystectomy

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Abstract

Purpose—Psychological distress has been associated with an impaired immune response and poor wound healing. We hypothesized that preoperative patient reported mental health would be associated with high grade 30-day complications after radical cystectomy.

Materials and Methods—We retrospectively identified patients who underwent radical cystectomy for bladder cancer who completed Short Form 12 (SF-12) surveys for self-assessment of health status less than 6 months before surgery. Median physical and mental composite scores were calculated. An expert model including known predictors of postoperative high grade complications was developed, and SF-12 physical composite score and mental composite score were added to determine their association with this end point.

Results—From January 2010 to August 2014, 472 patients underwent radical cystectomy for bladder cancer, of whom 274 (58.1%) completed preoperative SF-12 questionnaires. Responders were more likely to be white ($p=0.024$), have higher preoperative albumin ($p=0.037$), receive neoadjuvant chemotherapy ($p=0.002$), have pT3/T4 disease ($p=0.044$) and have positive soft tissue surgical margins ($p=0.006$). Median SF-12 physical composite score was 43.1 (IQR 33.0–51.5) and mental composite score was 48.5 (IQR 39.5–54.7) in responders. Overall 46 (16.8%) responders experienced a high grade 30-day complication. Patients with a high grade complication had a lower preoperative median SF-12 mental composite score (44.8 vs 49.8, $p=0.004$) but no difference in physical composite score (39.2 vs 43.8, $p=0.06$). SF-12 mental composite score was also a significant predictive variable when added to our expert model ($p=0.01$).

Conclusions—Preoperative patient reported mental health was independently associated with high grade complications after radical cystectomy. Therefore, patient self-assessment of health status before surgery through validated questionnaires may provide additional information useful in predicting short-term postoperative outcomes.

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Keywords

mental health; postoperative complications; cystectomy; urinary bladder neoplasms

RADICAL cystectomy is an effective treatment for locally advanced bladder cancer but is associated with a high degree of patient morbidity. A recent population based analysis reported 30-day complication, hospital readmission and mortality rates of 66.0%, 32.2% and 5.3%, respectively. Several clinical based measures, such as comorbidity, BMI and hypoalbuminemia, have been examined as predictors of complications after RC, and proposed as targets to reduce adverse outcomes.¹⁻³ However, some evidence has suggested that patient self-assessment of health is an important prognostic marker of outcomes and may be superior to physician reported assessments as predictors of all cause mortality.⁴ Patient self-appraisal of health status has also been shown to be predictive of mortality, regardless of clinical, lifestyle and socio-demographic factors in certain patients with cancer after initial treatment.

Prior studies have suggested that poor baseline mental health can lead to more significant postoperative complications due to the impaired immune response associated with higher levels of stress. This can delay wound healing and the ability to fight infection in the postoperative state. Although self-appraisal of overall well-being may mediate physiological responses to surgery, patient reported health status has not been extensively studied among patients with BC to date, and to our knowledge its use for predicting postoperative outcomes, such as complications, has not been previously examined.

Quality of life surveys, such as the Medical Outcomes Study Short Form (SF-12), allow patients to appraise their own health, and quantify the effects of disease and treatment on their overall well-being. The SF-12 is a standardized, validated questionnaire that measures physical and mental components of health that can be benchmarked to normative population scores.⁵ It has been used to measure health related QOL in patients with chronic conditions such as diabetes as well as in postoperative settings.⁶ In this study we evaluate the association of preoperative patient reported physical and mental health measured by the SF-12 with short-term postoperative outcomes after RC.

METHODS

Patients and Data Source

The study population included patients with BC treated with radical cystectomy and urinary diversion from January 2010 to August 2014 who were identified retrospectively in an institutional review board approved departmental cystectomy database. The departmental cystectomy database collects demographic, clinical and postoperative outcomes data on patients who undergo RC at our institution, and is updated by departmental data analysts.

We used SF-12 data collected as part of the HLMCC (H. Lee Moffitt Cancer Center) New Patient Questionnaire. The NPQ is an electronic clinical intake form designed to replace nonstandardized paper forms that had previously been used to collect demographic and personal health information from patients. The majority of patients complete the NPQ at

home via the Internet using a patient portal account. Otherwise patients complete the NPQ on electronic tablets in the clinic waiting area at their first appointment. NPQ findings were reported into the electronic health record for use by clinicians and discretely captured in the HLMCC Health and Research Informatics platform.

For this study we used the Health and Research Informatics data warehouse to identify patients who completed SF-12 questionnaires as part of the NPQ less than 6 months before RC. Patients were identified using an algorithm using the codes for bladder cancer (C670–C679) filtered by SEER (Surveillance, Epidemiology, and End Results) site specific surgery codes for radical cystectomy (60–64 in males, 71 in females). No patient captured had an incomplete or partial response on the SF-12 questionnaire.

Study Variables and Measures

SF-12 is a multipurpose survey with 12 questions selected from the SF-36 Health Survey which, when combined, scored and weighted, results in physical and mental composite scores. The SF-12 is a validated QOL instrument that is not age or disease specific, and provides a comprehensive, psychometrically reliable and efficient way to measure patient reported physical and mental health. PCS and MCS were computed using the responses of the 12 questions, and range from 0 to 100 with lower scores corresponding to lower levels of health and higher scores corresponding to higher health states.

Complications were captured via retrospective chart review of the patient's postoperative course (ie progress notes and discharge summary) and subsequent clinic visits up to 30 days after RC. The Clavien-Dindo classification was used to categorize 30-day complications. The primary end point of this study was the development of a high grade complication (defined as Clavien IIIa or greater) within 30 days after surgery and the highest grade was assigned to cases of multiple complications. Length of stay, defined from the time of RC until the date of initial discharge home, was also captured in a similar fashion.

Clinical study variables such as patient demographics (age, gender, race), smoking status, BMI (kg/m²), age adjusted CCI, ASA score, preoperative albumin and creatinine levels, use of neoadjuvant chemotherapy, number of NAC cycles administered and history of prior pelvic radiation therapy were abstracted from the departmental cystectomy database. Conditions contributing to CCI were identified through review of individual patient health records at the time of surgery. ASA score was recorded based on anesthesiologist assessment of the patient 2 to 3 hours before surgery. Finally, preoperative albumin and creatinine levels were obtained from solitary measurements drawn 1 to 2 weeks before surgery.

Disease specific characteristics such as clinical tumor histology, pathological tumor (pT) and nodal stage (pN), and soft tissue margin status were also abstracted from the departmental cystectomy database. Clinical tumor histology was based on the examination of the most recent transurethral resection specimen, and all tumor specimens (transurethral resection and RC) were reviewed by our institution's pathologists with expertise in genitourinary malignancy. Staging was assigned according to the 2010 American Joint Committee on Cancer system.

Intraoperative factors such as surgical approach, type of urinary diversion, extent of lymphadenectomy, median number of lymph nodes removed, median operative time and median estimated blood loss were recorded for each analytic case in our population. RC was performed with an open or robotic assisted laparoscopic approach, and extent of pelvic lymph node dissection was defined as none, limited (obturator nodes), standard (obturator, internal and external iliac nodes) or extended (obturator, internal, external and common iliac nodes).

Statistical Analysis

Continuous variables were reported as medians and IQRs, and categorical variables were reported as frequency counts and percentages. We used the Mann-Whitney U test to determine any difference in medians between groups and the chi-square test for proportions. An expert model was created with known predictors of high grade complications after RC (age, BMI, age adjusted CCI, ASA, preoperative albumin and pT stage). To identify whether SF-12 PCS and SF-12 MCS were clinically meaningful predictors above and beyond known predictors, we tested each in a series of likelihood ratio tests via multivariable regression. ROC curves of SF-12 PCS and MCS with the incidence of high grade 30-day complications after surgery were also plotted. Optimal cutoff points were determined visually by minimizing the Euclidean distance between the curve and the upper left corner of the graph (point [0,1]), and by the Youden index, which maximizes the vertical distance from the curve to the line of equality, thereby maximizing the sum of sensitivity and specificity. Statistical analyses were performed with SPSS® 21.0 and SAS® 9.4 software packages. All tests were 2-sided with $p < 0.05$ considered statistically significant.

RESULTS

During the study period, 472 patients underwent radical cystectomy for BC at our institution. The overall NPQ response rate was 66% and 274 patients (58.1%) completed the SF-12 component. Median time between survey completion and RC was 2.9 months (IQR 1.5–4.4). SF-12 responders were more likely to be white (95.3% vs 89.9%, $p = 0.024$), have a higher median preoperative albumin (4.1 vs 4.0 gm/dl, $p = 0.037$), receive NAC (42.7% vs 28.8%, $p = 0.002$), have pT3/T4 disease (47.4% vs 42.9%, $p = 0.044$) and have positive soft tissue surgical margins (15.3% vs 7.1%, $p = 0.006$, data not shown). Neither the incidence nor the distribution of complications or high grade complications differed in SF-12 responders and nonresponders ($p = 0.88$, 0.38 and 0.18, respectively). Basic clinicodemographic information and disease specific characteristics of the SF-12 group are listed in tables 1 and 2.

Preoperative median SF-12 PCS was 43.1 (IQR 33.0–51.5) and MCS was 48.5 (IQR 39.5–54.7) in responders. SF-12 MCS was significantly lower in patients who had a high grade 30-day complication (44.8 vs 49.8, $p = 0.004$) but PCS was not (39.2 vs 43.8, $p = 0.06$). Our expert model alone was not statistically associated with the development of high grade 30-day complications after RC ($p = 0.18$), nor was the expert model + SF-12 PCS ($p = 0.14$), but the expert model + SF-12 MCS was significant ($p = 0.02$). SF-12 MCS was independently associated with high grade 30-day complications after surgery (OR 0.96, 95% CI 0.93–0.99,

p=0.01, table 3). The likelihood ratio test was significant (likelihood ratio statistic=7.42, df=1, p=0.0065) for the expert model + SF-12 MCS vs the expert model alone. Higher SF-12 MCS was also associated with a decreased incidence of high grade complications. For the expert model + SF-12 PCS vs the expert model alone, the likelihood ratio test was insignificant (likelihood ratio statistic=2.15, df=1, p=0.14).

Based on the ROC curve a cutoff of 45 and 48, respectively, was chosen for SF-12 PCS and MCS with the highest combined sensitivity (65% and 68%, respectively) and specificity (47% and 55%, respectively) (see figure). The distribution of complications seen in SF-12 responders with low (48 or less) vs high (greater than 48) baseline MCS is shown in the supplementary table (<http://jurology.com/>).

DISCUSSION

The interaction between self-appraisal of health status before surgery and postoperative outcomes is under studied and poorly understood among patients with BC. However, baseline patient reported physical and mental QOL scores may serve as important prognostic factors in the risk stratification of patients undergoing RC. In this study lower patient reported baseline mental QOL was statistically associated with an increased incidence of high grade complications after RC. Although there is responder subjectivity associated with survey based health related QOL measures, this finding suggests that measuring baseline mental health before surgery may provide additional information that can improve the risk stratification of patients undergoing RC.

Prior literature has associated poor psychological health with worse short-term outcomes after major abdominal surgery. In a landmark study by Saxton and Velanovich preoperative mental QOL as measured by the role-emotional domain of the SF-36 was shown to be an independent predictor of postoperative complications in more than 200 patients undergoing general surgical operations. This was found even after controlling for patient age, comorbidities and functional status as measured by the frailty index.

A history of psychiatric disorders has also been shown to increase complication rates in morbidly obese patients undergoing bariatric surgery. The presence of previous psychiatric conditions increased the incidence of surgical complications threefold, most commonly malnutrition from vitamin deficiency.

Previous studies have also reported that preoperative anxiety and depression can impact the rates of hospital readmission and overall mortality in patients undergoing cardiac surgery. Additionally, preoperative mood disorders have been suggested to predict graft rejection rates in patients undergoing kidney transplantation. In a metaanalysis Walburn et al actually identified 17 studies associating preoperative stress with impaired wound healing due to a diminished immune response (Pearson's $r = -0.42$). However, preoperative psychological counseling and relaxation exercises have been shown to improve the surgical wound healing response after cholecystectomy in a randomized controlled trial. What is not clear from this trial is how many patients had poor baseline mental health before surgery and whether these patients benefited the most from the intervention.

There are several limitations to our study. We present a single institutional experience at a high volume cancer center with a relatively small patient sample, so lack of power is a potential issue. This may explain why components of the expert model were not statistically significant on multivariable regression. Our smaller sample size also precluded analysis of SF-12 PCS or MCS with specific types of complications since there were too few occurrences. In addition, because we evaluated patients retrospectively, only a noncausal association between preoperative SF-12 MCS and high grade 30-day complications after RC can be suggested.

Similar to other retrospective literature on RC outcomes, surgical treatment was not randomized, resulting in a selection bias of more surgically appropriate patients with relatively good performance status. Only 58.1% of patients treated with RC completed the SF-12 component of the NPQ within 6 months of surgery. Although responders were similar to nonresponders for most abstracted study variables, they had a more aggressive disease pathology and a higher positive soft tissue surgical margin rate. Additionally, NAC was used more frequently in SF-12 responders, resulting in more pathological down staging (pT0—15.3% vs 11.1%). This selection bias could have occurred because patients receiving NAC were more likely to have multiple preoperative visits before surgery and, therefore, were more likely to complete the NPQ and SF-12. However, it is important to note that NAC was not associated with high grade 30-day complications in the overall study population ($p=0.84$) or in the SF-12 responder subgroup ($p=0.83$).

Although we distinguished physical and mental domains in the SF-12, we could not account for other life stressors (ie death in family, job firing, financial difficulties etc) that may have influenced the SF-12 MCS at the time of survey completion. Additionally, results of this study cannot be extrapolated to other disease states since patients with BC are in a specific age group with baseline SF-12 scores that may not reflect those of the general population. Although more distal health complications (ie 90-day) could provide additional important information regarding the relationship between complications occurring later and patient reported mental health status, those outcomes are not reliably captured in our electronic medical record or database for all patients, so they could not be included as an alternative outcome in this study.

Despite these limitations, this study shows a relevant association between patient reported baseline mental health and high grade complications after RC for patients with bladder cancer. This relationship remained significant even in the setting of other known clinical risk factors and measures of physician reported patient health. SF-12 is a relatively broad instrument, and other more specific mental health measures such as the Beck Depression Inventory and Burns Anxiety Inventory could be evaluated in future prospective studies to understand the particular types of concerns of these patients. Future research should prospectively examine the psychosocial and QOL impact of RC and urinary diversion on patients with bladder cancer and their spouses using more discrete patient reported instruments. Recognition of poor preoperative mental health may also represent a potential signal warranting more proactive psychological counseling and relaxation techniques preoperatively, although these potential interventions need to be tested in future prospective trials.

CONCLUSIONS

Lower SF-12 MCS was independently associated with more high grade 30-day complications in patients with BC undergoing radical cystectomy. Larger, multi-institutional studies are needed to clarify this relationship and to test causal pathways with more specific QOL measures.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations and Acronyms

ASA	American Society of Anesthesiologists®
BC	bladder cancer
BMI	body mass index
CCI	Charlson comorbidity index
MCS	mental composite score
NAC	neoadjuvant chemotherapy
NPQ	New Patient Questionnaire
PCS	physical composite score
QOL	quality of life
RC	radical cystectomy
SF	Short Form

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SF-12 PCS and MCS as predictors of high grade 30-day complications after RC.

Table 1

Clinicodemographic characteristics of SF-12 complete responders

Median age at RC (IQR)	70.1	(62.7–76.1)
No. male (%)	209	(76.3)
No. female (%)	65	(23.7)
No. race (%):		
White	261	(95.3)
Nonwhite	13	(4.7)
No. smoking status (%):		
Never	55	(20.1)
Former	172	(62.8)
Current	47	(17.2)
Median kg/m ² BMI (IQR)	27.8	(24.9–30.7)
No. age adjusted CCI (%):		
5 or Less	86	(31.4)
6–8	153	(55.8)
9 or Greater	35	(12.8)
No. ASA score (%):		
2	127	(46.4)
3	140	(51.1)
4	7	(2.6)
No. clinical histology (%):		
Pure urothelial carcinoma	194	(70.8)
Urothelial carcinoma variant	65	(23.7)
Nonurothelial carcinoma	15	(5.5)
Median gm/dl preop albumin (IQR)	4.1	(4.0–4.3)
Median mg/dl preop creatinine (IQR)	1.0	(0.8–1.2)
No. neoadjuvant chemotherapy (%)	117	(42.7)
Median NAC cycles (IQR)	3	(3–4)
No. previous pelvic radiation (%)	34	(12.4)

Table 2

Operative and pathological features of SF-12 complete responders

No. surgical approach (%):		
Open	238	(86.9)
Robotic	36	(13.1)
No. urinary diversion (%):		
Cutaneous ureterostomy	18	(6.6)
Ileal conduit	198	(72.3)
Neobladder	43	(15.7)
Continent cutaneous pouch	14	(5.1)
None	1	(0.4)
No. lymphadenectomy (%):		
Limited	6	(2.2)
Standard	84	(30.7)
Extended	177	(64.6)
None	7	(2.6)
Median lymph nodes removed (IQR)	18	(12–24)
Median mins operative time (IQR)	329	(264–386)
Median ml estimated blood loss (IQR)	800	(500–1,200)
Median days length of stay (IQR)	7	(6–10)
No. 30-day complications (%): *		
None	114	(41.6)
I	38	(13.9)
II	76	(27.7)
III	23	(8.4)
IV	18	(6.6)
V	5	(1.8)
No. pathological T stage (%):		
T0	42	(15.3)
Tis–T1	70	(25.5)
T2	32	(11.7)
T3–T4	130	(47.4)
No. pathological N stage (%):		
N0	197	(71.9)
N1	26	(9.5)
N2	22	(8.0)
N3	22	(8.0)
NX	7	(2.6)
No. pos soft tissue margin (%)	42	(15.3)

* Highest grade assigned to patients with multiple complications during 30-day postoperative period.

Table 3

Predictors of high grade 30-day complications

	OR	95% CI	p Value	High Grade Complications (%)			
				Low - Q1	Q1 - Med	Med - Q3	Q3 - High
Expert model:							
Age at RC	1.00	0.96–1.05	0.99				
BMI (kg/m ²)	1.03	0.97–1.09	0.40				
Age adjusted CCI	1.21	0.93–1.56	0.15				
ASA score	1.07	0.48–2.36	0.87				
Preop albumin (gm/dl)	0.44	0.18–1.06	0.07				
Pathological T stage	1.05	0.78–1.40	0.77				
Model comparison: *							
SF-12 PCS	0.98	0.95–1.01	0.14	32.6	23.9	28.3	15.2
SF-12 MCS	0.96	0.93–0.99	0.01	32.6	34.8	21.7	10.9

* Expert model vs expert model + SF-12 component.