# Identifying patients at risk for depression after radical cystectomy

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Cite as: Savin Z, Dekalo S, Dayan LB, et al. Identifying patients at risk for depression after radical cystectomy. *Can Urol Assoc J* 2024;18(7):E228-32. http://dx.doi.org/10.5489/cuaj.8611

Published online March 1, 2024

## ABSTRACT

**INTRODUCTION:** We aimed to assess rates of depression in patients with bladder cancer undergoing radical cystectomy and identify its predictors.

**METHODS:** Depressive symptoms in 42 consecutive patients were evaluated using the Beck's Depression Inventory (BDI) on the day prior to surgery, postoperative day (POD) 6, six weeks after surgery, and 12–18 months postoperatively.

**RESULTS:** Fifteen patients (36%) presented with BDI scores ≥10 before the operation; this rate increased to 64% on POD 6 and 69% at six weeks post-surgery. Depression score rose from a preoperative median of seven to 11 on POD 6 (p=0.003) and to 15 at six weeks after surgery (p=0.001). Patients who arrived with a BDI score of <10 had a higher increase in the BDI at six weeks compared to patients with depressive symptoms prior to surgery (average increase of 9.8 vs. 0.8, p<0.01). Age, gender, type of diversion, and complications were not associated with depression at presentation or progression of depression. Patients who did not receive neoadjuvant chemotherapy tended to be at increased risk for depression progression (57.1% vs. 14.3%, p=0.093). Twenty-four patients completed a fourth questionnaire 12–18 months postoperatively. The median BDI score was eight; three patients with disease recurrence had a higher increase in the BDI score (average 12.7 vs. -5.2, p<0.01).

**CONCLUSIONS:** Depression among patients facing cystectomy is high, and postoperative progression is substantial. Patients without depressive symptoms preoperatively are at increased risk of developing postoperative depression. After 12–18 months, the most influential risk factor for depression is recurrence. These findings highlight the need to consider interventions in selected patients.

## INTRODUCTION

The diagnosis of cancer and anticipated surgery are closely associated with depression and psychological distress. Nearly 25% of patients with cancer have some degree of depression,[1] and this rate appears to increase when the cancer is more advanced.[2] Patients requiring some surgical interventions, including bariatric surgery, spine surgery, and coronary bypass, are reportedly more prone to developing depression. Data on these procedures and their relation to depression and distress are accumulating.[3-5]

Radical cystectomy preceded by neoadjuvant chemotherapy is the recommended standard treatment option in patients with muscle-invasive bladder cancer.[6] Patients advised to undergo this major surgery may face multiple stressors even prior to the operation itself. Postoperative changes in urinary function and body image, as well as a prolonged rehabilitation period may add more stress and anxiety, particularly given the advanced age and high complication rates associated with this operation.

In the current study, we endeavored to study the impact of radical cystectomy on patients' mental health recovery by administering the Beck's Depression Inventory (BDI) to patients before and after radical cystectomy. We aimed to assess the rates of depression before and after surgery and to determine characteristics of depressive symptoms before the operation. We also sought to identify predictors for developing depression after surgery.

## METHODS

### Sample population

After receiving approval from our institutional review board, we enrolled 44 consecutive patients with bladder cancer who underwent radical cystectomy and urinary diversion at our tertiary care center during 2018. All patients underwent open radical cystectomy and pelvic lymph node dissection with an ileal conduit or orthotopic neobladder.

### Depression assessment

Depressive symptoms were evaluated using the BDI,[7] a 21-question multiple-choice self-reported inventory. In essence, the questionnaire is composed of items assessing thoughts of hopelessness, guilt, or feelings of being punished, as well as physical symptoms such as fatigue, weight loss, and lack of interest in sex. Patients were asked to complete the questionnaire on the day prior to surgery, on postoperative day (POD) 6, at six weeks following the operation during their outpatient clinic visit, and 12–18 months postoperatively. Each question can receive a score of 0–3 and the total score is stratified into four categories to determine the severity of depression: 0–9 (minimal), 10–18 (mild), 19–29 (moderate), and 30–63 (severe). A BDI score of 10 or more was deemed a diagnosis of depression. Progression of a depressive state was considered when these criteria were met:

1. A patient had a worse second or third BDI score that placed them in a more severe BDI category.
2. The difference in BDI score was >3 points, which is considered clinically significant.[8]

### Statistical analysis

Categorical variables were reported as frequency and percentage. Continuous variables were evaluated for normal distribution using a histogram and a Q-Q plot. Normally distributed continuous variables were reported as mean and standard deviation (SD), while other variables were reported as median and interquartile range (IQR). Correlations between continuous and ordinal variables were evaluated using Spearman's correlation coefficient. Comparison of categorical variables was performed using the chi-square test or Fisher's exact test. Continuous variables were compared between time points using the Friedman test or Wilcoxon test. Continuous variables were compared between categories using the independent samples T-test or Mann-Whitney test. All statistical tests were two-sided and $p<0.05$ was considered statistically significant. SPSS Statistics software (version 25, IBM Corp., Armonk, NY, USA, 2017) was used for all statistical analyses.

## RESULTS

### Patient characteristics

Of the 44 consecutive patients who underwent radical cystectomy during 2018 and filled in the BDI, the data of two patients were incomplete and thus were excluded from final analysis. The characteristics of the remaining 42 patients are presented in Table 1. Of these patients, six (14.3%) were females, the mean age was 71.2 (SD, 10.3), eight patients (19%) received neoadjuvant chemotherapy prior to surgery, and five (12%) were receiving selective serotonin reuptake inhibitors (SSRIs) before surgery. Twenty-nine patients (69%) were married. Six patients (14%) had a neobladder urinary diversion, and the remaining had ileal conduits. Eight patients (19%) sustained major complications (Clavien Dindo category 3 or above[9]).

**Table 1. Patients' characteristics (N=42)**

| Characteristic | Value |
|---|---|
| Age, years, mean (SD) | 71.2 (10.3) |
| Gender, n (%) | |
| Male | 36 (86%) |
| Female | 6 (14%) |
| Urinary diversion, n (%) | |
| Ileal neobladder | 6 (14%) |
| Ileal conduit | 36 (86%) |
| SSRIs prior to operation, n (%) | |
| Yes | 5 (12%) |
| No | 37 (88%) |
| Complications (Clavien-Dindo ≥3), n (%) | |
| Yes | 8 (19%) |
| No | 34 (81%) |
| Neoadjuvant chemotherapy, n (%) | |
| Yes | 8 (19%) |
| No | 34 (81%) |
| Pathologic stage, n (%) | |
| T0 | 4 (9%) |
| T1 | 2 (5%) |
| T2N0 | 11 (26%) |
| T2N1 | 1 (2%) |
| T3N0 | 11 (26%) |
| T3N1 | 5 (12%) |
| T3N2 | 3 (8%) |
| T4N0 | 5 (12%) |

SD: standard deviation; SSRI: selective serotonin reuptake inhibitor.

| Table 2. Beck's Depression Inventory (BDI) with time | |
|---|---|
| BDI score (median) | |
| Pretreatment | 7 (IQR 3–14) |
| POD 6 | 11 (IQR7–16) |
| 6 weeks postoperatively | 15 (IQR 9–21) |
| 12-18 months postoperatively | 8 (IQR 5–17) |
| Patients with depression (BDI score of 10 or higher) | |
| Pretreatment | 15 patients (36%) |
| POD 6 | 27 patients (64%) |
| 6 weeks postoperatively | 29 patients (69%) |
| BDI score of 8 patients after neoadjuvant chemotherapy | |
| Pretreatment | 10 (IQR 7–16) |
| POD 6 | 11 (IQR 9–14) |
| 6 weeks postoperatively | 11 (IQR 9–15) |
| BDI score of 34 patients who did not get neoadjuvant chemotherapy | |
| Pretreatment | 5 (IQR 2–13) |
| POD 6 | 11 (IQR 7–20) |
| 6 weeks postoperatively | 15 (IQR 8–22) |
| **Level of depression (minimal BDI 0–9, mild BDI 10–18, moderate BDI 19–29, severe BDI 30–63)** | |
| Pretreatment | Minimal 27 (64%), mild 12 (29%), moderate 1 (2%), severe 2 (5%) |
| POD 6 | Minimal 15 (36%), mild 18 (43%), moderate 5 (12%), severe 4 (9%) |
| 6 weeks postoperatively | Minimal 13 (31%), mild 18 (43%), moderate 5 (12%), severe 6 (14%) |
| 12-18 months postoperatively | Minimal 13 (54%), mild 7 (29%), moderate 4 (17%), severe 0 (0%) |

IQR: interquartile range; POD: postoperative day.

## Prevalence and assessment of depression

Table 2 lists the BDI scores on the day before surgery, six days after surgery, at six weeks post-surgery, and after one year or more. Fifteen patients (36%) presented with a BDI score of 10 or higher on the day before the operation, indicative of depression to some degree. This rate increased to 64% (27 patients) on POD 6 and 69% (29 patients) at six weeks post-surgery. During the followup period, the depression score rose from a preoperative median score of seven (IQR 3–14) to 11 (IQR 7–16) on POD 6 (p=0.003), and to 15 (IQR 9–21) at six weeks after surgery (p=0.001, Figure 1).

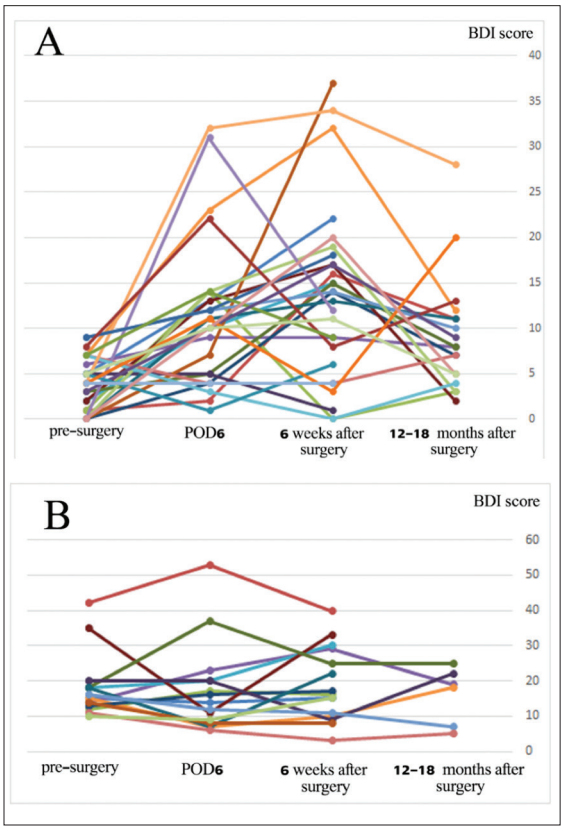


**Figure 1.** Beck's Depression Inventory (BDI) scores of (A) 27 patients who arrived to surgery without depressive symptoms (BDI score of <10) one day before radical cystectomy, on postoperative day (POD) 6, 6 weeks after the operation and 12–18 months postoperatively; (B) 15 patients who arrived to surgery with depressive symptoms (BDI score ≥10) one day before radical cystectomy, on POD 6, 6 weeks after the operation and 12–18 months postoperatively.

Moreover, patients who arrived to surgery with a BDI score of <10 had a higher increase in the BDI score at six weeks compared to patients who had already presented with depressive symptoms one day prior to surgery (average increase 9.8 vs. 0.8, p<0.01). A lower depression score before surgery was associated with progression of symptoms (median 3, IQR 0-9 vs. median 10, IQR 6–15, p<0.01). The median six-week post-surgery depression score was nine (IQR 4–15) for the 21 patients who did not experience progression in depressive symptoms (50%), compared to a median of 18 (IQR 15–27) in patients who did experience progression.

Age, gender, type of urinary diversion, preoperative use of SSRIs, marital status, and surgical complications were not associated with depression at presentation or progression of depression after the operation. Patients who did not receive neoadjuvant chemotherapy tended to be at increased risk for depres-

sion progression (57.1% vs. 14.3% who received the treatment, p=0.093). Patients who arrived to surgery after neoadjuvant treatment had a lower increase in BDI score at six weeks compared to patients who did not get prior chemotherapy (average increase 0 vs. 8, p=0.05). 24 patients (58%) were available to complete a fourth questionnaire 12–18 months post-operatively (14 patients died and 6 were unreachable). The median BDI score was 8 (IQR 5–17). 11 patients (46%) had a BDI score of 10 or higher at least one year postoperatively. 13 patients (54%) showed a clinically significant improvement (>3 points), and seven (29%) presented with clinically significant deterioration. At this stage, three patients (13%) with disease recurrence had a higher increase in the BDI score (average increase 12.7 vs. -5.2, p<0.01).

## DISCUSSION

The association between cancer, surgery, and depression has been receiving more attention, highlighting the pressing need to identify patients who might benefit from intervention. The evidence that 35% of our patients suffered from depressive symptoms even prior to radical cystectomy suggests that invasive bladder cancer may entail above-average levels of distress when compared to other solid malignancies.[10] The observed progression of depressive symptoms in the early and late postoperative periods serves to further emphasize the need for evaluation and treatment of patients at risk.

Many studies have evaluated quality of life issues in patients after radical cystectomy;[11] however, only a few specifically addressed depression, and even fewer identified risk factors for depression.[12,13] Our findings are in accordance with others showing no correlation between depression and age, gender, complications rate, and type of urinary diversion.[12] Interestingly, our patients who had no or minimal depressive symptoms prior to surgery were significantly more prone to progression of depression, while patients who were already mildly depressed before the procedure had stable BDI scores along their initial postoperative course. One possible explanation for this intriguing finding is that patients with preoperative depression were actually more realistic and ready to deal with the postoperative physical and mental challenges, while others were denying, unaware of, or not ready to deal with them. Our results emphasize the critical role of preoperative comprehensive and realistic discussions with patients regarding their anticipated postoperative course. The depression rates following other more common urological procedures are much lower. For example, a recent study that applied the BDI questionnaire to evaluate depression among a large cohort of patients who underwent radical prostatectomy revealed a substantially lower level of depression in the early and late postoperative period compared to our findings.[14]

Neoadjuvant chemotherapy is now part of the standard treatment for invasive bladder cancer.[15] Prior studies assessing depression among cystectomy patients did not stratify outcomes by neoadjuvant treatment status. In our study, only 20% of the patients were treated with neoadjuvant chemotherapy and they were less prone to progression of depressive symptoms. While the reason for this finding remains unclear, we again hypothesize that patients who had already received chemotherapy may have had more time to reconcile with the severity of their disease, and were consequently more appropriately prepared to cope with the difficulties of the operation. We believe that further investigation on larger cohorts in the post-neoadjuvant chemotherapy setting will substantiate our results.

Muscle-invasive bladder cancer is a lethal disease, and after a period of 12–18 months, only 60% of our patients were available to complete the fourth questionnaire. As expected, and in accordance with available literature, many patients had lower BDI scores,[14,16] although almost 50% had some sort of depressive symptoms at this stage. In this smaller group of patients, we observed that after a long period of adjustment and followup, the factors that were important before become negligible, and patients who are healthy with no recurrence are having fewer depressive symptoms as compared to those with disease recurrence.

### Limitations

We recognize several limitations of our study. First, like other self-reported questionnaires, BDI scores can be easily exaggerated or minimized by the person completing them, leading to over- or underestimation of the degree of depression. Second, the way the instrument is administered can affect the final score. The latter limitation was hopefully reduced in our study by having two invariable interviewers administer the questionnaire in a relatively uniform fashion. Third, the BDI was originally designed as a screening device rather than a diagnostic tool. Fourth, questionnaires were answered the day before the surgery, a day of stress and anxiety preceding a major life-changing procedure, which might have affected the scores. Lastly, we recognize that this is a relatively small cohort, and that larger studies are warranted to support our findings.

## CONCLUSIONS

The prevalence of depression among patients with bladder cancer facing radical cystectomy is high, and progression of depression after surgery substantial. Patients with no depressive symptoms preoperatively are at increased risk of developing postoperative depression, whereas patients with mild depression prior to surgery may experience less worsening of symptoms. After 12–18 months, the most influential risk factor for depression is disease recurrence. These findings highlight the need to consider psychological, and possibly, medical intervention in some of these patients confronting these challenging circumstances. Since there are no established guidelines regarding prevention of depressive progression after surgeries,[17] and because we hypothesize that preoperative perceptions and mental abilities contribute to the depressive progression, we would prefer to recommend non-medical psychiatric/psychologic interventions (e.g., consults, group therapies, cognitive behavioral therapy) as preventative measures.

COMPETING INTERESTS: The authors do not report any competing personal or financial interests related to this work.

This paper has been peer-reviewed.

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