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Educational Opportunities in Bladder Cancer: Increasing Cystoscopic Adherence and the Availability of Smoking-Cessation Programs

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Abstract

Cancer survivors who continue to smoke following diagnosis are at increased risk for recurrence. Yet, smoking prevalence among survivors is similar to the general population. Adherence to cystoscopic surveillance is an important disease-management strategy for non-muscle-invasive bladder cancer (NMIBC) survivors, but data from Surveillance, Epidemiology, and End Results program (SEER) suggest current adherence levels are insufficient to identify recurrences at critically early stages. This study was conducted to identify actionable targets for educational intervention to increase adherence to cystoscopic monitoring for disease recurrence or progression. NMIBC survivors ($n=109$) completed telephone-based surveys. Adherence was determined by measuring time from diagnosis to interview date; cystoscopies received were then

compared to American Urological Association (AUA) guidelines. Data were analyzed using non-parametric tests for univariate and logistic regression for multivariable analyses. Participants averaged 65 years (SD=9.3) and were primarily white (95 %), male (75 %), married (75 %), and non-smokers (84 %). Eighty-three percent reported either Ta- or T1-stage bladder tumors. Forty-five percent met AUA guidelines for adherence. Compared to non-smokers, current smokers reported increased fear of recurrence and psychological distress ($p<0.05$). In regression analyses, non-adherence was associated with smoking (OR = 33.91, $p<0.01$), providing a behavioral marker to describe a survivor group with unmet needs that may contribute to low cystoscopic adherence. Research assessing survivorship needs and designing and evaluating educational programs for NMIBC survivors should be a high priority. Identifying unmet needs among NMIBC survivors and developing programs to address these needs may increase compliance with cystoscopic monitoring, improve outcomes, and enhance quality of life.

Keywords

Urinary bladder cancer; Cystoscopy; Patient compliance; Smoking; Preventive health services

Introduction

Approximately 75,000 cases of urinary bladder cancer (BICa) are diagnosed annually, representing the second most common urologic malignancy in the USA [1]. Of new diagnoses, over 75 % are non-muscle-invasive bladder cancer (NMIBC) [2]. Cigarette smoking is the strongest modifiable risk factor for BICa, with cigarette smokers more than three times as likely to develop BICa as non-smokers [3]. However, previous studies indicate public awareness of the association between cigarette smoking and BICa is limited, highlighting current deficits in patient education regarding BICa prevention [4].

The risk for BICa recurrence is also high. Greater than one half of individuals with any stage NMIBC experience at least one recurrence within 3 years of initial treatment, higher for some high-grade NMIBC tumors [5]. Despite indications that rigorous surveillance is fundamental to early detection of NMIBC progression, data from the Surveillance, Epidemiology, and End Results program (SEER) suggest that current adherence is insufficient to identify recurrences at critically early stages [6]. However, SEER-Medicare does not provide users with necessary information to evaluate individual factors that may contribute to this dilemma.

Previous studies also indicate smoking is negatively associated with adherence and treatment efficacy in other malignancies [7]. Yet, evidence suggests continued smoking is common following diagnosis of BICa and other tobacco-related cancers [8, 9]. For many individuals, quitting smoking does not merely represent an isolated change in a person's life but an extensive transformation of a complex interconnected pattern of habits, gratification, and stress relief [10]. Quitting smoking is particularly challenging for individuals with certain psychological susceptibilities, e.g., anxiety-related disorders, which disproportionately affect smokers [11]. Additionally, tobacco users are often characterized by low educational attainment and health literacy that may complicate engagement in

prevention [12]. These indications, along with the limited research assessing psychosocial aspects of BICa, reveal the need for further investigations into behavioral and psychosocial factors that may contribute to NMIBC survivor adherence. Thus, we conducted the current study to examine the association between sociodemographic, psychological, and clinical characteristics, including current smoking status, and adherence to surveillance guidelines among a sample of NMIBC survivors and identify potential educational intervention points to increase adherence.

Methods

Study Population

The current cross-sectional study was conducted at Baylor College of Medicine (BCM) as one phase of the larger Bladder Cancer Outcomes Study. From 2007 to 2010, 202 individuals from our academic private practice (BCM) and affiliated Veterans Affairs hospital (VA) were sent study recruitment letters and 83 individuals responded to advertisements on BICa-survivorship websites (WEB; e.g., Bladder Cancer Advocacy Network) regarding study participation. Eligible study participants included English-speaking adults over age 18, diagnosed with NMIBC within 4 years of enrollment, and without previous radiotherapy. Following screening procedures, 117 eligible participants were enrolled. Given the different surveillance requirements, individuals treated with radical cystectomy were removed from the current analyses ($n=8$). Of the 168 individuals approached but not enrolled, the majority were not eligible for study participation, most commonly due to initial NMIBC diagnosis outside of the previous 4 years. This study was approved by BCM institutional review board, and patients provided informed consent.

Questionnaire

NMIBC survivors with an intact natural bladder ($n=109$; BCM=37, VA=29, WEB=43) completed telephone-based questionnaires containing a core of validated instruments focusing on general and disease-specific health-related quality of life (European Organization for Research and Treatment of Cancer Quality-of-Life Questionnaire core module (QLQ-C30), Bladder Cancer – Superficial – 24 (BLS-24)) [13] and psychosocial items including: (1) an assessment of fear of cancer recurrence using a five-item measure previously used in prostate cancer patients [14], (2) an evaluation of perceived lifestyle disruption using the illness intrusiveness rating scale (IIRS) [15], (3) the Brief Symptom Index-18 (BSI-18) measuring somatization, depression, and anxiety [16], (4) an assessment of traumatic stress via the Impact of Events Scale (IES) [17], and (5) a measure of the ability to draw emotional support from one's partner about one's illness using the Lepore social constraint measure [18]. Additionally, participants reported the types and number of therapeutic and surveillance treatments received since NMIBC diagnosis. Specifically, to measure cystoscopy, participants were asked "How many cystoscopies (have you had for BICa since diagnosis)?"

Primary Outcome

Surveillance protocols vary, but current American Urologic Association (AUA) guidelines suggest quarterly cystoscopy and urine cytology for the first 2 years, semiannual cystoscopic

and cytologic examinations for the following 2 years, and annual examinations from years 5–10 or potentially for the remainder of the patient's life [19]. To determine adherence, we measured the time interval between diagnostic treatment and interview and divided the self-reported number of cystoscopies received by the number suggested by AUA guidelines over this same interval. We then dichotomized adherence to cystoscopy as either adherent (>80 %) or non-adherent (≤80 %), implementing the threshold from previous studies assessing medication adherence [20]. Electronic medical records (EMRs) were available for 66 of 109 individuals in our sample (61 %). For these individuals, the number of cystoscopies collected from EMR was used in place of self-report.

Statistical Analysis

All analyses were performed using SAS® v9.2 (SAS Institute Inc., Cary, NC, USA). We calculated the prevalence of adherence to cystoscopic surveillance in the overall population and in specific subgroups. Additionally, we compared the characteristics of smokers versus non-smokers. To evaluate the significance of any potential differences between groups, we computed the non-parametric Wilcoxon signed-rank test for continuous variables and Fisher's exact test for categorical variables.

We generated a logistic regression model to determine the odds of non-adherence to AUA BICa-surveillance guidelines among smokers versus non-smokers. We used the change-in-estimates method for covariate selection [21]. Thirteen candidate variables were assessed for inclusion in the final model, including demographic characteristics (e.g., age, gender, ethnicity, education, relationship status), tumor stage, recruitment site, disease-specific quality of life (e.g., urinary symptoms, perceived impact of repeated treatments, future perspective (i.e., worry related to future BICa test results, treatments, and outcomes)), and psychosocial scales (e.g., fear of recurrence (FOR), IES, BSI-18). Variables producing at least a 10 % difference in the estimate for the association between smoking status and non-adherence were retained. Of the proposed variables, seven met the criteria for inclusion as potential confounders in the final logistic regression model (i.e., education, marital status, tumor stage, recruitment site, IES, FOR, EORTC perceived impact of repeated treatments).

Sensitivity Analysis

In the 43 WEB patients, adherence was obtained by self-report and potentially subject to recall bias. Because EMR data were not available for determining adherence in this group, we performed sensitivity analyses using three different strategies to assign adherence values in which we assumed: (1) all 43 patients were adherent; (2) 50 % were randomly selected to be adherent; and (3) none were adherent. We repeated the regression analysis, using the EMR-derived adherence for BCM and VA patients and each of the three assumed values of adherence for WEB patients.

Results

Participant Characteristics

Mean age for participants and frequency distributions for gender, ethnicity, education, relationship status, and tumor stage are shown in Table 1. Participants averaged 65.0 years

of age (range= 29–87; SD = 9.3) and were primarily non-Hispanic white, male, and married, with at least some college coursework. Of participants with tumor-stage information (self-report or EMR; n=91), the majority reported either Ta- or T1-stage tumors (82.7 %). Average time between diagnosis and interview was approximately 2 years.

Characteristics of Current Smokers

Participants primarily reported non-smoking at the time of interview (83.5 %). However, participants indicating current tobacco use began smoking at 22.3 years of age (SD=14.0) and sustained cigarette smoking behaviors for 42.4 years (SD=14.7), on average. The majority of smokers reported smoking their first cigarette within 1 h of waking (58.8 %) and smoking 11 or more cigarettes per day (53.9 %).

Smokers and non-smokers were similar in age, gender, ethnicity, relationship status, average time between diagnosis and interview, severity of disease-specific symptoms, and perceived intrusiveness of BICa on one's lifestyle. However, a higher percentage of non-smokers reported achieving at least a bachelor's degree compared to current smokers (55.0 versus 16.7 %, $p<0.01$). Additionally, smokers and non-smokers reported differences across several psychosocial characteristics (Table 2). Smokers reported higher psychological distress ($p = 0.03$), traumatic stress ($p = 0.05$), and FOR ($p = 0.02$). Smokers and non-smokers indicated comparable levels of overall social support. However, smokers reported higher levels of misunderstanding and diminished levels of support from their relationship with their spouse ($p<0.01$).

Adherence

More than one half of participants (55.0 %) were non-adherent to AUA guidelines for cystoscopic surveillance. A greater percentage of smokers (89 %) than non-smokers (48 %) were non-adherent ($p<0.001$). Adherence was not different when stratified by NMIBC tumor stage ($p=0.98$; not shown). In the 66 patients (61 % of sample) on whom adherence was measured via both self-report and EMR, we found self-reported and EMR-derived cystoscopy data yielded equivalent adherence results in 57 of the patients evaluated (84.9 %). When stratified by smoking status, there was an agreement between self-report and EMR for 84.6 and 84.9 % of smokers and nonsmokers, respectively.

Regression Analyses

Smoking was identified as a strong predictor of non-adherence to cystoscopic surveillance. Smokers were more likely to be non-adherent to AUA surveillance guidelines than non-smokers (OR=33.91, $p<0.01$; Table 3). Several additional covariates (education, relationship status, tumor stage, recruitment site, IES, FOR, and the impact of repeated bladder treatments) were retained as potential confounders of the not meet entrance criteria for the final regression model. Results from three separate sensitivity analyses showed the association between smoking and non-adherence persists when different values for adherence were assigned to individuals without available EMR validation (data not shown; ORs = 4.7–19.1, $p < 0.05$).

Discussion

Previous studies have reported poor adherence to BICa surveillance. However, to our knowledge, this pilot study is the first to assess clinically modifiable behavioral and psychosocial factors associated with non-adherence in NMIBC survivors. Our results reveal several key findings. First, overall, adherence was low, demonstrating the need for more effective patient-provider communication regarding the importance of adherence. Second, smoking was associated with nonadherence. Third, univariate analyses indicated smokers were less educated than non-smokers and reported increased fear of recurrence, psychological distress, and traumatic stress.

Analyses of SEER-Medicare databases have reported limited adherence to surveillance among NMIBC survivors [22, 6]. Similarly, in our sample, adherence to cystoscopic surveillance guidelines in NMIBC survivors was low (45.0 %). Our findings mirror previously documented adherence rates and support the need to improve adherence in NMIBC survivors. Due partly to surveillance requirements, BICa is one of the most expensive cancers in the US [23]. Some survivors may consider monetary costs to be prohibitive to routine surveillance [24]. However, given BICa's high recurrence rate, regular surveillance is essential to identify emergent tumors at an early stage. Subsequently, non-adherence to surveillance guidelines may only defer expenses away from regular monitoring onto later, more costly treatments for disease progression (e.g., cystectomy).

Several patient- and systems-level approaches have been developed to target adherence and various aspects of care for cancer and other chronic conditions. For example, improving health literacy through self-care training has been proven to positively influence cardiac outcomes (e.g., improve adherence, reduce hospitalization and direct health-care costs) [25, 26]. Additionally, patient navigation services, while diverse, have been shown to improve adherence to care and quality-of-life outcomes for breast cancer patients [27]. Development and integration of multimodal self-care education programs and patient navigation services into care for NMIBC survivors should be evaluated to determine if similar benefits can be achieved for rates of adherence to surveillance cystoscopy in this population.

In addition to supporting evidence of low overall adherence in NMIBC survivors, our results offer new insights into a subgroup of survivors that report particularly high noncompliance. Almost all current smokers in our sample were non-adherent (89 %), suggesting smokers represent a survivor group with unmet educational needs that may contribute to low adherence. Several factors may influence persistent smoking. Previous research underscores the current lack of patient awareness regarding the relationship between smoking and BICa. In one study surveying 280 urology patients about the relationship between smoking and several different malignancies (e.g., bladder, colon, lung), only 36 % of participants identified smoking as a risk factor for BICa, compared to 98% for lung cancer [28]. These findings are not surprising given the primary focus of previous anti-smoking campaigns on lung cancer. However, it does demonstrate an immediate target for BICa patient education. Additionally, while public campaigns are useful for widespread dissemination of antismoking information for BICa, frontline urologists should also assume a more active role in informing patients of the risks associated with smoking and providing appropriate

referrals for smoking-cessation intervention [29]. A recent study of American urologists indicated that only a small percentage of providers offered regular smoking-cessation counseling, while over one half reported never discussing smoking cessation with BICa survivors [30]. Nearly all surveyed urologists reported never having received smoking-cessation training. Consequently, most described themselves as unqualified to provide these services to patients. The limited smoking-cessation training among urologists suggests a need to partner with other providers who have the necessary expertise.

Additional evidence suggests this communication deficit between providers and patients may negatively impact NMIBC survivor smoking rates. Despite its role in cancer recurrence, evidence indicates continued cigarette smoking is not uncommon following BICa diagnosis. Studies have shown that up to 50 % of NMIBC survivors continue smoking following diagnosis [8]. In our sample, the prevalence of persistent smoking was lower, approximately 20 %. Smoking-cessation education holds additional significance, considering that cessation decreases the risk of recurrence and improves cancer outcomes in NMIBC survivors [31]. Our findings expand upon previous indications of worse disease-free survival in persistent smokers. Beyond being an independent risk factor for subsequent disease recurrence, smoking describes a survivor group with decreased participation in preventive strategies (e.g., routine cystoscopy), possibly compounding the prospect for worse outcomes.

The strong association between smoking and non-adherence in our sample suggests further exploration of the differences between smokers and non-smokers. In univariate analyses, a higher percentage of non-smokers reported achieving at least a bachelor's degree compared to current smokers ($p<0.01$). Education may correlate with additional factors that influence health-care utilization. For example, lower education among smokers may be associated with limited financial resources that preclude completion of smoking-cessation programs (e.g., pharmacotherapy, psychological counseling).

In addition to education-related disparities, our results describe several other differences between smokers and non-smokers. While there was no significant variation between groups in the severity of disease-specific symptoms, smokers reported significantly higher psychological distress, traumatic stress, fear of recurrence, and social constraint. These findings are consistent with previous studies describing cancer as a traumatic event with similar psychosocial effects associated with post-traumatic stress disorder (PTSD) [32]. Similarly, previous studies have linked smoking with increased depression and anxiety. Results from our sample suggest additional challenges that command attention in smoking-cessation programs targeting NMIBC survivors. Effective approaches for incorporating smoking cessation into treatment programs for individuals with similar psychosocial profiles have been demonstrated. In one trial of veterans with PTSD, study participants receiving smoking cessation integrated into mental health care experienced increased smoking abstinence compared to participants randomized to receive standard referral to smoking-cessation clinics [33]. Our results suggest NMIBC survivors may benefit from a similar multi-faceted approach integrating informational and skill-building sessions regarding distress management, as well as pharmacologic intervention, into smoking-cessation efforts.

The current findings should be viewed within the context of the study design. Our data were collected from a convenience sample, instead of randomly selected. Therefore, our results may not generalize to other populations. Yet, the distribution of participant characteristics in our sample was consistent with NMIBC epidemiology in the USA. Additionally, due to the cross-sectional design, we were unable to implicate smoking as a causal determinant of non-adherence. However, the strength of the association, along with evidence from previous studies of other cancers, permits generating specific hypotheses to be tested in larger research studies. This study is also not designed to differentiate between individuals who were instructed to receive cystoscopy at different monitoring intervals than described by current AUA guidelines. Future studies should account for these potential differences. Additionally, we cannot rule out unmeasured factors and self-report as potential sources of bias. For example, recall bias may have factored into cystoscopy reporting. However, we attempted to limit bias by collecting cystoscopy data from EMR, when available. There was substantial agreement between self-report and EMR data, supporting the reliability of self-report in the current sample. There were also slight differences by recruitment site which may suggest systemic characteristics requiring more detailed investigation in future studies. We aimed to control for potential site-specific differences by adjusting for recruitment site in our analyses. Further, smoking may have been underreported due to potential stigma associated with tobacco use. We also did not collect smoking history information in individuals that did not report smoking at the time of interview, which limited our ability to make comparisons between current and historical smoking behavior.

Conclusions

Substantial numbers of NMIBC survivors are non-compliant with surveillance; although our findings cannot distinguish between individual non-adherence and those survivors monitored by providers using different monitoring regimens than currently suggested by AUA guidelines. Non-adherence was associated with smoking, suggesting that smoking status may be a valuable indicator to identify survivors with underlying unmet psychoeducational needs that could be targeted with multimodal smoking-cessation and distress-management programs. Urologists treating BICa patients need a current list of resources to provide appropriate referrals to current smokers. Integrating psychoeducational support to address potential unmet needs within this survivor group may decrease disease burden and improve adherence and outcomes in NMIBC survivors.

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Table 1

Participant characteristics

	Overall	Current smokers	Non-smokers	<i>p</i> value
Age (mean (SD))	65.0 (9.3)	65.0 (10.8)	65.0 (9.1)	0.99
Time since diagnosis (months)	23.3 (13.6)	24.3 (14.0)	23.1 (13.6)	0.73
	<i>N</i> (%)	<i>N</i> (%)	<i>N</i> (%)	
Gender				0.55
Male	82 (75.2)	15 (83.3)	67 (73.6)	
Female	27 (24.8)	3 (16.7)	24 (26.4)	
Ethnicity				0.99
White	103 (94.5)	17 (94.4)	86 (94.5)	
Non-white	6 (5.5)	1 (5.6)	5 (5.5)	
Education				0.02
High school diploma	15 (13.8)	4 (22.2)	11 (12.1)	
Some college	41 (37.6)	11 (61.1)	30 (33.0)	
College degree	31 (28.4)	2 (11.1)	29 (31.9)	
Postgraduate	22 (20.2)	1 (5.6)	21 (23.0)	
Relationship status				0.08
Married	82 (75.2)	10 (55.5)	72 (79.1)	
Single, never married	2 (1.8)	1 (5.6)	1 (1.1)	
Separated or divorced	16 (14.7)	5 (27.8)	11 (12.1)	
Widowed	9 (8.3)	2 (11.1)	7 (7.7)	
Tumor stage				0.98
Ta	37 (42.5)	8 (44.4)	29 (42.0)	
Tis	15 (17.3)	2 (11.2)	13 (18.8)	
T1	35 (40.2)	8 (44.4)	27 (39.2)	
Adherent (AUA guidelines)				<0.01
Yes	49 (45.0)	2 (11.1)	47 (51.7)	
No	60 (55.0)	16 (88.9)	44 (48.3)	

SD standard deviation, *AUA* American Urological Association

Table 2

Psychosocial and disease-specific symptoms stratified by current smoking status

	Current smokers (mean (SD))	Non-smokers (mean (SD))	<i>p</i> value
Psychological distress (Brief Symptom Index)	10.6 (9.8)	5.8 (8.4)	0.03
Traumatic stress (Impact of Events Scale)	23.1 (20.0)	14.8 (15.4)	0.05
Fear of recurrence (CaPSURE™)	62.7 (18.3)	51.3 (18.9)	0.02
Social constraint (Lepore)	28.1 (11.0)	21.2 (7.2)	0.01
Social support (REACH)	30.6 (9.1)	31.9 (7.1)	0.67
Illness intrusiveness (EORTC BLS-24)	22.6 (16.2)	16.1 (16.0)	0.06
Urinary symptoms (EORTC BLS-24)	1.9 (0.6)	1.7 (0.7)	0.12
Impact of repeated treatments (EORTC BLS-24)	1.7 (0.8)	1.3 (0.1)	0.03
Future perspective (EORTC BLS-24)	2.2 (1.0)	1.9 (0.8)	0.29

Higher scores indicate worse symptoms/worse functioning *SD* standard deviation, *CAPSURE* Cancer of the Prostate Strategic Research Endeavor, *REACH* Resources for Enhancing Alzheimer's Caregiver Health, *EORTC BLS-24* European Organization for Research and Treatment of Cancer: Bladder Cancer – Superficial-24

Table 3

Logistic regression predicting non-adherence to cystoscopic surveillance

	Adjusted OR (95 % CI)
Smoking status (versus non-smoker)	
Current smoker	33.91 (3.69–311.4)
Recruitment site (versus VA)	
BCM	1.40 (0.38–5.20)
WEB	0.33 (0.07–1.51)
Education (versus high school diploma)	
Some college	0.47 (0.09–2.41)
College degree	1.97 (0.35–10.9)
Postgraduate	0.35 (0.06–2.07)
Relationship status (versus married)	
Separated or divorced	1.15 (0.26–4.99)
Single and never married	0.04 (0.01–1.77)
Widowed	0.65 (0.09–4.24)
Disease stage (versus T1)	
Ta	1.04 (0.32–3.38)
Tis	1.00 (0.21–4.84)
Impact of Events Scale (IES)	0.96 (0.92–1.00)
EORTC – impact of repeated treatments	0.76 (0.26–2.23)
CaPSURE fear of recurrence (FOR)	1.02 (0.99–1.06)

OR odds ratio, CI confidence interval