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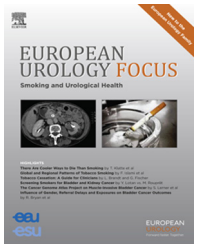

Epidemiology

Accuracy of Self-reported Smoking Exposure Among Bladder Cancer Patients Undergoing Surveillance at a Tertiary Referral Center

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Abstract

Background: Smoking is a risk factor for developing bladder cancer (BCa). Even though continued exposure after diagnosis may adversely affect prognosis, patients may be reluctant to disclose to their physicians that they are currently smoking, leading to inaccurate reporting of exposure and missed opportunities to deliver smoking-cessation advice and treatment in the context of cancer care.
Objective: We examined the extent of misclassification of recent smoking exposure among patients undergoing BCa surveillance.
Design, setting, and participants: A consecutive sample of 145 patients with a self-reported smoking history and prior initial diagnosis of BCa was recruited from a tertiary referral urology clinic.
Outcome measurements and statistical analysis: Patients were asked if they had smoked a cigarette or used nicotine replacement therapy (NRT) within the past week and whether they lived with a smoker. At the same visit, we collected urine under a biospecimen protocol. We used urinary cotinine, the primary metabolite of nicotine, as an objective biomarker of recent smoking exposure. Nine patients whose urine could not be interpreted for cotinine were excluded. We calculated the smoking status misreporting rate by comparing biochemically verified smoking status ($\geq$31.5 ng/ml vs $<$31.5 ng/ml) against self-reported current smoking status (yes vs no) while considering recent NRT use.
Results and limitations: Overall, 11% (15 of 136) of patients had cotinine values consistent with current smoking. Of these 15 patients, 7 reported being former smokers, resulting in a 47% misclassification rate. However, three of the seven patients who denied smoking in the past week were currently using NRT. Excluding NRT users, the misclassification rate was 33%.
Conclusions: Future studies investigating the impact of postdiagnosis nicotine exposure on BCa outcomes should use biochemical verification combined with self-reported smoking exposure to classify patients accurately.
Patient summary: Bladder cancer patients may misreport smoking exposure, thereby missing opportunities for smoking cessation.

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1. Introduction

Cigarette smoking is an established risk factor for developing bladder cancer (BCa), and continued exposure after diagnosis may adversely affect prognosis by increasing the risk of recurrence and progression as well as compromising intravesical therapy response [1–4]. Moreover, emerging data suggest that nicotine exposure after diagnosis may enhance tumor growth and metastasis [5–9]. An accurate assessment of smoking exposure is essential for reducing misclassification in studies on the impact of smoking on BCa outcomes and for referring patients to smoking-cessation programs. Identifying BCa patients who are current smokers is especially important in light of the recent findings that smokers are less likely to adhere to American Urological Association guidelines regarding surveillance cystoscopies [10].

All prior studies investigating associations between smoking and BCa outcomes have relied on self-report to capture patient smoking history and recent exposure [1,3,4,11,12]. Studies in smokers without cancer suggest that 32% of smokers require biochemical assessment to identify true tobacco use [13]; the limited studies among cancer patients suggest that misreporting rates are variable and that self-reported smoking may be inaccurate in up to 55% of patients [14–18]. Most recently, Morales et al. [17] found that patients who had a smoking-related cancer (ie, lung cancer) were more likely to misrepresent tobacco use than those patients who had breast cancer or prostate cancer (PCa). Among 77 lung cancer patients, the misreporting rate was 60% versus 23% in 79 PCa patients. Even when patients were aware of secondary biochemical verification of their smoking status, Alberg et al. found a 39% misreporting rate in a cohort of 108 head and neck cancer patients [18]. To our knowledge, no prior study has evaluated the accuracy of self-reported cigarette smoking among BCa patients. This population is noteworthy because BCa patient awareness of smoking as a risk factor for their disease is limited [19–22]. The purpose of this study was to describe the extent of misclassification of recent smoking exposure among BCa patients undergoing surveillance at a tertiary referral center.

2. Material and methods

Over 4 mo in 2013, we recruited 145 consecutive BCa patients who had a smoking history, were being treated at Memorial Sloan Kettering Cancer Center, and had consented to an existing specimen-collection protocol. We used urinary cotinine, the primary metabolite of nicotine, as an objective biomarker to determine recent smoking exposure [23]. The treating physician asked patients if they had smoked a cigarette within the past 7 d (yes vs no), had used nicotine replacement therapy (NRT) products within the past 7 d (yes vs no), and currently lived with an active smoker (yes vs no). At the same visit, urine was collected for biochemical assessment of cotinine using established methods of liquid chromatography coupled with tandem mass spectrometry and atmospheric pressure chemical ionization. Patients were blinded to the purpose of the study. We could not assess the urine of nine patients for cotinine because of interference, leaving a total of 136 patients for this analysis.

Continuous cotinine values were categorized into three groups—≥31.5 ng/ml, 0.5–31.4 ng/ml, and <0.5 ng/ml—which represented current, passive, and no recent smoking exposure, respectively [24,25]. We derived our cut-off points from clinical pharmacology studies that were designed to determine the optimal cut-off point of cotinine to discriminate active versus passive versus no recent nicotine exposure. We dichotomized patients into cotinine-positive (≥31.5 ng/ml) or cotinine-negative (<31.5 ng/ml) subgroups to represent current smoking status (yes vs no). We calculated sensitivity, specificity, false-positive, and false-negative rates from a 2 x 2 classification table comparing biochemically verified smoking status (≥31.5 ng/ml vs <31.5 ng/ml) against self-reported current smoking status (yes vs no). We abstracted additional patient and disease characteristics, such as a more detailed smoking history, from electronic medical records. All statistical analyses were performed using SAS version 9.4 software (SAS Institute, Cary, NC, USA).

3. Results

Table 1 presents the demographic, clinical, and smoking characteristics of the 136 BCa patients who had a smoking history. Patients were predominantly male and white; mean age at sample collection was 73 yr. The year patients were initially diagnosed with BCa ranged from 1994 to 2013. The majority of patients presented with early stage disease (<pT2; 95.6%) and high-grade tumors (68.4%). The median number of months since diagnosis was 31. The median number of cigarettes smoked per day and lifetime duration of smoking was 1 pack and 25 yr, respectively. Among self-reported former smokers, the median number of years since quitting was 27, with an interquartile range of 13–38 yr.

Table 2 compares self-reported smoking status with biochemically verified urinary cotinine levels. Overall, 11% (15 of 136) of patients had cotinine values consistent with current smoking (range: 118.3–2047.8 ng/ml). Of these 15 patients, 7 reported being a former smoker, resulting in a misclassification rate of 47%. Three of the seven patients who reported being a former smoker said they currently

Table 1 – Demographic, clinical, and smoking characteristics of bladder cancer (BCa) patients with a smoking history currently under surveillance for BCa recurrence (*n* = 136)

Characteristics	Total no. (%)
Age in yr, median (IQR)	73 (66–78)
Gender	
Male	115 (85)
Female	21 (15)
Race	
Caucasian	129 (94.9)
Black	3 (2.2)
Asian	2 (1.5)
Other	1 (0.7)
Missing	1 (0.7)
Year of initial BCa diagnosis	1994–2013
Months since initial diagnosis, median (IQR)	31 (19–73)
Stage	
<pT2	130 (95.6)
≥pT2	6 (4.4)
Grade	
High	93 (68.4)
Low	38 (27.9)
Missing	5 (3.7)
Average no. cigarettes smoked per day, median (IQR)	20 (20–40)
Lifetime duration of smoking in years, median (IQR)	25 (15–35)
Years since quitting, median (IQR)*	27 (13–38)

BCa = bladder cancer; IQR = interquartile range.
* Among 128 former smokers.

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