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Brief Report

Wake-Up Call to Address Sleep Health in Non-Muscle Invasive Bladder Cancer: Underappreciated Contributor to Poor Quality of Life

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Abstract.
BACKGROUND: Few studies have specifically examined sleep health in patients with non-muscle invasive bladder cancer (NMIBC). Further study is warranted to inform future strategies in patients with NMIBC.
OBJECTIVE: We aim to describe sleep health in a cohort of patients with NMIBC, and its relationship with quality of life (QOL).
METHODS: We conducted an observational cross-sectional study in patients undergoing surveillance for NMIBC. The validated Pittsburgh Sleep Quality Index (PSQI) was used to assess sleep health (scores from 0-21) in the overall study population as well as stratified. We assessed QOL among participants with and without poor sleep quality using the SF-12 and QLQ-NMIBC-24.
RESULTS: In a cohort of 94 NMIBC patients, median age was 67 years (IQR: 58, 72) and median time since initial diagnosis was 27 months (IQR: 9, 41). The mean PSQI score was 6.3 (SD: 3.8) and 64% percent of participants met or exceeded the PSQI cut-off score of 5, with a score of 5 or more indicating overall poor sleep quality. In those with poor sleep quality, there were statistically significant detriments in multiple QOL domains.
CONCLUSIONS: In patients undergoing surveillance for NMIBC, there is a substantial burden of sleep disturbances and resulting decrements in QOL. These data support the need for future interventions to support sleep quality and highlight the importance of addressing sleep health as part of NMIBC survivorship care to improve QOL in patients with NMIBC.

Keywords: Sleep, bladder cancer, epidemiology, observational

INTRODUCTION

Few studies have specifically examined sleep health in patients with non-muscle invasive bladder cancer (NMIBC), a chronic diagnosis requiring dedicated surveillance [1] with significant implica-

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tions for quality of life (QOL) [2]. An improved understanding of sleep quality in patients with NMIBC is warranted to inform future management strategies and survivorship care. Our objective was to describe sleep quality and its impact on QOL in patients with NMIBC. Other cancers, such as prostate cancer, have shown high rates of sleep disturbances due to both psychological issues like anxiety as well as physical issues such as nighttime urination [3]. Given that NMIBC can also involve some of these same issues, we hypothesized that sleep disturbances are common and associated with decrements in QOL in the NMIBC population.

MATERIALS AND METHODS

We conducted an IRB-approved study (#10-04057) at the University of California, San Francisco (UCSF) using validated questionnaires to assess sleep disturbances and QOL in patients undergoing surveillance for NMIBC using a cross-sectional study design. We identified patients with histopathologic diagnosis of NMIBC (Ta or T1 urothelial carcinoma, carcinoma in situ [CIS]). Exclusion criteria included preferred language other than English, history of muscle-invasive bladder cancer (MIBC), predominant variant histology, and prior radical cystectomy. All consecutive new and follow-up patients with an eligible diagnosis were prospectively offered participation during in-person clinic visits and consented. Consenting participants independently completed surveys electronically via Research Electronic Data Capture (REDCap) or paper questionnaire. Additional clinical information was abstracted via medical record review.

Sleep was evaluated using the validated Pittsburgh Sleep Quality Index (PSQI) [4], which assesses 7 components of sleep during the past month: subjective sleep quality, duration, efficiency, sleep onset latency, sleep disturbances, use of sleep medications, and daytime dysfunction. Each category was rated from 0–3, with a score of 0 corresponding to less impairment. The component scores were summed to calculate a global PSQI score (range: 0–21); consistent with prior research studies, a score ≥ 5 indicated "poor" sleep quality.

We assessed general QOL using the short form health survey (SF-12) [5] and report on the summary mental component score (MCS-12) and physical component score (PCS-12). We assessed NMIBC-specific QOL using the European Organization for Research and Treatment of Cancer's (EORTC) QLQ-NMIBC-24 [6] which has 11 scales or single items (urinary symptoms, malaise, intravesical issues, future worries, bloating and flatulence, sexual function, sexual intimacy, risk of contaminating a partner, sexual enjoyment, and sexual problems (women only, men only).

Sleep and QOL measures were assessed overall and by age (<65, ≥ 65) and participant-reported gender (women, men). We assessed QOL among participants with and without poor sleep quality. We used the mean (standard deviation) to present results for PSQI as it is typically reported, and the median (IQR) for QOL surveys. We conducted *t*-tests or one-way analysis of variance (ANOVA) for continuous variables. Alpha was set at 0.05. We report the *p*-values and a Bonferroni adjustment for the age and gender-specific analyses. Statistical analyses were performed using SAS version 9.4.

RESULTS

We contacted and consented 143 potential participants; 94 (66%) completed the PSQI, SF-12 and QLQ-NMIBC-24. The cohort is predominantly men (70%), White (87%), well-educated (70% with 4-year college degree or higher), retired (49%), and lives at home with a partner/spouse (77%). At the time of the questionnaire, median age was 67 (IQR: 58, 72), with 60% aged 65 or greater, median BMI was 26 (IQR: 24, 29), and median time between initial bladder cancer diagnosis and the survey was 27 months (IQR: 9, 41). The patients had predominantly intermediate- and high-risk NMIBC; 67% presented with high-grade urothelial carcinoma. Most (74%) received intravesical therapy. The most frequent comorbidities in these patients were elevated cholesterol (50%), high blood pressure (42%), and arthritis, rheumatism, or other conditions of the joints or bones (35%).

Among ninety-four participants, the mean PSQI was 6.3 (SD: 3.8), with sleep disturbances, sleep latency, and subjective sleep quality being the three greatest contributors with the worst scores. Sixty-four percent of participants met or exceeded the PSQI cut-off score of 5, indicating overall poor sleep quality. The median mental component score (MCS-12) and physical component score (PCS-12) were 52 (IQR: 44, 56) and 55 (48, 58) respectively (the SF-12 defines 50 as the U.S. average) [5] among

Table 1
Health-Related Quality of Life Differences by Sleep Quality in Patients with NMIBC

Characteristic	Median (IQR) among all participants	Mean among those with PSQI < 5	Mean among those with PSQI ≥ 5	*P*-value[1]
SF-12		*N* = 34	*N* = 47	
PCS12	52 (44, 56)	51.5	47.1	0.03
MCS12	55 (48, 58)	56.1	48.4	<0.0001
QLQ-NMIBC-24 (0-100)[2]				
Scales				
Urinary symptoms	19 (14, 33)	16.2	26.2	0.0009
Malaise	0 (0, 0)	2	6.2	0.04
Future worries	33 (25, 42)	29.3	40.8	0.03
Bloating and flatulence	17 (0, 33)	11.7	24.2	0.0014
Sexual function	33 (17, 50)	40.6	34.4	0.27
Sexual problems (men only)	17 (0, 50)	18.1	33.9	0.048
Single items				
Intravesical treatment issues	0 (0, 33)	3.9	15.7	0.0009
Sexual intimacy	0 (0, 33)	5.6	23.8	0.0018
Risk of contaminating a partner	0 (0, 33)	9.7	23.5	0.04
Sexual enjoyment	66 (33, 100)	70.8	55.1	0.06
Sexual problems (women only)	33 (0, 33)	33.3	21.2	0.52

[1] *T*-tests for continuous variables. [2] Responses were converted onto a numeric scale from 0–100 for all scales and items: Urinary symptoms (higher score = more symptoms), Malaise (higher score = more symptoms), Future worries (higher score = more worries), Bloating and flatulence (higher score = more symptoms), Sexual function (higher score = better functioning), Sexual problems (men only) (higher score = more problems), Intravesical treatment issues (higher = worse), Sexual intimacy (higher = worse), Risk of contaminating partner (higher = worse), Sexual enjoyment (higher = better), Sexual problems (women only) (higher = worse). *Abbreviations:* NMIBC, Non-muscle invasive bladder cancer; PSQI, Pittsburgh Sleep Quality Index; SF-12, short form health survey; QLQ, quality of life questionnaire.

all participants (Table 1). However, both physical health-related ($p = 0.03$) and mental-health related ($p < 0.0001$) QOL were lower in those with poor sleep quality than in those with higher sleep quality; and medians for both scores in those with poor sleep quality were below the national average. Moreover, in those with poor sleep quality, the QLQ-NMIBC-24 revealed statistically significant detriments in QOL related to urinary symptoms, malaise, future worries, bloating and flatulence, sexual problems (men only), intravesical treatment issues, sexual intimacy, and risk of contaminating partner (all $p < 0.05$, Table 1).

Those under age 65 demonstrated worse subjective sleep quality ($p = 0.001$), shorter sleep duration ($p = 0.007$), worse mental health-related QOL ($p = 0.009$), more future worries ($p = 0.003$), and fewer issues with sexual problems (men only) ($p = 0.04$) than those who were 65 or older. Women were more likely to report longer sleep latency ($p = 0.05$), lower sleep efficiency ($p = 0.01$), and more sexual function-related QOL issues ($p = 0.0004$) than men. With a Bonferroni adjustment for age and gender subgroup analyses, *p*-values <0.0038 for age-specific analyses and gender-specific analyses would be statistically significant.

DISCUSSION

In summary, sleep disorders are common in patients with NMIBC with the majority (64%) reporting poor sleep quality. In those reporting poor sleep quality, overall physical and mental health-related QOL and urinary symptom-related QOL were decreased. The subgroup data suggest that patients with NMIBC under the age of 65 and women have a greater risk of sleep and other QOL issues, and may benefit from additional support. These findings are consistent with prior non-cancer specific studies which have demonstrated poorer sleep quality in women than men [7].

These data are from a small observational study of NMIBC patients from a single institution; however, to our knowledge this is the largest study examining sleep quality in patients with NMIBC. This study sought to explore associations between sleep, QOL, and by age and gender to provide data to support future interventions which could target at-risk NMIBC patients. Future observational studies could examine whether sleep and other QOL parameters are associated with risk of recurrence or cancer status and concurrent treatments over follow-

up, and by comorbidities and other covariates, to better support patients while undergoing treatment and in survivorship. Additionally, future studies could examine sleep quality at varying time points for patients diagnosed with NMIBC using a prospective study design. Our study population was comprised of highly educated, mostly White bladder cancer patients with intermediate- and high-risk NMIBC, which limits generalizability. While our study population mirrors the age and gender ratio impacted with NMIBC, a concerted effort to recruit diverse study participants is essential in understanding sleep quality and QOL in women, patients of racial/ethnic minorities [8] and of lower education/SES. Future qualitative studies are warranted to examine the barriers and facilitators of sleep among patients with NMIBC. Strengths of the study include the use of validated instruments to assess sleep health, and the first demonstration of a relationship between poor sleep quality with worse QOL in NMIBC. This study contributes to an understanding of the substantial burden of sleep disturbances and resulting decrements in QOL for patients with NMIBC and supports the need for future interventions to support sleep quality in this population. Our findings suggest that addressing sleep health in clinical practice may be beneficial to improve QOL in patients with NMIBC.

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AUTHOR CONTRIBUTIONS

Contributions are as follows:

SAK and SPP conceptualized the study. SAK and SPP led the methodology. SAK led the statistical analysis. EYW, MAP, SAK, and SPP led the investigation. SPP provided resources. EYW, MAP, SAK, and SPP curated the data. EYW and SAK wrote the original draft. All authors were involved in data interpretation and reviewing and editing the manuscript. SAK and SPP supervised the study. SAK and SPP administered the project and acquired funding.

CONFLICTS OF INTEREST

MVM is an Editorial Board member of this journal, but was not involved in the peer-review process nor had access to any information regarding its peer-review.

EYW, MAP, MVM, SL, SAK and SPP have no disclosures that are related to the current study.

DATA AVAILABILITY

Data are available for bona fide researchers who request it from the authors.

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