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Elucidating the associations between sleep disturbance and depression, fatigue, and pain in older adults with cancer

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ABSTRACT

Objectives: Sleep disturbance is prevalent and often coexists with depression, fatigue, and pain in the cancer population. The aim of this study was to describe the prevalence of sleep disturbance with co-existing depression, fatigue, and pain in older patients with cancer. We also examined the associations of several socio-demographic and clinical variables with sleep disturbance.

Methods: This cross-sectional study consisted of 389 older patients with solid and hematologic malignancies who were referred to the Specialized Oncology Care & Research in the Elderly (SOCARE) clinics at the Universities of Rochester and Chicago between May 2011 and October 2015 and completed a sleep and geriatric assessment (that inquires about fatigue, pain, and depression). Multivariate logistic regression was used to identify variables associated with sleep disturbance.

Results: The prevalence of sleep disturbance was 40%. Of those with sleep disturbance ($n = 154$), 84% also had at least one of the other three symptoms (25% had one symptom, 38% had two symptoms, and 21% had three symptoms). Sleep disturbance was more likely to be reported in those with comorbidities (45% vs. 28%, $P = 0.002$), depression (49% vs. 36%, $P = 0.015$), fatigue (49% vs. 23%, $P < 0.001$), and pain (45% vs. 31%, $P = 0.010$). On multivariable analysis, only fatigue (adjusted odds ratio (AOR) 1.90, 95% CI 1.10–3.30, $P = 0.020$) was independently associated with sleep disturbance.

Conclusions: Sleep disturbance is prevalent and often co-occurs with depression, fatigue, or pain in older patients with cancer. Fatigue was significantly associated with sleep disturbance and future studies should explore interventions that target sleep disturbance and fatigue.

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1. Introduction

Cancer incidence increases exponentially with advancing age. By 2030, 65% of cancers are expected to occur in adults aged 65 or above [1]. Patients with cancer often suffer from a variety of symptoms related to their underlying disease and its treatment. In the older population, which is already susceptible to other comorbidities and geriatric syndromes, the consequences of these symptoms can be debilitating and can lead to decreased quality of life as well as functional status [2].

When assessed systematically, sleep disturbance is one of the more common symptoms experienced by patients throughout their disease and treatment trajectories. A history of cancer increases the likelihood of patients reporting sleep disturbance when asked on surveys [3]. In

a convenience sample of older patients with cancer, the prevalence of sleep disturbance was reported to be 60% [4]. Our group also previously reported a 40% prevalence of sleep disturbance in 389 older patients with cancer evaluated at two geriatric oncology-based clinics [5]. Sleep disturbance typically does not exist in isolation; prior studies found that sleep disturbance often co-exists with depression, fatigue, and pain in the cancer population [6,7]. In a study involving 120 older patients receiving active chemotherapy or radiation, 20% and 29% of patients reported co-occurrence of any two and any three of the aforementioned symptoms, respectively [4].

Approximately one-third also reported co-occurrence of all of the four symptoms. However, this study had a small sample size and the majority (84%) was in the young-old group (defined as ages 65 to 74). Despite the high prevalence and occurrence with other symptoms, sleep disturbance is usually not addressed during clinic visits, either because patients do not report their symptoms to their physicians or when reported, these were not addressed by physicians [8,9].

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A number of risk factors for sleep disturbance have been described in the cancer population. In a prospective study of 180 patients with advanced cancer, factors such as well-being, pain, dyspnea, and obstructive sleep apnea were independent predictors of sleep disturbance [10]. In a separate longitudinal study of 80 patients with prostate cancer undergoing radiation, factors such as younger age, presence of anxiety and depression as well as baseline sleep disturbance predicted the occurrence of sleep disturbance following treatment [11]. However, these studies did not focus on older patients.

In this study, we aimed to examine the prevalence of sleep disturbance with co-occurring depression, fatigue, and pain in the largest sample to date of older patients with cancer presenting for evaluation at two university-based geriatric oncology clinics. For those who reported sleep disturbance on surveys, we examined whether sleep was addressed by physicians and pattern of sleep medication use. In the entire study cohort, we also evaluated the associations of depression, fatigue, pain, and several socio-demographic and clinical variables with sleep disturbance.

2. Methods

2.1. Design, Setting and Population

This was a cross-sectional study conducted at two university hospitals: University of Rochester Medical Center and University of Chicago Medical Center. We included patients aged 65 years or older with cancer who were referred to the Specialized Oncology Care & Research in the Elderly (SOCARE) clinics between May 2011 and October 2015. The SOCARE clinics are staffed by a team of healthcare professionals including physicians with expertise in geriatric oncology, nurses, a social worker, a nutritionist, a physical therapist, and an occupational therapist. All patients undergo either a brief or comprehensive geriatric assessment (GA) on their initial visit depending on when they were referred to the clinics (i.e. those who were referred early prior to their clinic visits received the comprehensive GA). The assessment is used by the physicians to assist in treatment decision-making. The GA consists of a number of validated tools to assess functional status, cognition, nutritional status, comorbidities, medications, psychological status, social support, and symptom burden. A sleep assessment was included in the comprehensive GA. Between May 2011 and October 2015, a total of 680 patients were seen in the clinics and consented to the study. Brief GA was administered in 208 patients and they were excluded. For the remaining 472 patients, 83 patients did not complete the sleep assessment. A total of 389 patients were included in our final study population.

2.2. Patient and Clinical Characteristics

We collected demographic variables including age, gender, race, marital status, education level, and employment status. In addition, clinical variables such as comorbidity as well as depression, fatigue, and pain were collected with the GA [12]. Cancer type and stage were assessed via the GA (if available) or extracted from the clinic notes. For patients seen at the University of Rochester, we also collected data on the use of sleep medications (such as benzodiazepines, nonbenzodiazepine hypnotics, melatonin and melatonin receptor agonist, antidepressants, and antihistamines) and whether sleep disturbance was mentioned in any clinic notes within three months before the initial visit. This data was not available at the University of Chicago due to inability to review the medical record (N = 101).

We used the Older Americans Resources and Services Questionnaire (OARS) Physical Health subscale to define the presence of comorbidity [13]. OARS contains 13 comorbidities including other cancer or leukemia, arthritis or rheumatism, glaucoma, emphysema or chronic bronchitis, hypertension, heart disease, peripheral vascular disease, diabetes, gastrointestinal disorders, osteoporosis, chronic liver or kidney

disease, stroke, depression. Patients were considered to have a comorbidity if they reported one or more illnesses that affected them “great deal”, or three or more illnesses that affected them “somewhat”. Depression was defined using the 15-item Geriatric Depression Scale. A score of 5 or above was considered positive [12]. The presence of fatigue was assessed based on the dichotomous question, “Do you have fatigue now?” Pain was assessed using a Clinical Symptom Inventory, which is a multi-symptom patient-reported outcome measure. Patients were asked to rate the severity of their pain at its worst during the last week on a scale of 0 to 10 with 0 being “not present” and 10 being “as bad as you can imagine.” We defined the presence of pain as a score of 1 or above.

2.3. Dependent Variable

The dependent variable was the presence of sleep disturbance assessed with the GA. This was self-reported based on the dichotomous question, “Do you have sleep problems now?” A simple question was used to minimize respondent burden.

2.4. Statistical Analysis

Descriptive statistics (mean, standard deviation, range, and percentages, as appropriate to the scale of measurement) were used to describe our study population and the prevalence of symptoms. A chi-square test was used to compare the characteristics of patients with and without sleep disturbance. Multivariate logistic regression was used to examine the associations of the various demographic variables (age, gender, race, marital status, education level, and employment status), clinical characteristics (cancer type, stage, and comorbidity) and symptoms (fatigue, pain, and depression) with sleep disturbance. We evaluated for interactions between sleep disturbance, depression, fatigue, and pain. All analyses were carried out using SAS statistical software (Version 9.3, Cary, NC). The project was approved by the University of Rochester and the University of Chicago Medical Center's Research Subjects Review Boards.

3. Results

3.1. Demographics and Clinical Characteristics

A total of 389 patients were included in our study. The median age of the patients was 81 years (SD = 6.9, range 55–97; three patients were below the age of 65 and were referred because they were experiencing geriatric syndromes); 45% were female and 74% were white. Approximately half were married and 45% had higher than a high school diploma. For cancer subtypes, genitourinary (30%), gastrointestinal (25%), and lung cancer (18%) were the most common. Almost half (48%) had stage III or IV cancer. Comorbidity was present in 70%. Other demographics are shown in Table 1.

3.2. Prevalence of Sleep Disturbance and Co-occurring Pain, Fatigue and Depression

The prevalence of sleep disturbance, depression, fatigue, and pain were 40% (154/389), 31% (119/389), 60% (223/389), and 56% (193/389), respectively. There was a high rate of co-occurrence between sleep disturbance and depression, fatigue, and pain. Of those with sleep disturbance (n = 154), 84% also had at least one of the other three symptoms (25% had one additional symptom, 38% had two additional symptoms, and 21% had three additional symptoms) (Fig. 1). Among those patients who reported sleep disturbance at the University of Rochester (n = 116), sleep disturbance was mentioned in at least one of the clinic notes three months prior to the initial visit in 15 patients. In total, 52 sleep medications were present in 38% of patients (44/116) (Table 2). Seven patients were on more than one of these medications.

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