Review Article

Sleep disturbance in patients with cancer

ABSTRACT

Patients diagnosed with cancer often experience sleep disturbance in the form of poor sleep patterns or insomnia that can start on diagnosis and continue until the end of the individual's life. The aim of this review is to discuss current definitions and theories of sleep disturbance, its prevalence, the underlying physiological and psychological correlates, measurement scales, and possible intervention and management strategies. Equally important, regular assessment is worthwhile for sleep disturbance and quality of life among cancer patients. Therefore, it is advisable for health-care professionals to conduct regular assessment of sleep disturbance for cancer patients and provide appropriate management.

Keywords: Definition, etiology, prevalence, risk factors, scale, sleep disturbance

INTRODUCTION

Diagnosis of cancer is a major life stressor that can affect the physiological, psychological, and physical state of a person. The cancer journey can involve pain, weakness, sleep problems, and fatigue, and may cause limited function in terms of active daily living. People with cancer may experience symptoms related to their treatment and/or disease type and stage. One of the most common and distressing symptoms is sleep disturbance, which negatively affects the quality of life.[1] Patients diagnosed with cancer often experience sleep disturbance, especially insomnia. Sleep disturbance among cancer patients is a familiar problem and can start with the diagnosis and continue to the end of the patient's life.[2,3]

This review will discuss the current definitions and theories of sleep disturbance, its prevalence, the underlying physiological and psychological correlates, measurement scales, and possible intervention and management strategies.

DEFINITIONS OF SLEEP DISTURBANCE

There are potential difficulties in defining sleep disturbance or disorder, as sleep quality is a multidimensional concept. Buysse[4] defines sleep health as, "a multidimensional pattern of sleep-wakefulness, adapted to individual, social, and environmental demands, that promotes physical and mental well-being." Good sleep health is characterized by subjective satisfaction, appropriate timing, adequate duration, high efficiency, and sustained alertness during waking hours.

The National Institute of Health[5] defines sleep disturbance as, "dysregulation of sleep homeostasis, sleep deficiency, sleep fragmentation, insufficient sleep or impairment of sleep quality or quantity caused by a sleep disorder." Specifically, sleep disturbance may include difficulty falling asleep, problems with the initiation and maintenance of sleep, poor sleep timing, quality, efficiency, and excessive daytime sleepiness.[6-8]

The International Classification of Sleep Disorder-3 divides sleep symptoms into the following three diagnostic sections: insomnia, sleepiness, or abnormal events during sleep.[9] Insomnia is a sleep disturbance symptom that has been excessively used in the literature to describe sleep symptoms

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among patients diagnosed with cancer. Roth *et al*.[10] defined insomnia as difficulty initiating or maintaining sleep or nonrestorative sleep; it is also associated with daytime distress or impairment.

Difficulty sleeping is a phrase regularly used by patients to describe their sleep. The major challenge facing the researcher is to verify what this means and how to measure it. The following nine parameters of sleep disturbance have been recommended to measure sleep problems: total sleep time, sleep latency, awakenings, wake time after sleep sunset, napping during the day, excessive daytime sleepiness, quality of perceived sleep, stability of circadian rhythms, and sleep efficiency.[11] Adult parameters of sleep disturbance include sleeping for <7 h, sleep latency of >20 min, awakening >7 times during the night, waking after sleep onset >10% of the time, napping during the daytime for >2 h, minimal opportunities for daytime sleepiness while engaging with routine activities, satisfaction with the quality of perceived sleep, circadian rhythms within a 27 h period, and <80% sleep efficiency indicating a bad night.[6]

Sleep disturbance, thus, is a multidimensional concept that is, accordingly, measured across multiple aspects or dimensions. Understanding the differences between normal sleep and poor sleep can help health-care professionals in designing interventions to improve sleep, through a comprehensive care plan that meets the needs of patients with cancer. Defining sleep disturbance will, thus, guide the researcher and promote the health of such patients.

PREVALENCE OF SLEEP DISTURBANCE

Sleep disturbance is reported to be the second most common symptom among cancer patients.[12] Identifying the prevalence of sleep disturbance is important in understanding the underlying problem and developing treatment or a particular intervention for patients with cancer. A systematic review by Otte *et al*.[13] found that the prevalence for specific types of sleep disturbance in cancer remains unclear.

Sleep disturbance prevalence, type, and severity are difficult to assess in patients diagnosed with cancer, with incidences ranging from 50%[11] to 88%.[14] This is approximately three times higher than the rate within the general population.[15] Differences in prevalence among cancer patient populations may be partially dependent on cancer types, stages, and time of measurement such as pre- or post-chemotherapy/pre- or post-radiotherapy.

In a recent study, Akman *et al*.[16] examined the prevalence of sleep disturbance in 314 patients with different types of cancer; these researchers found 40.4% of patients suffered from poor quality sleep. An integrative review of 27 studies evaluating sleep quality in women with breast cancer found that the prevalence of sleep disturbance ranged from 65% to 87%.[17] In a large population-based study, Voiss *et al*.[18] reported sleep problems from the 2017 US National Health Interview Survey of 23,222,976 cancer survivors and found that 59.2% reported sleep problem. Al Maqbali *et al*.[19] conducted a cross-sectional study to identify sleep disturbance in 369 cancer survivors and found that the prevalence of poorer sleep among participants was 78%. A prospective study of 73 patients with breast cancer reported that 97% of patients experienced poor-quality sleep.[20]

Different types of cancer can lead to different percentages of patients experiencing sleep disturbance; for example, thyroid, 54.32%;[21] lung, 93.1%;[22] head and neck, 83%;[23] leukemia, 67.5%;[24] and melanoma, 60.7%.[25] Savard *et al*.[26] conducted a longitudinal study of patients with breast (n = 465) and prostate (n = 263) cancer to evaluate the relationship between adjuvant treatment and insomnia. They found that for breast cancer patients, insomnia was 66.2% at baseline, 51% at 6 months, and 38.8% at 18 months, whereas for prostate cancer patients, insomnia was 36.9% at baseline, 29% at 6 months, and 25% at 18 months.

Sleep disturbance may occur during the treatment of cancer, before and after surgical interventions, during radiotherapy and/or chemotherapy, and even after completing treatment. A longitudinal study by Halle *et al*.[27] explored sleep disturbance in 264 lung cancer patients who had undergone surgery and found that sleep disturbance was 60.9% at baseline, 68.5% at 1 month, 55.4% at 5 months, and 49.7% at 9 months.

Hong *et al*.[28] assessed sleep disturbance every 4th week during chemotherapy treatment for 706 patients with mixed types of cancer. They found that sleep quality was 51.86% at baseline and 68.54%, 83.48%, 89.36%, and 96.43% every 4th week, showing an increase in sleep disturbance during chemotherapy treatment. An observational study conducted by Tian *et al*.[29] involving 76 cervical cancer patients undergoing chemotherapy found that sleep quality was 61.84% before and 64.50% after adjuvant therapy.

Radiotherapy is a primary form of treatment for cancer patients. A prospective study by Mo *et al*.[30] investigated sleep changes before and after radiotherapy for 51 nasopharyngeal cancer patients; the results showed that 37.3% of patients

had poor sleep quality before starting radiotherapy, which increased to 64.7% after radiotherapy. Similarly, a longitudinal study of eighty breast cancer patients found that poor sleep before, during, and after radiotherapy was 61%, 56%, and 59%, respectively.[31]

Sleep disturbance may increase even after completing treatment. For instance, Lowery-Allison *et al*.'s[32] study of breast cancer survivors, 1–10 years posttreatment, found that 38% (76 out of 200) of patients experienced poor quality sleep. Findings from a cross-sectional survey of 337 cancer survivors by Ness *et al*.[33] found that 50% of participants reported sleep disturbance.

A systematic review of 254 studies by Otte *et al*.[13] found that the prevalence of sleep disorders could not be ascertained from research on patients with cancer. This was primarily due to the conceptualization and operationalization of "poor sleep," as the studies used different terminology that did not fully assess sleep disorder; thus, most of the studies (89.8%; 228) did not define sleep disorders. A cross-sectional study in South Korea by Park *et al*.,[34] of 30,400 patients diagnosed with cancer, found the prevalence of insomnia to be 8.21%; this was highest among lung cancer patients. However, the study did not use an instrument to measure insomnia, which means the percentage only reflects patients diagnosed with insomnia. Sleep disturbance can be assessed using objective measures and through self-reports. Wrist actigraphy is one such objective measure; however, many researchers have used a self-report instrument to measure sleep disturbance. The different findings between the studies reported above could be due to the variety of assessment methods used.

Consequently, understating the level of poor sleep among patients with cancer before, during, and after treatment is an important research area that will help in the development of an intervention for specific types of cancer and different stages of the cancer patient journey. However, as this review of the literature shows, it is important to use a valid and standard method of assessing "poor sleep".

IMPACT OF SLEEP DISTURBANCE

Sleep disorders are reported to be associated with decreased quality of life, increased use of health-care resources, and poor mood. Sleep disturbance has also been linked with the likelihood of cancer recurrence[35,36] and may result in poor healing,[13] decreased cognitive functioning,[37] and reduced work activity.[38]

Evidence of sleep disturbance impact is provided by surveys from the USA and five European countries, which found that people with insomnia experienced significantly worse health-related quality of life compared to people with normal sleep.[39] Sleep disturbance can cause changes in metabolism,[40] immune pathways,[41] and endocrine functioning.[42] Similarly, sleep disturbance in cancer patients can have a negative impact on health-related quality of life, which includes physical and psychological functioning.[43,44]

Research indicates that sleep disorders or poor sleep can have other negative effects on health, insofar as it can significantly increase the risk of developing Type 2 diabetes[45] and hypertension[46] and increase the risk of cardiovascular disease.[47] However, it is important to note that the consequences of sleep disorders are not confined to the individual; they may also have implications at a societal level in terms of public health and economic burdens.[48]

ETIOLOGY AND INFLUENCIAL FACTORS OF SLEEP DISTURBANCE

Sleep disturbance in patients with cancer may be attributable to the physiological and psychological effects of the cancer and the effects of treatment, surgery, chemotherapy, radiotherapy, and medications. Thus, it is difficult to establish the etiology of sleep disturbance.

In terms of demographic factors, being female, older age, having a lower level of education, and engaging in less physical activity have all been linked to sleep disturbance.[49-51] In a cross-sectional study of 209 mixed cancer patients, Akechi *et al*.[52] found a significant relationship between sleep disturbance and younger age, marital status (unmarried), living alone, higher psychological distress, pain, and diarrhea. However, the age relationship may be influenced by other factors that could increase sleep disturbance. For instance, Coles *et al*.[53] found that pain, anxiety, fatigue, and multiple comorbid conditions were significantly associated with worsening sleep disturbance among colorectal cancer patients. Galiano-Castillo *et al*.[54] also found a significant relationship between insomnia and types of treatment, depression, and anxiety among breast cancer patients.

In the context of cancer, tumor type and the treatments used may influence sleep disturbance. For example, Savard *et al*.[55] conducted a longitudinal study of 962 mixed patients over 18 months and found a significant association between insomnia and different types of cancer, including breast, prostate, gynecologic, urinary, and gastro-intestinal cancer. Furthermore, studies conducted on cancer patients to assess treatment efficacy found that chemotherapy[56] and radiotherapy[57] were significantly associated with an increase in sleep disturbance.

Furthermore, chemotherapy and radiotherapy have been associated with an increase in sleep disturbance and the level of pro-inflammatory cytokine markers such as interleukin (IL)-1β and IL-6 and tumor necrosis factor-α.[58-60] Current evidence shows that immune mediators are released as a response to pathogen invasion tissue injury or cytotoxic factors.[61] Even though some studies have found a relationship between cytokine markers and sleep disturbance, this is still not fully understood and further research is required in this area. Cancer-induced changes in metabolism, immunity, or endocrine function likely disrupt sleep via the promotion of aberrant activity within some neural populations.[62]

Overall, research findings suggest that sleep disturbance is associated with several different factors, but these factors will change from patient to patient. Further research should, therefore, explore these factors to facilitate their appropriate management and develop a strategy to prevent or reduce sleep disturbance.

MEASUREMENT OF SLEEP DISTURBANCE

Sleep disturbance can be assessed either objectively or subjectively. The two most common objective measurements for patients with cancer are polysomnography (PSG) and actigraphy, whereas the following three subjective scales have been used and validated in cancer populations: the Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scales (ESS), and the Insomnia Severity Index (ISI). However, each of the assessment methods has both advantages and disadvantages.

Objective measures

PSG is the gold standard for recording sleep.[63,64] The components of PSG consist of electroencephalography, electrocardiogram, electrooculography, electromyography, arterial oxygen saturation, respiratory effort, oral and nasal airflow, body position, and limb movement.[65] The data derived from PSG involve sleep latency, wake after sleep onset time, total sleep time, and sleep efficiency. However, PSG is expensive and does not provide information about sleep habits at home.

Actigraphy involves wearing a wrist device that measures movement activity between sleep and awake states.[66] The advantages of actigraphy are that it is easy to use, it is cheaper than PSG, and it can record for 24 h for a month.

Subjective measures

The PSQI is a 19-item scale designed to measure different aspects of sleep quality and sleep disturbance.[67] The scale reports the sleep quality of the previous month. The PSQI is divided into seven subscale scores, namely, subjective sleep quality, sleep latency (time to full sleep), duration, habitual sleep efficiency (proportion between total sleep time and time in bed), sleep disturbances (waking up during the night), use of sleeping medication, and daytime dysfunction (difficulty staying awake during daytime). The overall score ranges between 0 and 21; the high score indicates poor sleep quality. The original PSQI was tested on both psychiatric patients and a healthy sample; however, it has been validated in different clinical populations. Two studies have validated the PSQI in patients with cancer and showed internal consistency (Cronbach's alpha = 0.89).[68,69]

The ESS was constructed to assess daytime sleepiness and diagnose sleep disorders across eight items in a 4-point Likert scale.[70] The total score ranges between 0 (normal sleep) and 24 (very sleepy).

The ISI has seven items on a 5-point Likert scale; it has three subscales assessing the nature, severity, and impact of insomnia.[71] The scale measures the interval in the last 2 weeks. The overall score ranges between 0 and 28; the higher score indicates more severe insomnia. The total score can be categorized as follows: 0–7 (absence of insomnia); 8–14 (subthreshold insomnia); 15–24 (moderate insomnia); and 22–28 (severe insomnia).

All subjective measures are easy to administer and cheap, however they cannot roll out the subjective recall biases.[72] Consideration should be given when choosing an appropriate instrument of measuring sleep quality for research or clinical proposes, as each objective or subjective measure has advantages and disadvantages.

MANAGEMENT OF SLEEP DISTURBANCE

The management of sleep disturbance has involved a range of interventions that can be divided into pharmacological and nonpharmacological approaches. Several studies have investigated the effectiveness of nonpharmacological interventions on sleep disturbance in cancer patients, whereas no pharmacological interventions have been included in studies involving cancer patients. For example, cognitive behavioral interventions (CBIs) have had significant effects on reducing sleep disturbance, with several reviews recommending their use.[73,74] CBIs include sleep hygiene, stimulator control, relaxation therapies, sleep restriction, and cognitive restructuring. In a meta-analysis of nine studies, Johnson *et al*.[74] found that CBIs lead to reductions in insomnia, sleep-onset latency, and improved sleep efficiency in cancer survivors. A randomized controlled trial of 248 patients with breast cancer was undertaken by

Savard *et al*.[75] who found that CBIs had a significant effect on insomnia at a 12-month follow-up.

In a study by Reich *et al*.[76] involving 320 breast cancer patients, a mindfulness-based stress reduction (MBSR) was applied for 12 weeks; it had a significant effect on sleep quality. This result was supported by a randomized controlled trial evaluating the effectiveness of MBSR among breast and colorectal cancer patients, which also showed a significant reduction in sleep disturbance.[77,78]

Other mind–body practices focusing on the interaction between the brain, mind, body, and behavior, have demonstrated an improvement in sleep disturbance, such as yoga;[79] warm shower or baths;[80] acupuncture;[81] Qi Gong/Tai Chi;[82] and massage.[83]

Exercise interventions to reduce sleep disturbance among cancer patients have been undertaken and reported in several reviews. However, the evidence was inconclusive due to biases in several studies. In a recent systematic review and meta-analysis of 17 randomized controlled trials (RCTs) and four non-RCTs involving a total of 1595 participants, Mercier *et al*.[84] concluded that exercise interventions have no significant effect on sleep outcomes in patients with cancer. However, in comparison, a systematic review by Chiu *et al*.[85] of nine RCTs involving 599 patients found a modest effect of walking exercise on reducing sleep disturbance.

A number of clinical practice guidelines have been published for pharmacological management of the general population. For example, the American Academy of Sleep Medicine (AASM) conducted a meta-analysis of 46 studies and found weak evidence to support the use of 14 agents (suvorexant, eszopiclone, zaleplon, zolpidem, triazolam, temazepam, ramelteon, doxepin, trazodone, tiagabine, diphenhydramine, melatonin, tryptophan, and valerian).[86] The AASM guidelines concluded that these agents are not recommended for the treatment of chronic insomnia in adults.

To conclude, the Oncology Nursing Society published guidelines that critically appraised evidence for the safety and efficacy of using pharmacological and nonpharmacological interventions to reduce sleep disturbance in patients with cancer.[87] The guidelines found sufficient evidence to use CBIs, while MBSR and exercise intervention were likely to be effective, but required further research. Research on pharmacological interventions in cancer populations has yet to be conducted.

CONCLUSION

Sleep disturbance is a multidimensional concept whose prevalence and severity is higher among patients with cancer. The impact of sleep disturbance has been linked to the recurrence of cancer and a reduced life span among cancer survivors. This review has provided important evidence for measuring and managing sleep disturbance that can help in understanding sleep disturbance among cancer patients. Assessing sleep disturbance should be routine in clinical settings, thus identifying proper interventions, treatment, and management to improve sleep quality among cancer patients.

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Conflicts of interest

There are no conflicts of interest.

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