Interactive CardioVascular and Thoracic Surgery 25 (2017) 285–291
doi:10.1093/icvts/ivx076 Advance Access publication 8 May 2017

ORIGINAL ARTICLE

Cite this article as: Halle IH, Westgaard TK, Wahba A, Oksholm T, Rustøen T, Gjeilo KH. Trajectory of sleep disturbances in patients undergoing lung cancer surgery: a prospective study. Interact CardioVasc Thorac Surg 2017;25:285–91.

Trajectory of sleep disturbances in patients undergoing lung cancer surgery: a prospective study

Ingrid Helene Halle[a,†], Therese Krystad Westgaard[a,†], Alexander Wahba[a,b], Trine Oksholm[c,d], Tone Rustøen[e,f] and Kari Hanne Gjeilo[a,b,g,h,*]

[a] Department of Circulation and Medical Imaging, Faculty of Medicine, Norwegian University of Science and Technology (NTNU), Trondheim, Norway
[b] Department of Cardiothoracic Surgery, St. Olavs Hospital, Trondheim University Hospital, Trondheim, Norway
[c] VID Specialized University, Haraldsplass, Bergen, Norway
[d] Department of Respiratory Medicine, Oslo University Hospital, Rikshospitalet, Oslo, Norway
[e] Department of Nursing Science, Faculty of Medicine, University of Oslo, Oslo, Norway
[f] Department of Research and Development, Division of Emergencies and Critical Care, Oslo University Hospital, Ullevål, Oslo, Norway
[g] Department of Cardiology, St. Olavs Hospital, Trondheim University Hospital, Trondheim, Norway
[h] National Competence Centre for Complex Symptom Disorders, St. Olavs Hospital, Trondheim, Norway

* Corresponding author. Department of Cardiothoracic Surgery, St. Olavs Hospital, PO Box 3250 Sluppen, 7006 Trondheim, Norway. Tel: +47-72-826924; fax: +47-72-826714; e-mail: kari.hanne.gjeilo@stolav.no (K.H. Gjeilo).

Received 1 November 2016; received in revised form 27 January 2017; accepted 15 February 2017

THORACIC

Abstract

OBJECTIVES: Patients with lung cancer report sleep difficulties to be frequent and bothersome symptoms. This study describes the trajectory of sleep from before and up to 12 months after surgery for lung cancer. Further, it investigates possible associations between sleep disturbance, demographic and clinical characteristics before surgery.

METHODS: This study is part of a longitudinal multicentre study. Sleep disturbance was measured by The General Sleep Disturbance Scale (GSDS) that investigates frequencies of sleep difficulties (21 items) and a total sum score ≥43 indicates a clinically meaningful level of sleep disturbance (score range 0–147). Linear mixed models were used to study changes in sleep from baseline to 1, 5, 9 and 12 months after surgery.

RESULTS: The percentage of patients (n = 264) reporting sleep disturbances was 60.9% at baseline, 68.5% at Month 1, 55.4% at Month 5, 51.3% at Month 9 and 49.7% at Month 12. The increase to and decrease from Month 1 was the only significant alteration in the occurrence of sleep disturbance. The patients reported most problems within the subscales sleep quantity, early awakenings and sleep quality. Factors associated with sleep disturbance were lower age, use of pain medication and psychotropic medication and higher comorbidity score.

CONCLUSIONS: Lung cancer patients sleep poorly, before as well as after surgery. There is a need to address sleeping disturbance routinely in clinical practice and screening for sleeping problems is indicated. Further studies are warranted concerning factors that contribute to sleep disturbance and how they best can be treated.

Keywords: Lung cancer • Surgery • Sleep • Symptoms • Patient-reported outcomes

INTRODUCTION

Increased long-term survival after lung cancer has led to a growing interest in addressing issues and symptoms faced by long-term survivors [1]. Hence, the importance of measuring patient-reported outcomes is increasingly emphasized [2]. Studies on quality of life in lung cancer patients after surgery show diverging long-term results. However, all show a marked reduction in the quality of life in the first postoperative months [3, 4]. Sleep disorders are often assumed to be part of a cluster of symptoms reducing the quality of life, such as pain, fatigue, depression and anxiety [5].

Previous studies have shown that sleep disturbances are common in cancer patients [6] and insomnia has been rated the second most bothersome symptom based on cancer and treatment status [7]. Chronic sleep deficiency is a growing and an underappreciated determinant of health status [8]. Few studies have focused on possible associations between clinical and demographic characteristics and the course of sleep disturbances in patients undergoing surgery for lung cancer. In previous studies, sleep has mainly been examined as one of many symptoms [9] and not been described in detail. In these studies, patients with sleep disturbances exhibited worse psychological and

†The first two authors contributed equally to this work.

physiological symptoms such as more pain, anxiety, depression and fatigue [9, 10]. Further, studies in the general population and other cancer populations suggest that gender, age and comorbidity are predictors for sleep disturbances [11, 12]. Few studies have examined sleep longitudinally in patients with lung cancer. A study by Gooneratne *et al.* [1] found that lung cancer survivors had significant sleep problems even 8 years after diagnosis. However, to our knowledge, no studies have focused especially on sleep in patients undergoing surgery for lung cancer. Hence, the main aim of the present study was to describe the trajectory of sleep from before and up to 12 months after surgery for lung cancer. Secondary aims were to examine the prevalence of self-reported sleep disturbances in the same time span and to investigate possible associations between sleep disturbance and demographic and clinical characteristics before surgery.

METHODS

Patients, settings and study procedure

This study is part of a larger, descriptive, longitudinal multicentre study investigating several dimensions of patient-reported outcomes among lung cancer patients before and after surgery [13]. Patients scheduled for surgery for primary lung cancer who were 18 years or older and were able to read, write and understand Norwegian were eligible for inclusion. Exclusion criteria were cognitive impairment, cancellation of surgery, surgical exploration without curative resection or cases where histological examination after surgery revealed that the patient had benign or metastatic disease.

Patients were recruited from 3 university hospitals in Norway (i.e. Oslo University Hospital in Oslo, St. Olavs Hospital in Trondheim and Haukeland University Hospital in Bergen). Recruitment started in November 2010 and was completed in March 2012. The study was approved by the Regional Ethical Review Committe (REK number 2010/1508 b) and supported by the institutional review boards (Personvernombudet) at these hospitals.

The majority of the patients (91%) were recruited in the hospital 1 to 3 days before surgery. The remaining 9% of the sample was recruited in the outpatient clinic prior to surgery. After giving written informed consent, patients completed the baseline study questionnaires before surgery. Data were also collected by postal surveys at Months 1, 5, 9 and 12 after surgery.

Instruments

Demographic and clinical characteristics. Patients provided information on sociodemographic variables at enrolment. Research nurses completed information on age, smoking status, height, weight and use of preoperative medication. Medical records were reviewed for information on tumour histology, type of surgery and tumor node metastasis classification [14].

Self-Administered Comorbidity Questionnaire. The Self-Administered Comorbidity Questionnaire (SCQ) includes 16 common medical conditions and 3 optional conditions, adding points for treatment or limitations in activities. The total SCQ score can range from 0 to 57. The total SCQ has well-established validity and reliability for a variety of conditions [15].

General Sleep Disturbance Scale. The General Sleep Disturbance Scale (GSDS) was used to obtain information on sleep. The GSDS is a self-rated 21-item questionnaire investigating the frequencies of defined sleep difficulties in the past week. Frequencies of the respective items are indicated on a numeric rating scale ranging from 0 (never) to 7 (every day). The total sum score thus has a possible range of 0–147. Higher scores indicate more severe sleep disturbance. The 21 items are divided into 7 subscales: sleep onset latency (1 item), mid sleep wakes (1 item), early awakenings (1 item), quality of sleep (3 items), quantity of sleep (2 items), excessive daytime sleepiness (7 items) and medications for sleep (6 items). This study has made use of cut-off points for GSDS scores consistent with most previous studies [16], a GSDS total sum score $\geq$43 and mean subscale scores $\geq$3 indicate a clinically meaningful level of sleep disturbance [16]. In the calculations of total and mean GSDS scores, adjustments were made for missing data. If at least 70% of the questions were answered, a total value for all questions was estimated by replacing missing data with the mean scores from the other answers before calculating the total score. The GSDS has well-established validity and reliability in cancer patients [16]. The Cronbach's α was 0.86 for the 21 GSDS items at baseline and 0.85 at Month 12, suggesting a satisfactory internal consistency in the present study.

Statistical analyses

The data are given as means and standard deviations or frequencies and percentages. Linear mixed models fitted by restricted maximum likelihood were used to study changes in sleep over the 5 time points of measurement. Candidate covariates were chosen based on previous research [9–12] and statistical significance in univariate analyses. Age, analgesics, psychotropic medicine, comorbidity (assessed by SCQ) and work status were found to be significantly related to sleep (Table 1). Work status is highly related to age and was therefore not included in the linear mixed model. Gender was not significantly related to sleep in univariate analyses in our study but was included in the model based on previous studies [11]. The model was first fitted with total GSDS as the dependent variable, gender, time, analgesics and psychotropic medicine as fixed factors while age and SCQ score as continuous covariates. Within-subject correlation was accounted for by including a subject-specific random intercept. Two interaction terms, Time x Age and Time x Gender, were included in the model. A more parsimonious model was fitted with total GSDS as the dependent variable, gender and time as fixed factors and age as continuous variable.

Goodness of fit was evaluated by Akaike's information criteria [17]. Q–Q plots of the residuals were inspected visually to assess the normality assumption. *Post hoc* pairwise comparisons were performed with Bonferroni adjustment.

P-values <0.05 were considered statistically significant. Statistical analyses were performed using IBM SPSS statistics 21.

RESULTS

Patient characteristics and comorbidities

A total of 375 patients with presumptive primary lung cancer were asked to participate in the study and 307 agreed (81%).

Table 1: Demographic and clinical characteristics of the lung cancer patients before surgery

Characteristic (n = 245–264[a])	Mean (SD)	n (%)
Age (years)*	65.8 (8.5)	
Gender (female)		112 (42.4)
Lives alone		59 (23.5)
Education		
Primary/secondary school		211 (83.7)
University/college		41 (16.3)
Work status*		
Full- or part-time		75 (29.9)
Sick leave or disability		66 (26.3)
Retired or other		110 (43.8)
Smoking status		
Smoked until surgery		120 (45.6)
Stopped at least 1 year before surgery		126 (47.9)
Never smoked		17 (6.5)
Body mass index	25.9 (4.7)	
Tumour type		
Adenocarcinoma		149 (56.4)
Squamous-cell carcinoma		81 (30.7)
Small cell		6 (2.3)
Carcinoid		6 (2.3)
Other		22 (8.3)
Stage of cancer		
IA		80 (32.7)
IB		79 (29.9)
II		45 (18.4)
IIIA		40 (16.4)
IIIB/IV		1 (0.4)
Psychotropic drugs before surgery (yes)*		53 (20.1)
Pain medication before surgery (yes)*		42 (15.9)
SCQ-19[b,*]	4.4 (3.8)	

[a]*n* varies due to missing values.
[b]The Self-administered comorbidity questionnaire (SCQ) includes 16 common comorbidities and 3 optional conditions. The total SCQ-19 score can range from 0 to 57.
*$P < 0.05$: significantly related to sleep measured by General Sleep Disturbance Scale in univariate analyses at one or more time points (e.g. baseline, 1, 5, 9 or 12 months after surgery).

Based on prespecified exclusion criteria, 22 patients were excluded. Of the remaining 285 patients, 264 patients completed the questionnaire at baseline (92.6%). The flow chart in Fig. 1 shows inclusion and exclusion of patients throughout the entire study. Demographic and clinical characteristics for the patients at baseline are presented in Table 1. The patients' mean age was 65.8 (±8.5) years, and 152 (58%) of them were men. The patients had a mean SCQ score of 4.4 (±3.8) ranging from 0 to 21.

Sleep disturbances

The percentage of patients reporting sleep disturbances, defined as GSDS total sum score ≥43, was 60.9% at baseline, 68.5% at Month 1, 55.4% at Month 5, 51.3% at Month 9 and 49.7% at Month 12. Figure 2A illustrates how the mean GSDS total sum score varied from baseline through Month 12. The patients reported the highest GSDS total sum score at Month 1. Figure 2B illustrates how the GSDS mean scores for the 7 subscales varied from baseline through Month 12. The patients reported most problems within the subscales 'sleep quantity', 'early awakenings' and 'sleep quality'. 'Quantity of sleep' was the subscale in which the patients overall scored the highest, while the subscale 'medications for sleep' had the lowest mean scores, all below 1.0. Figure 3 displays the patients' individual trajectories for total GSDS over the 5 measurement points. The figure shows that the trajectory had individual variations beyond that for the total sample illustrated in Fig. 2A.

Factors associated with sleep disturbance are presented in Table 2. Lower age, use of pain medication, use of psychotropic medication and higher comorbidity score (SCQ) were significantly associated with higher sleep disturbance severity (total GSDS). The interaction terms Age x Time ($P = 0.596$) and Gender x Time ($P = 0.938$) did not reach statistical significance in the overall test and were removed from the model. Table 3 presents a more parsimonious model, not adjusting for pain medication, psychotropic and comorbidity (SCQ). The model presented in Table 2 gave a better fit (e.g. lower Akaike's information criteria). Gender differences were not significant in any of the models. However, the estimated effect of gender was higher in the model in Table 3. This may imply multicollinearity between gender, pain medication, psychotropic medication and comorbidity.

The highest sleep disturbance score was reported at Month 1. *Post hoc* pairwise comparisons showed that the total GSDS at Month 1 was the only time point that differed significantly from the other time points. The estimated marginal mean GSDS total sum score, based on mean age and SCQ for the total sample, was 61.3 at Month 1 compared with 56.2 at baseline ($P = 0.001$), 54.9 at Month 5 ($P < 0.001$), 54.2 at Month 9 ($P < 0.001$) and 54.7 at Month 12 ($P < 0.001$).

DISCUSSION

This study is the first to comprehensively describe the sleep trajectory of surgically treated lung cancer patients up to 12 months after surgery. The findings demonstrate that lung cancer patients in general sleep poorly, before as well as after surgery. Younger age, comorbidity, use of psychotropic and analgesic medication at baseline contributed significantly to worsening sleep. These are important findings, indicating a possible need for intervention to prevent chronification of sleep disturbances especially in the younger patients, patients with psychiatric comorbidities and patients on medication for pain.

In concordance with previous studies on sleep disturbances in cancer patients [5, 18], we found a higher prevalence of sleep disturbances in this data material than in the general population. Although specific sleep disorders (e.g. insomnia) are not diagnosed by GSDS, a large proportion of the patients reported GSDS scores well above the clinically meaningful cut-off points. The prevalence varied between 49.7% and 68.5% (GSDS total sum score ≥43) throughout the study period. A previous study found insomnia in 15.5% of the adult Norwegian population (using the DSM-IV inclusion criteria) [19] and a review of epidemiological studies from across the world found prevalence of insomnia in the general population to vary from 6% to 33% (based on 4 different criteria) [11]. These prevalence rates are much lower than in the present study, where 50% of the patients reported sleeping problems 1 year after surgery. The prevalence in our study is comparable to the findings in a small cross-sectional study reporting that more than half of the patients with lung cancer had sleep disturbances [10]. Long-term lung cancer survivors have some of the highest rates of insomnia when compared with other cancer survivors [1], suggesting that unique factors related to lung cancer diagnosis, treatment and survivorship influence sleep.

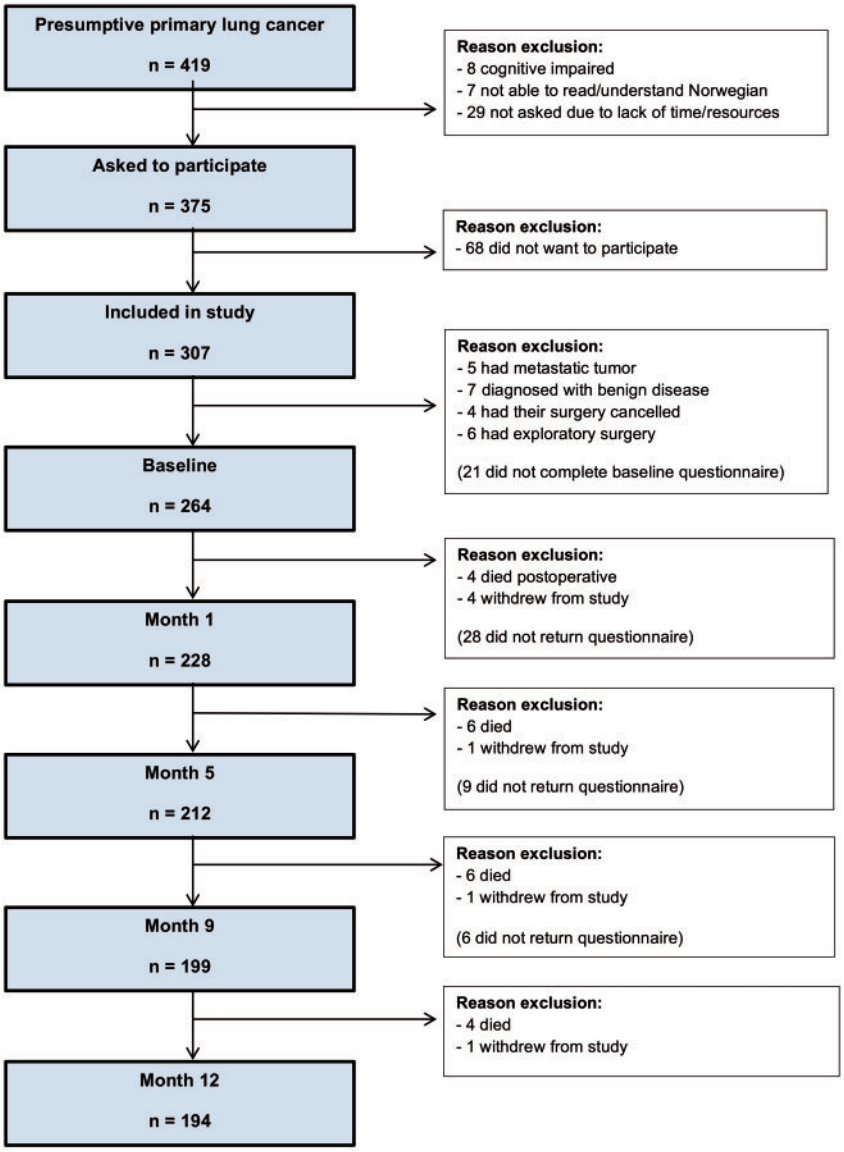

Figure 1: Study flowchart. The flowchart shows the enrolment and exclusion of patients throughout the study.

However, in surveys of insomnia among cancer patients, the patients appear not to report their sleep problems to their physician [5]. Savard and Morin [18] claim that insomnia is perceived only as a symptom secondary to depressive or anxiety disorders, with the sometimes erroneous assumption that it will resolve with adequate treatment of the underlying anxiety and depression and that sleeping problems are viewed as normal and temporary reactions to the cancer diagnosis and treatment. Hence, Savard and Morin emphasize the need for direct treatment of the condition because of both the elevated prevalence in cancer patients and the potential negative consequences on daytime functioning and quality of life.

The sample as a whole scored above the cut-off point for sleep disturbances at all measurement points, with a high mean score already before surgery. The score peaked, as expected, 1 month postoperatively and fell below the baseline level at 5 months. However, the reduction from baseline to 12 months was not statistically significant, indicating that the patients did not sleep better 12 months after surgery than preoperatively. A previous study found that 56.6% of elderly long-term lung cancer survivors had poor sleep more than 5 years post diagnosis compared with 29.5% of elderly non-cancer controls [1]. For the majority of these patients, the sleep problems did not predate their cancer diagnosis. This suggests that sleep disturbance is a problem not solely before surgery and in the postoperative phase and that there is a risk of developing chronic complaints.

For sleep disturbance on the subscale level, the mean varied substantially. This shows that the different dimensions of sleep disturbance in varying degrees contributed to the compound experience of sleep disturbance. Problems with sleep quantity, sleep quality and mid sleep wakes had the highest mean scores in this sample at all time points. Consistent findings have been reported in prostate cancer patients [16] but have not been reported after lung cancer surgery.

Lower age was related to the sleep disturbance trajectory. This is opposed to the tendency in the general population, where prevalence of insomnia symptoms increases with age [11]. However, consistent findings have been reported in other studies of sleep

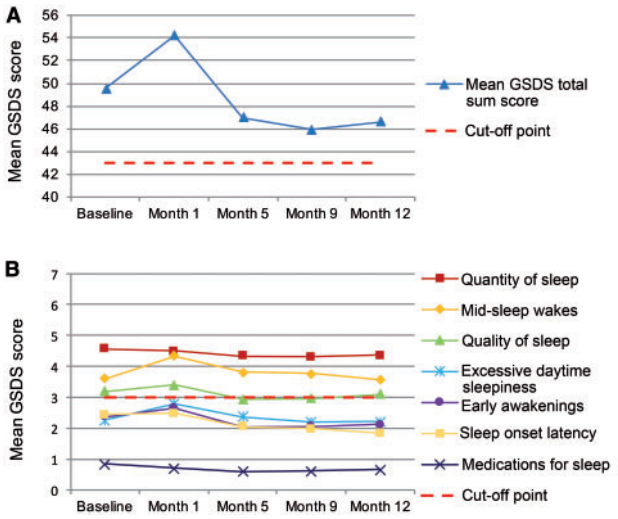

Figure 2: Mean General Sleep Disturbing Scale (GSDS) total sum scores for the total sample. (**A**) Mean GSDS total sum score for the total sample at baseline and through Month 12, the dotted line represents the cut-off point ≥43. The GSDS has a score range of 0–147; the *y*-axis has been cropped in this figure. (**B**) Mean GSDS scores for all subscales at baseline and through Month 12, with the dotted line representing the cut-off point ≥3.

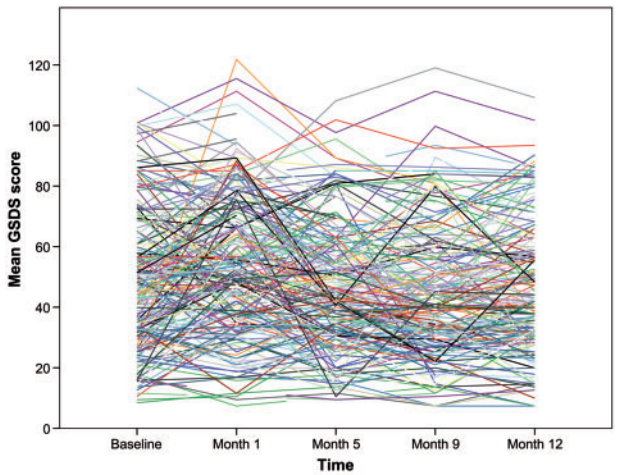

Figure 3: Plot of individual General Sleep Disturbance Scale (GSDS) scores. Plot of the patients' ($n = 261$) individual trajectories of total scores on the GSDS over the 5 measurement points during the first year after surgery for lung cancer. Of the total 1320 GSDS scores, 260 were missing, making interruptions to some of the trajectories.

disturbance in cancer patients [12, 20]. It may be that younger patients experience a lung cancer diagnosis differently and more burdensome than elderly patients, hence influencing sleep to a larger degree. This is supported by studies concluding that older and younger oncology patients experience a differently symptom burden [21, 22]. Further, it has also been found that younger females have the highest symptom burden [22]. In the general population, women are more likely to suffer from insomnia than men [11]. Gender was not found to be a risk factor for sleep disturbances in this study population, indicating that gender may be a less important predictor of sleep disturbance in lung cancer patients. However, in the linear mixed model, the estimate was higher in the model without medication and comorbidity. This may indicate that higher comorbidity and medication may be important factors concerning gender and sleep disturbances.

Higher comorbidity score was found to be an explanatory variable of the total GSDS score. Sleep disturbances are strongly associated with a wide range of diseases. For example, one study concluded that insomnia was a significant risk factor for depression, anxiety, fibromyalgia, rheumatoid arthritis, whiplash, arthrosis, osteoporosis, headache, asthma and myocardial infarction [23]. Consistent with our findings, it has been found that patients with breast cancer and higher GSDS scores, scored higher on comorbidity than the patients with lower GSDS scores [12]. Whether the sleep disturbances were caused by pre-existing diseases or the comorbidities were caused by the sleep disturbances, is not known, but awareness of the link between the degree of comorbidities and sleep disturbances is in any case of importance.

Long-term lung cancer survivors have been reported to have higher rates of sleep medication use relative to non-cancer controls [15]. This indicates that treatment other than medication might be necessary to accomplish satisfying sleep patterns. Cognitive–behaviour therapy for insomnia in patients with cancer is generally recommended both during and after cancer treatment [24]. The quality of the evidence supports a strong recommendation for the use of cognitive–behaviour therapy for insomnia among cancer survivors [24]. In addition, routinely screening patients for sleep disturbances is recommended and indicated as best practice for oncology practice [25]. However, most of the evidence comes from studies in other cancer populations; hence further studies on lung cancer patients are warranted.

Strengths and limitations

Some limitations need to be acknowledged. First of all, the GSDS determines the prevalence of sleep disturbances solely based on frequency of symptoms, leaving out information on what reasons the patients assign their sleep disturbances and how severe and/or distressing they experience these. However, frequency quantifiers are the most common in epidemiological studies on insomnia [11], and data already published from this study showed that our patients ranked difficulty sleeping both as one of the most severe and as one of the most distressing symptoms they experienced [13, 26]. Another limitation is the lack of objective sleep measures such as polysomnography. However, self-report measures of sleep are the most common approach and have some advantages (e.g. their ease of use, convenience, low expense and reflection of the natural setting) [27].

Both the modern Scandinavian lifestyle and seasonal changes in the photoperiod may be viewed as limitations concerning generalization. Modern lifestyle may change the sleep–wake rhythm and the prevalence of sleeping problems [19]. However, these features are typically found in other Western countries as well [28]. The evidence concerning seasonal changes is inconclusive. Some epidemiological studies suggest that significant seasonal changes (e.g. time of sunrise and hours of daytime light) may influence the sleep–wake rhythm of humans in the North [29]. However, a large epidemiological study did not find evidence for seasonal variations in sleeping problems [30].

The main strengths of this study are the prospective design, the large number of participants, the high response rate, the consecutive inclusion and the homogeneous sample including only patients with primary lung cancer undergoing surgical treatment. It is a multicentre study with patient inclusion from 4 of the 7 centres performing lung cancer surgery in Norway. We therefore consider this cohort to be representative of the lung cancer

Table 2: Results from a linear mixed model for sleep disturbance severity including gender, age, SCQ-19, use of pain and/or psychotropic medication

	Estimate	95% Confidence interval	*P*-value
Intercept	83.47	66.44 to 100.51	<0.001
Month 1	5.09	2.60 to 7.59	<0.001
Month 5	-1.30	-3.86 to 1.27	0.322
Month 9	-1.98	-4.58 to 0.63	0.137
Month 12	-1.45	-4.07 to 1.16	0.276
Baseline	Reference		
Gender: men	0.15	-4.24 to 4.53	0.947
Gender: women	Reference		
Pain medication before surgery: no	-10.46	-16.53 to -4.40	0.001
Pain medication before surgery: yes	Reference		
Psychotropic medication before surgery: no	-11.37	-17.11 to -5.64	<0.001
Psychotropic medication before surgery: yes	Reference		
Age	-0.30	-0.56 to -0.04	0.026
SCQ-19	0.74	0.15 to 1.33	0.014

The Akaike's Information Criterion was 8733.8 for this model.
SCQ: Self-administered comorbidity questionnaire.

Table 3: Results from a linear mixed model for sleep disturbance severity including age and gender

	Estimate	95% Confidence interval	*P*-value
Intercept	76.70	58.80 to 94.60	<0.001
Month 1	4.83	2.37 to 7.30	<0.001
Month 5	-1.41	-3.95 to 1.12	0.274
Month 9	-2.10	-4.68 to 0.47	0.109
Month 12	-1.68	-4.27 to 0.91	0.204
Baseline	Reference		
Gender: men	-2.20	-6.82 to 2.43	0.350
Gender: women	Reference		
Age	-0.40	-0.67 to - 0.12	0.004

The Akaike's Information Criterion was 8990.9 for this model.

patients receiving surgical treatment. We used GSDS, which is validated for cancer populations, and the internal consistency of the GSDS questionnaire was good.

CONCLUSIONS

Lung cancer patients in general sleep poorly, before as well as after surgery. This study provides a more complete picture of the trajectory of sleep disturbances in lung cancer patients undergoing surgery. There is a need to address sleep disturbances routinely in clinical practice and screening for sleep problems is indicated. Further studies are warranted concerning factors that contribute to sleep disturbance after lung cancer surgery and how they best can be treated.

ACKNOWLEDGEMENTS

We would like to thank Turid Follestad for valuable statistical advices.

Funding

This work was supported by the Norwegian Cancer Society.

Conflict of interest: none declared.

REFERENCES

[1] Gooneratne NS, Dean GE, Rogers AE, Nkwuo JE, Coyne JC, Kaiser LR. Sleep and quality of life in long-term lung cancer survivors. Lung Cancer 2007;58:403–10.
[2] Pompili C. Quality of life after lung resection for lung cancer. J Thorac Dis 2015;7:S138–44.
[3] Brunelli A, Socci L, Refai M, Salati M, Xiume F, Sabbatini A. Quality of life before and after major lung resection for lung cancer: a prospective follow-up analysis. Ann Thorac Surg 2007;84:410–6.
[4] Ilonen IK, Rasanen JV, Knuuttila A, Sihvo EI, Sintonen H, Sovijarvi AR *et al*. Quality of life following lobectomy or bilobectomy for non-small cell lung cancer, a two-year prospective follow-up study. Lung Cancer 2010;70:347–51.
[5] Induru RR, Walsh D. Cancer-related insomnia. Am J Hosp Palliat Care 2014;31:777–85.
[6] Otte JL, Carpenter JS, Manchanda S, Rand KL, Skaar TC, Weaver M *et al*. Systematic review of sleep disorders in cancer patients: can the prevalence of sleep disorders be ascertained? Cancer Med 2015;4:183–200.
[7] Cleeland CS, Zhao F, Chang VT, Sloan JA, O'Mara AM, Gilman PB *et al*. The symptom burden of cancer: evidence for a core set of cancer-related and treatment-related symptoms from the Eastern Cooperative Oncology Group Symptom Outcomes and Practice Patterns study. Cancer 2013;119:4333–40.
[8] Luyster FS, Strollo PJ Jr, Zee PC, Walsh JK. Sleep: a health imperative. Sleep 2012;35:727–34.
[9] Lin S, Chen Y, Yang L, Zhou J. Pain, fatigue, disturbed sleep and distress comprised a symptom cluster that related to quality of life and functional status of lung cancer surgery patients. J Clin Nurs 2013;22:1281–90.
[10] Nishiura M, Tamura A, Nagai H, Matsushima E. Assessment of sleep disturbance in lung cancer patients: relationship between sleep disturbance and pain, fatigue, quality of life, and psychological distress. Palliat Support Care 2015;13:575–81.
[11] Ohayon MM. Epidemiology of insomnia: what we know and what we still need to learn. Sleep Med Rev 2002;6:97–111.
[12] Van Onselen C, Cooper BA, Lee K, Dunn L, Aouizerat BE, West C *et al*. Identification of distinct subgroups of breast cancer patients based on self-reported changes in sleep disturbance. Support Care Cancer 2012;20:2611–9.

[13] Oksholm T, Rustoen T, Cooper B, Paul SM, Solberg S, Henriksen K *et al*. Trajectories of symptom occurrence and severity from before through five months after lung cancer surgery. J Pain Symptom Manage 2015;49:995–1015.
[14] Goldstraw P. International Association for the Study of Lung Cancer. Staging Manual in Thoracic Oncology. Orange Park, FL: EditorialRx Press, 2009.
[15] Sangha O, Stucki G, Liang MH, Fossel AH, Katz JN. The Self-Administered Comorbidity Questionnaire: a new method to assess comorbidity for clinical and health services research. Arthritis Rheum 2003;49:156–63.
[16] Miaskowski C, Paul SM, Cooper BA, Lee K, Dodd M, West C *et al*. Predictors of the trajectories of self-reported sleep disturbance in men with prostate cancer during and following radiation therapy. Sleep 2011;34:171–9.
[17] Casals M, Girabent-Farres M, Carrasco JL. Methodological quality and reporting of generalized linear mixed models in clinical medicine (2000-2012): a systematic review. PLoS One 2014;9:e112653.
[18] Savard J, Morin CM. Insomnia in the context of cancer: a review of a neglected problem. J Clin Oncol 2001;19:895–908.
[19] Pallesen S, Sivertsen B, Nordhus IH, Bjorvatn B. A 10-year trend of insomnia prevalence in the adult Norwegian population. Sleep Med 2014;15:173–9.
[20] Lee K, Cho M, Miaskowski C, Dodd M. Impaired sleep and rhythms in persons with cancer. Sleep Med Rev 2004;8:199–212.
[21] Yates P, Miaskowski C, Cataldo JK, Paul SM, Cooper BA, Alexander K *et al*. Differences in composition of symptom clusters between older and younger oncology patients. J Pain Symptom Manage 2015;49:1025–34.
[22] Miaskowski C, Cooper BA, Melisko M, Chen LM, Mastick J, West C *et al*. Disease and treatment characteristics do not predict symptom occurrence profiles in oncology outpatients receiving chemotherapy. Cancer 2014;120:2371–8.
[23] Sivertsen B, Lallukka T, Salo P, Pallesen S, Hysing M, Krokstad S *et al*. Insomnia as a risk factor for ill health: results from the large population-based prospective HUNT Study in Norway. J Sleep Res 2014;23:124–32.
[24] Johnson JA, Rash JA, Campbell TS, Savard J, Gehrman PR, Perlis M *et al*. A systematic review and meta-analysis of randomized controlled trials of cognitive behavior therapy for insomnia (CBT-I) in cancer survivors. Sleep Med Rev 2016;27:20–8.
[25] Howell D, Oliver TK, Keller-Olaman S, Davidson JR, Garland S, Samuels C *et al*. Sleep disturbance in adults with cancer: a systematic review of evidence for best practices in assessment and management for clinical practice. Ann Oncol 2014;25:791–800.
[26] Oksholm T, Miaskowski C, Kongerud JS, Cooper B, Paul SM, Laerum L *et al*. Does age influence the symptom experience of lung cancer patients prior to surgery? Lung Cancer 2013;82:156–61.
[27] Beck SL, Schwartz AL, Towsley G, Dudley W, Barsevick A. Psychometric evaluation of the Pittsburgh Sleep Quality Index in cancer patients. J Pain Symptom Manage 2004;27:140–8.
[28] Gamaldo AA, Beydoun MA, Beydoun HA, Liang H, Salas RE, Zonderman AB *et al*. Sleep disturbances among older adults in the United States, 2002-2012: nationwide inpatient rates, predictors, and outcomes. Front Aging Neurosci 2016;8:266.
[29] Borisenkov MF. The pattern of entrainment of the human sleep-wake rhythm by the natural photoperiod in the north. Chronobiol Int 2011;28:921–9.
[30] Sivertsen B, Overland S, Krokstad S, Mykletun A. Seasonal variations in sleep problems at latitude 63 degrees -65 degrees in Norway: The Nord-Trondelag Health Study, 1995-1997. Am J Epidemiol 2011;174:147–53.