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A Scoping Review of the Literature on Sleep Quality in Adult Lung Transplant Recipients

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A Scoping Review of the Literature on Sleep Quality in Adult Lung Transplant Recipients

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Abstract

Introduction: Lung transplant recipients face challenging postoperative complications and are at risk for poor sleep quality. Sleep quality, as a complex clinical phenomenon, has multiple subjective and objective connotations. Measures and definitions of sleep quality are not standardized. **Objective:** A scoping review methodology was used to systematically map the relevant literature, provide an overview of available sleep quality measures, and to identify knowledge gaps. **Methods:** A systematic search of published and gray literature enabled knowledge synthesis of the last 10 years of evidence documenting sleep quality in lung transplant recipients. The search revealed 246 articles with only 12 sources meeting the eligibility criteria. **Results:** Sources varied in terms of definitions and measures of sleep quality. Subjective, objective, or a combination of both measures were used across the relevant literature with findings confirming that poor sleep quality was common in lung transplant recipients. Significant associations with poor sleep quality included younger age, female gender, exposure to tacrolimus, anxiety, and depression. **Discussion:** Systematic literature assessing sleep quality in lung transplant recipients is sparse and lacks conceptual and operational definitions. Future research can focus on designing prospective observational studies. Subjective and objective measures for sleep quality need to be validated in lung transplant recipients. Further rigorous research is needed to standardize measures of sleep quality and to further examine potential risk factors that affect sleep after lung transplantation.

Keywords

lung transplantation, lung transplant recipients, sleep, sleep quality, scoping review

Introduction

Lung transplantation is a treatment strategy for individuals with end-stage lung disease that is no longer amenable to conventional treatments. After the lung transplant surgery, patients continue to face a plethora of complications. Risks of allograft rejection and infections become a lifelong concern while the complicated posttransplant medical regimen may lead to the development of diabetes, hypertension, osteoporosis, and malignancies.[1,2] Hence, the median survival for adults undergoing lung transplantation is only 6.7 years,[1] which is an improvement from previous decades due to advances in immunosuppressive, medical, and surgical techniques. In conjunction with these improvements, there is an increased awareness of the role of sleep in the development and management of chronic diseases and health. Sleep is an essential physiological function to maintain one's physical, cognitive, and psychological health.[3,4] Circulatory, respiratory, musculoskeletal, and central nervous systems are repaired during sleep.[5] Consistent lack of sleep or sleeping less than the recommended amount is associated with adverse health outcomes such as obesity, diabetes, cardiovascular disease, impaired immunity, neurocognitive dysfunction, depression, anxiety, poor quality of life and increased risk of death.[4,6–8]

Sleep Quality

The term sleep quality is often used by patients, clinicians and research professionals alike who have all associated it with health and vitality.[9] Often, patients who are dissatisfied with their sleep quality refer to difficulties with nighttime sleep when provided with an opportunity to sleep (eg, insomnia), daytime consequences due to poor sleep (eg, daytime sleepiness), nocturnal movements (eg, jerking of legs and sleep walking), or a combination of these concerns.[7,8] Yet, despite its common use, sleep quality as a concept has not been rigorously defined.[3,9–12] Sleep quality is likely to have different connotations from one person to the next.[13]

Sleep Quality Assessment

Standardized measurements of sleep quality have also not been universally agreed upon due to the vague definitions of the underlying concept.[13] Buysse et al[11] postulated that sleep quality included quantitative measures of sleep, such as sleep duration and sleep latency, in addition to subjective aspects such as restfulness of sleep. Hence, sleep quality assessments have been attempted using subjective and objective sleep parameters and self-report questionnaires.[13]

Sleep quality can be measured by sleep parameters related to the sleep-wake cycle.[14] These measures include total sleep

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time, sleep onset latency, and sleep efficiency (Table 1).[9,12,15,16] These indices can be measured subjectively, via patients' self-reports, or objectively from the physiological parameters generated from polysomnography), actigraphy, and wearable sleep trackers.[11,12,17–22]

While polysomnography is the gold standard for physiologically measuring sleep and diagnosing sleep disorders,[17] it is expensive and takes place in a medical setting as opposed to actigraphy, which is an activity-based assessment of sleep quality worn as a wristwatch or as an attachment to the belt.[23] Actigraphy devices measure motions with an idea that people move when awake with progressive reduction in motion when asleep, discriminating sleep and wake cycles.[18] The sleep efficiency and total sleep time measured with actigraphy devices reflect the polysomnographic sleep parameters and have been validated in healthy and clinical populations.[19] Spielmanns et al[18] found that these devices have advantages of convenience of use, cost effectiveness, and continuous recording. Compared to polysomnography, sleep data are collected an individual's home, as opposed to a sleep laboratory.

Similar to actigraphy devices, wearable sleep-trackers, show high sensitivity (above 90%) in detecting sleep but lower specificity in detecting wake cycle due to an overestimation of total sleep time and underestimation of wake after sleep onset.[19] Further investigations are recommended to establish their empirical validity in monitoring sleep.[19]

Several instruments are available to measure sleep quality using self-report questionnaires that evaluate various domains of the sleep experience.[13] The most commonly used self-reports are the Pittsburgh Sleep Quality Index (PSQI),[11] Insomnia Severity Scale (ISI),[20,21] and Epworth Sleepiness Scale (ESS).[22] These tools allow for an individual's subjective appraisal of sleep and are summarized in Table 2.

Table 1. Sleep Quality Indices and Definitions.

Sleep Quality Index	Definition	Accepted Values
Total sleep time (TST)	"Total amount of sleep time scored during the total recording ime",[15pg.2]	A low TST (<6 hours) may be indicative of insufficient sleep duration while prolonged TST may suggest effects of medications, medical conditions, or prior sleep deprivation[15]
Sleep latency (SL) or sleep onset latency	Duration of time in minutes that it takes for an individual to fall asleep[15,16]	Falling asleep within 30 minutes or less after going to bed[16]
Sleep efficiency (SE)	Calculates the percentage of total time in bed that is spent in sleep[15]	This measurement should be 85% or more for optimal health benefits[16]
Rapid eye movement (REM) sleep	Percentage of time spent in REM sleep compared to total sleep[16]	REM sleep of 21%-30% indicates good objective sleep quality[9]
Wake time after sleep onset	Calculates amount of time awake after initiation of sleep[16]	

Lung Transplantation

Patients after lung transplantation, similar to other solid organ recipients, are at an increased risk for poor sleep due to medications and comorbidities.[24] However, the understanding of sleep quality and its measures in lung transplant recipients is unclear. A preliminary search for existing scoping or systematic reviews on the topic was conducted using Cochrane Database of Systematic Reviews, JBI Evidence, and PubMed, and none were identified. Given the absence of evidence synthesis on this topic, the authors pursued a scoping review methodology to raise awareness of this gap among the clinical and academic transplant community.

Objective

The objective of this scoping review was to systematically map the literature available in the area of sleep quality in lung transplant recipients, provide an overview of available measures, and to identify knowledge gaps. It aimed to address the following research questions: (*a*) What is the range of research that examined sleep quality in lung transplant recipients and what were the characteristics of these studies? (*b*) What instruments (subjective and objective) were used to measure sleep quality in lung transplant recipients? (*c*) What were the primary results of the studies of sleep quality in lung transplant recipients?

Methods

Protocol and Registration

The protocol was developed a priori following guidelines for conducting scoping reviews recommended by methodology outlined by Arksey and O'Malley[25] and subsequently adapted by Joanna Briggs Institute.[26] The Preferred Reporting Items for Systematic reviews and Meta-Analyzes extension for Scoping Reviews (PRISMA-ScR)[27] was used to provide reporting guidance.

Eligibility Criteria

The primary concept of the review was sleep quality and, therefore, to be included in this review, articles had to discuss the concept of sleep quality, its associated constructs, or measures. This scoping review included literature of lung transplant recipients, male or female, 18 years and older, of any ethnicity, transplanted at any global transplant center. Studies of sleep quality in solid organ transplant patients that included sub-samples of lung transplant recipients were also considered. Research designs inclusive of quantitative, qualitative, and mixed

Table 2. Sleep Quality Measures and Instruments with Associated Descriptions.

Measure	Description
Objective Measures	
Polysomnography	Quantifies sleep latency, total sleep time, wake time after sleep onset, as well as sleep phases such as REM sleep and non-REM sleep[12,17]
Actigraphy	Relies on an accelerometer to measure motion with the premise that people move when awake with progressive reduction in motion when asleep, especially in the deepest stages of sleep, discriminating sleep and wake cycles[18] Convenient to use, cost effective, and provide continuous recording[18]
Wearable sleep-trackers	Measure signals such as heart rate, skin conductance, and motion from which the information about sleep is derived[19]
Self-report Instruments	
Pittsburgh Sleep Quality Index (PSQI)[11]	19-item self-report questionnaire assessing global sleep quality score and 7 component scores: Sleep Quality, Sleep Latency, sleep duration, habitual sleep efficiency (the ratio of sleep duration by time spent in bed), sleep disturbance (eg using the washroom), use of sleeping medications, and daytime dysfunction.[11] A global PSQI score of 5 or higher provides a sensitive and specific measure of poor sleep quality[11]
Insomnia Severity Scale (ISI)[20,21]	7-item instrument that measures patient's perceptions of insomnia. It evaluates insomnia over the past 2-4 weeks with particular attention to sleep onset, sleep maintenance, early morning awakenings, satisfaction with current sleep pattern, interference with daily functioning, and noticeability of sleep problems by others. An ISI score of greater than 7 is classified into various levels of insomnia from mild to severe and a score greater than 10 is a clinical threshold for insomnia.[20,21]
Epworth Sleepiness Scale (ESS)[22]	Assesses daytime sleepiness.[22] Evaluates the probability of falling asleep in common situations of daily life. The ESS score ranges from 0-24 with higher scores reflecting excessive daytime sleepiness[22]

REM = rapid eye movement.

methods studies were eligible. Gray literature, including conference abstracts, poster presentations, and dissertations was also eligible. Studies of pediatric populations under the age of 18 years and articles in a language other than English were excluded. Literature published over 10 years ago were excluded to target results relevant to a practicing audience and minimize introducing biases that may be associated with outdated transplant practices.

Information Sources

The database selection was based on a consultation with two librarians: clinical and academic. Source, for the purposes of this scoping review, refers to the included literature. To minimize missed sources and bias, several electronic databases were searched and included Medline PubMed, Embase, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, PsycINFO, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Scopus, and Web of Science. The trials register, clinicaltrials.gov, was searched for additional trials. The search for gray literature included the ProQuest Dissertations and Thesis, New York Academy of Medicine, and Google Scholar. Additional search strategies included hand searches of included key studies found through the database searches. The searches took place on multiple dates between January and February 2021, with the last search taking place on February 20, 2021.

Search Strategy

The search strategy aimed to identify both published and unpublished sources. A 3-step search strategy was used. The first step was an initial limited search of two online databases (PubMed and Embase) relevant to the topic. This initial search was constructed around the terms lung transplant and sleep quality, followed by an analysis of the text words in the title and abstracts of retrieved articles and of the index terms used to describe the article. The authors conducted a second search using all identified keywords and index terms. Examples of keyword strings, medical subject headings (MeSH) terms and truncated words in different groupings were combined using the Boolean operators and/or and included: sleep initiation and maintenance or sleep or insomnia or sleep quality or PSQI and lung transplant*. The literature search was adapted to each database. Limits of English language and date filter were applied at the end of each search. The reference list of all the identified articles was searched for additional sources. The final search strategy in Medline PubMed and Embase are presented in the Supplementary Appendix.

Selecting the Evidence

Zotero reference management software was used to import, manage, and de-duplicate references. Once de-duplicated, results were imported into a systematic review manager, Covidence (Veritas Health Innovation). The authors examined titles and abstracts of the retrieved articles in Level 1 of screening and when considered eligible, sources were reviewed in full text in Level 2. Inclusion and exclusion of

Table 3. Literature Regarding Sleep Quality in Lung Transplant Recipients.

Author, Year, Location, and Literature Source	Purpose	Design and Sample	Sleep Quality Measure	Key Findings
Burkhalter et al, 2017[28] Switzerland Quantitative Study	1. To detect and compare changes in sleep quality in solid organ transplant recipients over time (pre-, and four timepoints post-transplant) 2. To compare global quality of life and survival (until 3 years post-transplant) in subjects with persistently poor sleep quality to those with consistently good and variable sleep quality	• Prospective multi-center design • Convenience sample • N = 1173 organ transplant patients • Subsample of 123 lung transplant recipients • Mean age: 49.9 years • Gender: 59% male and 41% female	• Subjective: single item derived from the 'Kidney Disease Quality of Life–Short Form' instrument, which was initially developed for patients with end-stage renal disease	• 30% of lung transplant recipients experienced poor sleep quality 36 months post-transplant • Poor sleep quality had the lowest occurrence at 12 months after lung transplant (24%). No significant change over time was found in lung transplant recipients. • Patients with persistently poor sleep quality score higher on the depressive symptomatology and have lower mean global quality of life • No increased mortality risk was found
Fatigati et al, 2016[29] USA Quantitative Study	1. To identify the pattern, predictors, and impact of poor sleep quality on self-management behaviors and HRQOL outcomes during the first year after a lung transplant	• Secondary analysis of data from patients who participated in a randomized controlled trial to evaluate a mobile health intervention • Convenience sample • N = 75 • Mean age: 56.1 years • Gender: 66% male and 34% female	• Subjective: PSQI • PSQI Global Score > 8 used to identify poor sleep	• 32.0 to 37.5% were categorized as poor sleepers • Poor sleepers improved their sleep quality at 12 months and good sleepers showed stability in sleep quality over time • The only significant predictor of poor sleep quality was female gender ($P = .026$; odds ratio = 3.421). • A significant inverse relationship was found between poor sleep quality and the mental component of HRQOL ($r = 0.348$, $P < .01$)
Gilmour et al, 2015[30] Australia Poster Abstract	1. To assess the prevalence of depression, anxiety, and quality of life in a cohort of BOS patients and to investigate self-reported sleep disruptions	• Design not stated • Convenience sample • 47 lung transplant recipients n = 29 without BOS n = 18 with BOS	• ISI • ESS	• Symptoms of insomnia were found in 51.7% of patients with BOS and in 44.4% of those without BOS • Analysis of measures of anxiety and sleep disturbance did not reveal any significant differences between the groups

(continued)

Table 3. (continued)

Author, Year, Location, and Literature Source	Purpose	Design and Sample	Sleep Quality Measure	Key Findings
Hernandez Voth et al, 2015[31] Spain Quantitative Study	1. To analyze the evolution of SDB during a follow-up period of 1 year after the lung transplant.	• Prospective observational descriptive design • Convenience sample • N = 20	• Objective: PSG, TST, SE • Subjective: ESS	• TST 6 months after transplant 360.2 ± 61.8 minutes; 12 months post-transplant 333.2 ± 74.9 minutes. • SE 6 months after transplant 82.152 ± 13.3 minutes; 12 months post-transplant 81.8 ± 17.9 minutes
Reilly-Spong et al, 2013[24] USA Quantitative Study	1. To investigate the prevalence, characteristics, and correlates of sleep difficulties in solid organ transplant recipients	• Cross-sectional design • Convenience sample • 143 solid organ transplant recipients • Subsample of 12 lung transplant recipients • Mean age: 54.1 years • Gender: 42% male and 58% female	• Subjective: PSQI Global score >5 and >8 Objective: Actigraphy	• 27% lung transplant recipients had PSQI > 8 and 54.5% > 5 • SL > 15 minutes = 66.7% • TST < 7 hours = 30% • SE < 85% = 54.6% • Use of sleep aids = 25% • Sleep disorder diagnosis = 42% Actigraphy • TST 6.9 hrs. • TST< 6 hours = 33% • SL = 33.3 minutes • wake after sleep onset = 48.5 minutes • SE% = 80.9%
Rohde et al, 2017[32] USA Quantitative Study	1. To evaluate the prevalence of insomnia within lung transplant clinic 2. To determine whether a relationship exists between insomnia and exposure to immunosuppressant medications following transplantation	• Cross-sectional design • Convenience sample • N = 125 • Mean age with insomnia 57 years; without insomnia 55 years • Gender with insomnia: Male 30%; without insomnia: Male 62%	• Subjective: ISI (ISI score >10) • Wisconsin Sleep Cohort Study to assess the frequency of sleep complaints related to insomnia • ESS	• The prevalence of insomnia was 40% • Higher prevalence in women • ISI cutoff greater than 10. • Those with ISI score >10 had greater ESS scores and Sheehan disability scores. • No difference in time since transplant was found, mean tacrolimus exposure was significantly higher in patients with insomnia versus those without insomnia.
Sawhney et al, 2020[33] USA	1. To identify the reasons for poor sleep quality in lung transplant recipients	• Observational; cross-sectional design • Convenience sample • N = 167	• Subjective • PSQI Global score >5 • ESS >9	• 30% had high ESS scores • 74% reported poor sleep • Participants with PSQI

(continued)

Table 3. (continued)

Author, Year, Location, and Literature Source	Purpose	Design and Sample	Sleep Quality Measure	Key Findings
Quantitative Study		• Mean age: 60.6 years • Gender: 48% male and 52% female		> 5 were younger with no difference in gender distribution and mean body mass index. • SL was prolonged (33.2 minutes) with mean sleep time of 6.7 hours and low subjective SE of 78%. • Almost 1/3 of patients reported sleep initiation insomnia and more than 2/3 reported maintenance insomnia. • A higher score on ESS was noted for individuals with poor sleep quality
Sommerwerck et al, 2016[35] Germany Quantitative Study	1. To determine the prevalence and clinical predictors of obstructive sleep apnea in a cohort of lung transplant recipients	• Cross-sectional design • Convenience sample • N = 77 • Mean Age: • SDB: 56.1 years • Non-SDB 52.4 years • Gender: 58% male and 42% female	Objective: PSG, TST, SE Subjective: ESS	• No statistically significant differences in TST or SE in SDB or non-SDB groups • TST in SDB was 323 ± 79 minutes; in non SDB 326 ± 73 minutes • SE was 72.4 ± 13 in SDB group 71.2 ± 16.8 in non-SDB group
Smith & Blumenthal, 2016[34] USA Letter to the Editor	Not stated	• Post-hoc analysis • Sample not described	• Single item of sleep disturbance on BDI-II	• 8% of lung transplant recipients reported that their sleep was very disturbed • 5% of lung transplant recipients reported more severe sleep problems • A post hoc exploratory analysis of the HPI revealed that self-reported sleep disturbance was associated with greater depressive
Testelmans et al, 2021[36] Belgium Quantitative Study	1. To evaluate SDB prevalence and its associated factors at 1 year after lung transplant in a large cohort	• Design not stated • Convenience sample • N = 219 • Mean age for those with SDB was 57.9 years and 44.4 years for those with Non SDB	• Objective: PSG, SE • Subjective: ESS	• SE in lung transplant recipients was 70.7% ± 16% • ESS 5.8 ± 4.1

(continued)

Table 3. (continued)

Author, Year, Location, and Literature Source	Purpose	Design and Sample	Sleep Quality Measure	Key Findings
		• Gender: 73% male with SDB, 36% male without SDB		
Tokuno et al, 2020[37] Japan Abstract	1. To assess changes in sleep quality and other patient reported measures including health-related quality of life after lung transplantation	• Prospective multi-center design • Convenience sample • N = 56	• Subjective: PSQI Global score >5	• 62.5% lung transplant recipients had poor sleep quality • In PSQI subscales, sleep medication worsened significantly (p = .04) after lung transplantation
Yo et al, 2019[38] Australia Quantitative Study	1. To evaluate the prevalence and potential associations of insomnia in a lung transplant cohort	• Cross-sectional design • Convenience sample • N = 81 • Mean age: 57 years • Gender: 57% male and 43% female	• Subjective: ISI score >15	• The prevalence of insomnia was 32% • Insomnia was more common among women (51% vs 17%) • There was a significant association between the HADS scores and insomnia

BDI-II = Beck Depression Inventory II; BOS = bronchiolitis obliterans syndrome; ESS = Epworth Sleepiness Scale; HADS = Hospital Anxiety and Depression Scale; HPI = Health Practices Index; HRQOL = health-related quality of life, ISI = Insomnia Severity Index; PSG = polysomnography; PSQI = Pittsburg Sleep Quality Instrument; SDB = sleep disordered breathing; SE = sleep efficiency; SL = sleep latency; TST = total sleep time.

citation abstracts and full-text articles was tracked using Covidence. After full-text articles were screened for eligibility, the reference lists of all included papers were hand-searched for additional sources.

Data Extracting and Charting

Data were extracted from the final list of the eligible sources and charted in Excel (Microsoft Corporation, Redmond, WA) using a standard data charting form adapted from the Joanna Briggs Institute. The following information was recorded: author, year of publication and location; aim of the study; sample characteristics; methodology; sleep quality measures; key findings as they related to the scoping review questions; and literature source. Table 3 summarizes descriptive characteristics and key findings of the included sources.[24,28–38]

Results

Literature Search

After duplicates were removed from the initial 246 sources, the literature search yielded 184 citations. One hundred thirty-three sources were found irrelevant after Level 1 screening of titles and abstracts due to their focus on the populations with pulmonary diseases; pre-transplant or caregivers of lung transplant recipients; studies of pediatric populations; or focus on pathophysiology or medications. Fifty-one sources were moved for a full-text review. Level 2 screening excluded 39 sources due to reasons such as wrong patient population, lack of relevance, and older than 10 years. Sources from the same group of authors using identical cohorts of participants were excluded if identical sleep quality measures were used and reported. After all the combined searches and completion of Level 2 screening, 12 sources met the inclusion criteria. The number of studies identified and selected at each stage of the scoping review, along with the number of articles excluded at each stage with reasons for exclusion, are presented in a PRISMA flow diagram in Figure 1.

Source Characteristics

Nine sources were quantitative studies published in peer-reviewed journals, 2 were conference abstracts, and 1 was a letter to the editor. Almost half the sources identified in this scoping review were from the United States transplant centers (N = 5), 4 sources were from European groups (Belgium,

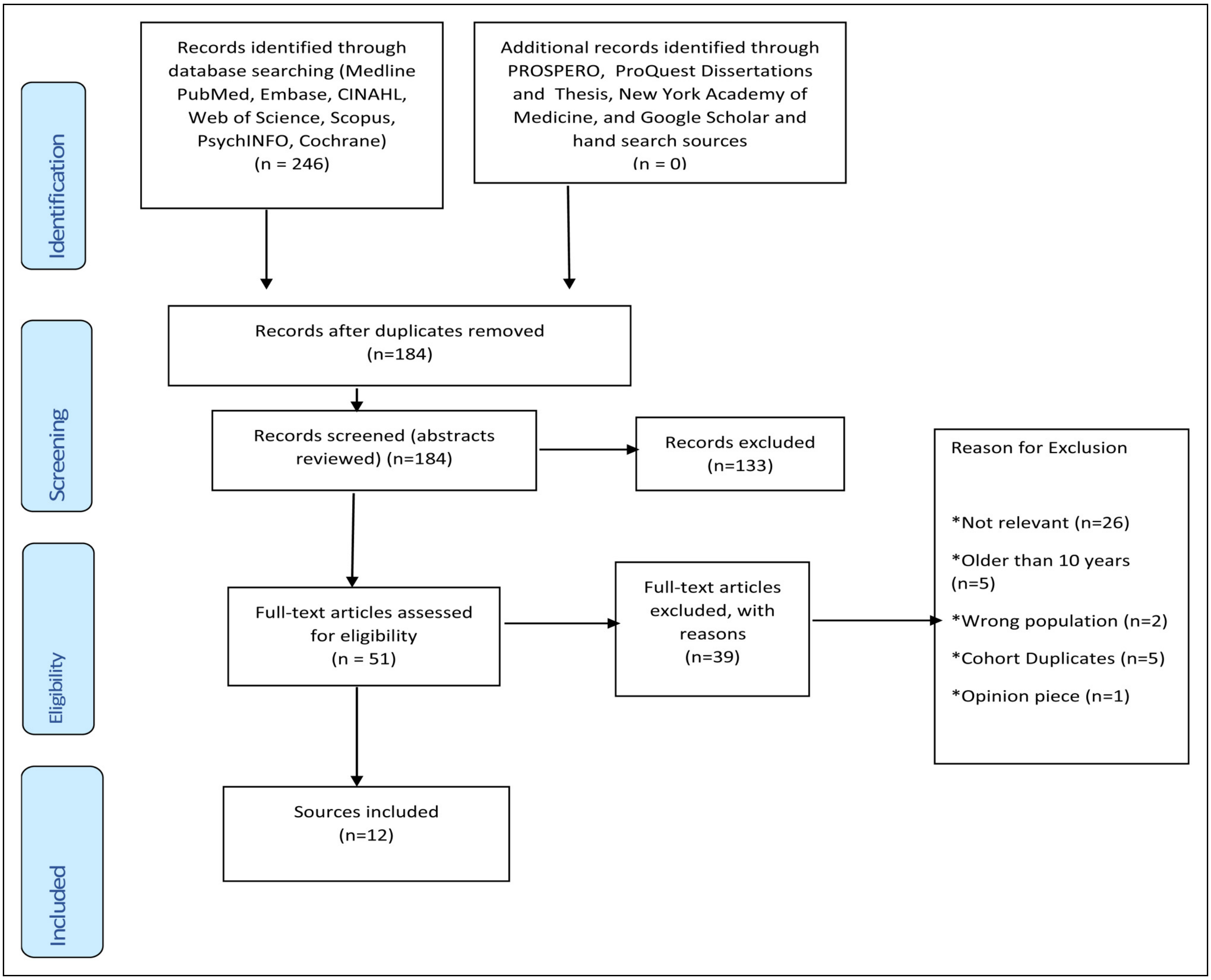

Figure 1. PRISMA flow diagram showing the final sources included in the scoping review.

Germany, Spain, and Switzerland), and the remaining 3 were from Australia and Japan. Quantitative studies and conference abstracts used predominantly observational cross-sectional and prospective methodologies; one was a secondary analysis. The letter to the editor involved a post-hoc analysis of the data collected in an earlier study.

Sample Characteristics

Studies' participant sample sizes of lung transplant recipients ranged from 12 to 219 patients. While participant samples were comprised exclusively of recipients of lung transplant in 10 sources, 2 studies used a sub-sample of lung transplant recipients among other solid organ transplant recipients.[24,28] Convenience sampling strategy was the predominant sampling method of the selected sources.

Terminology

Definitions of sleep quality as a clinical or theoretical concept were not consistent. Poor sleep quality was referred to as poor sleep,[28,29,33] sleep difficulty,[24] insomnia,[32,38] and sleep disturbance.[34]

Findings and Topic Areas

The authors analyzed 12 included sources and grouped the findings according to the 4 major topics: objective sleep quality measures, subjective sleep quality measures, combination of subjective and objective sleep quality measures, and the studies of risk factors and associations of sleep quality. Subjective, objective or a combination of both sleep quality measurement tools were used across all sources and the majority of sources (N = 9) were reported under more than 1 topic area. Table 4 provides a visual representation of the distribution of reported instruments across included sources.

Table 4. Subjective and Objective Measures of Sleep Quality in Lung Transplant Recipients Across Included Sources.

Author and Year	Objective SQ Measures		Subjective SQ Measures			
	PSG	Actigraphy	PSQI	ISI	ESS	Single Question
Burkhalter et al, 2017[28]						X
Fatigati et al, 2016[29]			X			
Gilmour et al, 2015[30]				X	X	
Hernandez et al, 2015[31]	X				X	
Reilly-Spong et al, 2013[24]		X	X			
Rohde et al, 2017[32]				X		
Sawhney et al, 2020[33]			X		X	
Sommerwerck et al, 2016[35]	X				X	
Smith & Blumenthal, 2016[34]						X
Testelmans et al, 2021[36]	X				X	
Tokuno et al, 2020[37]			X			
Yo et al, 2019[38]				X		

ESS = Epworth Sleepiness Scale; ISI = Insomnia Severity Index; LTR = lung transplant recipients; PSG = polysomnography; PSQI = Pittsburgh Sleep Quality Instrument; SQ = sleep quality.

Objective sleep quality measures. Of the objective measures, actigraphy was used in 1 study.[24] In lung transplant recipients who wore actigraphy devices, benchmarks for poor sleep inclusive of sleep latency greater than 30 minutes was present in 33%; total sleep time of less than 6 hours was present in 33%; and lack of sleep efficiency < 85% was present in 50%.[24] Three sources[31,35,36] used PSG to explore sleep characteristics. They found that although there was a high prevalence of sleep disordered breathing in their respective samples, of significance to sleep quality measures, mean total sleep time in patients with and without sleep disordered breathing were all equally poor (eg, under 6 hours). Lack of sleep efficiency, as reported under 85% via PSG, was consistent across all 3 publications;[31,35,36] however, slightly better in recipients without sleep disordered breathing.[35]

Subjective sleep quality measures. Subjective measures of sleep quality were used in most sources (N = 9). The PSQI was used in 4 studies,[24,29,33,37] ISI in 3 studies,[30,32,38] and ESS was used in 6 studies.[30–33,35,36] Additional subjective measures of sleep quality included questions from the Wisconsin Sleep Cohort study to assess the frequency of sleep complaints as they related to insomnia,[32] single item question from the Kidney Disease Quality of Life Short Form instrument,[28] and a single item of sleep disturbance on the Beck Depression Inventory-II.[34]

Perceived subjective sleep quality as measured by PSQI demonstrated that between 32%-81% of recipients experience poor sleep.[24,29,33,37] While 3 researchers used a PSQI cutoff greater than 5,[24,33,37] Fatigati et al[29] found that one-third of their sample were categorized as poor sleepers as evidenced by a higher PSQI cutoff score (PSQI > 8). In the PSQI subscales, reported subjective findings included increase in the use of sleeping aids,[37] sleep disturbances,[29] prolonged sleep latency,[29,33] decreased sleep duration,[29,33] and decreased sleep efficiency.[24,33] Both Sawney et al[33] and Reilly-Spong et al[24] found that most common factors for sleep initiation insomnia were getting up to use the bathroom, coughing or snoring loudly, feeling too hot or cold, and having pain.

The prevalence of insomnia as measured by ISI was found to be 32%-52%.[30,32,38] While Gilmour et al[30] did not specify the cutoff ISI score, Rohde et al[32] used the cutoff score equal or greater to 10, while Yo et al[38] used the ISI cutoff score of greater than 15. Both Rohde et al[32] and Yo et al[38] found that there was a higher prevalence of insomnia in female recipients. Additionally, Gilmour et al[30] differentiated the presence of insomnia in patients diagnosed with a form of chronic rejection bronchiolitis obliterans syndrome with findings that symptoms of insomnia were found in 52% of patients with bronchiolitis obliterans syndrome and 44% of patients without it.

The prevalence of daytime sleepiness as measured by ESS varied across sources.[30–33,35,36] Sawney et al[33] reported the prevalence of excessive daytime sleepiness (ESS > 9) in 29% of the sample. Both Rohde et al[32] and Sawney et al[33] noted that a higher score on ESS was documented for individuals with poor sleep quality or insomnia. For example, Rohde et al[32] found that higher ISI score was correlated with greater ESS score (mean score 9.7 in insomnia group vs 6.9 with no insomnia). Similarly, Sawney et al[33] described an ESS mean score of 8.3 in those recipients with PSQI > 5 compared to ESS mean score of 5.6 in those with PSQI < 5. This was divergent from findings of Hernandez et al[31] and Testelmans et al,[36] who postulated that ESS scoring was remarkably low in participants with and without SDB and deemed this measure of low predictability for sleep problems.

The 3 additional measures of subjective sleep quality in revealed that the most frequently reported sleep complaints as assessed via Wisconsin Sleep Questionnaire were *waking up repeatedly during the night* at 42%, followed by not feeling rested during the day, no matter how many hours of sleep you had at 35% and difficulty getting to sleep (32%).[32] One item from the Kidney Disease Quality of Life-Short Form instrument revealed that, in the sub-sample of 123, poor sleep quality (cutoff value less than 6) was prevalent in approximately one-third of participants at various time trajectories after transplant. Sleep quality was best 12 months after transplant (23%) and worst at 6 months (36%).[28] Conflicting with these reports were findings from the post hoc analysis on the single item of sleep of the Beck Depression Inventory-II revealing that only 8% of recipients reported that their sleep was disturbed and 5% reported more severe sleep problems.[34]

Combined (subjective and objective) sleep quality measures. Four studies used objective and objective measures within their studies.[24,31,35,36] When comparing self-report and actigraphy metrics, sleep durations were similar (6.78 and 6.65 hours, respectively) and sleep latencies also correlated (29.82 minutes and 28.2 minutes). However, the correlations between overall PSQI scores and actigraphy data for total sleep time and sleep latency were not sufficient.[24] Similarly, the 3 studies[31,35,36] using sleep indices via PSG and subjective reports of day-time sleepiness by ESS did not report significant correlations as ESS scores were surprisingly low even in recipients with SDB.

Risk factors and associations with sleep quality. Risk factors for poor sleep quality were assessed only in a few studies. On univariate analyzes, associations with poor sleep quality were noted in those patients who were younger[29,32,33] and were females.[29,38] Only female gender was a significant predictor of poor sleep quality on a multivariate level.[29] Several investigators found an inverse relationship between poor sleep quality or insomnia scores and the mental health domains of health related quality of life such as anxiety and depression.[28,29,33,34,38] This was consistent with Reilly-Spong et al[24] who found moderately strong correlations between self-reports of sleep on the PSQI and symptoms of depression, anxiety, fatigue, and pain across all organ transplant recipients in their sample. Furthermore, patients with persistently poor sleep quality over time experienced lower mean global quality of life in a study by Burkhalter et al[28]

Discussion

The authors conducted a scoping review to collect and summarize available evidence on sleep quality after lung transplantation and its associated subjective and objective measures. Although findings demonstrated that some research was available, information on sleep quality after lung transplantation was limited as only 12 sources met the eligibility criteria for the review. Yet, the results are multi-dimensional, highlighting the complexity of sleep quality as a clinical concept. Results suggest that while the majority of selected sources agreed that recipients experience poor sleep, this area of research is understudied.[24,28–30,32,33,37]

Only 4 of the selected sources explored objective measures of sleep quality. They all consistently demonstrated decreased total sleep time and lack of sleep efficiency in at least one-third of their respective samples.[24,31,35,36] Currently accepted measures of sleep quantity, such as total sleep time, sleep latency, sleep efficiency, and wake after sleep onset, may not completely characterize people's total sleep experiences.[12] Literature notes that they may reflect non-sleep phenomena such as overall health status or pain. Alternatively, there is a possibility that sleep quality may translate into different aspects of sleep for different individuals.[12] Several investigators highlighted increased rates of sleep disordered breathing after lung transplantation, which may also result in inadequate sleep duration or sleep fragmentation[33] affecting one's sleep quality. It is largely unknown whether variations in these objective indices were due to a high prevalence of sleep disordered breathing (eg, obstructive sleep apnea) and whether correction of the underlying pathology of sleep disordered breathing may lead to an improvement in these markers and overall sleep quality. While PSG is expensive and intrusive and actigraphy can be considered an alternative, researchers need to consider variabilities in techniques as measures obtained in the sleep lab may differ from those obtained by actigraphy.[9] Currently, there is no literature correlating these measures in the population of lung transplant recipients.

Most of the available data on sleep quality in recipients were obtained from self-report questionnaires. Their advantages involve low cost and non-invasive nature. At this time it was unclear whether they correlated well with objective measures. It is recognized that self-report data may be prone to the response bias affecting estimation of the targeted construct.[39] For example, those recipients who are affected by poor sleep quality may be more eager to participate in studies of sleep quality. Sleep experts also noted that since certain stages of sleep involve loss of consciousness, patients may not be reliable self-observers of particular behaviors that were being documented in self-reports.[19] Despite these disadvantages, patients' experiences about sleep contribute to a rich and meaningful information to aid with the study of sleep quality domains.

Lung transplant recipients may be especially predisposed to the effects of poor sleep. The complex interactions of the recipient, graft, immunosuppression, and underlying comorbidities may create complex challenges in relation to sleep and sleep quality. Recipients undergo physiological changes from impaired immunity due to immunosuppressive therapy and may experience further health challenges as a result of post-transplant complications. Complications such as episodes of acute or chronic organ rejection may result in dyspnea, although Gilmour et al[30] found similar rates of insomnia in individuals with and without bronchiolitis obliterans syndrome. Several studies found that female recipients were at a higher risk for poor sleep. One possible explanation may relate to the presence of menopausal symptoms since the average age included in the study samples was over 50 years old. Only 1 study investigated an association between immunosuppression and insomnia symptoms in lung transplant recipients with findings that there was a relationship between calcineurin drugs such as tacrolimus and poor sleep.[32] Rohde et al[32] explained that pharmacodynamics of tacrolimus may influence sleep and wake cycles with infusion of interleukin-2 into the central nervous system. Other agents known for their adverse sleep side effects include corticosteroids, which are the cornerstone of immunosuppressive regimens after transplantation. The association between corticosteroids and sleep quality after lung transplantation has not been investigated.

Psychosocial health states, such as anxiety and depression, were also found to be correlated with poor sleep. This relationship, however, may be bi-directional as anxiety and depression have an established relationship with altered sleep.[40]

Gaps

This scoping review highlighted that significant gaps exist not only in our understanding of sleep quality in lung transplant recipients but also in standardized definitions of the concept and its associated operational measures. Subjective measures, such as PSQI, ISI, and ESS, used in most publications possess strong psychometric properties, but none of them are validated in the population of lung transplant recipients. Objective indices across PSG and actigraphy have not been assessed for inter-measure reliability. Additionally, although sleep parameters can be measured by self-reports (eg sleep duration in PSQI), it can be argued that studies are strengthened by having both subjective and objective measurements especially of physiological variables.[41] This scoping review included 4 studies using a combination of actigraphy or PSG and self-reports but with variable results.

Implications for Research and Clinical Practice

This scoping review helped to identify several areas for future research in the arena of sleep quality after lung transplantation. Lack of standard conceptual and operational definitions of sleep quality limits its research and, therefore, greater conceptual clarity is warranted. This could be achieved by a concept analysis or formal concept mapping. Given the availability of sleep measures, psychometric testing of the existing subjective sleep quality in lung transplant recipients would further enhance validity of the studies. Systematic studies of correlations between objective and subjective constructs can provide further insight on standardization of measures. Furthermore, as wearable sleep monitoring devices become more widely used, further research can focus on evaluation of sleep metrics and their relationship to sleep quality via this novel technology. Ultimately, given the positive effects of sleep on health, the end goal is the formation of best practices around assessments of sleep quality to mitigate negative consequences that poor sleep may have on different domains of lung recipients' health and well-being.

Limitations

To the authors' knowledge, this is the first scoping review investigating the concept of sleep quality after lung transplantation. Several limitations were identified. Sources in a language other than English and those available before the year 2011 were excluded, limiting review of the literature to the last 10 years to reflect current practices and evolution of transplantation over the years. There was always a possibility of selection bias if the authors did not identify all available published and unpublished sources pertinent to the topic. The available research included in the review was predominantly observational, single-center, first-phase, and lacked replication. Cross-sectional designs precluded measurements of incidence and were not able to make causal inferences. Absence of methodological appraisal and risk of bias evaluation were limitations of the scoping review methodology.[42]

Conclusion

Poor sleep quality, a prevalent problem after lung transplantation, remains an under-studied clinical problem. Extant research is limited in standardized definitions and operationalized sleep quality measures. Subjective and objective assessments are available to measure sleep quality but need to be validated in lung transplant recipients. This review highlights the need for multi-dimensional examination of sleep quality after lung transplantation. Further rigorous research is needed to standardize measures of sleep quality and to further examine potential risk factors that affect sleep after lung transplantation.

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Supplemental Material

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Asterisks indicate sources used in the review

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