DOI: https://doi.org/10.53555/nnmhs.v9i4.1644 Publication URL: https://nnpub.org/index.php/MHS/article/view/1644

THE IMPACT OF NOCTURIA ON MORTALITY : A SYSTEMATIC REVIEW

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Abstract

The International Classification of Sleep Disorders (ICS) describes nocturia as "voiding that occurs during the main sleep period". However, there are some medical specialists who do not believe that feeling one emptiness while sleeping qualifies as a clinically important occurrence. They believe that this viewpoint is supported by the evidence. This might be owing to the fact that some studies have indicated that having fewer than two voids every night is not an issue, whilst other studies have found that having more than two voids every night can reduce quality of life. Having fewer than two voids every night is not a problem. Having more than two voids every night is a problem. The most common and bothersome symptom related to urination is called nocturia. 10 million people in the United States suffer with nocturia, yet only 1.5 million get treated for it. This annoys seventy percent of individuals over the age of thirty who get up at least twice throughout the night to use the toilet. People who suffer from the illness known as nocturnal enuresis are characterized by their inability to recognize when they have a full bladder and their involuntary need to empty while sleeping. Nocturia is quite similar to nocturnal frequency, with the exception that sleep comes before and after episodes of urination. Even though voiding diaries call it nocturia, getting up in the middle of the night for any reason other than to urinate is not considered to be nocturia. Convenience void. Nocturia is frequently caused by overactive bladders rather than illnesses of the urinary system. Patients who experienced urine urgency in the afternoon were also likely to have nocturia. Mortality is increased in patients with nocturia who have three or more nocturnal voids per night. The condition known as nocturia has been linked to an increased risk of death. Those who have had nocturia more than three times are at an increased risk of mortality.

Keyword: *Mortality; Nocturia; Sleed Disorder; Voiding*

INTRODUCTION

Nocturia is the most prevalent and annoying urine symptom. 10 million Americans have nocturia, but only 1.5 million receive treatment. 70% of adults over 30 who make at least two restroom excursions per night are annoyed by this.[1] 50% of persons over 65 void at least once a night, and 24% experience two or more nocturia episodes.Nocturia causes annoyance and long-term sleep deprivation. Nocturia is waking up at night to urinate. Nocturnal voids require sleep before and after the urination. Nocturia episodes do not include the first-morning void.[2,3]

Nocturnal enuresis is a distinct condition in which individuals are unaware of a full bladder and void involuntarily while sleeping. Nocturia is comparable to nocturnal frequency, except sleep precedes and follows voiding episodes. Although voiding diaries label it nocturia, waking up at night for any purpose other than urination is not. Convenience void. Overactive bladders without urinary tract infections often cause nocturia. Half of midday urinary urgency patients had nocturia. Nocturia of three or more nocturnal voids per night increases mortality.[4–6]

Nocturia disrupts sleep, risks nighttime falls and injuries, impairs quality of life, productivity, and even the partner's health. Older persons with nocturia who make repeated nighttime restroom trips are more at risk of serious falls. 25% of older people fall overnight. 25% connect directly to nocturia. Fractures and fall-related traumas are more than doubled in patients who make two or more nighttime restroom visits. Nocturia frequently occurs in conjunction with an overactive bladder that is not explained by urinary tract infections or other recognized illnesses.

Approximately half of patients who experience daytime urine urgency will also have nocturia. Those who have three or more nocturnal voids per night have a far greater overall death rate than the general population. There is evidence that indicates that nocturia is a risk factor for mortality. However, there is a lack of evidence and a significant possibility of it being biased.[7,8] Bladder diaries did not record nocturia, another downside. Patients often overestimate their nocturia episodes when self-estimating.[9] The discussion of the information concerning the influence that nocturia has on the risk of death.

METHODS

The Recommended Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 initiative complied with the requirements for data collection, processing, and reporting. Several factors influenced the decision to implement new restrictions. This review examines the effects of nocturia on mortality. According to the primary findings of the study, all written materials concerning the effect of nocturia on mortality must be composed in English. This systematic review examined scholastic articles published after 2016 that satisfied the study's inclusion criteria. The collection will exclude editorials, entries without a DOI, reviews of previously published books, and excessively lengthy duplicate journal articles. The search for studies to be included in the systematic review was carried out from April, 10th 2023 using the PubMed and SagePub databases by inputting the words: “nocturia” and “mortality”. Where *("nocturia"[MeSH Terms] OR "nocturia"[All Fields]) AND ("mortality"[MeSH Terms] OR "mortality"[All Fields] OR "mortalities"[All Fields] OR "mortality"[MeSH Subheading])* is used as search keywords.

The acceptability of studies was affected equally by their abstracts and their titles. Therefore, they must rely on historical records. Since study results are typically consistent, unpublished English papers are necessary. Only studies meeting the inclusion criteria were considered for the systematic review. This narrows the search results to only match your criteria. The evaluation process is divided into the sections listed below. The study considered authors, publication dates, geographical locations, activities, and motives. After EndNote had recorded a search's results, the database went through and eradicated any duplicate articles.

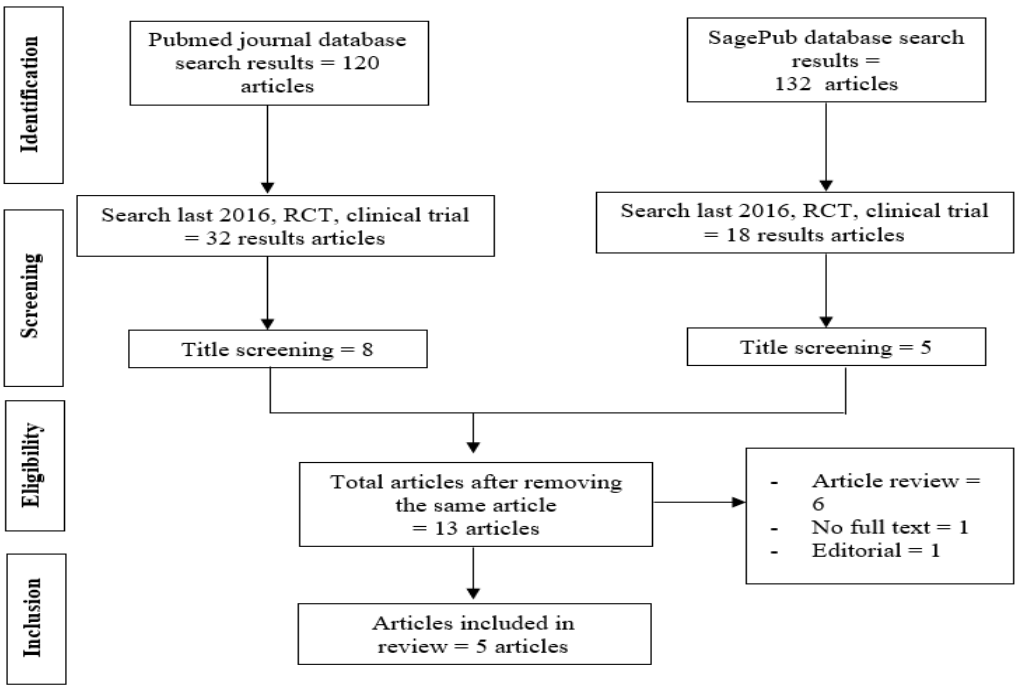

Figure 1. Article search flowchart

It was determined that two individuals would review the titles and abstracts of all the papers. Before deciding which article to discuss, each author meticulously considered the abstract and title of the relevant article. Every paper that satisfies the review criteria will be subjected to a comprehensive and exhaustive analysis. After completing our investigation, we will review any relevant scholarly publications that we may have missed the first time. This rule specifies the evaluation criteria to be applied to documents. The process of identifying objects that will be inspected in the future should be streamlined for optimal efficiency. Why was a single study selected over all others for inclusion in the literature review?

RESULT

Bliwise, et al (2019)[10] conducted a study with 7,343 men. They showed independent of demographic factors and medical comorbidities, nocturia was found to be related with an elevated risk of mortality (hazard ratio [HR] = 1.72; 95% confidence interval [CI] = 1.15-2.55). The magnitude of the connection was reduced when disrupted sleep was included in the model (HR = 1.43; 95% CI = 0.93-2.19). Even though the study was only conducted on men and only half of those men took dutasteride, the researchers believe that the disruption of sleep caused by nocturia could have long-term effects on health and may require targeted intervention.

Funada, et al (2020)[11] showed the prevalence rates of nocturnal voiding at 0, 1, 2, and 3 or more times were, respectively, 44.3%, 39.1%, 11.7%, and 4.7%. 263 participants perished in total. The follow-up evaluation was conducted 3,224 ± 537 days after the baseline. According to multivariable Cox proportional hazard regressions, mortality increased dose-dependently with the nocturnal voiding frequency: HR = 1.46 for 1 time (95% CI = 1.02-2.09), HR = 1.85 for 2 times (95% CI = 1.23-2.77), and HR = 2.06 (95% CI = 1.28-3.32) for 3 or more times versus 0 times (p for trend=0.00084). The association remained significant (p for trend = 0.0017) in the time-varying Cox proportional hazard regression.

Table 1. The litelature include in this study

Author	Origin	Method	Sample	Conclusion
Bliwise, 2019[10]	United State of America (USA)	Cross sectional study	7,343 men	Even though the study was only conducted on men and only half of those men took dutasteride, the researchers believe that the disruption of sleep caused by nocturia could have long-term effects on health and may require targeted intervention.
Funada, 2020[11]	Japan	Prospective cohort study	9,762 participants	According to the findings of this long-term study that had a high representation of the general population and a low prevalence of missing data, nocturia is linked to an increased risk of death.
Moon, 2022[8]	Republic of Korea	Cross-sectional study	9,892 adults	After taking into account a number of potential confounding factors, it was revealed that nocturia had a substantial correlation with mortality in both men and women.
Endeshaw, 2016[12]	United State of America (USA)	Cross-sectional study	1,478 older men	Independent of the symptoms of insomnia and the total amount of time spent sleeping, nocturia has been linked to an increased risk of death. The prevalence of cardiovascular disease and diabetes mellitus may help to explain the link, at least in part. The findings highlight the impact of these medical problems on the association between three or more bouts of nocturia and an elevated risk of mortality in older men. nocturia is defined as involuntary urination during sleep.
Chow, 2021[13]	Taiwan	Cross-sectional study	8,284 participants	The quality of life, as well as job productivity and mental health, are all greatly impacted by nocturia. However, consumption of healt-hcare services is still very low, which calls for more awareness and education on the part of patients, carers, and medical professionals.

Moon, et al (2022)[8] showed nocturia was significantly associated with all-cause mortality (HR = 1.23; 95% CI = 1.10–1.39) and cardiovascular disease (CVD) mortality (HR = 1.55; 95% CI = 1.19–2.01). Nocturia severity increased mortality risk. Nocturia was still related with all-cause and CVD mortality after propensity score matching. Men with nocturia had higher all-cause and CVD mortality. Moderate-to-severe nocturia increased all-cause and CVD mortality in women. Nocturia was related with CVD mortality in baseline diabetics, hypertensives, dyslipidemics, and CVD patients. Nocturia significantly increased all-cause mortality in people without diabetes, hypertension, or CVD.

Other study showed mortality rate was significantly higher for participants with 3 or more nocturia episodes per night compared to those with 0-1 episodes (HR = 1.21 95% CI = 1.00-1.47, p = 0.055), even after controlling for baseline characteristics including demographic variables, body mass index, lower urinary tract symptoms, use of loop diuretics,

insomnia symptoms, excessive daytime sleepiness / daytime naps, sleep duration, and use of sleep medications. Once prevalent diabetes mellitus and cardiovascular disease were included in the model, the association between 3 nocturia episodes per night and mortality risk was no longer statistically significant (HR = 1.18; 95% CI = 0.97-1.44, p = 0.100).[12] Other study showed there was a 35% prevalence of nocturia 2 in males and a 37% prevalence in females. The quality of life of individuals of both sexes declined in proportion to the frequency of nocturia. In addition to nocturia, other factors that were linked with HADS anxiety and depression scores of 8 were hypertension, the existence of a neurological illness, lower urinary tract symptom measurements, and being a female. There was a substantial impact on work ability across all WLQ measures caused by nocturia. Even while the use of prescription drugs increased with the rise in frequency of nocturia, it was also noticed that up to thirty percent of the participants who reported nocturia frequency of three or less did not seek any treatment for their symptoms. This was despite the fact that the use of prescription medications increased with the increase in frequency of nocturia.[13]

DISCUSSION

Nocturia, also known as waking up during the night to urinate, is a common condition that has been linked to a wide range of conditions, such as urologic diseases (such as prostate cancer, but also overactive bladder), cardiovascular disease in its broadest sense and heart failure in particular, chronic pain, central diabetes insipidus, and diabetes mellitus (DM), as well as medications such as diuretics.[14] Insomnia in general, as well as specific sleep disorders such sleep apnea and restless legs syndrome have been linked to nocturia.[15,16]

The International Classification of Sleep Disorders (ICS) describes nocturia as "voiding that occurs during the main sleep period". However, there are other medical professionals who do not think that having one emptiness while sleeping constitutes a clinically relevant event. This could be due to the fact that some research have found that having fewer than two voids every night is not a problem, while other studies have found that having more than two voids per night can lower quality of life.[17]

The question of whether this suggests that nocturia, in the absence of such competing comorbidities, has a causative role in mortality and, for that reason, deserves intervention, is one that cannot be answered by the observational data that has been presented here. Clinical research have shown, without a shadow of a doubt, that reduced nocturnal voiding is connected to improvements in various elements of sleep, improved quality of life, and increased work productivity. This suggests that therapies unquestionably bring benefits in the psychosocial domain.[18,19]

The REDUCE data suggest that in otherwise healthy individuals, voiding 3 times per night is indicative of a condition that could portend a fatal outcome. This should expedite the clinician's decision to take the condition's presence more seriously and consider available treatment options. Whether a targeted intervention should preferentially target nocturnal urine production, bladder function, or even sleep itself is yet to be determined, as is whether treatment for nocturia reduces the risk of such adverse outcomes.[10]

Other studies looked at the link between nighttime urination and death, and a systematic review and meta-analysis of 11 observational studies found a link between nighttime urination and death. In this study, nocturia was defined as going to the bathroom at night twice or three times at different times. It was linked to a higher chance of death (risk ratio [RR] = 1.27; 95% CI = 1.16–1.40). In a 5-year study of 9,762 Japanese men and women from the general population, those with nocturia had a higher risk of dying than those without it. The risk increased with the number of times nocturia happened (HR = 1.46 for 1 time, 95% CI = 1.02–2.09; HR = 1.85 for 2 times, 95% CI = 1.23–2.77; and HR = 2.06 for 3 times, 95% CI = 1.28–3.32).[11,20]

The link between nocturia and mortality is thought to be mediated by many routes.[11] Sleep deprivation can have a deleterious impact on health by lowering immunological function and raising the risk of CVD, obesity, and type 2 diabetes mellitus.[8] This suggests that chronic illnesses are connected to nocturia and mortality, which is a potential outcome of these co-morbidities. The interruption of sleep induced by nocturia in particular may increase the risk of mortality from cardiovascular disease by preventing the natural nighttime reductions in blood pressure and increasing sympathetic activity.[21]

In addition, fractures and other injuries brought on by falls that are associated with significant nocturia and daytime sleepiness can bring about a deterioration in performance status and generate frailty, both of which can lead to death. As a consequence of this, nocturia has been connected to incidents such as falling and breaking bones, in addition to an increased risk of developing chronic illnesses. (including CVD, hypertension, and diabetes).[11,22] Moon, et al (2022)[8] showed nocturia was associated with a greater baseline prevalence of CVD events and CVD death in this study. Cardiovascular disease mortality was higher than all-cause mortality.

CONCLUSION

Nocturia is associated with a higher mortality rate. Mortality is increasing in those who experience nocturia more than three times.

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