International Journal of Medicine Research
www.medicinesjournal.com
ISSN: 2455-7404
Received: 04-08-2026, Accepted: 03-09-2026, Published: 18-09-2026
Volume 11, Issue 3, 2026, Page No. 26-33

Sleep disturbances and sudden unexpected death in epilepsy (SUDEP): Narrative review

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DOI: https://doi.org/10.66856/ijmr.2026.11.3.11031

Abstract

Background: Sudden unexpected death in epilepsy (SUDEP) is a major cause of epilepsy-related mortality, particularly among individuals with chronic and drug-resistant epilepsy. Although generalized tonic-clonic seizures are the strongest established risk factor, the predominance of SUDEP during sleep suggests that sleep-related physiological disturbances may contribute importantly to its pathogenesis.

Objective: To review contemporary evidence on the relationship between sleep disturbances and SUDEP, emphasizing sleep physiology, cardiorespiratory dysfunction, autonomic instability, neurocardiology mechanisms, and potentially modifiable risk factors.

Methods: A narrative review of the literature was conducted using PubMed, Web of Science, Scopus, Embase, and Google Scholar, with primary emphasis on studies published from January 2020 through March 2026. Earlier landmark studies were included when necessary to establish key definitions, epidemiological observations, and mechanistic concepts. Relevant clinical studies, systematic reviews, meta-analyses, consensus statements, practice guidelines, and clinically relevant translational studies were evaluated.

Results: Evidence indicates that sleep disturbances are common in epilepsy and may increase SUDEP vulnerability through interacting mechanisms involving nocturnal seizures, intermittent hypoxemia, impaired arousal, autonomic dysfunction, cardiac arrhythmogenesis, postictal generalized EEG suppression, and brainstem respiratory dysregulation. Obstructive sleep apnea is particularly prevalent and potentially modifiable. Emerging evidence also supports a brain–heart–lung axis linking recurrent seizures with progressive cardiorespiratory and autonomic abnormalities. However, direct evidence that treatment of sleep disorders reduces SUDEP incidence remains limited.

Conclusions: Sleep disturbances may represent clinically important and potentially modifiable contributors to SUDEP risk. Routine sleep assessment, optimization of seizure control, and identification and treatment of sleep-disordered breathing may strengthen comprehensive SUDEP prevention. Prospective studies are needed to determine whether targeted sleep interventions reduce SUDEP incidence.

Keywords: Sudden unexpected death in epilepsy, SUDEP, sleep disturbances, obstructive sleep apnea, epilepsy, autonomic dysfunction, neurocardiology, sleep-disordered breathing

Introduction

Epilepsy is a common chronic neurological disorder associated with substantial morbidity, impaired quality of life, and increased premature mortality. Among epilepsy-related causes of death, sudden unexpected death in epilepsy (SUDEP) remains one of the most serious and difficult-to-predict complications. SUDEP is generally defined as the sudden, unexpected, non-traumatic, and non-drowning death of an individual with epilepsy, with or without evidence of a preceding seizure, excluding documented status epilepticus and cases in which an alternative structural or toxicological cause of death is identified [1,6]. Although its mechanisms remain incompletely understood, contemporary evidence supports a multifactorial process involving seizure-related respiratory dysfunction, autonomic instability, cardiac abnormalities, impaired arousal, and dysfunction of central cardiorespiratory regulatory networks [1, 2, 9].

Generalized tonic-clonic seizures, particularly when frequent or poorly controlled, remain the most consistently recognized clinical risk factor for SUDEP [6, 9]. However, an important feature of SUDEP epidemiology is its association with sleep. Many events occur during sleep or are discovered in bed, frequently following nocturnal seizures [9, 14, 15]. This temporal relationship has increased interest in the possibility that physiological changes accompanying sleep may create a state of heightened vulnerability to seizure-induced cardiorespiratory compromise.

The relationship between epilepsy and sleep is itself complex and bidirectional. Sleep stage and architecture influence neuronal synchronization, epileptiform activity, and seizure susceptibility, while recurrent seizures and antiseizure medications can disrupt normal sleep organization [11, 12]. Sleep disturbances are consequently common among people with epilepsy and include insomnia, excessive daytime sleepiness, sleep fragmentation, altered sleep architecture, and sleep-disordered breathing [11-13]. Systematic evidence demonstrates substantial impairment of sleep quality and increased daytime sleepiness among individuals with epilepsy, reinforcing the importance of sleep as a component of comprehensive epilepsy care [13].

Obstructive sleep apnea (OSA) is of particular interest because it is common among people with epilepsy and produces recurrent nocturnal hypoxemia, sleep fragmentation, and autonomic stress. Recent clinical evidence has demonstrated an association between OSA and increased estimated SUDEP risk, although this relationship

does not establish causality [14, 15]. Treatment of coexisting OSA may improve seizure-related outcomes in selected patients, further supporting identification and management of sleep-disordered breathing as part of epilepsy care [16, 43]. Nevertheless, whether treatment of OSA or other sleep disturbances directly reduces SUDEP incidence remains uncertain.

Beyond sleep-disordered breathing, several interacting mechanisms may explain the relationship between sleep and SUDEP. Postictal generalized EEG suppression has been investigated as a marker of severe postictal cerebral dysfunction, although its predictive significance remains inconsistent [21-25]. Autonomic abnormalities, including altered heart-rate variability, have also been described in epilepsy and investigated as potential indicators of SUDEP vulnerability [26-29]. Respiratory and arousal mechanisms involving brainstem serotonergic pathways provide an additional biological framework through which seizures occurring during sleep could progress from postictal respiratory impairment to catastrophic cardiorespiratory failure [5, 31, 32].

These observations support an integrated view of SUDEP in which the brain, respiratory system, cardiovascular system, autonomic nervous system, and sleep-wake regulatory networks interact rather than operate as independent mechanisms. Within this brain–heart–lung framework, recurrent seizures may generate acute and cumulative physiological disturbances, while sleep-related reductions in arousal and respiratory responsiveness may further compromise recovery following a nocturnal seizure [30, 42]. Sleep disturbances are therefore clinically important not merely as comorbidities of epilepsy but as potential contributors to the physiological environment in which SUDEP occurs.

Accordingly, this narrative review examines the relationship between sleep disturbances and SUDEP, with particular emphasis on sleep architecture, obstructive sleep apnea, sleep deprivation, autonomic dysfunction, heart-rate variability, postictal generalized EEG suppression, brainstem respiratory dysfunction, serotonergic mechanisms, and neurocardiology. It further evaluates potentially modifiable sleep-related factors and emerging approaches to risk stratification while identifying important limitations in the current evidence and priorities for future investigation.

Methods

A narrative review of the literature was conducted using PubMed, Web of Science, Scopus, Embase, and Google Scholar, with primary emphasis on studies published from January 2020 through March 2026. Earlier landmark studies were included when necessary to establish key definitions, epidemiological observations, and mechanistic concepts. Relevant clinical studies, systematic reviews, meta-analyses, consensus statements, practice guidelines, and clinically relevant translational studies were evaluated.

Search terms were used individually and in combination and included “SUDEP,” “epilepsy,” “sleep disturbances,” “sleep-disordered breathing,” “obstructive sleep apnea,” “insomnia,” “circadian rhythm,” “autonomic dysfunction,” “heart-rate variability,” “brainstem dysfunction,” “neurocardiology,” “arrhythmias,” “postictal generalized EEG suppression,” and “sleep deprivation.”

Eligible evidence included original clinical research, prospective and retrospective observational studies, systematic reviews, meta-analyses, narrative reviews, consensus statements, practice guidelines, and clinically relevant translational studies. Selected preclinical studies were included when they provided mechanistic evidence directly relevant to SUDEP, particularly regarding serotonergic signaling, respiratory regulation, arousal, and seizure-induced cardiorespiratory dysfunction. Emphasis was placed on evidence addressing interactions among sleep physiology, epilepsy, cardiorespiratory regulation, autonomic function, and seizure-related mortality.

Duplicate publications, conference abstracts without sufficient full-text data, editorials lacking substantive scientific evidence, and studies without direct relevance to epilepsy, sleep, or SUDEP were excluded. Publications for which reliable English-language information was unavailable were also excluded.

Given the narrative design, evidence was synthesized qualitatively rather than through formal meta-analysis. Findings were compared across study designs and clinical contexts, with greater interpretive weight given to peer-reviewed human studies, systematic reviews, contemporary clinical evidence, and established landmark investigations. Conflicting findings and methodological limitations were considered when interpreting associations, and mechanistic or preclinical evidence was not regarded as establishing clinical causality.

Epidemiology

Sleep disturbances represent some of the most common non-motor comorbidities among individuals with epilepsy and occur substantially more frequently than in the general population. Sleep disturbances are common among people with epilepsy and include impaired sleep quality, excessive daytime sleepiness, sleep fragmentation, insomnia, and sleep-disordered breathing [11-13]. These disturbances encompass insomnia, obstructive sleep apnea, excessive daytime sleepiness, circadian rhythm disorders, restless legs syndrome, parasomnias, and sleep fragmentation. Sleep-related problems may be particularly relevant in people with difficult-to-control epilepsy and in those with comorbid conditions that adversely affect sleep [11, 12].

Sudden unexpected death in epilepsy remains the leading cause of epilepsy-related mortality among adults with chronic epilepsy. SUDEP occurs at an estimated rate of approximately 1 per 1,000 patient-years in adults with epilepsy, with substantially greater risk among individuals with frequent generalized tonic-clonic seizures and poorly controlled epilepsy [1, 6, 9]. SUDEP contributes substantially to premature mortality and years of potential life lost among people with epilepsy [1, 7].

One of the most consistent epidemiological observations in SUDEP research is the predominance of nocturnal events. Case-control, observational, and monitored-event evidence indicates that SUDEP frequently occurs during sleep or in bed and is strongly associated with generalized tonic-clonic and nocturnal seizures [2, 4, 8, 9]. Many SUDEP victims are found in bed, sometimes in the prone position, supporting concern about interactions among nocturnal seizures, impaired arousal, and postictal cardiorespiratory dysfunction [1, 2, 8].

Obstructive sleep apnea has emerged as a particularly important comorbidity in epilepsy populations. Obstructive

sleep apnea is common and frequently underrecognized among people with epilepsy [11, 12, 16, 18]. Clinical factors such as obesity and other established OSA risk characteristics should heighten suspicion for sleep-disordered breathing in patients with epilepsy [12, 16]. Because OSA produces intermittent hypoxemia, sleep fragmentation, and autonomic stress, it has been investigated as a potentially modifiable contributor to SUDEP vulnerability [14-16, 42].

Sleep deprivation also appears to be highly prevalent among people with epilepsy. Systematic evidence demonstrates poorer sleep quality and greater daytime sleepiness among people with epilepsy than among controls [13]. These abnormalities may contribute not only to seizure worsening but also to cardiorespiratory instability and autonomic dysregulation.

The relationship between sleep and epilepsy is bidirectional: sleep disruption can increase seizure susceptibility, while seizures and epilepsy-related factors can further disturb sleep, potentially increasing physiological vulnerability [11, 12, 19, 20].

Sleep Architecture and Epilepsy

Sleep is a highly organized physiological process consisting of non-rapid eye movement (NREM) and rapid eye movement (REM) sleep. NREM sleep is further subdivided into stages N1, N2, and N3, each characterized by distinct neurophysiological features and levels of cortical synchronization. These sleep stages influence neuronal excitability, epileptiform activity, and seizure susceptibility in different ways [11].

NREM sleep, particularly slow-wave sleep, is associated with increased neuronal synchronization and enhanced propagation of epileptiform activity. Consequently, interictal epileptiform discharges and many seizures are facilitated during NREM sleep [11]. In contrast, REM sleep is generally associated with reduced epileptiform activity and may inhibit seizure propagation [11, 39].

Several studies have demonstrated that epilepsy significantly alters normal sleep architecture. Patients with epilepsy frequently demonstrate impaired sleep quality, sleep fragmentation, and alterations in sleep architecture, including reduced REM sleep in some populations [13, 38-40]. Recurrent seizures disrupt physiological sleep cycling and may impair restorative functions normally associated with healthy sleep.

Antiseizure medications also influence sleep architecture. Antiseizure medications can variably affect sleep quality, daytime alertness, and sleep architecture [41]. These medication-related effects further complicate the relationship between epilepsy and sleep.

Disrupted sleep architecture may contribute to SUDEP through multiple pathways. Fragmented sleep impairs autonomic stability, increases sympathetic activation, promotes systemic inflammation, and may reduce the effectiveness of protective arousal mechanisms following seizures. These physiological disturbances provide a plausible pathway by which disrupted sleep could increase vulnerability to severe postictal cardiorespiratory events [1, 11, 30].

Recent investigations suggest that alterations in sleep microarchitecture may also influence SUDEP risk. Alterations in sleep architecture and sleep-stage distribution have been documented in epilepsy, although their specific value for predicting SUDEP remains uncertain [38-40]. Although additional research is needed, these findings suggest that subtle sleep abnormalities may contribute to seizure-related mortality beyond traditional sleep disorder diagnoses.

Obstructive Sleep Apnea and SUDEP

Obstructive sleep apnea has become one of the most intensively studied sleep disorders in epilepsy populations because of its potential contribution to seizure burden, cardiovascular disease, and SUDEP risk. OSA is characterized by recurrent upper-airway obstruction during sleep, producing intermittent hypoxemia, sleep fragmentation, and repeated autonomic stress [16, 42].

The prevalence of OSA among epilepsy patients exceeds that observed in the general population. Clinical studies and reviews indicate that OSA is common and may be underrecognized among adults with epilepsy [11, 16, 18]. The coexistence of OSA and epilepsy appears particularly common among individuals with obesity, older age, cardiovascular disease, and long-standing seizure disorders.

Intermittent hypoxia associated with OSA exerts profound effects on cardiovascular and autonomic physiology. Repeated oxygen desaturation and arousal associated with OSA can impose substantial autonomic and cardiovascular stress [16, 42]. These abnormalities overlap significantly with mechanisms implicated in SUDEP pathogenesis.

OSA may increase SUDEP risk through several pathways. First, recurrent nocturnal hypoxemia may reduce physiological reserve during postictal respiratory depression. Second, chronic sympathetic activation may increase susceptibility to cardiac arrhythmias. Third, sleep fragmentation and impaired sleep quality may adversely affect seizure control and thereby compound established SUDEP risk factors [11, 16, 42].

Evidence suggests that treatment of OSA may improve seizure outcomes. Continuous positive airway pressure therapy has been associated with improved seizure-related outcomes in patients with epilepsy and coexisting OSA [16-18, 43]. Although direct evidence demonstrating SUDEP reduction remains limited, these observations support aggressive screening and treatment of sleep-disordered breathing in epilepsy populations.

Given the strong biological plausibility and increasing epidemiological evidence, OSA is increasingly regarded as a potentially modifiable SUDEP risk factor. Future prospective studies are needed to determine whether systematic OSA treatment can reduce seizure-related mortality.

Insomnia and Seizure Susceptibility

Insomnia and poor sleep quality are frequently reported among people with epilepsy [11-13]. Difficulties initiating sleep, maintaining sleep, or achieving restorative sleep may substantially affect neurological function, cardiovascular health, and seizure control.

The relationship between insomnia and epilepsy is bidirectional. Recurrent seizures, nocturnal epileptiform activity, medication side effects, anxiety, depression, and psychosocial stressors may all contribute to insomnia development. Conversely, inadequate or disrupted sleep can increase seizure susceptibility and contribute to seizure recurrence [11, 19, 20].

Experimental and clinical evidence supports sleep deprivation as a facilitator of epileptiform activity and

seizures [19, 20]. These physiological changes may contribute not only to seizure occurrence but also to increased cardiovascular vulnerability.

Sleep disruption may also interact with autonomic and cardiorespiratory mechanisms implicated in SUDEP, although direct evidence linking insomnia itself to SUDEP remains limited [1, 30]. Because similar mechanisms have been implicated in SUDEP pathogenesis, insomnia may contribute indirectly to seizure-related mortality through cumulative effects on autonomic and cardiovascular function.

Recognition and management of insomnia and other sleep disturbances should therefore form part of comprehensive epilepsy care, alongside optimization of antiseizure therapy and management of relevant comorbidities [11, 12].

Circadian Rhythm Dysfunction

Circadian rhythms regulate numerous physiological processes including sleep-wake cycles, hormone secretion, autonomic function, metabolism, cardiovascular regulation, and neuronal excitability. These rhythms are coordinated by central sleep-wake and neuroendocrine regulatory systems.

Epilepsy exhibits strong circadian influences. Seizure occurrence can vary with the sleep-wake cycle, and some epilepsies demonstrate characteristic relationships with sleep and awakening [11]. Circadian regulation therefore appears closely linked to seizure generation and propagation.

Disruptions of circadian organization may adversely affect epilepsy outcomes. Irregular or insufficient sleep may adversely affect seizure control, although the independent contribution of circadian misalignment to SUDEP risk remains incompletely defined [11, 19, 20]. These effects likely result from altered melatonin secretion, impaired sleep quality, autonomic imbalance, and disruption of neuronal homeostasis.

Circadian dysfunction may also influence SUDEP risk. A substantial proportion of SUDEP events occur during nighttime hours, suggesting that circadian factors contribute to periods of increased physiological vulnerability [14, 15]. Reduced arousal responsiveness, altered respiratory control, and changes in autonomic tone during sleep may interact with seizure-related abnormalities to increase physiological vulnerability [1, 2, 30-32].

Emerging research suggests that melatonin signaling, clock-gene expression, and circadian regulation of autonomic pathways may represent important areas for future investigation. Improved understanding of temporal and sleep-wake influences on seizures may inform future approaches to seizure management and SUDEP research [11, 30].

Neurocardiology and the Epileptic Heart

The concept of the "epileptic heart" has emerged as a compelling framework for understanding the cardiovascular consequences of chronic epilepsy and their potential contribution to SUDEP. This concept proposes that recurrent seizures may produce cumulative autonomic and electrophysiological disturbances that increase susceptibility to adverse cardiac events [1, 3, 30]. Although epilepsy has traditionally been viewed as a disorder confined to the central nervous system, increasing evidence demonstrates that recurrent seizures exert profound systemic effects involving the autonomic nervous system, myocardium, vasculature, and cardiorespiratory regulatory networks.

Seizures can produce acute cardiovascular disturbances, including changes in heart rate, rhythm, and autonomic tone [1, 3, 30]. Repeated exposure to these physiological stresses may promote myocardial remodeling, endothelial dysfunction, vascular stiffness, and chronic autonomic imbalance. Abnormalities in autonomic cardiac regulation, including reduced heart-rate variability, have been demonstrated in epilepsy and investigated in relation to SUDEP risk [26-29].

Sleep may amplify these vulnerabilities because normal sleep is associated with dynamic fluctuations in autonomic tone and cardiovascular regulation. During non-rapid eye movement sleep, parasympathetic activity predominates, whereas rapid eye movement sleep is characterized by greater autonomic variability and sympathetic surges. Seizures occurring during sleep may therefore interact with sleep-related autonomic and respiratory physiology to increase postictal vulnerability [1, 2, 42].

Neuroimaging studies further suggest that recurrent seizures may affect central autonomic networks involving the insula, amygdala, hypothalamus, anterior cingulate cortex, and brainstem nuclei. Dysfunction of central autonomic and cardiorespiratory networks has been proposed as one component of the multifactorial mechanisms underlying SUDEP [1, 30]. Consequently, the epileptic heart hypothesis provides an important bridge linking epilepsy, sleep disorders, cardiovascular disease, and SUDEP.

Autonomic Dysfunction and Heart-Rate Variability

Autonomic dysfunction represents one of the most consistently identified physiological abnormalities among individuals at elevated SUDEP risk. The autonomic nervous system plays a critical role in regulating cardiovascular stability, respiratory control, blood pressure, thermoregulation, and arousal responses. Seizure activity can disrupt autonomic regulation through effects on central autonomic networks [1, 30].

Heart-rate variability (HRV) is widely recognized as a noninvasive measure of autonomic function and reflects the dynamic balance between sympathetic and parasympathetic influences on cardiac rhythm. Reduced HRV has been investigated as a potential marker of autonomic dysfunction and SUDEP vulnerability [26-28]. Studies have demonstrated HRV abnormalities in epilepsy and associations between HRV measures and established SUDEP risk characteristics [26-29].

During seizures, profound fluctuations in autonomic tone may occur. Sympathetic activation frequently results in tachycardia and hypertension, whereas excessive parasympathetic activation may produce bradycardia, atrioventricular block, or asystole. Such peri-ictal autonomic disturbances may contribute to a period of postictal physiological instability [1, 2, 30].

Sleep disturbances may exacerbate autonomic dysfunction through chronic sympathetic activation, impaired vagal activity, sleep fragmentation, and intermittent hypoxemia. OSA can add intermittent hypoxemia and repeated autonomic stress to the autonomic abnormalities already observed in epilepsy [16, 42]. The coexistence of epilepsy and sleep-disordered breathing may therefore create a synergistic effect that increases SUDEP susceptibility.

Postictal Generalized EEG Suppression

Postictal generalized electroencephalographic suppression (PGES) has emerged as one of the most extensively investigated electrophysiological phenomena associated with SUDEP. PGES refers to a transient period of diffuse suppression of cortical electrical activity occurring after generalized tonic-clonic seizures and is characterized by markedly reduced EEG amplitude and cortical responsiveness [21-25].

Several investigations have reported associations between prolonged PGES and increased SUDEP risk. Although not all studies have produced consistent findings, prolonged cortical suppression has been investigated as a marker of severe postictal cerebral dysfunction, although its relationship with SUDEP risk is inconsistent [21, 22, 25]. This suppression may impair arousal mechanisms, delay recovery of respiratory drive, and contribute to persistent autonomic instability following seizures.

The physiological significance of PGES remains incompletely understood. Some investigators propose that PGES reflects widespread neuronal exhaustion following intense seizure activity, whereas others suggest that it may represent dysfunction within critical arousal networks involving the thalamus, brainstem, and reticular activating system [22, 30]. Regardless of its precise mechanism, prolonged PGES appears to identify patients who experience more severe postictal physiological disturbances.

The interaction between PGES and sleep may be particularly important. Because sleep is already associated with reduced cortical responsiveness and elevated arousal thresholds, postictal cortical suppression occurring during sleep may further impair protective awakening responses. This combination may increase vulnerability to respiratory arrest, cardiac dysfunction, and SUDEP [21, 22, 30].

Brainstem Respiratory Dysfunction

Respiratory dysfunction is increasingly regarded as a central component of SUDEP pathophysiology. Numerous witnessed and monitored SUDEP cases have demonstrated that respiratory abnormalities frequently precede cardiovascular collapse, suggesting that respiratory failure may represent a critical initiating event [1, 2].

The brainstem contains multiple nuclei responsible for generating respiratory rhythm, regulating airway patency, sensing blood gas concentrations, and coordinating cardiorespiratory responses. Seizure propagation into these regions may disrupt respiratory control and result in central apnea, hypoventilation, oxygen desaturation, and hypercapnia [1, 2, 30].

Several studies have demonstrated prolonged postictal apnea following generalized tonic-clonic seizures. These respiratory disturbances may be particularly dangerous during sleep because ventilatory responsiveness to hypoxia and hypercapnia is physiologically reduced during sleep states [30-32]. Consequently, seizure-induced respiratory depression may persist longer and produce more severe oxygen desaturation than would occur during wakefulness.

Neuropathological investigations have identified abnormalities within brainstem structures among individuals who died from SUDEP. Alterations involving serotonergic nuclei, respiratory regulatory centers, and autonomic pathways support the hypothesis that impaired brainstem function contributes to fatal seizure-related outcomes [1, 5, 30, 32]. These findings further emphasize the importance of the brain–heart–lung axis in understanding SUDEP.

Serotonergic Pathways and SUDEP

Serotonergic neurotransmission plays a central role in respiratory regulation, autonomic function, arousal mechanisms, and sleep-wake transitions. Brainstem serotonin neurons respond to changes in oxygen and carbon dioxide concentrations and contribute to protective responses during respiratory stress [5, 31, 32].

Experimental and clinical evidence suggests that impaired serotonergic signaling may contribute to postictal respiratory dysfunction and SUDEP. Animal models have demonstrated that serotonin deficiency is associated with impaired autoresuscitation, reduced arousal responses, and increased mortality following seizure-induced respiratory compromise [33-37]. Similar mechanisms have been proposed in human SUDEP.

The relationship between serotonin and sleep is particularly relevant because serotonergic pathways participate in regulating sleep architecture, wakefulness, and respiratory stability during sleep. Dysfunction within these pathways may simultaneously impair sleep quality, reduce arousal responsiveness, and increase vulnerability to seizure-induced respiratory depression [5, 31-37].

Interest in serotonergic mechanisms has generated investigation into potential therapeutic approaches. Although definitive clinical evidence remains limited, serotonergic modulation represents a promising area of future SUDEP prevention research and may ultimately contribute to targeted interventions for high-risk patients [5, 32-37].

Biomarkers and Future Directions

Reliable biomarkers capable of identifying individuals at elevated SUDEP risk remain one of the most important unmet needs in epilepsy research. Current risk stratification relies heavily on clinical characteristics such as seizure frequency, generalized tonic-clonic seizures, nocturnal seizures, and treatment resistance. However, these factors lack sufficient specificity to accurately predict individual risk [1, 6, 9].

Several candidate biomarkers have emerged from recent investigations. Reduced heart-rate variability, impaired baroreflex sensitivity, prolonged PGES, nocturnal oxygen desaturation, sleep-disordered breathing indices, autonomic dysfunction metrics, and neuroimaging abnormalities involving central autonomic and respiratory mechanisms have all been investigated as potential components of SUDEP risk assessment [21-30, 42].

Advances in wearable technologies offer exciting opportunities for future monitoring. Continuous assessment of heart rate, oxygen saturation, respiratory rate, sleep architecture, seizure activity, and autonomic parameters may facilitate earlier detection of physiological deterioration and may provide opportunities for future physiologic risk assessment. However, these approaches require prospective validation before they can be incorporated into routine SUDEP prediction.

Future research should prioritize large prospective studies examining the effects of sleep disorder treatment on seizure burden, cardiovascular function, and SUDEP incidence. Particular emphasis should be placed on evaluating whether systematic screening and treatment of obstructive sleep

apnea and other clinically significant sleep disturbances can improve relevant physiological outcomes and, ultimately, whether such interventions reduce SUDEP incidence [14-18, 42, 43].

Discussion

The growing body of evidence linking sleep disturbances to SUDEP has fundamentally transformed understanding of epilepsy-related mortality. Historically, SUDEP was viewed primarily as a seizure-related phenomenon. Contemporary research instead supports a multifactorial model involving interactions among sleep physiology, respiratory regulation, autonomic function, cardiovascular stability, and brainstem integrity. This expanded perspective provides a more comprehensive explanation for why many SUDEP events occur during sleep and why specific sleep disorders appear to increase risk.

The neurocardiology framework offers particularly important insights into SUDEP pathogenesis. Recurrent seizures may exert cumulative adverse effects on cardiovascular regulation, autonomic balance, and myocardial function. These abnormalities may remain clinically silent for years before contributing to fatal postictal events. Sleep disorders further amplify these vulnerabilities through intermittent hypoxemia, sympathetic activation, inflammation, and impaired arousal mechanisms.

Obstructive sleep apnea deserves particular attention because it is common, underdiagnosed, and potentially treatable. Existing evidence suggests that treatment of OSA may improve seizure control, cardiovascular health, and overall quality of life. Although definitive proof that OSA treatment reduces SUDEP risk remains unavailable, the biological plausibility and clinical benefits strongly support routine screening in epilepsy populations.

The brain–heart–lung axis provides a valuable conceptual model integrating many of the mechanisms implicated in SUDEP. Respiratory depression, autonomic dysfunction, arrhythmogenesis, impaired arousal, and brainstem abnormalities appear to converge in a final common pathway leading to cardiorespiratory collapse. Future preventive strategies will likely require multidisciplinary approaches involving neurology, sleep medicine, cardiology, pulmonology, and autonomic neuroscience.

Limitations

Several limitations affect current understanding of sleep disturbances and SUDEP. Most available studies are observational and cannot establish definitive causal relationships. Considerable heterogeneity exists regarding sleep disorder definitions, SUDEP classification, monitoring methodologies, and outcome measures. Many mechanistic hypotheses are derived from small cohorts or indirect evidence, limiting generalizability. Furthermore, prospective interventional trials evaluating whether treatment of sleep disorders reduces SUDEP incidence remain scarce. These limitations highlight the need for larger multicenter studies incorporating standardized definitions, advanced physiological monitoring, and long-term follow-up.

Recommendations

Sleep assessment should become a routine component of comprehensive epilepsy care. Patients with refractory epilepsy, recurrent nocturnal seizures, obesity, excessive daytime sleepiness, cardiovascular disease, or suspected sleep-disordered breathing should undergo formal sleep evaluation. Screening for obstructive sleep apnea should be prioritized because of its high prevalence and potential contribution to SUDEP risk. Optimization of seizure control remains the most effective strategy for reducing mortality; however, treatment of coexisting sleep disorders should be considered an important adjunctive intervention. Multidisciplinary collaboration among neurologists, sleep medicine specialists, cardiologists, pulmonologists, and primary care physicians may facilitate identification of modifiable risk factors and improve long-term outcomes. Future guidelines should incorporate sleep assessment and neurocardiology considerations into standardized SUDEP risk-reduction strategies.

Conclusions

Sleep disturbances have emerged as important contributors to SUDEP pathogenesis through complex interactions involving respiratory dysfunction, autonomic instability, cardiac arrhythmogenesis, impaired arousal mechanisms, and brainstem dysregulation. The majority of SUDEP events occur during sleep, emphasizing the importance of understanding sleep-related physiological vulnerability in epilepsy. Contemporary neurocardiology research supports the concept of a brain–heart–lung axis in which recurrent seizures produce cumulative effects on autonomic and cardiovascular regulation that may ultimately contribute to fatal outcomes. Recognition and treatment of sleep disorders, particularly obstructive sleep apnea, represent promising opportunities for improving seizure control, cardiovascular health, and potentially reducing SUDEP risk. Future investigations integrating sleep medicine, neurocardiology, and precision monitoring technologies may substantially improve risk stratification and prevention strategies for this devastating complication of epilepsy.

Declarations

Funding

The authors received no specific funding for this work.

Conflicts of Interest

The authors declare no conflicts of interest related to this manuscript.

Author Contributions

All authors contributed to the conceptualization, literature review, manuscript preparation, critical revision, and approval of the final version of the manuscript.

Data Availability

No new datasets were generated or analyzed during the preparation of this narrative review.

Ethics Statement

Ethical approval was not required because this narrative review synthesized previously published literature and did not involve the recruitment of human participants or the conduct of animal experiments.

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