

## Short Commentary

### From Neglected Symptom to Early Precision Medicine: Should We Pay More Attention to Sleep Disorders in Patients with Liver Cirrhosis?

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Sleep disorders are common clinical symptoms in patients with liver cirrhosis. Prolonged sleep deprivation not only exacerbates anxiety and panic symptoms, impairing quality of life, but also adversely affects disease prognosis. Based on our team's recently published review titled "Liver Cirrhosis and Sleep Disorders", this article provides a short commentary from three perspectives: the research motivation, key findings during the manuscript writing, and the ultimate clinical objectives. It also reiterates the important clinical significance and necessity of early diagnosis and standardized interventions for patients with liver cirrhosis complicated by sleep disorders.

#### From Clinical Observation to Critical Reflection: Should We Pay More Attention to Sleep Disorders in Cirrhotic Patients?

In clinical practice, we have observed that sleep disorders are present in the vast majority of patients with liver cirrhosis, manifesting as symptoms such as nocturnal insomnia and daytime sleepiness. Studies indicate that approximately 26%–77% of cirrhotic patients experience insomnia, while 29.5%–71% suffer from excessive daytime sleepiness [1]. However, such symptoms are often simplistically attributed to psychological factors or discomfort from the hospital environment, leading to neglect by both physicians and patients, and

consequently, a lack of systematic assessment and intervention. In recent years, studies on liver cirrhosis have predominantly focused on traditional complications such as hepatic fibrosis and portal hypertension, while systematic studies on sleep disorders as an independent or comorbid factor remain scarce. There is a lack of integrated cross-mechanism analysis, as well as explicit clinical practice guidelines or consensus statements. Notably, existing studies have shown that sleep disorders may exacerbate the progression of hepatic fibrosis through chronic intermittent hypoxia [2]. This implies that the relationship between sleep disorders and liver cirrhosis is not merely one of simple causality, but rather a complex interplay of mutual influence and promotion. Therefore, early assessment and intervention for sleep disorders in cirrhotic patients may hold significant clinical value for improving quality of life and delaying disease progression.

#### Refocusing on the Core of the Disease: From Mechanistic Exploration to Novel Diagnostic and Therapeutic Strategies

The diagnosis and treatment of diseases generally follow the principle of moving from presentation to etiology, and from cause to strategy. Currently, clinical management of sleep disorders associated with cirrhosis relies primarily on pharmacological interventions aimed at improving sleep quality. Examples include lactulose combined with rifaximin to alleviate hepatic encephalopathy [3], or the use of traditional hypnotics such as non-benzodiazepines to aid sleep [4]. However, there remains a lack of targeted therapeutic regimens addressing the specific pathological mechanisms. This is primarily due to the complexity of its pathogenesis. Sleep disorders triggered by different etiologies and complications exhibit distinct mechanisms. For instance, sleep apnea syndrome associated with metabolic dysfunction-associated fatty liver disease, the ammonia toxicity hypothesis in hepatic encephalopathy, and elevated inflammatory cytokines in infections [5-7]. At present, no unified mechanistic theory or clinical standard has been established. Furthermore, emerging mechanisms such as melatonin metabolism dysregulation and gut microbiota dysbiosis have gradually garnered attention, yet there remains a lack of systematic clinical validation and translational applications [8,9]. These ongoing investigations highlight the need for future diagnostic and therapeutic approaches to focus on deeper mechanistic insights and personalized treatment, tailoring sleep intervention strategies according to the specific etiology and complications of cirrhosis in individual patients.

What deserves emphasis is that screening and diagnosis form the foundation of treatment. The presence of sleep disorders and the quality of sleep largely depend on the patient's subjective perceptions, lacking a unified objective assessment standard. Currently, commonly used sleep evaluation methods in clinical practice primarily include polysomnography and the Pittsburgh Sleep Quality Index [10,11], among others, each with its own advantages and limitations. However, due to comprehensive considerations of cost and efficiency, systematic assessment is often not routinely conducted in actual clinical

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practice by either patients or physicians. Yet, as previously mentioned, sleep disorders and liver cirrhosis may interact in a bidirectional, mutually reinforcing manner. Therefore, we still recommend early sleep quality assessment for patients with certain clinical indicators (such as inflammatory markers, blood ammonia levels, etc.) suggesting a higher risk of sleep problems [7,12]. Early screening and early intervention hold positive significance for delaying disease progression and improving patients' quality of life.

### Addressing the Core Question: Promoting Early Screening and Advancing Toward Precision Medicine

Our review aims to construct a multidimensional framework for understanding the relationship between liver cirrhosis and sleep disorders. However, the causal and interactive mechanisms between the two have not yet been fully elucidated, and clinical evidence remains limited. We anticipate that this work will facilitate multidisciplinary collaboration among hepatology, psychiatry, sleep medicine, and other relevant fields, collectively driving the transformation of sleep disturbance from a neglected comorbid symptom to a modifiable prognostic factor. Moreover, we intend that our commentary will provide insights for clinicians, jointly promote the early screening and management of sleep disorders in cirrhotic patients, and contribute to the future development of widely recognized clinical guidelines or consensus statements.

### Author's Contribution

Qing Ye designed the structure of the article and revised its content, Jiawen Feng drafted the manuscript.

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