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**Small bites, big impact: the importance of evening snacks in patients with advanced chronic liver disease**

Nocturnal snacks and body composition

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## **Abstract**

People with advanced chronic liver disease (ACLD) have an enhanced risk of malnutrition, which has multifactorial etiology and is mainly linked to a reduced energy and protein intake; malnutrition is critical for patients with cirrhosis since it is often associated with sarcopenia, a skeletal muscle depletion with a loss of muscle mass and function. Late-evening snacks have been extensively studied, and guidelines are recommended to counteract the effects of prolonged fasting at night in patients with ACLD. However, it has not been fully explored whether late evening snacking is clarified as a milestone to address the nutritional needs of people with ACLD or whether it has a potential role in improving body composition. In this randomised control trial, Yu YB et al demonstrated that long-term nocturnal snacks have the potential to significantly improve body composition by body fat mass (BFM), visceral fat area (VFA) and body cell mass (BCM) in patients with ACLD. While the improvement in skeletal muscle mass was minor, the promising results in other compositions provide hope for future research and patient care.

**Key Words:** Nutrition; Cirrhosis; Advanced chronic liver disease; Malnutrition; Sarcopenia; Skeletal muscle mass.

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**Core Tip:** This editorial discusses a randomized control trial by Yu YB *et al* published in the *World Journal of Hepatology*, examining the effect of nocturnal snacks on patients with advanced chronic liver disease. The study aimed to assess late evening snacks' impact on body composition in cirrhosis patients. Findings suggest that nocturnal snacks may improve body fat mass, visceral fat area, and body cell mass, though their effect on skeletal muscle mass is limited. This result underscores the need for additional research on optimizing nutritional interventions in these patients.

## INTRODUCTION

Cirrhosis, also named advanced chronic liver disease (ACLD), is the final stage of progressive liver disease, marked by extensive fibrosis where regenerative hepatic nodules substitute the normal liver structure due to chronic liver injury, ultimately leading to liver failure. ACLD is often linked to significant morbidity and mortality.<sup>[1]</sup> In the early phases, this condition is asymptomatic, configured as compensated (cACLD), but subsequently, it evolves into decompensated (dACLD), defined as the first episode of ascites, esophageal variceal bleeding and hepatic encephalopathy<sup>[2]</sup>.

Malnutrition results in changes to body composition and cellular functions caused by insufficient protein and energy intake. This definition is supported by <sup>1</sup>both the Global Leadership Initiative on Malnutrition (GLIM) and the European Society for Clinical Nutrition and Metabolism (ESPEN)<sup>[3]</sup>. Diagnosing, evaluating, and grading malnutrition requires a blend of phenotypic criteria—such as weight loss, decreased body mass index, or reduced muscle mass—and etiological factors, including diminished food intake, poor assimilation, and the existence of acute or chronic disease-related inflammation. Malnutrition is a major concern among ACLD patients, with prevalence rates ranging from 5% to 92%<sup>[4]</sup>. This prevalence rises with greater disease severity (dACLD) but is also observable in the compensated stage<sup>[5,6]</sup>.

Frequently, in patients with ACLD, malnutrition is associated with sarcopenia, a skeletal muscle depletion with a loss of muscle mass and strength function<sup>[7]</sup>; in patients with cirrhosis, sarcopenia prevalence varies between 40% and 70%, significantly depending on the specific population studied, methods of assessment and the definition of sarcopenia used<sup>[8]</sup>. The etiology of sarcopenia is complex and multifactorial and involves gastrointestinal symptoms -prevalent in patients with cirrhosis- (nausea and early satiety) and also connected to high levels of leptin, hypermetabolism due to systemic inflammation, and low levels of physical activity; alcohol consumption, besides worsening liver disease, contributes to developing sarcopenia<sup>[9]</sup>.

Malnutrition, particularly when linked to sarcopenia, complicates ACLD and acts as a standalone risk factor for both disease advancement and outcomes, including increased hospitalization rates and mortality. It also contributes to other ACLD-related complications like hepatic encephalopathy and infections<sup>[10,11]</sup>.

### **THE IMPORTANCE OF NOCTURNAL LATE-EVENING SNACKS**

Patients affected by ACLD experience an imbalance between muscle protein synthesis, typically during the fed state, and protein breakdown, which is present during the fasting state<sup>[12-14]</sup>. Cirrhosis is characterised by hypermetabolism that leads to accelerated starvation even after a brief fasting period, with an early shift from glucose to lipid metabolism due to reduced glycogen storage<sup>[15,16]</sup>. Indeed, during fasting, in patients with ACLD, glucose oxidation and glycogenolysis diminish in favour of fat oxidation and gluconeogenesis<sup>[16]</sup>, which determine increased protein consumption and, finally, skeletal muscle depletion and sarcopenia<sup>[17]</sup>.

Since the most prolonged period of starvation occurs during the night, between dinner and breakfast, late-evening snack consumption counteracts the progression to a catabolic state and improves sarcopenia<sup>[18]</sup>. Moreover, late-evening snacks help stabilise glucose levels in the blood<sup>[18]</sup>. Finally, nocturnal snacks prevent muscle depletion and promote metabolic homeostasis<sup>[18]</sup>.

### **NOCTURNAL SNACKS AND BODY COMPOSITION**

Body composition is a crucial tool in indirectly assessing the nutritional state since it allows the evaluation of fat and muscle mass, thus indirectly evaluating the presence of sarcopenia<sup>[19]</sup>.

Several studies have explored the impact of nocturnal snacks on liver disease. Recently, we summarised the evidence about the impact of late-evening snacks in patients with ACLD<sup>[14]</sup>.

Most papers studied the positive effect of nocturnal snacks on strong outcomes, such as liver enzymes, hepatic encephalopathy and death<sup>[20,21]</sup>. Nevertheless, a prospective study by Kobayashi *et al*<sup>[22]</sup> evaluated the modifications in body composition through bioelectrical impedance analysis (BIA) after introducing late evening snacks in patients undergoing liver surgery for hepatocellular carcinoma or for metastasis from colorectal cancer. The authors<sup>[22]</sup> found that body cell mass and skeletal muscle volume were higher in the nocturnal snack group compared with the control group.

However, the effect of late-evening snacks on body composition still needs to be explored further.

In this relevant paper “Effects of nocturnal snacks on body composition in patients with liver cirrhosis” to be published in *World Journal of Hepatology*, Yu YB *et al*<sup>[23]</sup> studied the effect of late-evening snacks on body composition in a cohort of 70 patients with ACLD compared to 30 healthy controls. The differences in body composition were evaluated using multi-frequency bioelectrical impedance analysis (InBody 720, a body composition analyser). Bioelectrical impedance permits the detection of body composition utilising the different impedances encountered by the current passing through the cells and intercellular mass, to calculate the intracellular and extracellular fluid content of the subject and to derive the protein, fat, skeletal muscle substance, body cell count, and mineral contentment. Although computed tomography is the gold standard for body composition assessment, bioelectrical impedance avoids radiation exposure and allows regular monitoring of changes. The authors confirmed that at baseline, body fat mass (BFM), skeletal muscle mass (SMM), free fat mass (FFM), visceral fat area (VFA) and body cell mass (BCM) were significantly lower in ACLD patients than in the healthy control group. Subsequently, the patients were randomised into a standard diet group (three meals a day) and a late evening snacks group (three meals a day + nocturnal snacks) for three months of intervention. The authors showed,

at the end of follow-up, that in patients with ACLD, late-evening snacks ameliorate the body composition indicators with an improvement in BFM, VFA and BCM; on the other side, however, SMM was not improved in both groups. In light of these results, several considerations could be made. First, since there are different proportions between patients with cACLD *vs.* dACLD with distinct etiologies of liver disease, it could be intriguing to evaluate if differences in body composition are detectable after intervention, considering the basal condition. Second, as the duration of intervention was limited, it could be considered that a longer supplementation may positively impact body composition, including SMM. In fact, in a randomized controlled trial, Ruiz-Margáin *et al*<sup>[24]</sup> highlighted that a six-month supplementation with branched-chain amino acids - in addition to a high-fibre, high-protein diet - increases muscle mass without raising the levels of ammonia or development of hepatic encephalopathy. Third, since the authors showed that VFA increased after three months in the nocturnal snack group, this result could be insidious, especially for patients with an elevated body mass index at the baseline. Indeed, the increase in VFA exposes the patient to the risk of developing or worsening insulin resistance, a critical mechanism which may exacerbate liver damage. In fact, further investigations are required to clarify if a specific composition of late evening snack may impact positively on SMM without worsening VFA.

## **CONCLUSION**

Nocturnal snacks are fundamental to addressing the specific nutritional needs of patients with ACLD. Still, it remains to be seen if they may have a potential role in ameliorating skeletal muscle mass content detected through body composition analysis. Moreover, further studies are necessary to investigate if the different formulations (quantity of proteins, carbs and lipids) of the nocturnal snack may specifically affect body composition, particularly in preserving skeletal muscle mass and preventing sarcopenia.

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