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NUTRITIONAL ASSESSMENT AND ITS CLINICAL IMPLICATIONS IN A COHORT OF PATIENTS WITH HEPATIC FIBROSIS AND ADVANCED CHRONIC LIVER DISEASE

Tesi di laurea in Scienze Tecniche Dietetiche Applicate

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ABSTRACT

Background: Chronic liver disease is strongly influenced by nutritional status, and malnutrition is highly prevalent in patients with hepatic fibrosis and cirrhosis. Dietary patterns characterized by poor nutrient quality and increasing reliance on ultra-processed foods (UPFs) may contribute to disease progression through metabolic and inflammatory pathways. However, the role of UPF intake in advanced chronic liver disease still requires elucidation.

Aims: To comprehensively assess the nutritional status of patients with MASLD-related liver fibrosis and evaluate its association with fibrosis severity. The study investigated body composition, dietary intake, dysfunctional eating behaviors, and particularly the quantitative and qualitative contribution of ultra-processed foods (UPFs). Nutritional changes after intervention were also analyzed during follow-up.

Methods: This observational study included 41 outpatients with MASLD and significant liver fibrosis (F2–F4), followed at the Steatosis Outpatient Clinic of S. Orsola Hospital (Bologna). Patients were consecutively enrolled between July 2024 and October 2025. Liver fibrosis and steatosis were assessed using vibration-controlled transient elastography (FibroScan®), with liver stiffness (LSM) and controlled attenuation parameter (CAP) used to stage fibrosis and quantify hepatic fat. Biochemical analysis included glucose and lipid profile, liver enzymes, albumin, and bilirubin. Anthropometric measurements, body composition (BIA), and—only in cirrhotic patients—muscle strength and frailty (handgrip dynamometry and Liver Frailty Index) were assessed at baseline and after a median 4-month follow-up. Dietary intake was evaluated using a 7-day food diary analyzed with Handydiet® software and compared with disease-specific nutritional recommendations. Ultra-processed food (UPF) intake was assessed qualitatively using a UPF-focused FFQ and quantitatively through diary data, according to the NOVA classification.

Conclusions: MASLD patients with fibrosis frequently presented nutritional imbalances and a high reliance on UPFs, which was significantly associated with greater fibrosis severity. The nutritional intervention led to improvements in anthropometric and body composition parameters. These findings reinforce the importance of early and structured nutritional management to support liver disease care and potentially slow progression.

Contesto: Lo stato nutrizionale rappresenta un determinante fondamentale nella malattia epatica cronica, e la malnutrizione è altamente prevalente nei pazienti con fibrosi e cirrosi epatica. Modelli alimentari caratterizzati da bassa qualità nutrizionale e da un crescente consumo di alimenti ultraprocessati (UPF) possono contribuire alla progressione della malattia attraverso meccanismi metabolici e infiammatori. Tuttavia, il ruolo degli UPF nella progressione dell'epatopatia cronica avanzata richiede ulteriori approfondimenti.

Obiettivi: Valutare in maniera completa lo stato nutrizionale di pazienti con fibrosi epatica correlata a MASLD e indagare la sua associazione con la severità della fibrosi. Lo studio ha considerato la composizione corporea, l'intake alimentare, la presenza di comportamenti alimentari disfunzionali e, in particolare, il contributo quantitativo e qualitativo degli UPF. È stata inoltre analizzata la variazione dello stato nutrizionale dopo intervento dietetico durante il follow-up.

Metodi: Studio osservazionale su 41 pazienti ambulatoriali affetti da MASLD con fibrosi significativa (F2–F4), seguiti presso l'Ambulatorio Steatosi dell'Ospedale S. Orsola (Bologna). I pazienti sono stati arruolati consecutivamente tra luglio 2024 e ottobre 2025. Fibrosi e steatosi sono state valutate mediante elastografia epatica (FibroScan®), utilizzando Liver Stiffness Measurement (LSM) e Controlled Attenuation Parameter (CAP). Sono stati analizzati i profili glucidico e lipidico, enzimi epatici, albumina e bilirubina. Le valutazioni antropometriche e della composizione corporea (BIA) sono state condotte al baseline e dopo un follow-up mediano di 4 mesi; nei pazienti cirrotici è stata inoltre misurata la forza muscolare e la fragilità (handgrip test e Liver Frailty Index). L'intake alimentare è stato analizzato tramite diario alimentare di 7 giorni elaborato con Handydiet® e confrontato con le raccomandazioni nutrizionali per patologia. Il consumo di UPF è stato valutato qualitativamente tramite questionario FFQ mirato e quantitativamente dai diari, secondo classificazione NOVA.

Conclusioni: I pazienti con MASLD e fibrosi presentano frequentemente squilibri nutrizionali e un'elevata dipendenza dagli UPF, associata significativamente a una maggiore severità della fibrosi. L'intervento nutrizionale ha determinato un miglioramento dei parametri antropometrici e della composizione corporea. Questi risultati rafforzano l'importanza di una gestione nutrizionale precoce e strutturata come supporto alla cura della malattia epatica e per potenzialmente rallentarne la progressione.

1. **LIVER CIRRHOSIS**

1.1 **Introduction**

The liver plays an essential role in nutritional metabolism, being essential for glucose homeostasis, protein synthesis, and the metabolism of drugs and toxins. With the establishment and progression of chronic liver disease, a clinical condition often emerges, characterized by the presence of malnutrition, sarcopenia, and overall frailty. This complications affects more than 50% of patients with cirrhosis and significantly contribute to increased morbidity and mortality, primarily due to reduced quality of life and a higher risk of hepatic decompensation. ([1])

Recent studies in the literature increasingly highlight the importance of including the nutritional aspect in the assessment and management of patients with cirrhosis. Early identification of nutritional status and evaluation of common complications such as malnutrition and sarcopenia plays a crucial role. Therefore, it is necessary to define a personalized, evidence-based nutritional plan aimed at counteracting the accelerated catabolic state, protein depletion, and micronutrient deficiencies characteristic of the disease. ([2], [3])

Optimizing care for the cirrhotic patient should be achieved through a multidisciplinary approach involving physicians, nurses, and dietitians, with the goal of slowing the progression of liver damage and improving clinical outcomes and survival. ([2],[3])

1.2 **Definition**

Liver cirrhosis, also known as advanced chronic liver disease (ACLD), is a consequence of chronic liver inflammation and represents the end stage of progressive liver fibrosis, in which the normal hepatic architecture is replaced by regenerative nodules, which eventually leads to liver failure. ([4],[5])

1.3 **Epidemiology**

Cirrhosis represents a major public health burden in many countries, with its global impact increasing since 1990, partly as a consequence of population growth and ageing, specifically in low-income and middle-income countries. ([5])

Although the age-standardised death and DALY rates of cirrhosis decreased from 1990 to 2017, numbers of deaths, DALYs and the proportion of all global deaths due to cirrhosis

increased.([5])

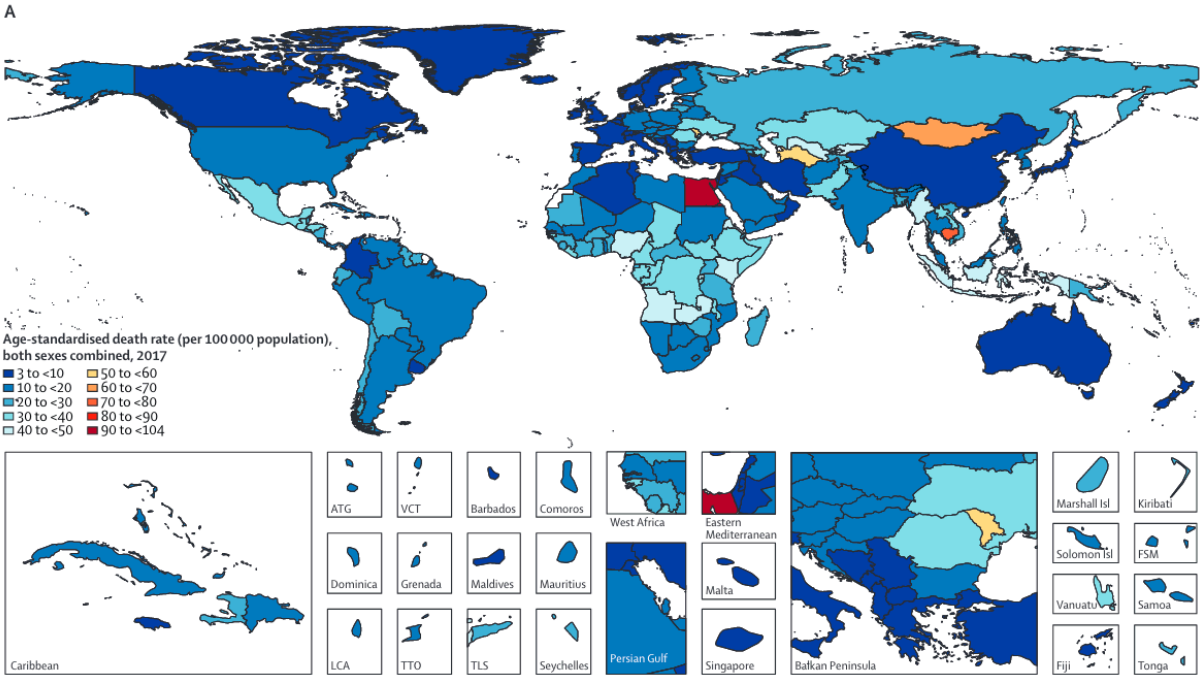

Figure 1. Age-standardised death rate for cirrhosis, both sexes combined, 2017 ([5])

About 2 million deaths worldwide annually are attributable to liver disease: 1 million due to cirrhosis and 1 million due to viral hepatitis and hepatocellular carcinoma. More than 60% of all liver disease-related deaths are in men. ([4])

Globally, liver cirrhosis is the 11th leading cause of death, the third most common cause of death in people aged 45–64 years and the 15th leading cause of morbidity, accounting for 2.4% of deaths (more than 1.32 million) and nearly 41.4 million of disability-adjusted life years worldwide in 2017. In the same year, hepatitis B, hepatitis C, and alcohol-related liver disease were the leading causes of cirrhosis-related deaths in men, whereas in women deaths from hepatitis B and alcohol-related liver disease were less frequent, hepatitis C had a similar impact, and non-alcoholic fatty liver disease and other causes were more common compared with males. ([1],[4],[5]).

Despite the availability of effective interventions for the prevention and treatment of hepatitis B and C, they were still the main causes of cirrhosis burden worldwide, particularly in low-income countries. ([1],[4],[5])

1.4 **Causes and risk factor**

The most common causes of cirrhosis worldwide are alcohol-related liver disease, non-alcoholic fatty liver disease, and chronic viral hepatitis B and C. ([4])

In addition to the major causes, several less frequent aetiological factors can lead to cirrhosis, including genetic disorders causing iron and copper overload such as haemochromatosis and Wilson's disease, respectively, α1-antitrypsin deficiency, as well as autoimmune diseases for instance autoimmune hepatitis, cholestatic diseases including primary biliary cholangitis and primary sclerosing cholangitis. ([4])

The occurrence of more than one causative factor in a single patient can lead to more rapid progression to cirrhosis: for example, components of metabolic syndrome and alcohol use disorder often coexist and constitute a cumulative risk. ([4])

In recent decades, a shift in the primary cause of liver disease has been observed, due to the rising prevalence of non-communicable chronic diseases in the general population, along with major advances in pharmacological treatments that have significantly improved the prognosis of viral hepatitis. Metabolic dysfunction has now become the leading cause of liver disease, previously known as non-alcoholic fatty liver disease (NAFLD) and currently redefined as metabolic dysfunction-associated steatotic liver disease (MASLD). ([1]). This condition is characterised by excessive fat accumulation in more than 5% of hepatocytes in the presence of at least one cardiometabolic risk factor, and includes a spectrum of liver pathologies ranging from simple steatosis to metabolic dysfunction–associated steatohepatitis (MASH), fibrosis, cirrhosis, and hepatocellular carcinoma. ([6])

Type 2 diabetes and obesity (particularly abdominal obesity) are the metabolic diseases with the strongest impact on the natural history of MASLD, including progression to MASLD/MASH-related advanced fibrosis, cirrhosis and hepatocellular carcinoma. ([7])

The presence of overweight or obesity in individuals with compensated cirrhosis at baseline is associated with a higher risk of clinical decompensation, independently of liver function, portal pressure and underlying aetiology of liver disease. ([7])

Moreover, specific demographic and metabolic profiles are associated with a higher likelihood of disease progression. In particular, males over 50 years of age, postmenopausal women, and individuals with multiple cardiometabolic risk factors are at increased risk of developing progressive fibrosis, cirrhosis, and its related complications. ([7])

1.5 **Diagnosis of cirrhosis**

The diagnostic evaluation of patients with suspected cirrhosis aims to quantify the degree of hepatic fibrosis, assess the presence of portal hypertension, and identify the underlying cause or causes of the disease. ([4])

Liver fibrosis is commonly classified into four stages of increasing severity. Stage 3 fibrosis and stage 4 fibrosis (which classify as cirrhosis) are strongly associated with future liver-related morbidity and mortality, representing a critical point at which timely intervention is essential to prevent further progression. ([4])

Chronic liver inflammation does not progress to cirrhosis in all patients, but when progression does occur, the rate at which it happens varies from weeks in case of complete biliary obstruction to decades in patients with longer-term causes, such as viral hepatitis C. Cirrhosis typically begins with an asymptomatic phase which is eventually followed by a short symptomatic phase of months to years. This latter stage, commonly referred to as decompensated cirrhosis, is characterized by various complications such as ascites, esophageal variceal bleeding (EVB), and hepatic encephalopathy (HE) leading to frequent hospitalizations, a marked decline in the quality of life of both patients and caregivers, and, in the absence of liver transplantation, ultimately to death. ([4])

A liver biopsy is the gold standard for the assessment of liver fibrosis although it is being increasingly replaced by noninvasive methods. However, the current indication for liver biopsy is mainly to determine the cause of liver disease in selected cases, and not to stage fibrosis. ([4], [7],[8])

Elastography, which measures the stiffness of the liver, can be used to assess the degree of hepatic fibrosis in the fasted state, in the absence of inflammation, biliary obstruction, and hepatic congestion. Transient elastography has been validated for the assessment of various causes of liver disease and is the preferred test for its ease of use and utility as a point-of-care assessment, but is not generally available in primary care. ([4])

Serologic measures and imaging-based indices are used to diagnose cirrhosis. Compared with biopsy, these measures are less expensive, safer, and simpler to follow longitudinally. The most common serologic tests capture indirect signs of liver fibrosis and dysfunction (eg, thrombocytopenia, reflecting reduced platelet production and splenic sequestration and a higher ratio of aspartate aminotransferase to alanine aminotransferase). ([8])

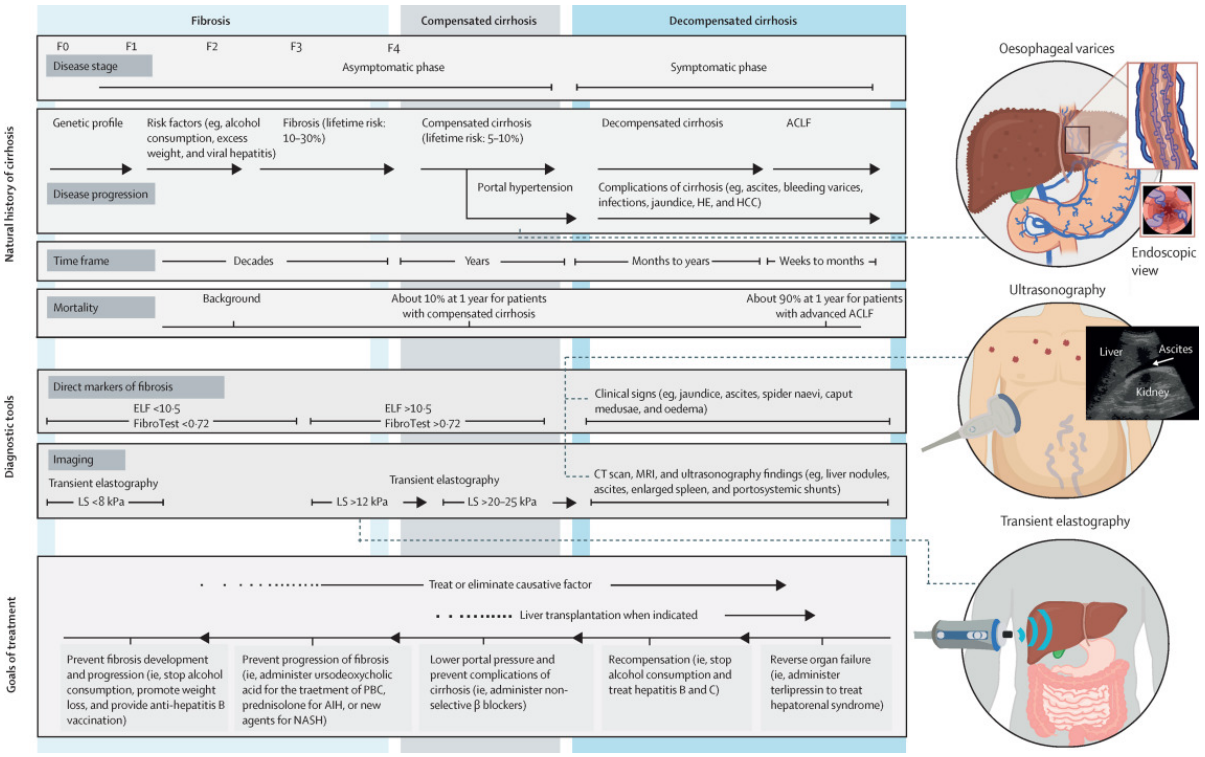

Figure 2. Natural history, diagnostic tools, and goals of treatment according to different stages of chronic liver diseases. ([4])

1.6 **Patophisiology of cirrhosis: portal hypertension and its complications**

The histological structural alterations distort the hepatic angioarchitecture, which increases resistance to portal blood and is the initial factor leading to portal hypertension. An additional dynamic component is related to the imbalance between intrahepatic vasoconstrictors and vasodilators, which favors vasoconstriction and contributes to rapid changes in portal pressure. Nitric oxide is the most extensively studied mediator in this process; its production by sinusoidal endothelial cells is reduced in cirrhosis and can decline further during acute events such as infections, thereby exacerbating intrahepatic resistance and portal pressure. ([4])

The initial increase in portal pressure as a result of higher intrahepatic vascular resistance leads to circulatory abnormalities, the most important of which is the development of splanchnic arterial vasodilation. In contrast to what occurs in hepatic circulation, in splanchnic circulation the production of nitric oxide by endothelial cells is increased. Vasodilation in the splanchnic capillary beds and arterioles results in an increase in portal blood flow that, in combination with an increase in intrahepatic vascular resistance, results in increased portal pressure (known as portal hypertension). ([4])

Progressive splanchnic vasodilation decreases effective arterial blood volume, leading to systemic hypotension, arterial underfilling, and activation of neurohumoral vasoconstrictive systems (sympathetic nervous system, renin–angiotensin–aldosterone system, and non-osmotic vasopressin release). These mechanisms aim to counteract vasodilation by promoting sodium and water retention, increasing plasma volume. Part of the excessive plasma volume is compartmentalised to the peritoneal space as ascites, due to portal hypertension. As cirrhosis progresses, vasodilation increases and systemic blood pressure continues to drop, with maximal vasoconstrictor activation. This results in marked vasoconstriction in the renal circulation and can lead to hepatorenal syndrome. The increased plasma volume also raises cardiac output, causing a hyperdynamic circulation that, together with splanchnic vasodilation, further increases portal blood flow and perpetuates portal hypertension. ([4])

Increased portal pressure leads to reversal of flow and dilation of preexisting collateral vessels at sites where portal and systemic circulation connect, such as the gastroesophageal junction, and also stimulates angiogenesis, promoting the formation of new collaterals. The most clinically significant portosystemic collaterals are gastroesophageal varices, which can bleed when intravariceal pressure exceeds the vessel wall's elastic limit. ([4])

Portosystemic shunting, along with worsening liver function, contributes to hepatic encephalopathy by reducing the clearance of gut-derived ammonia. ([4])

The importance of portal hypertension in cirrhosis complications is demonstrated by the correlation between its severity and complication risk, as well as by the reduction in risk following portal pressure lowering. ([4])

Progression of cirrhosis is also associated with systemic inflammation, which impairs circulatory function via vasodilator release. This inflammation is triggered by bacterial translocation due to increased intestinal permeability and altered microbiota. Impaired liver function and immune dysfunction in decompensated cirrhosis further increase susceptibility to bacterial infections. ([4])

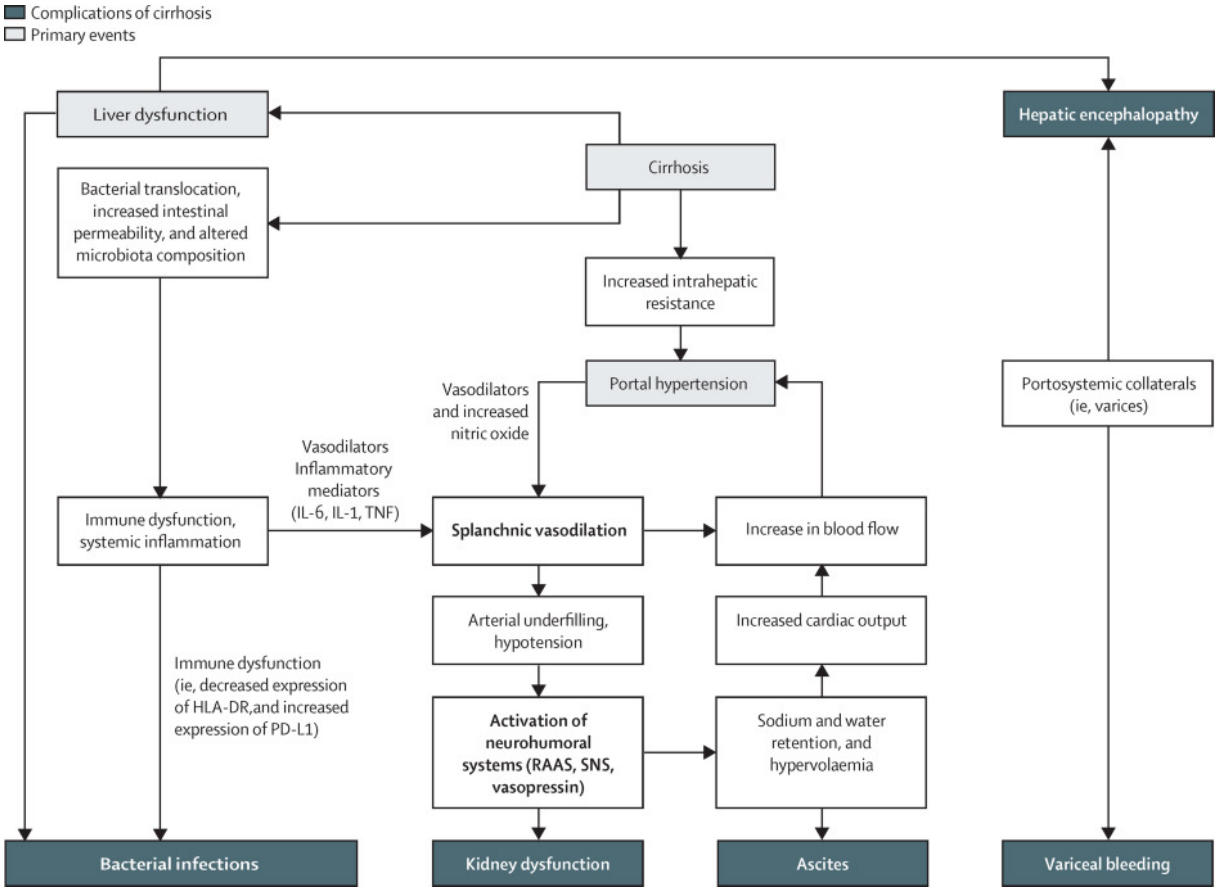

Figure 3. Summary of the pathophysiology of cirrhosis complications. ([4])

2. NUTRITIONAL STATUS AND ITS CLINICAL IMPACT ON CHRONIC LIVER DISEASE

Cirrhosis is an irreversible disease, and in the absence of antifibrotic therapies, clinical management must prioritize not only the treatment of underlying causes and complications but also the early assessment of nutritional status. ([1])

Malnutrition and, consequently, sarcopenia and physical frailty are frequent in these patients and strongly influence prognosis. ([1],[2],[3])

2.1 **Malnutrition: screening and assessment of nutritional status**

The classical clinical presentation of cirrhotic patients has changed significantly in recent years, with a marked increase in the proportion of individuals who no longer appear underweight, but rather normal weight, overweight, or even obese. However, a body weight within or above the normal range does not necessarily reflect an adequate nutritional status. ([1])

Malnutrition is highly prevalent in patients with liver cirrhosis, largely due to an altered catabolic state that causes an imbalance between energy requirements and dietary intake, leading to protein depletion and micronutrient deficiencies. Despite its clinical relevance, malnutrition is frequently underdiagnosed and has been reported in 5–92% of patients, depending on the screening methods and populations studied. Multiple factors -including reduced energy and protein intake, inflammation, malabsorption, altered nutrient metabolism, hypermetabolism, hormonal disturbances, and gut microbiome dysbiosis -contribute to its development; moreover, external factors such as prolonged fasting and alcohol consumption may further contribute to the development of malnutrition. ([2], [3],[9])

The prevalence and severity of protein-energy malnutrition correlate with the clinical stage of chronic liver disease, ranging from approximately 20% in patients with well-compensated disease to over 60% in those with advanced cirrhosis. Body composition in cirrhotic patients is profoundly altered, characterized by protein depletion and increased total body water, which may be present even in individuals with early-stage disease (Child-Pugh class A). ([2], [3]) For this reason, early identification of malnutrition risk is crucial in all patients with cirrhosis, particularly those who are underweight (BMI <18.5 kg/m²), sarcopenic, or have decompensated liver disease (Child-Pugh C). ([2])

Prompt nutritional screening can help reduce hospital stay, lower healthcare costs, improve quality of life, and decrease mortality. However, nutritional intervention is often delayed due to insufficient assessment of malnutrition risk. ([2])

2.1.1 **Application of the RFH-NPT**

The European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines recommend the Royal Free Hospital-Nutritional Prioritizing Tool (RFH-NPT) for identifying the risk of malnutrition in patients with liver disease. In a direct comparison, the RFH-NPT proved to be more sensitive than the NRS-2002 in detecting at-risk patients with liver disease. Therefore, the RFH-NPT remains the best option currently available and is easily applicable in clinical practice. ([3])

According to the RFH-NPT, patients are classified into three nutritional risk categories (low, moderate, and high) based on a combination of 1) presence of acute hepatitis or need for enteral nutritional support, 2) low BMI, unexplained weight loss, maintenance of volitional nutritional intake, and 3) whether fluid overload interferes with ability to eat. Patients at high risk for malnutrition based on the RFH-NPT classification system have been shown to experience worse clinical outcomes including reduced survival, worsened liver function, and reduced quality of life. Improvement in the RFH-NPT has been associated with improved survival. ([10])

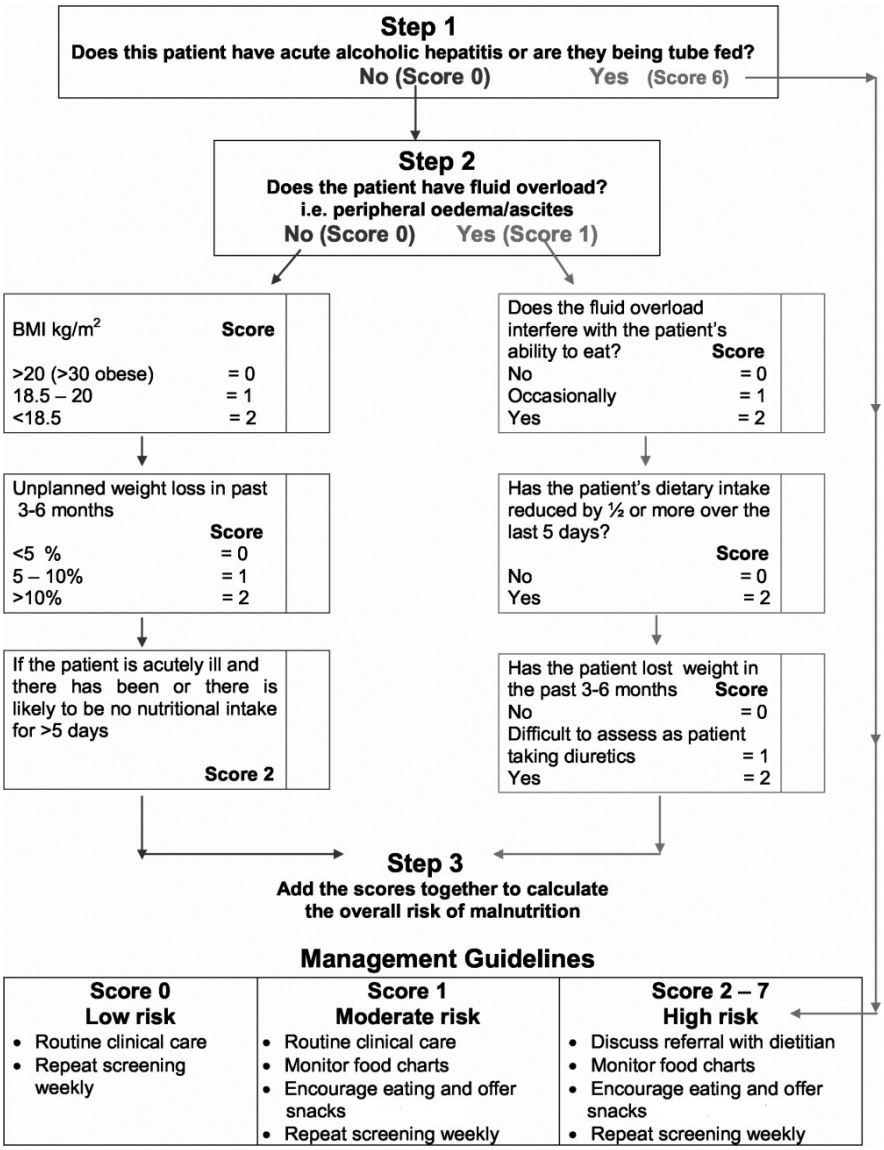

Figure 4. RFH-NPT screening flowchart for malnutrition risk in patients with cirrhosis. ([11])

In cases of fluid retention, body weight should be adjusted by estimating the patient's dry weight. This can be done using post-paracentesis weight, pre-fluid retention weight if available, or by subtracting a percentage of body weight according to the severity of ascites (5% for mild, 10% for moderate, and 15% for severe), with an additional 5% reduction if bilateral pedal edema is present. ([2])

A detailed assessment of dietary intake should be performed using either a three-day food diary completed by the patient or a 24-hour dietary recall. This evaluation should include daily caloric intake, protein quantity and quality, meal frequency and timing, fluid intake, supplements, and dietary sodium, as well as potential barriers to eating, such as nausea, vomiting, food aversions, taste changes, early satiety, gastrointestinal discomfort, and bowel

disturbances. Patients should also be asked whether their intake has changed, by how much, and over what period. ([2])

While the three-day food diary is the most accurate method, requiring minimal reliance on memory, it depends on patient cooperation and may be difficult to implement in advanced disease. The 24-hour recall is less burdensome, less likely to alter eating behaviour, and can be used across diverse populations, regardless of literacy. ([2])

2.2 **Sarcopenia and frailty**

2.2.1 **Definitions**

In patients with cirrhosis, sarcopenia is a major component of malnutrition. ([2]) Sarcopenia is defined as a progressive and generalized skeletal muscle depletion that involves a loss of muscle mass and strength function, and it is associated with increased adverse outcomes and mortality. ([12])

Frailty has most commonly been described as a clinical state of decreased physiologic reserve and increased vulnerability to health stressors, a definition that has its roots in the field of geriatrics. However, in patients with cirrhosis, existing evidence has primarily concentrated on a single component of frailty: physical frailty. Although this representation deviates somewhat from the classic "geriatric" definition of frailty as a global construct, physical frailty represents clinical manifestations of impaired muscle contractile function that are commonly reported by patients with cirrhosis such as decreased physical function, decreased functional performance, and disability. ([10])

2.2.2 **Prevalence and clinical impact of sarcopenia in cirrhosis**

The prevalence of sarcopenia and frailty in cirrhotic patients ranges from 40 to 70%, with a large variability depending on the population evaluated (sex, ethnicity, degree of liver failure), methods of assessment, and the definition of sarcopenia used. ([13])

A meta-analysis published in the *Journal of Hepatology* by X. Tantai et al. estimated the overall prevalence of sarcopenia in patients with advanced chronic liver disease (ACLD) at 37.5%, with higher rates observed in males, individuals with alcohol-related liver disease, and patients with more severe cirrhosis (28.3% in Child-Pugh A, 37.9% in Child-Pugh B, and 46.7% in Child-Pugh C). The same authors reported that sarcopenia is associated with an approximately two-fold higher risk of death in patients with cirrhosis and mortality rates at 1, 3, and 5 years of 23.4%, 35.7%, and 54.7%, respectively. ([14]) This elevated mortality risk is

linked to a higher incidence of falls, fractures, impaired quality of life, and the progression of liver-related complications. ([10])

In parallel, the presence of physical frailty is associated with an approximately 1.9-fold higher adjusted risk of waitlist mortality compared with non-frail patients. ([13])

2.2.3 **Pathophysiological mechanisms**

The development of sarcopenia in cirrhosis is driven by an imbalance between skeletal muscle protein synthesis and breakdown, leading to progressive muscle mass depletion. Hepatocellular dysfunction and portosystemic shunting further contribute by inducing biochemical and hormonal perturbations, including hyperammonemia, reduced testosterone and growth hormone levels, endotoxemia, and decreased dietary nutrient intake. In addition, alterations in amino acid metabolism - particularly reduced levels of the branched-chain amino acid L-leucine - impair global protein synthesis and exacerbate muscle wasting. ([2], [3])

Particularly during the decompensated phase, cirrhotic patients often exhibit reduced daily food intake: ascites can compress the stomach, leading to early satiety and decreased appetite, while hepatic encephalopathy may impair the ability to perform daily activities, including meal preparation and consumption. Additionally, to prevent fluid retention, edema, and ascites, patients are frequently advised to follow a low-sodium diet (<2 g/day), which is typically less palatable and may further reduce dietary intake, thereby promoting malnutrition and sarcopenia. Even in compensated stages, dysgeusia - likely due to combined zinc and vitamin A deficiencies - is common, often resulting in monotonous, nutritionally inadequate diets and an increased nutritional risk. ([2], [3])

2.2.4 **Sarcopenic obesity**

Obesity has been increasingly recognized as a factor contributing to frailty and sarcopenia in these patients, highlighting its growing significance amid the rising prevalence of obesity-related liver diseases. An obesogenic lifestyle - marked by physical inactivity and qualitative malnutrition, with excessive caloric intake but inadequate protein and micronutrients - predisposes these patients to sarcopenic obesity. This is a condition characterized by the coexistence of skeletal muscle loss and increased adiposity. defined as low sex-adjusted SMI and BMI $\geq$ 25 kg/m², and represents an independent risk factor for mortality in patients with cirrhosis. ([1],[7],[10])

The prevalence of sarcopenic obesity in cirrhosis ranges from 20% to 35%. This condition is highly prevalent among patients with MASH-related cirrhosis and is associated with a poorer prognosis, negatively affecting both morbidity and mortality. ([1],[7],[10])

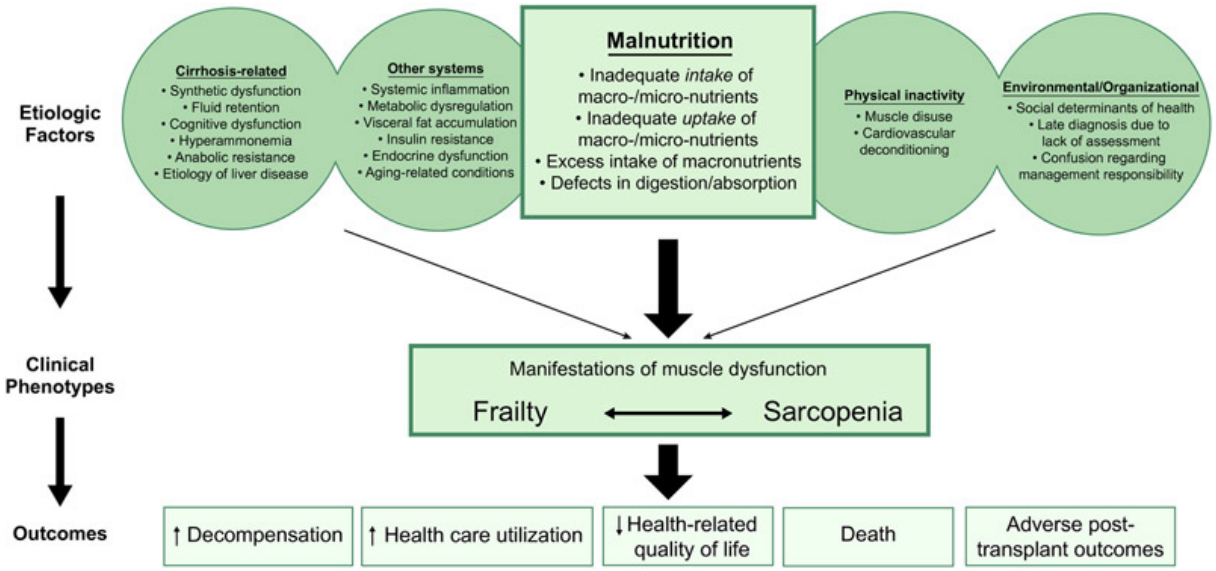

Figure 5. Overview of the key factors contributing to malnutrition, frailty, and sarcopenia, and their interconnections. ([10])

2.2.5 **Strategies to improve muscle mass**

To counteract the pathophysiological mechanisms of sarcopenia and improve muscle mass and function, nutritional strategies are recommended, including dietary modifications to ensure adequate energy and protein requirements. ([2])

Other therapeutic approaches currently under investigation include hormone replacement, antibiotics and gut microbiota manipulation, ammonia reduction, myostatin antagonists, nutritional supplementation such as branched-chain amino acids (BCAA) and L-carnitine supplements, and treatment of portal hypertension. ([2], [15])

At the same time, avoiding sedentary behavior and progressively increasing physical activity (preferably >150 minutes per week of moderate-intensity or 75 minutes per week of vigorous-intensity exercise) is strongly raccomended to prevent and/or ameliorate sarcopenia. A combined approach incorporating both resistance and endurance exercise is considered most effective, as aerobic training predominantly enhances functional capacity, whereas resistance training primarily supports increases in skeletal muscle mass. ([2], [7], [13], [10])

2.3 **Identification of sarcopenia and frailty in clinical practice**

The recognition of sarcopenia highlights the importance of a comprehensive nutritional assessment, incorporating malnutrition screening alongside a range of validated tests and tools currently available to identify sarcopenia and frailty. ([12])

Sarcopenia is considered probable when reduced muscle strength is detected, and the diagnosis is confirmed by evidence of low muscle quantity/quality. When low muscle strength, low muscle quantity/quality and low physical performance are all detected, sarcopenia is considered severe. ([12])

In clinical practice, case-finding may begin when a patient reports symptoms or signs of sarcopenia, such as recurrent falls, perceived weakness, slow walking speed, difficulty rising from a chair, or unintentional weight loss and muscle wasting. When these features are present, the European Working Group on Sarcopenia in Older People (EWGSOP2) recommends the use of the SARC-F, a 5-item questionnaire that is self-reported by patients as a screen for sarcopenia risk. Responses are based on the patient's perceived limitations in strength, walking ability, rising from a chair, stair climbing, and experiences with falls. ([12])

In its 2018 definition, the EWGSOP2 identifies low muscle strength as the principal parameter of sarcopenia, as it currently represents the most reliable indicator of muscle function and can be assessed through measurements of grip strength and chair stand performance. ([12]) Grip strength correlates moderately with muscle strength in other body regions, making it a reliable surrogate for more complex assessments of arm and leg strength. Accurate measurement of grip strength requires the use of a calibrated handheld dynamometer, which is simple and inexpensive. The Jamar dynamometer, a validated and widely used device, is commonly employed for this purpose. During the assessment, the patient is instructed to grip a dynamometer using the dominant hand with their best effort. ([10],[12]) The chair stand test (also called chair rise test) can be used as a proxy for strength of leg muscles (quadriceps muscle group). It measures the time required for a patient to rise from a seated position five times without using the arms. As the test involves both strength and endurance, it represents an indirect practical measure of muscle strength. ([12])

The evaluation of muscle using DXA and BIA methods is recommended to provide evidence confirming low muscle quantity or quality, although BIA may be preferred over DXA for the assessment of muscle mass because of its affordability and portability. BIA equipment does not measure muscle mass directly, but instead derives an estimate of muscle mass based on whole-body electrical conductivity. Muscle quantity or mass can be reported as total body

Skeletal Muscle Mass (SMM), as Appendicular Skeletal Muscle Mass (ASM), or as muscle cross-sectional area of specific muscle groups or body locations. ([12])

Physical performance has been defined as an objectively measured whole-body function related to locomotion. This is a multidimensional concept that not only involves muscles but also central and peripheral nervous function, including balance. Various tests, such as gait speed, the Short Physical Performance Battery (SPPB), and the Timed-Up and Go (TUG) test, can be employed to assess physical performance and determine the severity of sarcopenia. ([12])

A commonly used gait speed test is called the 4-m usual walking speed test. The SPPB is a composite test which includes assessment of gait speed, a balance test, and a chair stand test. The maximum score is 12 points, and a score of ≤ 8 points indicates poor physical performance. The TUG evaluates physical function. For the TUG test, individuals are asked to rise from a standard chair, walk to a marker 3 m away, turn around, walk back and sit down again ([12])

Considering both its practicality and its ability to predict sarcopenia-related outcomes, gait speed is recommended by EWGSOP2 as the primary measure for evaluating physical performance. ([12])

Test	Cut-off points for men	Cut-off points for women
EWGSOP2 sarcopenia cut-off points for low strength by chair stand and grip strength		
Grip strength	**<27 kg**	**<16 kg**
Chair stand	**>15 s for five rises**	
EWGSOP2 sarcopenia cut-off points for low muscle quantity		
ASM	**<20 kg**	**<15 kg**
ASM/height^2	**<7.0 kg/m^2**	**<5.5 kg/m^2**
EWGSOP2 sarcopenia cut-off points for low performance		
Gait speed	**≤0.8 m/s**	
SPPB	**≤8 point score**	
TUG	**≥20 s**	
400 m walk test	**Non-completion or ≥6 min for completion**	

Figura 6. EWGSOP2 sarcopenia cut-off points ([12])

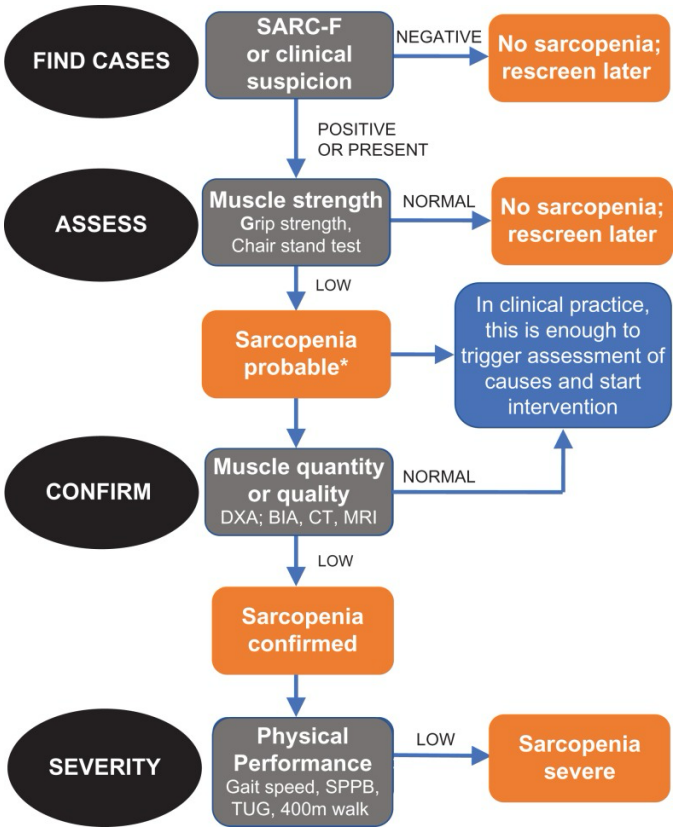

Figure 7. Sarcopenia: Find-Assess-Confirm-Severity (F-A-C-S). ([12])

2.3.1 **The role of Liver Frailty Index (LFI)**

Frailty overlap with sarcopenia; low grip strength and slow gait speed are characteristic of both. Weight loss, another diagnostic criterion for frailty, is also a major etiologic factor for sarcopenia. ([12])

Physical frailty can also be easily assessed both at baseline and longitudinally in the outpatient setting using the Liver Frailty Index (LFI), a cirrhosis-specific tool consisting of grip strength, chair stands, and balance testing. It establishes cut-points to classify patients as robust (LFI <3.2), prefrail (LFI 3.2–4.3), and frail (LFI ≥4.4). ([10])

Changes in Liver Frailty Index are associated with outcomes. ([10])

3. PREVENTION AND NUTRITIONAL INTERVENTION IN CHRONIC LIVER DISEASES

3.1 **Management and implementation of oral nutrition according to disease-specific requirements**

As cirrhosis progresses, a stage-dependent impairment of carbohydrate, protein, and lipid metabolism occurs. These alterations - characterized by hepatic glycogen depletion, impaired non-oxidative glucose metabolism, and reduced albumin synthesis - further contribute to the development of malnutrition and muscle wasting. This imbalance leads to an accelerated fasting state typical of cirrhosis, evidenced by a reduced respiratory quotient that reflects a shift from glucose to fatty acids as the predominant energy substrate. In this context, protein synthesis decreases, whereas gluconeogenesis from amino acids increases, driving proteolysis and thereby contributing to sarcopenia. Furthermore, these patients often develop complications such as insulin resistance and hepatogenic diabetes, which contribute to the progression of muscle wasting. ([2], [3], [15])

The multidisciplinary nutritional care process should provide guidance for achieving nutritional goals, which include optimizing metabolic profile, nutritional status, and quality of life through a personalized dietary approach. This should aim to meet energy and protein requirements, prevent or correct malnutrition and micronutrient deficiencies. Adequate nutritional education and counseling are essential to help patients understand the benefits of a healthy diet tailored to their clinical condition, sustain motivation for lifestyle changes, and improve adherence to dietary therapy. ([2], [3])

According to established nutritional guidelines, smaller, frequent meals with no more than a 3–4 hour gap between each meal are recommended to maintain a consistent meal schedule, minimize prolonged fasting periods and support total body protein stores. Therefore, daily food intake should be divided into three main meals, namely early breakfast, lunch, and dinner, while also including three snacks which may be consumed in the mid-morning, mid-afternoon, and late evening. ([3], [7], [10])

The late evening snack (LES) has been shown to help stabilize blood glucose levels, reducing sudden fluctuations in glucose and insulin and supporting overall metabolic homeostasis. Consequently, in patients with ACLD, a late-evening snack serves a dual role by preserving muscle mass and mitigating cirrhosis-related complications, including insulin resistance. Although current guidelines recommend an LES, they do not specify its optimal nutritional composition. ([2], [3], [15]) Recent reviews and meta-analyses, however, suggest that a late evening snack containing both complex carbohydrates and proteins may reduce lipid

oxidation and improve nutritional status, nitrogen balance, muscle mass, liver function, and overall quality of life in patients with cirrhosis. Most clinical studies report beneficial effects with LES composition providing at least 30 g of complex carbohydrates and approximately 13.5 g of protein, corresponding to an energy intake of around 200–250 kcal. No specific recommendations have been established for other nutrients. Due to the pathophysiology of ascites, a moderate sodium intake (about 60 mmol/day, equivalent to 1360 mg/day) is generally advised. ([15])

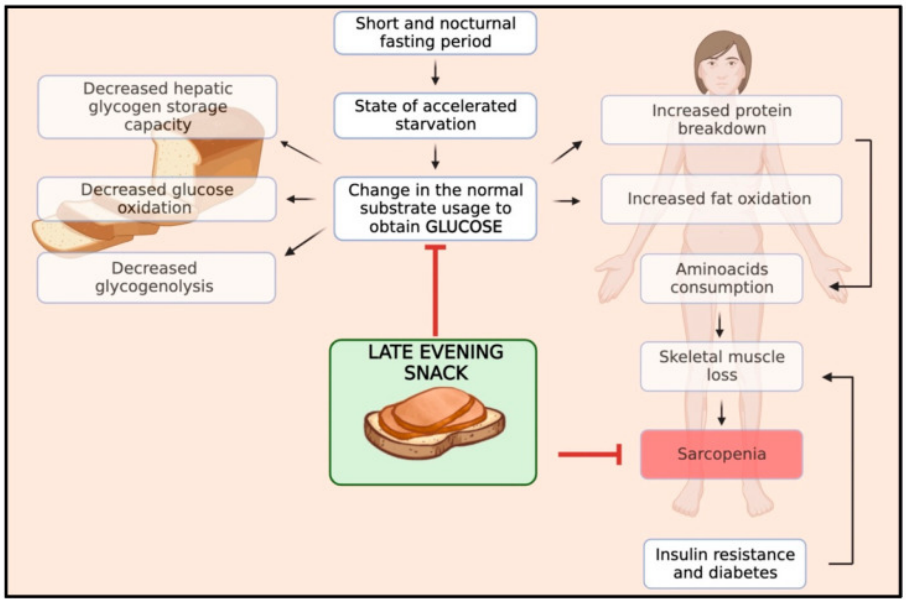

Figure 8. Impact of a late-evening snack (LES) on sarcopenia in cirrhosis ([15])

3.1.1 **Energy and protein requirements**

Energy intake should balance total energy expenditure (TEE). The energy requirements of compensed cirrhosis patients are not greater than those of healthy individuals (calculated as REE × 1.3). Accordingly, for non-obese patients, guidelines recommend an energy intake of 30–35 kcal/kg/day based on actual body weight, adjusted if ascites is present. ([2], [3], [7])

In the case of body mass index (BMI) >30 kg/m², weight-based energy intake recommendations may be modified to 25–35 kcal/kg/day for patients with BMI 30–40 kg/m² and 20–25 kcal/kg/day for those with BMI ≥ 40 kg/m², even if data are lacking. ([10])

A gradual weight reduction of ≥5–10% is considered an appropriate goal, as it is associated with a slower disease progression, including a reduction in portal hypertension. In these cases, dietary intake should ensure moderate caloric restriction through a tailored,

moderately hypocaloric diet (−500–800 kcal/day), while providing adequate protein intake to preserve muscle mass, given the potential risk of exacerbating sarcopenia. ([2], [3], [7])

The protein depletion characteristic of cirrhosis necessitates a higher protein intake compared with healthy individuals. Non-malnourished patients with compensated cirrhosis should consume 1.2 g/kg/day of protein, whereas malnourished and/or sarcopenic cirrhotic patients should aim for 1.5 g/kg/day to restore protein stores. This latter group is characterized by protein depletion due to both increased whole-body protein catabolism and reduced muscle protein synthesis; therefore, increasing protein intake enhances protein anabolism. In obese patients, protein requirements of 1.2–1.5 g/kg/day should be calculated based on ideal body weight. ([2], [3], [7])

For those with compensated ACLD, protein intake should come from a balanced combination of sources. This includes one-third of dairy protein (which contains casein), one-third of vegetable protein (which is rich in branched-chain amino acids), and one-third of animal protein (which is of high quality). Animal proteins are rich in aromatic amino acids not metabolised by skeletal muscle and may worsen HE if present. For patient who expresses a preference for different dietary habits, adjustments can be made to prioritise their overall daily protein intake rather than focusing exclusively on exact proportions. ([15])

Regarding the remaining macronutrient composition, adherence to a Mediterranean dietary pattern is recommended, given its proven benefits on body weight, insulin sensitivity, hepatic steatosis and fibrosis, even in the absence of weight reduction. ([3]) According to LARN 2024, in patients with cirrhosis, carbohydrates should constitute the basis of the diet, providing 45–60% of non-protein daily energy requirements, primarily from complex carbohydrate sources, while simple sugars should contribute less than 15% of total energy intake. ([16])
Compared with carbohydrate and protein metabolism, lipid metabolism appears to be less impaired in liver cirrhosis; ([1]) therefore, in the absence of specific contraindications, the distribution of lipid calories should follow the principles of the Mediterranean diet, providing approximately 20–35% of total energy, with the majority derived from unsaturated and polyunsaturated fats, and less than 10% from saturated fats. ([16])

3.2 **The nutritional impact of ultra-processed foods on liver cirrhosis**

The term “ultra-processed food” originates from the NOVA classification, a system that categorizes foods based on the degree of industrial processing rather than their nutrient composition. The NOVA classification currently distinguishes four groups of foods: group I,

unprocessed or minimally processed foods obtained directly from plants or animals; group II, unprocessed or minimally processed foods with the addition of salts, sugars, or oils for culinary purposes; group III, processed foods consisting of class I or class II foods that undergo further industrial manipulations; and group IV, ultra-processed foods. ([17],[18])

Ultra-processed foods (UPFs) are products made from ingredients that are mostly used in industry and result from multiple industrial processes. They consist of food substances often modified chemically and then assembled into ready-to-eat, hyper-palatable products. Flavours, colours, emulsifiers, and a variety of other additives are added to extend shelf life, preserve original properties, and prevent microbial growth. Common ingredients include sugars (such as fructose, high-fructose corn syrup, fruit juice concentrates, invert sugar, maltodextrin, and lactose), oils and fats (including hydrogenated or interesterified oils), salt, and protein sources (such as hydrolysed proteins, soy protein isolate, gluten, casein, whey protein, and mechanically separated meat). These ingredients are often combined in energy-dense products that have a poor nutritional composition (i.e., high sugar, unhealthy fats, salt, low dietary fibre, protein, vitamins and minerals). Therefore, these products cannot be considered "real food" at all. ([19])

There is growing evidence linking the overconsumption of ultra-processed foods to an increased risk of various disorders, including insulin resistance, type 2 diabetes, obesity, gut dysbiosis, and, more recently, MASLD. The hypothesis that excessive UPF intake contributes to MASLD pathogenesis has emerged from the parallel rise in both UPF consumption and MASLD prevalence. ([18])

The nutritional profile of UPFs promotes weight gain and increased adiposity, while their high content of refined carbohydrates contributes to postprandial hyperglycemia, which has been linked to hepatic fat accumulation. ([18])

Excess adipose tissue leads to increased lipolysis and elevated circulating free fatty acids (FFAs), which are transported to the liver and esterified into triglycerides (TGs). Consequently, hepatocellular TG overload induces oxidative and endoplasmic reticulum stress, both of which activate inflammatory pathways. Additional pro-inflammatory stimuli may arise from endocrine-disrupting chemicals (EDCs) and advanced glycation end products (AGEs) present in UPFs. Moreover, emulsifiers, together with EDCs and AGEs, can impair gut barrier integrity, leading to the development of a "leaky gut". This condition facilitates the translocation of lipopolysaccharides (LPS) into the systemic circulation and, consequently, to the liver. These combined mechanisms highlight the gut–liver axis as a major determinant in MASLD pathogenesis and may drive its progression to metabolic dysfunction-associated steatohepatitis (MASH). ([18])

A recent cross-sectional study published in *Clinical Nutrition ESPEN* also reported that higher UPF intake was significantly associated with increased odds of hepatic steatosis, with a clear dose–response relationship, while no significant association was observed with fibrosis. ([20])

Reducing UPF consumption is therefore recommended not only to lower the risk of MASLD but also as a nutritional strategy for patients to slow or reverse progression to MASH and liver fibrosis/cirrhosis. In contrast, adherence to a Mediterranean diet, naturally low in UPFs, has been suggested to mitigate the progression of MASLD to MASH and prevent further liver damage. ([18])

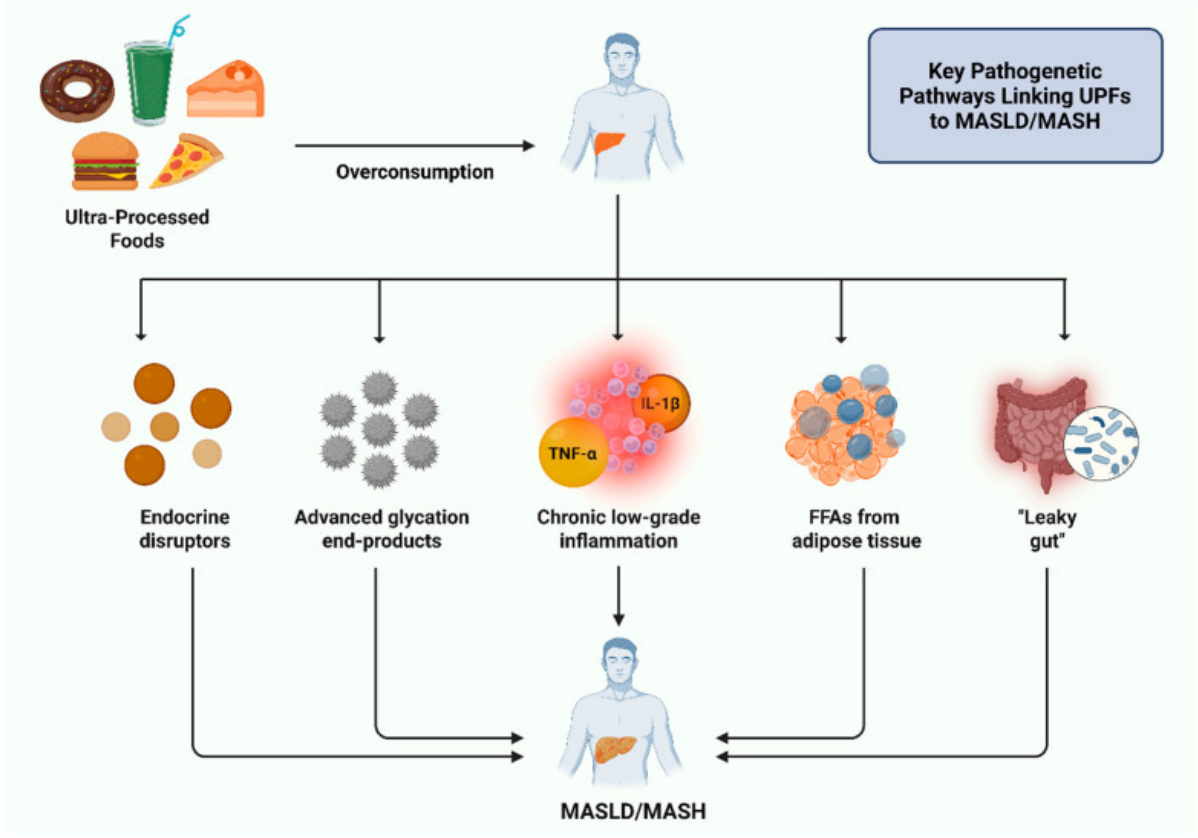

Figure 9. Pathophysiological mechanisms linking UPFs to MASLD/MASH ([18])

3.3 **Hepatic Encephalopathy and the role of nutrition**

Hepatic encephalopathy (HE) is defined as a spectrum of potentially reversible neuropsychiatric abnormalities resulting from hepatic dysfunction, portosystemic shunting, or both, ranging from covert (grades 0 and 1) to overt (grades 2, 3, and 4) forms, and profoundly affects the quality of life of patients and their caregivers. ([4])

Covert hepatic encephalopathy consists of subclinical alterations that cannot be detected through routine physical examination but can be identified using neuropsychological or electrophysiological tests. In 2017, the Animal Naming Test (ANT) was introduced as a simple and rapid screening tool to evaluate cognitive dysfunction (particularly executive function) during the early stages of hepatic encephalopathy. In this semantic fluency test, patients are asked to name as many animals as possible in 60 seconds. Identifying less than ten animals correctly suggests a high probability of covert hepatic encephalopathy. ([4])

Overt manifestations of hepatic encephalopathy develop in 30–45% of patients with cirrhosis and range in severity from mild cognitive impairment to coma (grade 4) ([4]).

Nitrogen metabolism plays a central role in the pathogenesis of hepatic encephalopathy in patients with cirrhosis. ([11]) HE occurs more frequently in malnourished individuals, and an inverse correlation exists between muscle mass and blood ammonia levels. The use of amino acids for gluconeogenesis leads to depletion of tissue protein stores and increased ammonia production. Consequently, appropriate timing of caloric intake is essential to optimize substrate utilization and limit unnecessary gluconeogenesis required to sustain splanchnic glucose output. ([2],[11]) Prolonged fasting should be avoided, and patients should be encouraged to consume small, frequent meals to ensure adequate dietary intake. ([2])

Energy and protein requirements in patients with cirrhosis and HE are considered comparable to those of patients with cirrhosis without HE. Protein restriction provides no benefit in the clinical course of acute hepatic encephalopathy and may increase protein catabolism. ([2],[3])

Current guidelines encourage the consumption of vegetable and dairy proteins, as human studies have shown that dairy protein is better tolerated than mixed protein sources and that vegetable protein is better tolerated than meat protein. ([2],[3],[10])

A recent randomized clinical trial demonstrated that nutritional intervention (30–35 kcal/kg BW/day and 1.0–1.5 g vegetable protein/kg BW/day for six months) improved neuropsychiatric performance in patients with minimal HE and reduced the risk of progression to overt HE compared with no nutritional support. ([21])

The beneficial effects of vegetable protein diets may be partly attributed to their higher fiber content, which exerts prebiotic and laxative effects leading to reduced transit time, lower intraluminal pH, and increased fecal ammonia elimination. ([2],[11])

BCAA supplementation, administered in divided daily doses of 0.25 g/kg/day, can help achieve adequate nitrogen intake in patients intolerant to meat protein. Replacing meat with dairy or vegetable protein combined with BCAA supplementation is preferable to reducing total

protein intake. Long-term oral BCAA supplementation in cirrhotic patients improves neuropsychiatric performance and nutritional status, and has been associated with increased event-free and overall survival; however, poor palatability continues to limit its use. ([2], [3])

Small studies suggest that L-carnitine, alone or with BCAAs, may lower ammonia levels and improve muscle mass in cirrhotic patients, but evidence is still insufficient to recommend its regular use in clinical practice. ([10])

3.4 **Micronutrients deficiencies and oral supplementation**

In patients with cirrhosis, micronutrient deficiencies should be assessed at least annually, corrected when present, and reassessed after repletion, targeting only confirmed or clinically suspected deficiencies. ([3], [10])

In chronic liver disease, fat- and water-soluble vitamin deficiencies are common and generally result from hepatic dysfunction, reduced reserves, and as the disease progresses, poor dietary intake and malabsorption. ([2])

In ACLD, low levels of vitamins D, E, and K frequently occur due to multiple factors, including vitamins sequestration in adipose tissue in patients with coexisting obesity. ([1])

In patients with cirrhosis, the prevalence of vitamin D deficiency has been reported to range from 64 to 92% and increases with disease progression. ([22], [23])

Vitamin D deficiency is generally defined as a serum 25(OH)D concentration below 50 nmol/L (20 ng/mL), while levels between 50 and 75 nmol/L (20–30 ng/mL) indicate insufficiency. Optimal status is considered between 75 and 125 nmol/L (30–50 ng/mL) ([22]).

According to EASL and ESPEN guidelines, vitamin D supplementation in patients with liver disease is indicated only for the correction of deficiency, with no proven benefits beyond those observed in the general population. Specifically, EASL recommends supplementing all patients with chronic liver disease who have serum vitamin D levels below 20 ng/mL with oral vitamin D until concentrations exceed 30 ng/mL. No specific dosage is established, although daily intakes of 800–2000 IU are the most commonly used. ([1],[2], [3])

Dietary intake contributes only marginally to overall vitamin D status. With the exception of fatty fish (such as herring, salmon, tuna) and cod liver oil, the natural vitamin D content of most foods is minimal, unless they are fortified, as in the case of milk. ([22], [24])

Patients with both alcohol-related and non-alcohol-related cirrhosis are prone to deficiencies in water-soluble vitamins, especially thiamine (B1). Severe thiamine deficiency can compromise cardiovascular, nervous, and immune function, potentially causing life-threatening conditions such as beriberi and Wernicke–Korsakoff encephalopathy, which require

urgent parenteral administration of high doses of thiamine. ([1],[2]) Deficiencies of pyridoxine (B6), folate (B9), and cobalamin (B12) may also occur rapidly due to reduced hepatic stores, though data on prevalence and/or need for supplementation are limited. Considering the difficulty in assessing vitamin status and the safety and low cost of multivitamins, a course of oral multivitamin supplementation may be justified in decompensated patients. ([2])

Regarding minerals, in cirrhotic patients with ascites who are on a sodium-restricted diet (recommended daily intake of 2 g of sodium corresponding to 5 g of added salt daily, according to EASL guidelines), it is important to focus on improving the palatability of the diet, as such restrictions may lead to reduced overall energy and protein intake. ([2])

Circulating levels of calcium, magnesium, and iron should be monitored and corrected if reduced in cirrhotic patients. Zinc deficiency, reflected by reduced tissue concentrations, has been implicated in the pathogenesis of hepatic encephalopathy. While evidence on its effect on mental performance is contrasting, zinc supplementation has been associated with improvements in dysgeusia and muscle cramps, particularly when combined with vitamin A. By enhancing taste perception, supplementation may indirectly support food intake and nutritional status. In general, zinc should be administered until serum levels normalize, at a dose of 50 mg of elemental zinc (229 mg zinc sulphate) once daily. ([1],[2],[3])

3.5 **Medical nutrition therapy**

In critically ill cirrhotic patients, ensuring adequate nutritional support is essential. Indications for artificial nutrition follow the same principles as in non-cirrhotic patients. Nutritional interventions (oral, enteral, or parenteral) should be implemented according to current guidelines for non-cirrhotic patients, as this is crucial to provide metabolic substrates and support protein anabolism. ([2],[3])

In patients who are unable to meet nutritional targets orally, either through diet alone or combined with oral nutritional supplements (ONS), enteral nutrition should be administered. ([3]) Parenteral nutrition is reserved for cases where oral and/or enteral feeding are ineffective or not feasible. ([3])

4. **EXPERIMENTAL STUDY**

4.1 **Aims of the study**

The aim of the present study was to comprehensively assess the nutritional status of a cohort of patients with chronic liver disease related to Metabolic Dysfunction–Associated Steatotic Liver Disease (MASLD) complicated by liver fibrosis, and to investigate its relationship with the severity of liver fibrosis and cirrhosis (advanced chronic liver disease; ACLD). To this end, several nutrition-related parameters were evaluated, including body composition, energy and nutrient intake, and eating behavior patterns. Particular attention was devoted to both the quantitative and qualitative characterization of dietary habits, with a specific focus on the contribution of ultra-processed foods (UPFs), in order to explore potential associations between UPF-rich diets and fibrosis progression.

Nutritional status was further monitored longitudinally through follow-up assessments, enabling the evaluation of changes following nutritional intervention and their consistency with current clinical guidelines and reference standards for chronic liver disease.

4.2 **Materials and methods**

4.2.1 **Cohort**

The study was conducted on a cohort of outpatients diagnosed with Metabolic Dysfunction–Associated Steatotic Liver Disease (MASLD) complicated by liver fibrosis, who were followed at the “Steatosis Outpatient Clinic” of the Unit of Internal Medicine, Hepatobiliary and Immunoallergologic Diseases (Director: Prof. F. Piscaglia), IRCCS Azienda Ospedaliero-Universitaria di Bologna, S. Orsola Hospital.

All patients were consecutively enrolled between June 2024 and October 2025. The diagnosis of MASLD and the stage of liver fibrosis were established according to the European Association for the Study of the Liver (EASL) Clinical Practice Guidelines, based on clinical, biochemical, and imaging criteria.

Inclusion criteria were: (1) a confirmed diagnosis of hepatic steatosis; (2) the presence of significant liver fibrosis ($F \geq 2$); (3) willingness to participate in a nutritional intervention program; and (4) non-eligibility for concurrent experimental protocols, including pharmacological trials or very-low-calorie ketogenic diet (VLCKD) interventions.

4.2.2 **Liver fibrosis and steatosis assessment by Vibration-Controlled Transient Elastography**

At baseline, all patients underwent liver stiffness and steatosis assessment using vibration-controlled transient elastography (VCTE) (FibroScan®, Echosens, Paris, France), a non-invasive, ultrasound-based technique that allows the quantitative evaluation of both hepatic fibrosis and fat accumulation.

The Liver Stiffness Measurement (LSM), expressed in kilopascals (kPa), was used to estimate and stratify the degree of liver fibrosis. Increasing LSM values are indicative of progressive fibrotic remodeling and have been validated as reliable surrogate markers for the histological stage of fibrosis and the presence of advanced chronic liver disease (ACLD). LSM thus enabled the identification and staging of fibrosis across the cohort, ranging from significant (F2) to advanced (F4) disease.

The Controlled Attenuation Parameter (CAP), expressed in decibels per meter (dB/m), was employed to quantify hepatic steatosis. CAP values correlate with the extent of lipid accumulation in hepatocytes, providing a reproducible and operator-independent measure of liver fat content. This parameter allows differentiation between absent, mild, moderate, and severe steatosis, and is particularly useful in patients with Metabolic Dysfunction–Associated Steatotic Liver Disease (MASLD), in whom hepatic fat deposition frequently coexists with fibrotic progression.

In addition, Spleen Stiffness Measurement (SSM) values were also recorded in all patients to provide complementary information on portal hypertension and the degree of hemodynamic involvement.

4.2.3 **Biochemical assessment of metabolic and liver function parameters**

At enrolment, a comprehensive biochemical evaluation was performed to assess parameters of particular nutritional and metabolic relevance. The glucidic and lipid profiles were analyzed, including plasma glucose, total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides. These markers provide an overview of metabolic homeostasis and are essential for characterizing the metabolic dysfunctions commonly associated with MASLD.

In addition, liver function tests were conducted to evaluate hepatocellular integrity, cholestatic involvement, and synthetic capacity. The enzymatic profile included aspartate aminotransferase (AST/GOT), alanine aminotransferase (ALT/GPT), gamma-glutamyl transferase (GGT), and alkaline phosphatase (ALP). Serum albumin and total bilirubin

concentrations were also measured as indicators of hepatic synthetic function and excretory efficiency, respectively.

The combined assessment of these biochemical markers provided a detailed picture of both the metabolic and hepatic status of each participant at baseline, facilitating the interpretation of nutritional findings in the broader context of liver disease severity and progression.

4.2.4 **Anthropometric measurements, muscle function, and frailty assessment**

At the first visit (baseline evaluation), comprehensive anthropometric data were collected, including body weight and height (for body mass index, BMI, calculation), changes in body weight over time, detailed dietary history, and habitual physical activity levels. Additional anthropometric parameters included selected body circumferences—waist, hip, neck, arm, and thigh—which served as indirect indicators of body fat distribution and muscle mass. Together, these measurements provided a direct overview of the participants' nutritional status and body composition.

Body weight was measured using a calibrated electronic scale (Seca 877, Seca GmbH & Co. KG, Hamburg, Germany), with participants wearing light underwear and no shoes. Height was measured with a wall-mounted stadiometer (Seca 217, Seca GmbH & Co. KG, Hamburg, Germany), while participants stood barefoot, upright, and with heels together. Body circumferences (waist, hip, neck, arm, and thigh) were measured using a non-stretchable, retractable measuring tape, following standardized anthropometric procedures to ensure measurement accuracy, consistency, and reproducibility.

In patients with cirrhosis, and in accordance with EASL/ESPEN Clinical Practice Guidelines [ref], muscle strength—a key component in the diagnosis of sarcopenia and frailty—was assessed using a handgrip dynamometer (DynX®, Akern, Italy). Muscle function and frailty status were further evaluated through the Liver Frailty Index (LFI) to provide complementary insights into physical performance and sarcopenia-related risk, thus broadening the overall assessment of functional status in advanced chronic liver disease.

Regarding the handgrip strength assessment, patients were instructed to perform the test while seated, holding the dynamometer with their dominant hand and exerting maximum effort while maintaining the elbow flexed at a 90° angle. Prior to measurement, the operator demonstrated the correct positioning and grip technique, emphasizing that a firm and complete grasp would yield the highest score. The hand was positioned so that the thumb encircled one side of the handle and the four fingers the other. Each participant performed three maximal

contractions, with a one-minute rest interval between attempts to minimize fatigue bias. The mean value of the three trials was used for subsequent analyses [27]. Handgrip strength values were compared with sex- and age-specific percentile reference data (5th–95th) available in the literature [28]

The Liver Frailty Index (LFI) was calculated using the online tool developed by the University of California, San Francisco [29,30]. The score was derived by entering the patient's sex, the three handgrip strength measurements, the time required to complete five chair stands, and the cumulative time (in seconds) spent maintaining balance in three positions (side, semi-tandem, and tandem). This multidimensional approach provided an integrated assessment of both muscle strength and functional performance in patients with cirrhosis.

These anthropometric and body composition assessments were conducted in all patients at both the first (baseline) visit and during follow-up evaluations, allowing the monitoring of changes over time in relation to the nutritional intervention and disease progression.

4.2.5 **Body composition assessment by Bioelectrical Impedance Analysis (BIA)**

Body composition was assessed using a portable bioelectrical impedance analyzer (BIA; Akern, Florence, Italy). The device measures resistance (Rz), reactance (Xc), impedance (Z), and phase angle (PhA) by applying a 50 kHz alternating current of 800 μA. These parameters enable the evaluation of intracellular and extracellular water distribution, providing insight into hydration status, cellular integrity, and nutritional condition.

For the procedure, participants were positioned supine on a non-metallic examination bed, ensuring that no part of the body was in contact with metal surfaces. The upper and lower limbs were slightly abducted to prevent skin contact. Four electrodes were placed on the right side of the body—two on the hand and two on the foot—on previously cleansed skin, maintaining a minimum distance of 5 cm between them. Electrodes were then connected to the corresponding tetrapolar cables of the analyser.

Quantitative body composition parameters were derived using predictive equations from the BODYGRAM® software (Akern, Italy). The analysis provided estimates of fat mass (FM), fat-free mass (FFM), skeletal muscle mass (SM), body cell mass (BCM), total body water (TBW), and extracellular water (ECW), along with several nutritional indices—including the Fat Mass Index (FMI), Fat-Free Mass Index (FFMI), Skeletal Muscle Index (SMI), Appendicular Skeletal Muscle Mass (ASMM), and Specific Phase Angle (SPA°).

The software also generated a Biavector® nomogram, allowing graphical visualization of each subject's hydration and nutritional status in comparison with a healthy reference population.

The proportions of %FFM and %FM were compared with literature-based reference values (80–85% FFM and 15–20% FM of body weight) to evaluate changes in body composition over time relative to baseline [24]. Reference ranges for phase angle (typically 5–7°) were also derived from published studies [31], serving as an indicator of cellular health and nutritional adequacy.

4.2.6 **Qualitative and quantitative dietary analysis and Ultra-Processed Food (UPF) evaluation**

The average daily dietary intake was calculated based on a 7-day food diary that patients were instructed to complete prior to their first nutritional visit. Participants were asked to record all foods and beverages consumed over seven consecutive days, specifying both the type of food and the portion size, as well as cooking methods and condiments used. Clear written and verbal instructions were provided by trained dietitians to ensure consistency and accuracy in data collection. Patients were encouraged to report food quantities as precisely as possible, including snacks and out-of-home meals, and to specify brands or product names when relevant.

Once returned to the clinical staff, the completed diaries were reviewed for completeness and accuracy together with each patient, and subsequently analysed using the dedicated software (Handydiet®, Milan, Italy). This validated digital tool facilitates the quantitative and qualitative analysis of nutrient intake and energy distribution. Unlike conventional software that relies exclusively on gram-based entries, Handydiet® integrates volume-based and anthropometric portion estimates, improving accuracy and patient compliance. The software enables food portions to be expressed not only in grams but also through reference volumes, using either anthropometric measures (hand, fist, palm, or finger) or common household units (cup, glass, spoon, or bowl). This flexible approach allows better translation of real-world eating behaviour into quantifiable data. To personalize the anthropometric references, each patient's hand was traced on paper during the initial assessment and classified into one of four categories - Small, Medium, Large, or Extra-Large - based on predefined Handydiet® criteria. This individualized calibration ensures greater accuracy in portion-size estimation and minimizes bias due to inter-individual variability in hand size [32].

The Handydiet® software automatically calculates energy intake and the distribution of macronutrients and micronutrients, using an integrated food composition database aligned with national and international standards. Data were then exported for further statistical analysis and comparison with disease-specific nutritional recommendations.

Specifically, energy intake, proteins, carbohydrates, soluble sugars, lipids, saturated fatty acids, and fiber were analyzed and compared with disease-specific reference values. Energy requirements were estimated using the Mifflin–St Jeor equation, considering ideal body weight (corresponding to a BMI of 25 kg/m²), as recommended for obese individuals. Protein requirements were calculated based on ideal body weight and multiplied by 1.2–1.5 g/kg/day, according to EASL (2019) and ESPEN (2019) guidelines. Recommendations from the LARN 2024 served as reference values for the intake of other macronutrients [24].

The qualitative dietary analysis focused on the identification and quantification of ultra-processed foods (UPFs), classified according to the NOVA system, which stratifies foods into four categories based on the degree and purpose of industrial processing. The classification process was carried out through a detailed review of the 7-day food diaries and the Food Frequency Questionnaire (FFQ) completed by each participant.

When product labels or packaging information were insufficient to determine the appropriate NOVA category, the Open Food Facts database (*https://world.openfoodfacts.org/*) was consulted as a complementary reference source. Open Food Facts is a freely accessible, collaborative, and continuously updated open database that provides standardized information on ingredient composition, level of processing, and nutritional labeling of commercial food products. The use of this database ensured greater objectivity and reproducibility in the classification of food items, particularly for branded or packaged products for which limited compositional details were available.

At the first (baseline) visit, patients completed a UPF Food Frequency Questionnaire (UPF-FFQ) (**Appendix 1**) specifically focused on UPF consumption. This questionnaire was developed by the Global MASH Council (GMC, https://www.globalnashcouncil.org/) and is currently undergoing evaluation and validation as a standardized tool for assessing UPF-FFQ exposure in populations with MASLD and related metabolic disorders. The UPF-FFQ included food items representative of NOVA groups 1–3 (unprocessed or minimally processed foods, culinary ingredients, and processed foods such as fruits, vegetables, grains, legumes, fish, olive oil, and dairy products) and NOVA group 4 (UPFs, including industrially processed packaged snacks, sweetened beverages, desserts, and ready-to-eat meals). Reported consumption frequencies were used to compute a UPF intake score, obtained by summing the frequency of

intake of all NOVA group 4 items, with proportional weighting assigned to each frequency category (*never = 0; 1–2 times/week = 1; 3–4 times/week = 2; ≥1 time/day = 3*). The resulting total UPF score allowed intra-cohort stratification according to the degree of UPF exposure (low, moderate, or high consumption).

In parallel, data from the 7-day food diaries were analyzed to determine the quantitative intake of UPFs, the total caloric intake derived exclusively from UPFs, and the percentage of total daily energy intake attributable to these foods. Additional indicators were computed, including the weekly number of UPFs consumed, the number of UPF-free days, and the number of days including ≥1, ≥3, or ≥5 UPFs.

This integrated approach, combining the UPF-FFQ and quantitative diary analysis, provided a comprehensive and multidimensional characterization of both the frequency and intensity of UPF exposure across the study cohort.

4.2.7 **Nutritional intervention**

Nutritional plans were individualized according to each patient's habitual eating patterns and preferences, with the objective of aligning their diet with the principles of the Mediterranean dietary pattern and the recommendations outlined in the EASL and AISF Clinical Practice Guidelines for the management of metabolic dysfunction–associated steatotic liver disease.

The dietary intervention was formulated and tailored using the Handydiet® software (Milan, Italy), which enabled clinicians to design precise, personalized meal plans based on both the quantitative and qualitative analyses of each patient's 7-day food diary. The patients' individual food preferences, which formed the foundation of each dietary plan, were derived directly from these food diaries.

The software facilitated the calculation of individual energy and macronutrient targets, translating nutritional goals into practical, patient-specific portions expressed in grams or through anthropometric and household reference units (hand, fist, palm, or cup). This approach ensured that the prescribed diet was both nutritionally adequate and realistic for long-term adherence.

Each nutritional plan was developed collaboratively with the patient during counseling sessions, allowing real-time adjustments to enhance acceptability, adherence, and self-efficacy. Participants also received personalized nutritional education and motivational support, aimed at reinforcing adherence to the Mediterranean diet and promoting sustainable dietary and lifestyle changes over time.

4.2.8 **Statistical analysis**

All statistical analyses were performed using Stata 19 SE (StataCorp LLC, College Station, TX, USA). Descriptive statistics were reported as mean ± standard deviation (SD) or median and interquartile range (IQR) for continuous variables, depending on data distribution, and as counts and percentages for categorical variables. The Shapiro–Wilk test was applied to assess normality.

Comparisons between groups were conducted using parametric tests (Student's t-test or ANOVA) for normally distributed variables, and non-parametric tests (Mann–Whitney U or Kruskal–Wallis) for skewed variables. Categorical variables were compared using the Chi-square or Fisher's exact test, as appropriate. Correlations were examined using Pearson's or Spearman's coefficients according to data distribution.

Boxplots were generated to visually explore the distribution of key nutritional and biochemical variables across fibrosis stages and between subgroups. Reclassification analyses were also performed to assess changes in nutritional status and fibrosis category over time, particularly in response to dietary intervention.

Receiver operating characteristic (ROC) curve analysis was carried out to evaluate the discriminative ability of the percentage of total caloric intake derived from ultra-processed foods (UPFs) in identifying cirrhosis (F4) versus non-cirrhotic fibrosis (F2–F3). The area under the curve (AUC) and 95% confidence interval (CI) were calculated to assess model performance. The optimal cut-off was determined using the Youden index. In addition, rule-out and rule-in thresholds were explored to improve clinical interpretability, prioritizing high sensitivity and high specificity, respectively.

A p-value < 0.05 was considered statistically significant for all tests.

4.2.9 **Ethical considerations**

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and approved by the Ethics Committee of the IRCCS Azienda Ospedaliero-Universitaria di Bologna (study title: BOMASH; Internal Code: 252/2024/Sper/AOUBo_PI Piscaglia). All participants provided written informed consent prior to enrolment.

4.3 **Results**

4.3.1 **Patient characteristics**

A total of 41 patients with MASLD meeting the inclusion criteria were enrolled and analysed. Following the nutritional intervention, the median follow-up period was 4 months (IQR, 4–8), allowing for the longitudinal monitoring of nutritional and anthropometric changes over time in response to the dietary program.

Table 1 summarizes the main demographic and clinical characteristics of the study cohort. The majority of patients (93%) were of Caucasian ethnicity. The median age of the cohort was 63 years (IQR, 55–69) and females accounted for 56% of participants, while males represented 44%. Patients were stratified according to the degree of liver fibrosis: 24% presented F2 fibrosis, 44% had F3, and 32% showed F4, corresponding to a diagnosis of cirrhosis.

Regarding comorbidities, 75% of patients had arterial hypertension, 70% had dyslipidemia, and 64% had a diagnosis of type 2 diabetes mellitus. At baseline, 78% of participants met the criteria for obesity, while none presented clinical signs of hepatic encephalopathy or ascites.

Variable	All (n=41)	F2 (24%)	F3 (44%)	F4 (32%)
Demographic				
Age; years, median (Q1-Q3)	62.5 (55-69.3)	69 (66-69.5)	60.5 (52-69.5)	65 (60.5-71)
Male n (%)	18 (43.9%)	3 (75%)	6 (31.6%)	7 (53.8%)
Female n (%)	23 (56.1%)	1 (25%)	13 (68.4%)	6 (46.2%)
Race, white (causasian) n (%)	38 (92.7%)	4 (100%)	16 (84.2%)	13 (100%)
Past medical history				
Family history of type 2 diabetes mellitus n (%)	16 (40%)	3 (75%)	6 (31.6%)	5 (41.7%)
Family history of obesity n (%)	12 (30%)	0 (0%)	5 (26.3%)	4 (33.3%)
Family history of liver diseases n (%)	14 (35%)	1 (25%)	4 (21.1%)	7 (58.3%)
Family history of HCC n (%)	1 (2,5%)	0 (0%)	0 (0%)	1 (8.3%)
Family history of heart attack n (%)	5 (12.8%)	1 (25%)	4 (21.1%)	0 (0%)
Family history of stroke n (%)	4 (10.3%)	0 (0%)	3 (15.8%)	1 (8.3%)
Family history of neoplasms n (%)	13 (33.3%)	3 (75%)	9 (47.4%)	1 (8.3%)
Glucose metabolism alteration n (%)	28 (70%)	4 (100%)	12 (63.2%)	9 (75%)
Obesity n (%)	32 (78%)			
Type 2 diabetes mellitus n (%)	18 (64.3%)	3 (75%)	8 (66.7%)	6 (66.7%)
Arterial hypertension n (%)	30 (75%)	4 (100%)	15 (78.9%)	8 (66.7%)
Dyslipidaemia n (%)	28 (70%)	4 (100%)	16 (84.2%)	4 (33.3%)
Hypothyroidism n (%)	11 (27.5%)	1 (25%)	7 (36.8%)	2 (16.7%)
Obstructive sleep apnea syndrome n (%)	3 (7.5%)	1 (25%)	1 (5.3%)	0 (0%)
Polycystic ovary syndrome n (%)	2 (10%)	0 (0%)	2 (16.7%)	0 (0%)
Depression n (%)	3 (7.5%)	1 (25%)	0 (0%)	1 (8.3%)
Osteoporosis/Osteopenia n (%)	3 (7.5%)	0 (0%)	1 (5.3%)	1 (8.3%)
Gallstones n (%)	10 (25%)	0 (0%)	6 (31.6%)	4 (33.3%)
Chronic kidney disease n (%)	2 (5%)	0 (0%)	0 (0%)	2 (16.7%)
Cardiovascular diseases n (%)	9 (22.5 %)	2 (50%)	3 (15.8%)	3 (25%)
Atrial fibrillation n (%)	3 (7.5%)	0 (0%)	0 (0%)	1 (8.3%)

Table 1. Baseline population characteristics

Blood glucose levels indicated the presence of glucidic alterations in the majority of the study population, with values increasing in parallel with the severity of fibrosis (median 132.5 mg/dL, IQR 116.8–157.0 mg/dL in patients with F4 stage fibrosis). In contrast, lipid profile parameters generally remained within the normal range, although a slight increase in triglycerides was observed among patients with F2 fibrosis.

Furthermore, as liver fibrosis advanced, a progressive and significant reduction in serum albumin level platelets count were noted, reflecting the reduction of hepatic synthetic function and presence of portal hypertension associated with disease progression (**Table 2**).

Biochemical exams	**All** (n=41)	**F2 (24%)**	**F3 (44%)**	**F4 (32%)**
White blood cells; ×10⁹/L, median (Q1-Q3)	6.8 (5.2-7.8)	6.8 (6.7-9)	6.8 (5.5-7.5)	5.3 (3.1-6.9)
Hb; g/dL, median (Q1-Q3)	14.3 (13.5-15)	14.4 (14.3-15.5)	14.5 (13.5-15.4)	14.2 (12.8-14.4)
Platelets; ×10⁹/L, median (Q1-Q3)	203 (130.5-259)	259 (234.5-298)	205 (155-259)	106 (46-161)
INR; median (Q1–Q3)	1 (1-1.1)	1 (1-1)	0.9 (0.9-1)	1.1 (1.1-1.2)
Glucose; mg/dL, median (Q1-Q3)	125 (96-132)	118.5 (104.3-130.5)	119 (91.8-129)	132.5 (116.8-157)
HbA1c; mmol/mol, median (Q1-Q3)	42 (37-48)	45.5 (42.5-48.8)	42 (38-46.5)	34.5 (26.9-39.8)
Total cholesterol; mg/dL, median (Q1-Q3)	162 (161-183.5)	161.5 (158.5-163.8)	162 (161-230)	161.5 (161-162)
HDL cholesterol; mg/dL, median (Q1-Q3)	46 (43-53)	40.5 (37.3-44.8)	47 (43-66)	43 (43-52)
LDL cholesterol; mg/dL, median (Q1-Q3)	90 (90-122)	90 (83.4-95.2)	90 (90-145)	90 (87-90)
Triglycerides; mg/dL, median (Q1-Q3)	120 (95-158)	176 (172-206.5)	105 (95-138)	102.5 (67-186.5)
Serum uric acid; mg/dL, median (Q1-Q3)	6.5 (5.4-30)	5.8 (5.6-6)	6.3 (5.6-7.6)	126 (23.7-284)
AST/GOT; U/L, median (Q1-Q3)	31 (22-38.5)	23.5 (20.3-26)	31.5 (22-38.5)	32 (21-40)
ALT/GPT; U/L, median (Q1-Q3)	26 (22-41)	23.5 (23-27.8)	26 (23-44.5)	25 (18-40)
AST/ALT Ratio, median (Q1-Q3)	1 (0.8-1.4)	0.9 (0.7-1)	1 (0.8-1.1)	1.6 (1.2-1.7)
GGT; U/L, median (Q1-Q3)	52 (24.8-87.3)	47 (30.5-66.3)	37 (23-96)	74 (54-96)
ALP; U/L, median (Q1-Q3)	74 (62-93)	63 (62.5-65.5)	62 (62-76.3)	91 (66.5-114)
Albumin; g/dL, median (Q1-Q3)	4.3 (4.1-4.2)	/	4.3 (4.2-3.3)	3.5 (2.4-4.3)
Total Bilirubin; mg/dL, median (Q1-Q3)	0.8 (0.6-1.4)	1.1 (0.8-1.4)	0.7 (0.6-1)	1.7 (0.8-1.8)
Creatinine; mg/dL, median (Q1-Q3)	0.8 (0.8-1)	0.9 (0.8-1)	0.8 (0.8-1.1)	0.9 (0.7-1)
Serum sodium; mmol/L, median (Q1-Q3)	140 (138-141)	144.5 (144.3-144.8)	140 (138-141)	139 (138.3-140.8)
Serum potassium; mmol/L, median (Q1-Q3)	4.2 (4.1-4.5)	4 (3.9-4)	4.1 (3.9-4.4)	4.3 (4.2-4.7)

Table 2. Baseline biochemical exams

In this cohort, Controlled Attenuation Parameter (CAP) values showed a progressive decline with advancing stages of fibrosis. This trend reflects the expected histopathological evolution of liver disease, in which hepatic fat accumulation diminishes as steatotic tissue is progressively replaced by fibrotic tissue in the later stages of disease progression.

Conversely, both Liver Stiffness Measurement (LSM) and Spleen Stiffness Measurement (SSM) values increased in parallel with fibrosis severity, consistent with the progressive rise in tissue stiffness associated with advanced fibrotic remodeling (**Table 3**).

Fibroscan	All (n=41)	F2 (24%)	F3 (44%)	F4 (32%)	P value
LSM; kPa, median (Q1-Q3)	10.2 (8.9-15.4)	8.7 (8.3-8.9)	10 (9.7-11.2)	19.7 (15.7-24.4)	**<0.001**
SSM; kPa, median (Q1-Q3)	38.6 (29.8-51.5)	35 (33.5-36.6)	30.1 (27.4-40.6)	42.9 (40.1-80)	
CAP; dB/m, median (Q1-Q3)	303 (276-326.3)	338 (315.8-361)	312 (277-325)	275 (233.5-305.8)	0.077

Table 3. Summary of CAP, LSM, and SSM values

4.3.2 **Anthropometric assessment and body composition**

The overall trend showed a significant reduction in body weight across the cohort, from a median of 92.5 kg (IQR 83.0–100.6) at baseline to 85.2 kg (IQR 74.8–99.8) at follow-up ($p < 0.001$). Body weight loss varied according to fibrosis stage, ranging from a 5.4% decrease in F2 patients to an 11.6% decrease in F4, with the difference reaching statistical significance ($p < 0.050$). Overall, the cohort exhibited a median weight loss of 7.9% between baseline and follow-up.

At baseline, the median BMI was 34.2 kg/m² (IQR 30.4–37.7). The reduction in body weight led to a decline in BMI at follow-up, with a median of 31.8 kg/m² (IQR 28.0–37.2), indicating a shift from class I obesity (BMI ≥30–34.9 kg/m²) toward values approaching the upper limit of the overweight range, though without reaching it.

The median waist circumference at baseline was 112 cm (IQR 103–120), exceeding the WHO reference thresholds (<102 cm for men and <88 cm for women), thereby indicating a substantially increased metabolic risk due to excessive visceral adiposity [33]. A general reduction in waist circumference was observed at follow-up, although values remained above reference ranges for all patients.

Bioelectrical impedance analysis (BIA) revealed favourable changes in body composition following the nutritional intervention. The fat-free mass percentage (%FFM) increased from a median of 69.5% (IQR 62.3–72.1) at baseline to 71.9% (IQR 63.7–81.6) at follow-up, reflecting an improvement in lean tissue proportion. Conversely, the fat mass percentage (%FM) decreased from 30.5% (IQR 27.9–37.7) to 28.1% (IQR 18.5–36.4), suggesting a reduction in overall adiposity.

The phase angle (PhA) remained stable (6.6, IQR 5.9–7.0 at baseline vs. 6.6, IQR 6.0–6.9 at follow-up), within the physiological reference range, indicating preserved cellular integrity and membrane function.

When compared with reference values for body composition (fat-free mass: 80–85%; fat mass: 15–20%), the post-intervention data demonstrated a clear trend toward normalization, supporting the positive impact of the dietary intervention on body composition.

A detailed summary of anthropometric and bioimpedance parameters at baseline and follow-up is provided in **Table 4**.

4.3.3 **Dietary intake assessment**

Before the nutritional intervention, the average daily dietary composition, obtained from the analysis of weekly food diaries, was compared with disease-specific reference values. Macronutrient intake was expressed both in grams and as a percentage of total energy intake, while protein intake was also reported as grams per kilogram of ideal body weight per day (g/kg IBW/day).

The mean protein intake was approximately 1 g/kg IBW/day, predominantly derived from animal sources even in the cirrhotic patients. Total fat intake frequently exceeded 35% of total energy, with saturated fatty acids (SFAs) contributing >10%, particularly among individuals in the upper quartile (≥75th percentile) of intake distribution. The median percentage of n-3 polyunsaturated fatty acids (PUFAs) was 0.5% (IQR 0.4–0.7), corresponding to the lower limit of the recommended range (0.5–2% of total energy). When considering EPA and DHA, median values were close to desirable reference levels; however, the wide interquartile range (0–0.4 g) reflected marked interindividual variability, suggesting that a proportion of subjects did not meet the minimum recommended intake.

The median percentage of total carbohydrate intake was 45.2% (IQR 40.1–48.7), lying at the lower end of the adequate range (45–60%). Patients below the 25th percentile (Q1) failed to reach the recommended 45% of total energy from carbohydrates. A noteworthy finding concerns the median percentage of soluble carbohydrates (15.0%, IQR 12.8–18.3), which was at the upper limit of the recommended threshold (<15% of total energy). Notably, more than one third of participants (upper quartile, Q3) had values exceeding 18%, indicating a high intake of rapidly absorbable sugars within this subgroup. Moreover, the median intake of free sugars was 15.4 g (IQR 6.7–22.5).

Median dietary fiber intake was 16 g/day (IQR 13.2–22.3), well below the recommended minimum of 25 g/day, indicating insufficient fiber intake across the study population and the different liver fibrosis stages.

With respect to micronutrients, several deviations from recommended dietary levels were observed. Median calcium intake was 514 mg/day (IQR 408–619), considerably below the recommended 1000–1200 mg/day, while median iron intake (6.9 mg/day, IQR 5.8–9.1) was also suboptimal compared with the reference range (10–18 mg/day). Sodium intake generally

remained within recommended limits (<2 g/day), though higher intakes were recorded among subjects in the upper quartile.

Regarding vitamin intake, most fat-soluble and B-group vitamins were below recommended levels, except for vitamin B12, which fell within the adequate range. Vitamin C intake was close to reference values, although characterized by marked interindividual variability.

The overall dietary intake of the study cohort is summarized in **Table 5**.

4.3.4 **Nutritional diagnosis**

Analysis of the weekly food diaries revealed suboptimal dietary patterns in the cohort at baseline. The energy balance was insufficient in 43.9% of patients, excessive in 34.1%, and adequate in 22%, when compared with the estimated basal metabolic rate (BMR) calculated using the Mifflin–St Jeor equation and ideal body weight (BMI = 25 kg/m²).

Total fat intake exceeded the recommended range in 46.3% of patients, accompanied by a high proportion of saturated fatty acids (SFAs), which surpassed suggested limits in 41.5% of the cohort.

Protein intake was largely below the nutritional requirements recommended for patients with chronic liver disease, with the majority of participants failing to reach the target protein intake per kilogram of ideal body weight. This inadequacy was particularly evident in patients with advanced fibrosis, as those with F3 and F4 stages showed the highest prevalence of insufficient protein consumption (60% and 50%, respectively). Notably, protein adequacy differed significantly across fibrosis stages ($p = 0.050$), and the association remained significant when comparing patients with early fibrosis (F2) to those with advanced stages (F3–F4) ($p = 0.015$).

Regarding minerals, excessive sodium intake was observed in 77.4% of patients when assessed according to LARN reference values. However, when applying the stricter threshold recommended by the EASL guidelines for patients with chronic liver disease (<2 g/day), the proportion classified as excessive decreased to 38.7%. Conversely, iron intake was below recommended levels in 82.9% of the cohort, while calcium intake was inadequate in all patients, remaining well below established dietary requirements.

A detailed summary of the baseline nutritional assessment is provided in **Table 6**.

Variable	All (n=41)	F2 (24%)	F3 (44%)	F4 (32%)	
	Baseline	Baseline	Baseline	Baseline	
Nutritional diagnosis					P value
	18 (43.9%) insufficient	1 (25%) insufficient	10 (50%) insufficient	8 (57.1%) insufficient	
Energy balance; n, %	9 (22%) adequate	0 (0%) adequate	5 (25%) adequate	3 (21.4%) adequate	
	14 (34.1%) excessive	3 (75%) excessive	5 (25%) excessive	3 (21.4%) excessive	
	0 (0%) insufficient	0 (0%) insufficient	0 (0%) insufficient	0 (0%) insufficient	
Dietary lipids; n, %	22 (53.7%) adequate	2 (50%) adequate	13 (65%) adequate	7 (50%) adequate	
	19 (46.3%) excessive	2 (50%) excessive	7 (35%) excessive	7 (50%) excessive	
Dietary satured lipids; n, %	17 (41.5%) excessive	3 (75%) excessive	5 (25%) excessive	6 (42.9%)	
	19 (46.3%) insufficient	0 (0%) insufficient	12 (60%) insufficient	7 (50%) insufficient	**0.050**
Dietary protein; n, %	22 (53.7%) adequate	4 (100%) adequate	8 (40%) adequate	7 (50%) adequate	
	0 (0%) excessive	0 (0%) excessive	0 (0%) excessive	0 (0%) excessive	
	14 (34.1%) insufficient	2 (50%) insufficient	3 (15%) insufficient	6 (42.9%) insufficient	
Dietary carbohydrates; n, %	27 (65.9%) adequate	2 (50%) adequate	17 (85%) adequate	8 (57.1%) adequate	
	0 (0%) excessive	0 (0%) excessive	0 (0%) excessive	0 (0%) excessive	
carbohydrates (>=15%); n, %	13 (31.7%) excessive	1 (25%) excessive	7 (35%) excessive	5 (35.7%) excessive	
	36 (87.8%) insufficient	1 (25%) insufficient	19 (95%) insufficient	14 (100%) insufficient	
Dietary fiber; n, %	5 (12.2%) adequate	3 (75%) adequate	1 (5%) adequate	0 (0%) adequate	
	0 (0%) excessive	0 (0%) excessive	0 (0%) excessive	0 (0%) excessive	
Excessive intake of Sodium; LARN, >1.5g/day	24 (77.4%)	2 (50%)	11 (73.3%)	8 (80%)	
Sodium; EASL, >2g/day	12 (38.7%)	2 (50%)	5 (33.3%)	4 (40%)	
Excessive intake of Potassium; LARN, 3.9g/day	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
Excessive intake of Phosphorus; LARN, 0.7g/day	24 (77.4%)	4 (100%)	10 (66.7%)	9 (90%)	
Insufficient intake of Iron; LARN, < 10 (M+F>60aa) or <18 (F<60aa) mg/day	34 (82.9%)	2 (50%)	17 (85%)	12 (85.7%)	
Insufficient intake of Calcium; LARN, < 1000 mg/day	41 (100.0%)	4 (100%)	20 (100%)	14 (100%)	

Table 6. Baseline nutritional diagnosis

4.3.5 **Nutritional history and eating behaviors of the study cohort**

From the nutritional history collected during the first dietary assessment, it emerged that 90% of the evaluated patients had undertaken several previous dietary attempts. The most common approaches included general dietary advice from a nutritional specialist (83.8%), calorie-restricted diets (75.7%), self-administered diets (37.8%), very-low-calorie ketogenic diets (VLCKD, 10.8%), very-low-calorie diets (2.7%), and group-based cognitive–behavioral therapy programs (2.7%).

When exploring eating motivations, most patients reported hunger (85.4%) as the main driver. However, a substantial proportion indicated eating for pleasure (58.5%) or boredom (29.3%), while only a small minority reported eating out of habit or by rule (4.9%).

Meal duration analysis revealed that more than half of participants (51.2%) consumed their meals within 0–10 minutes, 29.3% within 10–20 minutes, and only 19.5% took more than 20 minutes to finish eating.

The presence of dysfunctional eating behaviours—including night eating disorder, nibbling, and emotional eating—was identified in 61% of patients. Specifically, a large subset reported nibbling on small amounts of food either occasionally (28%) or frequently (44%). A detailed distribution of dysfunctional eating behaviours within the cohort is provided in **Table 7**.

4.3.6 **UPF consumption patterns**

Baseline dietary habits were analyzed with a specific focus on UPF consumption, assessed through a UPF-FFQ (Appendix 1). This assessment enabled the calculation of a UPF score proportional to each patient's exposure to these foods, with a median value of 5.4 (IQR 4.2–6.9). The detailed distribution of FFQ-derived UPF consumption patterns is reported in **Table 8.** Caloric intake derived exclusively from UPFs was estimated using the weekly food diary, with a median value of 330 kcal (IQR 215–430). The corresponding proportion of total daily energy intake provided by UPFs averaged 22% (IQR 15.7–27.7). Data on the total weekly number of UPFs, the number of UPF-free days, and the frequency of days including at least 1, 3, or 5 UPFs are summarized in **Table 9.**

4.3.7 **Association between UPF intake and liver steatosis and fibrosis stage**

To explore the relationship between UPF consumption and liver fibrosis severity prior to the nutritional intervention, the percentage of total caloric intake derived from UPFs was compared across fibrosis stages (F2, F3, F4) and steatosis grade (S1, S2, S3).

Figure 12 illustrates the distribution of the percentage of total caloric intake derived from UPFs across steatosis grades (S1, S2, S3). In contrast to the pattern observed for fibrosis, no significant differences were found among the three steatosis grades. Median values and interquartile ranges were comparable across groups, and the p-value (0.8654) confirmed the absence of a statistically significant association between UPF intake and steatosis severity.

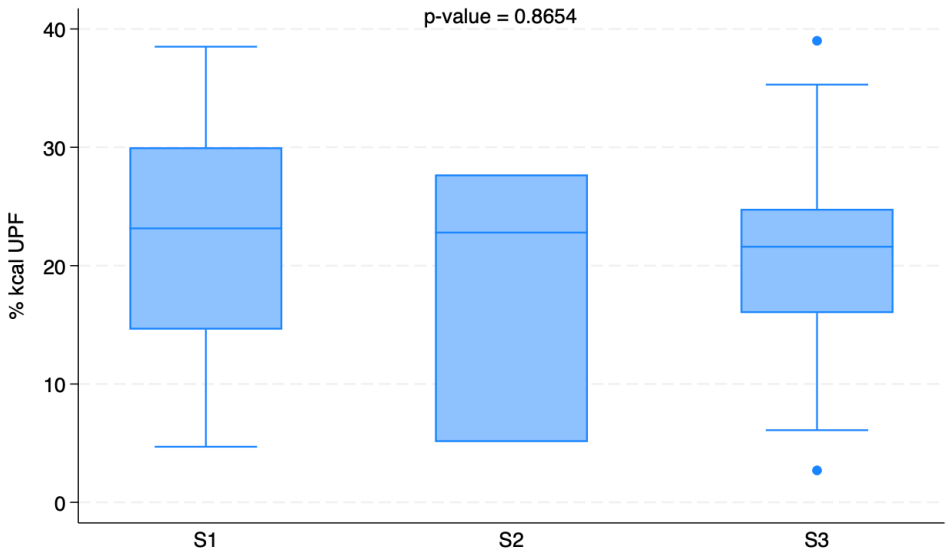

*Figure 12. Percentage of kcal from ultra-processed foods (UPFs) across steatosis grades (S1–S3). No significant differences were observed (*p = *0.8654).*

Beyond the caloric contribution of UPFs, the total weekly number of UPFs was analyzed in relation to fibrosis stage. No significant differences were observed among the three groups (F2, F3, F4), as indicated by a p-value of 0.7950. Although patients with F4 fibrosis exhibited greater interindividual variability, median values were comparable across stages. These findings suggest that the frequency of UPF consumption does not substantially differ with fibrosis severity.

Similarly, the median UPF score derived from the UPF-FFQ did not differ significantly across fibrosis stages. Nevertheless, the FFQ provides valuable insight into patients' habitual dietary patterns and the frequency of UPF consumption throughout the week. However, it does not adequately capture the quantitative caloric impact of UPFs, which is more accurately represented by the percentage of total energy intake derived from these foods.

However, when the percentage of total caloric intake derived from UPFs was considered, a significant association with fibrosis progression emerged. This indicates that the caloric contribution of UPFs—rather than their absolute frequency—may play a more meaningful role in the worsening of liver disease (**Figure 13**).

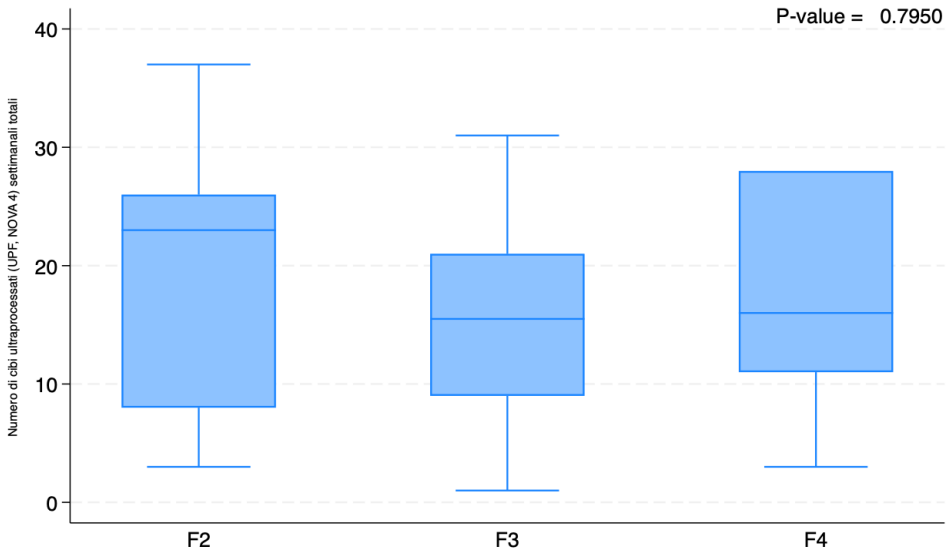

*Figure 13. Total weekly number of ultra-processed foods (UPFs, NOVA 4) consumed by patients according to fibrosis stage (F2–F4). No significant differences were found among groups (*p = *0.7950).*

As shown in **Figure 10**, the median percentage of calories from UPFs progressively increased with fibrosis severity, reaching the highest values among patients with F4 fibrosis. The F4 group also exhibited greater variability in UPF intake compared with F2 and F3, suggesting heterogeneous dietary patterns in advanced disease stages. A statistically significant difference among groups was observed (p = 0.0415), supporting a positive association between higher UPF consumption and more advanced liver fibrosis.

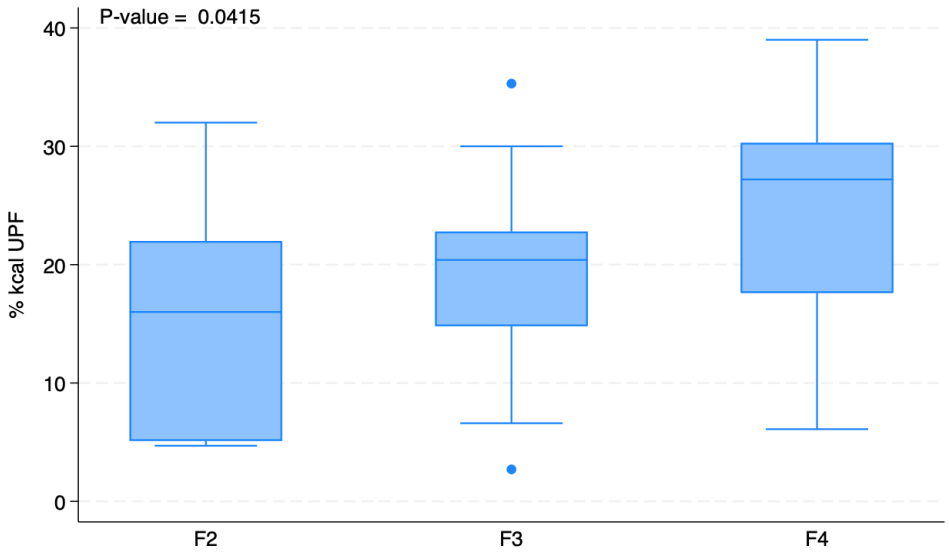

Figure 10. Distribution of % kcal from ultra-processed foods (UPFs) according to fibrosis stage (F2–F4). Higher UPF intake is associated with more advanced liver fibrosis (p = 0.0415).

Figure 11 provides a direct comparison between patients with moderate fibrosis (F2–F3) and those with advanced fibrosis (F4) in terms of the percentage of total caloric intake derived from UPFs. A clear increase in both the median value and the variability of UPF-derived calories was observed in the F4 group compared with F2–F3, indicating a higher and more heterogeneous consumption of UPFs among patients with advanced liver disease.
The difference between groups was statistically significant (p = 0.0411), confirming that the percentage of energy from UPFs not only increases with fibrosis severity but also discriminates between fibrosis and cirrhosis. This finding supports the potential role of UPF consumption as dietary marker of disease progression.

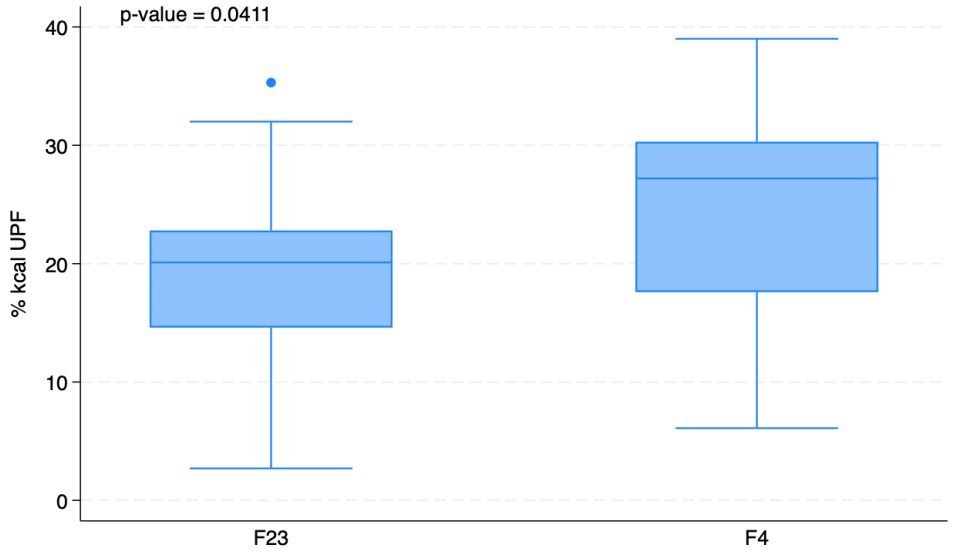

Figure 11. Percentage of kcal from ultra-processed foods (UPFs) in patients with moderate (F2–F3) and advanced (F4) liver fibrosis. Higher UPF intake is observed in the F4 group (p = 0.0411).

4.3.8 **Predictive accuracy of UPF-derived caloric intake for cirrhosis**

A receiver operating characteristic (ROC) curve analysis was performed to assess the discriminative ability of the percentage of total caloric intake derived from ultra-processed foods (UPFs) in identifying cirrhosis. The comparison between non-cirrhotic (F2–F3) and

cirrhotic (F4) patients yielded an area under the curve (AUC) of 0.7074, indicating moderate discriminative accuracy (95% CI, 0.5124–0.9023).

The optimal cut-off identified by the Youden index was 25.2% of total kcal from UPFs, corresponding to a sensitivity of 0.62 and a specificity of 0.87.

For clinical interpretability, additional rule-out and rule-in thresholds were explored. A percentage of kcal from UPFs ≥10.3% provided high sensitivity (92.3%) but low specificity (17.4%), supporting its potential use as a rule-out threshold. Conversely, a stricter threshold of ≥35.3% achieved high specificity (95.7%) but limited sensitivity (15.4%), suggesting its applicability as a rule-in criterion for advanced fibrosis.

Overall, these findings indicate that a greater caloric contribution from UPFs is associated with an increased likelihood of cirrhosis, and that extreme values may serve as practical dietary thresholds for risk stratification (Figure 14).

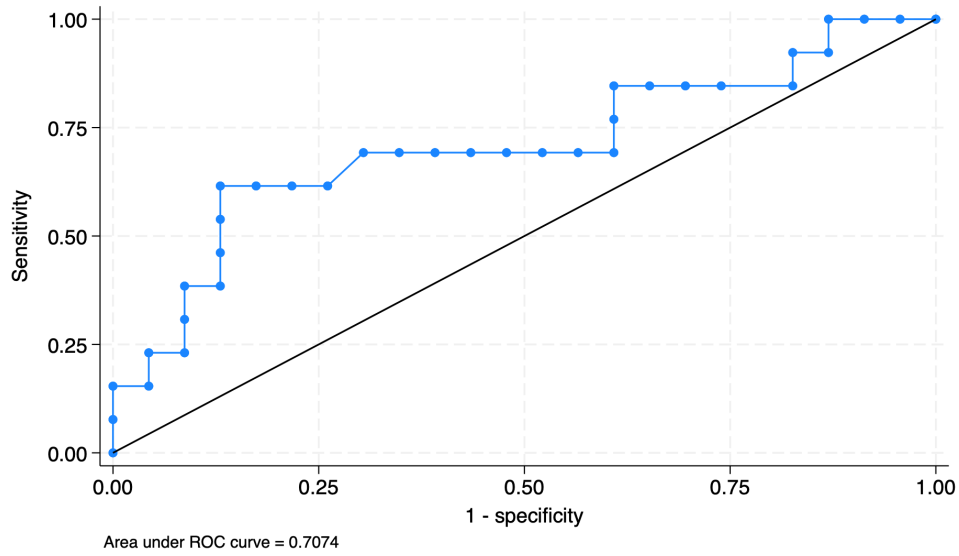

Figure 14. ROC curve evaluating the ability of % kcal from UPFs to discriminate cirrhosis (F4) from F2–F3 fibrosis stages. AUC = 0.7074 (95% CI: 0.5124–0.9023), best cut-off: 25.2%, sensitivity: 62%, specificity: 87%.

4.4 **Discussion**

Recent evidence increasingly underscores the importance of nutritional assessment in the clinical management of chronic liver disease, especially MASLD. In this context, evaluating dietary history played a key role in understanding patients' eating habits and their potential influence on disease progression. The 7-day food diary served a dual purpose: it enabled clinicians to assess meal structure and food choices, while encouraging patients to reflect on the quantity and quality of their diet, thereby increasing awareness of eating behaviours.

Although the 7-day diary provided a comprehensive overview of habitual intake, it required considerable motivation to ensure accuracy. Its validity may decrease over time as patients consciously or unintentionally omit certain foods or beverages. To mitigate these limitations, a shorter diary (e.g., 3 days) could be integrated with information obtained during the dietetic interview (24-h recall), clarifying often-overlooked aspects such as alcohol consumption, added sugars, and the use of condiments like olive oil. Providing a practical guidance sheet may further improve the accuracy and reliability of patient reporting.

The use of the HandyDiet software supported the nutritional analysis of food diaries in clinical practice and allowed clinicians to tailor dietary plans more efficiently according to each patient's individual needs and habits. In particular, the volume-based dietary approach proposed by O. Sculati and implemented in the software helped overcome the difficulties commonly associated with portion-size estimation during dietary history collection. This method simplified communication with patients and made dietary prescriptions easier to understand and apply.

The analysis of dietary composition revealed several nutritional imbalances that may contribute to the worsening of metabolic dysfunction in chronic liver disease. Although total energy intake varied widely among individuals, a substantial proportion of patients presented either insufficient or excessive caloric intake, resulting in a suboptimal energy balance at baseline.

An unexpected finding of this study was the high proportion of patients classified as having insufficient energy intake despite the presence of obesity in the cohort. This apparent paradox requires careful interpretation, considering both the method used to estimate energy requirements and the potential limitations of dietary self-reporting. Energy needs were estimated using the Mifflin–St Jeor equation applied to ideal body weight (BMI = 25 kg/m^2) and adjusted for lifestyle (PAL = 1.3), as recommended for subjects with obesity to avoid overestimation. However, this approach may yield higher target values compared with the

patient's spontaneous intake, resulting in a more frequent classification of "insufficient" energy consumption.

Furthermore, the food diary method is intrinsically vulnerable to underreporting, particularly among individuals with obesity, who may omit or underestimate certain foods—either consciously or unconsciously. It is also possible that patients modified their eating behavior during the recording week, knowing that their intake would be evaluated, thus temporarily reducing energy consumption and further contributing to the apparent mismatch. Taken together, these factors suggest that the diagnosis of "insufficient" energy intake may partially reflect measurement bias and self-correction behaviours, rather than a true chronic energy deficit. Nonetheless, these findings highlight the importance of combining objective nutritional assessment with repeated monitoring to better capture habitual intake patterns in this population.

Particular attention should be paid to protein intake, which was insufficient in most patients. Inadequate protein intake is especially concerning in individuals with chronic liver disease, given its close association with sarcopenia and reduced functional capacity. Advanced fibrosis stages (F3–F4) showed the highest prevalence of protein inadequacy, suggesting that nutritional deterioration may parallel disease progression. Ensuring an adequate protein intake per kilogram of ideal body weight therefore represents a key therapeutic priority to prevent further muscle loss and counteract the catabolic state typical of chronic liver disease.

Conversely, total fat intake frequently exceeded the recommended range of 20–35% of total energy (LARN 2024), and all patients exhibited a consistently high consumption of saturated fatty acids (>10% of energy)—a pattern known to worsen cardiometabolic and hepatic outcomes. Interestingly, dietary cholesterol intake remained below the upper recommended threshold, which is consistent with the generally acceptable lipid profiles observed in terms of total cholesterol, HDL-C, and LDL-C values. This favourable lipid pattern may also be partly explained by the predominant use of extra-virgin olive oil as the main culinary fat in this cohort. Extra-virgin olive oil is rich in monounsaturated fatty acids and bioactive phenolic compounds, which have been widely documented to exert beneficial effects on lipid metabolism and cardiovascular risk. These protective dietary components could therefore contribute to mitigating the negative impact of other less favourable aspects of the diet.

The excessive intake of soluble carbohydrates observed in this cohort appears consistent with the reported eating habits. A predominant consumption of refined grain products and industrially processed foods—almost always rich in added sugars—was described by most participants. At the same time, dietary fiber intake was markedly inadequate, with median

values reaching only about half of the recommended minimum, indicating a limited consumption of whole grains, pulses, fruits, and vegetables. This dietary pattern, characterized by a high proportion of rapidly absorbable carbohydrates and low fiber content, is known to worsen glycemic control and promote hepatic fat accumulation. Such findings are consistent with the high prevalence of diabetes and other glucose metabolism disorders reported in the patients' medical histories and documented by baseline biochemical assessments.

These same dietary behaviours may also explain the widespread inadequacy of micronutrient intake, particularly regarding fat-soluble and B-group vitamins. A low intake of fresh plant-based foods reduces the availability of antioxidant vitamins, such as vitamin C, as reflected by the marked interindividual variability observed in this cohort. Similarly, the deficiency of B-complex vitamins is partly attributable to reduced dietary diversity and lower consumption of plant-derived foods. Conversely, vitamin B12 intake remained within adequate ranges, likely due to a preserved consumption of animal-derived foods.

Regarding micronutrients, calcium intake was substantially below the Population Reference Intake (PRI = 950–1100 mg/day), as commonly observed in the general population, while iron intake was also suboptimal in a relevant proportion of patients (PRI = 10 mg/day for men and postmenopausal women, 18 mg/day for women ≤64 years). Excessive sodium intake—according to EASL recommendations (<2 g/day)—was mainly observed among individuals above the 75th percentile, reflecting the impact of processed food consumption and the difficulty of achieving sodium restriction in daily life. When applying the more stringent LARN threshold (<1.5 g/day), an even greater proportion of patients exceeded recommended intakes, further confirming the relevance of sodium excess in this population.

Overall, these findings reinforce the concept that a diet characterized by high levels of soluble sugars and saturated fatty acids, together with low nutrient density, represents a critical determinant of the nutritional risk profile in MASLD patients

A key finding of this study is the significant association between the percentage of total energy derived from ultra-processed foods (UPFs) and fibrosis severity. Patients with cirrhosis (F4) showed a markedly higher caloric contribution from UPFs compared with those with moderate fibrosis (F2–F3), indicating a progressive shift toward poorer-quality diets as liver disease advances. These results are further supported by ROC curve analysis, which demonstrated a moderate predictive accuracy of UPF-derived energy intake in identifying cirrhosis (AUC = 0.7074). Notably, the absolute number of UPFs consumed per week did not differ significantly among fibrosis stages, suggesting that the caloric contribution of UPFs, rather than their absolute frequency, may be more relevant in liver disease worsening. In other

words, patients with advanced fibrosis do not necessarily consume UPFs more often, but they derive a greater proportion of their daily caloric intake from these foods—an observation consistent with a progressive deterioration in overall dietary quality.

This finding aligns with growing evidence linking UPF-rich diets to systemic inflammation, metabolic dysfunction, and hepatic fat accumulation—mechanisms known to accelerate fibrosis progression. However, because only patients with established fibrosis (F2–F4) were included, comparison with a non-fibrotic control group was not possible. As such, while the results support a significant association between higher UPF-derived energy intake and fibrosis severity, causality cannot be inferred, and findings should be interpreted within this methodological limitation.

Additionally, estimating the percentage of kcal from UPFs may be affected by challenges inherent to the NOVA classification system. Food diaries do not always provide sufficient detail to accurately determine the processing level of specific products. The current food market offers a wide range of industrial products that appear similar to consumers but differ substantially in formulation and processing, leading to potential misclassification between NOVA categories 3 and 4. In such cases, minor inconsistencies in categorization could have influenced UPF quantification. These challenges highlight the need for careful interpretation of UPF intake estimates and for methodological standardization in future studies.

The FFQ, while useful for characterizing habitual UPF consumption patterns and identifying patients with higher exposure, remains a frequency-based tool and lacks precision in quantifying the actual caloric contribution of UPFs—particularly when compared with the time-anchored 7-day diary. Moreover, the reliance on self-reported recall introduces potential under- or overestimation bias, especially among individuals with obesity.

Following the nutritional intervention, the cohort exhibited a favourable shift in body composition, characterized by an increase in the relative proportion of fat-free mass and a reduction in fat mass. This change reflects a healthier redistribution of body compartments, clinically relevant for the prevention of sarcopenia and metabolic deterioration in chronic liver disease. Consistent with these improvements, all anthropometric parameters—including body weight, BMI, and waist circumference—showed a decreasing trend at follow-up. The reduction was more pronounced among individuals with advanced fibrosis (F3–F4), possibly due to heightened awareness of disease severity and greater adherence to nutritional and medical recommendations.

Despite these improvements, median BMI and waist circumference at follow-up remained above normal ranges (BMI >30 kg/m² and WC >102 cm in males / >88 cm in

females), indicating persistent obesity in most patients. Nonetheless, the observed downward trend suggests a gradual shift toward less severe weight categories, which, if sustained, may yield long-term benefits on hepatic and cardiometabolic outcomes.

Given the limited nutritional literacy observed in this cohort and the difficulty many patients face in retaining dietary advice provided during clinic visits, additional educational support is warranted. Visual and easy-to-use materials—such as brochures, illustrative meal guides, or the “healthy plate” model—can substantially improve patients’ understanding and adherence to dietary recommendations. Once provided, these tools remain accessible for continuous consultation, reinforcing concepts that may otherwise be forgotten and ultimately enhancing the effectiveness of nutritional intervention.

Altogether, these findings support the integration of comprehensive nutritional assessment, structured education, and individualized dietary counselling as a cornerstone of chronic liver disease management, aiming not only to slow disease progression but also to empower patients toward sustainable, long-term lifestyle change

5. **CONCLUSION**

The present study focused on the nutritional assessment and its clinical implications in MASLD patients with hepatic fibrosis and advanced chronic liver disease, aiming to clarify how dietary habits and nutritional status relate to disease severity.

Analysis of weekly food diaries and dietary histories revealed multiple nutritional imbalances, including suboptimal protein intake, excessive consumption of saturated fats and soluble sugars, insufficient dietary fiber, and frequent micronutrient inadequacies. Furthermore, a higher proportion of total energy derived from ultra-processed foods (UPFs) was significantly associated with more advanced fibrosis stages, supporting the hypothesis that poor dietary quality contributes to hepatic disease progression.

The nutritional intervention implemented during follow-up produced measurable improvements in body weight, composition, and anthropometric risk indicators, underscoring the benefits of personalized dietary management in this population.

Overall, these findings highlight the need for systematic and early nutritional assessment in patients with chronic liver disease to promptly identify those at nutritional risk. Integrating structured nutritional care and targeted counseling delivered by specialized professionals into routine hepatology practice may represent a key strategy to improve clinical outcomes and slow disease progression.

6. **APPENDIX**

Appendix 1. Food Frequency Questionnaire (FFQ)

Alimento	**Porzione STANDARD sec. CREA 2018**	**Mai/Raramente**	**1-2 volte/ settimana**	**3-4 volte/ settimana**	**5-6 volte/ settimana**	**1 volta al giorno**	**2-3 volte al giorno**	**4 o più volte al giorno**
Prodotti lattiero-caseari zuccherati come yogurt alla fragola o vaniglia o bevande a base di latte	1 unità o 1 tazza (125ml)							
Cereali integrali come farina d'avena cotta, quinoa, orzo, farro, o legumi come fagioli o lenticchie	1 tazza (150g cotto/50g secco)							
Verdure (fresche o cotte) o insalata fresca	1 porzione media (200g)							
Frutta	1 porzione media (150g)							
Pesce o frutti di mare (freschi o congelati)	1 porzione media (150g)							
Frutta secca al naturale (es. noci, mandorle…)	5 unità (30g)							
Burro/margarina/ strutto	1 cucchiaino (10g)							
Olio d'oliva per cucinare e condire	1 cucchiaino (10ml)							
Zucchero	1 cucchiaino (5g)							
Torte, biscotti, merendine confezionati	1 fetta/unità (100g)							
Cereali per la colazione dolci (zuccherati)	1 bicchiere (30g)							
Pollo fritto/impanato pronto da mangiare o da fast-food	1 unità (100g)							
Polpette di carne pronte da mangiare o da fast-food, come hamburger o kebab	1 unità (100g)							
Sostituti della carne a base vegetale processati (es. burger o nuggets confezionati	1 unità (100g)							
Hot dog/ Wurstel/ Salsicce	2 unità (100g)							
Salumi (es. salame, mortadella, pancetta, speck…)	2 fette (50g)							
Cibo pronto per una preparazione rapida o da fast food: pizza, patatine fritte, anelli di cipolla, pasti pronti da scaldare	1 porzione (150-200g)							
Gelato, sorbetto, ghiacciolo confezionati	2 piccole palline/unità (100g)							
Maionese, ketchup, salse da condimento industriali	1 cucchiaio (10g)							
Barrette dolci (es. barrette di cioccolato, barrette energetiche)	1 unità (30g)							
Snack salati confezionati (es. pretzel, patatine, popcorn)	1 bicchiere (30g)							
Bevande zuccherate acquistate (es. succhi, punch, bevande gassate, bevande energetiche, tè freddo zuccherato)	1 bicchiere (200g)							
Bevande dietetiche dolcificate (es. bevande zero o light a basso contenuto calorico)	1 bicchiere (200ml)							

Table 4. Anthropometric measurements and BIA at baseline and follow up

Variable	All (n=41)	All (n=41)	F2 (24%)	F2 (24%)	F3 (44%)	F3 (44%)	F4 (32%)	F4 (32%)		
	Baseline	Follow up	Baseline	Follow up	Baseline	Follow up	Baseline	Follow up		
Anthropometric measurements									P value	REFERENCE VALUES
Weight; Kg, median (Q1-Q3)	92.5 (83-100.6)	85.2 (74.8-99.8)	97.3 (92.4-100.5)	92 (76.5-94.5)	90 (84-100.2)	81.8 (74.1-99.5)	90.5 (81-97)	80 (70.7-89.6)	0.634	
Weight loss; %, median (Q1-Q3)		7.9 (9.9-0.8)		5.4 (17.2-6)		9.1 (11.8-0.7)		11.6 (12.7-7.6)	**0.050**	
Body mass index; kg/m², median (Q1-Q3)	34.2 (30.4-37.7)	31.8 (28-37.2)	33.8 (32.4-34.8)	33 (30.3-33.4)	34.8 (31.3-38.1)	30.2 (27.4-37.3)	30.8 (28.8-35.9)	30.4 (26.9-33.1)	0.216	overweight (25-29,9); obesity (≥30)
Waist circumference (WC); cm, median (Q1-Q3)	112 (103-120)	107 (99.9-115)	116.3 (112.9-117.1)	109 (99-111)	113 (104.5-120)	108.3 (101.4-117.1)	104.3 (101.3-115.8)	103.5 (97.5-113)	0.532	<94-102 cm (M); <80-88 cm (W)
Hip circumference (HC); cm, median (Q1-Q3)	113 (107.5-122.5)	107.8 (102.1-119)	110.5 (108.8-111.8)	107 (102.5-107)	119 (107-124.8)	105 (100-123)	109 (106-113.5)	108.5 (101.8-111)	0.180	
Neck circumference; cm, median (Q1-Q3)	38 (36.5-40)	37 (35-40)	41 (40-42.5)	40 (36.5-41.5)	38 (37.3-40.3)	38 (37-39.8)	36.5 (35-37.5)	36 (35-38.5)	0.042	<43 cm (M); <41 cm (W)
Arm circumference; cm, median (Q1-Q3)	34.5 (31.5-37)	32.5 (30.1-36)	34 (33.5-34.5)	35.5 (31.5-36)	34.5 (31.8-37)	32.5 (29.6-34.9)	32 (31-34.5)	31 (29-32.8)	0.327	
Thigh circumference; cm, median (Q1-Q3)	55.5 (51.5-60)	53 (50.5-57)	53.8 (53.1-54.4)	52 (48-53)	57 (50.3-59.5)	52 (50.3-56.3)	53 (50-57.5)	53 (50.3-54.5)	0.584	
Liver frailty index (LFI); median (Q1-Q3)	3.64 (3.48-3.91)	3.47 (3.31-3.75)	/	/	3.37 (3.17-3.58)	3.13 (2.95-3.55)	3.64 (3.48-3.84)	3.5 (3.38-3.72)	0.050	Robust (LFI <3.2)
TAA, total arm area; cm², median (Q1-Q3)	0.47 (0.45-0.48)	0.45 (0.44-0.48)	0.46 (0.46-0.47)	0.47 (0.45-0.48)	0.47 (0.45-0.48)	0.45 (0.43-0.47)	0.45 (0.44-0.47)	0.44 (0.43-0.46)		
Waist-hip ratio (WHR); median (Q1-Q3)	0.97 (0.91-1.03)	0.97 (0.93-1.03)	1.06 (1-1.07)	1.02 (0.93-1.07)	0.96 (0.92-1)	0.99 (0.93-1.03)	0.98 (0.85-1.03)	0.97 (0.95-1.03)		
Waist-to-height ratio (WtHR); median (Q1-Q3)	0.68 (0.63-0.71)	0.66 (0.61-0.72)	0.67 (0.66-0.68)	0.65 (0.62-0.66)	0.68 (0.63-0.71)	0.66 (0.62-0.72)	0.63 (0.61-0.71)	0.63 (0.58-0.7)		<0,90 (M); <0,85 (F)
Ideal weight (BMI 25); kg/m², median (Q1-Q3)	67.2 (62.8-73.9)	68.9 (63.2-72.9)	73.1 (68.7-75.9)	68.9 (63.2-68.9)	67.2 (62.4-74)	68.9 (66.2-74)	69.3 (64.6-75.5)	68.9 (65.2-74.4)		
BMR (Mifflin-St Jeor); kcal, median (Q1-Q3)	1329 (1149-1417)	/	1416 (1265-1475)	/	1357 (1210-1409)	/	1210 (1149-1446)	/		
BMR (Mifflin-St Jeor) adj. lifestyle; kcal, median (Q1-Q3)	1728 (1494-1842)	/	1841 (1645-1918)	/	1764 (1573-1832)	/	1573 (1494-1880)	/		
Lifestyle; median	Sedentary (PAL 1.3)	Sedentary (PAL 1.3)	Sedentary (PAL 1.3)	Sedentary (PAL 1.3)	Sedentary (PAL 1.3)	Sedentary (PAL 1.3)	Sedentary (PAL 1.3)	Sedentary (PAL 1.3)		
BIA									p value	
Rz; ohm, median (Q1-Q3)	390.2 (351.2-438.6)	386.3 (353-415.1)	339.5 (328.3-350.8)	353.7 (351-394)	380.5 (350-440.4)	378 (351.4-433.9)	421.3 (387.7-438.8)	390.8 (368.8-416.4)		
Xc; ohm, median (Q1-Q3)	47 (39.4-51.8)	44.8 (41-48.6)	36.4 (36.3-36.6)	46.2 (44.2-49.9)	50.7 (39.4-55.2)	43 (39.3-47.5)	45.7 (42-51.6)	43.4 (41.6-45.5)		
PA (°), median (Q1-Q3)	6.6 (5.9-7)	6.6 (6-6.9)	6.2 (6-6.3)	7.1 (6.9-7.2)	6.9 (6.3-7.6)	6.5 (6-6.9)	6.1 (5.8-6.7)	6.2 (5.6-6.7)	0.350	5-7°
Total Body Water (TBW); lt/kg, median (Q1-Q3)	46.3 (42.1-53.2)	48.2 (41.1-52)	56.2 (55.8-56.5)	53.7 (41.1-53.9)	46.3 (42.1-50)	48.6 (40.3-52.2)	43.6 (39.1-54.7)	48.7 (40.2-51.7)		60-62 % (M); 56-58% (F)
ExtraCellular Water (ECW), lt/kg, median (Q1-Q3)	19.3 (17-22.6)	20.7 (16.8-22.8)	25.3 (24.7-25.9)	21.3 (16.8-22.1)	19.3 (16.2-20.9)	21.4 (17-23)	18 (17-24.2)	21.5 (18.6-24)		40 % of TBW
Fat-Free Mass (FFM); kg, median (Q1-Q3)	62.8 (57.3-70.7)	65.6 (56.1-70.2)	72 (70.9-73.2)	70.9 (55.9-73.1)	62.8 (57.3-68.1)	66.5 (54.9-70.1)	59.2 (53.2-73.8)	64.9 (54.6-69.7)	0.356	
Fat-Free Mass (FFM); %, median (Q1-Q3)	**69.5 (62.3-72.1)**	**71.9 (63.7-81.6)**	**72.1 (69.2-75)**	**70.9 (70.9-70.9)**	**70.6 (61.8-71.9)**	**75.8 (64.2-85.2)**	**69.7 (67.8-76.5)**	**72.7 (65.9-79.8)**		80-85% body weight
Body Cell Mass (BCM); Kg, median (Q1-Q3)	36.4 (30.6-39.4)	34.9 (32.9-40.4)	39.1 (39.1-39.1)	40.8 (33.2-43.2)	36.4 (30.6-41.2)	36.3 (31-40.9)	34.3 (29.6-38.2)	33.8 (29.5-35.6)		
Fat Mass (FM); Kg, median (Q1-Q3)	29.8 (21.9-35.9)	20.9 (15.3-33.4)	28.3 (24.7-31.8)	21.2 (19.6-21.7)	30 (23.2-35.4)	18.3 (10.7-30.3)	23.6 (19.5-35.8)	19.4 (11.8-30.9)	0.526	
Fat Mass (FM); %, median (Q1-Q3)	**30.5 (27.9-37.7)**	**28.1 (18.5-36.4)**	**27.9 (25.1-30.8)**	**29.1 (29.1-29.1)**	**29.4 (28.1-38.2)**	**24.2 (14.9-35.8)**	**30.3 (23.5-32.2)**	**27.3 (20.2-34.1)**		15-20% body weight
Skeletal Muscle mass (SM); Kg, median (Q1-Q3)	30.8 (26.4-35.5)	32.4 (25.9-36.3)	38.6 (38.3-38.8)	35.3 (25.9-35.6)	29.1 (26.3-33.1)	34.4 (25-36.6)	34.4 (25.7-36.6)	30.9 (25.1-36.8)	0.134	
Skeletal Muscle Index (SMI); kg/m², median (Q1-Q3)	11.4 (9.9-12.3)	11.5 (9.7-12.9)	12.7 (12.5-12.8)	12.8 (10.3-12.9)	11.2 (9.9-11.8)	12.2 (9.4-12.6)	10.7 (9.7-12.2)	11 (9.6-12.1)	0.277	
Appendicular Skeletal MM (ASMM); Kg, median (Q1-Q3)	25.9 (22.7-27.7)	25.2 (22-27.3)	29 (28.5-29.5)	26.9 (21-26.9)	25.7 (21.9-27.5)	25.1 (20.1-28.2)	26.1 (22.9-29.4)	25 (20.7-26.7)	0.376	
Fat Free Mass Index (FFMI); kg/m², median (Q1-Q3)	23.7 (22.3-25)	23.4 (22-24.3)	23.7 (23.3-24)	23.4 (22.1-26.5)	23.2 (22.5-25.1)	23.6 (21.8-24.8)	23.3 (21.2-24.6)	23 (21.7-23.8)	0.616	
Fat Mass Index (FMI); kg/m², median (Q1-Q3)	11.1 (8.8-13.4)	8.7 (6.2-13.6)	9.3 (8.1-10.5)	7.7 (7.7-8.6)	11 (8.9-14)	7.3 (4.3-12.7)	8.4 (8-11.2)	7.6 (5.9-12.3)	0.411	
Standardized Phase Angle (SPA°); median (Q1-Q3)	1.1 (0.3-2.1)	1 (0.6-1.4)	0.5 (0.3-0.7)	1.2 (1.1-1.3)	1.1 (0.4-2.2)	0.9 (0.7-1.6)	1.2 (-0-3.3)	0.6 (0.1-0.9)	0.419	
Body Cell Mass Index (BCMI); median (Q1-Q3)	12.8 (12.1-14.4)	13.1 (12.3-13.7)	12.9 (12.8-12.9)	13.5 (13.1-15.7)	13.2 (12.3-14.7)	12.9 (12.2-13.6)	12.3 (11.8-12.7)	12.5 (12-13.2)		
BMR; Kcal, median (Q1-Q3)	1805 (1638-1891)	1769 (1702-1920)	1885 (1884-1885)	1934 (1712-2002)	1805 (1638-1942)	1802 (1647-1935)	1743 (1609-1859)	1729 (1605-1782)		

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Table 5. Baseline dietary intake evaluated through a 7-day food diary

Variable	All (n=41)	F2 (24%)	F3 (44%)	F4 (32%)		
	Baseline	Baseline	Baseline	Baseline		
Macronutrients					**P value**	REFERENCE VALUES
Energy; kcal, median (Q1-Q3)	1578 (1285-1795)	2300 (2064-2436)	1493 (1238-1749)	1507 (1306-1662)		/
Protein; %, median (Q1-Q3)	15.9 (14.7-17.2)	13.1 (12.8-14.5)	15.7 (14.5-17.6)	16.4 (15.8-17.5)		/
Protein; g, median (Q1-Q3)	**63.9 (50.8-74.7)**	**78.4 (74.6-80.3)**	**56.6 (47.2-72.4)**	**63.7 (54.6-75.3)**		
Proteine pro/kg; g, median (Q1-Q3)	**1 (1-1)**	**1 (1-1)**	**1 (1-1)**	**1 (1-1)**	0.442	1.2-1.5g/kg IBW/day
Animal protein; %, median (Q1-Q3)	52.9 (45.3–59.6)	42.6 (42.8–45.5)	57.4 (47–58.8)	56 (46.5–60.2)		/
Vegetal protein; %, median (Q1-Q3)	47.1 (40.4–54.7)	57.4 (54.5–57.2)	42.6 (41.2–53)	44 (39.8–53.5)		/
Lipids; %, median (Q1-Q3)	35.7 (32.1-39.2)	36.3 (34.6-41.3)	34.6 (29.8-36.5)	36.1 (32.9-41.1)		20-35% total energy
Lipids; g, median (Q1-Q3)	58.3 (50.2-79.5)	92.9 (79.6-112.1)	53.1 (44.5-63.9)	57.1 (51.1-67.5)		/
Saturated; %, median (Q1-Q3)	**9.5 (8.7-11.5)**	**10.7 (9.8-11.6)**	**9.2 (8.6-9.7)**	**9.9 (8.9-12.7)**		<7% total energy
PUFA n-3; %, median (Q1-Q3)	0.5 (0.4-0.7)	0.7 (0.5-0.8)	0.5 (0.4-0.6)	0.6 (0.4-0.8)		0.5-2% total energy
Alpha-linolenic acid (ALA); g, median (Q1-Q3)	0.7 (0.6-0.9)	1.5 (1.2-1.6)	0.7 (0.6-0.8)	0.9 (0.5-1)		/
EPA; g, median (Q1-Q3)	0.1 (0-0.1)	0.1 (0-0.3)	0.1 (0-0.1)	0.1 (0-0.3)		EPA-DHA 0.25 mg
DHA; g, median (Q1-Q3)	0.1 (0-0.2)	0.2 (0-0.4)	0.1 (0-0.2)	0.1 (0-0.3)		EPA-DHA 0.25 mg
Animal lipids; %, median (Q1-Q3)	38.3 (33.5–34.2)	29.6 (33-26.1)	36.2 (35.7-38.5)	37.8 (29.7-39.1)		/
Vegetal lipids; %, median (Q1-Q3)	61.7 (65.8-66.5)	70.4 (73.9-67)	63.8 (61.5-64.3)	62.2 (60.9-70.3)		/
Cholesterol; mg, median (Q1-Q3)	162 (118-202)	191 (149-226)	155 (131-181)	183 (110-205)		<300mg
Carbohydrates; %, median (Q1-Q3)	45.2 (40.1-48.7)	**44.3 (41-46.1)**	46.4 (44.7-50.2)	45.4 (38.6-47,6)		45-60% En
Carbohydrates; g, median (Q1-Q3)	181.7 (151.8-218.9)	247.5 (210.2-286.2)	200.5 (151.2-221.9)	166.9 (153.3-188)		/
Soluble carbohydrates; %, median (Q1-Q3)	**15 (12.8-18.3)**	**17 (15.5-17.5)**	**16 (13.8-18.3)**	**14 (12.3-19)**	0.219	<15% En
Soluble carbohydrates; g, median (Q1-Q3)	56.3 (44.3-74.9)	76.2 (73.3-83.9)	55.5 (48.1-74.2)	53.8 (40.8-64.5)		/
Free sugars; g, median (Q1-Q3)	15.4 (6.7-22.5)	26.9 (16.3-40.2)	14.5 (8.5-22.8)	10.2 (6.7-17.7)		<10% En
Dietary fiber; g, median (Q1-Q3)	**16 (13.2-22.3)**	**32.9 (26.4-35.1)**	**16 (13.7-18)**	**17.3 (14-22.8)**		At least 25g/day
BCAA						
Isoleucine; mg, median (Q1-Q3)	1514 (1089-2027)	1622 (1506-1756)	1421 (1012-1927)	1621 (1150-2028)		
Leucine; mg, median (Q1-Q3)	2764 (2145-3565)	2910 (2798-3091)	2645 (1913-3447)	2982 (2219-3719)		
Valine; mg, median (Q1-Q3)	1766 (1325-2298)	1901 (1755-2055)	1662 (1213-2232)	1904 (1333-2331)		
Minerals						
Iron; mg, median (Q1-Q3)	**6.9 (5.8-9.1)**	**10.5 (8.5-12.7)**	**6.8 (5.8-8.9)**	**8 (5.7-9.3)**		10-18 mg/day
Calcium; mg, median (Q1-Q3)	**514 (408-619)**	**683 (573-798)**	**505 (406-596)**	**517(436-656)**		1000-1200 mg/day
Sodium; mg, median (Q1-Q3)	**1812 (1353-2135)**	**1980 (1520-2447)**	**1623 (1252-2112)**	**1711 (1242-2042)**		<1.5 g/day or <2g/day
Potassium; mg, median (Q1-Q3)	2018 (1677-2444)	3274 (2851-3453)	2028 (1712-2387)	2082 (1606-2495)		3900 mg/day
Phosphorus; mg, median (Q1-Q3)	878.8 (676-1010)	1159 (976-1352)	819 (684-941)	932 (596-1040)		700 mg/day
Vitamins						
Retinol eq.; µg, median (Q1-Q3)	**559.3 (422.7-721.2)**	**647.8 (563.2-921.1)**	**571.3 (420.3-729.8)**	**636.2 (417.9-744.9)**		600 (F)-700(M) µg/day
Retinol; µg, median (Q1-Q3)	146.3 (110.9-201)	199.2 (183.3-202.8)	137.3 (109.2-203.4)	170.4 (133.1-222.3)		
Beta carotene eq.; µg, median (Q1-Q3)	**2705 (1618-3661)**	**2859 (2214-4542)**	**2780.1 (1742-3719)**	**2776.3 (1745.5-3705)**		3600 (F)-4200 (M) µg/day
Vitamin D; µg, median (Q1-Q3)	**1.6 (0.8-3.1)**	**2.7 (1.2-4.1)**	**1.4 (1-2.2)**	**2 (1.1-3.4)**		15 µg/day
Vitamin E; mg, median (Q1-Q3)	**9.2 (7.6-11.6)**	**14.4 (11.2-19.7)**	**8.5 (7.5-10)**	**8.6 (6.6-10.3)**		12 (F)-13 (M) mg/day
Vitamin K; µg, median (Q1-Q3)	**0.2 (0-4.6)**	**6 (1.2-21.1)**	**0.1 (0-1.7)**	**0.3 (0-5.2)**		140-170 µg/day
Vitamin B1 (thiamine); mg, median (Q1-Q3)	0.9 (0.7-1.1)	1.2 (1-1.3)	0.8 (0.7-1)	1 (0.6-1.1)		1.1 (F)-1.2 (M) mg/day
Vitamin B2 (riboflavin); mg, median (Q1-Q3)	**1.1 (0.9-1.3)**	**1.2 (1.1-1.2)**	**1.1 (0.9-1.2)**	**1.2 (0.9-1.3)**		1.3 (F)-1.6 (M) mg/day
Niacina (Vitamin B3); mg, median (Q1-Q3)	**12.2 (9.7-15.1)**	**17.5 (13-21.8)**	**12.2 (9.9-14)**	**12.3 (9.4-15.4)**		18 mg/day
Pantothenic acid (Vitamin B5); mg, median (Q1-Q3)	**2 (1.7-2.6)**	**2.1 (1.8-2.5)**	**2.1 (1.8-2.6)**	**2.3 (1.6-3.1)**		5 mg/day
Vitamin B6; mg, median (Q1-Q3)	1.4 (1.1-1.8)	2.3 (1.9-2.3)	1.4 (1.1-1.6)	1.4 (1.1-1.8)		1.3-1.7 mg/day
Biotin (Vitamin B7); µg, median (Q1-Q3)	**12.5 (8.8-16.4)**	**19.1 (16.9-22.2)**	**12.2 (8.6-15.7)**	**12.7 (8.1-15.2)**		30 µg/day
Total folate (Vitamin B9); µg, median (Q1-Q3)	**201.9 (164-271.9)**	**342.4 (304.2-356.3)**	**203.9 (171.1-258.9)**	**190.4 (139.4-251.8)**		400 µg/day
Cobalamin (Vitamin B12); µg, median (Q1-Q3)	3.2 (2.3-4.3)	3.4 (3-4)	2.8 (2.2-3.9)	3.8 (2.6-4.5)		2.4 µg/day
Vitamin C; mg, median (Q1-Q3)	88.1 (61.9-116.9)	182.4 (139-218.6)	92.7 (67.7-111.3)	89.5 (77.1-117.7)		85 (F)-105(M) mg/day

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Table 7. A detailed distribution of dysfunctional eating behaviors at baseline

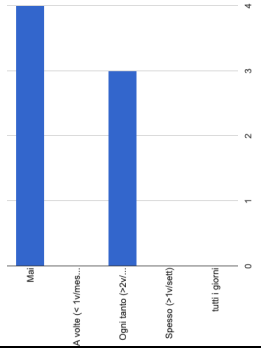
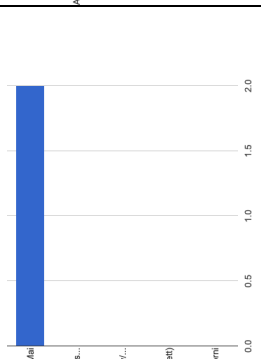
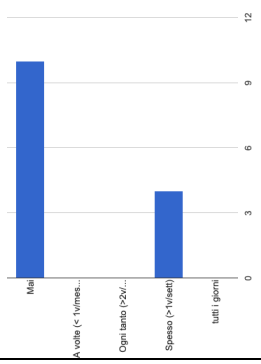
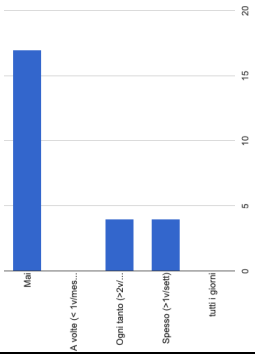
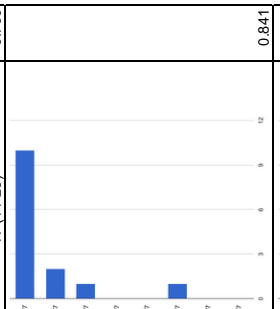
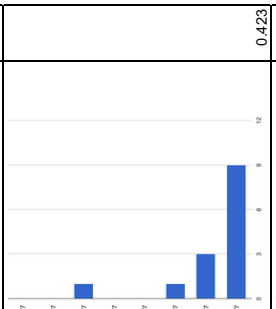
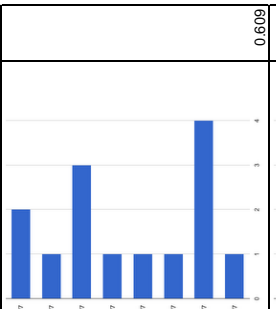
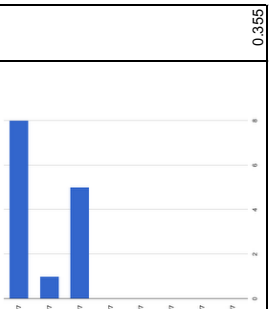
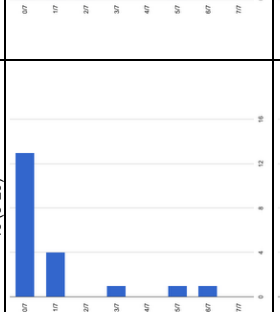
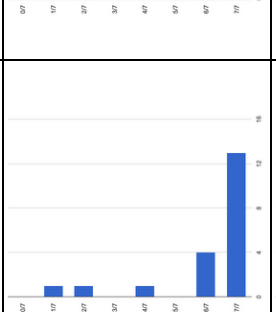
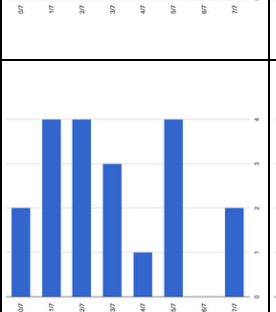
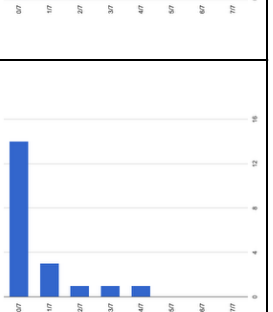
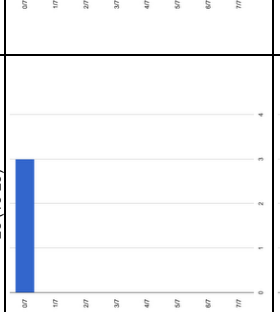
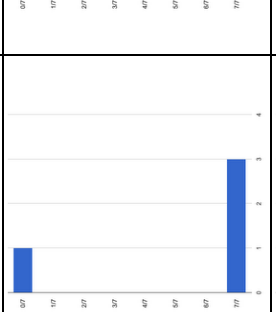
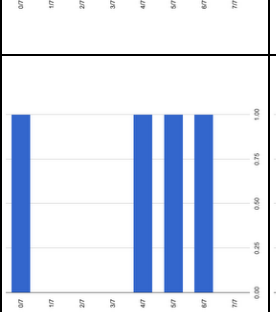
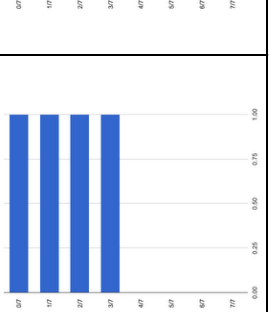
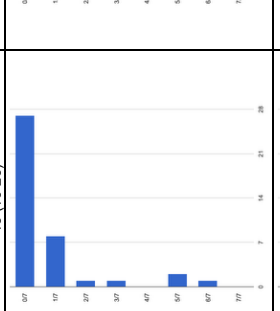
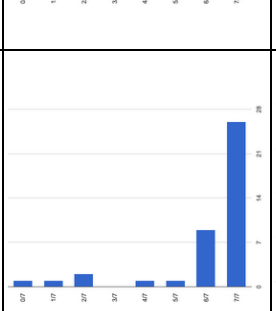
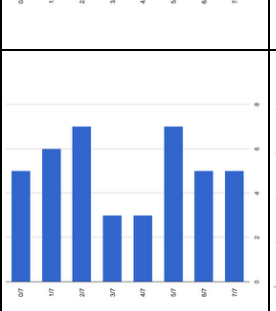
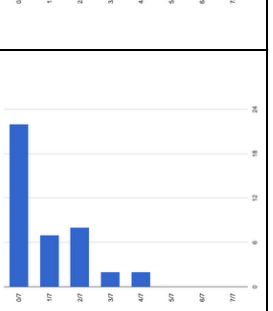
Variable	All (n=41)	F2 (24%)	F3 (44%)	F4 (32%)
Eating behavior				
Disfunctional eating; n, %	25 (61%)	2 (50%)	14 (70%)	7 (50%)
Night eating disorder; n, %				
Nibbling (small amounts of food); n, %				
Emotional Eating; n, %				

Table 8. A detailed distribution of FFQ-derived UPF consumption patterns

Variable	All (n=41)	F2 (24%)	F3 (44%)	F4 (32%)	LEGEND
					Never/rarely
ood Frequency Questionnaire					1–2/week
					3-4/week
					5-6/week
					1/day
					2-3/day
					≥4/day
Sweetened dairy products (e.g., strawberry or vanilla yogurt, milk-based drinks)					
Whole grains (e.g., cooked oatmeal, quinoa, barley, farro) or legumes (e.g., beans, lentils)					
Canned pulses					
Vegetables (fresh or cooked) or fresh salad					
Fruit					
Fish or seafood (fresh or frozen)					
Unsalted nuts (e.g., walnuts, almonds)					
Butter / margarine / lard					
Olive oil (for cooking or dressing)					
Sugar					
Packaged cakes, cookies, pastries					
Sweetened breakfast cereals					
Fried or breaded chicken (ready-to-eat or fast food)					
Ready-to-eat or fast-food meatballs (e.g., hamburgers, kebabs)					
Processed plant-based meat substitutes (e.g., packaged veggie burgers or nuggets)					
Hot dogs / wurstel / sausages					
Cured meats (e.g., salami, mortadella, bacon, speck)					
Ready-to-eat or fast-food items (e.g., pizza, French fries, onion rings, heat-and-eat meals)					
Packaged ice cream, sorbet, popsicles					
Industrial sauces and condiments (e.g., mayonnaise, ketchup)					
Sweet bars (e.g., chocolate bars, energy bars)					
Packaged salty snacks (e.g., pretzels, chips, popcorn)					
Sugar-sweetened beverages (e.g., juices, punch, soft drinks, energy drinks, sweetened iced tea)					
Diet or low-calorie sweetened beverages (e.g., zero or light drinks)					

Table 9. Baseline assessment of UPF Intake

Variable	All (n=41) Baseline	F2 (24%) Baseline	F3 (44%) Baseline	F4 (32%) Baseline	Pvalue
UPF (NOVA 4) intake					
UPF intake: Kcal, median (Q1-Q3)	330 (215-430)	433 (312-560)	285 (199-369)	345 (211-453)	0.550
UPF intake: % of total Kcal, median (Q1-Q3)	22 (15.7-27.7)	19 (13.3-24.5)	20 (14.7-22.7)	26.4 (18.7-30.3)	**0.042**
UPF score (FFQ): n, median (Q1-Q3)	5.4 (4.2-6.9)	8.1 (5.4-10.5)	5.4 (3.3-6.7)	5.1 (4.2-6.6)	0.850
Total weekly UPF: n, median (Q1-Q3)	16 (10-26)	25 (19-29)	16 (9-20)	17 (11-28)	0.760
Number of days with no UPF					0.841
Number of days with at least 1 UPF					0.423
Number of days with at least 3 UPF					0.609
Number of days with at least 5 UPF					0.355

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