T.C.
YEDITEPE UNIVERSITY
INSTITUTE OF HEALTH SCIENCES
DEPARTMENT OF NUTRITION AND DIETETICS

EVALUATION OF THE RELATIONSHIP BETWEEN MALNUTRITION AND SARCOPENIA IN PATIENTS WITH LIVER CIRRHOSIS WHO APPLIED TO THE GASTROENTEROLOGY DEPARTMENT OF UNIVERSITY HOSPITAL IN ISTANBUL

MSc THESIS

MELİKE TUNCER

Istanbul, 2023

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APPROVAL

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Title, Name-Surname

Director of Institute of Health Sciences

DECLARATION

I hereby declare that this thesis is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person nor material which has been accepted for the award of any other degree except where due acknowledgment has been made in the text.

Date
Signature
Name Surname

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LIST OF SYMBOLS AND ABBREVIATIONS

ALD	Alcoholic Liver Disease
BCAA	Branched-chain amino acid
BIA	Bioelectrical impedance analysis
BMI	Body Mass Index
CCM	Cirrhotic cardiomyopathy
CTP score	Child-Turcotte-Pugh Score
HE	Hepatic encephalopathy
HE	Hepatic encephalopathy
ICU	Intensive Care Unit
KFR	Kayser-Fleischer Rings
LFTs	Liver function tests
MELD	Model for end-stage liver disease
NAFL	Nonalcoholic fatty liver
NAFLD	Nonalcoholic fatty liver disease
NASH	Non-alcoholic steatohepatitis
PBK	Primary biliary cholangitis
PEM	Protein- Energy Malnutrition
SD	Standard Deviation

ABSTRACT

Tuncer, M (2023). Evaluation of the relationship between malnutrition and sarcopenia in patients with liver cirrhosis who applied to the gastroenterology department of a university hospital in Istanbul.

Malnutrition and sarcopenia are commonly encountered complications in liver cirrhosis. This study aimed to examine the relationship between cirrhosis-malnutrition-sarcopenia in 75 adult patients, followed up with the diagnosis of cirrhosis in the Gastroenterology outpatient clinic of Istanbul University Cerrahpaşa Medical Faculty. The FRAIL frailty index and the SARC-F sarcopenia index were used in this context. Liver function tests (LFTs) were retrospectively included in the study evaluation process. Based on the specified parameters, a significant relationship was found between muscle strength and body mass index (BMI) ($p<0.05$). In the last 3 months, a significant decrease in appetite and a significant relationship in muscle strength were observed in more than half of the patients in the nutritional status evaluation. At the same time, our study supports the positive correlation between decreased food consumption in liver cirrhosis and malnutrition, and sarcopenia. Especially the relationship between protein intake and sarcopenia is an important parameter revealed in this study. More studies are needed on the effects of dietary habits on liver cirrhosis.

Keywords: Cirrhosis, malnutrition, sarcopenia, liver diseases

ÖZET

Tuncer, M. (2023). İstanbul'da Bir Üniversite Hastanesinin Gastroenteroloji Bölümüne Başvuran Karaciğer Sirozlu Hastalarda Malnütrisyon Ve Sarkopeni İlişkisinin Değerlendirilmesi.

Karaciğer sirozunda malnütrisyon ve sarkopeni oldukça sık rastlanan komplikasyonlardır. Bu çalışmada, İstanbul Üniversitesi Cerrahpaşa Tıp Fakültesi Gastroenteroloji polikliniğinde siroz tanısı ile takip edilen 75 yetişkin hastada siroz-malnutrisyon-sarkopeni ilişkisinin incelenmesi amaçlanmıştır. Bu kapsamda hastalara FRAIL kırılganlık indeksi ve SARC-F sarkopeni indeksi kullanılmıştır. Karaciğer fonksiyon testleri (KCFT) retrospektif olarak çalışma değerlendirme sürecine dahil edilmiştir. Belirtilen parametrelerden yola çıkarak kas gücü ile beden kütle indeksi (BKİ) arasında anlamlı bir ilişki bulunmuştur ($p<0,05$). Son 3 ayda beslenme durum değerlendirilmesinde hastaların yarısından fazlasında belirgin bir iştah azalması ve bununla ilişkili kas gücünde anlamlı ilişki görülmüştür. Aynı zamanda çalışmamız karaciğer sirozundaki azalan besin tüketimi ile malnütrisyon ve sarkopeninin pozitif korelasyonunu desteklemektedir.. Özellikle protein alımı ve sarkopeni ilişkisi bu çalışmada ortaya koyulan önemli bir parametredir. Beslenme alışkanlıklarının karaciğer sirozu hakkındaki etkileri ile ilgili daha çok çalışmaya ihtiyaç vardır.

Anahtar Kelimeler: Siroz, malnutrisyon, sarkopeni, karaciğer hastalıkları

1. INTRODUCTION and PURPOSE

Cirrhosis is a severe form of chronic liver disease that is characterized by liver scarring. Sarcopenia and malnutrition are frequently seen in tandem in cirrhotic individuals and are linked to higher rates of morbidity and mortality. The precise relationship between malnutrition and sarcopenia and the effects of the stage of liver disease on either condition is not entirely understood, despite the fact that sarcopenia is a rather common condition in individuals with cirrhosis.

The overarching aim of this study is to illuminate the subtleties surrounding the coexistence of malnutrition and sarcopenia in the context of cirrhosis. The goal of this study is to understand the prevalence of sarcopenia and malnutrition in a cohort of cirrhotic people as well as their interactions and potential interdependence. The study also seeks to answer the riddle of dietary practices that may be causally related to the onset and progression of sarcopenia in patients with cirrhosis-induced malnutrition.

Through a rigorous investigation of the dietary behavior of cirrhotic patients combined with a comprehensive assessment of sarcopenia parameters, this study aims to shed light on the links between these critical health factors. Additionally, a retrospective analysis of disease and laboratory findings will be performed to gain insights from the historical trajectory of patients' health journeys. By examining these multifaceted aspects together, the study aims to contribute to a deeper understanding of the complex relationships underlying the co-occurrence of malnutrition and sarcopenia in cirrhotic individuals.

2. LITERATURE REVIEW

2.1. Malnutrition

The concept of malnutrition is generally evaluated as protein and/or calorie (protein-energy) malnutrition. However, inappropriate calorie intake due to obesity or vitamin toxicity can also cause malnutrition (1). The loss of more than 10% of body weight in the last 6 months can be used to identify malnutrition status, and many nutritional scoring systems are also practical in this regard. Subjective Global Assessment (SGA), Nutritional Risk Index (NRI), Mini Nutritional Assessment (MNA), the Malnutrition Universal Screening Tool (MUST), and Nutritional Risk Score (NRS-2002) are widely accepted diagnostic scales. In the elderly, diseases are the most important cause of malnutrition; as age advances, acute and chronic diseases increase, leading to a higher prevalence of these diseases (2).

On the other hand, this imbalance can also be due to insufficient food intake despite food being adequately available. Malnutrition is a major problem with significant biological, psychological, social, and economic consequences (3). Malnutrition manifests itself through weight loss and loss of muscle density (sarcopenia), resulting in decreased resilience in the elderly, increased risk of falls and hip fractures, more extended recovery periods in such cases, increased susceptibility to infections, delayed wound healing, and increased pressure ulcers (3,4).

2.1.1. Screening For Malnutrition

There is still no agreed-upon definition of malnutrition despite continuous discussion. To create malnutrition criteria that could be applied globally in all clinical settings, the four top clinical nutrition societies in the world (ESPEN, ASPEN, FELANPE, and PENSA) began a consensus process in 2016. These societies collectively represent more than 70 national scientific societies. Reduced muscle mass (based on validated body composition techniques), low body mass index (BMI) (20 kg/m^2 if 70 years old, or 22 kg/m^2 if >70 years old), and two etiologic criteria: decreased food intake or assimilation (50% of energy requirements for >1 week, any reduction for >2 weeks, or any chronic gastro-intestinal condition that adversely affects assimilation) (5).

2.1.2. Micronutrient Deficiencies

Micronutrient deficits are one type of malnutrition that affects elderly persons frequently. The causes of insufficient micronutrient consumption range from low food intake to, typically, poor food selection and a lack of variety. Prices and availability of foods high in vitamins, minerals, and trace elements may cause people to consume fewer micronutrients. On the other side, as people get older, changes occur that make it easier for people to become deficient in critical minerals, including calcium, vitamin D, vitamin B12, iron, magnesium, and zinc. Due to the expenses and difficulties, large investigations on the micronutrient serum status in older persons are uncommon (6).

2.1.3. Protein Energy Malnutrition

Protein-energy malnutrition (PEM) can be categorized into two main types: primary and secondary. Primary PEM occurs when there is inadequate intake of protein and/or calories, or less commonly, inadequate intake of essential amino acids, resulting in the inability to sustain normal metabolism. Secondary PEM, on the other hand, refers to malnutrition that develops due to illness or injury (6, 7). In cases of acute illness and injury, there is increased demand for protein and energy, inadequate intake due to loss of appetite, as well as insufficient digestion, absorption, and utilization of nutrients (7).

Restoration of muscle mass through nutritional support is not possible unless the underlying inflammatory process is addressed. In cases of disease-related catabolism, changes in energy-protein metabolism result in the redistribution of amino acids from the somatic compartment to the visceral compartment, primarily influenced by cytokines such as IL-1, TNF-alpha, IL-6, and IF-gamma. On the other hand, conditions like cancer cachexia have a different etiology due to the influence of disease-specific humoral mediators (e.g., proteolysis-inducing factor and lipid mobilizing factor) (8).

Elderly people who live at home may be more at risk for malnutrition if they use homecare services and reside in rural areas. Compared to men, females are far more likely to suffer from malnutrition (9).

The situation is slightly different in undernourished children during the growth and development period. The three main clinical presentations are Kwashiorkor, marasmus, and nutritional dwarfism. These conditions can also present with overlapping clinical features. Marasmus is characterized by significant weight loss and subcutaneous fat tissue and muscle mass loss. Kwashiorkor is distinguished by peripheral edema and characteristic skin and hair changes. The abdomen is prominent due to abdominal muscle weakness, distension, and hepatomegaly. Nutritional dwarfism refers to individuals who appear stunted despite a normal weight-to-height ratio and may have inadequate sexual development. They can return to normal with nutritional support. Marasmus and kwashiorkor can also occur in adults (10). Malnutrition affects 30-60% of hospitalized patients, with 10-25% being severely malnourished. A study found a higher mortality rate among PEM patients admitted to the hospital with diabetic ketoacidosis compared to non-PEM patients. Additionally, PEM patients had higher rates of complications, comorbidities, and a higher prevalence of the Charlson Comorbidity Index ≥3 (8). Malnutrition is observed in respiratory system diseases in 45% of cases, inflammatory bowel diseases in 80% of cases, and up to 85% of cases in individuals with malignancies (11).

The frequency of malnutrition varies among geographical regions, but it was not anticipated by national social and economic development. Elderly people who live at home may be more at risk for malnutrition if they use homecare services and reside in rural areas. Compared to men, females are far more likely to suffer from malnutrition (11).

2.1.4. Nutritional Deficiencies and Body Mass Index

BMI, often known as body mass index, is frequently used as a screening measure for obesity or overweight (12). The BMI, commonly known as Quetelet's Index, is calculated by dividing the weight in kilograms by the square of the height in meters. Diagnosing malnutrition in obese patients is quite challenging. To determine the development of malnutrition in a patient, nutrition and nutritional status assessment should be conducted (12). The most common methods of dietary assessment include 24/48-hour dietary recall, etc. The detection of malnutrition also relies on the following: anthropometric measurements, blood biochemical tests, and physical parameters. An important aspect in assessing nutritional status and diet is dietary assessment, which is

consumed by obese patients. Paradoxical malnutrition is defined as a state of nutritional deficiency associated with individual micronutrient insufficiency despite excessive energy consumption. Deficiency in essential micronutrients or lack of homeostasis can significantly affect daily performance, intellectual and emotional states, as well as physical condition (13). Nutritional deficiencies related to obesity may partially stem from excessive food intake, where a high-calorie but low-nutrient-dense diet pattern can contribute to such an issue (14). This phenomenon is most prevalent in developed countries. It is crucial to understand that obese patients can also be malnourished and prone to diseases like groups of patients with cachexia. Malnutrition has been shown to alter the course of the disease. The difficulty lies in improving the ability of common malnutrition screening and assessment techniques to detect malnutrition in obese patients. The most effective methods or biomarkers with clinical applicability for detecting malnutrition in the hospitalized obese and non-obese population require more study. Instead of utilizing BMI alone for outcome studies, additional criteria that truly indicate adiposity should be investigated in future research. There is not enough information available to draw broad generalizations about obesity and its outcomes. Future research on obese populations must first take nutritional status into account before thoroughly examining the obesity conundrum (15).

2.1.5. Treatment

While providing nutritional support, two main goals are considered: restoring cellular functions in the short term and replacing lost tissues in the long term. The decision of which patients require immediate nutritional support is evaluated using various criteria such as SGA, NRI, MNA, MUST, NRS-2002, etc. It is generally accepted as a treatment protocol to provide rapid nutritional support intervention in patients with acute illness and moderate to severe malnutrition (16). Serum visceral proteins such as albumin and prealbumin have traditionally been used to indicate patients' nutritional status (16). Regardless of the etiological cause, individuals with severe malnutrition, in addition to protein, fat, and glycogen, should also receive supplementation of elements such as potassium, phosphate, magnesium, zinc, selenium, as well as vitamins such as A, E, C, thiamine, pyridoxine, and riboflavin (17).

In cases of severe malnutrition, pancreatic secretory insufficiency, intestinal mucosal atrophy in the small and large intestine, and consequently, malabsorption and maldigestion can occur (18).

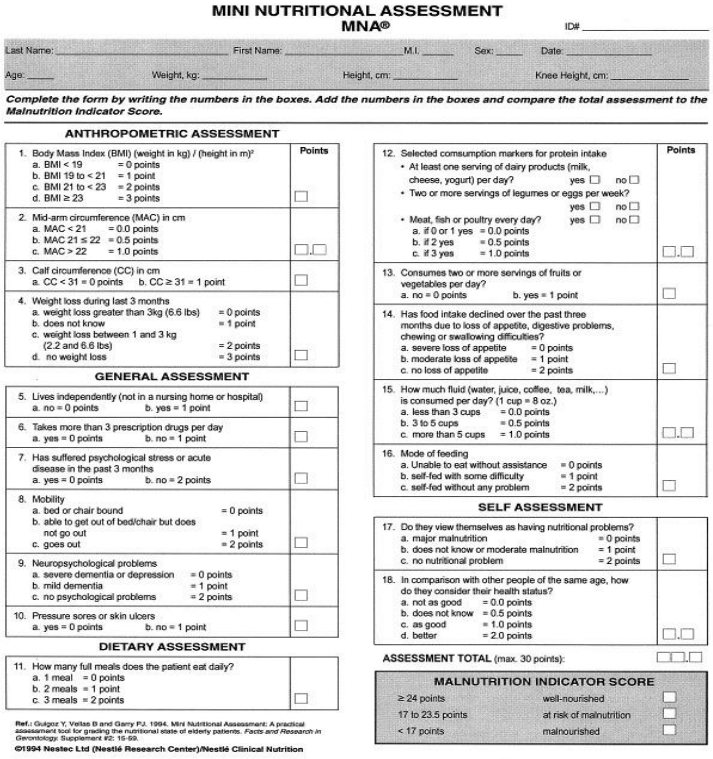
Refeeding syndrome is a life-threatening syndrome that occurs due to electrolyte and metabolic disturbances accompanying the start of refeeding after prolonged starvation or inadequate nutrition (19).

Patients who are gradually and cautiously initiated into nutrition should be evaluated to determine whether they can receive oral, enteral, or parenteral feeding. This route should be preferred if the patient is capable of oral intake. Potassium, magnesium, and phosphate replacement may be necessary to restore the patient's disturbed electrolyte balance. Support for water-soluble vitamins may be required. Despite normal intestinal function, enteral nutrition through a feeding tube placed in the stomach or jejunum may be necessary for some patients due to deficiencies in eating and swallowing functions. The patient's total energy requirement is achieved gradually over several days, following the "Refeeding Nutrition Protocol" (19, 20). Standard enteral nutrition products are designed to meet basic needs in terms of electrolytes, minerals, and trace elements, so additional monitoring may be required to bridge any gaps or meet the daily requirements in full (20).

When gastrointestinal dysfunction prevents oral or enteral feeding, parenteral nutrition is generally considered necessary. Additional salt, water, potassium, and phosphate are administered to address vomiting, diarrhea, or fistulas. The usual target energy intake is 35 kcal/kg/day, and the target protein intake is 1.5 g/kg/day (21). Malnourished patients typically progress in identifying their malnutrition status not only through clinical signs of malnutrition but also through worsening disease conditions. Hypermetabolism and malnutrition are common in intensive care patients, and nutritional therapy should be carefully managed, considering the frequency of malnutrition occurrence. On the other hand, each patient category, such as septic patients, inflammatory bowel disease patients, liver and kidney failure patients, pancreatitis patients, short bowel syndrome patients, diabetic patients, burn patients, cancer patients, patients with cardiac and pulmonary problems, neurological patients, AIDS patients, pregnant patients, children, and adolescents, should be approached individually (22). While providing nutritional support, it should not be forgotten that this intervention only

addresses one aspect of patient needs, and the main disease and accompanying conditions should be managed with equal care.

Table 2.1. Mini Nutritional Assessment



MINI NUTRITIONAL ASSESSMENT
MNA®

ID# _____

Last Name: _____ First Name: _____ M.I. _____ Sex: _____ Date: _____

Age: _____ Weight, kg: _____ Height, cm: _____ Knee Height, cm: _____

Complete the form by writing the numbers in the boxes. Add the numbers in the boxes and compare the total assessment to the Malnutrition Indicator Score.

ANTHROPOMETRIC ASSESSMENT

	Points
1. Body Mass Index (BMI) (weight in kg) / (height in m)² a. BMI < 19 = 0 points b. BMI 19 to < 21 = 1 point c. BMI 21 to < 23 = 2 points d. BMI ≥ 23 = 3 points	☐
2. Mid-arm circumference (MAC) in cm a. MAC < 21 = 0.0 points b. MAC 21 ≤ 22 = 0.5 points c. MAC > 22 = 1.0 points	☐.☐
3. Calf circumference (CC) in cm a. CC < 31 = 0 points b. CC ≥ 31 = 1 point	☐
4. Weight loss during last 3 months a. weight loss greater than 3kg (6.6 lbs) = 0 points b. does not know = 1 point c. weight loss between 1 and 3 kg (2.2 and 6.6 lbs) = 2 points d. no weight loss = 3 points	☐

GENERAL ASSESSMENT

5. Lives independently (not in a nursing home or hospital) a. no = 0 points b. yes = 1 point	☐
6. Takes more than 3 prescription drugs per day a. yes = 0 points b. no = 1 point	☐
7. Has suffered psychological stress or acute disease in the past 3 months a. yes = 0 points b. no = 2 points	☐
8. Mobility a. bed or chair bound = 0 points b. able to get out of bed/chair but does not go out = 1 point c. goes out = 2 points	☐
9. Neuropsychological problems a. severe dementia or depression = 0 points b. mild dementia = 1 point c. no psychological problems = 2 points	☐
10. Pressure sores or skin ulcers a. yes = 0 points b. no = 1 point	☐

DIETARY ASSESSMENT

11. How many full meals does the patient eat daily? a. 1 meal = 0 points b. 2 meals = 1 point c. 3 meals = 2 points	☐

	Points
12. Selected consumption markers for protein intake • At least one serving of dairy products (milk, cheese, yogurt) per day? yes ☐ no ☐ • Two or more servings of legumes or eggs per week? yes ☐ no ☐ • Meat, fish or poultry every day? yes ☐ no ☐ a. if 0 or 1 yes = 0.0 points b. if 2 yes = 0.5 points c. if 3 yes = 1.0 points	☐.☐
13. Consumes two or more servings of fruits or vegetables per day? a. no = 0 points b. yes = 1 point	☐
14. Has food intake declined over the past three months due to loss of appetite, digestive problems, chewing or swallowing difficulties? a. severe loss of appetite = 0 points b. moderate loss of appetite = 1 point c. no loss of appetite = 2 points	☐
15. How much fluid (water, juice, coffee, tea, milk,...) is consumed per day? (1 cup = 8 oz.) a. less than 3 cups = 0.0 points b. 3 to 5 cups = 0.5 points c. more than 5 cups = 1.0 points	☐.☐
16. Mode of feeding a. Unable to eat without assistance = 0 points b. self-fed with some difficulty = 1 point c. self-fed without any problem = 2 points	☐

SELF ASSESSMENT

17. Do they view themselves as having nutritional problems? a. major malnutrition = 0 points b. does not know or moderate malnutrition = 1 point c. no nutritional problem = 2 points	☐
18. In comparison with other people of the same age, how do they consider their health status? a. not as good = 0.0 points b. does not know = 0.5 points c. as good = 1.0 points d. better = 2.0 points	☐.☐

ASSESSMENT TOTAL (max. 30 points): ☐☐.☐

MALNUTRITION INDICATOR SCORE	
≥ 24 points	well-nourished ☐
17 to 23.5 points	at risk of malnutrition ☐
< 17 points	malnourished ☐

Ref.: Guigoz Y, Vellas B and Garry PJ. 1994. Mini Nutritional Assessment: A practical assessment tool for grading the nutritional state of elderly patients. *Facts and Research in Gerontology.* Supplement #2. 15-59.

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Source: Vellas, B., Guigoz, Y., Garry, P. J., Nourhashemi, F., Bennahum, D., Lauque, S., & Albarede, J. L. The Mini Nutritional Assessment (MNA) and its use in grading the nutritional state of elderly patients. Nutrition (Burbank, Los Angeles County, Calif.), 1999, 15(2), 116–122. https://doi.org/10.1016/s0899-9007(98)00171-3

2.2. Sarcopenia

Reduced skeletal muscle mass, reduced muscle strength, and/or diminished physical performance are characteristics of sarcopenia. Although primarily considered a geriatric syndrome, known causes of sarcopenia include chronic diseases, low physical activity, and inadequate nutrition (23). Physical inactivity, decreased mobility, sluggish walking, and limited physical stamina are frequently present in sarcopenia. Multiple factors play a role in the development of sarcopenia, including muscle mass and fiber loss, increased inflammation, changes in hormonal levels, poor nutritional status, and impaired renin-angiotensin system (23). Diagnosis requires measurements of muscle strength (handgrip strength), muscle mass, and physical performance assessment, such as walking speed (24). The prevalence of sarcopenia has been found to be 14% in men under

70 years, 20% in men aged 70-74, 27% in men aged 75-80, and 53% in men over 80 years old (24). Due to its high prevalence, sarcopenia leads to adverse outcomes such as physical disability, dependency, reduced quality of life, and increased mortality, resulting in significant personal and financial costs.

2.2.1. Categories of Sarcopenia

There are several factors contributing to the development of sarcopenia, including the aging process itself, nutritional deficiencies, immobility/sedentary lifestyle, chronic diseases, low physical activity, and the use of multiple medications (25). In some individuals, a single clear cause can be identified for sarcopenia. Sarcopenia is categorized as either primary or secondary.

Stages of Sarcopenia:

The European Working Group on Sarcopenia in Older People (EWGSOP) has classified sarcopenia into three stages:

- Presarcopenia: Muscle strength and physical performance are not affected, but there is a decrease in muscle mass.
- Sarcopenia: There is a decrease in muscle mass along with a reduction in muscle strength or performance.
- Severe sarcopenia: There is a decline in muscle mass, muscle strength, and performance (26).

Diagnosis of Sarcopenia: Diagnosing sarcopenia requires the evaluation of muscle mass, muscle strength, and physical performance. The diagnosis of inadequate nutrition relies on parameters such as clinical history (e.g., weight loss, activity level, disease-specific symptoms such as early satiety), physical examination (focused on muscle mass loss), body mass index (BMI) (e.g., $<18.5\ kg/m^2$), dietary intake (solid and liquid intake), laboratory findings, and global assessment tools (e.g., Subjective Global Assessment [SGA], Royal Free Hospital-Subjective Global Assessment [RFH-SGA]) (25, 26).

2.2.2. Relationship Between Sarcopenia And Disease

A clinically substantial number of patients with kidney disease have been observed to have sarcopenia, an important clinical disease that has been linked to a higher

mortality risk. However, the clinical heterogeneity brought on by various sarcopenia diagnostic thresholds, evaluation techniques, and diagnostic criteria is significant. Effective diagnostic criteria are essential for the quick detection of sarcopenia in patients, increasing patient outcomes and lessening the financial and social burdens associated with healthcare.

Sarcopenia and an elevated risk of falls are caused by a lack of muscle mass and/or strength in senior people with obesity or urinary tract problems.

Obesity is associated with a higher risk of fragility, impairment in daily living activities, and cognitive and nutritional impacts. Therefore, evaluating the patient's strength and mass and implementing the necessary therapies are especially important in geriatric practice to safeguard the patients' functionality (27). On the other hand, the loss of muscle mass in the group of patients with cardiovascular disease and cancer cachectic has a negative impact on the progression of the main illness.

2.2.3. Treatment Approach for Sarcopenia

The treatment of sarcopenia involves exercise and physical activity, hormonal therapy, nutritional therapy, and recently, angiotensin-converting enzyme (ACE) inhibitors have also been used (28).

2.2.4. Medical Nutrition Therapy in Sarcopenia

Sarcopenia, which causes a decline in muscle function, has been linked to malnutrition, especially in older people with low body weight (29). Skeletal muscles require energy for motor activity. An inadequate energy supply leads to weakness in muscle fibers due to impaired energy metabolism in the mitochondria. Prolonged fasting results in muscle tissue loss. Decreased energy intake is associated with changes in taste and smell perception, alterations in hormone levels, and slowing of the gastrointestinal system, which occurs with aging. Furthermore, other factors contributing to decreased energy intake in older adults include chewing difficulties, social isolation, and depression. These can lead to health problems and even malnutrition in older individuals (30).

The consumption of protein has been linked favorably to the maintenance of muscle mass, according to epidemiological studies (31). Dietary protein provides the necessary amino acids for the synthesis of muscle proteins, which directly affect protein

synthesis and function as anabolic stimuli. In a study, older individuals who consumed 0.8 g/kg/day of protein exhibited 40% less muscle mass loss compared to those who consumed 0.5 g/kg/day of protein (19). Another study determined that increasing protein intake from 0.8 g/kg/day to 1.0 g/kg/day in older adults was the minimum amount required to preserve muscle mass (31). It is recommended to achieve a daily protein intake of 1.2 g/kg/day in individuals with normal kidney function and no other contraindications (32).

Additionally, the type of protein is also crucial in increasing muscle strength. Other studies evaluated the effect of protein type on muscle strength and found that individuals who consumed the same amount of animal protein had higher muscle strength compared to those who consumed plant protein (33). To optimize protein synthesis, it is recommended to distribute protein intake evenly across three main meals (34). Branched-chain amino acids (BCAAs), especially leucine, have been shown to enhance skeletal muscle protein synthesis and reduce muscle loss, particularly in athletes (34). Vitamin D levels decrease with age. A meta-analysis of randomized controlled trials demonstrated a 19% reduction in falls in older individuals who consumed at least 700 IU of vitamin D daily. A study observed an oral nutritional supplement enriched with vitamin D and leucine-rich whey protein concentrate over a 13-week intervention period. The study found improvements in muscle mass and lower extremity function in sarcopenic older adults after supplementation with vitamin D and leucine (35).

Essential vitamins and minerals can contribute to the treatment of sarcopenia by preventing age-related muscle mass loss, decreased muscle strength, and impaired physical performance. Additionally, it is suggested that oxidative stress involving free radicals may play a role in the pathogenesis of sarcopenia. Therefore, the administration of antioxidants such as selenium, vitamin E, and vitamin C has been recommended in sarcopenia treatment (36).

2.3. Functions of the Liver

The liver is situated in the upper right part of the abdominal cavity, above the stomach and intestines, and below the diaphragm. It consists of two lobes, the right and left lobes. It is the largest glandular organ in the body and the second largest organ overall, following the skin. The liver exhibits both exocrine and endocrine functions and is surrounded by a fibrous capsule. It constitutes approximately 2.5% of the body weight, with an average weight of around 1600 grams in males and 1300 grams in females (37). The liver secretes bile, approximately 700 to 1200 ml per day, to aid in intestinal digestion (38).

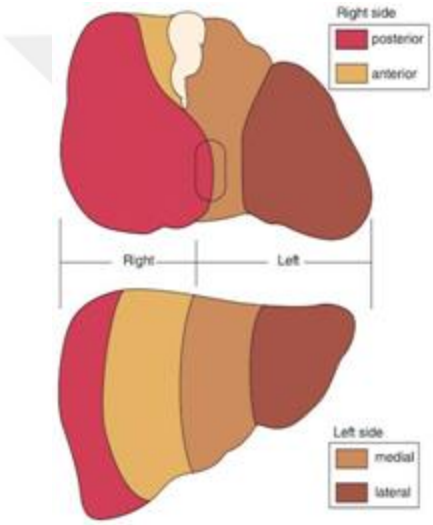

Figure 2.1. The Diagram İllustrates The Different Sectors Of The Human Liver

Source: Dooley, J. S., Lok, A. S., Garcia-Tsao, G., & Pinzani, M. (Eds.). Sherlock's diseases of the liver and biliary system. John Wiley & Sons, 2018.

The liver is a versatile and vital organ that plays a role in many metabolic functions of the body. It requires approximately 10-20% of the liver to be functional for it to carry out its duties (38).

The liver is largely in charge of several metabolic processes. It plays a crucial biochemical role in detoxification, storage, secretion, digestion, synthesis, elimination, erythropoiesis, homeostasis, and other metabolic functions. Its functions can be broadly categorized into four main areas: blood storage, blood purification, metabolic functions, and storage of vitamins and minerals (38).

In terms of metabolic functions, the liver maintains blood glucose levels within specific ranges through carbohydrate metabolism. It is involved in protein metabolism through processes such as transamination, oxidative deamination, synthesis of non-essential amino acids, and conversion to substrates used for energy production. Additionally, the liver converts ammonia into urea, a byproduct of amino acid deamination. The liver also plays a significant role in fat metabolism, including synthesizing triglycerides, phospholipids, cholesterol, and lipoproteins (39).

The liver is an important organ for bile production and secretion. Bile is synthesized by hepatocytes and stored in the gallbladder. When needed, bile is released into the small intestine, where it aids in the digestion of lipids, transportation of cholesterol, and absorption and elimination of metabolic waste and drugs. It secretes 250-1100 mL of bile per day (40).

Overall, the liver is a vital organ with many metabolic functions essential for maintaining homeostasis and overall health (40).

2.4. Liver Function Tests

Liver function tests (LFTs) are biochemical measurement parameters used to assess cell damage or cholestasis in the liver. A single test is insufficient for this evaluation, so these tests are collectively referred to as LFTs (41).

LFTs are important parameters used to determine abnormal findings, the specific metabolic pathway involved, and the severity of the disease in liver diseases. They include tests based on the detoxification and elimination functions of the liver, tests that provide information about the liver's biosynthetic function, clotting factors, and other diagnostic tests. According to WHO data, liver disease-related deaths in Turkey account for 1.52% of total deaths (42).

2.5. Classification of Liver Diseases and Nutritional Therapy

2.5.1. Medical Nutrition Therapy in Liver Diseases

The liver is a vital organ involved in many metabolic functions. Nutrition plays a significant role in certain liver diseases, whether chronic or acute. When appropriate conditions are provided, a proper dietary model for the disease can positively alter the

course of the disease or be implemented in the treatment protocol. This topic will be discussed in detail in the following pages.

2.5.2. Classification of Liver Diseases

Liver diseases can be classified based on various factors:

• Classification (acute, chronic)

• Pathophysiology (hepatocellular, cholestatic)

• Stage (end-stage liver failure, cirrhosis)

• Etiology (viral, alcohol-related, toxin-induced, autoimmune)

These factors help categorize liver diseases based on their nature, progression, and underlying causes.

2.5.2.1. Non-Alcoholic Fatty Liver Diseases (NAFLD)

Non-alcoholic fatty liver disease refers to a range of liver diseases encompassing steatosis and steatohepatitis, which can progress to cirrhosis (43). It is often considered in patients with asymptomatic elevation of liver enzymes, radiological evidence of liver fat accumulation, or idiopathic hepatomegaly (44). Diagnosis criteria exclude alcohol intake of 30 grams or more per day for men and 20 grams or more per day for women. Non-alcoholic steatohepatitis (NASH) is classified under the concept of "non-alcoholic fatty liver disease (NAFLD)." NAFLD has a worldwide prevalence of around 25% and is one of the most common liver diseases (45). It is primarily associated with obesity, type 2 diabetes, hyperlipidemia, and insulin resistance (45).

2.5.2.2. Non-Alcoholic Steatosis

Non-alcoholic steatosis refers to the condition where more than 5% of the liver weight is composed of fat in individuals who do not consume alcohol. It is the most easily reversible disease with medical nutrition therapy (46). Based on clinical and ultrasonographic findings, NAFLD can be categorized into four stages: steatosis, non-alcoholic steatohepatitis (NASH), liver fibrosis, and cirrhosis. The histopathological classification includes Type 1: the presence of only steatosis without inflammatory

infiltration, Type 2: steatosis + lobular inflammatory infiltration, Type 3: steatosis + hepatocyte ballooning (transition to fibrosis), and Type 4: steatosis + hepatocyte ballooning + fibrosis or Mallory bodies (47). Non-invasive methods such as FibroScan® (Echosens, Paris, France) assist in determining the extent of fibrosis (48).

2.5.2.3. Non-Alcoholic Steatohepatitis (NASH)

The second stage of the condition is called simple fatty liver or Non-alcoholic steatosis (NASH). The inflammatory subtype of non-alcoholic fatty liver disease (NAFLD), known as NASH, is characterized by inflammation, Mallory bodies, megamitochondria, and, in some cases, fibrosis in addition to the accumulation of fat in liver cells. Cirrhosis development and the requirement for liver transplantation are linked to the disease's progression (49).

2.5.2.4. Non-Alcoholic Fatty Liver Disease and Medical Nutrition Therapy

Non-alcoholic fatty liver disease (NAFLD) and its medical nutrition therapy have gained more attention due to the increasing prevalence and understanding of its pathophysiology. Although there is no standard protocol, the treatment approach aims to address commonly associated secondary conditions such as obesity, type 2 diabetes, insulin resistance, and hyperlipidemia (50). The main principles focus on weight loss, increasing physical activity through lifestyle changes, improving insulin sensitivity, and supporting dyslipidemia treatment with antioxidants such as vitamin E. In managing fatty liver disease, a weight loss of 10% of body weight should be achieved, with the majority of weight loss coming from fat while preserving muscle mass (50). Vitamin E, with its anti-obesity, hypoglycemic, and hypocholesterolemic properties, is believed to have an impact on the favorable clinical course of NAFLD and continues to be investigated (51). Silymarin, the main component of milk thistle (Silybum marianum), has been studied in relation to NAFLD. In one study, consumption of an optimal amount of Silymarin resulted in improvements in glucose and lipid profiles and reduced fibrosis, inflammation, and oxidative stress in a patient with NASH (52).

2.5.3. Alcoholic Liver Disease (ALD)

Alcoholic liver disease (ALD) refers to conditions that are brought on by excessive alcohol intake that harm the liver and its functions. Alcoholic beverages contain

ethanol, which, when processed by the liver, causes fat to accumulate in liver cells (53). Fatty liver disease, alcoholic hepatitis, steatohepatitis, and chronic hepatitis with fibrosis or cirrhosis are a few diseases that can manifest (53). Despite being connected to alcohol, the etiology involves extremely complex and harmful pathways, such as immune cells, adipose tissue, and genetic variety (54).

a) Alcoholic Steatosis (Fatty Liver)

Alcoholic steatosis is the most common type of liver disease associated with alcohol consumption. The liver has now become fat due to alcohol-related liver damage. Taking more than 20 grams of alcohol each day for an extended period of time usually results in a fatty liver. The likelihood of developing fatty liver depends on how much alcohol is consumed; for example, consuming more than 60 grams of alcohol per day increases the risk in more than 90% of persons. Usually, the condition progresses asymptomatically (55). Hepatomegaly, abnormal liver function tests, and ultrasound results are all examples of useful diagnostic criteria. It is essential to avoid drinking alcohol, adhere to a healthy diet, and engage in regular exercise in order to treat this stage of the ailment. For obese or slightly overweight individuals, reaching the target weight is a goal in the treatment protocol, but specialized medical care is often not provided (56).

b) Alcoholic Hepatitis

The second stage of the disease is alcoholic hepatitis, a severe form of the disease. In addition to fat accumulation in the liver, inflammation (swelling of liver cells) also occurs. It often presents as an acute illness. Symptoms in these patients may include loss of appetite, fever, jaundice, nausea, vomiting, weight loss, accumulation of fluid in the abdomen (ascites), and impaired consciousness (encephalopathy) (57). In severe cases, the risk of death reaches 50%, and more than 50% of surviving patients develop cirrhosis if they consume alcohol. Malnutrition is observed in most advanced cases of alcoholic hepatitis.

Many individuals with acute alcoholic hepatitis need nutritional care because they are malnourished. In a study that evaluated the nutritional status of 284 patients with alcoholic hepatitis using a thorough nutritional assessment, signs of severe protein-calorie malnutrition (such as hypoalbuminemia and edema) and tissue wasting were seen in nearly all of the patients (58).

Initiating nutritional support for patients aims to give them enough calories and protein in addition to the replacement of vitamins and minerals (59). It is crucial to emphasize that patients with prolonged prothrombin times typically get vitamin K, but this treatment is frequently ineffective since coagulopathy is more often a symptom of underlying liver insufficiency than a vitamin K shortage. Parenteral treatment may be chosen for these patients because oral vitamin K absorption is insufficient (59).

c) Alcoholic Cirrhosis

Long-term use of alcohol leads to fibrosis (hardening) of the normal liver tissue, followed by the progression of the disease and the development of cirrhosis. The process slows down and/or the worsening of the condition may decrease when alcohol is discontinued. Studies have shown that 80-100% of patients with alcoholic cirrhosis develop protein-energy malnutrition (60).

d) Nutritional Treatment of Alcoholic Cirrhosis

The aim is to address the underlying causes of the disease and prevent or treat complications. In the initial stage, medical nutritional therapy is achieved by completely discontinuing alcohol and avoiding toxic foods. The prothrombin time (PT) prolongs to 11-15 seconds. Monitoring of ALT, AST, albumin, alkaline phosphatase, total bilirubin, and ammonia levels is important to assess the liver's response and detect damage.

It is crucial to highlight that although I am an AI language model and may offer basic advice, it is always advised to seek the opinion of a medical expert or a certified dietician for individualized guidance and treatment suggestions for certain illnesses like alcoholic cirrhosis (61).

2.6. Cirrhosis

2.6.1. Liver cirrhosis

Hepatic fibrosis/cirrhosis is a significant global health problem that can result in liver failure or hepatocellular carcinoma (HCC) and causes numerous deaths each year (62). According to the World Health Organization (WHO), liver cirrhosis is "a widespread change characterized by fibrosis and the replacement of normal structure with abnormal nodules, which extensively involves the liver" (62). The term "cirrhosis," derived from

the Greek word "kirrhos," meaning "tawny or yellowish-brown," was coined by Laennec to describe the condition as a state where the liver is shrunk to about one-third of its normal size, has an orange appearance, is covered with nodules of varying sizes that can be distinguished from each other, and has hardened (63).

Various socioeconomic and cultural factors influence the etiology of cirrhosis. Alcohol intake is the leading contributor to liver cirrhosis in Western nations (64).

When sudden damage occurs in the liver, liver cells are lost, but the cells have a rapid regenerative capacity, and fibrosis or scarring does not occur. However, when the damaging factor is continuous or repetitive, scar tissue begins to accumulate in the liver as part of the cycle of cell death and regeneration. As scar tissue affects a certain amount of the liver, the organ becomes unable to perform some of its functions over time and becomes hardened. Among the chronic liver diseases that can progress to cirrhosis due to prolonged damage in the liver, viral hepatitis (hepatitis B, hepatitis C, hepatitis D), alcohol-related liver disease, and fatty liver disease are among the leading causes (64, 65).

The asymptomatic phase of cirrhosis progresses to a symptomatic decompensated phase, which is marked by the emergence of ascites, hemorrhage, encephalopathy, and jaundice. A liver transplant is necessary or fatal for patients who get into the symptomatic decompensated phase too quickly (65).

Approximately 5-7% of patients with compensated cirrhosis transition to the symptomatic decompensated phase annually (66). Steatosis, alcoholic hepatitis, and fibrosis are the three pathological features associated with the highest risk of progression to cirrhosis in patients with alcoholic hepatitis (66). When cirrhosis progresses to the decompensated stage, it becomes a systemic disease, and multiple organ and system dysfunctions develop. In the treatment approach to cirrhosis, two main strategies are employed: suppression of etiological causes and interventions aimed at preventing decompensation and progression of the underlying pathogenesis (67). The staging of cirrhosis often involves the Child-Pugh scoring system and the Model for End-Stage Liver Disease (MELD) score, which is automatically calculated based on total bilirubin, creatinine, and the international normalized ratio (INR) values and is used for liver transplantation prioritization (67, 68). Recent studies have shown that in advanced-stage

cirrhosis, systemic inflammation due to circulatory disturbances plays a role, and appropriate treatment can improve quality of life, prolong survival, and reduce healthcare expenses (68, 69).

2.6.2. Etiology of Liver Cirrhosis

Early implementation of specialized treatments that target the etiology delays the transition to the decompensated phase and the onset of complications in any phase of cirrhosis, increasing survival. These advantages are specifically provided by stopping drinking in cases of alcoholic cirrhosis, viral suppression in hepatitis B and C, and immunosuppressive medication in cases of autoimmune hepatitis. Due to the more complicated pathophysiology, these effects fluctuate in the decompensated phase even though they are more evident in the compensated phase (69). Therefore, when a diagnosis of cirrhosis is made, the first step is to investigate the etiology (Table 2.2).

Table 2.2. Major Etiological Causes Of Cirrhosis

1. Chronic hepatitis a. Viral hepatitis (B, C, D) b. Autoimmune hepatitis
2. Alcohol-related cirrhosis
3. Biliary diseases
a. Primary and secondary biliary cirrhosis b. Primary sclerosing cholangitis
4. Drug- and toxin-induced cirrhosis
5. Cirrhosis associated with inherited metabolic disorders a. Hemochromatosis b. Wilson's disease c. Galactosemia d. Alpha-1 antitrypsin deficiency e. Type IV glycogen storage disease f. Galactosemia g. Tyrosinemia h. Cystic fibrosis
6. Venous outflow obstruction a. Veno-occlusive disease b. Budd-Chiari syndrome
7. Heart failure a. Right-sided heart failure b. Constrictive pericarditis c. Tricuspid valve insufficiency
8. Rare causes of cirrhosis a. Congenital syphilis b. Fibrocystic disease c. Sarcoidosis
9. Intestinal bypass surgery
10. Malnutrition
11. Obesity and diabetes (NASH - Non-alcoholic Steatohepatitis)

Source: Godfrey, E. L., Malik, T. H., Lai, J. C., Mindikoglu, A. L., Galván, N. T. N., Cotton, R. T., ... & Rana, A. The decreasing predictive power of MELD in an era of changing etiology of liver disease. American Journal of Transplantation, 2019; 19(12), 3299-3307.

2.6.3. Classification of Liver Cirrhosis

2.6.3.1. Classification of Liver Cirrhosis According to Clinical Stage

It is classified into two groups: decompensated and compensated cirrhosis. Decompensated cirrhosis is characterized by the presence of ascites, jaundice, and encephalopathy. In compensated cirrhosis, these symptoms are absent (70). If no underlying cause can be identified, it is referred to as cryptogenic (idiopathic) cirrhosis. In approximately 10-15% of cases, no etiology can be determined (70, 71).

2.6.4. Scoring Systems Used to Determine the Severity of Liver Cirrhosis

Two important classifications are used to determine the prognosis of liver cirrhosis patients. The first is the Child-Turcotte-Pugh (CTP) classification, and the second is the Model for End-Stage Liver Disease (MELD) classification. While the Child-Turcotte-Pugh (CTP) classification is essential in evaluating transplant patients, it has limitations in prioritizing patients on the transplant list (71, 72).

a) Child-Turcotte-Pugh Score (CTP Score)

In order to evaluate the surgical risk in cirrhotic patients, Child and Turcotte established a prognostic method unique to the liver in 1964 (73). This system was later modified by Pugh (73, 74). The CTP score has been widely used to assess the risk level of cirrhotic patients and evaluate the effectiveness of therapeutic interventions. CTP score, formulated over thirty years ago, is still the fundamental method for assessing prognosis in cirrhotic cases. It is the most commonly used scoring system in clinical practice and research. However, it is considered inadequate due to variations in the assessment of subjective data and the lack of evaluation of extrahepatic prognostic factors. The CTP score is calculated by assigning scores corresponding to ascites, encephalopathy, total bilirubin level, albumin level, and prothrombin time (INR value), and it is shown in (Table 2.3) (Table 2.4).

Table 2.3. Child-Pugh Classification Of The Severity Of Cirrhosis

Variable	**1 point**	**1 point**	**2 points**	**3 points**
Encephalopathy	absent	absent	Grade 1-2	Grade 3-4
Ascit	absent	absent	Slight to moderate	tense
Bilirubin (mg/dL)	<2	<2	2-3	>3
Albumin (g/dL)	>3.5	>3.5	2.8-3.5	<2.8
PT or INR	<4 <1.7	<4 <1.7	4-6 1.7-2.3	>6 >2.3

Source: Acharya, G., Kaushik, R. M., Gupta, R., & Kaushik, R. Child-Turcotte-Pugh score, MELD score and MELD-Na score as predictors of short-term mortality among patients with end-stage liver disease in Northern India. Inflammatory intestinal diseases, 2020; 5(1), 1-10.,

Table 2.4. Child-Pugh Classification Is Obtained By Adding A Score For Each Parameter

Score	**Classification**
5-6	Child class A
7-9	Child class B
10-15	Child class C

b) Model for End-Stage Liver Disease (MELD) Score/ MELD-Na Score

The Model for End-Stage Liver Disease (MELD) was developed in the United States by a logarithmic transformation of several parameter values (75). The MELD score is a significant scoring method used in evaluating liver transplantation, primarily to understand the severity of liver damage. It initially emerged as a system to prioritize and predict mortality in cases of allogenic (transplants from compatible individuals such as siblings or relatives) organ transplantation in patients with cirrhosis, aiming to determine the severity of the disease. The MELD score can be calculated and used according to the United Network for Organ Sharing (UNOS) scoring system, a standardized national organ allocation network (76).

As the disease progresses, the MELD scoring also changes. The MELD score increases as the disease diagnosis advances. Depending on the criticality of the disease, the MELD score can be recalculated weekly (77).

MELD score recommended follow-up frequency;

- 25 or higher: Every week
- 19-24: Every 30 days
- 11-18: Every three months
- 10 or less: Once a year

MELD=3.78 × loge (Bilirubin mg/dL) + 11.2 × loge (INR) + 9.57 × loge (creatinine mg/dL) + 6.43

The MELD score is calculated based on the International Normalized Ratio (INR), serum bilirubin, and creatinine levels. In 2016, the MELD scoring system was revised and renamed MELD-Na (MELD with Sodium), including sodium levels.

MELD-Na: MELD + 1.32 x (137 - Na) - [0.033 x MELD*(137 - Na)]

With the latest modification in the MELD scoring system, serum albumin levels have also been included in the calculation, and the score is now referred to as MELD 3.0 (55).

2.7. Complications of Liver Cirrhosis

Patients with liver cirrhosis can experience a wide range of complications. In some cases, the disease may remain asymptomatic until a complication arises, leading to a diagnosis of liver cirrhosis. Additionally, complications can develop as liver fibrosis progresses in patients already under surveillance for liver cirrhosis (78). Complications of cirrhosis indicate a significant decline in liver reserve. If the underlying liver disease is treatable and has not reached irreversible stages, it may be possible to improve and prevent the recurrence of complications through treatment (78, 79). However, if the

underlying liver disease is untreatable or has advanced significantly, liver transplantation becomes the only option to consider (80).

a) Esophageal Varices and Variceal Bleeding

Esophageal varices are dilated blood vessels that occur in the esophagus. In liver cirrhosis, the slowed blood flow through the portal vein and its branches within the liver leads to increased pressure in the portal vein. The high-pressure and sluggish blood flow within the portal vein creates alternative pathways, causing dilation of the veins in the esophagus and stomach, ultimately leading to the development of varices at a certain pressure level (81). The stretching and rupture of these veins in the esophagus and stomach due to increased pressure and other external factors can result in severe bleeding. The main symptoms experienced by patients with variceal bleeding include vomiting or passing bloody stools. Treatment should be administered in a hospital setting, which may involve medication and endoscopic interventions to control the bleeding (82).

b) Ascites and Spontaneous Bacterial Peritonitis

Ascites is the medical term for fluid accumulation in the abdominal cavity, commonly seen with the progression of liver cirrhosis. The presence of ascites can be detected during a physical examination or through imaging. One of the most significant complications of advanced liver cirrhosis is the infection of the accumulated fluid in the abdominal cavity, known as spontaneous bacterial peritonitis. Other complications, such as hepatorenal syndrome and hepatic encephalopathy, can also develop due to ascitic fluid infection. Once a patient with cirrhosis experiences spontaneous bacterial peritonitis, the risk of recurrence is very high, necessitating continuous prophylactic (preventive) antibiotic treatment. Spontaneous bacterial peritonitis is also an indicator of other complications and the need for liver transplantation (82, 83).

c) Hepatic Encephalopathy

Hepatic encephalopathy, also known as "hepatic coma," occurs as a result of impaired brain function in advanced liver cirrhosis. It is a reversible neuropsychiatric complication of cirrhosis and is observed in up to 50% of patients with cirrhosis (83). Factors such as constipation, dehydration, electrolyte imbalance, spontaneous bacterial peritonitis, gastrointestinal bleeding, and diuretic medications can trigger hepatic encephalopathy. Patients with hepatic encephalopathy may present with personality changes, sleep disturbances, slowed mental activities, and deteriorated speech. Tremors in the hands and impaired handwriting may also begin to manifest. In the advanced stage, the patient's consciousness becomes completely impaired, leading to a coma (83).

In treatment, the presence of any triggering factor for hepatic encephalopathy is investigated and addressed, as their elimination is of great importance. Treatment may involve using laxatives such as lactulose and intestinal antibiotics (such as rifaximin). When hepatic encephalopathy develops, it indicates a severe decline in liver reserve, and the possibility of liver transplantation should be considered (83, 84). Other potential treatment options include PEG, probiotics, and FMT, but further studies are ongoing regarding these potential treatment options (84, 85).

Ammonia detoxification has an alternative site in muscle tissue. In muscle tissue, ammonia is detoxified by using BCAAs to produce glutamine. BCAAs are branched-chain amino acids that include valine, leucine, and isoleucine. Malnutrition encountered in cirrhosis patients can accelerate recovery by increasing protein synthesis with BCAAs. Among the BCAAs, leucine is the most effective in stimulating multiple pathways. However, it is emphasized that BCAA supplementation has no significant impact on mortality, quality of life, or nutritional status, and further research is needed in this regard (85).

On the other hand, it has been observed that patients with sarcopenia have a predisposition to hepatic encephalopathy (HE) (85). A study showed that patients with cirrhosis who had sarcopenia and HE had low BCAA levels (85, 86). HE has multifactorial pathophysiological mechanisms in which hyperammonemia plays a central role. Adequate dietary protein and carbohydrate energy consumption are important in preventing protein-calorie malnutrition in patients with HE and cirrhosis (86).

In a study, Vidot et al. demonstrated a significant correlation between 25-OHD deficiency and the presence of HE ($p<0.0001$) (86). In patients with decompensated liver cirrhosis, vitamin D therapy has been demonstrated to increase survival, and it was discovered that individuals with low 25-OHD levels had a higher incidence of overt HE at identical disease severity levels (86, 87).

d) Hepatic encephalopathy (HE) severity can be assessed using the West-Haven criteria

• **Minimal HE**: Hepatic encephalopathy that does not show clinical signs but can be detected through psychometric tests.

• **Grade I:** Euphoria, anxiety, decreased attention and concentration, disturbances in sleep rhythm.

• **Grade II**: Lethargy, inappropriate behavior, impaired time orientation, significant personality changes, dispraxia, flapping tremor.

• **Grade III**: Confusion, severe and continuous impairment in time and space orientation, increased drowsiness, inability to perform mental tests, may respond to simple verbal questions.

• **Grade IV**: Severe drowsiness, initially responsive but gradually unresponsive; acute forms may show signs of cerebral edema.

- Minimal HE and Grade I HE: **Covert HE.**
- Grade II-III-IV HE: **Overt HE.**

Source: Fallahzadeh, M. A., & Rahimi, R. S. Hepatic encephalopathy and nutrition influences: a narrative review. Nutrition in Clinical Practice, 2020; 35(1), 36-48.

Table 2.5. Classification Of Hepatic Encephalopathy Based On The Underlying Cause

Type	Cause
TYPE 1	Hepatic encephalopathy due to acute liver failure.
TYPE 2	Hepatic encephalopathy due to portal-systemic shunting without liver disease.
TYPE 1	Hepatic encephalopathy due to portosystemic shunt or portal hypertension caused by cirrhosis.

Source: Harman, A. A. Hepatik ensefalopati tedavisi için rifaksimin ve laktuloz kullanan siroz hastalarının barsak mikrobiyotalarının tedavi ile değişiminin incelenmesi, 2020.

e) Hepatorenal Syndrome

Cirrhosis of the liver can lead to a kidney illness called hepatorenal syndrome. It can be ascribed to a number of modifications that occur as liver cirrhosis advances and causes a reduction in blood supply to the kidneys. Reduced urine output and other renal failure symptoms may be present. When problems in kidney function are seen in a patient with liver cirrhosis, a diagnosis is made. Hepatorenal syndrome can be treated with medication. However, the condition may be reversed by treating the underlying liver disease. A combined kidney and liver transplant may be required in some situations when renal failure develops into a chronic condition (88).

f) Hepatopulmonary Syndrome and Portopulmonary Hypertension

Hepatopulmonary syndrome and portopulmonary hypertension are lung complications associated with liver cirrhosis. Patients with portal hypertension are susceptible to the condition known as hepatopulmonary syndrome, which can enlarge blood vessels in the lungs and decrease oxygenation due to shunting (89). On the other hand, portopulmonary hypertension is pulmonary hypertension that is linked to liver cirrhosis and cannot be attributed to any other factors. Liver transplantation is the only available treatment for both pulmonary problems. However, mortality rates after liver transplantation are still significant in situations of advanced portopulmonary hypertension (90).

g) Hepatocellular Carcinoma (Liver Cancer)

It is among the most serious side effects of liver cirrhosis. Liver cancer can develop in cirrhosis caused by any underlying condition, but the risk of developing hepatocellular carcinoma is particularly high in hepatitis B, hepatitis C, fatty liver disease, and hemochromatosis characterized by iron accumulation in the liver. Treatment decisions depend on the type of underlying liver disease, liver reserve, and tumor stage (91). Hepatocellular carcinoma represents a life-threatening condition indicating the depletion of liver reserve and often requires liver transplantation.

2.8. Treatment Of Liver Cirrhosıs

The objective of treatment is to diagnose and initiate therapy in the pre-cirrhotic stage and attempt to control the disease. The treatment approach for liver cirrhosis primarily focuses on managing symptoms and complications. If the underlying cause of liver cirrhosis is known, specific medication targeting the underlying disease should be administered (92).

Complications that may arise from liver cirrhosis should be monitored, and appropriate treatments should be provided. Individualized medical treatment protocols should be applied for existing or potential complications (93).

Secondly, medical nutrition therapy should involve personalized dietary adjustments, considering any existing complications. A balanced diet rich in vitamins and achieving the required protein-energy balance should be maintained during medical nutrition therapy (94).

Finally, it is advisable to avoid intense physical activity and maintain a moderate pace that does not increase the metabolic burden and requirements of the liver. While individuals with compensated cirrhosis may be allowed to engage in daily routine activities, bed rest is recommended for those with decompensated liver cirrhosis (95).

In conclusion, complications of liver cirrhosis indicate the depletion of liver reserve and threaten the patient's life. It is crucial to evaluate these patients at liver transplant centers and determine the appropriate treatment. When complications of liver cirrhosis start to emerge, liver transplantation should be considered. For end-stage patients, liver transplantation is the only viable option (96).

a) Malnutrition in Liver Cirrhosis

The prevalence of malnutrition in cirrhosis ranges from 65% to 90%. Protein loss and decreased muscle function are commonly observed in cirrhosis, particularly in males and those with alcoholic cirrhosis. In patients classified as Child-Pugh class A, malnutrition can reach up to 25%. The assessment of malnutrition in cirrhotic patients typically involves a focused history, physical examination, and laboratory studies. The use of specialized tests such as bioelectrical impedance analysis (BIA) is limited to research settings due to availability, radiation/contrast exposure, special equipment requirements, and cost (97).

For assessing nutritional status in cirrhotic patients, there is no gold standard, and clinical practice may differ. Malnutrition in cirrhosis is caused by a variety of reasons. Low oral intake, malabsorption, metabolic abnormalities, increased energy needs, modifications in substrate oxidation (lower glucose oxidation and increased lipid oxidation), rapid protein breakdown, insufficient protein synthesis, and hypermetabolism are some of these (98).

Dietary restrictions on sodium and low-fat nutritional patterns, which can lead to decreased appetite, are also common due to the presence and severity of complications such as ascites and peripheral edema. On the other hand, reduced taste sensation due to zinc or magnesium deficiency has been identified. Depending on the screening techniques utilized and the patient groups under study, malnutrition is frequently underdiagnosed and affects anywhere from 5% to 92% of patients (99). Malnutrition can be exacerbated by increased calorie and protein intake, inflammation, malabsorption, altered nutritional metabolism, hypermetabolism, hormonal disturbances, and dysbiosis of the gut flora. The disease's side effect of malnutrition, which can also happen on its own, can cause morbidity. Therefore, it is advised to start medical nutrition therapy early (99, 100).

b) Cirrhosis-Sarcopenia

Frailty, impaired muscle contraction, and muscle weakness due to cirrhosis define a limited physical function (101). Although the exact mechanism of sarcopenia is not fully understood, several possible mechanisms exist. These processes include muscle fat content, neuromuscular integrity, proteolysis, and protein synthesis. The prevalence of sarcopenia varies between 8% and 40%, depending on the diagnostic criteria (102). The diagnosis of sarcopenia is based on measurements of muscle mass and functional tests that assess muscle strength or physical performance (such as walking and balance tests) (103). So far, no specific biomarker has been identified. Currently, the most widely accepted and studied approaches to combat the effects of sarcopenia include exercise and physical activity, nutritional support therapy, hormonal approaches, and novel pharmacological agents. Concerning older people's muscle mass, strength, and function, there is mounting evidence that nutritional therapy is crucial for controlling and preventing sarcopenia (103, 104).

c) Medical Nutrition Therapy in Liver Cirrhosis Patients

Nutrition therapy ought to boost liver regeneration, stop or treat malnutrition, and stop or handle problems (105).

Patients with cirrhosis frequently have protein-calorie malnutrition, which has been linked to problems such as variceal hemorrhage, ascites, increased surgical morbidity and mortality, lower survival, and even decreasing liver function. Regardless of the underlying cause, malnutrition can occur in cirrhotic patients and has a considerable negative impact on mortality and morbidity rates (105, 106).

Accurate diagnosis and early malnutrition identification are essential for controlling the condition's progression. Appropriate and prompt dietary treatment can have a positive effect on the patient's clinical result (107). Therefore, it is essential to give patients nutritional support therapy via oral, enteral, and/or parenteral routes. Therapeutic techniques are widely performed in connection to nutrition in liver patients due to the frequent occurrence of hypoglycemia (107). The liver is responsible for many functions, including controlling blood sugar levels. If the liver is not working effectively, blood sugar levels cannot be appropriately controlled, hastening the onset of issues (108). As a result, it is recommended to eat small, frequent meals and to promote the nutritional diversity of the meals.

Patients with cirrhosis also lose bone and muscle mass more quickly. Maintaining muscular mass, particularly in elderly individuals, can increase lifespan. As a result, nutrition is essential. Diets that are overly restrictive should be avoided by cirrhotic patients. Muscle loss might be accelerated by excessive protein restriction without sufficient biochemical value monitoring. Based on the patient's biochemical results during the acute phase and treatment term, controlled protocols should be followed (109).

d) Protein-Energy

For patients with cirrhosis, The European Society for Clinical Nutrition and Metabolism recommends an energy intake of 35-40 kcal/kg/day, while the American Society for Parenteral and Enteral Nutrition (ASPEN) suggests 30-40 kcal/kg/day. ESPEN and ASPEN recommend an energy intake of 25-35 kcal/kg/day for compensated cirrhosis patients (110).

Protein restriction should not be applied in compensated cirrhosis. Daily protein intake of up to 1.2-1.5 g/kg has beneficial effects (111). However, high protein intake should be avoided in decompensated cirrhosis (112). In cirrhosis, it is recommended that 20-30% of energy comes from protein, with a protein intake of 1.0-1.5 g/kg/day. If there is protein intolerance, a protein intake of 0.5-1.0 g/kg/day and BCAA supplementation are recommended (112, 113). Plant proteins with low methionine and aromatic amino acid content and high fiber content, as well as milk proteins, are well tolerated in cirrhosis. There are a few recommendations regarding the optimal glucose and fat ratio in the diet of liver patients. ESPEN suggests that non-protein energy should come from 50-60% glucose and 40-50% fat (113).

BCAAs (leucine, isoleucine, valine), which belong to the essential amino acid group, positively affect immune functions, especially in improving infections in patients with cirrhosis (114). There are three main purposes of BCAA supplementation in liver diseases: prevention and treatment of hepatic encephalopathy and hepatic cachexia and repair and regeneration of hepatic tissue. In patients with chronic liver disease, especially cirrhosis, plasma BCAA concentrations decrease while aromatic amino acids (phenylalanine, tyrosine, tryptophan) (AAAs) and methionine levels increase (115). In acute conditions where protein restriction is necessary, BCAA use of 0.25 g/kg/day is recommended (115).

In addition, BCAA supplementation increases serum albumin levels. In a prospective multicenter study, the effect of dietary BCAA supplementation on hypoalbuminemia in decompensated cirrhotic patients was investigated, and a significant increase in serum albumin levels, Child-Pugh scores, as well as the incidence of ascites and edema were found to decrease compared to baseline (116).

e) L-Ornithine L-Aspartate

L-Ornithine L-Aspartate is a substrate for urea synthesis and accelerates urea synthesis. It has been found to be as effective as lactulose (a disaccharide commonly used to treat constipation) in reducing ammonia levels. The benefits of ornithine aspartate have been demonstrated in randomized controlled trials in patients with mild hepatic encephalopathy (117).

In summary, studies have shown the positive results of using N-acetylcysteine in alcoholic hepatitis and probiotics and L-ornithine aspartate in the nutritional treatment of hepatic encephalopathy. However, further research is needed on this topic (118).

f) Sodium and Potassium

A sodium restriction of mostly 2 g/day is required in managing ascites, but fluid is generally not restricted. A sodium concentration of 120 mmol/L is at the severe hyponatremia threshold and is associated with renal failure (119). Maintaining the balance between sodium and potassium is important during the disease. The clinical condition should be closely monitored, and if the potassium level drops, supplementation may be necessary as it can hasten hepatic coma.

g) Vitamins and Minerals

Vitamin needs are generally increased by inadequate intake, aberrant metabolism, increasing demand, and losses. Cholestasis disrupts the enterohepatic circulation of bile secretions, which affects the absorption of lipids and fat-soluble vitamins (A, D, E, and K), increasing the requirement for these nutrients (120).

Vitamin E also functions as an antioxidant, halting the oxidation of unsaturated fatty acids and the production of peroxide. However, due to the prevalence of osteoporosis, osteomalacia, and osteopenia, vitamin D levels should be carefully watched, and supplementation should be started as needed. In addition, hemorrhoids and esophageal varices may increase the demand for vitamin K. Hypoprothrombinemia causes a prolonged prothrombin time, and vitamin K dosage is chosen based on the patient's clinical situation.

h) Nutrition Support and General recommendations

Enteral and parenteral support ensures daily energy and protein balance and compensates for inadequate oral intake in patients (121). Oral enteral nutrition support is usually selected based on the symptoms and laboratory findings of the disease, while total parenteral nutrition supplementation is administered to patients with a non-functional gastrointestinal system or those who cannot be adequately nourished orally or enterally. Alternative treatments are considered in cases of hepatic encephalopathy (122).

A small and frequent meal approach is recommended in the cirrhotic patient group according to the nutrition therapy protocol. Notably, a carbohydrate-rich evening meal helps improve nitrogen balance by limiting the necessary amino acid for gluconeogenesis in patients with cirrhosis. According to the 2015 ESPEN guideline, For those with liver problems, it is advised that should avoid fasting for more than 12 hours since ketogenesis and gluconeogenesis, which occur after 2-3 days of fasting in healthy individuals, occur in a much shorter period of time in cirrhotic individuals and 75% of energy comes from fat utilization during overnight fasting (123).

It has been shown that this bacterial balance is disrupted in liver diseases. Therefore, under appropriate conditions, the positive effects of the correct probiotic supplementation can be observed. Probiotics have been proven to be helpful in treating conditions including cirrhosis and fatty liver disease in several studies (124). However, more study is required.

In cases of abdominal ascites, a common complication of cirrhosis, excessive hydration should be avoided as it can increase ascites volume, decrease plasma sodium concentration, and sometimes accelerate gastrointestinal bleeding caused by varices (125). Therefore, maintenance fluids should not be routinely administered to patients without pre-renal azotemia, especially if they can tolerate oral fluids (126).

In conclusion, the Mediterranean diet has been found to be the most suitable for liver diseases based on the highest level of evidence. Additionally, fermented products should not be overlooked. Patients with cirrhosis should avoid unnecessary diets, should not restrict protein intake, and should focus on consuming plant-based proteins. (127)

3. MATERIALS & METHODS

3.1. Study Population

In this study, adult patients diagnosed with cirrhosis and followed up at the Gastroenterology outpatient clinic of Istanbul University Cerrahpaşa-Cerrahpaşa Medical Faculty were included (n=75). Those who voluntarily participated in the study among cirrhosis patients who underwent routine outpatient clinic examinations between September 2022 and March 2023 were evaluated within the scope of the study.

3.2. Inclusion Criteria

- Adult patients diagnosed with cirrhosis at least 6 months prior,
- Willingness to participate in the study,
- Adequate follow-up data related to the diagnosis of cirrhosis,

3.3. Exclusion Criteria

- Patients who refused to provide their consent to take part in the trial,
- Patients with hepatic encephalopathy who did not cooperate during the evaluation,
- Patients under 18 years of age,
- Patients with suspected cirrhosis or a diagnosis of cirrhosis for less than 6 months,
- Patients diagnosed with cirrhosis but with limited data related to follow-up.

3.4. Demographic and Clinical Parameters Assessed in the Study

The patients' demographic data (age, gender) and anthropometric measurements (height, weight) were recorded. The etiology of cirrhosis was categorized as cryptogenic, Hepatitis B, Hepatitis B+D, Hepatitis C, alcohol-related, non-alcoholic fatty liver disease, Wilson's disease, and other causes. The presence of comorbidities such as diabetes mellitus (DM), hypertension (HT), chronic obstructive pulmonary disease (COPD), history of myocardial infarction (MI) or angina, asthma, arrhythmia, stroke, chronic kidney disease, cancer, and other diseases was classified. Complications associated with cirrhosis, such as ascites, varices, variceal bleeding, encephalopathy, spontaneous

bacterial peritonitis (SBP), and hepatocellular carcinoma (HCC) were evaluated. These parameters were graded as shown in Table 3.1.

Table 3.1. Evaluation of Complication Parameters

Ascites	non	under control	uncontrolled
Variceal bleeding	non	no variceal bleeding	yes variceal bleeding
Encephalopathy	non	under controlled	frequent attacks
History of SBP (spontaneous bacterial peritonitis)	non	presence	non
HCC (hepatocellular carcinoma)	non	presence	non

The hospital or ICU admission status and number of patients were recorded during their last 1-year follow-up.

a) Laboratory parameters and disease scores evaluated in the study

Laboratory tests conducted within the last 1 month during patients' clinic follow-ups were taken into consideration. These parameters are presented in Table 3.2.

Table 3.2. Laboratory Parameters and Disease Scores Evaluated in the Study

Laboratory parameters		
Glucose	Iron-Total iron binding capacity (TIBC)	ALT
Albumin	INR	ALP
C reactive protein (CRP)	Total/ direct bilirubin	GGT
Total Cholesterol	Urea	Hemoglobin – hematocrit
HDL cholesterol	Creatinine	TSH
Triglyceride	Vitamin D	Na

The Child-Pugh score (84) and classification, as well as the MELD/MELD-Na scores, were calculated as indicators of liver disease severity. The Child-Pugh score is based on both clinical and laboratory evaluations. Clinical parameters, such as the presence and severity of cirrhosis-related ascites and encephalopathy, and laboratory parameters, including serum total bilirubin level, serum albumin level, and INR level, were considered. The Child-Pugh score was calculated according to the parameters' classification, as stated in Table 3.3. and a total score was determined. The score ranges from 5 to 15.

Table 3.3. The Child-Pugh Scores

	Point		
Laboratory	**1**	**2**	**3**
Total bilirubin (mg/dL)	<2	2-3	>3
Serum albumin (g/dL)	>3.5	2.8-3.5	<2.8
INR	<1.7	1.7-2.3	>2.3
Encephalopathy	absent	Mild–medium (Grade1/2)	Severe (Grade 3/4)
Ascite	absent	Mild-midium (under control with diuretics)	Severe-tens (diuretic resistant)

The Child-Pugh scores (Table 3.3) were also used to classify patients into Child-Pugh classes. According to this classification, a score of 5-6 corresponds to Class A, 7-9 corresponds to Class B, and 10-15 corresponds to Class C.

The MELD and MELD-Na scores were calculated using serum creatinine, INR, bilirubin, and sodium values. The formulas are as follows:

- MELD: [3.78xLoge(bilirubin (mg/dL))] + [9.57xLoge(creatinine (mg/dL))] + [11.2xLoge(INR)] + 6.43
- INR/creatinine or bilirubin values <1 were considered as "1" in the calculation since Loge would give negative results.
- Patients with creatinine values >4 mg/dL, patients who underwent dialysis at least twice in the last 7 days, or patients who underwent continuous hemofiltration for 24 hours in the previous 7 days were considered to have a creatinine value of 4 mg/dL.
- MELD-Na: MELD - (Na mmol/L) - [0.025xMELDx(137 - Na mmol/L)] + 137

Dietary habits, frailty, and sarcopenia-related questions and indices were assessed in the study. The questions in Appendix 1 were asked to assess patients' nutritional status, weight loss, eating habits, frailty status, and sarcopenia-related symptoms.

Chronic diseases were classified, and having more than 5 of them was scored as one point each. The total score was calculated, where 0 indicated normal, 1-2 points indicated pre-frail, and 3-5 points indicated frail. The SARC-F index was calculated based on strength, walking assistance, rising from a chair, climbing stairs, and frequency of falls, as shown in the last section of the mentioned questions. The response "None" was scored as 0 points, "Somewhat difficult" was scored as 1 point, and "Very difficult or unable to do" was scored as 2 points. A score of 4 or higher was considered a risk for sarcopenia.

3.5. Evaluation of Hand Grip Strength in Patients

After patients were assessed through routine clinic evaluations and questions related to nutrition, frailty, and sarcopenia, their hand grip strength was evaluated. After patients were informed and adequately rested, hand grip strength measurement was performed in a sitting position. The Baseline Hydraulic Hand Dynamometer (200 lb) was used for measurement. The measurement was taken with the patient sitting, the shoulder and arm in a neutral position, the elbow flexed at a 90-degree angle, and the forearm extended parallel to the ground while grasping the hydraulic hand dynamometer. Patients were asked to squeeze the dynamometer with all their strength in this position. This

measurement was repeated three times for both the right and left hands. Three measurements for each hand were recorded, and their averages were noted. Before the hand grip strength measurement, the physician demonstrated the correct position and use of the dynamometer to the patients.

Regarding the patient's dietary habits, the following factors were evaluated: meal frequency, presence of food allergies, frequency of red meat consumption, frequency of alcohol use, and use of dietary supplements.

3.6. Statistical Analysis

By use of the Kolmogorov-Smirnov test, the parameters' normal distribution was assessed. For non-parametric data that did not have a normal distribution, the median and interquartile range were used, while the mean and standard deviation were used for parametric data with a normal distribution. As frequencies or percentages, categorical data were displayed. The Student's t-test and the Mann-Whitney U test were both employed for comparisons between two groups when comparing numerical variables with normally distributed distributions. The Kruskal-Wallis test was used for numerical variables with non-normal distribution when there were more than two groups, while one-way analysis of variance (ANOVA) was used for regularly distributed numerical variables. With Spearman correlation for non-normally distributed data and Pearson correlation for normally distributed data, correlation analysis was utilized to assess the correlations between numerical variables. The symbol for correlation coefficients was "r." Between 0.2 and 0.5, the correlation coefficient denoted a weak correlation; between 0.5 and 0.7, a moderate correlation, and above 0.7, a strong correlation. Statistics were deemed significant at a p-value of 0.05 level of significance. Software from SPSS Inc., Chicago, IL, USA, IBM SPSS 29.0 was used for the statistical analysis.

4. RESULTS

A total of 75 patients' data were analyzed in the study. Of these, 58.7% (n=44) were men, and 41.3% (n=31) were women. With a median age of 66 and an (IQR) of 12, the age distribution did not follow a normal distribution. The minimum and maximum ages were 28 and 85, respectively. Table 4.1 provides a summary of the patient's height, weight, and demographic information.

Table 4.1. Demographic and Anthropometric Characteristics of the Patients

Character	**Result**
Gender - female % (n)	41.3 (31)
Age (years) median (IQR)	66 (12)
Height (cm) (±SD)	165.6 (±8.5)
Weight (kg) (±SD)	74.2 (±13.3)
BMI (kg/m^2) (±SD)	27 (±4.3)

Regarding the patient's dietary habits, the following factors were evaluated: meal frequency, presence of food allergies, frequency of red meat consumption, frequency of alcohol use, and use of dietary supplements. It is shown in Table 4.2.

Table 4.2. Meal frequency

Meals frequency	**%(n)**
Only one meal per day.	8 (6)
2 meals per day.	50.7 (38)
3 meals per day.	36 (27)
4 or more meals per day.	5.3 (4)

As can be seen from these data, the results were found to be 50.7% of the patients (n=38) reported having 2 meals per day, 36% of the patients (n=27) reported having 3 meals per day, 8% of the patients (n=6) reported having only one meal per day and 5.3% of the patients (n=4) reported having 4 or more meals per day as detailed in Table 4.2.

Table 4.3. Reports on Food Allergies

Allergenic food	**n**
Tomato	3
Hazelnut	2
Eggs	1
Strawberries	1
Seafood	1

Among the study group, 8 patients (10.7%) reported food allergies. These allergenic foods and their food groups are shown in Table 4.3.

Table 4.4. Frequency of Red Meat Consumption

Frequency (per week)	**%(n)**
0-1 time	42.7(32)
2-3 times	42.7(32)
4 times and more	15 (11)

According to the results of the questionnaire evaluation in the cirrhotic patient group, 10% of the patients were found to be 42.7% of the patients reported consuming red meat 0-1 times per week, and the same percentage (42.7%) reported consuming it 2-3 times per week, 14.7% of the patients reported consuming red meat 4 or more times per week. Detailed results are shown in Table 4.4.

Table 4.5. Frequency of Alcohol Use

Frequency (per week)	%(n)
Never	5.3 (4)
Rarely or never	80 (60)
1 time or more	12 (9)

The frequency of alcohol consumption was analyzed in three groups: non-drinkers, rare drinkers, and those who drank 1 or more drinks per week. 85.3% of the group reported none or very rare drinking, while a minority of the group (12%) reported 1 or more drinks per week. There were no patients in the never-smoker category. It was shown in Table 4.5.

Table 4.6. Defecation Patterns

Defecation	%(n)
Every day	78.7(59)
Twice a week	16 (12)
Once a week	5.3 (4)

Based on these data, the frequency of reported bowel movement was analyzed. The results are shown in Table 4.6.

Table 4.7. Evaluation of Nutritional Status in The Past 3 Months

Pattern	% (n)
No change	10.7 (8)
Moderate decrease	56 (42)
Severe decrease	33.3 (25)

When the patient's nutritional status in the last 3 months was assessed according to the questionnaire results, their oral intake and appetite were categorized into different categories as shown in Table 4.7: no change in nutritional status, moderate decrease, or severe decrease. Almost half of these categories were recorded as moderate decrease, followed by the severe decrease category with 33.3%. This was followed by 10.7% of patients who reported no change in attitude.

The etiology of cirrhosis is shown in Figure 4.1. NASH was the leading cause, followed by Hepatitis B and alcohol. Cryptogenic cirrhosis was present in 23.1% of the patients.

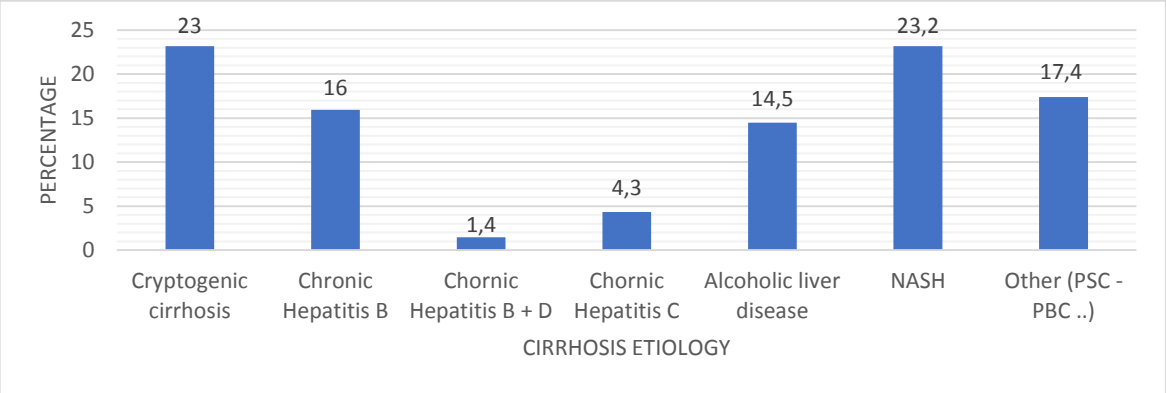

Figure 4.1. Patients' Cirrhosis Status and Laboratory Findings

Table 4.8. Laboratory Values and Child-Meld Scores Of The Entire Patient Group

Variable	Median (IQR) Mean (±SD)	Variable	Median (IQR) Mean (±SD)
Glucose (mg/dl)	116 (56)	**T.cholesterol (mg/dl)**	160 (59)
T. protein (d/dl)	7.2 (7.8)	**HDL cholesterol (mg/dl)**	45 (22)
Albumin (g/l)	34.5 (10.8)	**Triglyceride (mg/dl)**	98 (54)
Crp (mg/l)	7.3 (15.7)	**Serum iron (mg/dl)**	64 (60)
Urea (mg/dl)	35 (±12.3)	**Iron binding capacity (TIBC) (mg/dl)**	330 (96)
Creatinine (mg/dl)	0.89 (±0.27)	**Ferritin (mg/l)**	43 (33)
Total bilirubin (mg/dl)	1.4 (1.2)	**Vitamin D (ng/ml)**	26.5 (25)
INR	1.2 (0.4)	**TSH mU/l**	2 (1.85)
Na (mmol/l)	137 (2.75)	**PLT (K/uL)**	86000(39750)
ALT (U/L)	33.5 (28)	**HGB (g/dl)**	11.8 (±2.3)
AST (U/L)	48.5 (38.7)	**Child score**	7 (5)
GGT (U/L)	45 (55.5)	**Meld**	10.5 (6)
ALP (U/L)	86 (80.5)	**Meld - Na**	12 (8)

In 57.3% of the patients, there is no ascites, while in 16% of them, uncontrolled ascites is present. Similarly, 68% of the patients do not have encephalopathy, while 8% of them have encephalopathy despite treatment. The incidence of variceal bleeding history is 14.7%, while the incidence of varices without bleeding is 49.3%. Seven patients have a history of spontaneous bacterial peritonitis.

In Table 4.9, the results of the FRAIL and SARC-F index parameters of the patients are summarized

Table 4.9. FRAIL and SARC-F Index Parameters of the Patients

Frail İndeks	**%(n)**	Sarc-F Index	**Some tension %(n)**	**Inability to %(n)**
Feeling fatigued	46.7 (35)	Strength	30.7 (23)	16 (12)
Inability to climb 10 flights of stairs	45.3 (34)	Walking	32 (24)	6.7 (5)
Inability to walk 200 meters comfortably	49.3 (37)	Getting up from the chair	26.7 (20)	2.7 (2)
≥5 chronic disease	6.7(5)	Climbing steps	34.7 (26)	9.3 (7)
Frail score median (IQR)	2 (2)	Falling down	28 (21)	16 (12)
≥ 5% weight loss	25.3 (19)	Sarc -F score median (IQR)	1 (4)	
Frail / prefrail	30.7 (23) / 60 (45)	Risk of sarcopenia	32 (24)	

In the entire group, the median grip strength was found to be 33 kg for the right arm and 30 kg for the left arm. In males, these values were 34.5 (15) kg for the right arm and 32 (14) kg for the left arm, while in females, they were lower at 29 (13) kg for the right arm and 27 (11) kg for the left arm. However, the difference between genders did not reach statistical significance (p: 0.06, p: 0.163).

When examining the correlation between grip strength and age, MELD score, Child score, and BMI, it was observed that grip strength was moderately correlated with age for the left arm (p: 0.05, r: 0.638), but no significance was found for the right arm (p: 0.07, r: 0.504). On the other hand, there was a significant correlation between grip strength and BMI (right arm: $p < 0.001$, r: 0.483; left arm: $p < 0.001$, r: 0.466), but the correlation was weak. Correlation analysis was also performed between grip strength and MELD score, and Child score, revealing moderately significant negative correlations for

both (MELD: $p < 0.001$, -0.584; $p < 0.001$, -0.641; Child: $p < 0.001$, -0.565; $p < 0.001$, -0.585).

Among the laboratory values, grip strength was found to be correlated with albumin, bilirubin, INR, and vitamin D levels. The correlation between albumin and grip strength was $r = 0.528$ ($p < 0.001$) for the right arm and $r = 0.565$ ($p < 0.001$) for the left arm. INR and total bilirubin showed a negative correlation with grip strength (INR: $r = -0.411$, -0.416; bilirubin: $r = -0.411$, -0.513). Vitamin D levels were moderately correlated with grip strength ($p < 0.001$, r: 0.636; $p < 0.001$, r: 0.591). Total cholesterol and ferritin levels showed weak correlations with grip strength. For total cholesterol, the correlation was $r = 0.248$ ($p = 0.03$) for the right arm and $r = 0.244$ ($p = 0.03$) for the left arm, while for ferritin, higher ferritin levels were associated with lower grip strength ($r = -0.275$, $p = 0.01$; $r = -0.223$, $p = 0.04$). There was no significant relationship between grip strength and iron levels or iron-binding capacity ($p = 0.632$, $p = 0.458$).

Table 4.10. Correlation of Laboratory Findings and Right Hand Left Hand Grip Strength

	Right hand		Left hand	
	r	p	r	p
Albumin	0.528	<0.001	0.565	<0.001
Billirubin	-0.410	<0.001	-0.411	<0.001
INR	-0.416	<0.001	-0.513	<0.001
Vit - D	0.629	<0.001	0.616	<0.001
Total Cholesterol	0.248	0.032	0.244	0.035
Ferritin	-0.275	0.015	-0.223	0.040
Serum iron	-	0.632	-	0.497
Iron Binding capacity	-	0.622	-	0.668

While no relationship was observed between food allergies and grip strength ($p = 0.09$ for both arms), red meat consumption was found to be associated with grip strength. The group that consumed red meat 4 or more times per week had higher grip strength for both arms (Figure 4.3).

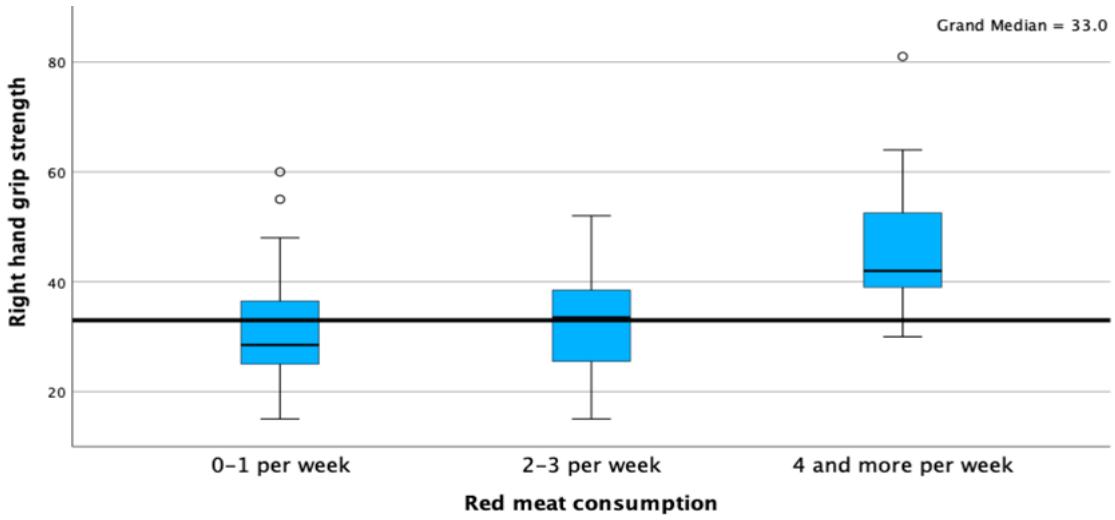

Figure 4.2. Association of Red Meat Consumption With Right Hand Grip Strength

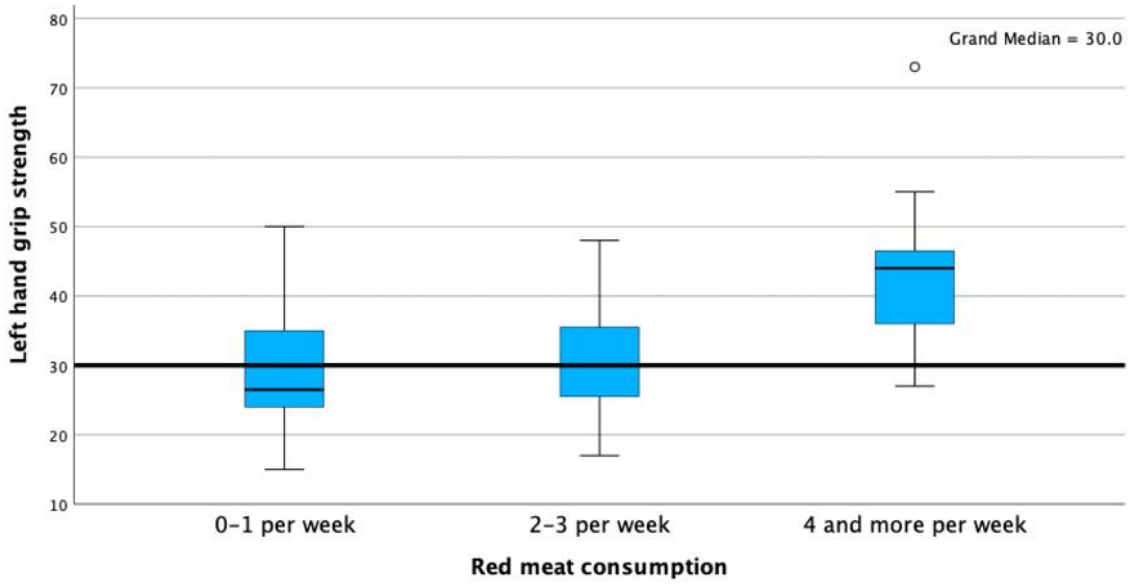

Figure 4.3. Association of Red Meat Consumption With Left Hand Grip Strength

There was no significant relationship observed between alcohol consumption frequency or the use of dietary supplements and grip strength (p: 0.104, p: 0.322; p: 0.354, p: 0.831). However, the nutritional status in the last 3 months was found to be associated with grip strength (Figure 4.6, Figure 4.7).

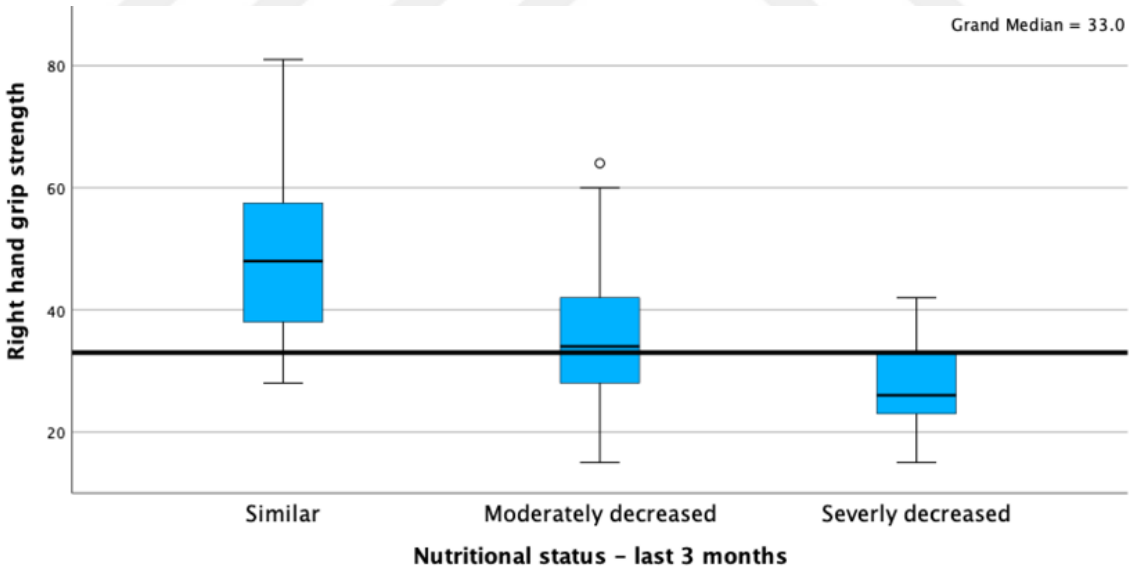

Figure 4.4. Association Of Nutritional Status in The Last 3 Months With Right Hand Grip Strength

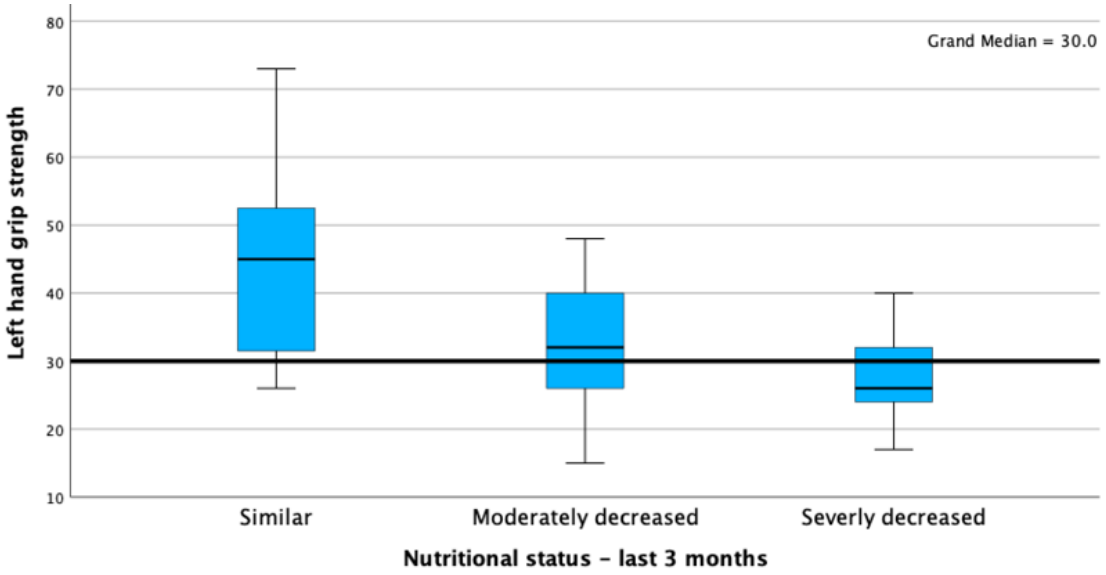

Figure 4.5. Association Of Nutritional Status in the Last 3 Months With Left Hand Grip Strength

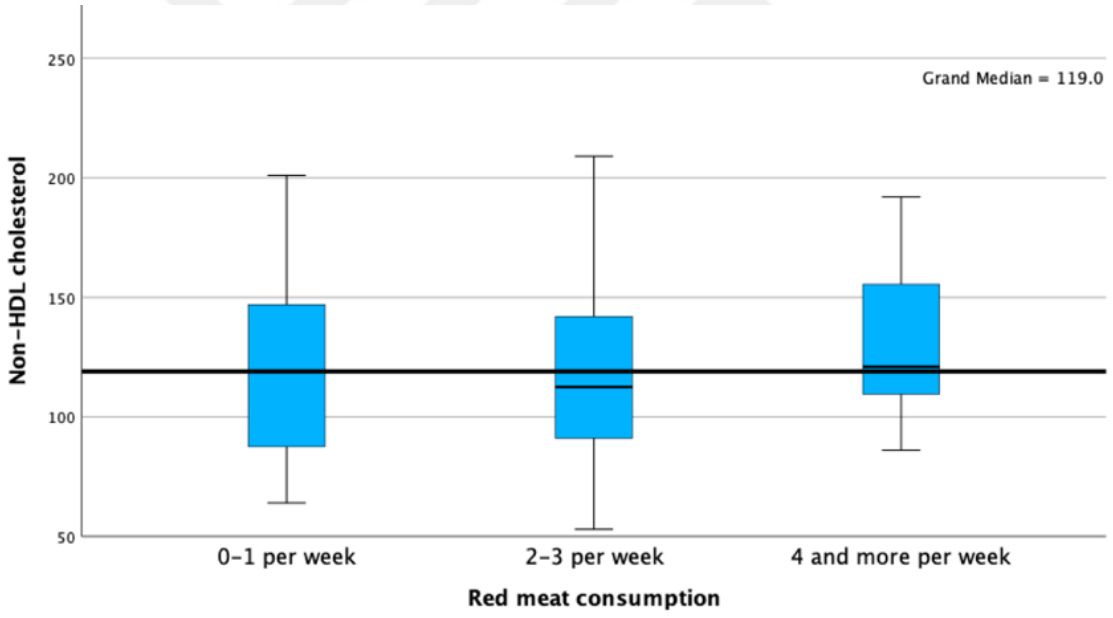

Figure 4.6. Association of Red Mear Consumption With Non-HDL Cholesterol

The frequency of red meat consumption was not associated with non-HDL cholesterol levels (p: 0.825). Furthermore, there was no significant effect of red meat consumption frequency on the presence of hepatic encephalopathy (p: 0.508). Figure 4.5.

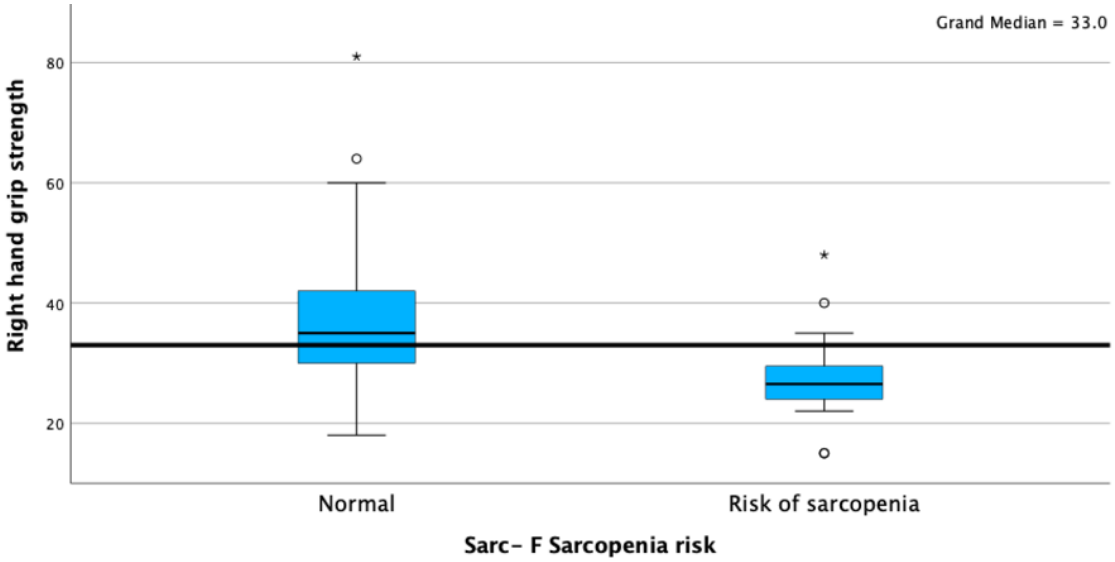

Figure 4.7. Association Sarc F With Right Hand Grip Strength

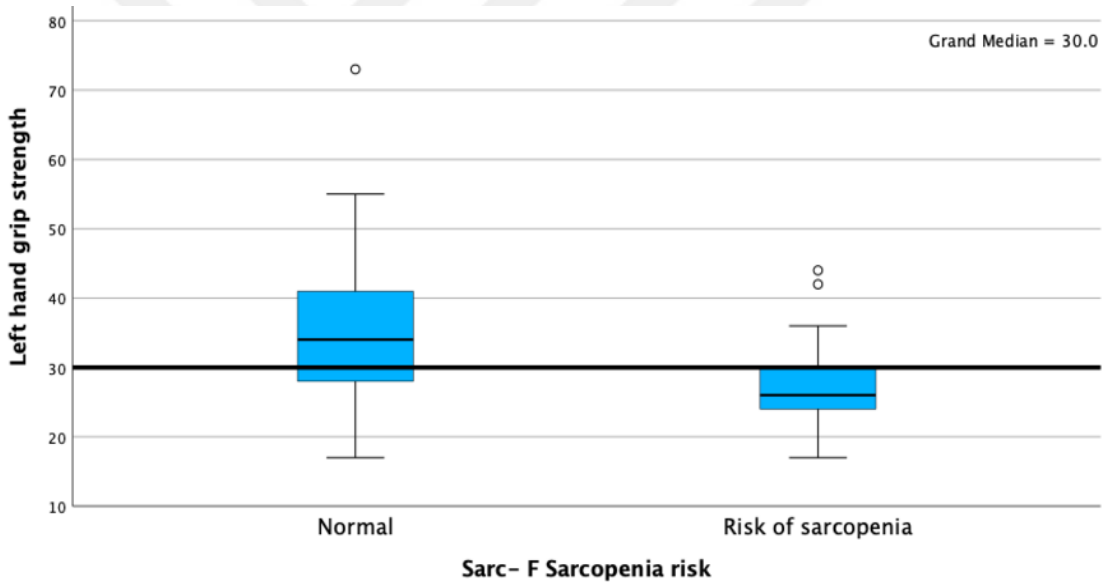

Figure 4.8. Association Sarc With Left Hand Grip Strength

The grip strength was negatively correlated with both the Sarc-F and Frailty indices ($p < 0.001$, r: -0.459; $p < 0.001$, r: -0.430). The median grip strength values were significantly different between the Sarc-F and Frailty index groups (Figure 4.9, Figure 4.10, Figure 4.11, Figure 4.12).

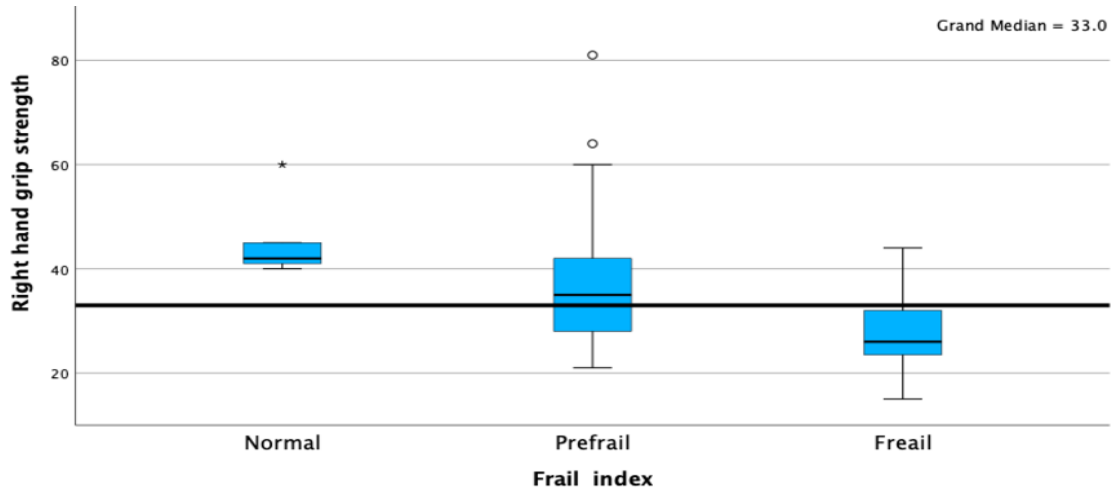

Figure 4.9. Association Frailty With Right Hand Grip Strength

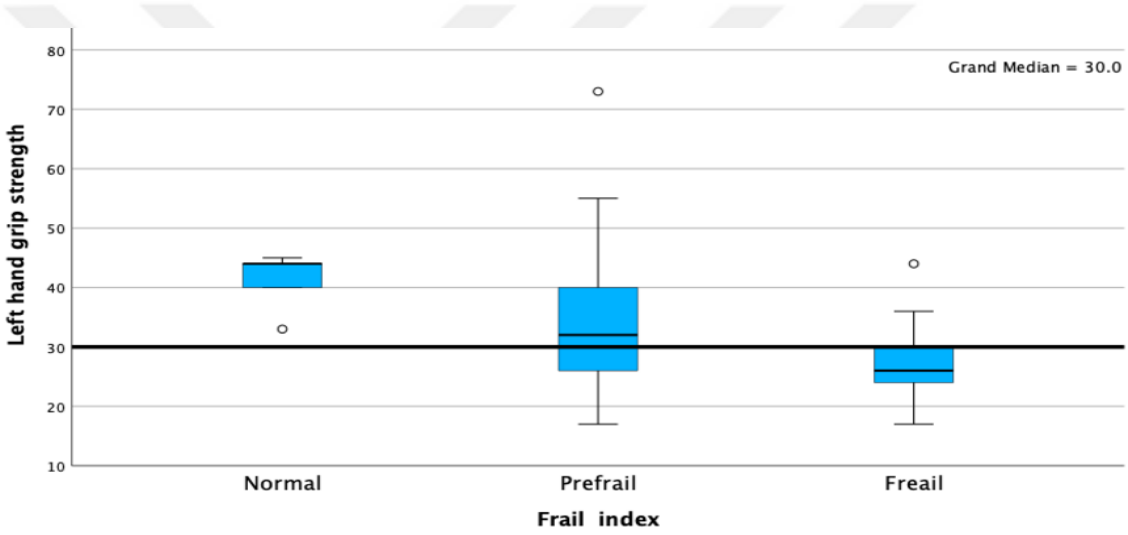

Figure 4.10. Association Frailty With Left Hand Grip Strength

Table 4.11. Table Of The Effect Of Various Variables On Right Hand, Left-Hand Grip Strength

	Strength (kg) median (IQR)			
Red meat consumption	**Right hand**	p	**Left hand**	p
0-1 / week	28.5 (12)		26.5 (11)	
2-3 / week	33.5 (14)	0.001	30 (11)	0.025
≥4 / week	42 (22)		44 (14)	
Nutritional status last 3 months				
Similiar	48(24)		45(24)	
Moderately decreased	34(14)	0.012	32(14)	0.036
Severly decreased	26(11)		26(9)	
Frail index				
Normal	42(5)		44(4)	
Prefrail	35(14)	<0.001	32(14)	<0.001
Frail	26(9)		26(6)	
Sarc-F index				
Normal	35(13)	<0.001	34(14)	0.001
Risk of sarcopenia	26.5(6)		26(6)	

5. DISCUSSION

After several well-known etiological processes, cirrhosis of the liver is a condition that shows similar clinical symptoms. However, the course of the disease and the nutritional treatment of cirrhosis still need to be clarified (128). Sarcopenia is a frequent side effect in people with liver disease, affecting 30% to 70% of patients (128). It is usually associated with weight loss but has a complex metabolism that cannot be explained solely by malnutrition and low protein intake (129).

According to our research, patients with liver cirrhosis are at an increased risk of developing sarcopenia and understanding how this condition affects muscle strength. Protein intake and sarcopenia are the variables we have found and should be emphasized in this investigation.

In our study, patients were also evaluated in terms of routine outpatient clinic evaluations and questions related to nutrition - frailty - sarcopenia, and handgrip strength. Hepatitis B and C infections, alcohol consumption, non-alcoholic fatty liver disease, and autoimmune liver illnesses are some of the etiologies of liver cirrhosis (130). While it is predicted that the number of patients will decrease in the future with advances in the treatment of chronic viral hepatitis, the increasing incidence of fatty liver and non-alcoholic fatty liver disease shows the potential for an increase in cases of liver cirrhosis on this basis. In our study group, the leading etiologic cause was NASH, followed by hepatitis B and alcohol. The majority of the study patients had cryptogenic cirrhosis. Different studies emphasize that patients with cryptogenic cirrhosis may be undiagnosed NASH patients at varying rates (131). Considering that this situation is valid in our study population, it can be easily said that NASH is a cause of cirrhosis well ahead of viral etiologies.

In the management of decompensated liver cirrhosis patients with complications, a careful approach should be followed in terms of prognosis management. Cirrhosis patients frequently experience ascites and hepatic encephalopathy (HE) (132). Chronic alcoholism symptoms such as Wernicke's encephalopathy, alcohol withdrawal-induced delirium, severe hyponatremia, encephalitis, and dementia may be mistaken for HE (133). In our study, patients who consumed alcohol infrequently or never had the highest alcohol consumption rates. In the records, there were no patients who regularly consumed

alcohol. The rate of alcohol usage may have decreased as a result of the patients having cirrhosis diagnoses. As a result, it was not viewed as a restriction. Nearly half of the patients had ascites, but only a third had encephalopathy as cirrhosis sequelae. In the study findings, the incidence of treatment-resistant ascites was higher than the incidence of encephalopathy. It was shown that patients who consumed red meat 2-3 days a week had greater muscle strength when this group of patients was evaluated. On detailed examination, it was found that both arm muscle strength was higher for the group consuming meat 2-3 days a week compared to the group consuming meat rarely. Supporting this result, the data of the group consuming red meat 4 days a week had the highest muscle strength. This effect of meat-eating frequency may be especially noticeable in patients with advanced liver damage because of the link between sarcopenia and elevated Child and Meld scores. Another interpretation that can be made from the obtained results is that the content of the meals may have a more significant impact on the frailty score than meal frequency.

It is known that excessive protein load can increase the ammonia burden in cirrhotic patients due to the effect on metabolism and can trigger hepatic encephalopathy (134). The preference for lactulose in the treatment of encephalopathy is based on its ability to reduce ammonia absorption and accelerate its passage through intestinal acidification (135). In our patient group, the consumption of red meat was not found to have a significant effect on the frequency of encephalopathy (p: 0.508). Increasing the frequency of red meat consumption did not trigger the complication of hepatic encephalopathy, which is an important point to emphasize. However, it is not possible to make a definitive conclusion regarding its impact on the course of patients with complications. On the other hand, predicting the consequences of a possible dietary modification and increased meat consumption in terms of encephalopathy based on this study is uncertain. Another important point is that the interpretation was based on the weekly frequency of meat consumption, and not specifying the protein/meat quantity is a limitation of the study.

In our study, the mean BMI was 27 kg/m^2, indicating that our group can be classified as mildly to moderately overweight. The median age of 66 suggests a significant presence of the geriatric population in our patient group. When examining the correlation between muscle strength and age, MELD score, Child score, and BMI, it was observed that muscle strength moderately correlated with decreasing age (left arm p: 0.05, r: 0.638). The relationship between BMI and muscle strength was found to be significant (right arm $p < 0.001$, r: 0.483; left arm $p < 0.001$, r: 0.466), but the correlation was weak. The relationship between age and arm strength can be explained by the sarcopenia associated with geriatric age, and the weaker relationship for the dominant arm may indicate the protective effect of active use. It is known that increasing age is a risk factor for higher BMI. On the other hand, it is known that in advanced stages of cirrhosis, sarcopenia and even cachexia can occur. This can be expected to lower the BMI, but at the same time, the acidosis associated with advanced liver disease will have an increasing effect on BMI calculation. In support of this, a study found no significant association between sarcopenic obesity and any anthropometric measurement in an elderly female population (136). In another study, it was emphasized that BMI and dry BMI were insensitive as diagnostic criteria for malnutrition in the presence of cirrhosis (137). Therefore, BMI may not be particularly suitable for evaluating the nutritional status of patients with cirrhosis. The Turdep-II study has shown an increase in the prevalence of overweight/obese individuals in our country (138). The patient population in our study may also reflect the general trend in our country, possibly influenced by the increased risk of overweight/obesity associated with age. On the other hand, the most common etiology of cirrhosis in our group NASH may have also had an impact on these results. The worsening of cirrhosis leads to a decrease in muscle strength. It is not possible to make a definitive interpretation in our study regarding the positive impact of disease progression on muscle gain or strength.

As mentioned above, BMI should not be evaluated as a standalone parameter. As we mentioned, in patients with cirrhosis, ascites create a separate confounding factor for BMI. However, as demonstrated in our study, low BMI may be an indicator of muscle strength loss, although it does not show a strong correlation. Muscle strength and MELD and Child scores proved moderate and substantial adverse correlations. (MELD: $p<0.001$, -0.584; $p<0.001$, -0.641; Child: $p<0.001$, -0.565; $p<0.001$, -0.585). In a study evaluating the cirrhotic patients' dietary history throughout the previous three months, a 56%

decrease in oral intake was found to be associated with muscle strength (139). This indicates a relationship between recent malnutrition (or risk) and the risk of sarcopenia. Even a change in this parameter alone should be alerting in rapidly decompensating cirrhotic patients. In the continuation of the study, the results obtained from frail and prefrail scoring were 30% and 60%, respectively, indicating an association between frailty and muscle strength. Similarly, the investigation of sarcopenia risk using the SARC-F questionnaire was found to be related to muscle strength in the cirrhosis patient group. Although these scores do not provide a definitive diagnosis for sarcopenia, their ease of evaluation and repeatability in outpatient settings suggest that they can be instructive and enable proactive management.

Our study shows that albumin, bilirubin, and INR values are correlated with muscle strength. When this correlation was examined in detail, mean albumin values of 3.4 g/dL were correlated with the results of muscle strength measurements in the arms ($p:<0.001$), whereas INR and total bilirubin were negatively correlated with muscle strength (r: -0.411, -0.411; -0.416, -0.513, respectively). Based on these results, even small changes in albumin values may be associated with muscle strength, as well as the relationship between INR and bilirubin levels, which are widely used in the literature as indicators of disease severity and muscle strength. The finding that albumin, a parameter that is strongly associated with mortality in cirrhotic patients, is associated with sarcopenia even at values close to normal may be interpreted as a sign that it may not be easy to evaluate the nutritional - sarcopenia status using only albumin.

In a literature review, it was thought that vitamin D deficiency might lead to NASH by changing the level of hepcidin, and the relationship between hepcidin and vitamin D was examined. However, no statistically significant difference was found in terms of hepcidin levels and, thus, vitamin D according to vitamin D classes in the patient and control groups ($p>0.05$) (140). In our study, no data supporting the development of frailty and malnutrition were observed with vitamin D levels (mean 26.5 nmol/L). Patients' replacement use and ultraviolet (UV) exposure were considered study limitations.

In one study, sarcopenia was not associated with increased mortality or rehospitalization after liver transplantation in patients with end-stage liver disease model scores (141), whereas in another study, the mortality rate was shown to increase as the severity of sarcopenia increased or its duration prolonged (142). In our study, it is not possible to comment on long-term survival. However, the fact that we showed a significant correlation between the Child score, which is known to be associated with survival, the MELD score, which is used to determine priority in transplantation lists, and serum albumin levels, which have been shown to be associated with complications and survival benefit of replacement in acute periods, and muscle strength of the patients suggests that sarcopenia may be associated with survival. Whether the assessment of sarcopenia has, a relative advantage over these scoring methods needs to be examined with different designs.

6. CONCLUSION

Our study showed that sarcopenia and malnutrition are common in patients with hepatic cirrhosis and that there is a substantial correlation between muscle strength and sarcopenia. Additionally, the patient's dietary habits were evaluated, including meal frequency, presence of food allergies, frequency of red meat consumption, alcohol use frequency, and use of dietary supplements. Muscle strength and BMI have been found to be significantly correlated based on these variables. To evaluate the prognosis of liver cirrhosis with malnutrition, the Child-Pugh score and classification, as well as the Model for End-Stage Liver Disease (MELD)/MELD-Na scores, were calculated, and a positive correlation was found. In the assessment of nutritional status in the last 3 months, more than half of the patients experienced a significant loss of appetite, which was significantly associated with muscle strength. Consequently, widespread development of malnutrition was observed in patients with liver cirrhosis, independent of etiological factors and due to decreased appetite and the increasing catabolic processes associated with the course of the disease. These factors were associated with decreased BMI, reduced muscle strength, and the development of sarcopenia. Additionally, the frequency of red meat consumption did not show a significant effect on hepatic encephalopathy.

Our study suggests that patients with liver cirrhosis are susceptible to the development of malnutrition due to decreased oral intake, which subsequently triggers muscle wasting and the development of sarcopenia. We still need to learn more about how nutrition affects the development of liver cirrhosis and how it relates to sarcopenia in our country.

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8. APPENDICES

Appendices 1: Anket Formu

Bu çalışmaya katılmak tamamen gönüllülük esasına dayanmaktadır. Çalışmanın amacına ulaşması için sizden beklenen, bütün soruları eksiksiz, ve size en uygun gelen şekilde cevaplamanızdır. Çalışmaya katılmama hakkına da sahipsiniz. Bu çalışmadan elde edilecek bilgiler tamamen araştırma amacı ile kullanılacaktır ve kişisel bilgileriniz gizli tutulacaktır.,

BU KISIM HASTA veya YAKINI TARAFINDAN DOLDURULACKTIR

Adınız: **Doğum Tarihi:**

Soyadınız :

1) **Günde kaç öğün yemek yersiniz:**
2) **Bildiğiniz herhangi bir besin alerjiniz var mı?**

Varsa nedir: ……

3) **Ortalama ne sıklıkla kırmızı et tüketirsiniz?**

Haftada 1 veya hiç b) Haftada 2 -3 c) Haftada 4 ve üzeri

4) **Ne sıklıkla alkol tüketirsiniz?**

a) Hiç b) Nadiren – sosyal içici c) En az Haftada 1 gün

b) d) Hergün

5) **Beslenme desteği amacıyla kullandığınız bir ürün var mı? Varsa nelerdir?**

a) Yok b) Var İsmi nedir:

6) **Kaç günde bir büyük tuvalete çıkarsınız?**

a) Her gün b) Haftada 2 gün c) Haftada 1'den daha az

7) **Son 4 haftanın ne kadarlık kısmında yorgun hissetttiniz?**

a) Nadiren b) Çoğu Zaman

8) **10 basamak merdiveni dinlenmeden, tek başınıza ve yardımsız yürümekte herhangi bir zorluk çekiyor musunuz?**

a) Evet b) Hayır

9) **200 metreyi tek başınıza yardımsız ve güçlük çekmeden yürümekte zorluk çekiyor musunuz?**

a) Evet b) Hayır

10) **1 yıl içerisinde kaç kilo kaybettiniz? Son 3 ayda besin alımında, yemek yemede bir azalma oldu mu?**

a) Şiddetli azalma b) Orta derecede azalma c) Azalma yok

11) **Son 3 ay içindeki kilo kaybı yaşadınız mı, kaç kilo kaybettiniz?**

a) 3 kg'dan fazla b) 1-3 kg arası c) kilo kaybı yok d) bilmiyorum

12) Kilo kaybı idrar söktürücü ilaç ile mi oldu ?

a) Evet b)Hayır

13) Hastanın hareketlilik durumu nedir?

a) Yatak veya sandalyeye bağımlı

b) Yataktan, sandalyeden kalkabiliyor ama evden dışarı çıkamıyor

c) Evden dışarı çıkabiliyor

14) Son 3 ayda psikolojik stress veya ciddi hastalık şikayeti oldu mu

a) Evet b) Hayır

15) Bunama veya psikolojik problemler var mı?

a) ciddi bunama ve depresyon

b) hafif düzeyde bunama

c) hiçbir psikolojik problem yok

5 kg kaldırıp taşıyabilir misiniz?	Hiç	Biraz zorlanırım	Çok zorlanırım veya yapamam
Odada yürümede zorlanır mısınız?	Hiç	Biraz zorlanırım	Çok zorlanırım veya yapamam
Sandalye ve yataktan geçişte zorlanır mısınız?	Hiç	Biraz zorlanırım	Çok zorlanırım veya yapamam
10 basamak çıkmakta zorlanır mısınız?	Hiç	Biraz zorlanırım	Çok zorlanırım veya yapamam
Son 1 yıl içinde kaç kez düştünüz?	Hiç	1-3 kez düştüm	4'den daha fazla düştüm

	El kavrama gücü ölçümleri	
	Sol El	Sağ El
Ölçüm		
Ölçüm		
Ölçüm		

KATILIMINIZ İÇİN TEŞEKKÜR EDERİZ.

BU KISIM RETROSPEKTİF OLARAK HASTA DOSYASINDAN ALINACAKTIR.

Appendices 2: Biyokimyasal ve Hematolojik Bulguların Referans Değerleri

Hasta no		**Doldurma Tarihi**	
Ad - Soyad		**Boy**	
Cinsiyet	E - K	**Kilo**	
Siroz Etiyolojisi:	Kriptojenik; Hep B/B+D / C ; Alkol; NASH; Wilson; Diğer:		
Ek hastalık:	HT – DM – KOAH – MI – KKY – Angina -Astım – Aritmi - İnme - Böbrek hastalığı –Kanser Diğer:		
Diuretik Tedavi:			
İlaçlar:			
Asit	Yok/Kontrol altında/Kontrolsüz		
Ödem	Yok/Hafif /Ciddi		
Varis -kanama	Yok/Var kanama olmamış/Kanama öyküsü var		
Ensefalopati	Yok/Var kontrol altında/Sık atak var		
SBP öyküsü	Yok/Var		
HCC	Yok/Var		
Son 1 yıl içinde hastane yatış sayısı		**Son 1 yılda yoğun bakım ünitesi yatışı**	

Glukoz		**Demir /TDBK**		**ALT**	
Total protein		**Ferritin**		**AST**	
Albumin		**INR**		**ALP**	
CRP		**Total/direkt bilirubin**		**GGT**	
Total kolesterol		**Üre**		**HGB/HCT**	
HDL kolesterol		**Kreatinin**		**TSH**	
Trigliserit		**D Vitamini**		**Na**	

Appendices 3: Etik Kurul Onayı

Çalışmamız için İstanbul Üniversitesi Cerrahpaşa Tıp Fakültesi Etik Kurulu'ndan (karar no:) onay alınmıştır.

Hasta Onayı:

Retrospektif çalışma.

Hakem Değerlendirmesi:

Editörler kurulu dışında olan kişiler tarafından değerlendirilmiştir.

İSTANBUL ÜNİVERSİTESİ-CERRAHPAŞA REKTÖRLÜĞÜ
KLİNİK ARAŞTIRMALAR ETİK KURULU KARAR FORMU

(2011-KAEK-55)

ARAŞTIRMANIN AÇIK ADI	**"İstanbul'da Bir Üniversite Hastanesinin Gastroenteroloji Bölümüne Başvuran Karaciğer Sirozlu Hastalarda Malnütrisyon ve Sarkopeni İlişkisinin Değerlendirilmesi"**
VARSA ARAŞTIRMANIN PROTOKOL KODU	---

DEĞERLENDİRİLEN BELGELER	Belge Adı	Tarihi	Versiyon Numarası	Dili
	ARAŞTIRMA PROTOKOLÜ	☒		TÜRKÇE
	BİLGİLENDİRİLMİŞ GÖNÜLLÜ OLUR FORMU	☒		TÜRKÇE
	OLGU RAPOR FORMU	-		
	ARAŞTIRMA BROŞÜRÜ	-		

DEĞERLENDİRİLEN DİĞER BELGELER	Belge Adı		Açıklama
	SİGORTA	-	
	ARAŞTIRMA BÜTÇESİ	☒	
	BİYOLOJİK MATERYEL TRANSFER FORMU	-	
	İLAN	-	
	YILLIK BİLDİRİM	-	
	SONUÇ RAPORU	-	
	GÜVENLİLİK BİLDİRİMLERİ		
	DİĞER	☒	Anabilim Dalı Üst yazısı, Gizlilik Taahhütnamesi, Araştırmacılara ait özgeçmiş,Helsinki Bildirgesi, Sorumluluk paylaşım belgesi, İyi klinik uygulamalar kılavuzu taahhütnamesi, Aynı anda birden fazla merkeze başvuru yapılmadığı ve reddedilmediğine dair taahhütname, Araştırma projesinin daha önce yapılmadığı ya da bitirilmemiş bir proje olmadığına dair taahhütname, Araştırma projesinin daha önce yapılmadığı ya da bitirilmemiş bir proje olmadığına dair taahhütname

KARAR BİLGİLERİ		
	Karar No: 217	**Tarih: 04.07.2023**
	Prof.Dr.İkbal Billur CANBAKAN, Dr.Öğr.Üye.Gönde DÜMLÜ BİLGİN danışmanlığında, Uzm.Dr.Oğuz Kağan BAKKALOĞLU yardımcı araştırmacılığında Dyt.Melike TUNCER'in yürütücülüğünde yapılacak olan, yukarıda başvuru bilgileri verilen klinik araştırma başvuru dosyası ve ilgili belgeler araştırmanın gerekçe, amaç, yaklaşım ve yöntemleri dikkate alınarak incelenmiş olup, gerçekleştirilmesinde etik sakınca bulunmadığına toplantıya katılan etik kurul üyelerinin oy birliği ile karar verilmiştir.	

ETİK KURUL BİLGİLERİ	
ETİK KURULUN ÇALIŞMA ESASI	**İyi Klinik Uygulamaları Kılavuzu**
BAŞKANIN UNVANI / ADI / SOYADI:	Prof. Dr. Mehmet Sarper ERDOĞAN (Başkan)

ETİK KURUL ÜYELERİ

Unvanı/Adı/Soyadı	Uzmanlık Alanı	Kurumu	Cinsiyet		Araştırma ile ilişki *		Katılım *	
Prof. Dr. Mehmet Sarper ERDOĞAN (Başkan)	Halk Sağlığı	İÜ Cerrahpaşa Tıp Fakültesi	E ☒	K ☐	E ☐	H ☐	E ☒	H ☐
Prof. Dr. Semra ÖZDEMİR (Başkan Yard.)	Biyofizik	İÜ Cerrahpaşa Tıp Fakültesi	E ☐	K ☒	E☐	H ☐	E ☒	H
Doç. Dr. Ömer Faruk Demirel (Raportör)	Ruh Sağlığı ve Hastalıkları	İÜ Cerrahpaşa Tıp Fakültesi	E ☒	K ☐	E☐	H ☐	E	H ☒
Prof. Dr. Sibel ÖZYAZGAN	Tıbbi Farmakoloji	İÜ Cerrahpaşa Tıp Fakültesi	E ☐	K ☒	E☐	H ☐	E	H ☒
Prof. Dr. Şükrü Öztürk	İç Hastalıkları	İÜ İstanbul Tıp Fakültesi	E ☒	K ☐	E ☐	H ☐	E	H ☒
Prof. Dr. Kerem Erkalp	Anesteziyoloji ve Reanimasyon	İÜ Cerrahpaşa Tıp Fakültesi-Kardiyoloji Enstitüsü	E ☒	K ☐	E☐	H ☐	E ☒	H ☐
Prof.Dr.Hidayet SARI	Fizik Tedavi ve Rehabilitasyon	Dış Üye	E ☒	K ☐	E☐	H ☐	E ☒	H
Prof.Dr.Mehmet Rıza ALTIPARMAK	İç Hastalıkları	İÜ Cerrahpaşa Tıp Fakültesi	E ☒	K ☐	E☐	H ☐	E ☒	H
Doç.Dr.Ayşe Ayzıt KILINÇ SAKALLI	Çocuk Sağlığı ve Hastalıkları	İÜ Cerrahpaşa Tıp Fakültesi	E ☐	K ☒	E	H ☐	E ☒	H
Dr.Öğr.Üye.Ahmet ÖZDİNÇ	Tıp Tarihi ve Etik	İÜ Cerrahpaşa Tıp Fakültesi	E ☒	K ☐	E☐	H ☐	E ☒	H
Dr.Öğr.Üye.Elif Altınay KIRLI EGEMEN	Çocuk Cerrahisi	İÜ Cerrahpaşa Tıp Fakültesi	E ☐	K ☒	E☐	H ☐	E	H ☒
Dr.Serdar Şirazi	Avukat	Dış Üye	E ☒	K ☐	E☐	H ☐	E ☒	H
Muhamet Fethi Aslaner	Sivil Üye	İÜ Cerrahpaşa Tıp Fakültesi Vakfı	E ☒	K ☐	E☐	H ☐	E ☒	H

Yönetmelik kapsamı dışında kalan araştırmalar ise Etik Kurul bünyesinde oluşturulmuş 11 kişilik alt komisyon tarafından değerlendirilmekte olup Sağlık Bakanlığı iznine tabi değildir.
"Kişisel Verilerin Korunması Kanunu kapsamında çalışmaya katılan gönüllülerin verilerinin korunması ile ilgili tedbirleri almak Araştırmacının sorumluluğundadır"

Appendices 4: Questionnaire in English

1- How many meals a day do you eat:

2- Do you have any known food allergies, and if so, what are they:

3- How often do you consume red meat on average?

a) One or none per week b) 2 -3 per week c) 4 or more per week

4- How often do you drink alcohol?

a) Never b) Rarely - social drinker c) At least one day a week d) Every day

5- Is there a product you use for nutritional support, and if so, what is it?

a) None b) Yes, what is the name:

6- How often do you go to the toilet?

a) Every day b) 2 days a week c) Less than once a week?

7- How much of the last 4 weeks have you felt tired?

a) Rarely b) Most of the time

8- Do you have any difficulty walking up 10 flights of stairs without rest, alone and unassisted?

a) Yes b) No

9- Do you have difficulty walking 200 meters alone without assistance and without difficulty?

a) Yes b) No

9- How many kilograms have you lost in the last 1 year?

11- Has there been a decrease in food intake and eating in the last 3 months?

a) Severe decrease b) Moderate decrease c) No decrease

12- Have you experienced weight loss in the last 3 months? How much weight did you lose?

a) More than 3 kg b) between 1-3 kg c) no weight loss d) don't know.

13- Was the weight loss caused by diuretics?

a) Yes b) No

14- What is the patient's mobility status?

a) Bed or chair dependent

b) Can get out of bed, or chair but cannot go out of the house

c) Can go out of the house

15- Has there been any psychological stress or serious illness in the last 3 months?
a) Yes b) No

16- Are there dementia or psychological problems?
a) severe dementia and depression
b) mild dementia
c) no psychological problems

Can you lift and carry 5 kg	Not at all	A little	Very difficult or unable
Do you have difficulty walking in the room?	Not at all	A little	Very difficult or unable
Do you have difficulty transferring from a chair to a bed?	Not at all	A little	Very difficult or unable
Do you have difficulty climbing 10 steps?	Not at all	A little	Very difficult or unable
How many times have you fallen in the past year?	Ever fallen	Fallen 1 - 3 times	Fallen more than 4 times

When evaluating the patients' responses to these questions, their answers were used to calculate the FRAIL frailty and SARC-F sarcopenia index scores based on their respective risks. The questions for the FRAIL frailty index can be found in Appendix 2.

- "How much of the past 4 weeks did you feel tired?"
- "Do you have any difficulty walking up 10 steps without resting, on your own, and without assistance?"
- "Do you have difficulty walking 200 meters on your own and without difficulty?"
- Answered responses to these questions and
- Weight loss of >5% in the past year.

9. CURRICULUM VITAE

Kişisel Bilgiler

Adı	MELİKE	**Soyadı**	TUNCER
Doğum Yeri			
Uyruğu			
E-mail			

Öğrenim Durumu

Derece	**Alan**	**Mezun Olduğu Kurumun Adı**	**Mezuniyet Yılı**
Yüksek Lisans	Beslenme ve Diyetetik	Yeditepe Üniversitesi	
Lisans	Beslenme ve Diyetetik	Bahçeşehir Üniversitesi	2020
Lise	-	Bahçelievler Anadolu Lisesi	2015

Bildiği Yabancı Dilleri	**Yabancı Dil Sınav Notu (#)**
İngilizce	B2-C1 (proficiency passed)
Almanca	A1-A2

Başarılmış birden fazla sınav varsa(KPDS, ÜDS, TOEFL; EELTS vs), tüm sonuçlar yazılmalıdır

İş Deneyimi (Sondan geçmişe doğru sıralayın)

Görevi	Kurum	**Süre (Yıl - Yıl)**
Klinik Diyetisyen	Koç Üniversitesi Hastanesi	halen
Araştırma Görevlisi	İstinye Üniversitesi	8 ay

Bilgisayar Bilgisi

Program	**Kullanma becerisi**
Microsoft Word	Giriş düzeyi
Microsoft Excel	Giriş düzeyi

*Çok iyi, iyi, orta, zayıf olarak değerlendirin

Diğer (Görev Aldığı Projeler/Sertifikaları/Ödülleri)

Global Health Dergisi içerik yazarlığı yaptı.
2019 Bahçeşehir Üniversitesi "Pediatride Vakalar Eşliğinde Beslenme Sempozyumu" organizasyon ve sunuculukta görev aldı.
2019 yılında İtalya Tuscany bölgesinde bulunan Ospedale Apuane, Ospedale Civile di Carrara ve Madre Cabrini DCA merkezlerinde gastroenteroloji, endokrinoloji, yeme bozukluğu eğitimlerine katıldı.
2020 Bahçeşehir Üniversitesi Psikoloji Yan dal sertifikası aldı.