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Study Protocol

The FraiLtx Study Protocol: A Prospective, Single-Center Observational Study on Frailty, Systemic Inflammation, and Monocyte Subsets in Liver Transplant Candidates

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Abstract: Introduction: Frailty is a multidimensional syndrome characterized by diminished physiological reserve and increased susceptibility to stressors, resulting in poor perioperative outcomes. While commonly associated with elderly patients, frailty is increasingly recognized in liver transplant candidates, where it significantly affects morbidity and mortality. The pathophysiological mechanisms underlying frailty in this population remain poorly understood. However, evidence from other distinct patient groups suggests that frailty is linked to a distinct immunophenotype involving altered monocyte subset distribution and elevated pro-inflammatory cytokines. The FraiLtx study aims to investigate the association between frailty, systemic inflammation, and monocyte subpopulations in liver transplant candidates. Methods and analysis: FraiLtx is a prospective, single-center, observational study. We aim to include 81 patients listed for liver transplantation and a control group of 20 individuals not being listed for liver transplantation. Frailty is assessed using both the Liver Frailty Index (LFI) and the FRAIL Scale. Routine blood sampling is performed to calculate the MELD score (model of end stage liver disease). Furthermore, plasma is isolated for quantification of key pro-inflammatory cytokines, and erythrocyte-lysed whole blood is used for detailed profiling of circulating monocyte subsets by flow cytometry. All participants undergo body composition analysis using whole-body MRI (EchoMRI™). Discussion: Although liver cirrhosis is known to be associated with an altered immune landscape, no studies to date have systematically examined the relationship between frailty and immunophenotype in liver transplant candidates. We hypothesize that frail patients listed for liver transplantation will exhibit a characteristic pattern of systemic inflammation, altered monocyte subset distribution, and distinct body composition features. By elucidating the biological correlates of frailty in this cohort, FraiLtx aims to enhance our understanding of its

pathophysiology, improve risk stratification, and support the development of targeted therapeutic strategies for this vulnerable population.

Keywords: liver transplantation; frailty; immunology; body composition

1. Introduction

Liver disease causes approximately two million deaths each year, making it the 11th leading cause of death worldwide. Liver transplantation (LT) remains the only curative therapy for patients with end-stage liver disease and improves outcomes in both acute and chronic hepatic failure [1,2]. However, LT faces persistent challenges, including a shortage of donor organs: currently, less than 10% of the demand is met, creating an ethical imperative to equitably allocate scarce resources amid increasing patient complexity [2,3]. To address these challenges, the model for end-stage liver disease (MELD) score has been widely adopted for prioritizing patients on the waiting list [3]. Despite its widespread use, the MELD score reflects laboratory markers but does not capture indicators of nutritional status or physical function [3,4]. This limitation may lead to the under-prioritization of patients who are physiologically compromised but have low MELD scores. Thus, the search for supplemental metrics has focused on filling these prognostic gaps [4,5].

A syndrome that describes this loss of function is frailty, which is a multidimensional syndrome with reduced reserve capacity and increased vulnerability to stressors, as a result of which it is associated with a significantly increased risk of perioperative morbidity and mortality [6,7]. Although frailty is estimated to affect 25–50% of patients over 85 years of age and therefore has a major impact on perioperative medicine, there is no standardized definition of frailty [8]. A common model for characterizing frailty is the phenotype model according to Fried et al. (2001), which is characterized by the presence of pronounced fatigue, muscle weakness, low physical activity, slowed walking speed and unintentional weight loss [9]. According on this phenotype, the Frail Scale is a tool that assesses frailty based on fatigue, resistance, ambulation, illnesses, and loss of weight and is associated with an increased postoperative complication rate and mortality in older surgical patients [10].

Although liver transplant candidates are generally younger than the previously described populations, they exhibit a comparable frailty phenotype. In this specific cohort, frailty is assessed using the Liver Frailty Index (LFI), a validated predictor of both waiting list and post-transplant mortality [11–13]. A key contributing factor is sarcopenia, which plays a central role in LFI assessment and is particularly relevant in liver transplant patients.

Although frailty is inherently multifactorial, alterations in body composition, particularly sarcopenia and the loss of muscle mass, are considered central to its pathogenesis [14,15]. Studies in community-dwelling older adults have shown that sarcopenia is highly prevalent among frail individuals [16]. Accordingly, sarcopenia has emerged as a biologically meaningful and potentially modifiable component of frailty [14,15]. Fumagalli et al. emphasize this concept by demonstrating that CT-derived measures of both muscle quantity and quality strongly correlated with patient frailty and independently predicted postoperative complications in patients who underwent abdominal surgery [17]. Their findings suggest that muscle phenotype may offer a dynamic framework for risk stratification independent of subjective functional testing or time-consuming clinical frailty scores [17]. However, these assessments rely on cross-sectional imaging (e.g., CT), which requires specialized software, trained personnel, and exposes patients to radiation—factors that limit routine or repeated implementation in LT candidates [18].

The detailed pathogenesis of frailty in elderly patients as well as other cohorts that leads to the poor prognosis has not yet been clarified. There is evidence that a change in the immune system which leads to "cold" chronic inflammation may play a decisive role [19–21]. While a correlation between frailty and inflammatory markers like IL-6, CRP, TNF-α and albumin has been shown in elderly patients, there are also some results in more specific patient groups like patients undergoing transcatheter aortic valve implantation (TAVI) that show similar correlations [6, 22–25].

In 120 patients undergoing TAVI a correlation between eyeball frailty, increased inflammatory parameters (CRP, IL-8) and the increase in intermediate monocytes could be shown, both frailty and elevated intermediate monocyte levels were associated with increased mortality following TAVI [6]. Cybularz et al. [6] conclude that an altered immunological status could be a possible mechanism underlying the increased mortality following TAVI in frail patients, which could be reflected not only in the extent of systemic inflammation but also in the type of cells involved, such as increased levels of intermediate monocytes.

In patients with liver cirrhosis, circulating monocyte subpopulations exhibit distinct phenotypic alterations. These include increased expression of CCR4, CXCR3, CXCR4, and CD62L, alongside reduced expression of CCR2 and HLA-DR, as well as elevated plasma levels of IL-6, IL-10, and IL-17A [25–27]. However, in patients with end stage liver disease, little is known about how frailty affects the monocyte phenotype or whether such phenotypic alterations are associated with poorer outcomes.

The aim of the FraiLtx study is to gain a better understanding of the pathogenesis of frailty in liver transplant candidates in order to optimize therapies for this vulnerable patient group by identifying potential bio markers. Therefore, we will examine whether the proinflammatory status—characterized by monocyte subpopulations and systemic inflammatory markers—correlates with frailty in patients with end-stage liver disease, and additionally define a body-composition phenotype in frailty-affected liver transplant candidates.

2. Methods

This study is a prospective, single center, observational study at the University Hospital Schleswig-Holstein, Campus Kiel. The aim is to interdisciplinary investigate the association between frailty and systemic inflammation by analysing monocyte subpopulations and cytokines in liver transplant candidates. Additionally, we seek to define the body composition phenotype of frail individuals in this population. Therefore, we screened liver transplantation listed patients attending a routine appointment in the transplant outpatient clinic as well as listed patients who are hospitalized due to decompensation.

Inclusion criteria

- Liver transplantation listed patient
- Age ≥ 18 years
- Capable of providing informed consent and willing to do so

Exclusion criteria

- Acute infection
- Participation in an interventional study within the last 30 days
- Previous participation in this study

Based on identical in- and exclusion criteria a control cohort of 20 individuals not being listed for liver transplantation were recruited. For a balanced frailty distribution (10 frail, 10 non-frail) in the control cohort, subjects were subjectively assessed for frailty before inclusion (Figure 1).

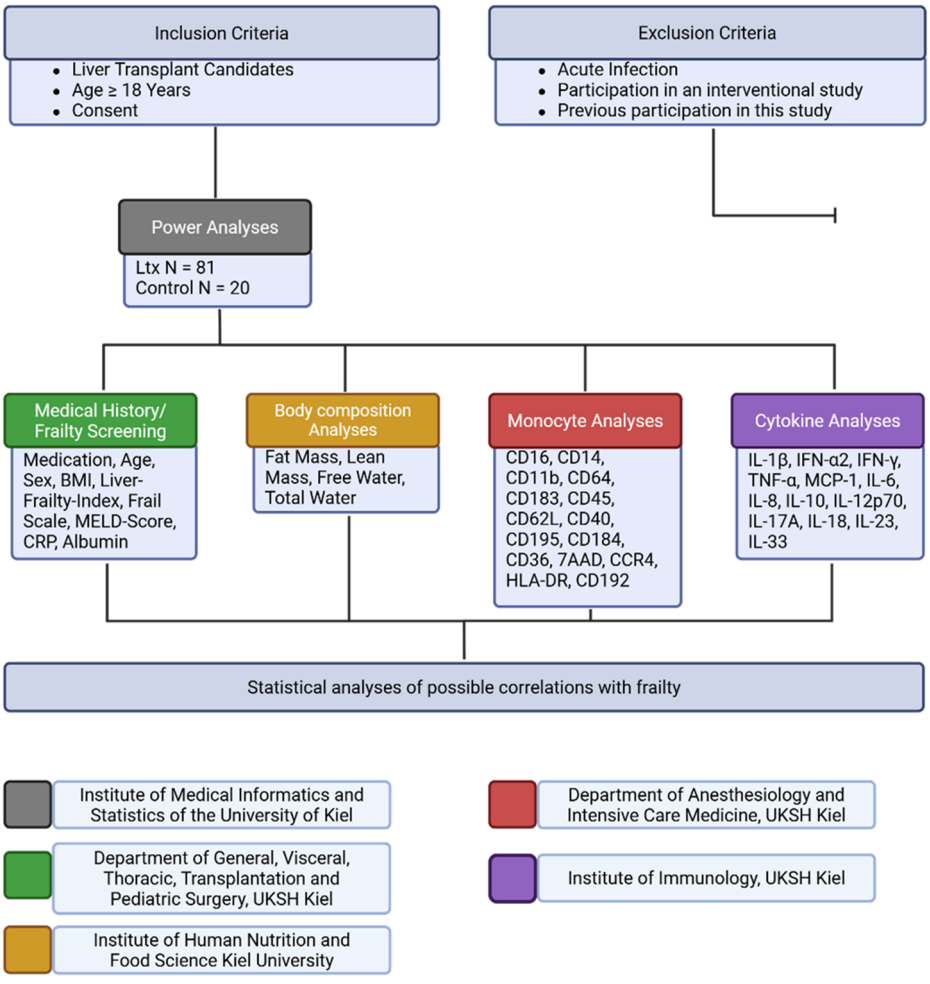

Figure 1. FraiLtx study protocol.

2.1. Assessments

A medical history was taken on all participants and their age, gender, height and weight were recorded. Furthermore, all participants were assessed for frailty using the Liver Frailty Index [7] and the Frail Scale [8]. At the day of frailty assessment, a routine blood sample was taken from all listed patients and C-reactive protein (CRP) and albumin concentrations, as well as the Model of end stage liver disease score (MELD-Score) [4] were determined. For immunophenotyping, 5 mL of citrated blood was taken from all participants. Furthermore, all participants without MRI specific contraindications underwent a body composition analysis using the EchoMRI™ Adolescent Humans Body Composition Analyzer (EchoMRI LLC, Houston, TX, USA). This non-imaging, whole-body MRI, which is specifically designed to assess body composition, provides precise absolute values for whole-body fat mass, lean mass, free water, and total body water in just a few minutes.

EchoMRI contraindications

- Immobilization
- Pregnancy
- Cardiac pacemakers
- Non-MRI-capable prostheses
- Prostheses implanted within the last 6 weeks
- Claustrophobia

Immunophenotyping of monocytes was done using a MACSQuant X (Miltenyi Biotec, Bergisch Gladbach, Germany; Tables 1 and 2).

Table 1. Antibody panel for monocyte analyses. (-): Unstained; (+): 7-AAD staining, FICT: Fluorescein, PE: Phycoerythrin, APC: Allophycocyanin, AF 647: Alexa Fluor 647, 7-AAD: 7-amino-actinomycin D

Tube	FICT	PE	APC	AF 647	7-AAD
1	-	-	-	-	-
2	Mouse IgG1	Mouse IgG2α,κ	Mouse IgG1	-	+
3	CD16	CD14	CD11β	-	+
4	CD64	-	CD183	-	+
5	CD45	-	CD62L	-	+
6	-	-	CD40	-	+
7	Mouse IgG2α	Mouse IgG1	Mouse IgG2α	-	+
8	CD195	CD194	CD184	-	+
9	HLA-DR	CD36	-	-	+
10	-	-	-	Mouse IgG2β	+
11	-	-	-	CD192	+

Table 2. Staining protocol for monocyte analyses.

Step	Staining Protocol
1	Add staining reagent (per manufacturer's instructions) to 0.2 mL citrated blood
2	Incubate at 4 °C for 25 min
3	Add 5 µL of 7-AAD
4	Incubate for 5 min in the dark
5	Add 2 mL FACS Lysing Solution
6	Incubate for 10 min in the dark
7	Centrifuge for 5 min at 1800 rpm
8	Discard the supernatant and add 2 mL PBS
9	Centrifuge for 5 min at 1800 rpm
10	Discard the supernatant and add 2 mL PBS
11	Centrifuge for 5 min at 1800 rpm
12	Discard the supernatant and add 0.2 mL PBS
13	Analyze the sample using MACSQuant

Pro-inflammatory cytokines are analysed employing the LEGENDplex™ Human Inflammation Panel 1 (IL-1β, IFN-α2, IFN-γ, TNF-α, MCP-1, IL-6, CXCL8 (IL-8), IL-10, IL-12p70, IL-17A, IL-18, IL-23, IL-33; BioLegend, San Diego, USA). Due to logistical constraints, cytokine measurements could not be performed on the day of sample collection. After blood for flow cytometry has been collected, the remaining citrated blood was centrifuged, and the plasma is aliquoted and stored at −80 °C for batch analysis after completion of recruitment.

2.2. Statistical Analysis

In a first step we plan to evaluate distinct liver cirrhosis, frailty, body composition and immune phenotypes. In a follow-up assessment we plan to correlate these phenotypes to identify potential associations. A key focus here will be on identifying independent variables in order to enable the most valid conclusions possible regarding morbidity and mortality, as well as the cause and effect of the phenotypes.

2.3. Sample Size

The sample size was determined using the Wilcoxon rank-sum test based on the results of Cybularz et al. [6] and calculated with G*Power (3.1.9.6, Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany). Assuming an effect size of d = 0.8, a power of 80%, and a significance level of 5%, the analysis indicated a required sample size of 81 patients.

Unfortunately, due to a lack of funding, it was not possible to recruit a control group of the same size as the cohort calculated for the study. In order to still obtain a comparison with non-cirrhotic individuals, a control group was recruited that was sized so as to use up the cytokine panels acquired for the study.

3. Discussion

The FraiLTx study aims to provide a comprehensive, interdisciplinary assessment of frailty in liver transplant candidates. While laboratory-based models for predicting outcomes in transplant candidates have been extensively validated, the increasing scarcity of donor organs and the resulting prolongation of waiting times require greater emphasis on patients' functional status and participation in everyday life. To the best of our knowledge, no previous study has adopted such a holistic approach to the assessment of frailty in this specific patient population.

Our first hypothesis is that selected concepts and approaches established in the care of classically frail patients can be transferred to liver transplant candidates. A central objective of geriatric medicine is the preservation and restoration of functional capacity and participation. However, important differences between these populations must also be acknowledged. In geriatric patients, biological aging is considered one of the principal drivers of frailty. Furthermore, curative treatment is often not available, whereas liver transplant candidates have the potential for definitive treatment through transplantation. Consequently, the primary therapeutic goal in this population is to bridge the waiting period while achieving the best possible preoperative stabilization. Demonstrating shared pathophysiological mechanisms between geriatric frailty and frailty in liver transplant candidates could identify common therapeutic targets, facilitate synergistic treatment strategies, and ultimately contribute to improved patient care.

Nevertheless, it should be acknowledged that the pathophysiology of frailty remains incompletely understood, even in geriatric populations. Sarcopenia appears to represent one of its major contributing factors. Therefore, we sought to characterize a body composition phenotype in our cohort. Conventional methods for assessing body composition have important limitations in liver transplant candidates. Recent studies have explored alternative modalities such as bioelectrical impedance analysis (BIA) to identify body composition phenotypes associated with frailty [16]. However, the use of BIA in patients with liver cirrhosis is problematic, as the method's underlying assumption of constant hydration of fat-free mass is frequently violated in clinical conditions such as ascites or peripheral edema, resulting in inaccurate estimates of lean and fat mass. Computed tomography (CT)-based body composition analysis represents another well-established approach but is associated with exposure to ionizing radiation and was therefore not considered appropriate for use in our exploratory study. Instead, we had the opportunity to perform magnetic resonance imaging (MRI)-based body composition analysis, a technique that remains relatively uncommon because of its limited availability and higher costs. In future work, we plan to compare MRI-based measurements with CT-derived body composition analyses to improve the generalizability and comparability of our findings.

Our second hypothesis is that an inflammatory profile is positively associated with frailty. The selection of inflammatory markers is critical in this context. We therefore focused on pro-inflammatory biomarkers and systemic inflammatory states that have previously been reported to correlate with frailty. Exploratory approaches of this kind require particularly careful statistical analysis and subsequent validation in independent cohorts, as well as a longitudinal follow-up, otherwise our ability to assess temporal changes in immune profiles and frailty progression is limited. Furthermore, a great challenge is distinguishing between dependencies, causes, and effects among the phenotypes studied. In particular, distinguishing the influence of frailty and liver disease on the phenotypes poses a major challenge, partly due to the size of the control cohort. One possible approach to differentiation is to consider the Frail Scale as well as the LFI and MELD scores. Frailty was assessed in all patients using the Frail Scale, which

provides reliable and liver-independent information about perioperative outcome and can be compared with the LFI and MELD scores which provide specific information about the severity of liver disease.

Nevertheless, we believe that this approach represents an important first step toward a better understanding of the underlying pathophysiology and may provide the basis for the development of targeted therapeutic strategies in future studies.

Author Contributions

A.L.H.: initiated the study; O.S.: coordinated participant recruitment and continues to coordinate assessments; A.B.-W.: planned and supervises the body composition analyses; G.E.: co-initiated the study and advises on body phenotype assessments; A.C.: calculated the statistical power and advised on the study design; C.P.: performs the cytokine assays and advised on their planning; K.S.Z.: planned and assists with the monocyte assays; M.A.: planned the monocyte assays and advised on the study design. F.B.: coordinated patient assessments and advised on the study design. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

The study protocol (version 1.0) was finalized and prospectively registered in the German Clinical Trials Register (DRKS00033886) on 13 March 2024 and was updated following ethical approval to version 1.1 on 21 February 2025. Participant recruitment commenced in June 2024 and was completed by the end of 2025, with all planned participants enrolled by that time. The Ethics Committee of the Faculty of Medicine at the University of Kiel approved the FraiLtx study protocol on 26 November 2023 (D606/23). Data collection was restricted to pseudonymized patient information.

Informed Consent Statement

All participants were enrolled voluntarily after providing written informed consent.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author OS.

Conflicts of Interest

The authors declare no conflict of interest.

Use of AI and AI-Assisted Technologies

During the preparation of this work, the authors used DeepL Translate, DeepL SE for translation and stylistic editing. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

List of Abbreviations

AF	Alexa Fluor
APC	Allophycocyanin
BIA	Bioelectrical Impedance Analysis
CRP	C-Reactive Protein
CT	Computed Tomography
FICT	Fluorescein
LFI	Liver Frailty Index
LT	Liver Transplantation
MELD	Model of End Stage Liver Disease
MRI	Magnetic Resonance Imaging
PE	Phycoerythrin
TAVI	Transcatheter Aortic Valve Implantation
7-AAD	7-amino-actinomycin D

References

1. Girish, V.; Mousa, O.Y. Liver Transplantation. In *StatPearls [Internet]*; StatPearls Publishing: Treasure Island, FL, USA, 2026. Available online: http://www.ncbi.nlm.nih.gov/books/NBK559161/ (accessed on 6 April 2026).
2. Devarbhavi, H.; Asrani, S.K.; Arab, J.P.; et al. Global burden of liver disease: 2023 update. *J. Hepatol.* **2023**, *79*, 516–537. https://doi.org/10.1016/j.jhep.2023.03.017.
3. Sandhu, S.; Goldberg, D. Update on Organ Allocation and Liver Transplantation. *Gastroenterol. Hepatol.* **2025**, *21*, 424–430.
4. van Vugt, J.L.A.; Alferink, L.J.M.; Buettner, S.; et al. A model including sarcopenia surpasses the MELD score in predicting waiting list mortality in cirrhotic liver transplant candidates: A competing risk analysis in a national cohort. *J. Hepatol.* **2018**, *68*, 707–714. https://doi.org/10.1016/j.jhep.2017.11.030.
5. Engelmann, C.; Aehling, N.; Schob, S.; et al. Body fat composition determines outcomes before and after liver transplantation in patients with cirrhosis. *Hepatol. Commun.* **2022**, *6*, 2198–2209. https://doi.org/10.1002/hep4.1946.
6. Cybularz, M.; Wydra, S.; Berndt, K.; et al. Frailty is associated with chronic inflammation and pro-inflammatory monocyte subpopulations. *Exp. Gerontol.* **2021**, *149*, 111317. https://doi.org/10.1016/j.exger.2021.111317.
7. Murphy, P.; Savage, S.; Zarzaur, B. Impact of Patient Frailty on Morbidity and Mortality after Common Emergency General Surgery Operations. *J. Surg. Res.* **2020**, *247*, 95–102. https://doi.org/10.1016/j.jss.2019.10.038.
8. Clegg, A.; Young, J.; Iliffe, S.; et al. Frailty in elderly people. *Lancet* **2013**, *381*, 752–762. https://doi.org/10.1016/s0140-6736(12)62167-9. Erratum in *Lancet* **2013**, *382*, 1328.
9. Fried, L.; Tangen, C.; Walston, J.; et al. Frailty in older adults: Evidence for a phenotype. *J. Gerontol. A Biol. Sci. Med. Sci.* **2001**, *56*, M146–M156. https://doi.org/10.1093/gerona/56.3.m146.
10. Gong, S.; Qian, D.; Riazi, S.; et al. Association between the FRAIL Scale and Postoperative Complications in Older Surgical Patients: A Systematic Review and Meta-Analysis. *Anesth. Analg.* **2023,** 136, 251–261. https://doi.org/10.1213/ANE.0000000000006272.
11. Lai, J.; Covinsky, K.; Dodge, J.; et al. Development of a novel frailty index to predict mortality in patients with end-stage liver disease. *Hepatology* **2017**, *66*, 564–574. https://doi.org/10.1002/hep.29219.
12. Lai, J.; Feng, S.; Terrault, N.; et al. Frailty predicts waitlist mortality in liver transplant candidates. *Am. J. Transplant.* **2014**, *14*, 1870–1879. https://doi.org/10.1111/ajt.12762.
13. Klein, C.G.; Malamutmann, E.; Latuske, J.; et al. Frailty as a predictive factor for survival after liver transplantation, especially for patients with MELD ≤ 15—A prospective study. *Langenbeck's Arch. Surg.* **2021**, *406*, 1963–1969. https://doi.org/10.1007/s00423-021-02109-9.
14. Ferriolli, E.; Roschel, H. Body Composition and Frailty: The Role of Adiposity. *J. Nutr. Health Aging* **2023**, *27*, 401–402. https://doi.org/10.1007/s12603-023-1930-0.
15. Lai, J.; Tandon, P.; Bernal, W.; et al. Malnutrition, Frailty, and Sarcopenia in Patients with Cirrhosis: 2021 Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology* **2021**, *74*, 1611–1644. https://doi.org/10.1002/hep.32049. Corrected in *Hepatology* **2021**, *74*, 3563.
16. Davies, B.; García, F.; Ara, I.; et al. Relationship Between Sarcopenia and Frailty in the Toledo Study of Healthy Aging: A Population Based Cross-Sectional Study. *J. Am. Med. Dir. Assoc.* **2018**, *19*, 282–286.
17. Fumagalli, I.A.; Le, S.T.; Peng, P.D.; et al. Automated CT Analysis of Body Composition as a Frailty Biomarker in Abdominal Surgery. *JAMA Surg.* **2024**, *159*, 766–774. https://doi.org/10.1001/jamasurg.2024.0628.
18. Reichelt, S.; Pratschke, J.; Engelmann, C.; et al. Body composition and the skeletal muscle compartment in liver transplantation: Turning challenges into opportunities. *Am. J. Transplant.* **2022**, *22*, 1943–1957. https://doi.org/10.1111/ajt.17089.
19. Laube, R.; Wang, H.; Park, L.; et al. Frailty in advanced liver disease. *Liver Int.* **2018**, *38*, 2117–2128. https://doi.org/10.1111/liv.13917.
20. Soysal, P.; Stubbs, B.; Lucato, P.; et al. Inflammation and frailty in the elderly: A systematic review and meta-analysis. *Ageing Res. Rev.* **2016**, *31*, 1–8. https://doi.org/10.1016/j.arr.2016.08.006. Erratum in *Ageing Res. Rev.* **2017**, *35*, 364–365.
21. Yao, X.; Li, H.; Leng, S.X. Inflammation and immune system alterations in frailty. *Clin. Geriatr. Med.* **2011**, *27*, 79–87. https://doi.org/10.1016/j.cger.2010.08.002.
22. Hubbard, R.; O'Mahony, M.; Savva, G.; et al. Inflammation and frailty measures in older people. *J. Cell. Mol. Med.* **2009**, *13*, 3103–3109. https://doi.org/10.1111/j.1582-4934.2009.00733.x.
23. Collerton, J.; Martin-Ruiz, C.; Davies, K.; et al. Frailty and the role of inflammation, immunosenescence and cellular ageing in the very old: Cross-sectional findings from the Newcastle 85+ Study. *Mech. Ageing Dev.* **2012**, *133*, 456–466. https://doi.org/10.1016/j.mad.2012.05.005.
24. Mehta, M.; Louissaint, J.; Parikh, N.S.; et al. Cognitive Function, Sarcopenia, and Inflammation Are Strongly Associated with Frailty: A Framingham Cohort Study. *Am. J. Med.* **2021**, *134*, 1530–1538. https://doi.org/10.1016/j.amjmed.2021.07.012.
25. Ha, N.; Seetharaman, S.; Kent, D.; et al. Serum and plasma protein biomarkers associated with frailty in patients with cirrhosis. *Liver Transpl.* **2023**, *29*, 1089–1099. https://doi.org/10.1097/lvt.0000000000000128.

26. Cardoso, C.; Matiollo, C.; Pereira, C.; et al. Patterns of dendritic cell and monocyte subsets are associated with disease severity and mortality in liver cirrhosis patients. *Sci. Rep.* **2021**, *11*, 5923. https://doi.org/10.1038/s41598-021-85148-y.
27. Gadd, V.L.; Patel, P.J.; Jose, S.; et al. Altered Peripheral Blood Monocyte Phenotype and Function in Chronic Liver Disease: Implications for Hepatic Recruitment and Systemic Inflammation. *PLoS ONE* **2016**, *11*, e0157771. https://doi.org/10.1371/journal.pone.0157771.