Appendix 1 Methods

(I) Diagnostic criteria for the etiology of chronic liver disease (CLD) and diagnostic procedures for hepatocellular carcinoma (HCC): steatotic liver disease (SLD) was diagnosed based on imaging findings (hepatic and renal contrast on abdominal ultrasonography; liver/spleen ratio <0.9 on abdominal computed tomography (CT); proton density fat fraction measured by magnetic resonance imaging (MRI), >5.2% (44). Additionally, alcohol-related liver disease was diagnosed in accordance with the diagnostic criteria of the Japanese Society for Biomedical Research on Alcohol (45), and metabolic dysfunction-associated SLD (MASLD) was diagnosed according to the new diagnostic criteria (46). HCC was diagnosed according to the guidelines as tumors marked in the arterial phase on contrast-enhanced CT and showing washout in the portal or delayed phase (47,48). In the case of gadoxetate disodium (EOB) contrast-enhanced MRI, tumors were also defined as those that stained in the early phase and showed washout in the portal venous phase.

(II) Diagnostic criteria for advanced CLD (ACLD), and procedures for diagnosing the severity of hepatic reserve dysfunction: the diagnosis of ACLD in this study was based on LS ≥3 kPa on magnetic resonance elastography (MRE) in accordance with the practice guidance by the American Association for the Study of Liver Diseases (AASLD) (49). Liver reserve function impairment was evaluated using an albumin-bilirubin (ALBI) score (24), and patients with ACLD were categorized based on severity, ranging from ALBI grade 1 to grade 3. The ALBI score is an index of hepatic reserve developed to assess the prognosis of patients with HCC. A number of publications have now shown that ALBI scores have a high prognostic ability in patients with CLD of all etiologies and stages (26).

Classification of mALBI grade is shown below (24,26)

The ALBI score was calculated using the formula ALBI score = (log10 bilirubin[μmol/L] × 0.66) + (albumin [g/L] × –0.085) and classified into grade 1 (ALBI score <–2.60), grade 2 (–1.39< ALBI score <–2.60), and grade 3 (ALBI score >–1.39). Grade 2 was further divided into grade 2a (–2.60< ALBI score <–2.27) and 2b (–2.27< ALBI score <–1.39). Thus, mALBI was classified into four grades: G1, G2a, G2b and G3.

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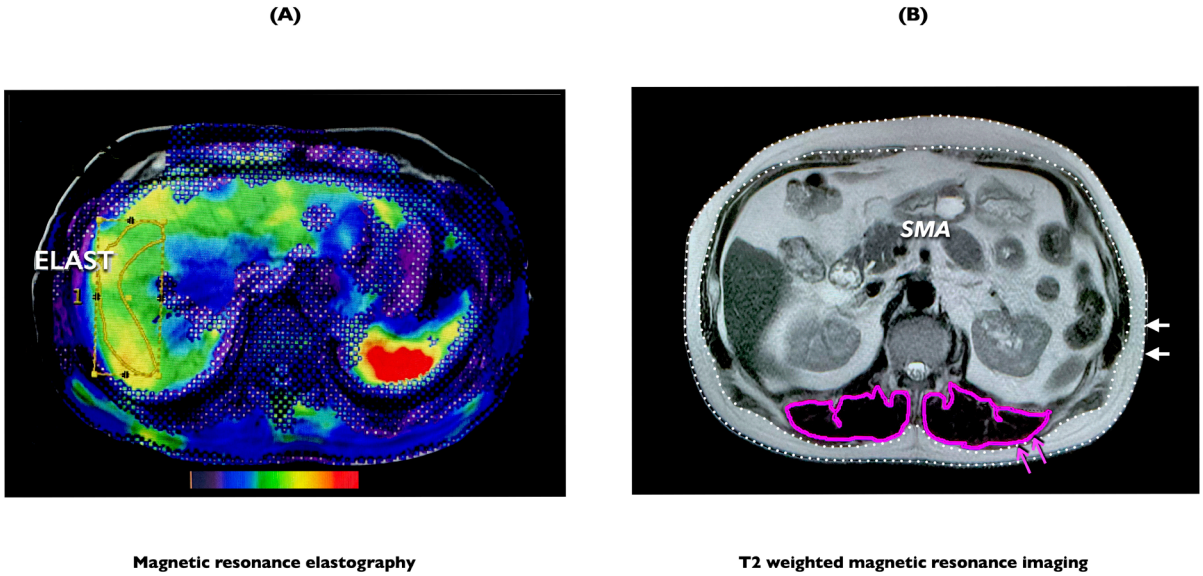

Figure S1 Magnetic resonance elastography (MRE) imaging and T2-weighted magnetic resonance imaging (MRI) with anthropometric measurements are presented. (A) Liver stiffness on MRE (kPa) was measured in the right lobe of the liver, avoiding blood vessels, bile ducts, and gallbladder. (B) MRI image analysis was performed on a separate workstation [OsiriX version 6.0 open-source software (64-bit, Pixmeo, Geneva, Switzerland; http://www.osirix-viewer.com)]. The bilateral paraspinal musculature was manually segmented at the level of the origin of the superior mesenteric artery (SMA) using a T2-weighted image single-shot fast spin-echo (SS-FSE) sequence (thin purple arrows). The subcutaneous fat area was also measured from the T2-weighted MRI images using the origin of the SMA as a landmark (white arrows).

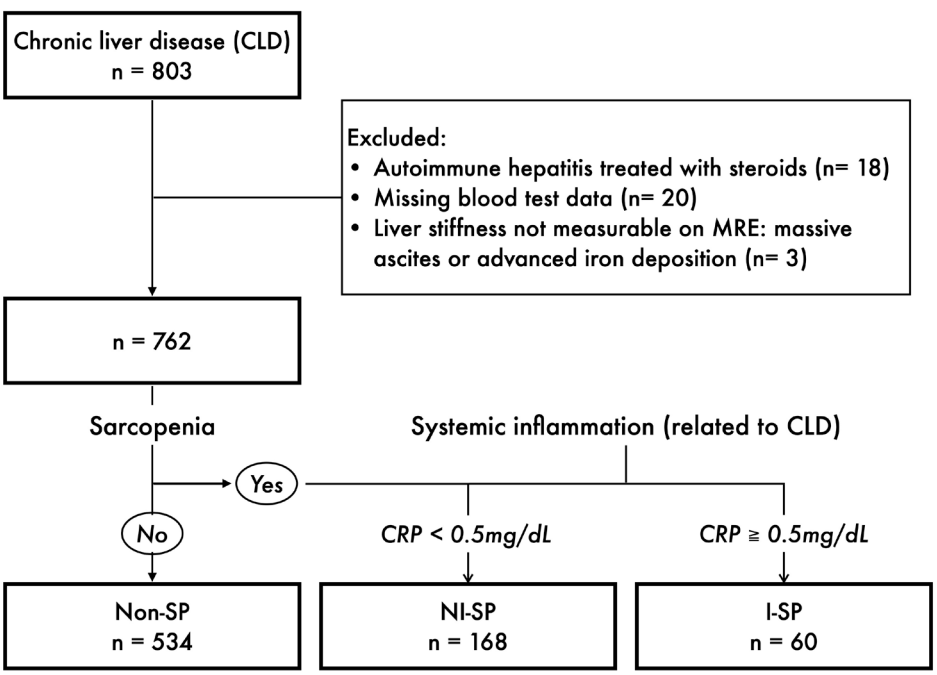

Figure S2 Flow chart for inclusion/exclusion of patients in this study. CRP, C-reactive protein; MRE, magnetic resonance elastography; NI-SP, non-inflammatory sarcopenia; I-SP, inflammatory sarcopenia; Non-SP, non-sarcopenia.

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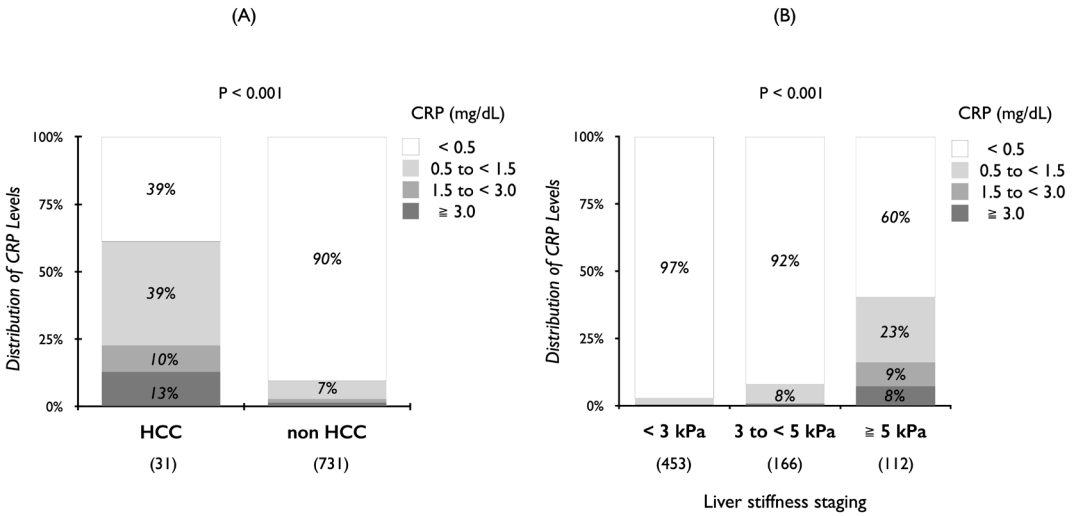

Figure S3 The relationship between C-reactive protein (CRP) levels (<0.5, 0.5 to <1.5, 1.5 to <3.0, ≥3.0 mg/dL) and the severity of liver disease in chronic liver disease (CLD). (A) Comparison of CRP levels between CLD patients with and without hepatocellular carcinoma (HCC). (B) Relationship between CRP levels and liver stiffness (LS) values (<3 kPa, 3 to <5 kPa, ≥5 kPa) in 731 CLD patients without HCC.

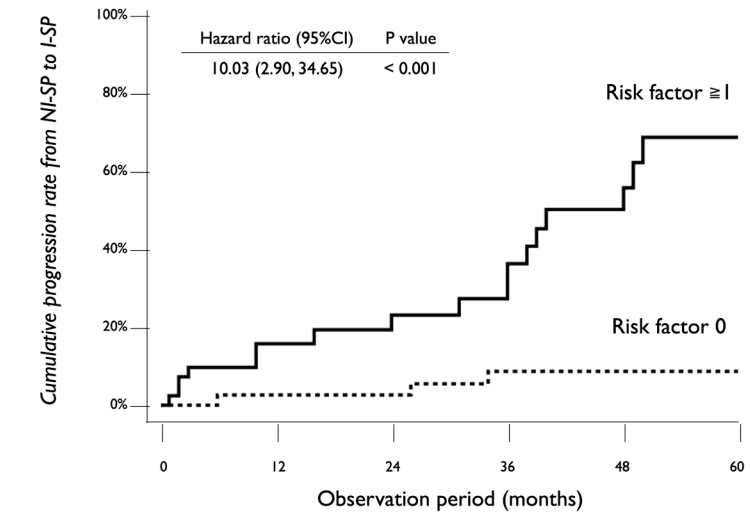

Figure S4 The results of a follow-up study involving 78 patients with non-inflammatory sarcopenia (NI-SP) in advanced chronic liver disease (ACLD), with a median follow-up of 36 months. Twenty patients progressed to inflammatory sarcopenia (I-SP). Among the NI-SP patients, those with any of the three risk factors (ALBI score ≥–2.42, alcohol-related liver disease, and hepatocellular carcinoma) as indicated in the figure under the "Risk Factor ≥1" group had a significantly higher progression rate to I-SP compared to those without these risk factors. ALBI, albumin-bilirubin.

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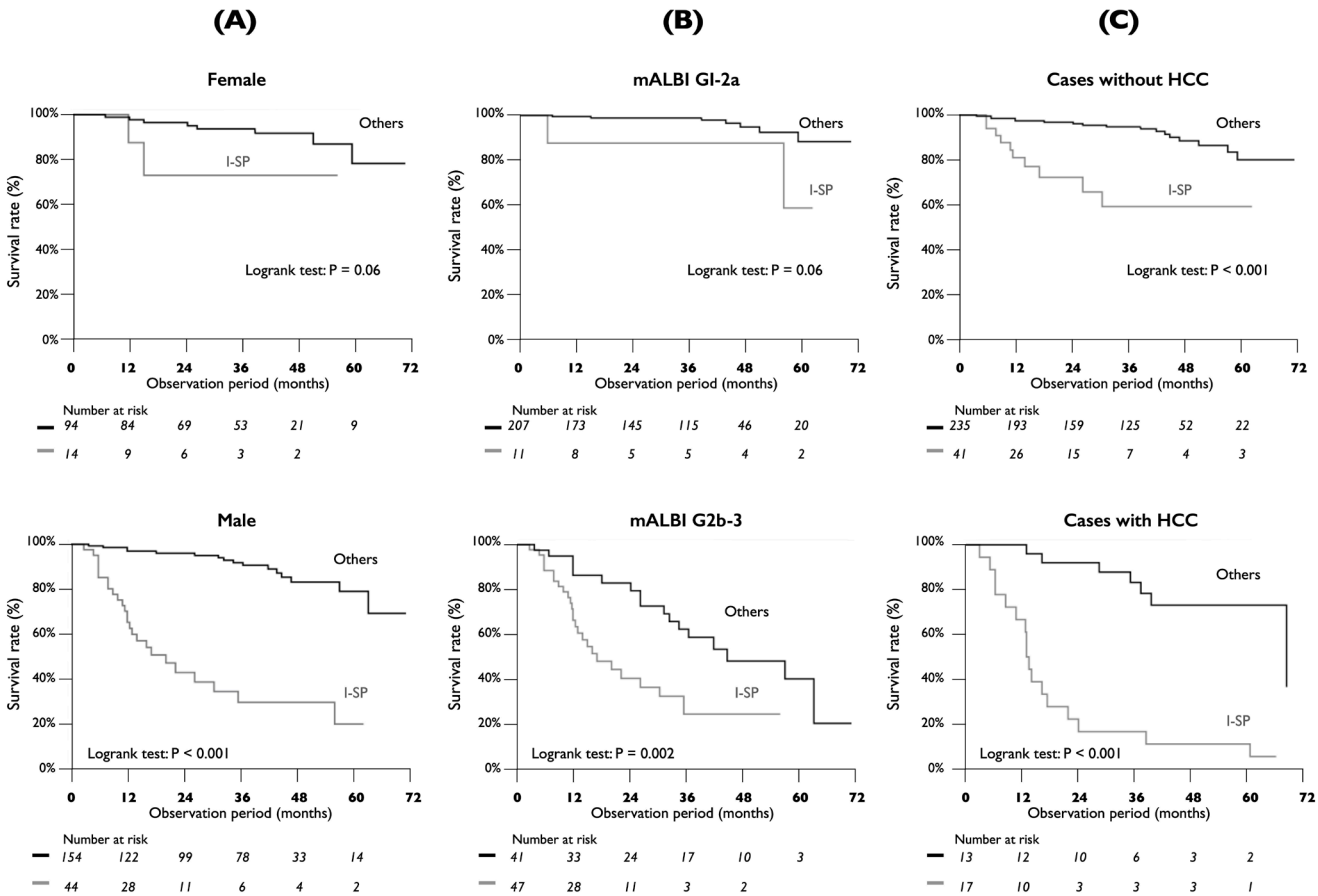

Figure S5 Kaplan-Meier survival curves stratified by (A) gender, (B) hepatic reserve function, and (C) presence or absence of hepatocellular carcinoma (HCC). mALBI, modified albumin-bilirubin.

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