Editorial Commentary

Validating the prognostic value of muscle changes in patients with cirrhosis undergoing transjugular intrahepatic portosystemic shunt

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A multicenter prospective observational study by Di Cola *et al.* (1) examined the significant impact of individual muscle changes and their combinations on the prognosis of cirrhosis. In their study (1), the 1-year cumulative incidence of death in patients with either sarcopenia and myosteatosis (13.8%) or isolated myosteatosis (13.4%) was more than twice that in patients without muscle changes (5.2%) or with isolated sarcopenia (5.6%). They also found that these muscle changes were associated with other adverse outcomes (such as hospitalization and liver decompensation) over a 1-year period (1). Our previous meta-analysis established the association between sarcopenia and long-term survival of patients with cirrhosis (2). This study by Di Cola *et al.* (1) further elucidated the prognostic value of muscle changes, with a particular emphasis on the prognostic significance of muscle quality (myosteatosis). To broaden the applicability of Di Cola *et al.*'s (1) conclusions, we aimed to validate their findings in a cohort of cirrhotic patients undergoing transjugular intrahepatic portosystemic shunt (TIPS) with long-term follow-up.

All patients with cirrhosis undergoing TIPS in our hospital who had an abdominal computed tomography (CT) scan within three months prior to the procedure were retrospectively screened for the study. The exclusion criteria, measurement methods, and definition criteria for muscle changes were consistent with those used in Di Cola *et al.*'s study (1). Sarcopenia and myosteatosis on CT images were assessed using SliceOMatic software (version 5.0, TomoVision, Montreal, Canada). Typical CT images of muscle changes are shown in *Figure 1*. The Ethical Committee of our hospital approved the study protocol (No. 2022032), and patient consent was waived due to the retrospective nature of the analysis. Our primary outcome was all-cause mortality, and secondary outcomes included the occurrence of first or further decompensation events, using the same definitions as in Di Cola *et al.*'s study (1). Since none of the included patients underwent liver transplantation during the follow-up period, the association between muscle changes and mortality was evaluated using the Cox proportional hazards model and Kaplan-Meier curves. Death was considered a competing event when assessing the risk of first and further decompensation, and the Fine-Gray model was used. The same variable selection approach used in Di Cola *et al.*'s study was adopted for the

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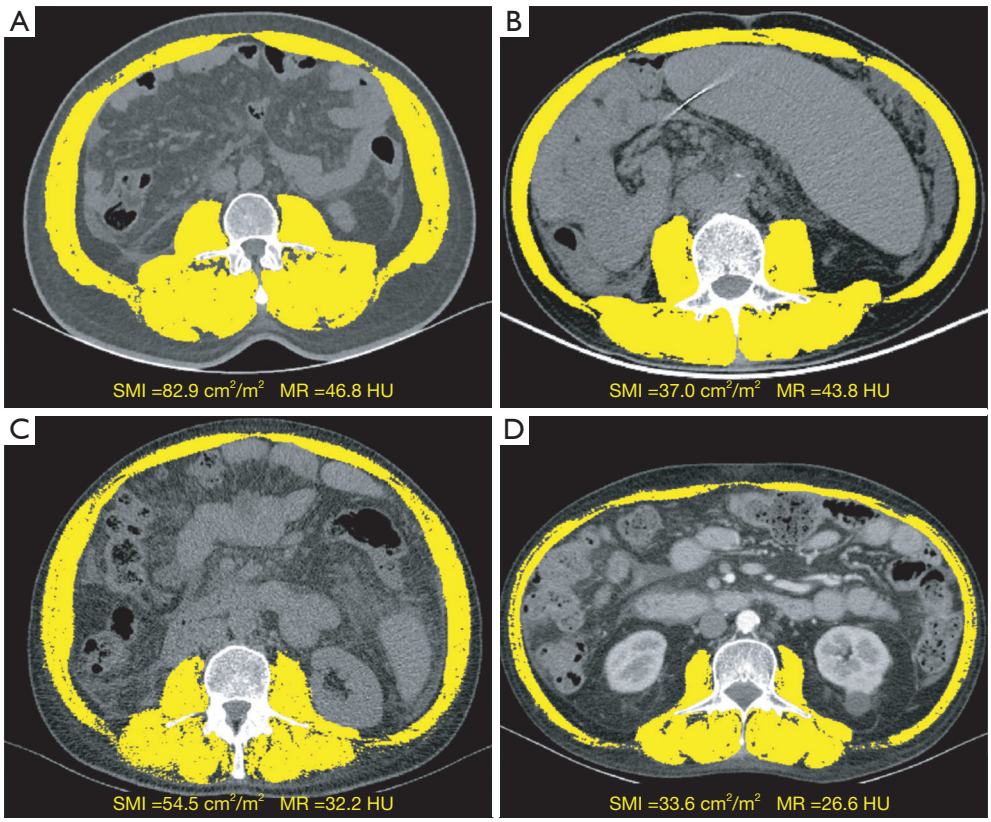

Figure 1 Typical CT images of muscle changes. (A) Patients without muscle changes; (B) patients with isolated sarcopenia; (C) patients with isolated myosteatosis; (D) patients with combined sarcopenia and myosteatosis. SMI, skeletal muscle index; MR, muscle radiodensity; CT, computed tomography; HU, Housefield unit.

multivariable model (1).

Finally, a total of 202 patients with cirrhosis were included in the study. The baseline characteristics of the included patients are shown in Table S1. The mean age was 55.8±11.0 years, and 54.0% of patients were male. The predominant etiology was chronic viral hepatitis (61.9%). The median Model of End Stage Liver Disease (MELD) at TIPS implantation was 10 (interquartile range, 8–12). The indications for TIPS in the included patients were primarily variceal bleeding (99.0%). All patients used covered stents, with the majority using stents with an 8 cm diameter (94.1%). Simultaneous variceal embolization was performed in 91.1% of cases. After stent placement, the mean hepatic venous pressure gradient decreased from a preoperative 25.9 mmHg to a postoperative 8.8 mmHg. All patients achieved an adequate decrease in portal pressure, defined as a portosystemic gradient of less than 12 mmHg or a 50% reduction from the initial gradient (3). Among all included patients, combined sarcopenia and myosteatosis was diagnosed in 88 patients (43.5%), isolated sarcopenia in 48 patients (23.8%), isolated myosteatosis in 19 patients (9.4%), and 47 patients (23.3%) had no evidence of muscle changes. During the median follow-up period of 33.6 months, 25 patients (12.4%) died (19 of liver-related causes), 55 patients (27.2%) experienced first decompensation events, and 81 patients (40.1%) had further decompensation events. As shown in *Figure 2A*, the incidence of death was significantly higher for patients with isolated myosteatosis (P=0.047), and those with both sarcopenia and myosteatosis (P=0.047), compared to those without muscle changes. However, the difference was not significant for patients with isolated sarcopenia (P=0.32). The adjusted hazard ratios (HRs) for 1-year mortality and overall mortality in patients with muscle changes were 3.72 (95% CI: 1.14–12.16) and 1.80 (95% CI: 1.11–2.92), respectively. However, the associations between muscle changes and the incidence of first or further decompensation events during the 1-year or the entire follow-up period were not significant (*Figure 2B-2E*).

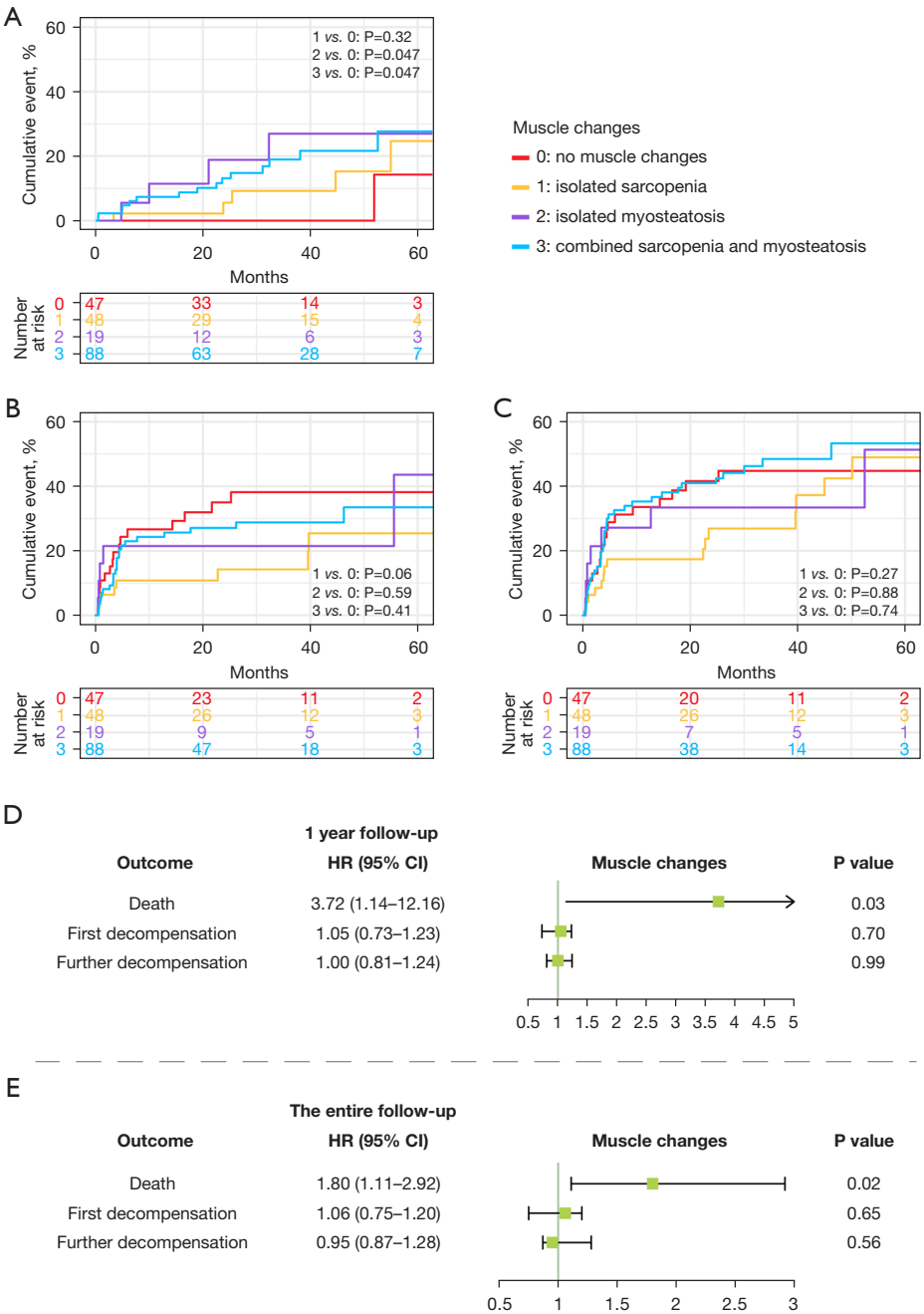

Figure 2 Associations between muscle changes and adverse outcomes in patients with cirrhosis undergoing transjugular intrahepatic portosystemic shunt. (A) Cumulative incidence of death in four patient subgroups according to the type of muscle changes during the entire follow-up period. (B) Cumulative incidence of first decompensation events, with death as competing risk, in four patient subgroups according to the type of muscle changes during the entire follow-up period. (C) Cumulative incidence of further decompensation events, with death as competing risk, in four patient subgroups according to the type of muscle changes during the entire follow-up period. (D) Adjusted hazard ratios of muscle changes for the risk of death, first and further decompensation during a 1-year period. MELD, hepatic encephalopathy and ascites were adjusted. (E) Adjusted hazard ratios of muscle changes for the risk of death, first and further decompensation during the entire follow-up period. MELD, hepatic encephalopathy and ascites were adjusted. Like in the study by Di Cola *et al.* (1), muscle changes were included in the model as a discrete variable scored as follows: no changes = 0, isolated sarcopenia = 1, isolated myosteatosis = 2, and combined sarcopenia and myosteatosis = 3. MELD, Model of End Stage Liver Disease; HR, hazard ratio; CI, confidence interval.

In patients with cirrhosis undergoing TIPS, our study found that muscle changes were highly prevalent, with a high proportion having both sarcopenia and myosteatosis, and only 23.8% exhibiting isolated sarcopenia. Additionally, the presence of muscle changes before the procedure significantly increased the risk of post-TIPS mortality but did not increase the risk of decompensation events. Our study supports and extends the findings of Di Cola *et al.* (1). Our study, along with the research by Di Cola *et al.* (1) and other studies (4), indicates that muscle abnormalities in cirrhotic patients often involve concurrent changes in both muscle mass and quality. This may be attributed to shared mechanisms such as hyperammonemia, insulin resistance, and mitochondrial dysfunction (5,6). Most previous studies on sarcopenia in cirrhosis have not simultaneously considered the impact of myosteatosis, which may raise questions about the independent prognostic value of sarcopenia. However, evidence has shown that both sarcopenia and myosteatosis are independently associated with long-term survival in patients with cirrhosis, with those exhibiting both conditions having a higher risk of mortality (7,8). Sarcopenia and myosteatosis are closely related and may represent different subtypes or stages of muscle damage resulting from liver-muscle axis mechanisms in the long-term progression of cirrhosis.

In summary, the independent prognostic value of muscle changes also applies to patients with cirrhosis undergoing TIPS. However, our conclusions require further validation due to the retrospective nature of the study, the relatively small sample size, and the lack of consideration of follow-up muscle changes after TIPS. Some studies have indicated that TIPS creation is significantly associated with improvements in both muscle mass and quality, along with subsequent improvements in prognosis for patients with cirrhosis (9,10). These findings need to be confirmed in future research.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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