Dynamic relationship between surrogates of skeletal muscle mass and MELD-Na score in three cirrhotic patients under cell-free and concentrated ascites reinfusion therapy

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DESCRIPTION

We studied the relationship of the score of model for end-stage liver disease with incorporated serum sodium concentration (MELD-Na) with parameters on sarcopenia using bioelectrical impedance analysis (BIA: InBody770, Inbody Japan Inc., Tokyo) in patients undergoing cell-free and concentrated ascites reinfusion therapy (CART).¹⁻³ When BIA was not available in a patient, serum creatinine (SCr; normal range:

Figure 1 Clinical courses of case 1 and case 2. In case 1, the bending points were at 9 months of model for end-stage liver disease with serum sodium (MELD-Na) score and at 5 months of skeletal muscle index (SMI). In case 2, the bending points were at 5 months of MELD-Na score and at 3 months of SMI. The SMIs at 12 months in case 1 and at 6 and 7 months in case 2 were not available due to deterioration of the patient's condition. All the data of MELD-Na in case 1 have been measured and written on a graph. The measured grip strength was 22.0 kg on the right and 22.1 kg on the left in case 1, 19.0 kg on the right and 18.8 kg on the left in case 2.

Figure 2 The changes of skeletal muscle index (SMI) and model for end-stage liver disease with serum sodium (MELD-Na) score before and after the respective bending points. The error bars represent the standard errors. The values of SMI or MELD-Na score at the bending points were set to 1, respectively. (A) Student's t-test showed significant difference of p=0.014 between SMI before (n=7) and after (n=6) the bending points. (B) Student's t-test showed significant difference of p=0.014 between MELD-Na score before (n=11) and after (n=7) the bending points.

Figure 3 Clinical course of case 3. The unit for serum creatinine is 10⁻¹ mg/dL. The cell-free and concentrated ascites reinfusion therapy implementation period was completed by 7 months. The measured grip strength was 25.5 kg on the right and 25.0 kg on the left in case 3. An irregularly measured skeletal muscle index level showed 6.9 kg/m².

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Figure 4 Approximate linear lines of model for end-stage liver disease with serum sodium (MELD-Na) score and skeletal muscle index (SMI) or serum creatinine (SCr) for case 1, case 2 and case 3. MELD-Na before, SMI before and SCr before represent the approximate lines before the respective bending points, and MELD-Na after, SMI after and SCr after represent the approximate lines after the respective bending points. The R^2 means the coefficient of determination, which ranges between 0.8325 and 1. The vertical axis indicates the y-coordinate, and the horizontal axis indicates the x-coordinate. In case 1; MELD-Na before: $y = -0.1455x + 15.4546$ ($R^2 = 0.9643$), MELD-Na after: $y = 6.4x - 46.2$ ($R^2 = 0.8325$). In case 1; SMI before: $y = 8.6$, SMI after: $y = -0.425x + 10.7417$ ($R^2 = 0.9988$). In case 2; MELD-Na before: $y = 0.5143x + 14.0476$ ($R^2 = 0.9868$), MELD-Na after: $y = 7.5x - 22.3333$ ($R^2 = 0.9643$). In case 2; SMI before: $y = -0.11x + 5.29$ ($R^2 = 0.9868$), SMI after: $y = -0.65x + 6.5666$ ($R^2 = 0.9530$). In case 3; MELD-Na before: $y = 5x + 11$ ($R^2 = 1$), MELD-Na after: $y = -1.8571x + 18.2857$ ($R^2 = 0.9769$). In case 3; SCr before: $y = 1.42x + 6.17$ ($R^2 = 0.9943$), SCr after: $y = -0.58x + 11.82$ ($R^2 = 0.9625$) (originally, $y = 0.142x + 0.617$, $y = -0.058x + 1.182$).

0.63–1.05 mg/dL) was used as a surrogate marker for skeletal muscle mass.⁴ Sarcopenia was reported to reduce life quality and worsen prognosis with liver cirrhosis (LC).⁵ Our three male patients suffered from decompensated LC, case 1 with non-alcoholic steatohepatitis with type 2 diabetes mellitus at age 83, case 2 with alcoholic liver disease with primary biliary cholangitis at age 81 and case 3 with alcoholic LC at age 64. They had CART administrations almost every 2 weeks to control ascites. BIA was performed every 1–3 months to estimate their nutritional states, and calculated

Figure 5 Coronal abdominal CT at porta hepatis showed that the liver area size was 4888 mm² in case 1.

skeletal muscle index (SMI: (skeletal muscle mass)/(body height)², kg/m²). Handgrip strength was assessed with a digital grip strength dynamometer (T.K.K.5401 GRIP D; Takei Scientific Instruments, Niigata, Japan). Sarcopenia was diagnosed using the Japan Society of Hepatology criteria, and defined as grip strength <26 kg and SMI <7.0 kg/m² for man in 2016.⁶ As a result, SMI and MELD-Na score showed reciprocal trends, with the MELD-Na score beginning to rise 2–4 months after SMI began to decline (figure 1). The bending points were considered as the boundary between the

Figure 6 Coronal abdominal CT at porta hepatis showed that the liver area size was 5894 mm² in case 2.

Figure 7 Coronal abdominal CT at porta hepatis showed that the liver area size was 13 271 mm² in case 3.

Patient's perspective

Case 1: My husband was not a heavy drinker, but he has been treated for diabetes mellitus since he was in his 30s. He is currently undergoing self-injection of insulin, and his total daily insulin dose is about 50 units. He was obese from a young age, his job was as a salesman, and he often ate out a lot. In that sense, I think it was a lifestyle-related disease.

Learning points

- Sarcopenia has been reported to be associated with worse prognosis in cirrhosis. In case 1 and case 2, we reported an increase in model for end-stage liver disease with serum sodium (MELD-Na) score after several months of muscle mass (skeletal muscle index) loss during cell-free and concentrated ascites reinfusion therapy (CART).
- In case 3, a cirrhotic patient with normal kidney function had a decrease in MELD-Na score and a concomitant gradual increase in serum creatinine (Scr) under CART. This means that if Scr reflects skeletal muscle mass without excess or deficiency, then the contraposition to the proposition 'If skeletal muscle mass decreases, MELD-Na score increases under CART', that is, 'If MELD-Na score decreases, skeletal muscle mass (Scr) increases under CART' is valid.
- Elevated serum myostatin levels have been reported to be associated with skeletal muscle mass loss and poor survival in cirrhotic patients, and although the involvement of cytokines was not examined in this paper, future studies of cytokine dynamics on sarcopenia in serum and ascites during CART are expected.

two trends. Significant differences on SMI and MELD-Na score were confirmed by Student's t-test/Mann-Whitney U test before and after the bending points during each course with $p=0.014/p<0.05$ and $p=0.014/p<0.05$, respectively (figure 2). The values at the bending points were set to 1. A p value of <0.05 was considered statistically significant (XLSTAT 2016: Addinsoft Inc., NY, USA). Case 3 showed that SCr peaked at a few months after the MELD-Na score began to decrease with normal kidney function (figure 3). Figure 4 showed that the time courses of MELD-Na score and surrogate markers of muscle mass in each case were well approximated by linear lines. All three patients were diagnosed with sarcopenia. The molecular weight (MW) of myostatin was reported to be 26 kDa, in comparing with albumin of 66 kDa.⁷ CART's filters for concentration are supposed to be able to concentrate molecules with the MW of 30 kDa or more. When compared imagingly, abdominal computed tomography (CT) showed that the liver area size (13 271 mm²) of case 3 was as 2.2–2.7 times as those of case 1 (4888 mm²) and case 2 (5894 mm²) (figures 5–7). These imaging studies would suggest that the liver size might be one factor in the ability of MELD-Na to improve as well as the age difference, which in turn might be linked to increased muscle mass. Detailed research on the molecular level of sarcopenia and LC under CART is expected in the future.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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