Chronic liver diseases are generally associated with physical inactivity,[3] which could result in osteoporosis and sarcopenia as recently discussed.[4] Thus, in addition to the possible mechanisms described by the authors,[1] physical inactivity appears to be another significant mechanism by which autoimmune liver diseases cause skeletal fragility. Appropriate physical activity is therefore recommended and its individual-level monitoring using accelerometers would be useful in clinical practice.

Denosumab treatment can continuously increase areal bone mineral density for a long time. This is regarded as a key distinguishing feature among currently approved osteoporosis agents, and its unique mechanisms of action has been proposed. Of note, experimental and clinical evidence has suggested enhancing physical activity.[5] Consequently, physical activity might be linked to the efficacy of long-term treatment with denosumab. The risk-benefit balance of denosumab treatment for up to 10 years would be acceptable for most postmenopausal osteoprotic women,[5] and I fully agree with the authors[1] that further clinical research is warranted.

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Potential conflict of interest: Nothing to report.

REPLY:

We thank Dr. Sugiyama for having interest in our work on denosumab therapy for osteoporosis in patients with autoimmune liver diseases.[1]

Osteodystrophy is a worrisome complication in chronic liver diseases (CLDS), especially in autoimmune liver diseases such as primary biliary cholangitis and autoimmune hepatitis accompanying vitamin D malabsorption and use of corticosteroid. Given that physical activity is closely associated with bone health,[2] physical inactivity in CLD is likely to worsen bone metabolism. We think that regular exercise should be recommended in patients receiving denosumab treatment.

Osteoporosis is closely associated with sarcopenia. For example, Hayashi et al. reported that the appendicular skeletal muscle mass index was significantly correlated with bone mineral density of the lumbar spine and femur neck.[3] Several studies demonstrated that exercise improved muscle strength and function in CLD patients. In addition, exercise ameliorated VO_2 peak, anaerobic threshold, 6-mintute walk distance, and quality of life in patients with compensated and decompensated cirrhosis.[4,5] Therefore, exercise programs should be incorporated in the management of CLD. However, appropriate type, intensity, and duration of exercise are largely unknown. These factors should be arranged based upon patients' liver function (compensated or decompensated) and physical condition. The combination of exercise and a specific treatment such as denosumab will be the focus of future trials.

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Letter to the Editor: Could Variceal Screening Stratified by Liver/Spleen Stiffness Replace the Role of Endoscopy?

TO THE EDITOR:

I read with interest regarding the noninferiority of screening strategy for varices guided by liver and spleen stiffness measurement (LSSM) to endoscopic screening.[1] Wong et al. designed a well-controlled study and demonstrated a similarly low risk of variceal bleeding in patients with cirrhosis between both methods. Moreover, the necessity of endoscopic screening was reduced up to one-half in individuals receiving LSSM as compared with conventional endoscopic screening. Though inspiring, several points need further clarification.

Among all the participants in both groups, 27 patients were noted to have clinically significant varices. A total of 50 patients received beta-blockers, and 27 patients received prophylactic banding ligation. This implied that 50 patients without clinically significant varices have received prophylactic therapy. Moreover, among the 23 patients with incident variceal bleeding, only 11 patients had clinically significant varices. Four patients in the LSSM group and 1 patient in the conventional arm were without antecedent varices detected. It appeared that some observation bias existed. The value of LSSM in reducing endoscopic screening of varices cannot be denied. However, endoscopic examinations have some additional advantages other than the detection of varices. A high incidence of peptic ulcers and congestive gastropathy has been noted in patients with cirrhosis.[2] The severity of peptic ulcer bleeding has been noted to be as bad as variceal bleeding.[3,4] Though LSSM could reduce endoscopic examinations, it is likely that routine endoscopic screening could as well detect the presence of peptic ulcers, resulting in the prevention and reduction of ulcer bleeding. The incidence of ulcer bleeding in both groups was not reported in the current study.

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