



## Cirrhotic cardiomyopathy: An independent prognostic factor for cirrhotic patients

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Cirrhotic cardiomyopathy (CCMP), which indicates cardiac dysfunction in cirrhotic patients, has received attention as a complication of liver cirrhosis. Cardiac dysfunction observed in cirrhotic patients is characterized by electrophysiological abnormalities, diastolic dysfunction, and impaired and blunted responsiveness to physiologic or pathologic stress in the absence of underlying heart disease.<sup>1-3</sup> Sinusoidal portal hypertension in advanced liver cirrhosis causes increased production of a number of vasoactive mediators, such as nitric oxide, endothelin, and prostaglandin production, which drives splanchnic vasodilation resulting in hyperdynamic circulation.<sup>2,4,5</sup> Electrophysiological abnormalities including QT-interval prolongation and echocardiographic findings reflecting diastolic and/or systolic dysfunction in cirrhotic patients have been demonstrated as typical findings indicating CCMP.<sup>2,6</sup> However, diagnostic criteria of CCMP have not yet been established, and the association between CCMP and the clinical outcome of cirrhotic patients has not been well clarified.

In this issue of *Clinical and Molecular Hepatology*, a Korean prospective study by Lee et al. implicates that the presence of left

ventricular diastolic dysfunction (LVDD), which is an early manifestation of CCMP, is associated with poor survival in patients with decompensated cirrhosis.<sup>7</sup> Seventy patients with decompensated cirrhosis were enrolled prospectively and cardiac function of the study patients was assessed using 2D echocardiography with tissue Doppler imaging. LVDD was diagnosed in 44 of 70 patients (62.9%), and 10 patients (22.7%) among 44 patients with LVDD at baseline were Child-Pugh class A. Overall survival was significantly worse in these patients with LVDD than those without LVDD (31.1 months vs. 42.6 months,  $P=0.01$ ). The presence of LVDD was an independent predictor of overall survival (vs. no LVDD; adjusted hazard ratio [HR], 4.69; 95% confidence interval [CI], 1.06–20.8;  $P=0.042$ ). These findings implicate that a considerable number of patients among cirrhotics with relatively preserved liver function may have CCMP. Moreover, CCMP was associated with poor survival outcome independently of severity of liver disease, suggesting the need for screening and monitoring for cardiac function in cirrhotic patients even if the patient is asymptomatic.

In a study by Lee et al., there was no difference in liver function index (Child-Pugh class and MELD score) according to the presence or absence of LVDD.<sup>7</sup> Recently, an European prospective,

### Abbreviations:

CCMP, cirrhotic cardiomyopathy; CI, confidence interval; CMR, cardiac magnetic resonance; ECV, extracellular volume; HR, hazard ratio; LVDD, left ventricular diastolic dysfunction; LV-GLS, left ventricular global longitudinal strain

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multicenter study investigating the presence of diffuse myocardial fibrosis in cirrhotic patients using cardiac magnetic resonance (CMR) was reported.<sup>8</sup> Structural myocardial changes including diffuse myocardial fibrosis were assessed by quantification of the extracellular volume (ECV) on CMR. Myocardial ECV was significantly higher in cirrhotic patients compared to the healthy controls (31.2% vs. 27.4%,  $P=0.04$ ), and furthermore, increased across the Child-Pugh class (26.9% in Child-Pugh class A, 31.5% in Child-Pugh class B, and 34.4% in Child-Pugh class C;  $P=0.02$ ). In addition, ECV was associated with worse transplant-free survival (HR, 3.6; 95% CI, 1.1–11.6;  $P=0.03$ ). The authors proposed a novel method for the diagnosis of subclinical CCMP by applying ECV measurement technique using CMR in patients with cirrhosis and showed possibility of ECV measurement as an index reflecting cardiac structural change of CCMP. Our group also reported results from a prospective study including 52 patients (32 cirrhotics and 20 healthy controls) to investigate the association between diffuse myocardial fibrosis and the severity of liver disease and to explore cardiac functional/structural changes after liver transplantation.<sup>9</sup> In our study, LV hypercontractility in patients with cirrhosis was reaffirmed via CMR-based LV ejection fraction and LV-global longitudinal strain (LV-GLS) measurements. We found that both increased LV-GLS and ECV in cirrhotic patients decreased at 1 year after transplantation, suggesting normalization of the LV systolic function and a decrease in diffuse myocardial fibrosis. In addition, our case-control study showed that non-alcoholic fatty liver disease was associated with increased risk for LVDD and the risk was incrementally increased according to fibrosis grade among subjects without cirrhosis.<sup>10</sup> These findings suggest that LVDD may develop in earlier stage of chronic liver disease.

CCMP is not just a phenomenon secondary to hyperdynamic circulation, but it has important prognostic value in cirrhotic patients. Moreover, CCMP is a concept that includes not only a functional change due to hemodynamic change but also a structural change in myocardium itself. It is necessary to establish diagnostic criteria for early diagnosis of CCMP in patients with cirrhosis. LVDD might be an early indicator of CCMP. Additionally, further studies to investigate whether thorough monitoring and management can improve long-term outcomes of cirrhotic patients are warranted.

## Authors' contribution

Manuscript writing: Yun Bin Lee and Jeong-Hoon Lee

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## Conflicts of Interest

The authors confirm that this article content has no conflict of interest.

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