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EDITORIAL



## Towards holistic integrative medicine based management strategy of liver cirrhosis

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### 1. Introduction

Nowadays, the development and popularity of evidence-based medicine (EBM) have greatly advanced our clinical practice into a new era [1], because the physicians' decisions on prescribing a drug or performing a test or procedure have become more accurate and reliable. Undoubtedly, the clinical decision-making is biased without the support of EBM. However, in the EBM era, we still focus on treating a specific complication of a disease or managing an individual organ of a patient by designing studies, collecting relevant data, performing statistical analyses, and achieving a conclusion. Notably, as stated in a milestone concept, holistic integrative medicine (HIM) [2], which has been for the first time proposed by Prof. Daiming Fan, a human should be considered a holistic system composing of multiple organs that are well integrative and is being greatly affected by the people around him or her and the society where he or she is living. Specifically, the liver, an essential organ of our body that is responsible for metabolism, closely correlates with other organs, such as brain, heart, kidney, and digestive tract. A diseased, even cirrhotic, liver not only causes metabolic dysfunction or failure, but can also induce the development of mental disorders (i.e. hepatic encephalopathy), cardiac dysfunction (i.e. cirrhotic cardiomyopathy), kidney failure (i.e. hepatorenal syndrome or acute kidney injury), and gastrointestinal bleeding (i.e. gastroesophageal variceal bleeding). Accordingly, the management of a patient with liver cirrhosis is not only to treat a liver itself, but also to manage the whole body. Understanding and application of HIM concept should be very critical to address such a complex issue. Herein, we would like to briefly introduce several aspects, where the concept of HIM is being used for the management of liver cirrhosis, to emphasize its effects on our future knowledge.

### 2. Evaluation of prognosis of liver cirrhosis

Child–Pugh and MELD scores are the most widely used models for evaluating the outcomes of patients with liver cirrhosis. Nearly half a century has been passed since the first

development of Child–Turcotte score in 1964 [3] and its modification as Child–Turcotte–Pugh score in 1973 [4]. MELD score has also been established for more than 20 years [5] and then continuously modified as MELD-Na [6] and MELD 3.0 [7]. In fact, their first proposal was specific for cirrhotic patients who underwent surgery or transjugular intrahepatic portosystemic shunt for portal hypertension related complications, but not general patients with liver cirrhosis. Certainly, they are the most classical and representative and have comprehensively assessed the function of multiple extrahepatic organs, such as prothrombin time or international normalized ratio as an indicator of coagulation system, creatinine as an indicator of renal function, and hepatic encephalopathy as an indicator of nervous system. However, the physicians still strive to more precise approaches for evaluating the prognosis of liver cirrhosis by integrating other clinical and laboratory parameters, seeking novel biomarkers, and incorporating imaging and histology features, especially in the contemporary era when artificial intelligence technology has been widely used in our lives. This behavior suggests the use of HIM concept in updating the evaluation of prognosis of liver cirrhosis.

### 3. Assessment of decompensation of liver cirrhosis

Traditionally, the primary endpoint that investigators observe and follow in previous studies regarding management and outcomes of liver cirrhosis and its complications is often a single decompensation event, such as the first or recurrent variceal bleeding [8,9], *de novo* or recurrent ascites [10], or hepatic encephalopathy [11] alone. By comparison, at present, it has been gradually accepted that decompensation, which is defined as the occurrence of any decompensation event, is a preferred outcome of interest in such studies [12–14]. Accordingly, the statistical methods used for assessing hepatic decompensation have also been changed. Kaplan–Meier curve analysis is conventionally used for calculating the cumulative incidence of developing decompensation or being free of decompensation during follow-up period. However, in the recent years, competing risk analysis, in which death and liver transplantation are considered competing events, is

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recommended for evaluating the risk of decompensation [15]. This is primarily because death or liver transplantation may be earlier than decompensation in some cases, underestimating the probability of decompensation. Taken together, hepatologists and gastroenterologists are increasingly recognizing the importance of assessing the progression of liver cirrhosis from an integrative point of view, instead of only one or two clinical events.

#### 4. Recognition of recompensation of liver cirrhosis

There is an old dogma that liver cirrhosis, especially decompensated stage, is irreversible. But it has been greatly challenged by contemporary knowledge [16]. Recent studies suggest that a proportion of patients with decompensated cirrhosis will be free of developing further decompensation events, especially after etiological cure, such as alcoholic abstinence, cure of hepatitis C, and viral suppression of hepatitis B. Thus, the definition of cirrhosis recompensation, which should be the removal/suppression/cure of the primary etiology of cirrhosis with stable improvement of liver function tests, but without cirrhosis-related complications, has been firstly proposed in the Baveno VII consensus [17] and then supported by recent evidence [18]. Collectively, the two definitions are obviously reverse, but the recognition of their coexistence indicates that the physicians are understanding the disease course of decompensated cirrhosis in a holistic point of view.

#### 5. Treatment of liver cirrhosis

How to prevent and treat various clinically significant complications of liver cirrhosis, such as variceal bleeding, ascites, hepatorenal syndrome, and hepatic encephalopathy, has been the primary responsibility of our physicians and investigators for decades. Recently, except for the injury of a single or multiple organs, the general condition of a patient with liver cirrhosis, including whether he or she has malnutrition, sarcopenia, and frailty, has been increasingly explored. This is mainly because cumulative evidence has clarified their impact on decreased survival of cirrhotic patients [19]. On the other hand, except for cirrhotic patients themselves, their caregivers also experience physical and psychological problems, compromising their quality of life. Accordingly, the importance of improvement of the caregivers' burden and distress is being highlighted [20]. Such a shift in the idea regarding how to treat liver cirrhosis more comprehensively also indicates the penetration of HIM attitude into physicians' perception.

#### 6. Conclusion

In conclusion, HIM, which provides more comprehensive and unbiased attitudes on the management of liver cirrhosis, has been deeply infiltrated in our every clinical practice, although maybe not all clinicians and investigators have heard or used this concept yet. In future, it should also be valuable and practical for us to enlighten novel perspectives and strategies in the field of hepatology.

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#### References

- Davidoff F, Haynes B, Sackett D, et al. Evidence based medicine. *BMJ*. 1995 Apr 29;310(6987):1085–1086. doi: [10.1136/bmj.310.6987.1085](https://doi.org/10.1136/bmj.310.6987.1085). PubMed PMID: 7742666; PubMed Central PMCID: PMCPMC2549494.
- Fan D. Holistic integrative medicine: toward a new era of medical advancement. *Front Med*. 2017 Mar;11(1):152–159. doi: [10.1007/s11684-017-0499-6](https://doi.org/10.1007/s11684-017-0499-6). PubMed PMID: 28044221; eng.
- Child CG, Turcotte JG. Surgery and portal hypertension. *Major Probl Clin Surg*. 1964;1:1–85. PubMed PMID: 4950264.
- Pugh RN, Murray-Lyon IM, Dawson JL, et al. Transection of the oesophagus for bleeding oesophageal varices. *Br J Surg*. 1973 Aug;60(8):646–649. doi: [10.1002/bjs.1800600817](https://doi.org/10.1002/bjs.1800600817). PubMed PMID: 4541913.
- Kamath PS, Wiesner RH, Malinchoc M, et al. A model to predict survival in patients with end-stage liver disease. *Hepatology*. 2001 Feb;33(2):464–470. doi: [10.1053/jhep.2001.22172](https://doi.org/10.1053/jhep.2001.22172). PubMed PMID: 11172350.
- Kim WR, Biggins SW, Kremers WK, et al. Hyponatremia and mortality among patients on the liver-transplant waiting list. *N Engl J Med*. 2008 Sep 4;359(10):1018–26. doi: [10.1056/NEJMoa0801209](https://doi.org/10.1056/NEJMoa0801209). PubMed PMID: 18768945; PubMed Central PMCID: PMCPMC4374557.
- Kim WR, Mannalithara A, Heimbach JK, et al. MELD 3.0: the model for end-stage liver disease updated for the modern era. *Gastroenterol*. 2021 Dec;161(6):1887–1895 e4. doi: [10.1053/j.gastro.2021.08.050](https://doi.org/10.1053/j.gastro.2021.08.050). PubMed PMID: 34481845; PubMed Central PMCID: PMCPMC8608337.
- García-Pagán JC, Morillas R, Bañares R, et al. Propranolol plus placebo versus propranolol plus isosorbide-5-mononitrate in the prevention of a first variceal bleed: a double-blind RCT. *Hepatol*. 2003 Jun;37(6):1260–1266. doi: [10.1053/jhep.2003.50211](https://doi.org/10.1053/jhep.2003.50211). PubMed PMID: 12774003; eng.
- García-Pagán JC, Villanueva C, Albillos A, et al. Nadolol plus isosorbide mononitrate alone or associated with band ligation in the prevention of recurrent bleeding: a multicentre randomised controlled trial. *Gut*. 2009 Aug;58(8):1144–50. doi: [10.1136/gut.2008.171207](https://doi.org/10.1136/gut.2008.171207). PubMed PMID: 19218249; eng.
- Bureau C, Thabut D, Oberti F, et al. Transjugular intrahepatic portosystemic shunts with covered stents increase transplant-free survival of patients with cirrhosis and recurrent ascites. *Gastroenterol*. 2017 Jan;152(1):157–163. doi: [10.1053/j.gastro.2016.09.016](https://doi.org/10.1053/j.gastro.2016.09.016). PubMed PMID: 27663604; eng.

11. Bass NM, Mullen KD, Sanyal A, et al. Rifaximin treatment in hepatic encephalopathy. *N Engl J Med.* **2010** Mar 25;362(12):1071–81. doi: [10.1056/NEJMoa0907893](https://doi.org/10.1056/NEJMoa0907893). PubMed PMID: 20335583; eng.
12. Frenette C, Kayali Z, Mena E, et al. Emricasan to prevent new decompensation in patients with NASH-related decompensated cirrhosis. *J Hepatol.* **2021** Feb;74(2):274–282. doi: [10.1016/j.jhep.2020.09.029](https://doi.org/10.1016/j.jhep.2020.09.029). PubMed PMID: 33038432; eng.
13. Ding M, Yin Y, Wang X, et al. Associations of gallbladder and gallstone parameters with clinical outcomes in patients with cirrhosis. *J Transl Int Med.* **2023**. In press. doi: [10.2478/jtim-2022-0076](https://doi.org/10.2478/jtim-2022-0076)
14. Wang L, Guo X, Bai Z, et al. Impact of asymptomatic Superior mesenteric vein thrombosis on the outcomes of patients with liver cirrhosis. *Thromb Haemost.* **2022** Dec;122(12):2019–2029. doi: [10.1055/s-0042-1756648](https://doi.org/10.1055/s-0042-1756648). PubMed PMID: 36179738; eng.
15. Jepsen P, Vilstrup H, Andersen PK. The clinical course of cirrhosis: the importance of multistate models and competing risks analysis. *Hepatol.* **2015** Jul;62(1):292–302. doi: [10.1002/hep.27598](https://doi.org/10.1002/hep.27598). PubMed PMID: 25376655; eng.
16. Marcellin P, Gane E, Buti M, et al. Regression of cirrhosis during treatment with tenofovir disoproxil fumarate for chronic hepatitis B: a 5-year open-label follow-up study. *Lancet.* **2013** Feb 9;381(9865):468–475. doi: [10.1016/s0140-6736\(12\)61425-1](https://doi.org/10.1016/s0140-6736(12)61425-1). PubMed PMID: 23234725; eng.
17. de Franchis R, Bosch J, Garcia-Tsao G, et al. Baveno VII - Renewing consensus in portal hypertension. *J Hepatol.* **2022** Apr;76(4):959–974. doi: [10.1016/j.jhep.2021.12.022](https://doi.org/10.1016/j.jhep.2021.12.022). PubMed PMID: 35120736; eng.
18. Wang Q, Zhao H, Deng Y, et al. Validation of Baveno VII criteria for recompensation in entecavir-treated patients with hepatitis B-related decompensated cirrhosis. *J Hepatol.* **2022** Dec;77(6):1564–1572. doi: [10.1016/j.jhep.2022.07.037](https://doi.org/10.1016/j.jhep.2022.07.037). PubMed PMID: 36038017; eng.
19. Lai JC, Tandon P, Bernal W, et al. Malnutrition, frailty, and Sarcopenia in patients with cirrhosis: 2021 practice guidance by the American Association for the study of liver diseases. *Hepatol.* **2021** Sep;74(3):1611–1644. doi: [10.1002/hep.32049](https://doi.org/10.1002/hep.32049). PubMed PMID: 34233031; PubMed Central PMCID: PMC9134787.
20. Tapper EB, Saleh ZM, Lizza S, et al. CAREGIVER randomized trial of two mindfulness methods to improve the burden and distress of caring for persons with cirrhosis. *Dig Dis Sci.* **2023** Sep;68(9):3625–3633. doi: [10.1007/s10620-023-08042-9](https://doi.org/10.1007/s10620-023-08042-9). PubMed PMID: 37498415.