

Symposium 1

Understanding of Liver Function Test and Functional Assessment

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Because most patients with hepatocellular carcinoma (HCC) have chronic liver diseases such as liver cirrhosis, the choice of treatment modality depends on tumor stage and the functional status of liver.¹ Although several treatment modalities including radio-frequency ablation, transarterial chemoembolization, radiotherapy are currently used for the treatment of HCC, hepatic resection is widely considered for the mainstay of curative therapy of HCC. Compared to radiofrequency ablation, surgical resection of liver parenchyma accompanies the reduction of the functioning liver volume which may cause postoperative hepatic failure. Therefore preoperative assessment of liver function and prediction of postoperative residual functional reserve are very important to minimize surgical risk. In this lecture, the current understanding of liver function test and preoperative evaluation of functional hepatic reserve are briefly reviewed.

Conventional liver function tests include the standard liver function tests, such as serum total bilirubin levels, serum albumin levels, and prothrombin time. The Child-Pugh classification is a simple but useful tool that provides an initial clue to the extent of hepatic resection that a cirrhotic patients tolerate.² The Child-Pugh class C cirrhosis is considered a contraindication for hepatic resection. For Child-Pugh class B cirrhotic patients, only minor hepatic resection would be considered. For Child-Pugh class A cirrhotic patients, the decision for a major hepatic resection requires additional liver function tests. Child-Pugh classification only provides a rather crude evaluation of liver function reserve.³

Quantitative liver function tests assess a specific aspect of liver function such as liver microsomal function, cytosolic function, hepatic perfusion, and synthetic function. Indocyanine (ICG) clearance test is the

most commonly used in Asian countries. After intravenous administration, the dye ICG almost completely binds to plasma protein and is distributed in the serum alone (no extravascular distribution). ICG is exclusively removed by the liver via a carrier-mediated mechanism, and it is excreted unchanged into bile and does not undergo any extrahepatic circulation. In cirrhotic patients, the ICG uptake by the liver from the plasma is decreased and the ICG excretion by the liver into the bile is maintained relatively intact. Because of this, ICG-R15, which are calculated from the distribution phase of disappearance curve up to 15 min, are thought to be adequate as indices of liver functional reserve in chronic liver disease including cirrhosis.⁴ The value of ICG clearance test in the preoperative assessment of liver function has been well documented from several studies.⁵ In patients without ascites and with normal serum bilirubin levels, ICG-R15 value becomes the main determinant for the respectability, i.e. right hepatectomy can be tolerated if the ICG-R15 is <10%. For patients with ICG-R15 within the range of 10~19%, one-third of the liver parenchyma can be resected. When the ICG-R15 value range is 20~29%, approximately one-sixth of the liver parenchyma can be resected. A limited resection is indicated in patients with ICG-R15 values of 30% or more.⁴ However, ICG-R15 may not be the only factor in predicting post-operative mortality or liver failure, therefore it should be interpreted with caution by taking into account other parameters that can affect liver function including serum alanine aminotransferase levels, platelet count, portal hypertension.

Recently analysis of postoperative prognosis was performed in 490 patients with liver cirrhosis who underwent surgery at Samsung Medical Center under general anesthesia from January 2003 to December

2008.⁶ The postoperative mortality in patients with cirrhosis was compared with respect to Child-Turcotte-Pugh (CTP), Model for End-stage Liver Disease score (MELD), and Model for End-stage Liver Disease and Serum Sodium Concentration score (MELDNa) systems. Ninety-day mortality in patients with CTP A, B, and C class were 2.1, 22.1 and 54.5%, respectively. Ninety-day mortality according to MELD score was as follows: 6~9, 3.5%; 10~14, 8.9%; 15~19, 14.3%; 20~24, 12.5%; and ≥ 25 , 63.6%. Ninety-day mortality according to MELDNa score was as follows: 6~9, 1.9%; 10~14, 6.2%; 15~19, 13.2%; 20~24, 20.6%; and ≥ 25 , 50%. Multivariable analysis showed that emergency surgery, American Society of Anesthesiologist class \geq IV, CTP score ≥ 7 , MELD score ≥ 10 , and MELDNa score ≥ 10 were independent risk factors for 90-day mortality. The area under the receiver operating curve of CTP, MELD, and MELDNa in predicting 90-day mortality were 0.859, 0.761, 0.818, and nonparametric approach using the generalized U-statistic showed that the CTP score was equal to the MELDNa score ($P=0.855$) and the CTP and MELDNa scores were superior to the MELD score ($P=0.027$ and 0.047) in predicting postoperative 90-day mortality.

References

1. Fattovich G, Stroffolini T, Zagni I, Donato F. Hepatocellular carcinoma in cirrhosis: incidence and risk factors. *Gastroenterology* 2004;127:S35-50.
2. Pugh RN, Murray-Lyon IM, Dawson JL, Pietroni MC, Williams R. Transection of the oesophagus for bleeding oesophageal varices. *Br J Surg* 1973;60:646-9.
3. Poon RT, Fan ST. Assessment of hepatic reserve for indication of hepatic resection: how I do it. *J Hepatobiliary Pancreat Surg* 2005;12:31-7.
4. Imamura H, Sano K, Sugawara Y, Kokudo N, Makuuchi M. Assessment of hepatic reserve for indication of hepatic resection: decision tree incorporating indocyanine green test. *J Hepatobiliary Pancreat Surg* 2005;12:16-22.
5. Hemming AW, Scudamore CH, Shackleton CR, Pudek M, Erb SR. Indocyanine green clearance as a predictor of successful hepatic resection in cirrhotic patients. *Am J Surg* 1992;163:515-8.
6. Cho HC, Jung HY, Sinn DH, et al. Mortality after surgery in patients with liver cirrhosis: comparison of Child-Turcotte-Pugh, MELD and MELDNa score. *Eur J Gastroenterol Hepatol* 2011;23:51-9.