



Is liver biopsy still useful in the era of non-invasive tests?

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See Article on Page 318

Liver biopsy has been referred to as the gold standard for the diagnosis of liver diseases and evaluation of liver fibrosis or liver damage. The American Association for the Study of Liver Disease guidelines have suggested the following indications for liver biopsy,¹ namely, diagnosis of parenchymal liver diseases, abnormal liver function tests of uncertain causes, fever of unknown origin, and abnormal findings on imaging studies; staging of parenchymal liver diseases; and development of treatment plans based on histopathologic findings. Among all indications for liver biopsy, its use in diagnosis is of utmost importance. For example, histological findings of interface hepatitis and lymphoplasmacytic infiltrates in portal tract are seen in autoimmune hepatitis,² and destruction of the interlobular bile duct and nonsuppurative destructive cholangitis are observed in primary biliary cholangitis.³ Liver biopsy plays an important role in the diagnosis of malignancies, such as hepatocellular carcinoma, which can also be diagnosed by typical imaging findings in multiphasic computed to-

mography (CT) or magnetic resonance imaging (MRI) in patients with risk factors, such as cirrhosis or chronic viral hepatitis. However, liver biopsy should be considered in patients who show typical image findings but do not have risk factors as well as in those who have risk factors but do not show typical image findings.⁴

Limitations to liver biopsy include invasive nature with possibility of complications, sampling variability and the subjective nature of the pathologist interpretation.⁵ Therefore, non-invasive methods have recently replaced or supplemented a significant portion of liver biopsy. As non-invasive tests, the scoring systems using serologic test such as fibrosis-4 (FIB-4) index, non-alcoholic fatty liver disease (NAFLD) fibrosis score, or aspartate transaminase to platelet ratio index (APRI) might be useful to screen advanced fibrosis or cirrhosis. These methods are easily obtained at no additional cost. Patients suspected of cirrhosis in these scoring systems might be confirmed without liver biopsy by imaging based non-invasive methods such as ultrasonography based elastography such as transient elastography and two-dimensional shear wave elastography, and magnetic resonance elastography.

In the current study, the changes in indications for liver biopsy

Abbreviations:

APRI, aspartate transaminase to platelet ratio index; CT, computed tomography; FIB-4, fibrosis-4; MRI, magnetic resonance imaging; NAFLD, non-alcoholic fatty liver disease; NAS, NAFLD activity score; NASH, non-alcoholic steatohepatitis

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in a single Korean tertiary care center were evaluated.⁶ In general, conducting liver biopsies for viral hepatitis has been found to decrease over time. This finding suggested the development of non-invasive methods replacing the reported indications of liver biopsy for fibrosis staging in viral hepatitis. Transient elastography is the most widely used non-invasive method in the tertiary care center, and has been validated for the evaluation of liver fibrosis in various liver diseases.⁷ Filtering out chronic hepatitis B patients with advanced fibrosis or cirrhosis is very important to determine the antiviral therapy or evaluate prognosis because current guidelines generally recommend antiviral therapy in patients with cirrhosis regardless of alanine transaminase levels,⁸⁻¹⁰ and thus, non-invasive test methods can be very beneficial in determining antiviral therapy without a liver biopsy. In addition, the results of transient elastography on the degree of fibrosis can predict hepatocellular carcinoma risk in patients with chronic hepatitis B.^{11,12} However, the degree of liver stiffness from transient elastography can be overestimated in case of severe inflammation of liver,¹³ and the measurement of fibrosis may be difficult in patients with obesity or ascites. Therefore, it should be interpreted in consideration of various situations. Similar to viral hepatitis, liver biopsies for malignancy were also decreased over time in the current study,⁶ and it seems to be possible to diagnose hepatocellular carcinoma in most patients who have risk factors such as viral hepatitis or cirrhosis without liver biopsy due to the development of CT or MRI techniques.

However, in the current study, liver biopsies for autoimmune hepatitis or primary biliary cholangitis were increased.⁶ Although various serologic markers may suspect autoimmune hepatitis, but most cases are confirmed by liver biopsy.² For primary biliary cholangitis, liver biopsy is especially helpful when anti-mitochondrial antibody is negative, or overlap syndrome with autoimmune hepatitis is suspected.³ In primary sclerosing cholangitis, "onion skin" can be observed in the biopsy sample. These pathological findings cannot be replaced by non-invasive tests. Non-invasive tests are helpful in NAFLD—transient elastography can measure not only fibrosis but also steatosis by controlled attenuated parameter. Despite the availability of non-invasive methods in the current study, liver biopsies for NAFLD also showed an increased pattern.⁶ This could have been due to an increased incidence of NAFLD, including non-alcoholic steatohepatitis (NASH) in recent years. A liver biopsy is considered as an important test if the degree of steatohepatitis or NAFLD activity score (NAS) needs to be determined because there has been no proven non-invasive test that reflects the degree of inflammation and fibrosis in NASH. A liver biopsy

also provides us useful informations when the cause of hepatitis is not clear. There is no alternative method or test that can replace liver biopsy for demonstrating the actual status of liver disease.

Percutaneous liver biopsy is the most widely used approach and is currently performed under ultrasonographic guidance. Conducting liver biopsy under guidance from ultrasonography has reduced the risk of complications.¹ Two retrospective studies reported that major adverse events after percutaneous liver biopsies were about 1.0%.^{14,15} Pain was the most common post-biopsy complication that occurred in 30–50% of the patients,¹⁶ but was not usually serious. Bleeding was the most common serious complication reported to occur in 0.6% of the patients.¹⁴ Rare complications of organ injury, such as pneumothorax, hemothorax, or bile peritonitis have also been reported.¹ The outcomes in the current study showed a comparatively lower incidence of major adverse events (0.05%) than previous studies.⁶ This study included patients with advanced cirrhosis and ascites belonging to Child-Pugh Class B or C. Study results suggested that ultrasonography-guided percutaneous liver biopsies were performed without serious complications in most patients, including advanced cirrhosis; however, this study did not record whether patients with advanced cirrhosis had any bleeding tendency, such as thrombocytopenia or prolongation of prothrombin time. Therefore, in cirrhotic patients with bleeding tendency, other approaches, such as transjugular liver biopsy should be considered.

Although various non-invasive methods have been developed and are currently available, liver biopsy has its own irreplaceable role and is still important. The indication of liver biopsy has been changed from assessment of fibrosis in viral hepatitis to diagnosis of autoimmune hepatitis, primary biliary cirrhosis, and NASH mainly due to the changes in disease incidence as well as due to the development of non-invasive test. A liver biopsy can be safely performed in most patients, and therefore, should be always considered, if necessary.

Conflicts of Interest

The authors have no conflicts of interests to disclose.

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