EASL Clinical Practice Guidelines on non-invasive tests for evaluation of liver disease severity and prognosis – 2020 update

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Recommendations that remained unchanged as in the previous EASL CPGs

General statements

- Even though liver biopsy has been used as the reference method for the design, evaluation and validation of non-invasive tests, it is an imperfect gold standard. In order to optimize the value of liver biopsy for fibrosis evaluation, it is important to adhere to the following recommendations: (i) sample length >15 mm by a 16G needle; (ii) use of appropriate scoring systems according to liver disease etiology; and (iii) reading by an experienced (and if possible specialized) pathologist.

- Non-invasive tests reduce but do not abolish the need for liver biopsy; they should be used as an integrated system with liver biopsy according to the context.

Currently available non-invasive methods

- Non-invasive tests should always be interpreted by specialists in liver disease, according to the clinical context, considering the results of other tests(biochemical,

radiological and endoscopic) and taking into account the recommended quality criteria for each test and its possible pitfalls (A1)

- Serum biomarkers can be used in clinical practice due to their high applicability (>95%) and good interlaboratory reproducibility. However, they should be preferably obtained in fasting patients (particularly those including hyaluronic acid) and following the manufacturer's recommendations for the patented tests (A1)

- TE is a fast, simple, safe and easy to learn procedure that is widely available. Its main limitation is the impossibility of obtaining results in case of ascites or morbid obesity and its limited applicability in case of obesity and limited operator experience (A1)

- TE should be performed by an experienced operator(>100 examinations) following a standardized protocol with the patient, fasting for at least 2 hours, in the supine position, right arm in full abduction, on the midaxillary line with the probe-tip placed in the 9th to 11[th]intercostal space with a minimum of 10 shots (A1)

- Correct interpretation of TE results in clinical practice must consider the following parameters:

  IQR/ median value (<30%),

  Serum aminotransferases levels (<5 x ULN),

  BMI (use XL probe above 30 kg/m2 or if skin-to-capsule distance is >25 mm),

  Absence of extra-hepatic cholestasis

  Absence of right heart failure, or other causes of congestive liver

  Absence of ongoing excessive alcohol intake (A1)

- Although alternative techniques, such as pSWE/ARFI or 2D-SWE seem to overcome limitations of TE, their quality criteria for correct interpretation are not yet well defined (A1)

- At present correct interpretation of pSWE/ARFI results in clinical practice should systematically take into account the potentially confounding parameter:

  fasting for at least 2 hours, transaminases levels (<5 x ULN), absence of extra-hepatic cholestasis and absence or right heart failure (A1)

Endpoints for staging liver fibrosis

- Detection of cACLD/cirrhosis represents the most relevant clinical endpoint in patients with chronic liver disease of any etiology (A1)

- Detection of cirrhosis indicates that patients should be monitored for complications related to PH and regularly screened for HCC (A1)

Performance of TE for staging liver fibrosis

- TE can be considered the non-invasive standard for the measurement of LS (A1)

- TE is well validated in untreated viral hepatitis with performance equivalent in hepatitis B and C and in HIV-HCV coinfection (A1)

- TE performs better for detection of cirrhosis than for detection of significant fibrosis (A1)

- TE is a reliable method for the diagnosis of cirrhosis in patients with chronic liver diseases, that generally performs better at ruling out than ruling in cirrhosis (with negative predictive value higher than 90%) (A1)

Performance of other ultrasound elastography techniques for staging liver fibrosis

- pSWE/ARFI performs better for detecting cirrhosis than significant fibrosis and is better validated in chronic hepatitis C than for hepatitis B, HIV-HCV coinfection, NAFLD and other liver diseases (A1)
- pSWE/ARFI shows equivalent performance to TE for detecting significant fibrosis and cirrhosis (A1)

Comparison of performance of TE and serum biomarkers for staging liver fibrosis

- TE and serum biomarkers have equivalent performance for detecting significant fibrosis in patients with untreated viral hepatitis (A1)
- TE is the most accurate non-invasive method for detecting cirrhosis in patients with untreated viral hepatitis (A1)

Algorithms combining different tests (LS and/or serum biomarkers)

- Among the different available strategies, algorithms combining TE and serum biomarkers appear to be the most attractive and validated one (A2)
- In patients with viral hepatitis C, when TE and serum biomarkers results are in accordance, the diagnostic accuracy is increased for detecting significant

fibrosis but not for cirrhosis. In cases of unexplained discordance, a liver biopsy should be performed if the results would change the patient management. (A1)

Indications for non-invasive tests for staging liver disease in untreated viral hepatitis

HCV including HIV-HCV

- All HCV patients should be screened to exclude cirrhosis by TE if available. Serum biomarkers can be used in the absence of TE (A1)
- HCV patients who were diagnosed with cirrhosis based on non-invasive diagnosis should undergo screening for HCC and PH and do not need confirmatory liver biopsy (A1)

HBV

- TE has better prediction for advanced liver fibrosis and cirrhosis than serum biomarkers in chronic hepatitis B(B1)
- TE is best used to determine liver fibrosis in hepatitis B patients with active viraemia (HBV DNA >2000 IU/ml)but normal ALT (A1)
- TE can be used to exclude severe fibrosis and cirrhosis in inactive carriers (HBeAg-negative, low viral load (HBV DNA <2000 IU/ml) and normal ALT). Liver biopsy should only be considered in doubtful cases after TE(A1)
- LS measurement should be interpreted with caution among patients with elevated ALT, and should not be used in patients with very high ALT levels (>10 x ULN)(A1)

Use of non-invasive methods when deciding for treatment in viral hepatitis B

- For the diagnosis of significant fibrosis a combination of tests with concordance may provide the highest diagnostic accuracy (A2)

- Non-invasive tests should be utilized prior to therapy by treating non-specialists to make sure that patients with severe fibrosis/cirrhosis are referred for appropriate disease specific specialist evaluation (A1)

- Non-invasive assessment of liver fibrosis, using either serum biomarkers or TE, should be considered for patients with significant viraemia (HBV DNA >2000 IU/ml) when liver cirrhosis is suspected (A1)

- Among patients who have HBV DNA >2000 IU/ml, antiviral therapy should be considered for patients who have advanced fibrosis or cirrhosis as determined by non-invasive assessment of liver fibrosis, either by serum biomarkers or TE, regardless of the ALT levels(A1)