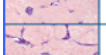
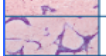
Assessment of the severity of liver disease – Full clinical guideline

Reference no.: CG-T/2023/191

The assessment of patients with abnormal LFTs is aimed at identifying the aetiology of their liver disease and the severity of underlying liver damage. Injury to hepatocytes leads to activation of immune cells and an inflammatory response. Inflammatory mediators stimulate hepatic stellate cell activation (may then be self perpetuating) which leads to fibrogenesis. It is fibrosis progression which may ultimately lead to cirrhosis. The assessment of severity of liver disease can be based on clinical, laboratory, imaging and histological findings.

Clinical: The presence of stigmata of chronic liver disease (spider naevi, palmar erythema, leuconychia and gynaecomastia) in a patient presenting with liver disease often indicates cirrhosis in the absence of an alternative cause.
Laboratory: thrombocytopenia in a patient with abnormal LFTs should always alert the clinician to the possibility of cirrhosis (low platelets largely secondary to hypersplenism resulting from cirrhosis and portal hypertension). An AST:ALT ratio > 1 in patients with HCV may indicate cirrhosis.
Imaging: A shrunken liver with an irregular surface may be seen on USS or CT in patients with advanced liver disease, but the liver can often appear normal on imaging in the presence of cirrhosis.
Tissue elastrography: See section on tissue elastrography
Histology: There are various scoring systems for the severity of liver fibrosis on biopsy. The Ishak modified HAI score was developed for the assessment of fibrosis in viral hepatitis and is frequently referred to in pathology reports and clinic letters in Derby. NAFLD is reported using Kleiner score – see NAFLD section.

Ishak fibrosis score

General Appearance	Categorical Description	Categorical Assignment
	No fibrosis (normal)	0
	Fibrous expansion of some portal areas (+/-) short fibrous septa	1
	Fibrous expansion of most portal areas (+/-) short fibrous septa	2
	Fibrous expansion of most portal areas with occasional portal to portal (P-P) bridging	3
	Fibrous expansion of portal areas with marked bridging (P-P) as well as portal to central (P-C)	4
	Marked bridging (P-P and/or P-C), with occasional nodules (incomplete cirrhosis)	5
	Cirrhosis, probable or definite	6

Assessment of severity of liver failure in patients with cirrhosis:
Scoring systems for the severity of liver failure in patients with cirrhosis help determine prognosis and are used to aid decisions on treatment (e.g Interferon therapy in HCV) and surveillance intervals for oesophageal varices. They are also used in decisions regarding the need for liver transplantation.

Child-Pugh score

Parameter	Points assigned		
	1	2	3
Ascites	Absent	Slight	Moderate
Hepatic encephalopathy	None	Grade 1-2	Grade 3-4
Bilirubin micromol/L (mg/dL)	<34.2 (<2)	34.2-51.3 (2-3)	>51.3 (>3)
Albumin g/L (g/dL)	>35 (>3.5)	28-35 (2.8-3.5)	<28 (<2.8)
Prothrombin time Seconds over control INR	 <4 <1.7	 4-6 1.7-2.3	 >6 >2.3
CPT classification: Child A: score 5-6 (well compensated); Child B: score 7-9 (significant functional compromise); Child C: score 10-15 (decompensated)			

Model of End-Stage Liver Disease (MELD score) - electronically calculated from the serum bilirubin, creatinine, and clotting (INR and prothrombin time). If using MD-Calc ensure click SI units. It is used for the allocation of livers for transplantation in the US. A similar scoring system which also incorporates the serum sodium is used by the UK transplantation services (UKELD).

Tissue elastography (Fibroscan) in the assessment of liver fibrosis

Tissue elastrography (TE) measures the velocity of a low frequency (50Hz) elastic shear wave propagated through the liver. The stiffer (more fibrosed) the liver the faster the shear wave progression.

The patient should have fasted for at least 2 hours, as a large meal will increase blood flow in the liver and potentially falsely increase the liver stiffness measurement.

Trainees should not perform TE on a patient until they have received appropriate training.

TE results are given as a median kPa. When interpreting the result the clinician should be aware that the reading may be falsely raised in the presence of ongoing excessive alcohol consumption, serum aminotransferase levels > 5 x ULN, extra-hepatic cholestasis and in right heart failure or other causes of hepatic congestion.

The M probe should be used in all patients, with the XL probe reserved for those patients with a raised BMI in whom no valid result can be obtained with the M probe. Be aware that the XL probe will in general give a slightly lower stiffness reading (Median 1.4kPa less).

Validity of result:
A reliable (valid) TE result requires:

- Number of valid shots ≥ 10
- IQR/ Median (variability of measurements) < 30%

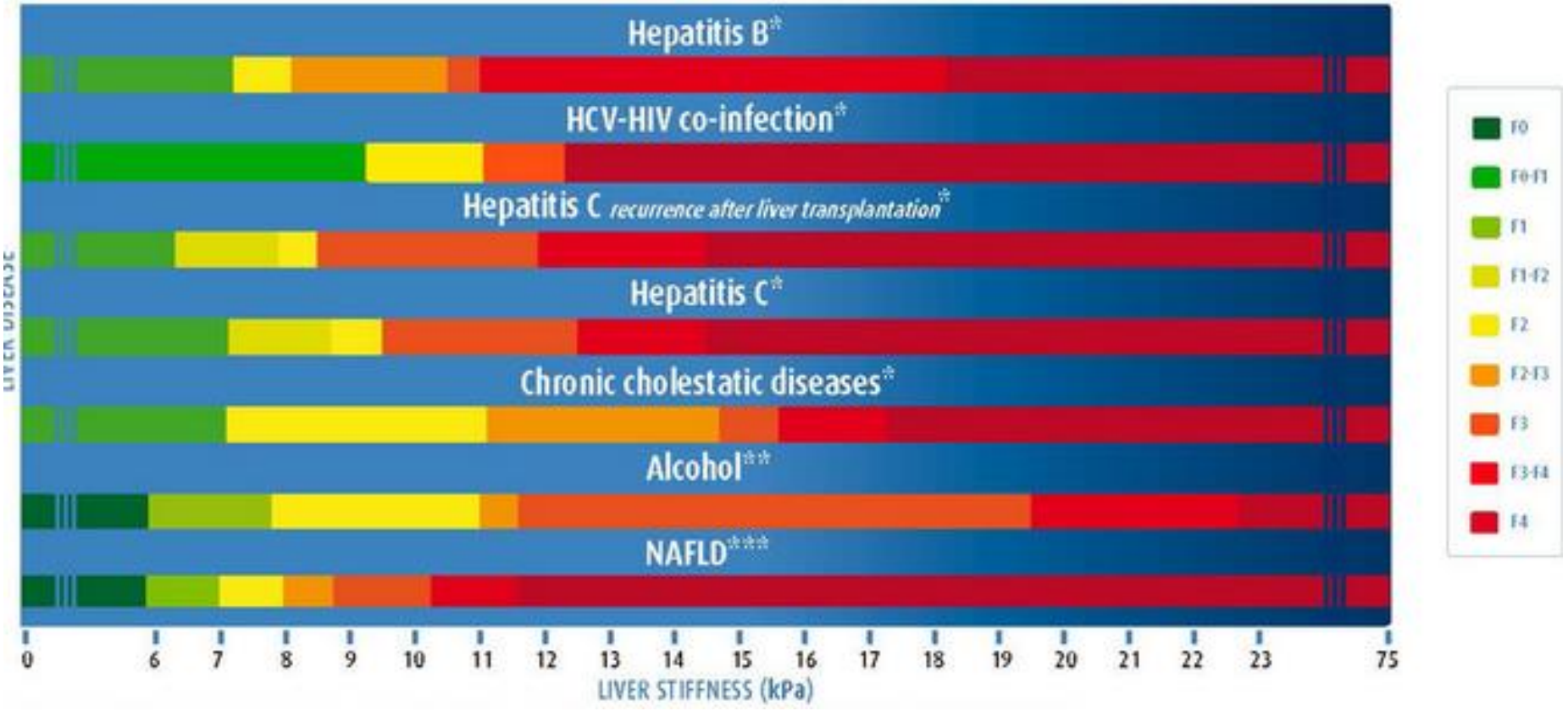
The failure rate is ≈ 3% and invalid results are obtained in 10-15% of patients

In patients in whom a valid measurement of tissue elastography cannot be obtained and in whom liver biopsy is not indicated, an assessment of fibrosis can be made using the Extended Liver Fibrosis (ELF) test. Specify on a black paper pathology form for the specimen to be sent to St James Hospital, Leeds. The sample (yellow top) should be obtained following an overnight fast.

Interpreting the result:

TE is better at assessing for cirrhosis rather than significant fibrosis (≥ F2 on biopsy) (cirrhosis mean AUROC 0.94, ≥ F2 mean AUROC 0.84)

It is also better at ruling OUT than ruling IN cirrhosis: Negative predictive value 96% Positive predictive value 74%



Further reading: [EASL guidelines on non-invasive tests for the evaluation of liver disease severity and prognosis 2021]

Documentation Controls (these go at the end of the document but before any appendices)

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Version / Amendment History	Version	Date	Author	Reason
	3	2022	Liver Management group	Previous version of guideline expired
Intended Recipients: Hepatology trainees, CNS' and consultants				
Training and Dissemination: Forms part of liver handbook which is disseminated to all clinicians rotating through Hepatology				
Development of Guideline: **Job Title: Dr A Lawson (Consultant Hepatologist)**				
Consultation with: Liver management group				
Linked Documents: State the name(s) of any other relevant documents NAFLD guideline				
Keywords: Fibroscan, Tissue elastography, Liver Fibrosis				
Business Unit Sign Off			**Group:Liver management group and cross-site teams** **Date:2022**	
Divisional Sign Off			**Group:Medicine division** **Date:Jan 2023**	
Date of Upload			June 2023	
Review Date			June 2026	
Contact for Review			Dr A Lawson	