Non-Alcoholic Fatty Liver disease (NAFLD) – Full Clinical Guideline

Reference no: CG-T/2023/209

NAFL is characterised by excessive hepatic fat accumulation, NASH (Non-alcoholic steatohepatitis) incorporates steatosis with ballooning of hepatocytes and lobular inflammation. They are estimated to be present in 20% and 5% of the general population respectively.

Diagnosis

1. **Demonstrate hepatic steatosis – USS/ CT/ MRI**
2. **Consider/ exclude secondary causes of steatosis**

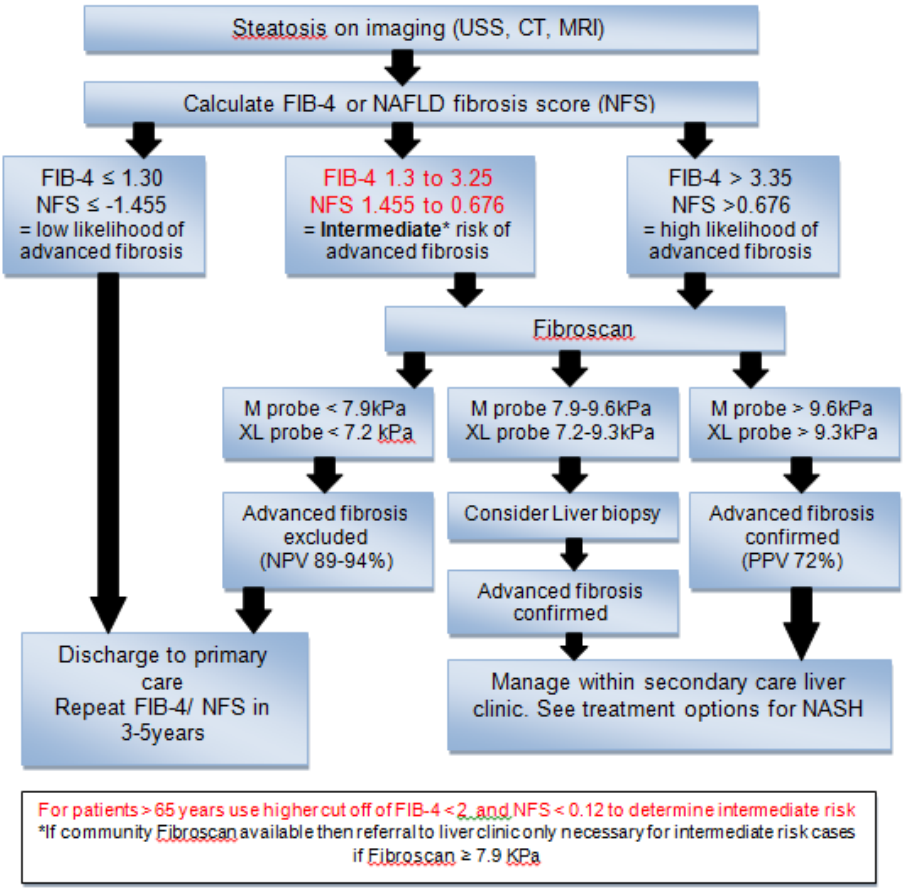
Macrovascular steatosis	Microvascular steatosis
Excessive alcohol consumption Hepatitis C (genotype 3) Wilson's disease Lipodystrophy Starvation Parenteral nutrition Abetalipoproteinaemia Medications (e.g. amiodarone, methotrexate, tamoxifen and corticosteroids)	Reye's syndrome Medications (e.g. Valproate, ART) Acute fatty liver of pregnancy HELP syndrome Inborn errors of metabolism (e.g. LCAT deficiency)

3. **Exclude co-existing causes of chronic liver disease** (Note - an elevated ferritin and low titre autoantibodies are common in NAFLD).

Staging

NALFD fibrosis score (http://nafldscore.com) - panel of age, hyperglycaemia, BMI, platelet, Albumin and AST/ ALT ratio (AUROC 0.84, NPV 92%, PPV 72%)

FIB-4 fibrosis score – uses age, platelet, AST and ALT



Liver biopsy – NAFLD (Kleiner NAFLD activity score (NAS) and staging system)

NASH activity grade: grade = total score: S + L + B (range 0–8)					
Steatosis	S score	Lobular inflammation	L score	Hepatocyte ballooning	B score
< 5%	0	None	0	None	0
5–33%	1	< 2	1	Few ballooned cells	1
34–66%	2	2–4	2	Many ballooned cells	2
> 66%	3	> 4	3		

NASH fibrosis stage	Stage
None	0
Mild, zone 3 perisinusoidal fibrosis	1a
Moderate, zone 3 perisinusoidal fibrosis	1b
Portal/periportal fibrosis only	1c
Zone 3 perisinusoidal and portal/periportal fibrosis	2
Bridging fibrosis	3
Cirrhosis	4

Natural History and risk of progression

NAFLD is in general a slowly progressive disease. Rate of progression corresponds to 1 fibrosis stage every 14 years in NAFL and every 7 years in NASH, and is doubled by arterial hypertension. NASH is associated with an increased SMR. Liver related mortality is increased, though cardiovascular is the most common cause of death

Treatment

Lifestyle approach to NAFLD treatment (see appendices for weight loss advice sheet)

- Energy restriction – 500-1000kcal energy defect. Aim for 7-10% weight loss
- Avoid fructose containing beverages
- Keep weekly alcohol less than 14 units
- 150-200 min/week of moderate intensity (brisk walking, cycling) aerobic exercise in 3-5 sessions

Drug treatments for risk factors associated with NAFLD:

Statins can be used to treat the dyslipidaemia in NAFLD and NASH (cardiovascular benefits are greater than for patients without NAFLD) but are yet to be established treatments for the liver disease.
Omega-3 fatty acids may be considered as first line agents to treat hypertriglyceridaemia in NAFLD
Metformin **in absence of diabetes** and ***Orlistat*** are not recommended

Drug treatment for NAFLD: indicated in NASH with Kleiner stage ≥ 2 fibrosis, high necroinflammatory activity or patients with NASH patients with risk factors for fibrosis progression (age > 50 yrs, diabetes, metabolic syndrome or increased ALT)

Vitamin E (α-tocopherol) 800 IU/day - but associated with increased all cause mortality, increased risk of prostate cancer in men and haemorrhagic CVA). Assess LFTs at 6/12 and discontinue if no response
Pioglitazone (30mg/day) - contraindicated in heart failure, previous or active bladder cancer and uninvestigated haematuria. This is only for existing T2DM patients and can only be initiated by a diabetologist.
*In patients with a raised ALT, stop Vitamin E and Pioglitazone if no reduction after 6 months

Iron depletion – improves insulin resistance and Kleiner NAS. Consider in patients with raised ferritin and increased siderosis on liver biopsy.

Foregut bariatric surgery is not contraindicated in otherwise eligible obese individuals with NAFLD or NASH (but without established cirrhosis). 1 year follow-up study showed NASH cleared in 85% and improved fibrosis in 34%

Further reading: EASL Clinical Practice Guidelines for the management of NAFLD 2016
NAFLD a patient guideline. EASL 2021
Diagnosis and Management of NAFLD. AASLD practice guideline 2018

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

<table>
<tr><td>Reference Number

CG-T/2023/209</td><td colspan="2">Version:

3</td><td>Status

Draft or Final</td><td>Final</td></tr>
<tr><td rowspan="3">Version / Amendment History</td><td>Version</td><td>Date</td><td>Author</td><td colspan="2">Reason</td></tr>
<tr><td>3</td><td>2022</td><td>Liver Management Group</td><td colspan="2">Previous version of guideline expired</td></tr>
<tr><td></td><td></td><td></td><td colspan="2"></td></tr>
<tr><td colspan="5">Intended Recipients: All clinicians managing patients with liver disease</td></tr>
<tr><td colspan="5">Training and Dissemination: Forms part of liver handbook which is disseminated to all clinicians rotating through Hepatology</td></tr>
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<tr><td colspan="5">Linked Documents: State the name(s) of any other relevant documents</td></tr>
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