PRACTICE AID

Screening for Advanced Fibrosis Related to NAFLD/NASH[1]

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Step 1: Identify patients at risk for clinically significant fibrosis

- T2D
- Two or more metabolic risk factors
- Incidental finding of hepatic steatosis or elevated aminotransferases

Step 2: Conduct blood tests and standard H&P (eg, assess for signs of advanced liver disease)

- Excessive alcohol intake
- CBC
- LFTs

Step 3: Conduct noninvasive testing for liver fibrosis[a,b]

FIB-4 is shown to have the best diagnostic accuracy for advanced fibrosis compared with other noninvasive markers of fibrosis in patients with NAFLD; the score also correlates with clinical outcomes in patients with NAFLD

FIB-4 <1.3 (<2.0 in those older than 65 years)	FIB-4 1.3-2.67	FIB-4 >2.67
LOW RISK Repeat NIT in 2-3 years unless clinical circumstances	**INDETERMINATE RISK**	**HIGH RISK** Refer to hepatologist

Step 4: Obtain a liver stiffness measurement[c,d]

LSM <8 kPa	LSM 8-12 kPa	LSM >12 kPa
LOW RISK Repeat NIT in 2-3 years unless clinical circumstances	**INDETERMINATE RISK** Refer to hepatologist for liver biopsy or MRE or monitoring with re-eval of risk in 2-3 years	**HIGH RISK** Refer to hepatologist

[a] Other NITs derived from routine laboratories can be used instead of FIB-4. [b] Many online FIB-4 calculators are available, such as https://www.mdcalc.com/calc/2200/fibrosis-4-fib-4-index-liver-fibrosis. [c] Ultrasound acceptable if VCTE (FibroScan) is unavailable. Consider referral to hepatologist for patients with hepatic steatosis on ultrasound who are indeterminate or high risk based on FIB-4. [d] LSM values are for VCTE (FibroScan); other techniques such as bidimensional shear wave elastography or point shear wave elastography can also be used to measure LSM; proprietary commercially available blood NITs may be considered for patients considered indeterminate or high risk based on FIB-4 or APRI, or where LSM unavailable.

1. Kanwal F et al. *Gastroenterology*. 2021;161:1657-1669.

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Management of NAFLD/NASH[1]

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	Lifestyle Intervention	Structured Weight-Loss Programs, Antiobesity Medications, Bariatric Surgery if Overweight/Obese	NASH Pharmacotherapy	CVD Risk Reduction	Diabetes Care
Patients at Low Risk of Advanced Fibrosis FIB-4 <1.3 or LSM <8 kPa or liver biopsy F0-F1	All patients require regular physical activity, a healthy diet, and avoidance of excess alcohol intake	May benefit	Not recommended	Yes	Standard of care
Patients at Indeterminate Risk of Advanced Fibrosis FIB-4 1.3-2.67 and/or LSM 8-12 kPa and liver biopsy not available		Greater need	Yes (Though no pharmacological agent is FDA approved for NASH, patients with T2DM and NASH may benefit from some diabetes medications, such as pioglitazone and some GLP-1 RAs; consider the use of vitamin E in patients with NASH without T2DM)		Prefer medications with efficacy in NASH (pioglitazone, GLP-1 RA)
Patients at High Risk of Advanced Fibrosis FIB-4 >2.67 or LSM >12 kPa or liver biopsy F2-F4		Strong need			

1. Kanwal F et al. *Gastroenterology*. 2021;161:1657-1669.

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AGA Clinical Practice Update on Lifestyle Modification in the Management of NAFLD: Best Practice Advice Statements[1]

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Lifestyle modification using diet and exercise to achieve weight loss is beneficial for all patients with NAFLD

Among patients with NASH, weight loss of ≥5% of total body weight can decrease hepatic steatosis, weight loss of ≥7% of total body weight can lead to NASH resolution, and weight loss of ≥10% of total body weight can result in fibrosis regression or stability

Clinically significant weight loss generally requires a hypocaloric diet targeting 1,200-1,500 kcal/d or a reduction of 500-1,000 kcal/d from baseline

Adults with NAFLD should follow the Mediterranean diet; minimize saturated fatty acid intake, specifically red and processed meat; and limit or eliminate consumption of commercially produced fructose

Regular physical activity should be considered for patients with NAFLD, with a target of 150-300 minutes of moderate-intensity or 75-150 minutes of vigorous-intensity aerobic exercise per week

Patients with NAFLD should be evaluated for coexisting metabolic conditions, such as obesity, DM, hypertension, dyslipidemia, and CV disease; these comorbidities should be managed aggressively

Alcohol consumption should be restricted or eliminated from the diets of adults with NAFLD

1. Younossi ZM et al. *Gastroenterology*. 2021;160:912–918.

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Medications to Treat Diabetes and Their Efficacy for the Treatment of NAFLD[1]

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Medication/Class	Liver Fat	Disease Activity (steatohepatitis/NAS)
Metformin	**Unchanged**	**Neutral**
DPP-IV inhibitors (sitagliptin and vildagliptin)	**Unchanged (in RCTs)**	**Effect unknown**
Insulin	**Decreased**	**Effect unknown**
SGLT2 inhibitors (dapagliflozin, empagliflozin, and canagliflozin)	**Decreased**	**Effect unknown**
Pioglitazone	**Decreased**	**Improved**
GLP-1 RAs (semaglutide and liraglutide)	**Decreased**	**Improved**

1. Kusi K et al. *Endocr Pract*. 2022;28:528-562.