AGA SECTION

Clinical Care Pathway for the Risk Stratification and Management of Patients With Metabolic Dysfunction–Associated Steatotic Liver Disease

[1]Metabolic risk factors:
increased waist circumference, high triglycerides, low high-density lipoprotein cholesterol, hypertension, prediabetes, or insulin resistance

If abnormal LFTs,
r/o mass lesions via liver ultrasound + below:

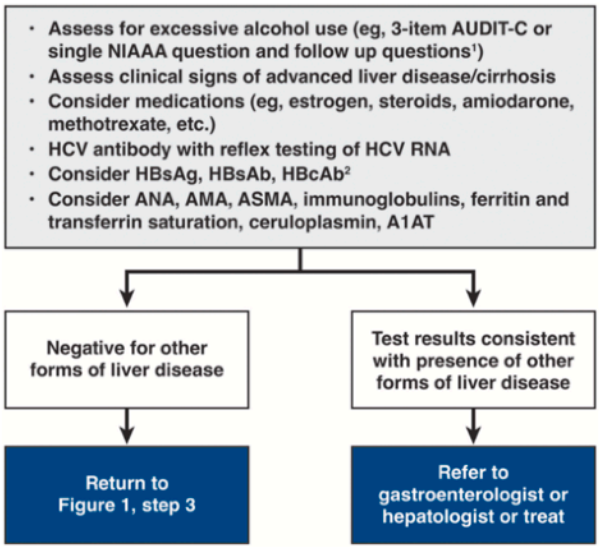
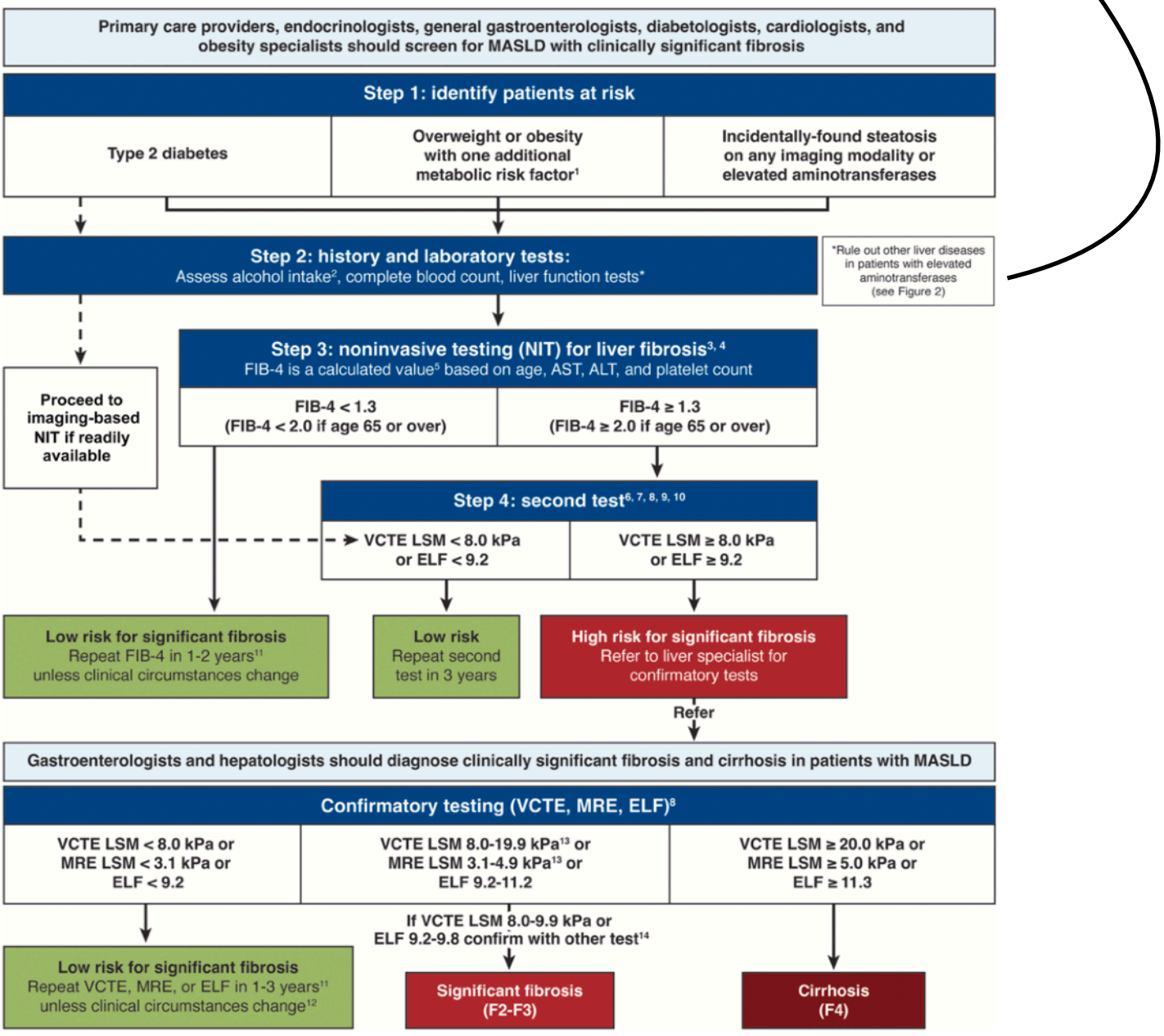


Figure 2. Evaluate for other forms of liver disease. [1]Use



	Low risk FIB-4 < 1.3 or VCTE LSM < 8 kPa or ELF < 9.2 or MRE LSM < 3.1 or Liver biopsy F0-F1	High risk VCTE LSM ≥ 8 kPa or ELF ≥ 9.2 or MRE LSM ≥ 3.1 or Liver biopsy F2+
	Management by primary care provider, dietitian, endocrinologist, diabetologist, obesity expert, cardiologist, others	Management by gastroenterologist, hepatologist, and/or other providers with experience with patients with MASH, together with multidisciplinary team
Lifestyle intervention, including cessation of alcohol use[1]	Yes	Yes
Structured weight loss programs and/or antiobesity medications[2]	Yes, target of at least ≥ 5%	Yes, target of at least ≥ 10%
Bariatric surgery if indicated	Yes	Yes, can be considered in compensated cirrhosis, but contraindicated in decompensated cirrhosis[3]
Control of CVD risk factors (LDL-C, BP, A1C, etc.)	Yes	Yes
Statins are safe if indicated	Yes	Yes, except in decompensated cirrhosis[4]. Adjust dose if patient is on resmetirom

Figure 3. Interventions to control cardiometabolic risk factors.

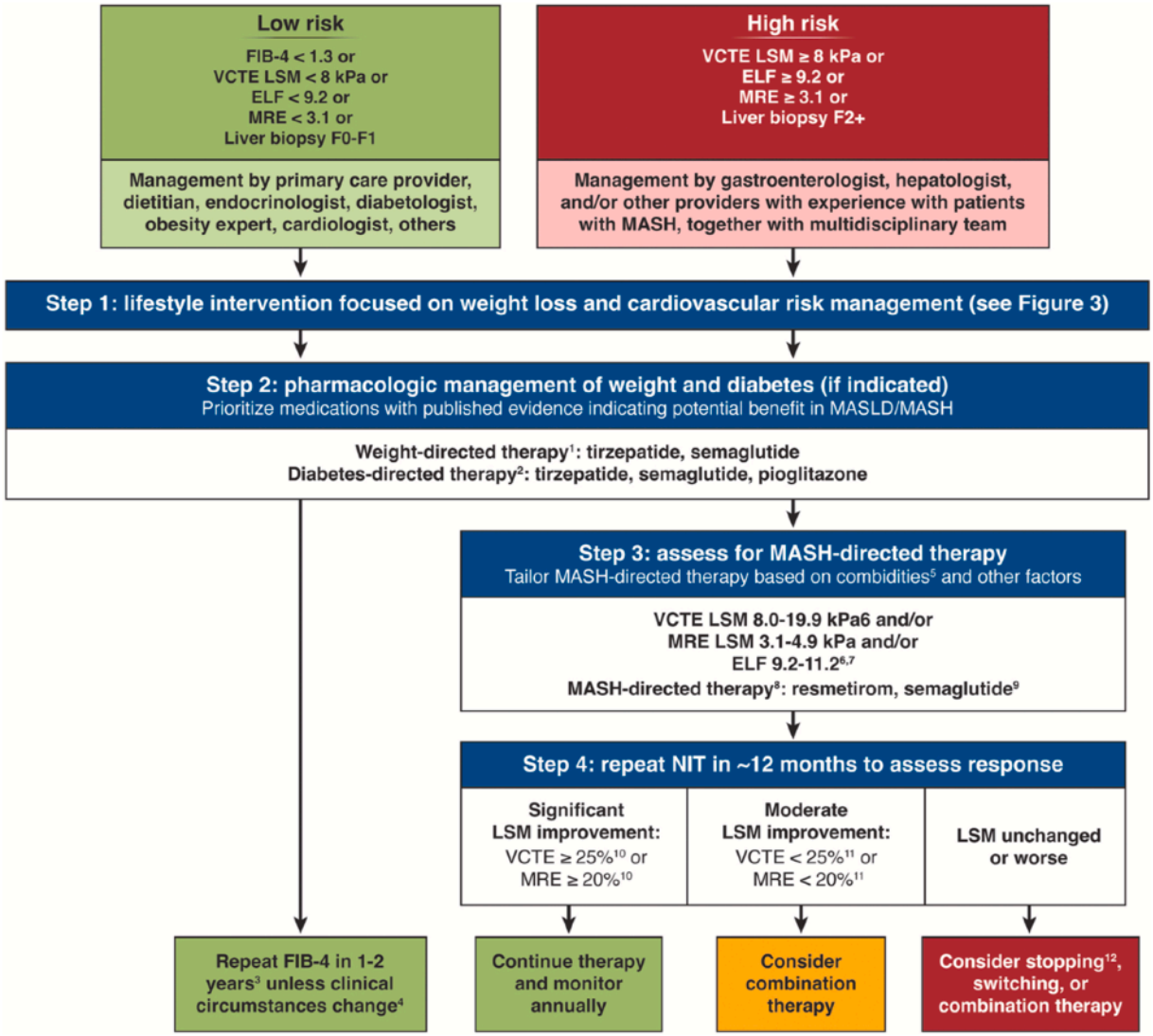


Figure 4. Pharmacologic management of MASLD/MASH.

Lifestyle Intervention:

- **Mediterranean diet** is based on daily consumption of vegetables and fresh fruit, unsweetened cereals rich in fiber, nuts, fish or white meat, olive oil, and minimal use of simple sugars and red (or processed) meats
- **Avoid Alcohol** - 0–9 g of daily non-wine alcohol use doubles the risk for adverse liver-related outcomes compared with lifetime abstainers
- **Exercise** - 150–300 minutes of moderate- intensity exercise or 75–150 minutes of vigorous-intensity exercise per week
- **Weight loss** recommended for cardiometabolic benefit and reversal of steatosis. Greater weight loss is often associated with more benefit, such as reversal of steatohepatitis (usually with weight loss ≥7%) or fibrosis (usually with weight loss ≥10%). Consider weight loss meds or bariatric surgery.

		Resmetirom	Semaglutide	Tirzepatide	Piogliatzone
Indications		MASH with F2–F3	MASH with F2–F3[1] Diabetes[1] Obesity or overweight with at least one weight-related comorbidity[1] ASCVD and overweight or obesity (or diabetes)[1] Diabetes with CKD[1]	Diabetes[2] Obesity or overweight with at least one weight-related comorbidity[2] Moderate to severe obstructive sleep apnea and obesity[2]	Diabetes
Mechanism of action		THR-β agonist	GLP-1RA	GLP-1/GIP RA	PPAR-γ agonist
Dose		< 100 kg: 80 mg daily ≥ 100 kg: 100 mg daily On CYP2C8 inh.: 60 mg daily	Start dose[3]: 0.25 mg SQ QW (Increase dose every 4 weeks as tolerated; i.e. 0.5, 1.0, 1.7, and 2.4 mg SQ weekly)	Start dose: 2.5 mg SQ QW (Increase dose every 4 weeks as tolerated, i.e. 5, 7.5, 10, 12.5, and 15 mg SQ weekly)	15–30 mg daily (Can be increased to 45 mg daily if needed)
EFFECTS	**Weight**	↔	↓↓	↓↓↓	↑
	Glycemia	↔	↓↓	↓↓↓	↓
	LDL-C	↓↓	↓	↓	↔
	Liver steatosis	+ (phase 3)	+ (phase 3)	+ (phase 2)	+ (phase 3)
	Liver fibrosis	+ (phase 3)	+ (phase 3)	+ (phase 2)	↔
	CV outcomes	Not studied	+ (phase 3)	+ (phase 3)[4]	+ (phase 3)
	CKD outcomes	Not studied	+ (phase 3)	Not studied[5]	Not studied[5]
	OSA severity	Not studied	Not studied[5]	+ (phase 3)	Not studied
	HFpEF severity	Not studied	+ (phase 3)	+ (phase 3)	–
	Other cardiometabolic considerations	↓ TG; ↓ Lp(a); ↑ SHBG with consequent increase in total testosterone and estradiol levels[6]	↓ TG; ↑ HDL-C; ↓ Blood pressure Rapid weight loss can lead to sarcopenia	↓ TG; ↑ HDL-C; ↓ Blood pressure Rapid weight loss can lead to sarcopenia	↓ TG; ↑ HDL-C Increases risk of bone fractures and anemia Change in fat distribution favorable

Key:

Weight:
- ↓ -2% to -3%
- ↓↓ -9% to -13%
- ↓↓↓ -14% to -19%
- ↑ +2% to +4%
- ↔ No significant change

Glycemia:
- ↓ -0.6% to -1.0%
- ↓↓ -1.2% to -1.9%
- ↓↓↓ -1.9% to -2.4%
- ↔ No significant change

LDL-C:
- ↓ -1% to -7%
- ↓↓ -13% to -20%
- ↔ No significant change

Data indicators:
- \+ Positive results in large RCT
- – Worsening of symptoms in RCT
- ↔ No significant change

Figure 5. Drugs with beneficial effects on MASLD/MASH and their cardiometabolic impact.