# NAFLD-associated metabolic risks in obesity and diabetes – Insights from clinical practice

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NAFLD occurs concomitantly with several end-organ diseases and is associated with metabolic disorders and increased cardiometabolic risk factors[1]

## Clinical evidence supporting metabolic risks associated with NAFLD

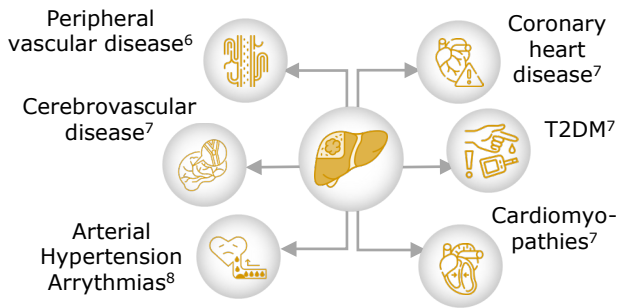
**Decreased survival** in patients with NAFLD/NASH vs reference population primarily due to CVD (p=0.04) and liver failure (p=0.04)[2]

**Cardiac-specific mortality rate** (4.2/1000 person-years) **was higher** than liver specific mortality rate (0.92/1000 person-years) amongst patients with NAFLD[4]

**Higher risk** of **CVD events** (fatal or non-fatal or both; HR=1.64; 95% CI 1.26–2.16) associated with NAFLD[3]

**Advanced fibrosis was predictor** of incident CVD vs non-advanced fibrosis (HR=2.86; 95% CI 1.36–6.04) in patients with MAFLD[5]

## NAFLD-associated metabolic comorbidities




## NAFLD is a multi-system disorder[9]

**Diet-induced obesity**

· Insulin resistance · Metabolic stress · Inflammation & fibrosis

Arteries (HTN, CVD, CAD) · Heart (Heart failure) · Liver (MAFLD) · Pancreas (T2DM) · Kidney (CKD)

## NAFLD may precede and promote T2DM[10]

T2DM promotes:
- Risk of NASH ⬆
- Risk of cirrhosis ⬆
- Risk of HCC ⬆

2.2-fold increase in risk

**T2DM** ⇄ **NAFLD**

2 to 6-fold increase in risk (fibrosis)

NAFLD promotes:
- Risk of T2DM ⬆
- Risk of CVD ⬆
- Risk of AD ⬆

## Monitoring metabolic risk factors in NAFLD

**Arterial hyper-tension?** ≥130/85 mmHg

**AD?** Non-HDL cholesterol >130 mg/dL; Apo B >120 mg/dL

**Prediabetes/ Diabetes?** HbA1c >6.4%; FBS>100 mg/dL; >140 mg/dL at 2 hours during OGTT

**Metabolic syndrome?** (2/3 criteria) Levels of TG to HDL-cholesterol ratio >3

## Management of cardiometabolic risk factors[11]

### Control obesity

**Weight loss**:
- Lifestyle (diet & physical activity)
- GLP-1RA & SGLT2i
- Bariatric surgery

### Reduce CVD risk

**Treat T2DM & CV risk factors**:
- GLP-1RA & SGLT2i
- Statins, ACEi/sartans
- Smoking cessation
- Antiplatelet drugs

### Target NASH

**Liver treatment**:
- Vitamin E
- Pioglitazone
- Semaglutide

- NAFLD increases risk of T2DM and CVD due to IR and atherogenic lipoprotein phenotype
- NAFLD associated metabolic risk factors and subclinical stages of atherosclerosis should be actively monitored
- Statins, anti-diabetic drugs and weight loss interventions are of proven efficacy in decreasing the metabolic risk factors of NAFLD

ACEi, angiotensin-converting enzyme inhibitor; AD, atherogenic dyslipidemia; Apo B, apolipoprotein; CAD, coronary artery disease; CI, confidence interval; CKD, chronic kidney disease; CVD, cardiovascular disease; FBS, fasting blood sugar; FLI, fatty liver index; GLP-1RA, glucagon like peptide-1 receptor agonist; HbA1c, hemoglobin A1c; HCC, hepatocellular carcinoma; HDL, high density lipoprotein; HR, hazard ratio; HTN, hypertension; IR, insulin resistance; MAFLD, metabolic-associated liver disease; NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis; OGTT, oral glucose tolerance testing; SGLT2i; sodium-glucose co-transporter-2 inhibitor; T2DM, Type-2 diabetes mellitus; TG, triglyceride.

1. Sanyal A. NASH in 2021: The Multi-System disease, webinar; 2. Ekstedt M, et al. Hepatology 2006;44:865–73; 3. Younossi ZM, et al. Hepatology 2023;77:1335–47; 4. Targher G, et al. J Hepatol 2016;65:589–600; 5. Henson JB, et al. Aliment Pharmacol Ther 2020;51:728–736; 6. Zou Y, et al. Intern Med J 2017;47:1147–1153; 7. Oikonomou D, et al. Eur J Gastroenterol Hepatol 2018;30:979–985; 8. Wong CR, et al. Clin Liver Dis 2018;12:39–44; 9. Friedman SL, et al. Nat Med 2018;24:908; 10. Budd J, et al. Current Diabetes Reports 2020;20:59; 11. Manikat R and Nguyen MH Clin Mol Hepatol 2023;29(Suppl):s86–s102.

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