Disease Progression Overview of Metabolic Dysfunction-Associated Steatohepatitis (MASH)

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STAGE

Normal Liver

Steatotic Liver

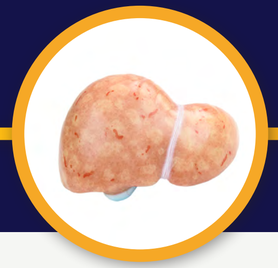
MASH

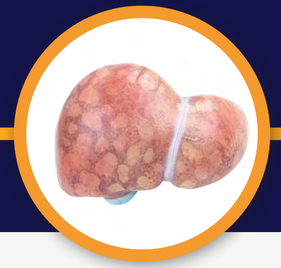
MASH with Fibrosis

Cirrhosis

Major Adverse Liver Outcomes (MALO)

THE LIVER AT EACH STAGE





OVERVIEW

The liver is located in the upper right of the abdominal cavity, is a dark reddish-brown colour and weighs about 1500 grams.[1]

The liver regulates many metabolite levels in the blood. Functions include production of bile, production of cholesterol, glucose homeostasis and production of certain proteins for blood plasma.[1]

What is the process of MASH progression?

The presence of excess triglycerides in the liver is called hepatic steatosis.[2-4]

MASLD

MASLD is defined as the presence of hepatic steatosis in conjunction with at least one cardiometabolic risk factor and no other discernible cause.[2-4]

38% of all adults and 7–14% of children and adolescents currently have MASLD worldwide.[5]

Some patients progress from simple steatosis to **MASH,** a condition characterised by histological features of liver injury, hepatocellular ballooning and lobular inflammation in the presence of hepatic steatosis, which can lead to liver fibrosis.[3,6]

Why some patients progress from simple steatosis to **MASH** with inflammation and increased fibrogenesis is complex and not fully understood.[6]

Prevalent MASH cases are forecasted to increase 45%, from 12.6 million (2015) to 18.2 million (2030) in the EU5.[7]

Fibrosis

As fibrosis accumulates, the risk of all-cause and liver-related mortality increases substantially.[8]

A study with a mean follow-up period of 20 years found that decompensated liver disease occurred in:

- **3.7%** of patients with fibrosis stage (F) 0
- **4.3%** in patients with F1
- **8.7%** in patients with F2
- **12.1%** in patients with F3
- **45%** of patients with cirrhosis (compared with **1.8%** in controls)[9]

Cirrhosis

Cirrhosis is the most important risk factor for progression to liver transplant, development of HCC, and death.[6]

Transition to cirrhosis involves inflammatory, hormonal, and structural changes that lead to portal hypertension.[6]

A meta-analysis found that cirrhosis was associated with an approximately:

- **13x** higher rate of liver-related events
- **11x** higher rate of liver-related mortality
- **4x** higher rate of all-cause mortality (compared with patients without fibrosis)[10]

MASH can progress to MASH with fibrosis, cirrhosis, or liver cancer and may ultimately lead to liver transplantation or death.[11]

MALO

Liver cancer remains a global health challenge, with an estimated incidence of >1 million cases by 2025.[12]

MASLD is becoming the second leading cause of HCC behind alcohol-related liver disease.[13]

Progression from compensated cirrhosis to decompensation events, liver transplant, or death may be rapid compared with progression at earlier stages of MASH.[14]

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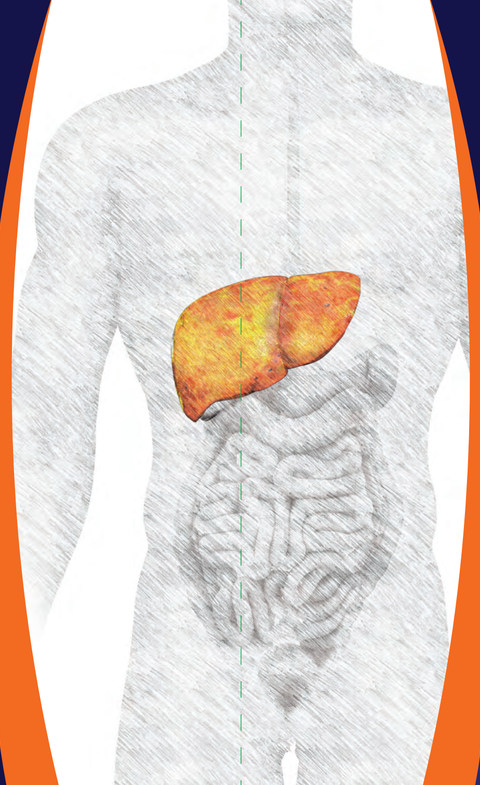

Disease Progression Overview of Metabolic Dysfunction-Associated Steatohepatitis (MASH)

Progression of MASH from steatosis to cirrhosis and MALO

The natural history of MASLD is complex and variable. A minority of patients develop inflammation and risk progressive fibrosis that can result in cirrhosis. Progression to cirrhosis occurs in 3–5% of patients and it takes 7 years on average to progress by 1 stage of fibrosis.[6,15] A subset of patients can progress to cirrhosis in as little as 3 years from the date of diagnosis.[16]

Healthy Liver	Steatotic Liver	MASH	MASH & Scarring	Cirrhosis	MALO
Normal amount of fat	Fat buildup	Toxic fat buildup and inflamation	Toxic fat buildup, inflamation, and scarring or fibrosis	Severe scarring or fibrosis and possible permanent damage	Loss of liver function, cancer or the need for transplantation

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Optimise patient outcomes
Early risk stratification for advanced fibrosis in patients with MASLD/MASH is critical for optimisation of patient outcomes.[3]

EU5, France, Germany, Italy, Spain, United Kingdom; **F**, fibrosis stage; **HCC**, hepatocellular carcinoma; **MALO**, major adverse liver outcomes; **MASLD**, metabolic dysfunction-associated steatotic liver disease; **MASH**, metabolic dysfunction-associated steatohepatitis.

1. Hopkins Medicine: https://www.hopkinsmedicine.org/health/conditions-and-diseases/liver-anatomy-and-functions. Accessed January 2025; **2.** Rinella et al. J Hepatol. 2023;79:1542-1556; **3.** Tacke et al. J Hepatol. 2024;81:492-542; **4.** Qadri S, Yki-Järvinen. Diabetologia. 2024;67:961-973; **5.** Younossi et al. Clin Mol Hepatol. 2024;doi:10.3350/cmh.2024.0431; **6.** Hagström et al. Lancet Gastroenterol Hepatol. 2024;9:944-56; **7.** Estes C. et al. J Hepatol. 2018;69(4):896-904; **8.** Ng et al. Clin Gastro Hep. 2024;21:931-939; **9.** Hagström et al. J Hepatol. 2017;67:1265-1273; **10.** Taylor. Gastroenterology. 2020;158:1611-1625; **11.** Diehl, Day. N Engl J Med. 2017;377:3063-3072; **12.** Llovet et al. Nat Rev Dis Primers. 2021;7:6; **13.** Qiu et al. JAMA Netw Open. 2024;7:e2445525; **14.** Allen et al. J Hepatol. 2022;77(5):1237-1245; **15.** Singh et al. Clin Gastroenterol Hepatol. 2015;13(4):643-e40; **16.** Schattenberg et al. Gastro Hep Adv. 2024;3(1)191-108.

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