

# Metabolic syndrome & non alcoholic fatty liver disease

## Abstract

Metabolic syndrome can be described as a batch of lipid and non-lipid risk factors for coronary hearth disease (CHD) of metabolic origin. A diagnosis of metabolic syndrome can be made when three or more of risk determinants are present. Risk determinants are consistent with abdominal obesity, atherogenic dyslipidemia (elevated triglyceride, small low density lipoprotein (LDL) particles, low HDL cholesterol), raised blood pressure, insulin resistance (with or without glucose intolerance) and prothrombotic and proinflammatory states. Metabolic syndrome is closely linked to a generalized metabolic disorder called insulin resistance in which the normal actions of insulin are impaired.

We now know that non-alcoholic fatty liver disease (NAFLD) is the hepatic manifestation of metabolic syndrome and might be an independent risk factor for coronary hearth disease. Metabolic Syndrome and its component are risk factors for development of liver fibrosis and advanced- stage liver disease. Non-alcoholic steatohepatitis (NASH) is an intermediate lesion characterized by hepatocytes injury death and inflammation. Patient with confirmed NASH, fibrosis or both can be managed with diet and intensive life style changes plus clinical management of hyperlipemia and type 2 diabetes. Obeticholic acid showed also promising preliminary results. NAFLD who progress to decompensate cirrhosis and HCC are candidate for liver transplantation.

**Keywords:** metabolic syndrome, non-alcoholic fatty liver disease, non alcoholic steatohepatitis, liver fibrosis, ketogenic diet, liver transplantation

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**Abbreviations:** NAFLD, non-alcoholic fatty liver disease; NASH, non alcoholic steatohepatitis; LDL, low density lipoprotein; CHD, coronary heart disease; PDFF, proton density fat fraction; MRE, magnetic resonance elastography; TE, transient elastography; ROS, reactive oxygen species

## Introduction

Prevalence of NAFLD is 20%- 30% in Western adults and 90% in extreme obesity; NAFLD might be an independent risk factor for CHD.<sup>1</sup> Prevalence of NASH is 2-3% in the general population and 37% in the morbidly obese.<sup>2</sup>

NAFLD is usually discovered quite incidentally for unexpected elevation of liver enzyme or "bright" liver at ultrasonography, in the absence of any clinical symptom of liver disease, but in the long term the condition may progress to advanced cirrhosis carrying an high risk of all cause and liver related mortality.<sup>3</sup> The accumulation of fat within hepatocytes stimulates compensatory mechanism to eliminate the excess lipid, these include: Induction of various mitochondrial microsomal and peroxisomal enzymes systems that oxidize fatty acids. Fatty acid oxidation generates reactive oxygen species (ROS) generating oxidative stress. Fatty liver causes insulin resistance because factors that primarily promote lipid accumulation in hepatocytes cause hepatocytes to become resistant to certain effects of insulin by stress activated protein kinases. Type 2 diabetes develops and might be an indicator of more serious hepatic inflammation. This helps to explain clinical association between type 2 diabetes and histologically advanced stages of NAFLD, i.e., NASH and cirrhosis.<sup>4</sup> The gold standard for diagnosis of NASH is liver biopsy, however

new interesting data are emerging in favour of magnetic resonance elastography (MRE) and proton density fat fraction (PDFF) and transient elastography (TE).<sup>5</sup>

Patients with confirmed NASH, fibrosis, or both can be managed with intensive life style modifications including weight loss and dietary changes. There is no consensus as to what diet or lifestyle approach is the right one for NAFLD and NASH patients, preliminary data on ketogenic diet are promising as it can reverse insulin resistance.<sup>6,7</sup> A recent phase II trial of treatment of NASH with obeticholic acid (FLINT trial, NCT01265498) has shown an improvement in liver histology including fibrosis over a period of 72 weeks.<sup>8</sup> This treatment might have the potential to change prognosis of this disease.

## Conclusion

Metabolic syndrome & NAFLD is a complex and potentially progressive condition, diet and life style changes are currently highly recommended. Associated conditions such as hyperlipemia and type 2 diabetes must be adequately managed. In addition patients with biopsy proved NASH might be candidate for clinical trials of promising drugs in development.

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## Conflicts of interest

The authors declare that there are no conflicts of interest.

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