



NAFLD and metabolic comorbidities – current understanding and perspectives



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Flash for webinar (~20 mins)

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Risk stratification

The development and progression of NAFLD is associated with a number of risk factors, including age, gender, BMI, ethnicity and comorbidities (e.g. type 2 diabetes, hypercholesterolemia and hypertension).¹ Personalization through clinical risk stratification is possible, for example with diabetes as a predictor of advanced fibrosis.²

In particular, there is a strong relationship between metabolic comorbidities and NAFLD severity – for patients with mild NAFLD, the odds ratio of having metabolic burden is 3.64 (95% CI: 1.5–8.8) vs no NAFLD; and for patients with moderate-to-severe NAFLD, the odds ratio of having metabolic burden is 9.4 (95% CI: 3.5–25.0) vs no NAFLD.³ The liver interacts with other organs in the context of metabolically-ill patients and data from population-based analyses in Germany suggest that NAFLD also contributes to extrahepatic diseases.⁴

Disease progression and importance of early diagnosis

NAFLD is a multifactorial, progressive disease and, as such, early diagnosis will better target treatment to those who are most likely to benefit from intervention. A meta-analysis of 13 studies including 4428 patients with liver histology, 65% of whom had NASH, found that more advanced fibrosis was associated with a higher risk of all-cause mortality.⁵

The pathogenesis of hepatic steatosis involves disruption of metabolic pathways – the DNL pathway is promoted and β -oxidation is impaired.^{6,7} Further to this, there is a correlation between steatosis progression and metabolic comorbidities. Steatosis, as an early change, may be a risk factor not only for NAFLD progression but also for other cardiometabolic disorders.³

Screening and diagnostics

According to clinical guidance, screening by ultrasound is recommended in high-risk groups.⁸ Since transaminases are not elevated in 80% of NAFLD patients,⁹ generally enzyme levels are not recommended as the screening modality as they do not reflect steatosis and NAFLD severity/stage.¹⁰ Importantly, recent guidance from the ADA advises that people with T2DM or pre-diabetes and elevated liver enzymes or fatty liver on ultrasound should be evaluated for the presence of NASH and liver fibrosis.¹¹

ADA: American Diabetes Association; **AST:** aspartate transaminase; **AUROC:** area under the receiver operating characteristic curve; **BMI:** body mass index; **CAP:** controlled attenuation parameter; **CI:** confidence interval; **DNL:** *de novo* lipogenesis; **EASL:** European Association for the Study of the Liver; **LSM:** liver stiffness measurement; **NAFLD:** non-alcoholic fatty liver disease; **NASH:** non-alcoholic steatohepatitis; **T2DM:** type 2 diabetes.

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Further to the ADA recommendations, EASL guidelines provide a flow-chart for diagnosis, indicating that metabolic work-up must carefully assess all components of the metabolic syndrome.¹² In addition, they also advise that the presence of obesity/T2DM or raised liver enzymes in patients with metabolic risk factors should prompt non-invasive screening to predict steatosis, NASH and fibrosis.¹²

While ultrasound represents the first-line imaging technique for diagnosing steatosis,¹³ additional non-invasive techniques are available, such as the Fatty liver index (FLI); NAFLD liver fat score (NAFLD-LFS) and hepatic steatosis index (HIS).¹⁴ The FibroScan-AST (FAST) score also provides an efficient way of non-invasively identifying patients at risk of NASH progression.¹⁵ This is a predictive model combining LSM, CAP and AST, and in a prospective study its predictive performance indicated an AUROC of 0.80 (95% CI: 0.76–0.85) across the validation cohorts tested (N=350).¹⁵

In the future, artificial intelligence may also be used for diagnosis NAFLD/NASH, as it has demonstrated capability of identifying 14 parameters which discriminate NASH from non-NASH.¹⁶

References

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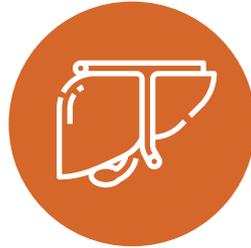
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Learning objectives:



Explore the relationship between metabolic comorbidities, such as type 2 diabetes and obesity, and NAFLD severity.

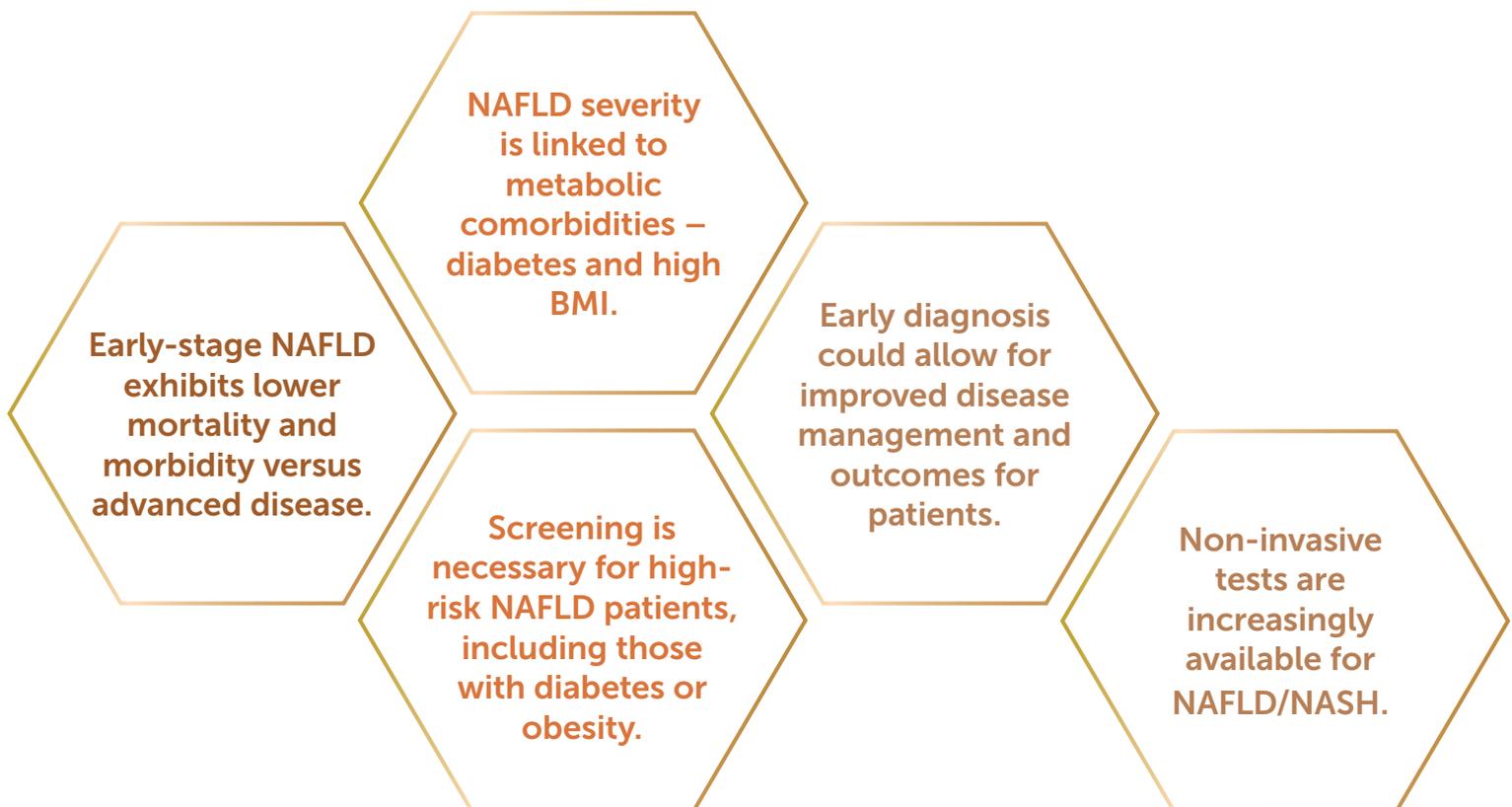


Understand the importance of early diagnosis of NAFLD and consider how this may impact patient outcomes.



Review the available diagnostic techniques in screening and staging of NAFLD/NASH.

Main take aways:



The logo features a stylized liver shape with a hexagonal pattern, transitioning from orange to red. The text '1st GLOBAL LIVER HEALTH FORUM' is overlaid in white.

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