Non-Alcoholic Fatty Liver Disease
Epidemiology, Clinical Course, Investigation, and Treatment
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**Difficult-to-Understand Point**
This very well researched review article lists “states of hunger” as one of the possible causes of non-alcoholic fatty liver disease. In this point, I do not fully understand the complex relationships involved. This phenomenon is also incomprehensible to me from a pathophysiological perspective. The opposite would be quite plausible. I think that many colleagues find it difficult to understand this point; therefore, I would like to ask the authors to briefly explain it.

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**REFERENCES**

**Conflict of interest statement**
The author declares that no conflict of interest exists.

**Benefit: “Therapeutic Indication”**
Liver biopsy as the gold standard for diagnosis should only be performed if a therapeutic indication can be derived from it. Ultrasonography as a non-invasive screening method loses accuracy in early stages of the disease and depends very much on the skills and experiences of the examiner. Therefore, we prefer the “Fatty Liver Index” (FLI) for screening. In their publications (1, 2), Bedogni et al. described a simple and accurate indicator which calculates the FLI using an algorithm based on triglycerides (mg/dL), BMI (kg/m²), gamma-GT (U/L), and waist circumference (cm). The FLI can vary between 0 and 100. An FLI <30 (negative likelihood ratio = 0.2) rules out fatty liver with a high degree of certainty, while an FLI >60 (positive likelihood ratio = 4.3) rules in fatty liver.

The significance of the FLI was confirmed in subsequent studies. An FLI >60 is indicative of fatty liver with 78% probability, while an FLI of 20 or less rules out fatty liver with 91% probability. Not only can the FLI be used for screening purposes, it is also an appropriate method for patient monitoring after dietary interventions. A multivariate adjusted analysis of data from more than 3000 patients undergoing coronary angiography (3) demonstrated for the group of patients with an FLI above 75.6 a highly statistically significant increase in cardiovascular mortality, non-cardiovascular mortality (infections, cancer,
liver disease), and a significantly increased overall mortality.

Since “doctors in private practice have an important steering function”, the FLI is ideally suited for both screening and follow-up, as it is easy to use and cost-effective.

REFERENCES

In Reply

W. Hofmann raises the question of the links between non-alcoholic fatty liver disease (NAFLD) and states of hunger, mentioned in the review as a possible cause of the disease. Here, we would like to point out that in the corresponding table states of hunger are not listed as a cause of NAFLD, but as a cause of secondary hepatic steatosis—this difference is important. Two exemplary conditions are kwashiorkor and marasmus which may be associated with fatty liver, besides muscle wasting. The most likely underlying pathomechanisms are proteolysis of the muscles as well as lipolysis which may lead to fatty liver as the result of an increased production of free fatty acids and a lack of lipoproteins; this was experimentally demonstrated for states of hunger (1). Both M. Hofmeister and H. Walle mention in their letters the “Fatty Liver Index” (2) which can identify patients with fatty liver with an accuracy of 0.84 based on the parameters body mass index, waist circumference, triglycerides, and gamma-glutamyl transpeptidase. Ultimately, various non-invasive scores are available which can be used to identify high-risk patients. We think that the “NAFLD Fibrosis Score” mentioned in our article, which was developed by the North American Clinical Research Network (CRN) working group (3), is perfectly suited for this purpose. This score is also based on few routine parameters, viz. age, body mass index, AST (GOT), ALT (GPT), platelet count, and albumin, and can be calculated online; at the same time, the interpretation of the result is provided. This score can rule out advanced fibrosis with a negative predictive value between 0.88 and 0.93 and diagnose advanced fibrosis with a positive predictive value between 0.82 and 0.90; with this, 75% of all liver biopsies could be avoided in the underlying study. The “Fatty Liver Index” has a negative likelihood ratio of 0.2 for ruling out hepatic steatosis for values <30 and a positive likelihood ratio of 4.3 for values ≥60 (2). However, there is the important difference that the “NAFLD Fibrosis Score” provides information about advanced fibrosis, while the “Fatty Liver Index” provides information about hepatic steatosis. A recently published study has demonstrated the superiority of the “NAFLD Fibrosis Score” over other non-invasive scores, such as the ratio of AST (GOT) and platelet count, the FIB-4 score, or the BARD score (4).

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