Non-alcoholic fatty liver disease (NAFLD) and current diagnostic approach and spa treatment options

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Bologna 3 -6 .11. 2022

Background

- Non-alcoholic fatty liver disease (NAFLD) is
  - The most common cause of chronic liver disease in Western countries
  - The most frequent indication for liver transplantation by 2030.
- ‚The prevalence
  - In the general population is about 25%,
  - In patients with type II diabetes up to 55%.
- NAFLD is not only confined to liver-related morbidity and mortality, but there is now growing evidence that NAFLD is a **multisystem disease**, affecting extra-hepatic organs and regulatory pathways.
- NAFLD increases risk cardiovascular and chronic kidney disease.

Non-alcoholic fatty liver disease (NAFLD)

Characterized by:

- Steatosis,
- Liver inflammation
- Hepatocellular injury
- Progressive fibrosis

NASH is common in patients with obesity, insulin resistance and T2DM and NASH increases the risk of HCC

Despite the progress made, there are currently no effective treatments for NAFLD.

Liver fibrosis

Causes of liver fibrosis

- Chronic HCV infection
- Alcohol abuse
- Nonalcoholic steatohepatitis

Liver fibrosis results from chronic damage to the liver in conjunction with the accumulation of ECM proteins, which is a characteristic of most types of chronic liver diseases .

Liver fibrosis to cirrhosis

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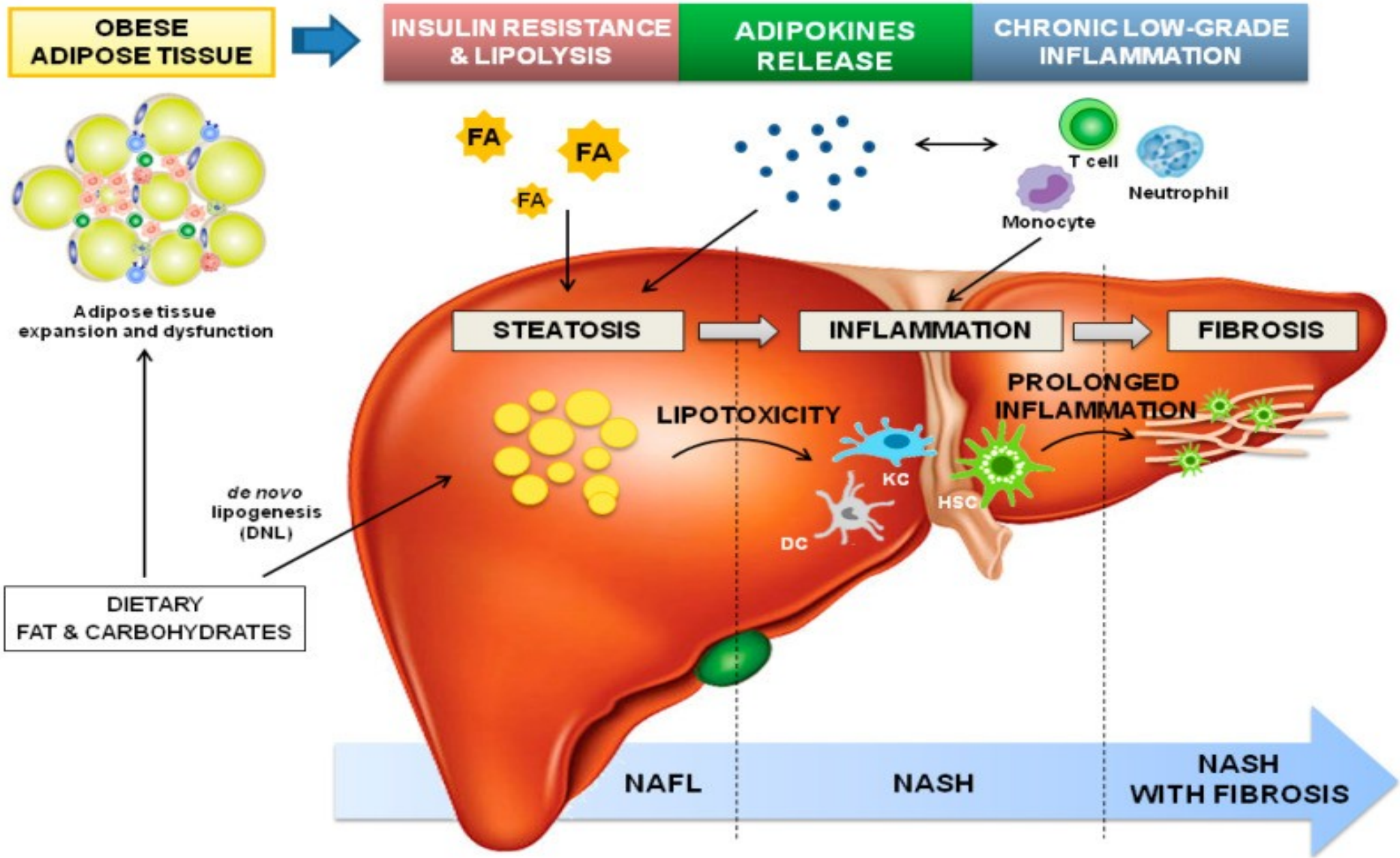
The accumulation of ECM proteins distorts the hepatic architecture by forming a fibrous scar, and the subsequent development of nodules of regenerating hepatocytes defines cirrhosis.

<u>Cirrhosis produces</u>

- hepatocellular dysfunction
- increased intrahepatic resistance to blood flow
- hepatic insufficiency
- portal hypertension, respectively


OBESE ADIPOSE TISSUE
INSULIN RESISTANCE & LIPOLYSIS
ADIPOKINES RELEASE
CHRONIC LOW-GRADE INFLAMMATION
FA
FA
FA
T cell
Neutrophil
Monocyte
Adipose tissue expansion and dysfunction
STEATOSIS
INFLAMMATION
FIBROSIS
PROLONGED INFLAMMATION
LIPOTOXICITY
KC
HSC
DC
de novo lipogenesis (DNL)
DIETARY FAT & CARBOHYDRATES
NAFL
NASH
NASH WITH FIBROSIS

NAFLD diagnostic methods

- When assessing a patient with nonalcoholic fatty liver disease (NAFLD), the key histological features of interest include the degree of steatosis, necroinflammation and fibrosis.
- MRI-estimated proton density fat fraction is the most accurate test to quantify hepatic steatosis and can be considered the gold standard.
- Magnetic resonance elastography is the most accurate fibrosis test, yet its use is limited by cost and availability.
- Transient elastography also enables simultaneous assessment of hepatic steatosis and fibrosis, albeit with lower accuracy and success rates than MRI-based methods.

Nonalcoholic fatty liver disease (NAFLD)

Current status:

- With an increasing number of patients developing NASH-related end-stage liver disease and pharmacological treatments on the horizon, there is a **pressing need to develop NAFLD and NASH biomarkers for prognostication, selection of patients for treatment and monitoring.**
- This requirement is particularly true as liver biopsy utility is limited by its invasive nature, poor patient acceptability and sampling variability.

NAFLD
Aim of our study and perspective for future

- Finding potential biomarkers for different features of NAFLD, namely, steatosis, necroinflammation and fibrosis.
- For each biomarker, we evaluate its accuracy, reproducibility, responsiveness, feasibility and limitations.
- We will correlate biochemical, imaging and genetic biomarkers and we select the optimal markers pro follow-up, prognosis of the disease, prediction of the effect of treatment .

Aim off study II
Spa treatment and longitudinal monitoring

Three groups of monitored persons:

1. **Pathological group -** three weeks of spa treatment - and continuous monitoring the course of treatment minimally every three months
2. **Pathological group -** standard treatment - and detailed examination after 1 year
3. **Healthy people** - initial examination and control after one year

Spa treatment and its components

- Education
- Diet modification
- Drinking cures
- Defined spa procedures
- Physical activity monitoring

Planned laboratory examinations

- Parameters of **glucose metabolism** – glycaemia, C-peptide (inzulin)
- Parameters of **lipid metabolism** - lipidogram, adiponectin, leptin
- **Fibrosis** parameters – procollagen I a II, hyaluronic acid, laminin, MMP and TIMP
- Parameters of **inflammation** - CRP, IL -6, TNF
- Parameters of **bone metabolism** - osteopontin , osteoprotegin
- **Tumor markers** - Pivka-II, AFP and chromogranin

Spa treatment - control examination

Control examination:

- Elastography at the beginning and end of the stay
- Laboratory examination at the beginning and end of the stay
- Special standardized questionnaire at the beginning and end of the stay

Conclusion

- **Expected result**:
- Standardization of laboratory methods
  - Creating program for NAFLD
    - A screening
    - A real monitoring system for follow up
  - Gain new knowledge
    - About etiopathogenesis of NAFLD
    - For optimalization and montoring treatment

Thank you for your attention

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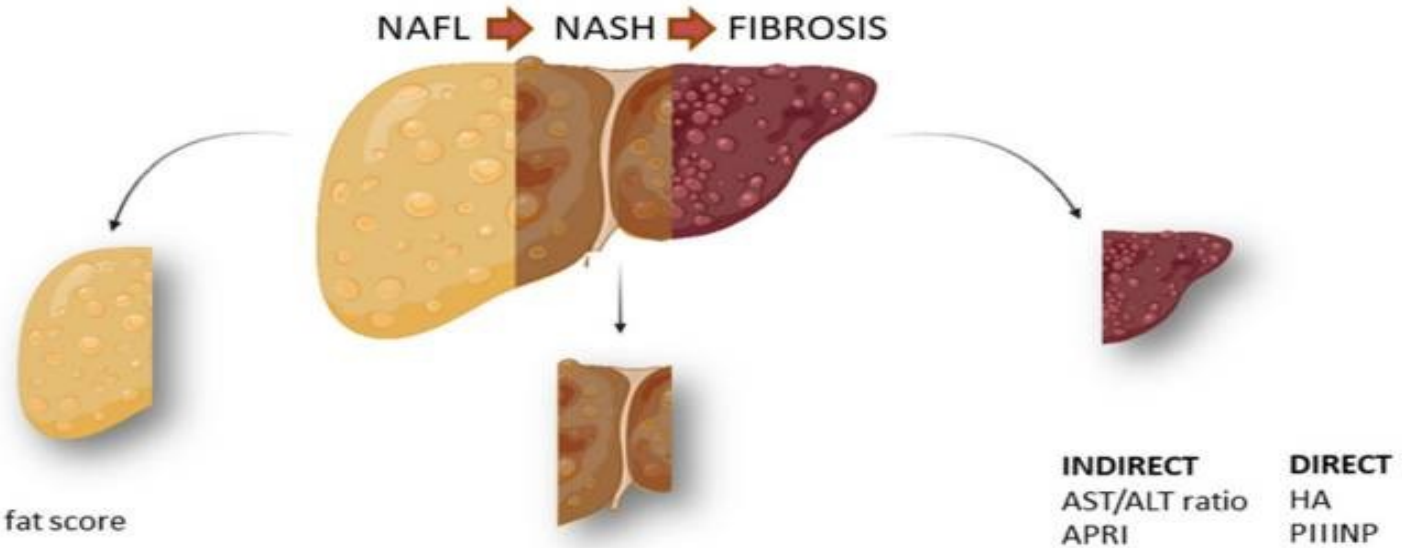
FAKULTNÍ NEMOCNICE PLZEŇ

Diagnosis NAFLD.



PANELS
FLI
HSI
NAFLD liver fat score
SteatoTest

IMAGING
Elastografy
CAP
MRI-PDFF

-OMICS
Proteomics
Lipidomics
Metabolomics

NON CODING RNAs
miRNAs
lncRNAs

APOPTOSIS AND INFLAMMATION
C Reactive Protein, TNF, IL-6, IL-1, CXCL10, CK-18

IMAGING
Paramagnetic iron oxide MRI
Phosphorus MRS

-OMICS
Lipidomics
Metabolomics

NON CODING RNAs
miRNAs
lncRNAs

INDIRECT
AST/ALT ratio
APRI
BARD score
FIB-4
NFS

DIRECT
HA
PIIINP
Pro-C3
TIMP-1
Laminin

IMAGING
Fibroscan
Elastografy with ARFI
MRE

NON CODING RNAs
miRNAs
lncRNAs

miR-122, miR-192, miR-16, miR-21, miR-27b, miR-197, miR-34a, miR-375, miR-451, miR-1290, miR-885, miR-181d, miR-99a, miR-146b, miR-29, miR-1296, miR-132, miR-135, miR-19a, miR-19b, miR-125, miR-223, lncRNA ARSR.

miR-122, miR-192, miR-16, miR-21, miR-27b, miR-197, miR-34a, miR-375, miR-30c, miR-22, lncRNA LeXis, lncRNA RP11-128N14.5.

miR-122, miR-192, miR-16, miR-21, miR-27b, miR-197, miR-30c, lncRNA APTR, lncRNA RP11- 128N14.5, lncRNA TGFB2/TGFB2-OT1, lncRNA GAS5.