LIFESTYLE FOR THE TREATMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE

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Physical activity

- Aerobic & Resistance activity independently:
  - Reduce liver fat
  - NASH and fibrosis – little evidence

Dietary composition

- Beneficial without weight loss
- The Mediterranean diet is the recommended diet by the EASL–EASD–EASO NAFLD Guidelines
  
  *Journal of Hepatology 2016*

Weight reduction

- Consistently beneficial
  - Steatosis ≥ 5%
  - NASH ≥ 7%
  - Fibrosis ≥ 10%
Added sugars pose dangers to health that justify controlling them like alcohol

Liver damage
Hyperuricemia
Hypertension
Insulin resistance
Heart disease
Habituation
Dyslipidemia
Obesity
Malnutrition
Diabetes
Pancreatitis

The toxic truth about sugar

Lustig RH., NATURE 2012
NAFLD independently related to sugared beverages consumption

Only cola sweetened with sugar increased liver fat
Fructose consumption independently associated with NASH in children

- 271 obese children with NAFLD
- Liver biopsy obtained

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio (95% CI)</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>Fructose, g/day</td>
<td>1.6 (1.3, 1.9)</td>
<td>0.001</td>
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<tr>
<td>Uric acid, mg/dl</td>
<td>2.5 (1.9, 2.8)</td>
<td>0.004</td>
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<tr>
<td>WC, cm</td>
<td>1.8 (1.1, 1.9)</td>
<td>0.03</td>
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<tr>
<td>HOMA-IR</td>
<td>3.2 (1.9, 5.7)</td>
<td>0.024</td>
</tr>
<tr>
<td>Triglyceride, mg/dl</td>
<td>1.2 (1.1, 1.6)</td>
<td>0.048</td>
</tr>
</tbody>
</table>

Adjusted association between fructose consumption and NASH (NAS≥5)

Mosca A., & Nobili V., Journal of Hepatology 2017
Short-term dietary fructose restriction reduces liver fat

- 9 days isocaloric fructose restriction
- Obese children (n=41) with habitual high sugar consumption

Changes in individual fat compartments

Schwarz JM., Gastroenterology 2017
Actual and estimated sugar content in a range of popular high-sugar beverages

Fruit juice has a similar sugar content as cola: 250 ml of juice - 26 g of sugar

Sugar content of fruit juices was underestimated by 48% on average

Nationally representative group of 2005 adults, living across the UK

Gill JM., Lancet Diabetes Endocrinol 2014
High red and processed meat consumption is positively associated with NAFLD and insulin resistance.

Volunteers 40-70 years old, who participated in screening study, n=789, 39% NAFLD (US)

Unhealthy cooking methods:
- grilled or broiled to well done level
- fried

↑ Temperature
↑ Cooking duration

Heterocyclic Amins (HCAs)

↑ Oxidative stress
↑ Inflammation

Insulin Resistance

NAFLD

Healthy Liver
The Mediterranean is superior to low fat diet in RCTs

High in
- Olive oil ≥4 tbsp/day
- Nuts handful/day
- Fish ≥3 /wk
- Legumes ≥3 /wk
- Fruits & Vegetables
- Fat - 40% /kcal, mostly MUFA and ω3 PUFA

Low in
- Soda drinks
- Sweets
- Red and processed meats
- Carbohydrate- 40% /kcal

Salas-Salvadó J., Ann Intern Med 2014
Ryan MC., Journal of Hepatology 2013
Nordmann AJ., The American Journal of Medicine 2011
Weight loss by lifestyle modification needed to reach NASH-resolution and Fibrosis regression

- Prospective study
- 293 NASH patients
- 52 weeks of lifestyle intervention (low fat diet + exercise + behavioral therapy)

% Weight loss

<table>
<thead>
<tr>
<th></th>
<th>5%</th>
<th>7%</th>
<th>10%</th>
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<tr>
<td>NASH-resolution</td>
<td>10%</td>
<td>26%</td>
<td>64%</td>
</tr>
<tr>
<td>FIBROSIS-regression</td>
<td>45%</td>
<td>38%</td>
<td>50%</td>
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<tr>
<td>STEATOSIS improvement</td>
<td>35%</td>
<td>65%</td>
<td>76%</td>
</tr>
</tbody>
</table>

Vilar-Gomez E., Gastroenterology 2015
Zelber-Sagi S., Journal of Hepatology 2017
<table>
<thead>
<tr>
<th>Association</th>
<th>Journal Year of publication</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>European Association for the Study of the Liver (EASL)</td>
<td>J of Hepatology 2016</td>
<td><strong>Total abstinence is mandatory in NASH-cirrhosis</strong></td>
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<tr>
<td>European Association for the Study of Diabetes (EASD)</td>
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<td>European Association for the Study of Obesity (EASO)</td>
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<tr>
<td>American Association for the Study of Liver Diseases (AASLD)</td>
<td>Hepatology 2017</td>
<td><strong>There are insufficient data to make recommendations to non-heavy consumption of alcohol</strong></td>
</tr>
<tr>
<td>The European Society for Clinical Nutrition and Metabolism (ESPEN)</td>
<td>Clinical Nutrition 2019</td>
<td><strong>NAFL/NASH patients shall be encouraged to abstain from alcohol in order reduce risk for comorbidity and to improve liver biochemistry and histology</strong></td>
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Aerobic vs. resistance exercise in NAFLD
Systematic review

Aerobic exercise
• Based on 13 protocols
  Effective protocol
    • 40 min/session, 3 times/week/12 weeks

Resistance exercise
• Based on 4 protocols
  Effective protocol
    • 45 min/session, 3 times/week/12 weeks

Resistance exercise - may be more feasible for patients with poor cardiorespiratory fitness

Hashida R., Journal of Hepatology 2017
Summary of lifestyle treatment options through the course of NAFLD

Healthy liver

Fatty liver

NASH/Fibrosis

Liver cancer

Hypocaloric or isocaloric - Mediterranean diet

Aerobic or resistance exercise (Clinical trials)

≥7-10% Weight reduction by energy deficit of 500-750 kcal/day through either diet:
• Low fat
• Low carb
• Mediterranean (Clinical trials)

Dietary composition modification
Reduced fructose
Mediterranean diet (Observational studies)

Mediterranean diet
• High fibres
• High fish
• High vegetables
• Low cholesterol
• Low sugar

Drinks
• Coffee ≥2-3 cups/day
• No alcohol in cirrhotics (Observational studies)
