Lifestyle Interventions in NASH Patients

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Lifestyle Leads to Development of NASH

- A Western diet/lifestyle has been associated with weight gain and obesity, and NAFLD\(^1\)

\[\begin{align*}
\text{High calorie intake} & \rightarrow \text{Excess (saturated) fat} & \rightarrow \text{Obesity} \\
& \rightarrow \text{High fructose intake} & \rightarrow \text{NAFLD} \\
& \rightarrow \text{Sedentary behavior} & \\
\end{align*}\]

Lifestyle leads to *Obesity*

- BMI and waist circumference are positively related to NAFLD
  - Predictors of advanced disease, particularly in the elderly
High calorie food

Excess saturated fats

High fructose corn syrup
High calorie food

Excess saturated fats

High fructose corn syrup

Sedentary Lifestyle
NAFLD Risk Factors

“NAFLD is the equivalent of this is foie gras. You have to force-feed ducks to get fatty liver, but people seem to be able to develop it on their own”
Food Insecurity

- The state of being without reliable access to a sufficient quantity of affordable, nutritious food and instead relying on low-cost, energy dense, nutritionally poor foods.
Food Insecurity

• Linked to obesity, metabolic syndrome and risk of diabetes
• Increases risk for advanced hepatic fibrosis
  – Especially diabetics
• 6.1% of diabetics report food insecurity
• Associated with:
  – Black or Hispanic
  – Lack of health insurance
  – Education below secondary school
  – Younger age
  – Women
  – BMI > 35

Rosenblatt et al. J Hepatology 2018; 68: S33-34 PS-060 (oral)
BAGEL

20 Years Ago

140 calories
3-inch diameter

Today

350 calories
6-inch diameter

Calorie Difference: 210 calories
Calorie Difference: 257 calories
SODA

20 Years Ago
85 Calories
6.5 ounces

Today
250 Calories
20 ounces

Calorie Difference: 165 Calories
MUFFIN

20 Years Ago

210 calories
1.5 ounces

Today

500 calories
4 ounces

Calorie Difference: 290 calories
CHICKEN STIR FRY

20 Years Ago

435 calories
2 cups

Today

865 calories
4 ½ cups

Calorie Difference: 430 calories
CHICKEN CAESAR SALAD

20 Years Ago

390 calories
1 ½ cups

Today

790 calories
3 ½ cups

Calorie Difference: 400 calories
NAFLD : TREATMENT
NAFLD : TREATMENT

• Weight loss
• Weight loss
• Weight loss
• Weight loss
• Weight loss
• Weight loss

• **Diet**
  • Increase complex carbohydrates
  • Avoid fructose
  • Coffee 2-4 cups/d
  • Exercise

Components of a lifestyle approach to NAFLD

Energy restriction
- Calorie restriction (500–1,000/day)
- 7–10% weight loss target
- Long-term maintenance approach

Macronutrient composition
- Low-to-moderate fat
- Moderate-to-high carbohydrate
- Low-carbohydrate ketogenic diets or high protein

Fructose intake
- Avoid fructose-containing food and drink
  - Non-alcoholic beverages

Daily alcohol intake
- Strictly below 30 g men and 20 g women

Coffee consumption
- No liver-related limitations

Physical activity
- 150–200 min/week moderate intensity in 3–5 sessions
- Resistance training to promote musculoskeletal fitness and improve metabolic factors

Lifestyle Modifications for Treatment of NAFLD

• Diets rich in polyunsaturated fats have been shown to reduce liver fat even without weight loss
  – Mediterranean diet

J Hepatol. 2017 May 23. pii: S0168 8278(17)32052-4
Mediterranean Diet
Western vs Mediterranean Diet in NAFLD

**Western diet** causes:
- Healthy liver ➔ Fatty liver ➔ NASH/Fibrosis ➔ Liver cancer

**Mediterranean diet** or Hypocaloric/isocaloric, with:
- Aerobic or resistance excercise
- ≥7-10% Weight reduction by energy deficit of 500-750 kcal/day through either diet:
  - low fat
  - low carb
  - Mediterranean diet
- Dietary composition modification:
  - Reduced fructose
  - Mediterranean diet
- Mediterranean diet:
  - High fibres
  - High fish
  - High vegetables
  - Low cholesterol
  - Low sugar
- Drinks:
  - Coffee ≥2-3 cups/day
  - No alcohol in cirrhosis

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*Journal of Hepatology* 2017 67, 829-846 DOI: (10.1016/j.jhep.2017.05.016)
Coffee consumption has been associated with a lower risk of metabolic syndrome and a reduced diabetes risk in a dose dependent manner.

A study in NAFLD patients indicated an inverse association between coffee consumption and liver fibrosis.

Large prospective cohort study demonstrated that those who drank 2-3 cups of coffee per day had a 38% risk reduction for HCC compared with non-coffee drinker.

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Coffee must be taken without sugar!!

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Summary: Management of NAFLD

- **Lifestyle changes – DIET**
  - Replace saturated and trans fat with monounsaturated and polyunsaturated fats
    - Monounsaturated fats
      - Olive, peanut and canola oils
    - Polyunsaturated fats
      - Corn, soybean and safflower oils
      - Many kinds of nuts
      - Omega 3 fatty acids
        » Salmon, walnuts, flaxseed oil
  - Eat low glycemic index foods
    - Fruits, vegetables, whole grains
  - Avoid foods and drinks that contain simple sugars, especially fructose
    - Soft drinks, sports drinks, sweetened tea, juices
  - Avoid heavy alcohol use

Recommendations for NAFLD: Dietary Nutrients

• 40-50% carbohydrates
• Fat < 30% of total calories
  – Saturated fatty acids > 7%
• 20 % protein
Recommendations for NAFLD: Dietary Nutrients

• Energy content
  – 1000-1200 kcal/day for women
  – 1200-1600 kcal/day for men

• Meal intake
  – 4-5 meals /day
  – Breaks between meals should not exceed 2-3 hrs
  – Meals should be consumed slowly
  – Finish eating before feeling full

NAFLD: Recommended Foods

• Coffee
• Green vegetables
  – Broccoli, spinach, Brussels sprouts, kale
• Tofu
  – Reduces fatty buildup in the liver
• Fish
  – Salmon, sardines, tuna, trout
• Oatmeal
  – Whole grain carbohydrates fill you up and help you maintain weight
• Walnuts, olive oil
  – High in omega 3 fatty acids
• Avocado
• Sunflower seeds
  – High in Vitamin E
• Garlic
  – Reduce body weight and fat
Summary: Management of NAFLD

- **Lifestyle changes – **WEIGHT LOSS
  - Explain diagnosis and set realistic target weight
  - Weight loss should be gradual
    - No more than 1 kg/week
    - Rapid weight loss may worsen NASH
  - Avoid very low calorie diets (388 kcal/day)
    - May increase inflammation and increase bilirubin levels
  - Nutritional counseling – refer to dietician
  - Exercise – 3-4 times per week, expend 400 kcal/session

Summary: Management of NAFLD

- Lifestyle changes – *EXERCISE*
  - Exercise – 5-7 times per week, expend 400 kcal/session
  - Aerobic exercise better than weight training
  - At least 30 minutes a day


Effects of Exercise on the Liver

Van der Windt et al. Gene Expr 2018;18:89-101
Effect of exercise on hepatic fatty acid synthesis

Van der Windt et al. Gene Expr 2018;18:89-101
Effect of NASH and exercise on Mitochondrial Function

Van der Windt et al. Gene Expr 2018;18:89-101

Peroxisome proliferator activated receptor
Benefits of Exercise in NAFLD

Changes in the liver
1. Peripheral insulin sensitivity $\uparrow = de$ novo lipogenesis $\downarrow$
2. Visceral fat $\downarrow = $ lipid supply to liver $\downarrow$
3. VLDL clearance $\uparrow = $ lipid storage $\downarrow$

Changes to cardiovascular system
1. Torsion $\downarrow = $ myocardial damage $\downarrow$
2. EDV $\uparrow = $ preload $\uparrow$
3. $Ca^{2+}$ handling $\uparrow = $ SV $\uparrow + $ EF $\uparrow$
4. FMD $\uparrow = $ O$^2$ supply $\uparrow$

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Treatment of NAFLD with diet and exercise

52 weeks of lifestyle intervention

<table>
<thead>
<tr>
<th>% Weight loss (WL)</th>
<th>5%</th>
<th>7%</th>
<th>10%</th>
</tr>
</thead>
<tbody>
<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>
</tr>
<tr>
<td>STEATOSIS improvement</td>
<td>35%</td>
<td>65%</td>
<td>76%</td>
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<tr>
<td>% Patients achieving WL</td>
<td>70%</td>
<td>12%</td>
<td>9%</td>
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