Nutrition and Non-alcoholic fatty liver disease

Carlton Li
QEH
Definition

1) Evidence of hepatic steatosis, either by imaging or histology
2) Lack of secondary causes of hepatic fat accumulation

NAFL - presence of >=5% hepatic steatosis without evidence of hepatocellular injury in the form of hepatocyte ballooning

NASH - presence of >=5% hepatic steatosis and inflammation with hepatocyte injury, with or without any fibrosis
Weight loss Works

![Diagram showing weight loss progression]

Vilar-Gomez et al. Gastroenterology 2015
Hypothesis

- IRS hypothesis
- ER stress hypothesis
- mTORC1 hypothesis
Biochemical changes in liver cells

- Overexpress SREBP-1c
- Increase in expression of genes encoding fatty acid synthase and acetyl-coA carboxylase (lipogenic enzymes)
Both carbohydrates and fat contribute to fatty liver
Nutritional induction of NAFLD

Overnutrition is the primary driver

- Increased energy uptake supports hepatic fat accumulation by delivery of excess fat and carbohydrates-> de-novo-lipogenesis
- Expansion of adipose tissue, if compounded with inflammation-> increase in nonesterified fatty acids pool in the serum
A calorie is a calorie

- Law of conservation of energy - energy can neither be created nor destroyed
- Prevention of obesity = Eat less and exercise more?
Theories behind manipulation of macronutrients

- alter overall calorie intake and expenditure
- corresponding change in energy stores of the body
- Alter endocrine factors that influence the propensity to accumulate body fat or direct the storage of fat to particular locations
Dietary interventional study for 2 years

- 750kcal calorie deficit
- 4 groups with different composition of carbohydrate/protein/fat

(HLL, MLH, MHL, LHH)
Key factors
Effect of low-fat diet interventions versus other diet interventions on long-term weight change in adults: a systematic review and meta-analysis

Deirdre K Tobias, Mu Chen, JoAnn E Manson, David S Ludwig, Walter Willett, Frank B Hu

Interpretation These findings suggest that the long-term effect of low-fat diet intervention on bodyweight depends on the intensity of the intervention in the comparison group. When compared with dietary interventions of similar intensity, evidence from RCTs does not support low-fat diets over other dietary interventions for long-term weight loss.
Macronutrient composition is not a key determinant in weight loss success. Adherence to the dietary protocol is more important.
## Clinical Practice Guidelines

### Table 5: Elements of a comprehensive lifestyle approach to NAFLD treatment.

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<th>Supportive literature</th>
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<td>Energy restriction</td>
<td>• 500-1000 kcal energy deficit, to induce a weight loss of 500-1000 kcal/week</td>
<td>Calorie restriction drives weight loss and the reduction of liver fat, independent of the macronutrient composition of the diet [107]</td>
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<td>• 7-10% total weight loss target</td>
<td>A 12-month intensive lifestyle intervention with an average 3% weight loss leads to significant reduction of hepatic steatosis [108]</td>
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<td>• Long-term maintenance approach, combining physical activity according to the principles of cognitive-behavioral treatment</td>
<td>Hispanic fat increases along with total body fat regain, but most of the beneficial metabolic effects are maintained and progression to T2DM is delayed [109]</td>
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<td>Macronutrient composition</td>
<td>• Low-to-moderate fat and moderate-to-high carbohydrate intake</td>
<td>Adherence to the Mediterranean diet has been reported to reduce liver fat on 1H-MRS, when compared with a low fat/high carbohydrate diet in a cross-over comparison [110, 111]</td>
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<td>• Low-carbohydrate ketogenic diets or high-protein</td>
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<td>Fructose Intake</td>
<td>• Avoid fructose-containing beverages and foods</td>
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<td>Alcohol intake</td>
<td>• Strictly keep alcohol below the risk threshold (30 g, men; 20 g, women)</td>
<td>In epidemiological surveys, moderate alcohol intake (namely, wine) below the risk threshold is associated with lower prevalence of NAFLD, NASH and even lower fibrosis at histology [112-114]. Total abstinence is mandatory in NASH-cirrhosis to reduce the HCC risk [115]</td>
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<td>Coffee drinking</td>
<td>• No liver-related limitations</td>
<td>Protective in NAFLD, as in liver disease of other aetiologies, reducing histological severity and liver-related outcomes [116]</td>
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<td>Exercise/physical activity</td>
<td>• 150-200 min/week of moderate intensity aerobic physical activities in 3-5 sessions are generally preferred (brisk walking, stationary cycling)</td>
<td>Physical activity follows a dose-effect relationship and vigorous (running) rather than moderate exercise (brisk walking) carries the full benefit, including for NASH and fibrosis [110, 117, 118]</td>
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<td>• Resistance training is also effective and promotes musculoskeletal fitness, with effects on metabolic risk factors</td>
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20. Weight loss generally reduces Hepatic Steatosis, achieved either by hypocaloric diet alone or in conjunction with increased physical activity. A combination of a hypocaloric diet (daily reduction by 500-1,000 kcal) and moderate-intensity exercise is likely to provide the best likelihood of sustaining weight loss over time.
Fructose
Fructose

- Potent stimulator of de-novo-lipogenesis
- Bypass the regulatory enzymes of the glycolytic pathway
- Provide lipogenic precursors for lipogenesis (acetyl coA)

KLINICAL—LIVER

Effects of Dietary Fructose Restriction on Liver Fat, De Novo Lipogenesis, and Insulin Kinetics in Children With Obesity

Jean-Marc Schwarz,1,2 Susan M. Noworolski,3 Ayca Erkin-Cakmak,4 Natalie J. Korn,3 Michael J. Wen,5 Viva W. Tai,5 Grace M. Jones,1 Sergiu P. Paliu,1 Moises Velasco-Alin,1,2 Karen Pan,2 Bruce W. Patterson,6 Alejandro Gugliucci,1 Robert H. Lustig,4 and Kathleen Mulligan1,2

1Touro University California College of Osteopathic Medicine, Vallejo, California; 2Department of Med Endocrinology, University of California, San Francisco, Zuckerberg San Francisco General Hospital, S 3Department of Radiology and Biomedical Imaging, University of California, San Francisco, San Fran 4Department of Pediatrics, University of California, San Francisco, Benioff Children’s Hospital, San F 5Clinical and Translational Science Institute Clinical Research Services, University of California, San Fr 6Department of Internal Medicine, Washington University School of Medicine, St Louis, M

CONCLUSIONS: Short-term (9 days) isocaloric fructose restriction decreased liver fat, VAT, and DNL, and improved insulin kinetics in children with obesity. These findings support efforts to reduce sugar consumption. ClinicalTrials.gov Number: NCT01200043.
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Mediterranean Diet

Adherence to Mediterranean Diet and Non-Alcoholic Fatty Liver Disease: Effect on Insulin Resistance

Francesco Baratta, MD1,2,9, Daniele Pastori, MD1,2,9, Licia Polimeni, MD1, Tommaso Bucci, MD1, Fabrizio Ceci, MD1, Cinzia Calabrese, MD1, Ilaria Ervesti, MD1, Gaetano Pannitteri, MD1, Francesco Violi, MD1, Francesco Angelico, MD1 and Maria Del Ben, MD1

OBJECTIVES: The prevalence of cardiometabolic disorders, including non-alcoholic fatty liver disease (NAFLD), is increasing in western countries, because of changes in lifestyle and dietary habits. Mediterranean Diet (Med-Diet) is effective for cardiovascular prevention, but its relationship with NAFLD has been scarcely investigated.

METHODS: We included 584 consecutive outpatients presenting with one or more cardiovascular risk factor such as type 2 diabetes mellitus (T2DM), arterial hypertension, overweight/obesity, and dyslipidemia. Liver steatosis was assessed using ultrasonography. Med-Diet adherence was investigated by a validated semiquantitative nine-item dietary questionnaire: patients were divided into low, intermediate, and high adherence. Insulin resistance was defined by the 75th percentile of homeostasis model of insulin resistance (HOMA-IR; ≥3.8).

RESULTS: The mean age was 56.2±12.4 years and 38.2% were women. Liver steatosis was present in 82.7%, and its prevalence decreased from low to high adherence group (96.5% vs. 71.4%, P<0.001). In a multiple logistic regression analysis, hypertriglyceridemia (odds ratio (OR): 2.913; P=0.002), log (ALT) (OR: 6.186; P<0.001), Med-Diet adherence (intermediate vs. low OR: 0.115; P=0.041, high vs. low OR: 0.093; P=0.030), T2DM (OR: 3.940; P=0.003), and high waist circumference (OR: 3.012; P<0.001) were associated with NAFLD. Among single foods, low meat intake (OR: 0.178; P<0.001) was inversely significantly associated with NAFLD. In 334 non-diabetic NAFLD patients, age (OR: 1.035, P=0.025), high waist circumference (OR: 7.855, P<0.001), hypertriglyceridemia (OR: 2.152, P=0.011), and Log (ALT) (OR: 2.549, P=0.002) were directly associated with HOMA-IR, whereas Med-Diet score was inversely associated (OR: 0.601, P=0.018).

CONCLUSIONS: We found an inverse relationship between Med-Diet and NAFLD prevalence. Among NAFLD patients, good adherence to Med-Diet was associated with lower insulin resistance. Our findings suggest that Med-Diet may be a beneficial nutritional approach in NAFLD patients.

Am J Gastroenterol 2017; 112:1832–1839; doi:10.1038/ajg.2017.371; published online 24 October 2017
Recommendations

- Intense nutritional education
- Hypocaloric diet is helpful to induce weight loss
- A diet with reduced simple sugar intake, especially fructose, to less than 10% of caloric intake
- Mediterranean diet maybe protective against NAFLD (high intakes of fruits, nuts, vegetables, whole grain cereals, olive oil, and moderate consumption of fish, poultry, wine, and low intake of dairy, red meats, and sweets)
Thank you for listening!