Ursachen, Therapie und Prävention der nichtalkoholischen Fettlebererkrankung

Nicolai Worm

www.logi-methode.de
www.leberfasten.de
www.heilkraft-d.de

Über die nicht-alkoholische Fettleber-Erkrankung wurde erstmals 1976 publiziert

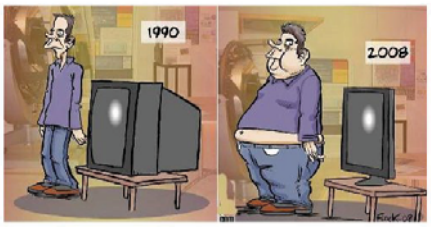
PUBMED-Suche „NAFLD“ am 04.09.2015

Zahl der Publikationen pro Jahr

Heute die häufigste Lebererkrankung in Industrienationen!

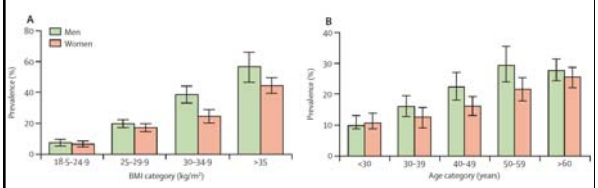
Was ist passiert?

Vom fetten Fernsehgerät – zur fetten Leber....



Prävalenz der nichtalkoholischen Fettleber in USA

NHANES III (1988–1994); n = 12.454;



Yki-Järvinen H. Lancet Diabetes Endocrinol 2014; aus Lazo M, et al. Am J Epidemiol 2013;178:38-45

NAFLD als kardiometabolisches Risiko: vor allem für Typ-2-Diabetes und KHK!

Diagnostik

Transaminasen sind ungeeignet zur NAFLD-Diagnose!

Prävalenz der NAFLD / NASH bei Typ-2-Diabetikern

- 103 Typ-2-Diabetiker mit normalen Transaminasen AST (= GOT), ALT (= GPT) aus San Antonio, Texas
- Außer MetS/T2DM keine manifesten Erkrankungen
- Diagnose mit MRT

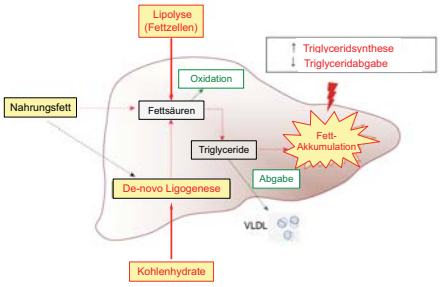
=> Prävalenz der NAFLD = 76 %

=> Prävalenz der NASH = 56 %

Portillo Sanchez P, et al. J Clin Endocrinol Metab. 2014 Oct 10; epub ahead of print

Pathophysiologie

Wie entsteht die nichtalkoholische Fettleber?



Ferramosca A, et al. World J Gastroenterol 2014;20:1746-1755

Woher stammt das Fett in der Leber?

Bei übergewichtigen Patienten mit nicht-alkoholischer Fettleber (mit Hypertriglyceridämie u. Hyperinsulinämie) stammt das Fett in der Leber zu

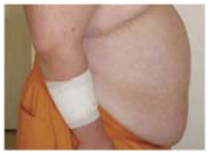
- 59 % aus der Lipolyse der Adipozyten
- 26 % aus der „de novo“ Lipogenese (Kohlenhydrate)
- 15 % aus dem Nahrungsfett

Donnelly KL, et al. J Clin Invest 2005;115:1343–1351

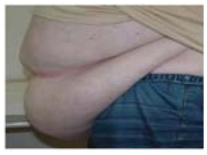
Gestörte Fettspeicherung, ektopes Fett und NAFLD

Dysfunktionelle Fettzellen; Insulinresistenz und NAFLD

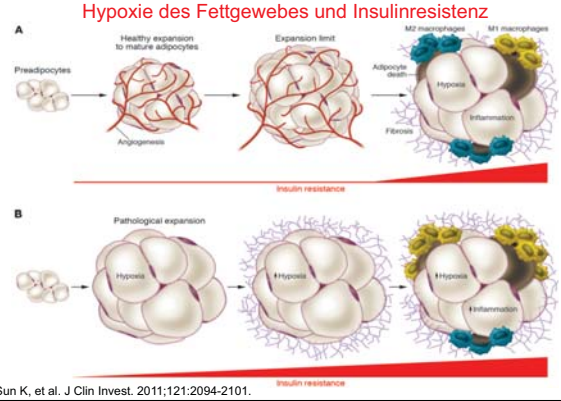
Klöting N, et al. Am J Physiol Endocrinol Metab 2010;299:E000–E000



BMI 45

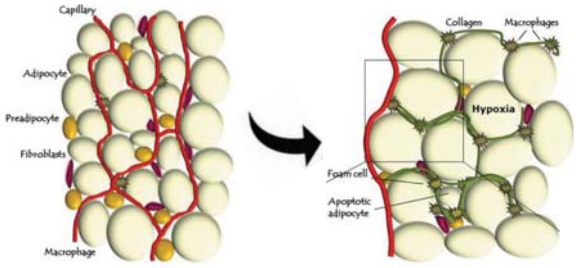


Hypoxie des Fettgewebes und Insulinresistenz



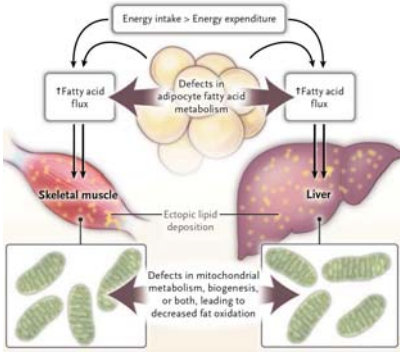
Sun K, et al. J Clin Invest. 2011;121:2094-2101.

Gestörtes Wachstum des Fettgewebes



Rodrigues T, et al. Arch Physiol Biochem 2014

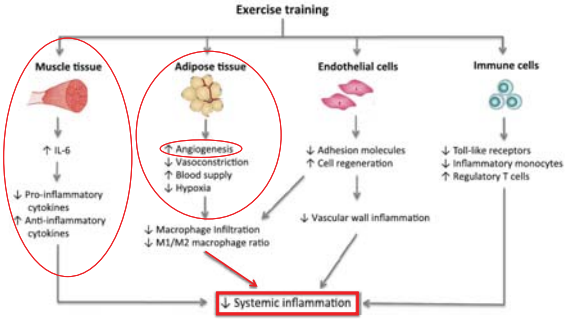
Dysfunktionale Fettzellen bedingen ektope Fetteinlagerungen



Shulman GI. N Engl J Med 2014;371:1131-41.

Sport bei Fettsucht erhält normnahe Stoffwechselfunktionen!

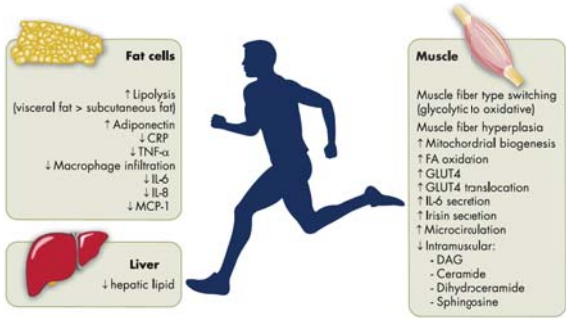
Einflüsse der körperlichen Aktivität



You T, et al. Sports Med 2013;43:243-256.

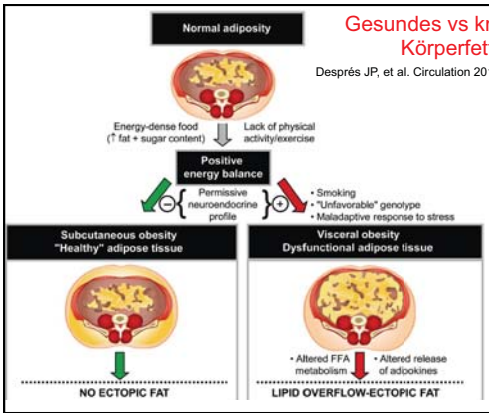
Muskeln, Myokine und Stoffwechselregulation

Hocking S, et al. Endocrine Reviews 2013

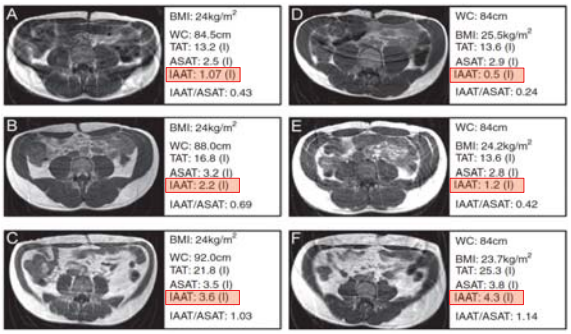


Gesundes vs krankes Körperfett

Després JP, et al. Circulation 2012;126:1301-1313.



BMI, Taillenumfang und ektopes Fett bei Normalgewicht

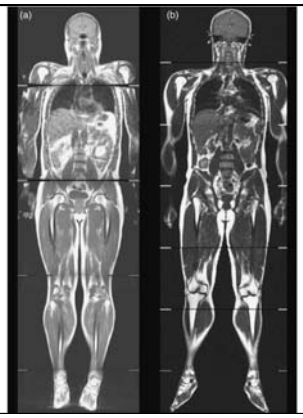


Thomas EL, et al. Obesity 2012;20:76–87

TOFI

BMI = 25,8 kg/m²

3,3 l viszerales Fett



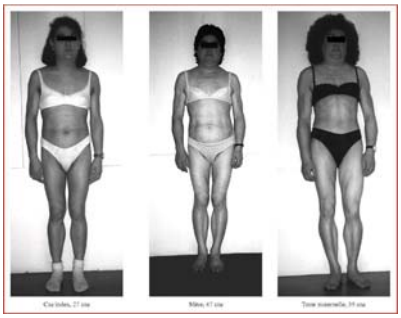
Gesunder

BMI = 26,5 kg/m²

2,2 l viszerales Fett

Thomas EL, et al.
Nutr Res Rev 2012

Lipodystrophie und ektope Fetteinlagerungen



Lipodystrophie und Folgen

- Schwund des Unterhautfettgewebes
- Starke Fettansammlung (Kinn, Innenseite Oberarm, Achselhöhle)
- Männliches Erscheinungsbild bei Frauen
- Auffallend kräftige Muskulatur
- Fettstoffwechselstörung
- Bauchspeicheldrüsenentzündungen
- Fettleber mit erhöhten Leberwerten
- Störung der Blutzuckerregulation
- Acanthosis nigricans (Achselhöhlen, des Halses u. der Leistenbeugen)
- Bluthochdruck (nicht bei allen Patienten)
- Erhöhtes Risiko von Arteriosklerose, Herz- u. Hirninfarkt u. Verschlüssen
- Hormonelle Störungen
- Nervenkompressionssyndrome

„Überlaufen“ von Fettzellen unabhängig von der Größe des Fettdepots

schlanker, gesunder Mensch ausgeglichene Energiebilanz

übergewichtiger, insulinresistenter Mensch

normalgewichtiger mit Fettspeicherstörungen in ausgeglichener Energiebilanz

Hocking S, et al. Endocrine Reviews 2013

Folgeerkrankungen

Medscape Deutschland | DIABETOLOGIE/ENDOKRINOLOGIE

Gesund trotz Übergewicht – die Geheimnisse der „glücklichen Dicken“

Inge Brinkmann | 11. September 2013 | 0 Kommentare

Prof. Norbert Stefan

- Der BMI trennt nicht zwischen gesund und krank

  „Der Body-Mass-Index (BMI) allein eignet sich nicht für eine scharfe Trennung zwischen ‚gesund‘ und ‚krank‘.“

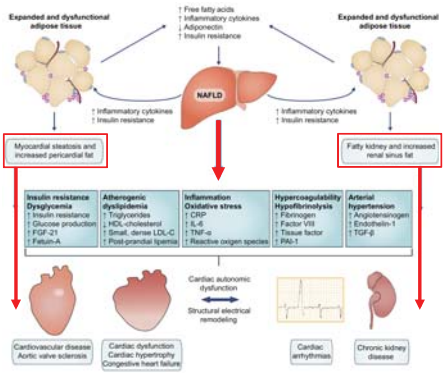
- Des Rätsels Lösung liegt in der Leber

  „Nur wenn die Leberzellen verfettet sind, verschlechtert sich auch die Prognose des Übergewichtigen. So wirkte sich der Fettgehalt der Leber in Studien wesentlich deutlicher auf die Insulinsensitivität bzw. die Inzidenz eines Typ-2-Diabetes aus als die Menge des Bauchfetts ganz allgemein. Außerdem ist zwischen den verfetteten Leberzellen und dem Auftreten von Gefäßschäden nachgewiesen – und zwar unabhängig von weiteren atherosklerotischen Risikofaktoren.“

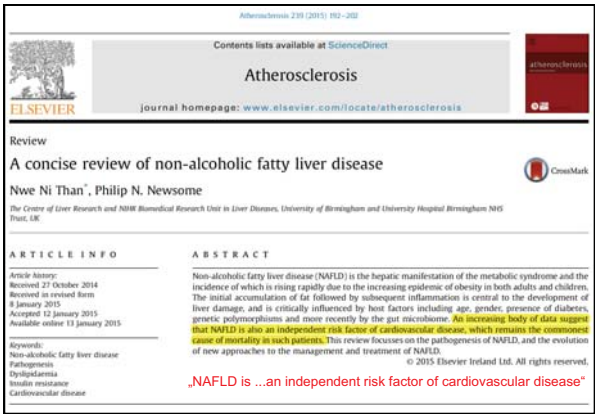
Ektope Fetteinlagerungen und Folgen

- erhöhtes Insulin
- erhöhter Nüchtern-Blutzucker
- erhöhter Blutdruck
- erhöhtes VLDL und Triglyceride
- erniedrigtes HDL-Cholesterin
- mehr kleine dichte LDL-Partikel
- gestörte Blutgerinnung
- erhöhte Harnsäure
- Nierenfunktionsstörungen
- etc.

Dysfunktionales Fettgewebe, NAFLD u. Folgeerkrankungen



Byrne CD, et al. J Hepatol 2015;62:S47–S64



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journal homepage: www.elsevier.com/locate/atherosclerosis

Review

A concise review of non-alcoholic fatty liver disease

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The Centre of Liver Research and NIHR Biomedical Research Unit in Liver Diseases, University of Birmingham and University Hospital Birmingham NHS Trust, UK

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Cardiovascular disease

ABSTRACT

Non-alcoholic fatty liver disease (NAFLD) is the hepatic manifestation of the metabolic syndrome and the incidence of which is rising rapidly due to the increasing epidemic of obesity in both adults and children. The initial accumulation of fat followed by subsequent inflammation is central to the development of liver damage, and is critically influenced by host factors including age, gender, presence of diabetes, genetic polymorphisms and more recently by the gut microbiome. An increasing body of data suggest that NAFLD is also an independent risk factor of cardiovascular disease, which remains the commonest cause of mortality in such patients. This review focusses on the pathogenesis of NAFLD, and the evolution of new approaches to the management and treatment of NAFLD.

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„NAFLD is ...an independent risk factor of cardiovascular disease“

Review

NAFLD: A multisystem disease

JOURNAL OF HEPATOLOGY

Christopher D. Byrne[1,2,*], Giovanni Targher[3]

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Summary

Non-alcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease in Western countries that is predicted to become also the most frequent indication for liver transplantation by 2030. Over the last decade, it has been shown that the clinical burden of 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. For example, NAFLD increases risk of type 2 diabetes mellitus (T2DM), cardiovascular (CVD) and cardiac diseases, and chronic kidney disease (CKD). Although the primary liver pathology in NAFLD affects hepatic structure and function to cause morbidity and mortality from cirrhosis, liver failure and hepatocellular carcinoma, the majority of deaths among NAFLD patients are attributable to CVD.

J Hepatol 2015;62:S47–S64

Inzidenz von Typ-2-Diabetes in Abhängigkeit von Übergewicht und NAFLD in China

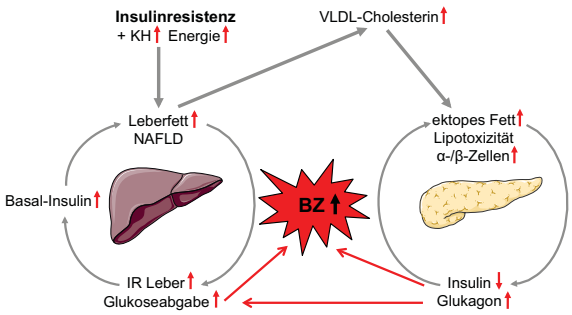
4.736 gesunde Teilnehmer, 4 Jahre Follow-up = 17.223 Personen-Jahre, 380 Fälle von T2DM (Inzidenzrate = 8,0 %); mittl. Alter = 57 Jahre;

BMI	NAFLD	*n*	T2DM	Incidence rate[1] (%)	RR[2] (95%CI)
< 24	Control	2383	85	3.6	1.0
	NAFLD	616	81	13.1	3.407 (2.461-4.717)
About 24	Control	712	35	4.9	1.0
	NAFLD	537	102	19.0	3.455 (2.269-5.262)
About 28	Control	229	15	6.6	1.0
	NAFLD	259	62	23.9	3.438 (1.841-6.420)

BMI-Cut-Off für Übergewicht bei Asiaten ist ≥ 24!

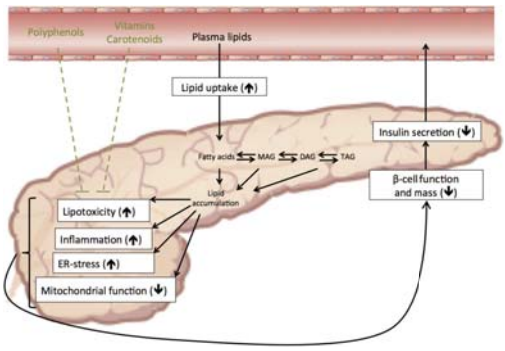
Li WD, et al. World J Gastroenterol 2015;21: 9607-9613

Der „Zwillings-Zyklus“ des Typ-2 Diabetes



Taylor R. Reversing the Twin Cycles of Type 2 Diabetes. Diab Med 2013;30:267-275

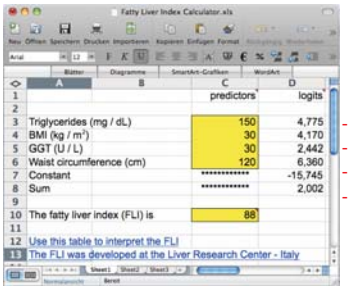
Ektopes Pankreasfett und Typ-2-Diabetes



Stinkens R, et al. Obes Rev 2015;16:715–757

Schätzung mit dem „Fatty Liver Index“-Rechner

http://www.giorgiobedogni.it/varie/flicalc.xls



	predictors	logits
Triglycerides (mg / dL)	150	4,775
BMI (kg / m²)	30	4,170
GGT (U / L)	30	2,442
Waist circumference (cm)	120	6,360
Constant	**********	-15,745
Sum	**********	2,002
The fatty liver index (FLI) is	88	
Use this table to interpret the FLI		
The FLI was developed at the Liver Research Center - Italy		

- Triglyceride
- γ-GT
- BMI
- Taillenumfang

FLI ≥ 60 => mit 78%iger Wahrscheinlichkeit eine Fettleber
FLI < 20 => mit 91%iger Wahrscheinlichkeit *keine* Fettleber

Fatty Liver Index und Diabetes-Risiko: EPIC-Potsdam

Genestete Fall-Kontrollstudie aus EPIC-Kohorte; n = 1.922 Kontrollen (1.215 Frauen u. 707 Männer) und n = 563 neue T2-Diabetes-Fälle (224 Frauen u. 339 Männer)

Ergebnis (multivariat adjustiert): T2-Diabetes-Risiko ist bei Frauen 18-fach und bei Männern 11-fach erhöht, wenn FLI > 60 (vs < 30)

	FLI categories women			FLI categories men		
	<30	30-<60	≥60	<30	30-<60	≥60
FLI, median (IQR)[b]	7.17 (10.4)	42.5 (15.2)	77.0 (22.0)	16.8 (14.5)	44.0 (13.5)	78.2 (19.1)
n (cases)	39	71	138	17	62	293
Model 1 (age-stratified)	1	7.03 (4.50–11.0)	17.1 (11.3–25.9)	1	3.05 (1.71–5.44)	11.4 (6.70–19.3)
Model 2 (multivariable-adjusted)	1	7.25 (4.51–11.7)	17.6 (11.1–28.0)	1	2.53 (1.37–4.67)	10.9 (6.22–19.2)

FLI, fatty liver index; PEE, Proportion of exposure effect

[a] women: n = 1439, men: n = 1046

[b] in sub-cohort

* significant change in β-coefficients compared to the multivariable-adjusted model

Model 2 is further adjusted for education (no vocational training or in training, vocational training, technical school, technical college or university), occupation (sedentary, standing, (heavy) manual work), smoking behavior (never smoker, ex-smoker, current smoker <20 units/day, current smoker ≥20 units/day), sport activities (no sport, ≤4 h/week, >4 h/week), biking (no biking, <2.5 h/week, 2.5–4.9 h/week, ≥5 h/week), alcohol intake (women: no alcohol intake, >0–6 g/day, >6–12 g/day, >12–24 g/day, >24–60 g/day, >60 g/day; men: no alcohol intake, >0–6 g/day, >6–12 g/day, >12–24 g/day, >24–60 g/day, >60–96 g/day, >96 g/day), coffee consumption (ml/day), red meat intake (g/day), intake of whole-grain bread (g/day).

Jäger S, et al. PLoS ONE 2015:10(4):e0124749

Fatty Liver Index und Diabetes-Risiko: EPIC-Potsdam

	FLI categories women			FLI categories men		
	<30	30-<60	≥60	<30	30-<60	≥60
FLI, median (IQR)[a]	7.33 (10.6)	42.3 (15.0)	78.3 (21.8)	17.2 (13.5)	44.0 (14.0)	78.2 (18.4)
n (cases)	37	70	125	15	50	213
Model 1 (age-stratified)	1	7.61 (4.83-12.0)	15.9 (10.4-24.4)	1	2.69 (1.44-5.04)	11.1 (6.26-19.5)
Model 2 (multivariable-adjusted)	1	7.80 (4.83-12.6)	15.8 (9.83-25.2)	1	2.20 (1.11-4.36)	10.2 (5.49-18.9)

FLI, fatty liver index

[a]women: n=1292, men: n=780; [b] in sub-cohort

Model 2 is further adjusted for education (no vocational training or in training, vocational training, technical school, technical college or university), occupation (sedentary, standing, (heavy) manual work), smoking behavior (never smoker, ex-smoker, current smoker <20 units/day, current smoker ≥20 units/day), sport activities (no sport, ≤4 h/week, >4 h/week), biking (no biking, <2.5 h/week, 2.5-4.9 h/week, ≥5 h/week), alcohol intake (women: no alcohol intake, >0-6 g/day, >6-12 g/day, >12 g/day; men: no alcohol intake, >0-6 g/day, >6-12 g/day, >12-24 g/day, >24 g/day), coffee consumption (ml/day), red meat intake (g/day), intake of whole-grain bread (g/day).

Jäger S, et al. PLoS ONE 2015:10(4):e0124749

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journal homepage: www.elsevier.com/locate/nmcd
Nutrition, Metabolism & Cardiovascular Diseases

The fatty liver index is associated with increased mortality in subjects referred to coronary angiography

E. Lerchbaum [a,*], S. Pilz [a,b], T.B. Grammer [c], B.O. Boehm [d], T. Stojakovic [e], B. Obermayer-Pietsch [a], W. März [c,e,f]

3316 Patienten bei Koronarangiographie; 8 Jahre Follow-Up

Lerchbaum E, et al. Nutr Metab Cardiovasc Dis 2013;23:1231-8.

Fatty Liver Index und Sterblichkeit: LURIC-Studie

Table 3: HRs with 95% CI of FLI levels in quartiles for all-cause, cardiovascular, non-cardiovascular, and cancer mortality. Data analyzed by Cox proportional hazard ratios.

	Model 1		Model 2		Model 3		Model 4	
	HR	p-value	HR	p-value	HR	p-value	HR	p-value
All-cause mortality								
Q1 (<31.0)	1.0 (reference)		1.0 (reference)		1.0 (reference)		1.0 (reference)	
Q2 (31.0-53.7)	1.14 (0.92-1.40)	0.228	1.24 (0.99-1.55)	0.059	1.20 (0.95-1.51)	0.120	1.17 (0.93-1.47	0.189
Q3 (53.8-75.6)	1.11 (0.90-1.37	0.322	1.33 (1.20-1.96)	0.001	1.47 (1.14-1.89)	0.003	1.39 (1.04-1.75)	0.023
Q4 (>75.6)	1.26 (1.02-1.54)	0.030	2.56 (1.90-3.43)	<0.001	2.38 (1.75-3.22)	<0.001	2.17 (1.58-2.99)	<0.001
Risk per 1 SD increase in FLI	1.00 (1.00-1.01)	0.025	1.02 (1.01-1.02)	<0.001	1.01 (1.01-1.02)	<0.001	1.01 (1.01-1.02)	<0.001
Cardiovascular mortality								
Q1 (<31.0)	1.0 (reference)		1.0 (reference)		1.0 (reference)		1.0 (reference)	
Q2 (31.0-53.7)	1.28 (0.97-1.69)	0.081	1.30 (0.96-1.74)	0.086	1.22 (0.90-1.66)	0.194	1.15 (0.84-1.56)	0.381
Q3 (53.8-75.6)	1.35 (1.03-1.77)	0.032	1.64 (1.19-2.26)	0.003	1.54 (1.11-2.14)	0.010	1.33 (0.95-1.86)	0.098
Q4 (>75.6)	1.32 (1.00-1.73)	0.047	2.17 (1.47-3.22)	<0.001	1.95 (1.30-2.93)	0.001	1.64 (1.07-2.51)	0.023
Risk per 1 SD increase in FLI	1.00 (1.00-1.01)	0.017	1.01 (1.01-1.02)	<0.001	1.01 (1.01-1.02)	<0.001	1.01 (1.00-1.02)	0.008
Cancer mortality								
Q1 (<31.0)	1.0 (reference)		1.0 (reference)		1.0 (reference)		1.0 (reference)	
Q2 (31.0-53.7)	1.10 (0.65-1.88)	0.717	1.15 (0.65-2.05)	0.633	1.14 (0.64-2.03)	0.662	1.24 (0.69-2.23)	0.472
Q3 (53.8-75.6)	0.75 (0.41-1.35)	0.333	0.96 (0.48-1.92)	0.911	0.94 (0.47-1.89)	0.866	1.04 (0.51-2.11)	0.917
Q4 (>75.6)	1.01 (0.59-1.76)	0.957	1.88 (0.83-4.16)	0.122	1.86 (0.83-4.17)	0.131	2.33 (1.01-5.41)	0.048
Risk per 1 SD increase in FLI	1.00 (0.99-1.01)	0.469	1.01 (0.99-1.02)	0.523	1.00 (0.99-1.02)	0.561	1.01 (0.99-1.02)	0.351
Non-cardiovascular mortality								
Q1 (<31.0)	1.0 (reference)		1.0 (reference)		1.0 (reference)		1.0 (reference)	
Q2 (31.0-53.7)	0.98 (0.69-1.38)	0.896	1.18 (0.81-1.72)	0.382	1.15 (0.79-1.68)	0.472	1.21 (0.82-1.77)	0.342
Q3 (53.8-75.6)	0.88 (0.62-1.26)	0.482	1.45 (0.95-2.21)	0.085	1.39 (0.91-2.13)	0.127	1.46 (0.95-2.26)	0.088
Q4 (>75.6)	1.27 (0.91-1.76)	0.161	3.49 (2.16-5.66)	<0.001	3.31 (2.03-5.41)	<0.001	3.72 (2.22-6.24)	<0.001
Risk per 1 SD increase in FLI	1.00 (1.00-1.01)	0.328	1.02 (1.01-1.03)	<0.001	1.02 (1.01-1.03)	<0.001	1.02 (1.01-1.03)	<0.001

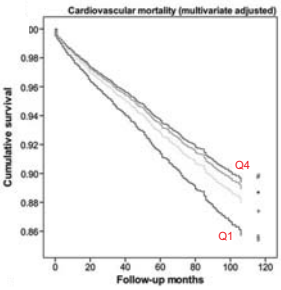
Model 1: crude; Model 2: adjusted for age, sex, and BMI; Model 3: adjusted for age, sex, BMI, and homeostatic model assessment-insulin resistance; Model 4: adjusted for age, sex, BMI, homeostatic model assessment-insulin resistance, systolic and diastolic blood pressure, prevalent diabetes, smoking, alcohol intake, C-reactive protein, fibrinogen, free fatty acids, total cholesterol, HDL, and statin use.

Lerchbaum E, et al. Nutr Metab Cardiovasc Dis 2013;23:1231-8.

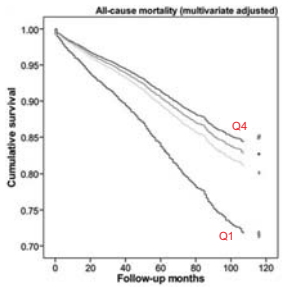
Fatty Liver Index und Überleben: LURIC-Studie

Q1: < 31,0 Q2: 31 – 53,7 Q3: 53,8 – 75,6 Q4: > 75,6

Herz-Kreislauf



Gesamt

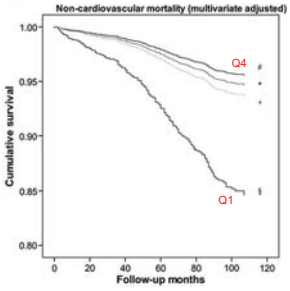


Lerchbaum E, et al. Nutr Metab Cardiovasc Dis 2013;23:1231-8.

Fatty Liver Index und Überleben: LURIC-Studie

Q1: < 31,0 Q2: 31 – 53,7 Q3: 53,8 – 75,6 Q4: > 75,6

Infektionen, Krebs, Lebererkrankungen



Lerchbaum E, et al. Nutr Metab Cardiovasc Dis 2013;23:1231-8.

Einfluss der Ernährung

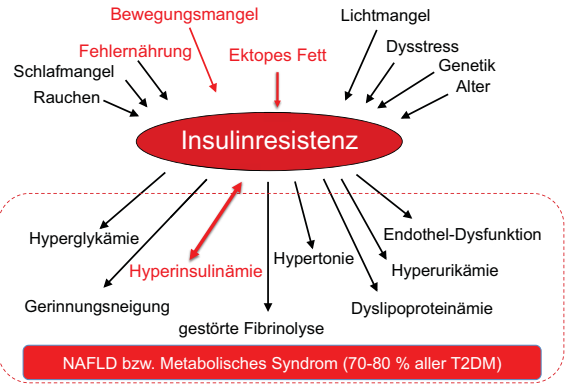
Woher stammt das Fett in der Leber?

Donnelly KL, et al. J Clin Invest 2005;115:1343–1351

Bei übergewichtigen Patienten mit nicht-alkoholischer Fettleber (mit Hypertriglyceridämie u. Hyperinsulinämie) stammt das Fett in der Leber zu

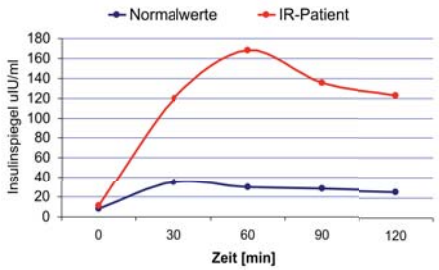
- 59 % aus der Lipolyse der Adipozyten
- 26 % aus der „de novo" Lipogenese (Kohlenhydrate)
- 15 % aus dem Nahrungsfett

Moderner Lebensstil und NAFLD



Insulinresistenz und Hyperinsulinämie

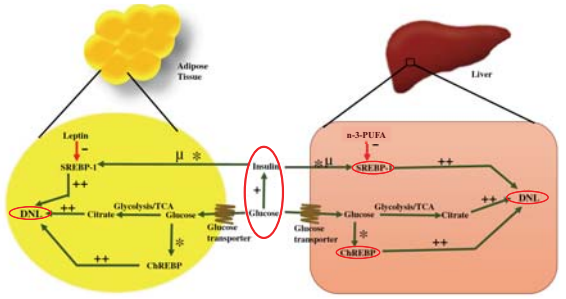
Patient mit MetS und gestörter Nüchternglukose
Insulinbestimmung während OGTT (75 g Glukose)



Scholl J. persönl. Mittl. 2008;

De-novo Lipogenese in Leber- und Fettzellen

Hohe Blutzucker- und Insulinspiegel aktivieren
die Transkriptionsfaktoren ChREBP und SREBP-1



Ameer F, et al. Metabolism 2014;63:895-902.

Hepatic de novo lipogenesis in normoinsulinemic and hyperinsulinemic subjects consuming high-fat, low-carbohydrate and low-fat, high-carbohydrate isoenergetic diets[1–3]

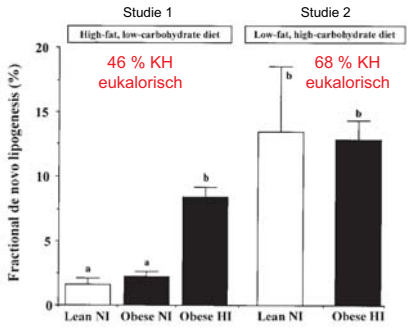
Jean-Marc Schwarz, Peter Linfoot, Doris Dare, and Karmen Aghajanian

5 Tage eukalorische Diät in geschlossenem Stoffwechsellabor:
kohlenhydrat-reich/fettarm *vs* kohlenhydratmoderat/fettmoderat
bei insulinsensitiven und insulinresistenten Probanden

[1] From the Department of Nutritional Sciences and Toxicology, University of California, Berkeley (J-MS and KA), and the Department of Medicine, University of California, San Francisco (J-MS, PL, and DD).

Schwarz JM, et al. Am J Clin Nutr 2003;77:43–50

De novo Lipogenese in Abhängigkeit der Insulinämie

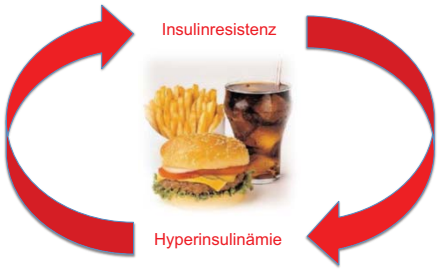


Schwarz JM, et al. Am J Clin Nutr 2003;77:43–50

Cave!

Insulinresistente haben bereits bei üblichen Kohlenhydratmengen eine deutlich gesteigerte de novo Lipogenese!

Insulinresistenz + Stärke u. Zucker bedingen eine Hyperinsulinämie...

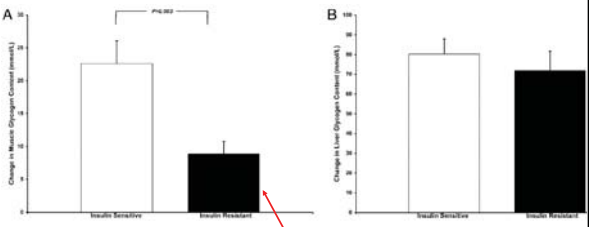


Hyperinsulinämie verstärkt wiederum die Insulinresistenz!

Gestörte Glykogensynthese Kost bei Insulinresistenz

Petersen KF, et al. PNAS 2007;104 :12587-94.

Identische Zufuhr an Kohlenhydraten



Muskel

Leber

geminderte muskuläre Glykogensynthese

De novo Lipogenese bei Insulinresistenz

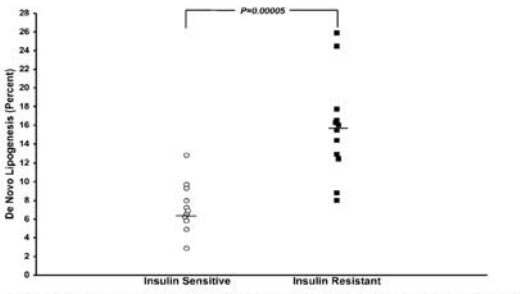


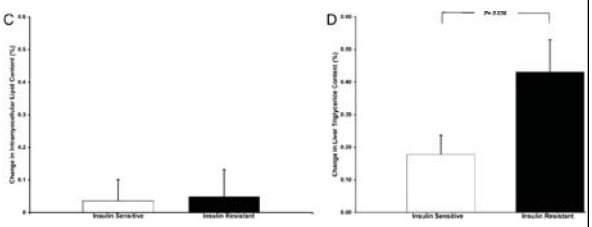
Fig. 4. Fractional *de novo* lipogenesis in insulin-sensitive and insulin-resistant subjects after the two high-carbohydrate mixed meals

Petersen KF, et al. PNAS 2007;104 :12587-94.

De Novo Lipogenese bei Insulinresistenz

Petersen KF, et al. PNAS 2007;104 :12587-94.

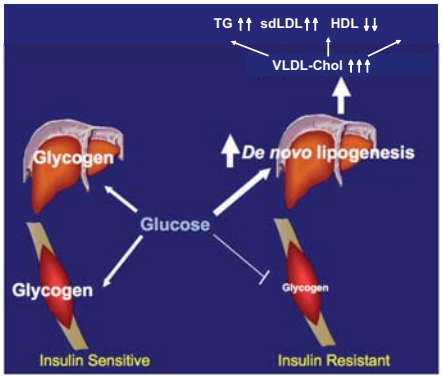
Identische Zufuhr an Kohlenhydraten



Muskel

Leber

Foie Gras - wie produziert man eine fette Leber?



Petersen KF, et al. PNAS 2007;104 :12587-94.

Cave!

Insulinresistente haben trotz Hyperinsulinämie eine gestörte Glykogensynthese in Muskel und Leber!

Kohlenhydratmenge und Kohlenhydratart

The Potential of a High Protein-Low Carbohydrate Diet to Preserve Intrahepatic Triglyceride Content in Healthy Humans

Eveline A. Martens*, Blandine Gatta-Cherifi*, Hanne K. Gonnissen, Margriet S. Westerterp-Plantenga
Department of Human Biology, Maastricht University, Maastricht, The Netherlands

12 Wochen eukalorische Kost bei gesunden, schlanken Probanden:

Low-Carb: **35 En% Kohlenhydrate**, 30 En% Protein, 35 En% Fett;

High-Carb: **50 En% Kohlenhydrate**, 5 En% Protein, 35 En% Fett;

	Baseline	
	Low-Carb	High-Carb
No. of subjects (M/F)	7 (4/3)	9 (3/6)
Age (y)	23±5	25±5
Baecke total score	9.4±1.0	8.9±1.1
Height (cm)	173±8	170±9
BW (kg)	67.6±6.6	64.5±8.2
BMI (kg/m²)	22.6±2.0	22.3±2.1

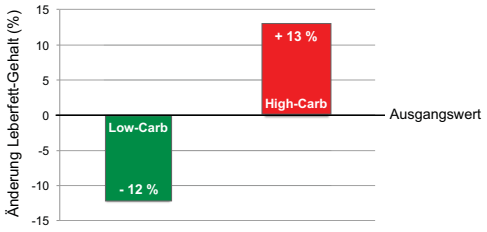
Martens EA, et al. October 2014;9:e109617

Low-Carb vs High-Carb und Leberfettgehalt

12 Wochen iso-energetische Kost bei gesunden, schlanken Probanden

Low-Carb: **35 En% Kohlenhydrate**, 30 En% Protein, 35 En% Fett;

High-Carb: **50 En% Kohlenhydrate**, 5 En% Protein, 35 En% Fett



Martens EA, et al. October 2014;9:e109617

Sucrose-sweetened beverages increase fat storage in the liver, muscle, and visceral fat depot: a 6-mo randomized intervention study[1–3]

Maria Maersk, Anita Belza, Hans Stødkilde-Jørgensen, Steffen Ringgaard, Elizaveta Chabanova, Henrik Thomsen, Steen B Pedersen, Arne Astrup, and Bjørn Richelsen

RCT bei 47 Übergewichtigen, 6 Monate täglich 1 Liter Test-Getränk;
Cola mit 50 % Fruktose/50 % Glukose; Cola-Light; Milch mit 1,5% Fett;

Composition and energy content of the 4 test drinks[1]

	Sucrose-sweetened regular cola	Milk	Aspartame-sweetened diet cola	Water
Carbohydrate (g/100 mL)	10.6	4.7	0	0
Protein (g/100 mL)	0	3.4	<0.1	0
Fat (g/100 mL)	0	1.5	0	0
Energy (kJ/d)	1800	1900	15	0
Volume (mL)	1000	1000	1000	1000
Energy density (kJ/g)	1.8	1.9	0.015	0

[1] The subjects drank 1 L of 1 of 4 test drinks daily for 6 mo.

Maersk M, et al. Am J Clin Nutr 2012;95:283–9.

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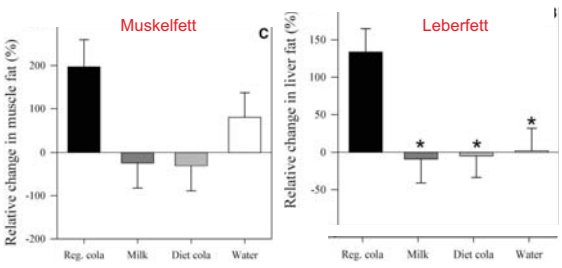

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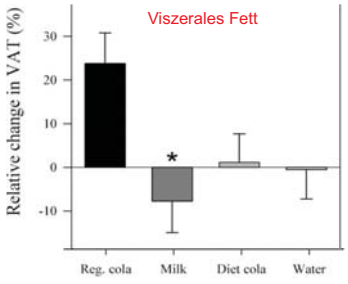

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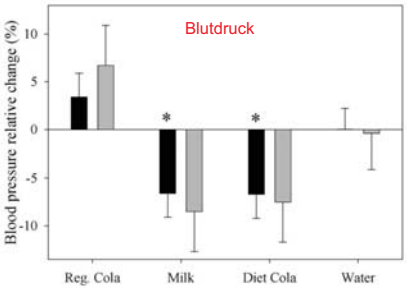


Maersk M, et al. Am J Clin Nutr 2012;95:283–9.

The Journal of Clinical Investigation http://www.jci.org Volume 119 Number 5 May 2009

Consuming fructose-sweetened, not glucose-sweetened, beverages increases visceral adiposity and lipids and decreases insulin sensitivity in overweight/obese humans

Kimber L. Stanhope,[1,2] Jean Marc Schwarz,[3,4] Nancy L. Keim,[5] Steven C. Griffen,[6] Andrew A. Bremer,[7] James L. Graham,[1,2] Bonnie Hatcher,[2] Chad L. Cox,[2] Artem Dyachenko,[3] Wei Zhang,[8] John P. McGahan,[8] Anthony Seibert,[8] Ronald M. Krauss,[9] Sally Chiu,[9] Ernst J. Schaefer,[10] Masumi Ai,[10] Seiko Otokozawa,[10] Katsuyuki Nakajima,[10,11] Takamitsu Nakano,[11] Carine Beysen,[12] Marc K. Hellerstein,[12,13] Lars Berglund,[6,14] and Peter J. Havel[1,2]

[1]Department of Molecular Biosciences, School of Veterinary Medicine, and [2]Department of Nutrition, UCD, Davis, California, USA. [3]College of Osteopathic Medicine, Touro University, Vallejo, California, USA. [4]UCSF, San Francisco, California, USA. [5]United States Department of Agriculture, Western Human Nutrition Research Center, Davis, California, USA. [6]Department of Internal Medicine and [7]Department of Pediatrics, School of Medicine, UCD, Sacramento, California, USA. [8]Department of Radiology, UCD Medical Center, Sacramento, California, USA. [9]Children's Hospital Oakland Research Institute, Oakland, California, USA. [10]Lipid Metabolism Laboratory, Jean Mayer United States Department of Agriculture Human Nutrition Research Center on Aging at Tufts University, and Tufts University School of Medicine, Boston, Massachusetts, USA. [11]Diagnostic Division, Otsuka Pharmaceutical Co., Tokyo, Japan. [12]KineMed, Emeryville, California, USA. [13]Nutritional Sciences and Toxicology, University of California, Berkeley, California, USA. [14]Veterans Affairs Northern California Health Care System, Sacramento, California, USA.

Fruktose- und Glukose-reiche Getränke und ihre Folgen

Study period	Setting	Duration	Diet
Baseline	Inpatient	2 wk	Energy balance diet: 55% complex carbohydrate, 30% fat, 15% protein
Intervention	Outpatient	8 wk	Ad libitum usual diet and sugar-sweetened beverages providing 25% of energy requirement positive energy balance!
Intervention	Inpatient	2 wk	Energy balance diet: 25% sugar-sweetened beverage, 30% complex carbohydrate, 30% fat, 15% protein

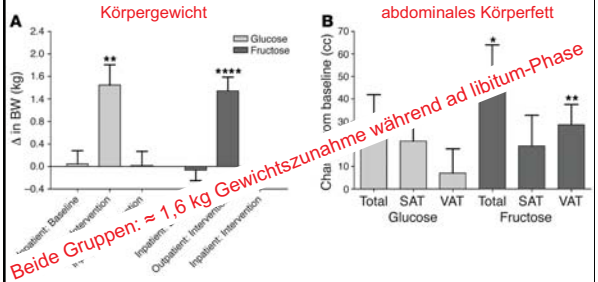
Parameter	Glucose Male (n = 7)	Glucose Female (n = 8)	Fructose Male (n = 9)	Fructose Female (n = 8)
Age (yr)	54 ± 3	56 ± 2	52 ± 4	53 ± 2
Weight (kg)	88.4 ± 2.9	84.0 ± 4.5	89.3 ± 2.9	81.9 ± 4.2
BMI (kg/m²)	29.3 ± 1.1	29.4 ± 1.3	28.4 ± 0.7	30.3 ± 1.0
Waist circumference (cm)	98.9 ± 2.6	91.0 ± 4.0	97.3 ± 3.3	91.8 ± 4.4
Body fat (%)	29.4 ± 1.1	43.2 ± 1.5	28.5 ± 1.3	39.6 ± 2.2
TG (mg/dl)	148 ± 31	145 ± 23	131 ± 21	159 ± 30
Total cholesterol (mg/dl)	179 ± 14	193 ± 10	176 ± 6	198 ± 15
HDL (mg/dl)	36 ± 3	41 ± 3	39 ± 4	41 ± 3
LDL (mg/dl)	124 ± 5	123 ± 11	107 ± 7	124 ± 15
Glucose (mg/dl)	89 ± 2	89 ± 3	88 ± 1	90 ± 1
Insulin (μU/ml)	14.3 ± 3.2	15.6 ± 2.9	16.3 ± 2.5	12.0 ± 1.6

Stanhope KL. J Clin Invest 2009;119:1322–1334;

Fruktose- und Glukose-reiche Getränke und ihre Folgen

Körpergewicht

abdominales Körperfett



Beide Gruppen: ≈ 1,6 kg Gewichtszunahme während ad libitum-Phase

Stanhope KL. J Clin Invest 2009;119:1322–1334

1 Kalorie ≠ 1 Kalorie

Editorial May 2015 EASL JOURNAL OF HEPATOLOGY

Sugar sweetened beverages and fatty liver disease: Rising concern and call to action

Manal F. Abdelmalek[1,*], Chris Day[2]

[1]Duke University School of Medicine, Durham, NC, United States; [2]Newcastle University Medical School, Framlington Place, Newcastle upon Tyne, United Kingdom

The potential danger of SSB, and in particular fructose, and its link with various metabolic disorders including NAFLD has been widely documented and counseling patients, particularly those with pre-existing metabolic syndrome and NAFLD, is prudent from a public health standpoint. Pending further investigation to support or refute the rising concerns, a call to action for health care providers to counsel patients at risk of or with diagnosed NAFLD on avoidance of SSB as a modifiable risk factor for NAFLD acquisition and progression, is warranted.

World Journal of Gastroenterology

Online Submissions: http://www.wjgnet.com/esps/
wjg@wjgnet.com
doi:10.3748/wjg.v19.i8.1166

World J Gastroenterol 2013 February 28; 19(8): 1166-1172
ISSN 1007-9327 (print) ISSN 2219-2840 (online)
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TOPIC HIGHLIGHT

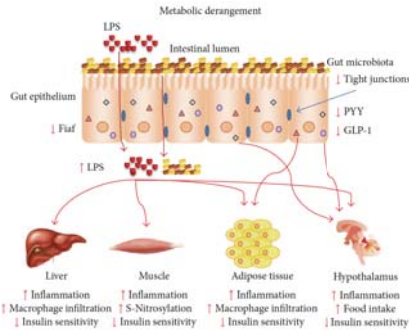
Metin Basaranoglu, MD, PhD, Associate Professor, *Series Editor*

Fructose as a key player in the development of fatty liver disease

Metin Basaranoglu, Gokcen Basaranoglu, Tevfik Sabuncu, Hakan Sentürk

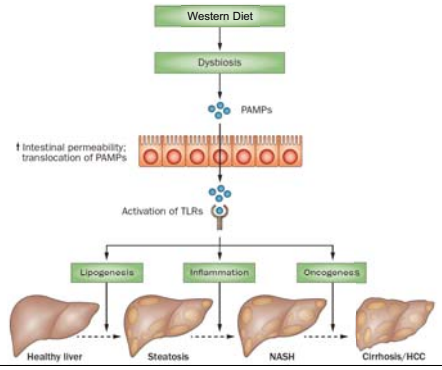
Dysbiose

Dysbiose, Inflammation und NAFLD/NASH



Carvalho BM. Mediat Inflamm 2013; Article ID 986734

Darmbakterien, Dysbiose und Fettleber

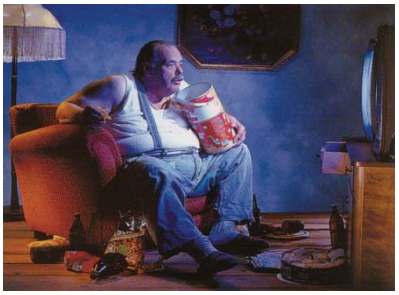


Mehal WZ. Nat Rev Gastroenterol Hepatol 2013;10:637–644

Pause

Prävention der NAFLD

Im Jahre 2015 lebt in mitteleuropäischen Ländern...



...mehr als die Hälfte der Erwachsenen
mit Übergewicht – und sie bewegen sich kaum!

Lebensstil-Facetten zur Prävention der NAFLD:

Vermeidung von Insulinresistenz!

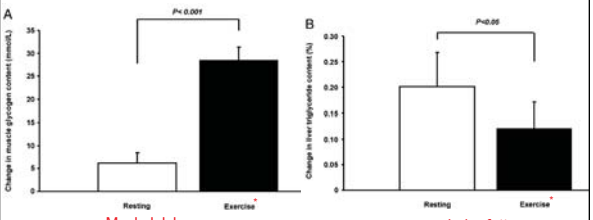
Gleiche Kost für alle?

Raus aus der Kohlenhydratfalle...

Reversal of muscle insulin resistance with exercise reduces postprandial hepatic de novo lipogenesis in insulin resistant individuals

Rasmus Rabøl[a], Kitt Falk Petersen[a], Sylvie Dufour[b], Clare Flannery[a], and Gerald I. Shulman[a,b,c,1]

Departments of [a]Internal Medicine and [c]Cellular & Molecular Physiology, [b]Howard Hughes Medical Institute, Yale University School of Medicine, New Haven, CT 06536



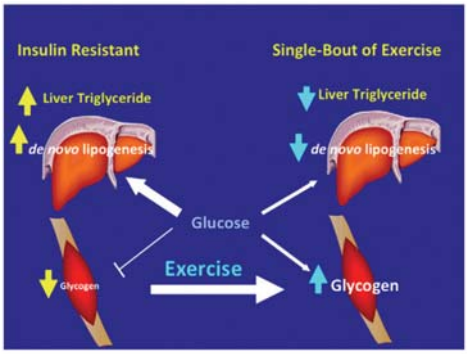
Muskelglykogen

Leberfett

* 3 x 15 min on Nautilus NE 2000 Elliptical Trainer

Rabøl R, et al. PNAS 2011;108:13705-13709

Bei Insulinresistenz müssen Kohlenhydrate erst „verdient" werden!



Rabøl R, et al. PNAS 2011;108:13705-13709

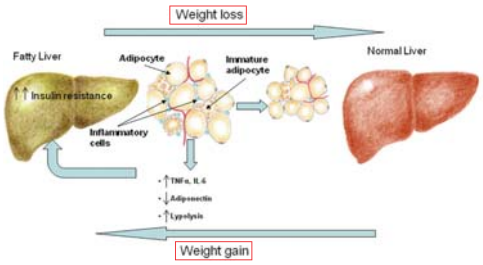
Fazit

Insulinresistente müssen sich Kohlenhydratmahlzeiten erst durch vorherige intensive Muskelarbeit verdienen!

Therapie

Noch gibt es keine etablierte medikamentöse Therapie!

Energierestriktion baut primär ektopes Fett ab!



McCarthy EM, et al. J Acad Nutr Diet 2012;112:401-409

Wie gelingt eine möglichst gezielte und effektive Leberfett-Reduktion?

VLCD bzw. Formula-Diäten bei NAFLD

Reducing Liver Fat by Low Carbohydrate Caloric Restriction Targets Hepatic Glucose Production in Non-Diabetic Obese Adults with Non-Alcoholic Fatty Liver Disease

Haoyong Yu [1], Weiping Jia [1] and ZengKui Guo [2,*]

[1] Department of Endocrinology and Metabolism, Shanghai Jiaotong University Affiliated Sixth People's Hospital, Shanghai Diabetes Institute, Shanghai Clinical Centre of Diabetes,

[2] Endocrine Research Unit, Division of Endocrinology, Diabetes, Metabolism and Nutrition, Department of Internal Medicine, Mayo Foundation, 5-194 Joseph, Rochester, MN 55905, USA

Leberfett und postprandiale hepatische Glukoseproduktion

8 Wochen Diät bei 8 nicht-diabetischen Übergewichtige mit NAFLD

Low-Carb (< 20 g KH/Tag) 800 kcal/Tag + Mikronährstoffsupplement

Yu H, et al. J Clin Med. 2014;3:1050-1063;

NAFLD und postprandiale hepatische Glukoseproduktion

8 Wochen Diät bei 8 nicht-diabetischen Übergewichtigen mit NAFLD

Low-Carb (< 20 g KH/Tag) 800 kcal/Tag + Mikronährstoffsupplement

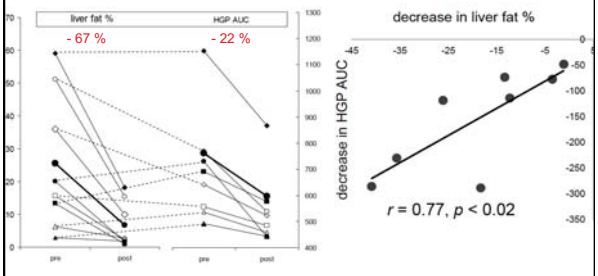
Parameters	Before	After	*p*	
body weight, kg	87.7 ± 3.8	80.9 ± 3.0	0.001	- 7 %
BMI, kg/m^2	32.0 ± 0.7	29.5 ± 0.4	0.0004	
waist, cm	100 ± 2.9	95.0 ± 1.2	0.04	
TG, mmol/L	1.85 ± 0.59	1.11 ± 0.34	0.04	
FFA, mmol/L	0.73 ± 0.03	0.57 ± 0.04	0.01	
HDL, mmol/L	1.28 ± 0.14	1.24 ± 0.11	0.29	
LDL, mmol/L	2.98 ± 0.29	3.14 ± 0.27	0.31	
ASQ fat, cm^2	321 ± 31	244 ± 21	0.005	
visceral fat, cm^2	99 ± 10	65 ± 4	0.007	
liver fat, %	28.8 ± 7.2	9.5 ± 2.7	0.004	- 67 %

Yu H, et al. J Clin Med. 2014;3:1050-1063;

NAFLD und postprandiale hepatische Glukoseproduktion

8 Wochen Diät bei 8 nicht-diabetischen Übergewichtigen mit NAFLD

Low-Carb (< 20 g KH/Tag) 800 kcal/Tag + Mikronährstoffsupplement



Yu H, et al. J Clin Med. 2014;3:1050-1063;

Reversal of type 2 diabetes: normalisation of beta cell function in association with decreased pancreas and liver triacylglycerol

E. L. Lim · K. G. Hollingsworth · B. S. Aribisala · M. J. Chen · J. C. Mathers · R. Taylor

- 11 Patienten mit Typ-2-Diabetes seit < 4 Jahren, 104 kg, BMI 34, HbA1c 7,4%, nü-Glucose 166 mg/dl
- 8 Wochen Diät: 3 x Formula (600 kcal) + Gemüse ad-libitum (200 kcal) Formula-Nährstoffrelation (46 % KH, 33 % EW, 20% F); 60 g KH/Tag
- eingestellt mit oralen Antidiabetika (ohne Glitazone)

Lim EL, et al. Diabetologia 2011:54:2506–2514

Formula-Diät und Diabetes-Remission

Lim EL, et al. Diabetologia 2011:54:2506–2514

Variable	Controls	Baseline	Week 1	Week 4	Week 8
Weight (kg)	101.5±3.4	103.7±4.5	99.7±4.5*	94.1±4.3*	88.4±4.3*†
BMI (kg/m²)	33.4±0.9	33.6±1.2	32.3±1.2*	30.5±1.2*	28.7±1.3*†
Fat mass (kg)	36.2±2.7	39.0±3.5	36.6±3.6*	31.7±3.7*	26.3±4.0*†
ffm (kg)	64.7±3.8	64.7±3.0	63.2±3.1	62.4±3.0*	62.1±3.0*
Waist circumference (cm)	105.0±1.5	107.4±2.2	104.4±2.2*	99.7±2.4*	94.2±2.5*†
Hip circumference (cm)	109.8±2.4	109.5±2.9	108.3±2.7*	105.0±2.6*	99.5±2.6*†
WHR	0.96±0.02	0.98±0.02	0.97±0.02	0.95±0.01	0.95±0.01

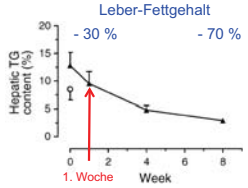
1. Woche

Gewicht: - 4,0 kg
Fettmasse: - 2,4 kg
Taille: - 3,0 cm

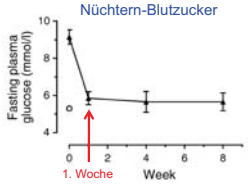
Formula-Diät und Diabetes-Remission

Lim EL, et al. Diabetologia 2011:54:2506-2514

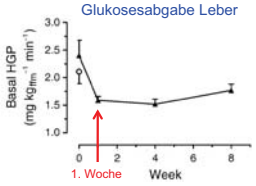
Leber-Fettgehalt



Nüchtern-Blutzucker



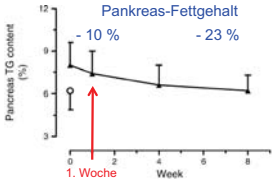
Glukosesabgabe Leber



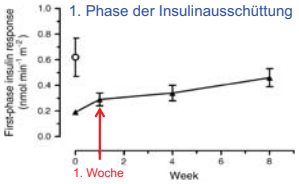
Formula-Diät und Diabetes-Remission

Lim EL, et al. Diabetologia 2011:54:2506–2514

Pankreas-Fettgehalt



1. Phase der Insulinausschüttung



Formula-Diät und Diabetes-Remission

Lim EL, et al. Diabetologia 2011:54:2506–2514

Variable	Controls	Baseline	Week 1	Week 4	Week 8
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Fat mass (kg)	36.2±2.7	39.0±3.5	36.6±3.6*	31.7±3.7*	26.3±4.0*†
ffm (kg)	64.7±3.8	64.7±3.0	63.2±3.1	62.4±3.0*	62.1±3.0*
Waist circumference (cm)	105.0±1.5	107.4±2.2	104.4±2.2*	99.7±2.4*	94.2±2.5*†
Hip circumference (cm)	109.8±2.4	109.5±2.9	108.3±2.7*	105.0±2.6*	99.5±2.6*†
WHR	0.96±0.02	0.98±0.02	0.97±0.02	0.95±0.01	0.95±0.01

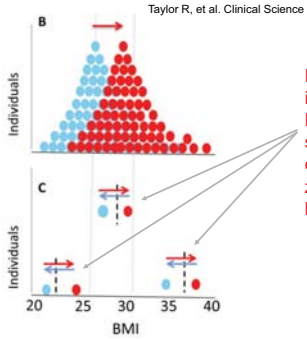
8. Woche

Gewicht: - 15,3 kg
Fettmasse: - 12,7 kg
Taille: - 13,2 cm

Diabetes-Remission mit Formula-Diät

DiRECT-Studie (Diabetes Remission Clinical Trial) Newcastle, UK

Taylor R, et al. Clinical Science 2015;128:405–410



Diese Patienten erreichen ihre persönliche individuelle Metabolische Verfettungs-schwelle und damit die volle endokrine Funktionsfähigkeit zur Glukosekontrolle unab-hängig vom BMI!

The effect of rate of weight loss on long-term weight management: a randomised controlled trial

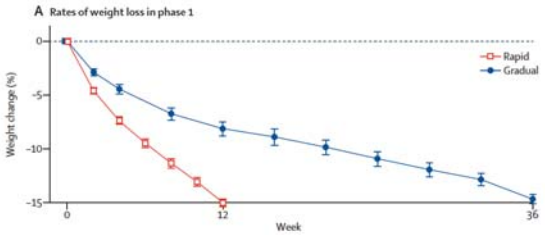
Katrina Purcell, Priya Sumithran, Luke A Prendergast, Celestine J Bouniu, Elizabeth Delbridge, Joseph Proietto

204 Teilnehmer (51 Männer, 153 Frauen); Alter: 18–70 Jahre, BMI 30 – 45;

- Phase 1: 12-wöchige schnelle Gewichtsreduktion vs 36-wöchige langsame Gewichtsreduktion zur Erreichung von 15 % Gewichtsverlust
- Schnell: 450 – 800 kcal/Tag mit drei Formula-Mahlzeiten pro Tag;
- Langsam: 400–500 kcal Defizit pro Tag mit „gesunder Mischkost" (15% E, 25–30% F, 55–60% KH) + Ersatz einer Mahlzeit/Tag mit identischer Formula
- Phase 2: 144-wöchige „Erhaltungsphase"; Ziel: 400–500 kcal Reduktion für alle mit „gesunder" Ernährung (15% E, 25–30% F, 55–60% KH)

Purcell K, et al. Lancet Diabetes Endocrinol 2014;2:954-62.

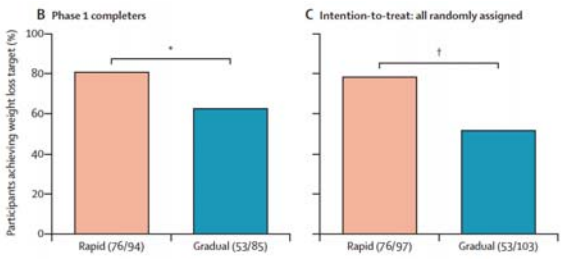
Starke vs moderate Kalorienreduktion bzw. rapides vs langsames Abnehmen



Purcell K, et al. Lancet Diabetes Endocrinol 2014;2:954-62.

Wieviele erreichen ihr Zielgewicht?

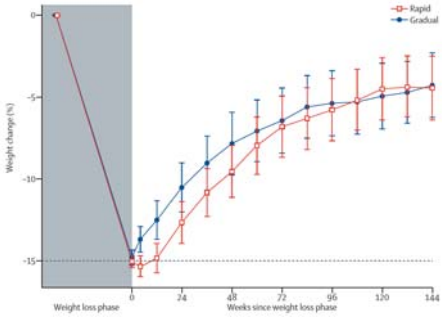
Rapides vs langsames Abnehmen



Purcell K, et al. Lancet Diabetes Endocrinol 2014;2:954-62.

Bedingen „Crash-Diäten" stärkeren Jojo-Effekt?

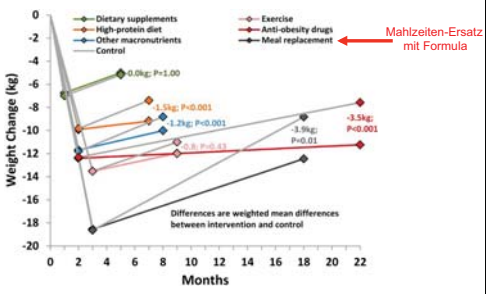
„Erhaltungsphase" mit „gesunder" kalorienreduzierter Mischkost



Purcell K, et al. Lancet Diabetes Endocrinol 2014;2:954-62.

Gewichtserhalt nach einer (Very-)Low-Calorie-Diet

Meta-Analyse: 20 randomisiert-kontrollierte Studien mit 27 Interventions-Armen; n = 3.017;



Johansson K, et al. Am J Clin Nutr 2014;99:14–23.

Kohlenhydratreduktion

Increased De Novo Lipogenesis Is a Distinct Characteristic of Individuals With Nonalcoholic Fatty Liver Disease

Jennifer E. Lambert,[1] Maria A. Ramos–Roman,[2] Jeffrey D. Browning,[3] and Elizabeth J. Parks

[1]Center for Human Nutrition, Divisions of [2]Endocrinology and [3]Digestive and Liver Diseases, University of Texas Southwestern Medical Center, Dallas, Texas

As the understanding of NAFLD has evolved, scientists have questioned whether it is excess lipolysis or lipogenesis that causes fatty liver disease.[55] The present data join the large number of studies currently available showing that elevated lipogenesis, in combination with excess adipose FA release, is a significant contributor to this condition. Excess lipolysis is found in other conditions such as hypertriglyceridemia and obesity, but the distinctive elevation of lipogenesis in NAFLD suggests a causative role. As a result, these data provide strong support for the recent emergence of carbohydrate restriction as a goal of dietary therapy.[56,57] Whether lipogenesis as a target for pharmaceutical development will benefit fatty liver has yet to be determined.

Gastroenterology 2014;146:726–735

Rationales Ernährungsprinzip bei NAFLD und T2DM

Die Umstellung der Energiebereitstellung
von kohlenhydratbetont auf fett-/proteinbetont:

Fettoxidation ⇧ Kohlenhydratoxidation ⇩

Jede starke Kalorienrestriktion reduziert auch die KH-Aufnahme!

Short-term weight loss and hepatic triglyceride reduction: evidence of a metabolic advantage with dietary carbohydrate restriction[1–3]

Jeffrey D Browning, Jonathan A Baker, Thomas Rogers, Jeannie Davis, Santhosh Satapati, and Shawn C Burgess

2 Wochen kalorienreduzierte Diät vs Low-Carb

	Low-calorie diet (n = 9)	Low-carbohydrate diet (n = 9)	P value[2]
Energy intake (kcal/d)	1325 ± 180	1553 ± 517	0.229
Diet composition			
Protein (%)	16 ± 3	33 ± 4	<0.001
Fat (%)	34 ± 6	59 ± 7	<0.001
Carbohydrate (%)	50 ± 4	8 ± 5	<0.001
Protein (g/d)	53 ± 12	121 ± 34	<0.001
Fat (g/d)	49 ± 9	105 ± 44	0.002
Carbohydrate (g/d)	169 ± 33	26 ± 8	<0.001
Fat intake (%)			
Saturated	42 ± 8	37 ± 4	0.134
Monounsaturated	37 ± 2	38 ± 6	0.634
Polyunsaturated	18 ± 7	15 ± 4	0.221

Browning JD, et al. Am J Clin Nutr 2011;93:1048–52

Low-Carb vs Low-Fat zur Leberentfettung

Browning JD, et al. Am J Clin Nutr 2011;93:1048–52

	Low-calorie diet (n = 9)		Low-carbohydrate diet (n = 9)	
	Before	After	Before	After
Age (y)	47 ± 12[1]	—	42 ± 11	—
Sex ratio (F:M)	6:3	—	7:2	—
Liver biopsy				
NAFLD activity score	4.3 ± 1.8	—	5.8 ± 1.6	—
Fibrosis stage	1.3 ± 1.4	—	0.8 ± 0.9	—
BMI (kg/m^2)	34 ± 9	33 ± 9	36 ± 4	35 ± 4
Body weight				
Absolute (kg)	96 ± 21	-4 kg 92 ± 20	97 ± 14	-5 kg 92 ± 15
Fractional (%)	100	96 ± 1	100	95 ± 1
Total cholesterol (mg/dL)	207 ± 29	204 ± 53	212 ± 34	175 ± 24
Triglycerides (mg/dL)	154 ± 65	115 ± 46	215 ± 90	103 ± 34
AST (U/L)	56 ± 28	15 ± 4	50 ± 18	17 ± 2
ALT (U/L)	77 ± 49	81 ± 45	80 ± 51	98 ± 25
AST:ALT ratio	0.8 ± 0.2	0.2 ± 0.1	0.7 ± 0.2	0.2 ± 0.1
Fasting glucose (mg/dL)	122 ± 55	106 ± 21	113 ± 34	87 ± 14
Hepatic TG content (%)				
Absolute	19 ± 10	14 ± 7	22 ± 13	10 ± 7
Fractional	100	-28 % 72 ± 23	100	-55 % 45 ± 14

Dietary Fat and Carbohydrates Differentially Alter Insulin Sensitivity During Caloric Restriction

ERIK KIRK, DOMINIC N. REEDS, BRIAN N. FINCK, MITRA S. MAYURRANJAN, BRUCE W. PATTERSON, and SAMUEL KLEIN

Center for Human Nutrition and Division of Geriatrics and Nutritional Science, Washington University School of Medicine, St Louis, Missouri

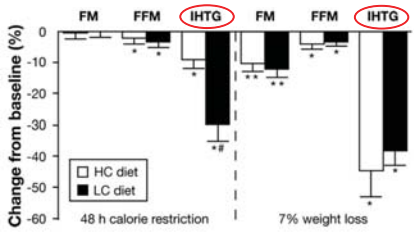
22 Übergewichtige (BMI = 37), randomisiert in 2 Gruppen mit hypokalorischer Diät: ≈ 1100 kcal/Tag;

- Low-Fat/High-Carb: > 180 g KH/Tag vs Low-Carb: < 50 g KH/Tag
- Low-Fat/High-Carb: 65 % KH, 20 % F, 15 % P;
- Low-Carb/High-Fat: 10 % KH, 75 % F, 15 % P;

Kirk E, et al. Gastroenterology 2009;136:1552-1560

High-Carb vs Low-Carb-Reduktionsdiät und Leberfett

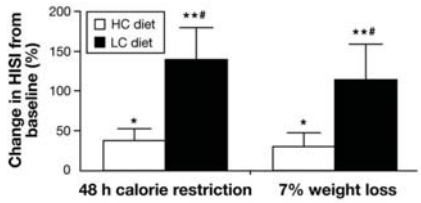
Kirk E, et al. Gastroenterology 2009;136:1552-1560



High-Carb vs Low-Carb-Reduktionsdiät und Leberfett

Kirk E, et al. Gastroenterology 2009;136:1552-1560

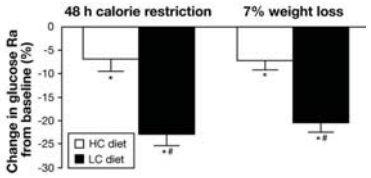
Insulinsensitivität der Leber



High-Carb vs Low-Carb-Reduktionsdiät und Leberfett

Kirk E, et al. Gastroenterology 2009;136:1552-1560

Geminderte Glukoseausgabe ans Blut



Anhebung der Proteinzufuhr

Molkenprotein!

Molkenprotein und NAFLD

Effects of a whey protein supplementation on intrahepatocellular lipids in obese female patients

Murielle Bortolotti [a,d], Elena Maiolo [a,d], Mattia Corazza [a,d], Eveline Van Dijke [a,d], Philippe Schneiter [a,e], Andreas Boss [b,f], Guillaume Carrel [a,e], Vittorio Giusti [c,g], Kim-Anne Lê [a,h], Daniel Guae Quo Chong [b,f], Tania Buehler [b,f], Roland Kreis [b,f], Chris Boesch [b,f], Luc Tappy [a,c,*]

[a] Department of Physiology, University of Lausanne, 7, rue du Bugnon, 1005 Lausanne, Switzerland
[b] Department of Clinical Research/MSM, University of Bern, Postbus 524, Inselspital, P.O. Box 35, 3010 Bern, Switzerland
[c] Service of Endocrinology, Diabetes and Metabolism, CHUV, 1011 Lausanne, Switzerland

- 11 übergewichtige Frauen mit 60 g Molkenprotein/Tag über 4 Wochen zusätzlich zur üblichen Kost
- nach 4 Wochen Molkenprotein-Supplement:
  - Leberfettgehalt: - 21 %
  - Serum Triglyceride: - 15 %
  - Serum Cholesterin: - 7 %
  - fettfr. Körpermasse: + 4 %

Bortolotti M, et al. Clinical Nutrition 2011;30:494-498

Eiweiß in der Adipositas-Therapie

Erhöhte Eiweißzufuhr bewirkt:

- Sättigung ↑
- Sattheit ↑
- Thermogenese ↑
- fettfreie Masse bei negativer Energiebilanz ↑

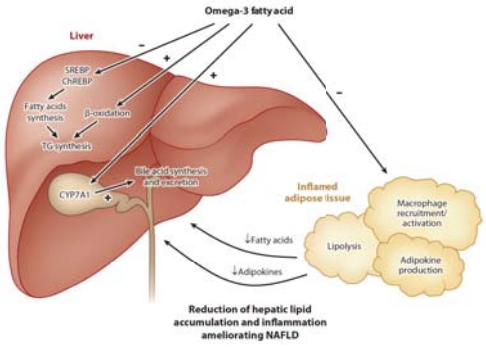
Modifikation der Fettzufuhr

n-3 PUFA + MUFA

Leberfasten! – Ernährungstherapie der NAFLD

Omega-3-Fettsäuren

Omega-3-Fettsäuren in der Therapie der NALFD



Scorletti E, Byrne CD. Annu Rev Nutr 2013;33:231–48

Omega-3 supplementation and non-alcoholic fatty liver disease: A systematic review and meta-analysis

Helen M. Parker[1], Nathan A. Johnson[1,3], Catriona A. Burdon[1], Jeffrey S. Cohn[2], Helen T. O'Connor[1,3], Jacob George[4,*]

[1]Discipline of Exercise and Sport Science, University of Sydney, Australia; [2]Nutrition and Metabolism Group, Heart Research Institute, Sydney, Australia; [3]Boden Institute of Obesity, Nutrition and Exercise, University of Sydney, Australia; [4]Storr Liver Unit, Westmead Millennium Institute and Westmead Hospital, University of Sydney, Australia

Authors, year [Ref.]	Effect size		p
	Hedge's g	95% CI	
Capanni et al., 2006 [45]	-0.938	-1.559, -0.316	0.003
Sofi et al., 2010 [53]	-0.811	-1.948, 0.326	0.162
Spadaro et al., 2008 [54]	-1.709	-2.460, -0.958	0.000
Zhu et al., 2008 [48]	-0.626	-0.971, -0.281	0.000
Cussons et al., 2009 [56]	-1.718	-2.326, -1.109	0.000
Tanaka et al., 2008 [47]	-0.476	-0.894, -0.058	0.026
Chen et al., 2008 [55]	-0.731	-1.441, -0.021	0.043
	-0.965	-1.348, -0.582	0.000

Effect size and 95% CI

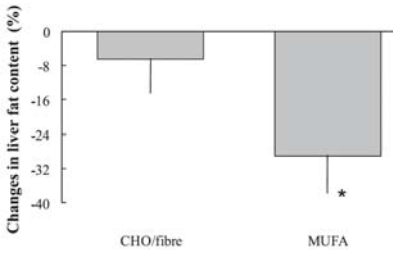
-3.00 -1.50 -0.00 1.50

Favors PUFA Favors control

Pa

Einfach ungesättigte Fette in der Therapie von NAFLD

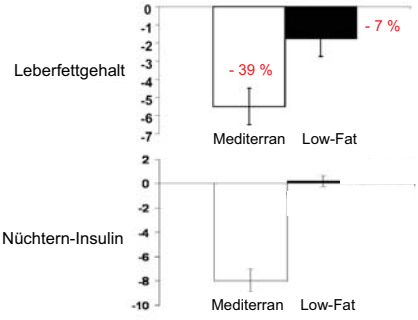
n = 45; randomisiertes Cross-over à 8 Wochen;
eukalorisch: KH-betont+Ballaststoff-reich vs MUFA-reiche Diät



Bozzetto L, et al. Diabetes Care 2012;35:1429–1435

Eukalorische mediterrane Kost vs Low-Fat/High-Carb

n = 12; Cross-over 6 Wochen eukalorisch, ohne Gewichtsreduktion



Ryan MC, et al. J Hepatol 2013;59:138-43

Ernährungstherapie der NAFLD

Die 5 Grundprinzipien:
- kalorienreduziert
- kohlenhydratreduziert
- eiweißbetont
- fettmodifiziert
- ballaststoffreich

Nährstoffspezifische Aspekte:
- Omega-3-Fettsäuren
- Vitamin E
- Cholin
- β-Glukan
- Inulin
- Carnitin
- Taurin
- Resveratrol
- Quercitin
- Koffein
- Kaffeesäure
- Kurkuma

„Leberfasten“ in der Therapie von NAFLD metabolischem Syndrom und Typ-2-Diabetes

Mahlzeiten-Ersatz-Konzept mit leberspezifischer Formula + kohlenhydrat-reduzierter, mediterraner Diät

Leberfasten® + LOGI in der Ernährungstherapie

bei NAFLD, metabolischem Syndrom, PCO-Syndrom, Gestationsdiabetes, Typ-2-Diabetes etc.

+

Leberfasten®

- 2 Wochen VLCD mit 3 x täglich Meal Replacement (Hepafast® => kohlenhydratarm, proteinreich, ballaststoffreich mit Milch (1,5 % Fett) zubereitet
- 780 kcal pro Tag
- ergänzt mit Rohkost, Salat, stärkearmem Gemüse und 1 TL MUFA-reichem Pflanzenöl, ca. 100-150 kcal

8 Uhr:
HEPAFAST®

13 Uhr:
HEPAFAST® + Gedünstetes Gemüse, Suppe, Salat oder Rohkost mit Dipp

18 Uhr:
HEPAFAST® + Gedünstetes Gemüse, Suppe, Salat oder Rohkost mit Dipp

Leberfasten®

Langfristiges Schema

Intensivphase: 2 Wochen – 3 x HEPAFAST + Rohkost + Öl ≈ 800-950 kcal/Tag

Reduktionsphase: 8-10 Wochen – 2 x Hepafast + 1 x LOGI-Mahlzeit ≈ 1.000-1.100 kcal/Tag

Stabilisierungsphase: 4 Wochen – 1 x Hepafast + 2 x LOGI-Mahlzeit ≈ 1.300-1.600 kcal

Erhaltungsphase: Dauerhaft – Ernährung nach LOGI ≈ 1.500-2.500 kcal/Tag

Regelmäßige Auffrischung: 1 x im Monat: 3 Tage à 3 x HEPAFAST/Tag

ALBIS Dr. Dirk Padberg, Jägerweg 16, 24941 Flensburg, Tel.: 0461-8400 550

Laborblatt vom 24.04.2015

[redacted], geb. [redacted]

Seite 1 von 1

			30.03.2015	29.01.2015	22.12.2014	28.11.2014	11.11.2014	07.11.2014
CREATININ	0.84 - 1.25	mg/dl	0,98	0,94	0,88			1,08
HARNSTOFF	19.0 - 44.0	mg/dl	47,8 (+)	46,6 (+)	40,0			25,2
GLUCOSE	74 - 106	mg/dl	101	107 (+)	100	103	189 (+)	183 (+)
GGT	< 55	U/l	17	20	18			32
CHOLESTERIN	140 - 250	mg/dl	146	160	140			202
TRIGLYCERIDE	< 200	mg/dl	72	88	61			193
HDL CHOLESTERIN	...	mg/dl	42 (-)	41 (-)	41 (-)			38 (-)
KALIUM	3.6 - 5.4	mmol/l	4,4	5,1	4,8			4,7
NATRIUM	135 - 145	mmol/l	141	140	144			140
HBA1C	...	%	6,1 (+)	6,6 (+)	8,3 (+)			11,7 (+)
HBA1C ALTERNATIV	26 - 42	mmol/mol Hb	43,2 (+)	48,6 (+)	67,2 (+)			104,4 (+)
HARNSAEURE	3.6 - 7.0	mg/dl	6,6	6,6	6,9			4,0
GPT	< 45	U/l	21	30	35			62 (+)
LEUKOZYTEN	4.0 - 10.0	G/l	7,3	6,5	9,7	5,2		6,2
ERYTHROZYTEN	4.5 - 6.0	T/l	5,5	5,5	5,4	5,2		5,4
HAEMOGLOBIN	13.0 - 18.0	g/dl	16,4	15,9	15,6	15,0		16,0
HAEMATOKRIT	0.40 - 0.47	l/l	0,47	0,46	0,45	0,43		0,45
MCH	27.0 - 33.0	pg/Ery	29,9	29,1	29,1	29,1		29,5
MCHC	32.0 - 37.0	g/dl	35,3	34,6	34,4	34,6		35,7
MCV	80.0 - 96.0	fl	84,7	84,1	84,5	83,9		82,7
THROMBOZYTEN	150 - 450	G/l	244	258	288	274		269
C REAKTIVES PROTEIN	< 5.0	mg/l				negativ		
NEUTROPHILE	47 - 72	%	57	49	63	38 (-)		53
LYMPHOZYTEN	25 - 40	%	31	38	25	45 (+)		32
MONOZYTEN	2 - 12	%	9	9	10	12		11
EOSINOPHILE	< 4	%	3	3	2	4		3
BASOPHILE	< 1	%	0	0	0	1		1
GOT	< 35	U/l	21	26	21			31
CALCIUM	2.20 - 2.65	mmol/l	2,33	2,31	2,39			2,42
EISEN	12.5 - 32.2	umol/l	14,0	10,6 (-)	7,7 (-)			11,5 (-)
PHOSPHOR ANORGANISCH	0.81 - 1.45	mmol/l	1,31	1,18	1,21			0,97
BILIRUBIN GESAMT	< 1.10	mg/dl	0,60	0,56	0,60			0,48
GLOM FILT RATE MDRD	...	kA	88	93	100			79 (-)
ALKAL PHOSPHATASE	30 - 120	U/l	58	59	66			52
AMYLASE	< 100	U/l	52	52	62			42
CHOLINESTERASE	4620 - 11500	U/l	10277	11489	11342			13447 (+)
LDH	< 248	U/l	124	157	123			145
LDL CHOLESTERIN DIRE	...	mg/dl	93	125	100			166 (+)
GESAMT EIWEISS	66 - 83	g/l	69,5	70,5	74,5			68,3
VITAMIN D 25 OH	...	nmol/l	99	118	119			12 (-)
ALBUMIN ELPHO	56.4 - 66.8	%	62,0	62,9	62,3			61,7
ALPH 1 GLOBUL ELPHO	3.2 - 4.8	%	4,0	3,5	4,3			4,5
ALPH 2 GLOBUL ELPHO	7.2 - 11.0	%	7,7	7,3	8,5			9,2
BETA 1 GLOBUL ELPHO	5.2 - 7.5	%	6,2	6,1	6,2			6,3
BETA 2 GLOBUL ELPHO	3.4 - 6.6	%	5,1	4,9	5,5			5,9
GAMMA GLOBUL ELPHO	10.2 - 18.7	%	15,0	15,3	13,2			12,4

Kasuistik

Patientin 45 Jahre, BMI 27, Bauchumfang 97 cm, FLI = 66

07.11.2014

HbA1c = 11,7 %

Therapie: 4 Wochen intensiv Leberfasten ohne Medikamente

22.12.2014

HbA1c = 8,3 %

30.03.2015

HbA1c = 6,1 %

Diskussionsforum zum „Leberfasten“ auf:

www.logi-methode.de

im LOGI-Forum unter:

„LOGI und Leberfasten“

mehr Infos unter:

www.leberfasten.de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LEBERFASTEN
NACH DR. WORM®
Save the Date!
Die Fortbildung
mit den Experten
persönlich
Jetzt anmelden und Expertenwissen sichern!
NUR 59,- CHF inkl. MwSt.
JA, ich bin dabei! Ich nehme an folgender Fortbildung „Leberfasten nach Dr. Worm®" zum Preis von nur 59,- CHF inkl. MwSt. teil.
Fr., 06. November 2015 in Olten
16:00 bis 20:00 Uhr
Termine 2016 im Überblick (Bitte ankreuzen)
☐ Sa., 16. April Nürnberg 10:00 bis 17:00 Uhr
☐ Sa., 11. Juni Wien 10:00 bis 17:00 Uhr
☐ Sa., 16. Juli Hamburg 10:00 bis 17:00 Uhr
☐ Sa., 17. September Köln 10:00 bis 17:00 Uhr


Dr. Nicolai Worm
Menschen stopf Leber
Die verharmloste Volkskrankheit Fettleber
Das größte Risiko für Diabetes und Herzinfarkt
Leberfasten nach Dr. Worm
VOLKS KRANKHEIT FETT LEBER
VERKANNT VERHARMLOST HEILBAR
TRIAS