The Ketogenic Diet

Edwin Cox, M.D.
OLLI

Actually, Ketogenic Diets

There isn't just one ketogenic diet

- An ensemble of diets, based on treatment goal

One is designed for "fast fat shedding" (AKA weight loss)

Another is designed for control of epilepsy

Yet others may be effective for control of Type II diabetes, hypertension, coronary heart disease (hyperlipidemia), acne, polycystic ovarian syndrome (PCOS), even neurologic diseases and cancer

Ketogenic Diet Applications

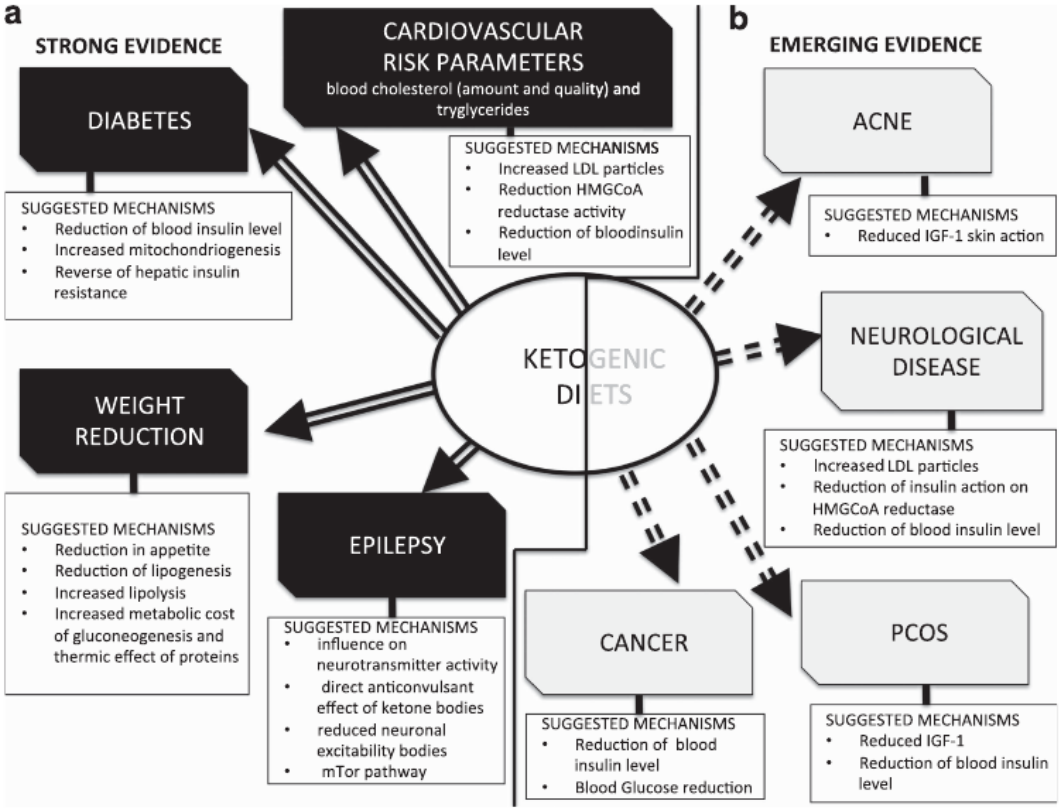


Figure 1. Suggested mechanisms for the therapeutic action of ketogenic diets in pathologies for which there exists strong (**a**) and emerging (**b**) evidence.

Ketogenic Diets Defined

Common denominator: Very low carbohydrate (VLC) consumption (<20 gm/day)

Triggers a switch to use fats as the primary energy source

The CARB-OFF diet?

How do we get fat?

We get fat when we repeatedly, day after day, consume more fuel (calories, energy) than the body needs

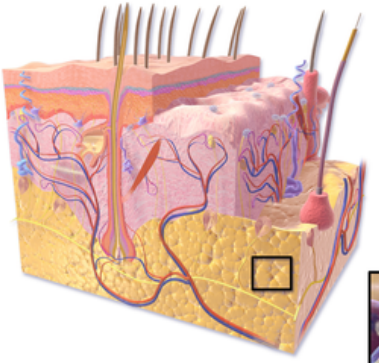
- Excess fuel not wasted; stored in fat cells (adipocytes) for future use

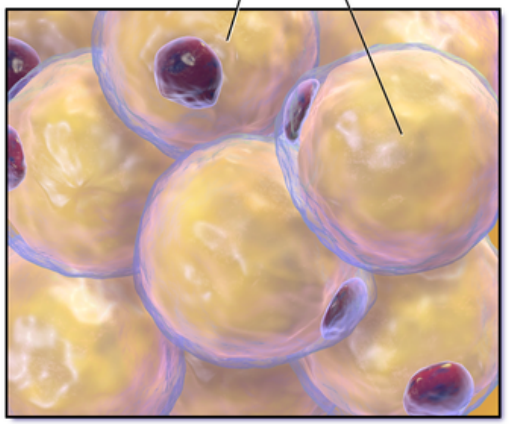
Not necessarily a bad thing in itself

- Mechanism to save up fuel for times when fuel is unavailable
- Likely had strong survival value

However, we live in an unprecedented time where food shortage is rare, as least in developed nations

- Too much cheap, alluring fuel in the form of sweets and starches
- We are in a growing epidemic of counter-productive energy storage, leading to distress and disease
- The best approach is prevention: education aimed at healthy nutrition





Adipose Tissue

Why ketogenic diets?

Impressive results in treating obesity in Italy and Spain with KDs are under-utilized in the U.S.

- Many obese individuals desperately seeking durable weight loss could benefit if these KD options were more available and publicized
- The other main option, bariatric surgery, is over-utilitized, and patients are not offered non-invasive opportunities

My hope is that discussing these methods will lead to demand for them and motivate health systems to offer them

Is this the Atkins diet?

The Atkins diet emphasizes low carbohydrate consumption, replacement with dietary protein and fats

Atkins diet, as it is commonly practiced, is sufficiently ill-defined that it may or may not produce ketosis

- If so, results may match other defined ketogenic approaches
- If not, results may be disappointing, less durable or take much longer to achieve

Is this the Atkins diet?

Popular belief: You can eat as much as you want of protein and fat on the Atkins diet; as long as it isn't carbs, it's "on the table"

Another popular belief: You should continue a low carbohydrate diet as your maintenance diet

- Risks consuming too little fiber to maximize its benefits

More productive to discuss specific elements of the ketogenic approach than to apply labels, such as Atkins

- Some Atkins materials may be useful guides to achieve a ketogenic diet

Ketogenic diet

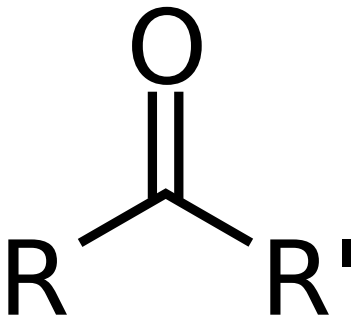
Keto-: refers to ketones, a category of chemical compounds

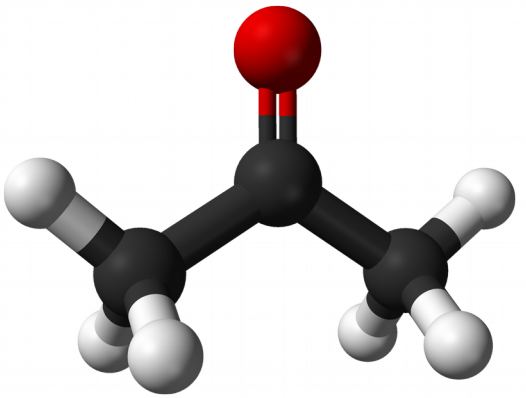
- Ketones have a carbon, double-bonded to oxygen, flanked by carbon-containing "chains" (R, R') on either side

-genic: generating

Ketogenic diet: a diet that generates large amounts of ketones, producing the state of "ketosis"

The simplest ketone, shown below, is acetone





Ketosis defined

Ketosis is the ketogenic state, that is, the metabolic state in which ketones make up a major energy source

Ketosis begins after a prolonged (>24 hours) very low carbohydrate intake, at which point glucose is no longer directly available from dietary carbohydrates and liver glycogen has been depleted

When inadequate glucose supply is sensed, the liver begins to convert fat – specifically, fatty acids - into "ketone bodies" (KBs): acetoacetate, acetone and 3-hydroxybutyric acid

Implications of ketosis

Free fatty acids (FFA) cannot directly fuel the brain because they are blocked by the blood-brain barrier

However, KBs can cross the blood-brain barrier into the brain, where they are a fully functioning substitute for glucose to fuel the brain

KBs can also be used as fuel by other organs - except the liver - in lieu of glucose

Dietary fat is the first source of FFA used by the liver

Implications of ketosis

If dietary fat is insufficient to make enough KBs to meet the body's needs, fatty acids are mobilized from adipose (fat) tissue stores to the liver, to serve as input to the production of KBs

- The normal role of fat storage is to serve as a source of fuel during severe food shortages, such as famine
- Ketosis is the physiologic response to starvation, keeping us alive when there is no food to eat
- Possibly our ancestors survived while their contemporaries died due to superior ability to store fat during times of abundant food supply

Implications of ketosis

A key aspect of ketosis is that a certain amount of glucose is necessary to drive the liver conversion of fatty acids to KBs

- In the absence of carb-derived glucose, the glucose is derived from protein
- If that protein is not provided in the diet, it comes from breaking down muscle
- Provision of sufficient dietary protein accompanying carb restriction will prevent breakdown of muscle - "protein-sparing"

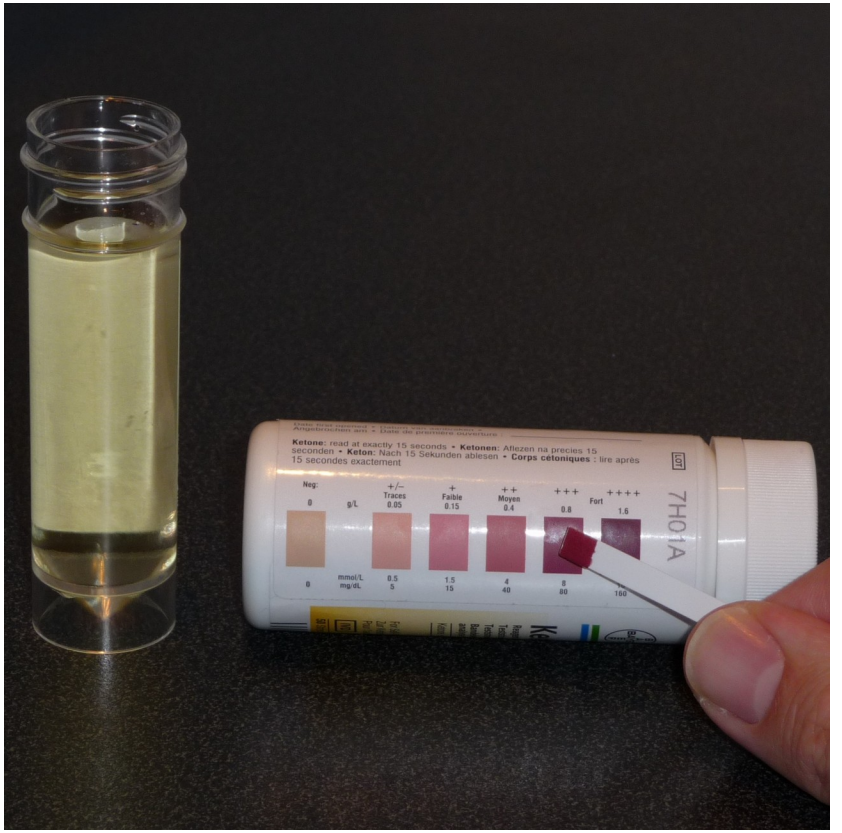
Monitoring ketosis

How do you know if you are in ketosis?

Ketone bodies pass into the urine based on their blood level

Dip a Ketostix into a urine sample

If it changes color, there are significant amounts of ketone bodies present



M.D.'s fear of ketosis

When ketosis is mentioned to most doctors, there is an instant recoil in horror

Diabetic ketoacidosis (DKA) is the state into which a diabetic slips when the amount of insulin is grossly insufficient; serious, sometimes life-threatening

- High levels of KBs are a hallmark
- However, major differences – acidosis, high glucose in DKA; not in physiologic ketosis

Table 1. Blood levels during a normal diet, ketogenic diet and diabetic ketoacidosis[11]

Blood levels	*Normal diet*	*Ketogenic diet*	*Diabetic ketoacidosis*
Glucose (mg/dl)	80–120	65–80	>300
Insulin (μU/l)	6–23	6.6–9.4	≅ 0
KB conc (mM/l)	0.1	7/8	>25
pH	7.4	7.4	<7.3

M.D.'s fear of ketosis

In our time of plenty, doctors rarely encounter physiologic ketosis but often see DKA

- Since ketosis in DKA is bad, common sense suggests that the ketosis in VLC diet *must* be a slippery slope that easily leads to trouble
- Wrong!

Table 1. Blood levels during a normal diet, ketogenic diet and diabetic ketoacidosis[11]

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M.D.'s fear of fasting

Protein-sparing modified fast (PSMF) was a trendy weight loss strategy in the 1960-70s

A number of reports documented sudden deaths associated with PSMF

- Common denominator was prolongation of QT interval, torsades de pointes on the EKG, abnormalities associated with sudden death
- Mechanism was not clearly defined

Risk factors were low quality of protein, lack of electrolyte supplementation (potassium, magnesium), and long duration of fast

Sudden cardiac death has not been seen with contemporary ketogenic diets

Three KD fat shedding diets

Cappello

- Italy, initially Rome and now several smaller cities
- Ketogenic enteral nutrition (KEN): Small feeding tube with pump to administer 24 hr/d x 10 days per cycle, at home
- Cycle may be repeated after rest period; average 2.5 cycles

Paoli

- Italy
- Oral VLCKD x 20 days, LCD X 20 days, Mediterranean diet x 4 mo
- Repeat one additional cycle
- KEMEPHY proprietary supplement of herbs and electrolytes

Moreno

- Spain
- Randomized trial: Oral VLCKD until 80% target weight loss achieved, low calorie until further 20% target achieved, then maintenance diet vs. low calorie diet
- PronoKal proprietary sachets of high protein foods and electrolytes

All three report weight loss typically 10% or more, maintained for a year

Ketogenic enteral nutrition

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- Cycle may be repeated after rest period; average 2.5 cycles

Cappello & KEN

Prof. Gianfranco Cappello at University of Rome 'La Sapienza'

- Surgeon, specialist in enteral and intravenous nutrition for 40 years
- Enteral nutrition for weight loss began 2006 (by chance!)
- Program grew rapidly by word of mouth; has never been advertised in Italy
- At last update, he and staff have treated 25,000 patients, who have shed 320 tons
- No major complications have occurred

Before and after KEN

KEN Orientation

Body composition analysis

Fat mass, body cell mass, total body water evaluated with impedance plethysmography

KEN tube placement

KEN tube

KEN tube and pump

KEN experience

Patients go about their normal activities

Decrease or discontinue diabetic and blood pressure medications

- Blood sugar and blood pressure predictably reduced on KEN

Supplemented with medication to suppress acid secretion and laxative to avoid constipation

Fluids *ad libitum* – coffee, tea, water – as long as they contain no carbs

Side effects: Tiredness, heartburn and acid reflux, constipation; no major complications

Tube feeding formula

Table 2 (g%) Composition of the nutrition powder (K1000®)

Proteins	90.0
Carbohydrates	1.80
Fats	0.80
Calcium	0.40
Potassium	1.00
Phosphorus	0.20
Sodium	0.10
Magnesium	0.05

Table 2 Composition of K1000® (Nutrimed 2000 srl, Italy), the nutrition feed used for the KEN, made of whey proteins enriched with potassium chloride, lecithin and bovine hydrolyzed collagen.

Costs of KEN

Initial visit: € 167

End of treatment visit: € 30

Followup visit: € 122

Protein solution, one cycle: € 60

Pump: No charge if returned

Costs of KEN partially or fully offset by avoided cost of food consumption

KEN Results

	Baseline (kg)	Followup (kg)	Change (kg)	Regain (kg)
Body weight	101.4	91.2	-10.2	+1.57
Fat mass	40.9	35.1	-5.8	
Body cell mass	31.6	29.4	-2.2	
Total body water	43.5	40.1	-3.4	
Body mass index	36.5	32.8	-3.7	

Average treatment was $2\frac{1}{2}$ cycles per patient

More than 25,000 treated

Benefits of KEN

Cosmetic

Metabolic syndrome +/or diabetes remediation; reduction of medication

Blood pressure reduction or normalization; reduction of medication

Reduction of cardiac risk factors – hyperlipidemia

Reduced stress on knees and hips, improved mobility

Reduce risk for surgical procedures, including bariatric surgery and orthopedic procedures

KEN web site

http://www.gianfranco-cappello.it/epazienti-obesi.html

Especially interesting is the large series of before-and-after photographs

KEN in the U.S.

Kediet.com

Oliver DiPietro, M.D.

- Bay Harbor Islands, FL

12 licensee practitioners across U.S.

- Dr. Wickham Simonds, Durham

Proprietary formula

Basic scheme based on and similar to Cappello KEN

Cost ??

Very low carb ketogenic diet

Paoli

- Italy
- Oral VLCKD x 20 days, LCD X 20 days, Mediterranean diet x 4 mo
- Repeat one additional cycle
- KEMEPHY proprietary supplement of herbs and electrolytes

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Article

Long Term Successful Weight Loss with a Combination Biphasic Ketogenic Mediterranean Diet and Mediterranean Diet Maintenance Protocol

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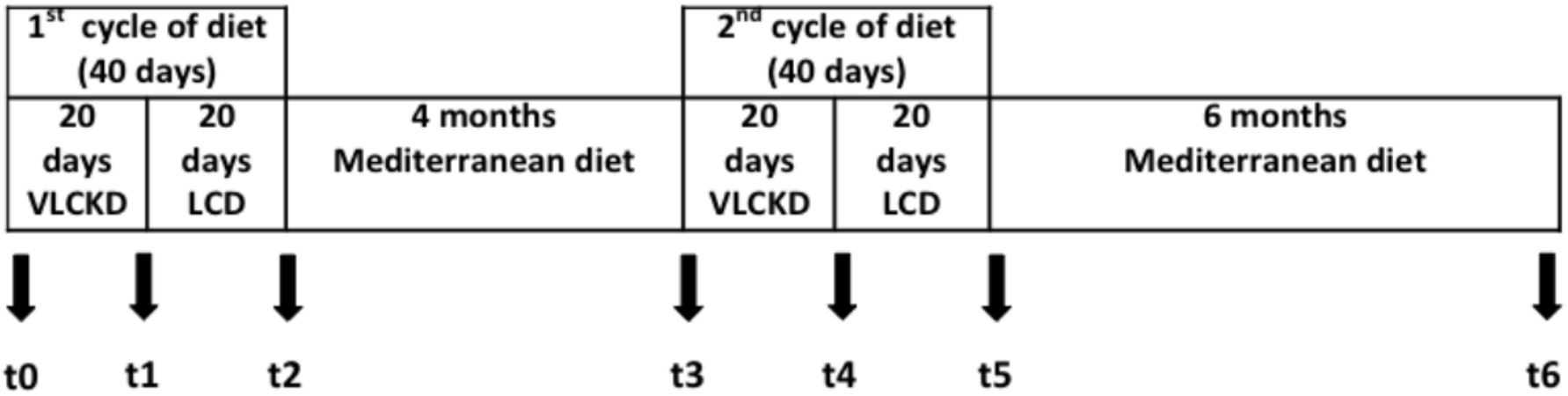
[2] Sport and Exercise Sciences Research Unit, University of Palermo, Palermo 90146, Italy;

Paoli: VLCKD/LCD/Med. diet



Paoli

Subjects: Age 25-65, BMI > 30, healthy

89 eligible, 81 evaluable, 68 completed 1 yr.

Permitted: Beef, veal, poultry, fish, cold cuts, eggs, seasoned cheese

Supplement: Specialty meals – protein blend from plant sources, herbal extracts, MVI

Avoided (ketogenic phase): Alcohol, pasta, bread, rice, milk, yogurt

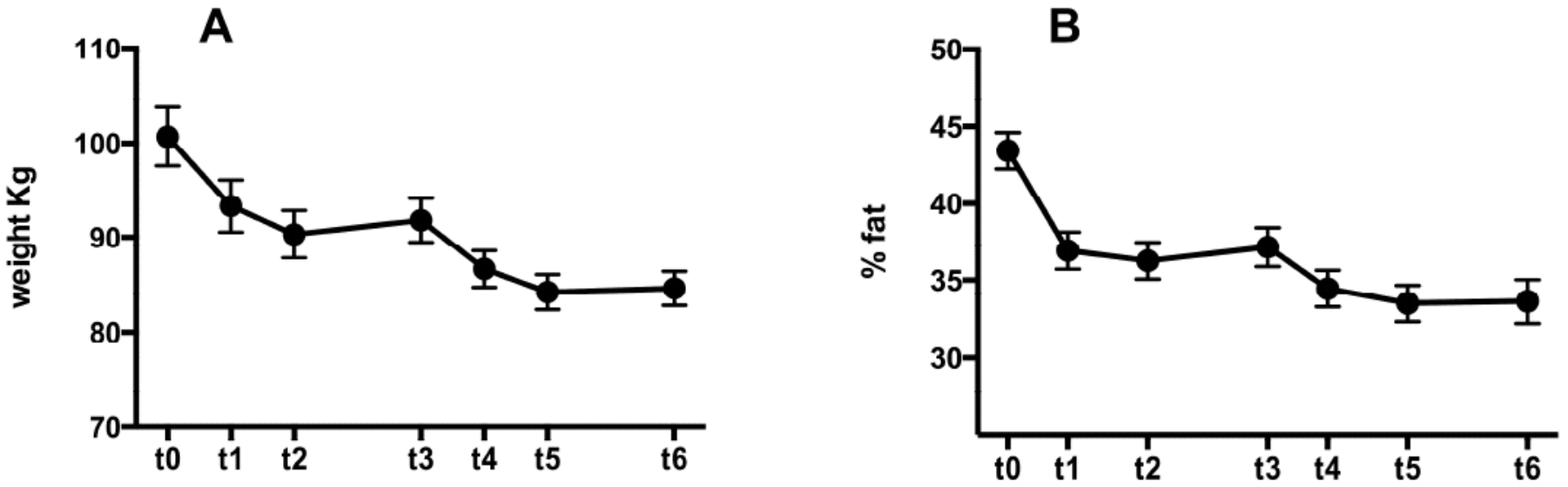
Mediterranean diet

Food	Goal
Mediterranean diet	
Recommended	
Olive oil*	≥4 tbsp/day
Tree nuts and peanuts†	≥3 servings/wk
Fresh fruits	≥3 servings/day
Vegetables	≥2 servings/day
Fish (especially fatty fish), seafood	≥3 servings/wk
Legumes	≥3 servings/wk
Sofrito‡	≥2 servings/wk
White meat	Instead of red meat
Wine with meals (optionally, only for habitual drinkers)	≥7 glasses/wk
Discouraged	
Soda drinks	<1 drink/day
Commercial bakery goods, sweets, and pastries§	<3 servings/wk
Spread fats	<1 serving/day
Red and processed meats	<1 serving/day

Table 4 Blood biomarker, anthropometric and body composition values, separated for male and female, before and after 6 weeks KEMEPHY diet. Values are expressed in mean and SD.

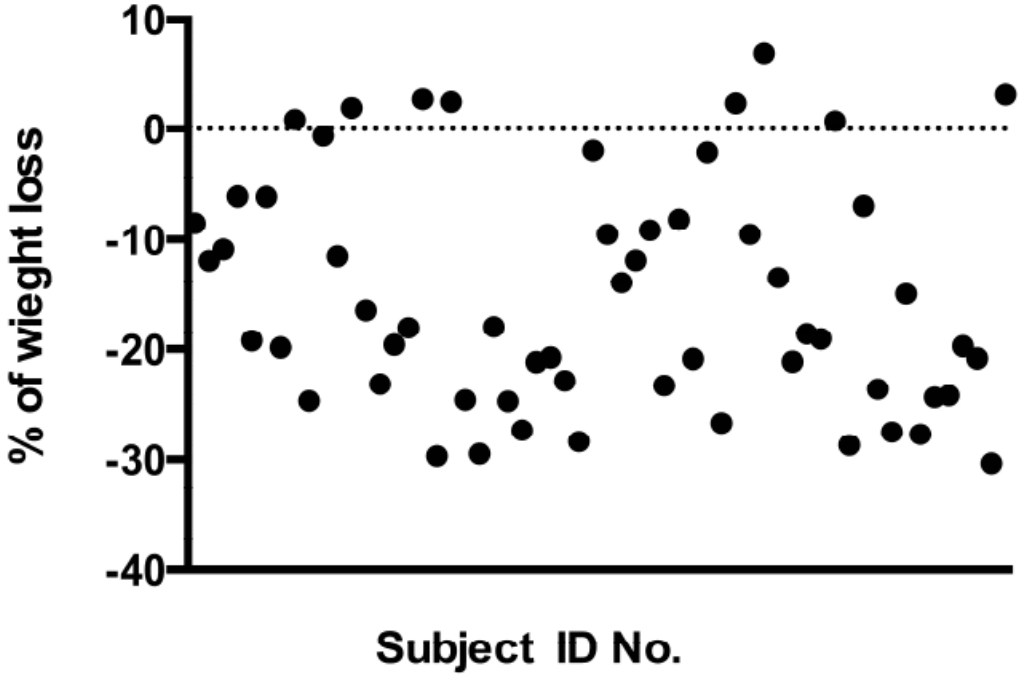
	Pre diet female	Post diet female	Pre diet male	Post diet male
BUN (mg/dl)	33.4 ± 9.5	33.2 ± 8.7	35.2 ± 6.0	33.8 ± 7.0
Uric acid (mg/dl)	5.0 ± 1.3	5 ± 1.2	4.8 ± 1.3	5.0 ± 1.3
VES (mm/hour)	14 ± 7.3	12.7 ± 7.6	16 ± 7.3	14.4 ± 6.3
Creatinine (mg/dL)	0.84 ± 0.15	0.77 ± 0.11	0.83 ± 0.2	0.85 ± 0.2
Total Cholesterol (mg/dl)	206.2 ± 41.4	182.8 ± 34.3	199.2 ± 29.8	176.9 ± 26.1
HDLc (mg/dl)	46.7 ± 7.2	52.6 ± 9.5	43.9 ± 8.5	50.1 ± 9.1
LDLc (mg/dl)	151.8 ± 28.3	137.1 ± 24.8	140.9 ± 32.9	130.4 ± 25.9
TG (mg/dl)	119.9 ± 60.3	94.2 ± 41.8	114.1 ± 61.8	93.9 ± 46.2
ALT (U/l)	20.5 ± 10.9	17.3 ± 5.1	18.4 ± 4.6	19.1 ± 6.8
AST (U/l)	18.5 ± 5.4	17.1 ± 4.7	17.8 ± 3.8	17 ± 5.1
GGT (U/l)	20.5 ± 10.9	17.3 ± 5.1	21.5 ± 11.7	15.4 ± 4.1
Glucose (mg/dl)	95.7 ± 12.5	90.5 ± 9.8	95.9 ± 11.2	90.6 ± 8
Weight Kg	82.6 ± 12.7	76.3 ± 12.1	102.4 ± 22.2	93.4 ± 21
BMI (Kg/m^2)	31 ± 4.8	28.7 ± 4.6	33.6 ± 6.2	30.6 ± 5.8
% Fat	42.3 ± 6, 8	36 ± 6, 9	37 ± 4.3	30.6 ± 4.1
Waist circumference cm	103.5 ± 14	94, 3 ± 10.3	120.8 ± 15.1	109.7 ± 14.1
Hip circumference cm	114.9 ± 11.6	107.2 ± 10.5	117.3 ± 9.9	111.2 ± 10.4

Paoli - Results



Paoli - Results

Figure 3. Changes in weight (% of change) of each subject (*t*6 compared to *t*0). Basal value is represented by the line zero. Each circle represents a single subject.



Paoli – Nutrition data

Table 1. Characteristics of diets (data are expressed as mean and SD).

Macronutrients	Ketogenic Phase	Lowcarbohydrates Phase	Mediterranean Phase
Kcal/day	976 ± 118	1111 ± 65	1800 ± 248
Protein (% totaldaily Kcal)	41 ± 2	27 ± 2	15 ± 2
Fat (% totaldaily Kcal)	46 ± 4	41 ± 2	27 ± 3
Carbohydrate (% totaldaily Kcal)	12 ± 2	33 ± 2	58 ± 4
Protein (g/day)	100 ± 11	74 ± 11	67.5 ± 9
Fat (g/day)	51 ± 9	50 ± 2	54 ± 6
Carbohydrates (g/day)	30 ± 0.2	91 ± 5	261 ± 18

Paoli – Biochem & BP results

Table 3. Changes in blood biochemical and pressure parameters at baseline (*t*0), after first period of ketogenic diet and low carbohydrate diet (*t*2) and after one year from the start (*t*6). Values are expressed as mean and standard deviation.

Blood Parameters	***t*0**	***t*2**	***t*6**	***t*0 *vs.* *t*2**	***t*0 *vs.* *t*6**	***t*2 *vs.* *t*6**
Chol-tot	193.2 ± 37.87	171.9 ± 31.94	179.8 ± 32.42	$p < 0.0001$	$p = 0.0003$	n.s.
HDL-C	43.03 ± 6.09	49.59 ± 8	44.59 ± 8	$p < 0.0001$	n.s.	$p < 0.001$
LDL-C	144.5 ± 58.4	108.0 ± 42.66	122.9 ± 42.25	$p < 0.0001$	$p = 0.0004$	$p < 0.0001$
TG	112.7± 61.02	88.62 ± 40.65	95.45 ± 39.99	$p = 0.0006$	$p = 0.0106$	n.s.
Glu	102.6 ± 11.5	90.31 ± 8.45	95.31 ± 8.45	$p < 0.0001$	$p = 0.0004$	$p < 0.0001$
ALT	18.75 ± 11.6	16.53 ± 6.72	17.11 ± 9.3	n.s.	n.s.	n.s.
AST	18 ± 8.69	17.13 ± 7.2	17.76 ± 5.43	n.s.	n.s.	n.s.
GGT	20.68 ± 16.16	16.1 ± 5.3	17.8 ± 6.8	$p = 0.012$	$p < 0.05$	n.s.
Creatinine	0.79 ± 0.16	0.76 ± 0.07	0.77 ± 0.1	n.s.	n.s.	n.s.
BUN	15.87 ± 3.83	16.1 ± 85.29	15 ± 3.87	n.s.	n.s.	n.s.
Uric acid	4.56 ± 0.86	4.2 ± 0.64	4.01 ± 0.91	$p < 0.01$	$p < 0.05$	n.s.
SBP	125 ± 10	117 ± 6	118 ± 4	$p < 0.01$	$p < 0.01$	n.s.
DBP	86 ± 5	82 ± 8	82 ± 5	n.s.	n.s.	n.s.

VLCKD vs. low calorie diet: Randomized controlled trial

Moreno

- Spain
- Randomized trial:
  - Oral VLCKD until 80% target weight loss achieved, low calorie until further 20% target achieved, then maintenance diet vs. low calorie diet
  - 10% reduced calorie diet
- PronoKal proprietary sachets of high protein foods and electrolytes

Moreno - 2014

Endocrine (2014) 47:793–805
DOI 10.1007/s12020-014-0192-3

ORIGINAL ARTICLE

Comparison of a very low-calorie-ketogenic diet with a standard low-calorie diet in the treatment of obesity

Basilio Moreno · Diego Bellido · Ignacio Sajoux · Albert Goday · Dolores Saavedra · Ana B. Crujeiras · Felipe F. Casanueva

Randomized control trial of ketogenic diet vs. low calorie diet

RCT – LC arm

Low calorie (LC)

- Designed to be 10% below calorie requirement calculated for the individual from WHO/UN formula
- 45-55% carbs, 15-25% protein, 25-35% fat (calorie %)
- Fiber 20-40 g / day

RCT – VLCK arm

VLCK – Very low carb ketogenic diet

- Pronokal commercial weight loss program, including behavioral and lifestyle modification; <50 g vegetable carbs; 10 g olive oil
- 100 cal sachets, 6-8 per day, plus low glycemic-index vegetables in phase I
- Above + one serving natural protein (meat or fish) in phase II
- Above + two servings natural protein in phase III
- Vitamin, mineral and omega-3 supplements to attain RDA
- VLC continued until 80% of target weight loss achieved; generally 30-45 days in total

LC – low calorie phase

- Continued until target weight achieved

Maintenance

RCT – VLCK diet vs. LC diet

80% of target weight loss			20% of target weight loss	Long-term maintenance of weight loss
Multidisciplinary team (dietary counselling / physical activity / psychological support)				
Stage 1 Active Stage			**Stage 2 Dietary re-education**	**Stage 3 Maintenance**
Phase 1	Phase 2	Phase 3	Gradual re-introduction of different foods	Balanced diet
VLCK diet[1] (600-800 kcal/day)			LC diet[2] (800-1500 kcal/day)	Maintenance diet (1500-2250 kcal/day)

RCT – VLCK vs. LC diet

Subjects:

- age 18-65
- BMI >30
- stable wt. for preceding 3 mo
- no serious medical conditions

Studies:

- DXA scans for body composition
- Blood work for hematology and chemistry

RCT – VLCK vs. LC diet

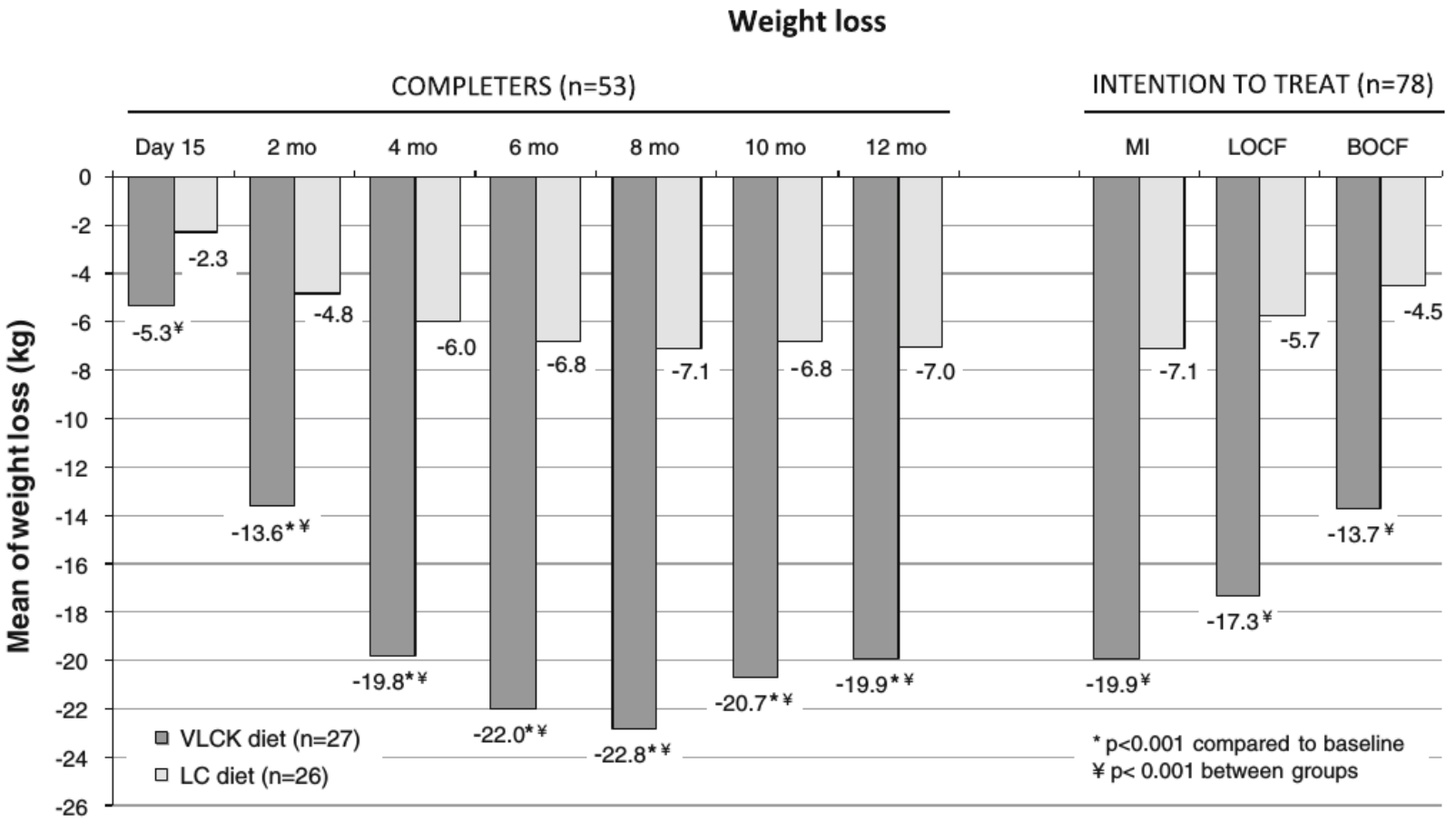
Randomized 79 patients

Withdrawals: 12 VLCK, 14 LC

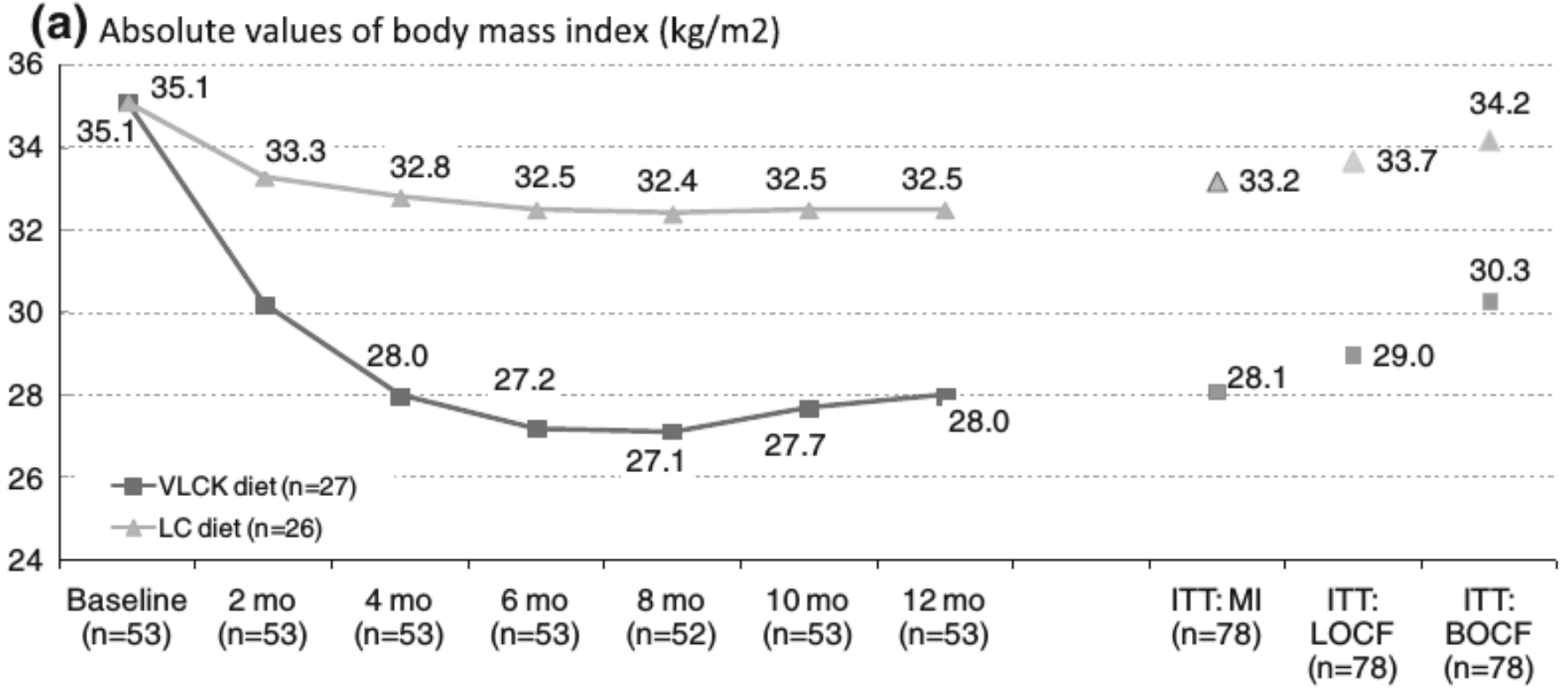
Analyzed: 27 VLCK, 26 LC

Outcomes: Total body mass (weight), waist circumference, BMI, DXA

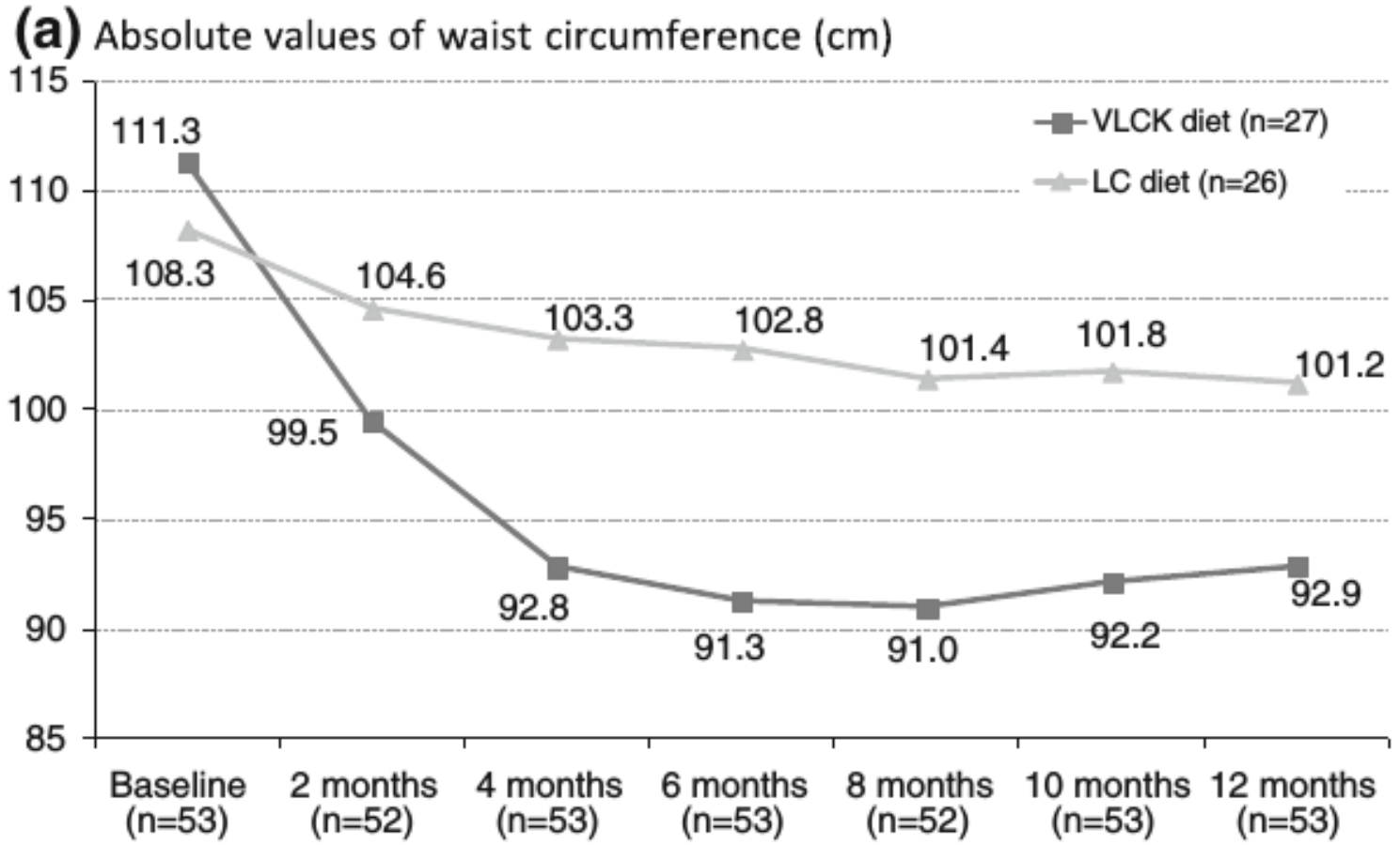
Weight change



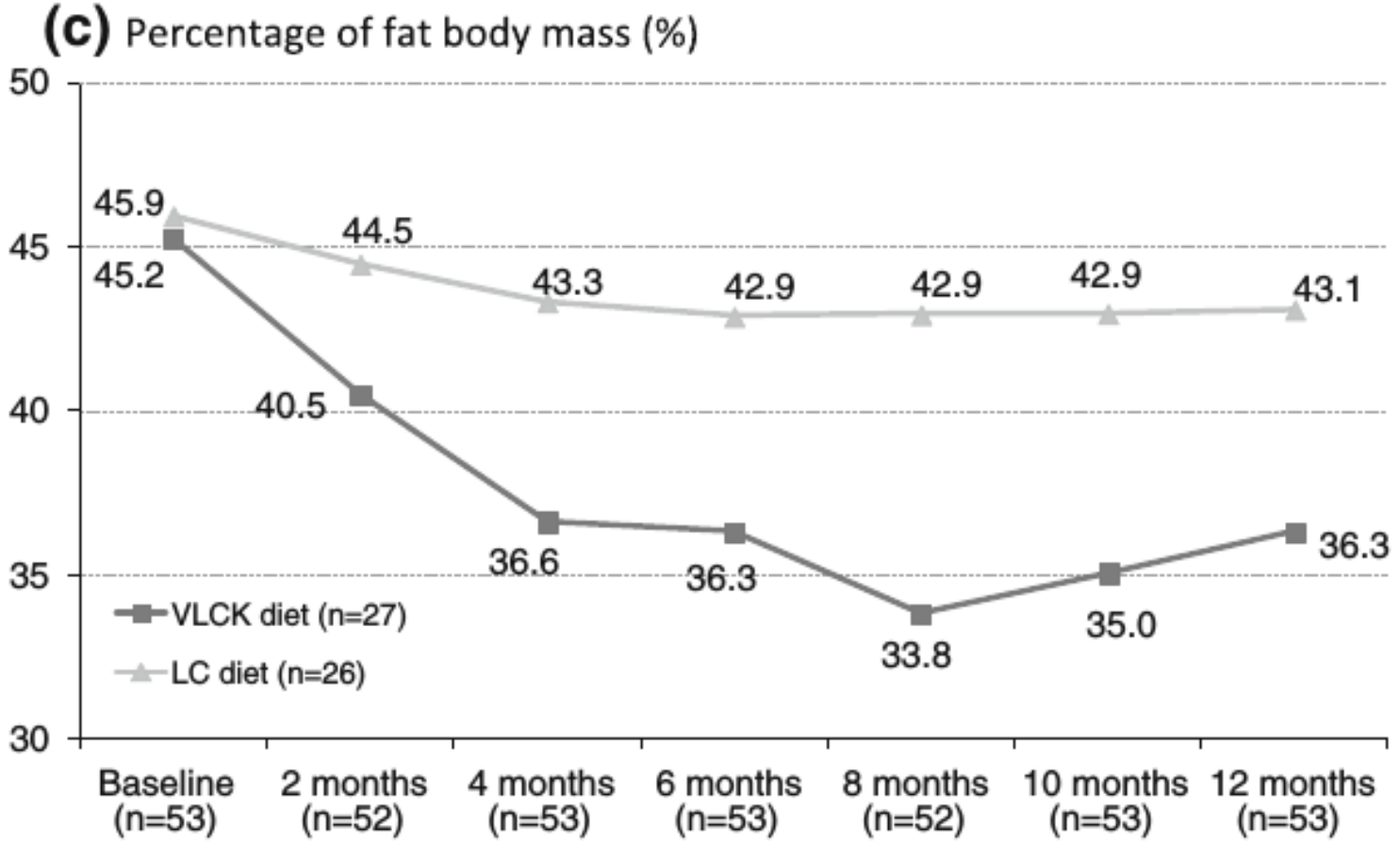
BMI


(a) Absolute values of body mass index (kg/m2)
36
34
32
30
28
26
24
35.1
35.1
33.3
32.8
32.5
32.4
32.5
32.5
28.0
27.2
27.1
27.7
28.0
33.2
33.7
34.2
28.1
29.0
30.3
VLCK diet (n=27)
LC diet (n=26)
Baseline (n=53)
2 mo (n=53)
4 mo (n=53)
6 mo (n=53)
8 mo (n=52)
10 mo (n=53)
12 mo (n=53)
ITT: MI (n=78)
ITT: LOCF (n=78)
ITT: BOCF (n=78)

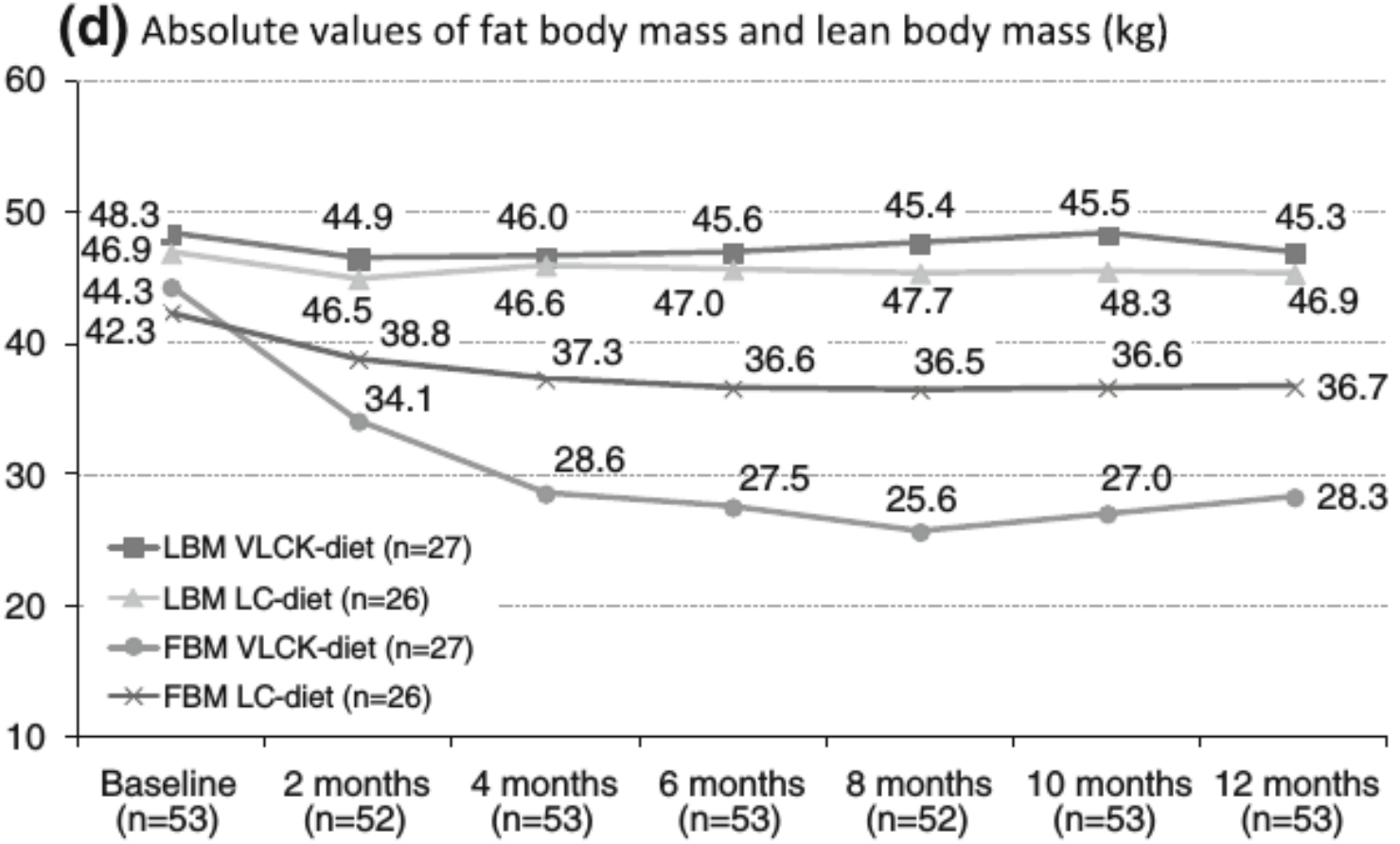
Waist circumference



Fat mass %


(c) Percentage of fat body mass (%)
50
45
40
35
30
45.9
45.2
44.5
43.3
42.9
42.9
42.9
43.1
40.5
36.6
36.3
33.8
35.0
36.3
VLCK diet (n=27)
LC diet (n=26)
Baseline (n=53)
2 months (n=52)
4 months (n=53)
6 months (n=53)
8 months (n=52)
10 months (n=53)
12 months (n=53)

DXA body composition



RCT – VLCK vs. LC – Side effects

Table 3 Side effects and patients drop out under the nutritional interventions

	15 days			4 months			12 months		
	VLCK diet	LC diet	*p*	VLCK diet	LC diet	*p*	VLCK diet	LC diet	*p*
Asthenia	8 (29.6 %)	0 (0 %)	0.004	5 (19.5 %)	0 (0 %)	0.051	1 (3.7 %)	0 (0 %)	1.000
Hair fall	1 (3.7 %)	0 (0 %)	1.000	8 (29.6 %)	0 (0 %)	0.004	2 (7.4 %)	0 (0 %)	0.491
Cramps	3 (11.1 %)	0 (0 %)	0.236	4 (14.8 %)	0 (0 %)	0.111	–	–	–
Headache	15 (55.6 %)	0 (0 %)	<0.000	–	–	–	–	–	–
Muscle weakness	6 (22.2 %)	0 (0 %)	0.023	–	–	–	–	–	–
Constipation	16 (59.3 %)	4 (15.4 %)	0.002	11 (40.7 %)	3 (11.5 %)	0.028	5 (18.5 %)	3 (11.5 %)	0.002
Hyperuricemia >6.5 mg/dL	11 (40.7 %)	1 (3.9 %)	0.002	1 (3.7 %)	0 (0 %)	1.000	–	–	
Orthostatic hypotension	4 (14.8 %)	0 (0 %)	0.111	–	–	–	–	–	–
Myalgia	2 (7.4 %)	0 (0 %)	0.491	–	–	–	–	–	–
Nausea	9 (33.3 %)	0 (0 %)	0.002	1 (3.7 %)	1 (3.9 %)	1.000	–	–	–
Leg heaviness and fatigue	6 (22.2 %)	0 (0 %)	0.023	2 (7.4 %)	0 (0 %)	0.491	–	–	–

RCT – VLCK vs. LC diet

Conclusions

- VLCK diet very tolerable and well-accepted by patients; dropout same as with LC
- No serious adverse effects
- Significantly greater loss of fat mass on VLCK, with no difference in lean body mass change, by comparison to LC
- Fat mass loss sustained out to one year on maintenance

Three KD fat shedding diets

Cappello

- Ketogenic enteral diet: 10 day cycle of tube feeding
- After average 2.5 cycles, 10% weight loss maintained to one year, with 15% regain
- 25,000+ patients treated
- No serious adverse effects

Paoli

- VLCKD, then LC diet, then Mediterranean diet maintenance
- 10% weight loss after two complete cycles, maintained to one year
- Patient selection and dropout not completely characterized

Moreno

- Randomized trial: Oral VLCKD until 80% target weight loss achieved, low calorie until further 20% target achieved, then maintenance diet vs. low calorie diet, vs. low calorie diet
- PronoKal proprietary sachets of high protein foods and electrolytes + behavior modification
- Significantly greater loss of weight, especially fat mass, in VLCKD
- 10% weight loss maintained to one year

KD for weight loss vs. others

Many weight loss strategies are successful for initial weight loss

Relapse is high, back to original weight

The body "defends" highest fat mass level attained and resists efforts to reduce

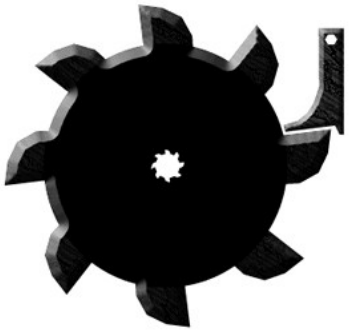
- Reduced resting energy expenditure
- More efficient low intensity movement
- Weight regain occurs at lower-than-normal caloric intake

KD for weight loss vs. others

VLCK diets may somehow bypass the fat-mass-maintenance mechanisms

Perhaps passing through the ketogenic state for weight loss "tricks" the body into giving up fat without making "defensive" adjustments

- Ratchet metaphor – Ketogenic diet releases the pawl from the gear, whereas standard low calorie diet merely pulls back against the gear



KD vs. bariatric surgery

KD deserves urgent attention, in view of the "epidemics" of obesity and bariatric surgery

- Could many patients get needed results with less invasive measures?

Curious that Cappello results not better known and applied in U.S.

- Why are KEN clinics in U.S. not catching on like Cappello, which spread dramatically by word-of-mouth?
- Adverse publicity by Academy of Nutrition and Dietetics; see Wikipedia article "KE diet"; no mention of Cappello!

Ketogenic diets and epilepsy

Epilepsy defined

- Abnormal electrical activity in the brain, either focally or widespread, leading to any of a number of patterns of altered motor activity, sensation, behavior, and other neurologic function
- May be mild, self-limited and not interfering with daily activities
- Often may be very disruptive

Causes

- Brain injury, such as trauma, strokes
- Brain tumors
- Often the cause is unknown

Ketogenic diets and epilepsy

Epilepsy treatment

- Medication
- Brain surgery
- Electrical stimulation
- Ketogenic diet

Epilepsy common in childhood

- Many spontaneously remit with time

Ketogenic diets and epilepsy

A major application of KD, for 100 years!

Before anticonvulsive drugs were available, astute clinicians made the observation that severely restricting carbohydrates led to complete remission of seizures in a few, partial remission in many

Drugs became available from 1930s on

- Ease of use allowed drugs to completely displace diet

Ketogenic diets and epilepsy

Substantial percent of patients remain resistant to drugs, even newest and best

In 1990s, Hollywood producer Jim Abrahams' son Charlie was successfully treated with KD

- Charlie Foundation was started to spread the word

KD has become a well-known option for drug-resistant seizures, and first-line therapy for certain rare specific seizure syndromes

KD and epilepsy

About 10% of patients with drug-resistant (DR) seizures attain complete, or nearly complete, remissions with KD

About 50% with DR seizures have a 50% or greater reduction

Some do not respond

KD and epilepsy - considerations

Mechanism of action not known with certainty

- Research on-going

Weight loss undesirable

- 100% of energy needs must be met from protein and fat
- Therefore, these are very high fat diets
- Challenging to provide palatable high fat diets
- Concern over side effects, including bone loss, especially in children

Summary

Ketogenic diets are those in which very-low carbohydrate consumption triggers a switch to fats as the predominant fuel source

The liver converts fats to ketone bodies, which can fuel the brain and other organs

- Exception: Liver, which must have glucose, derived from muscle breakdown or supplied by protein foods or dietary supplements

Summary – Ketogenic diets

Ketogenic diets are valuable for durable body fat mass reduction

- Apparently bypass defense mechanisms that usually lead to fat regain

Fat mass reduction is frequently accompanied by health benefits and reduced medication requirements

- Blood sugar reduction
- Blood pressure reduction
- Improved lipoprotein ("cholesterol") levels

Summary – ketogenic diets

Ketogenic diets are a useful adjunct in epilepsy not controlled by medication alone, and as first-line therapy in specific syndromes

- Required high-fat intake poses challenges in diet planning

Possible future applications on following slide

Ketogenic Diet Applications

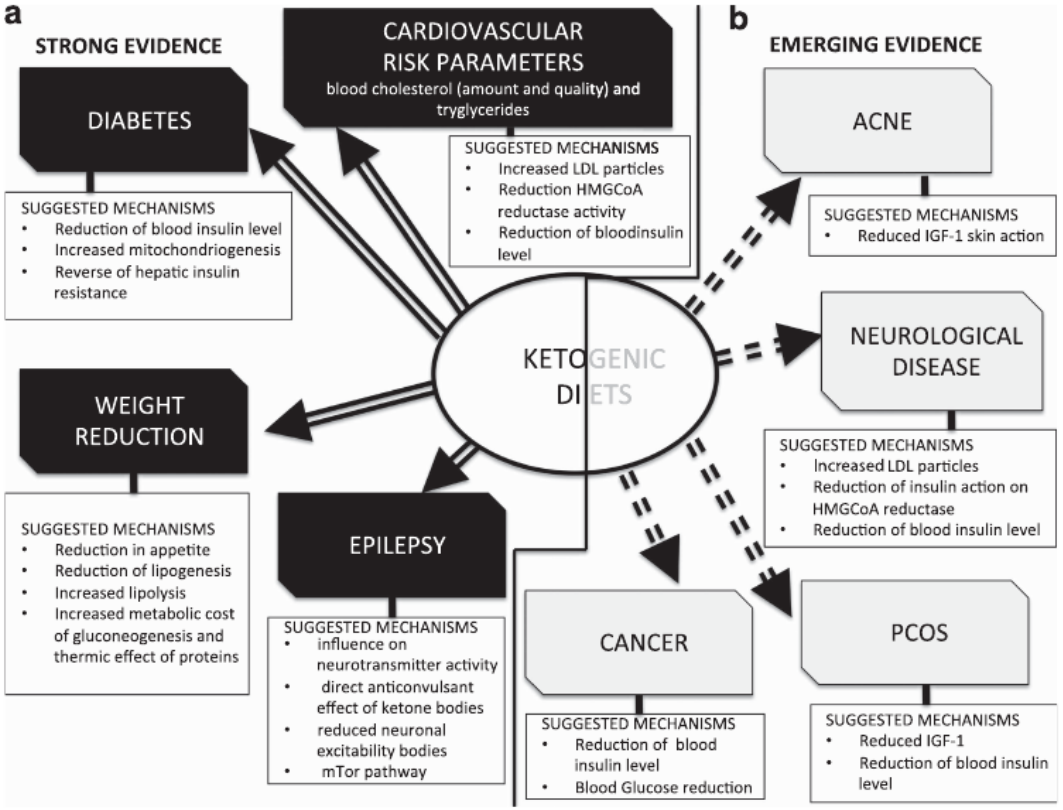


Figure 1. Suggested mechanisms for the therapeutic action of ketogenic diets in pathologies for which there exists strong (**a**) and emerging (**b**) evidence.

Thank you !

Questions or comments ?

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Basic metabolism

The human body requires energy 24/7 to run the brain, heart, muscles and all the other organs

There are two main fuels – glucose and fatty acids

- Proteins can be turned into glucose if needed to provide fuel, but this is an expensive source

Glucose normally fuels the brain and liver; both glucose and fatty acids fuel muscles

Glucose metabolism

Blood glucose generally comes from digested dietary starches and sugars

- Excess glucose is stored as glycogen (a starch) in the liver
- Further excess is converted to fat and stored in fat cells
- Insufficient glucose is initially covered by drawing on glycogen stores

Insulin is the major hormone that regulates glucose use and storage

- Insulin is secreted by the pancreatic islet cells in response to rising blood glucose and enables glucose uptake by muscle and other tissues

Fatty acid metabolism

Fat is transported to tissues in lipoproteins as triacylglycerides (TAG) AKA triglycerides

TAG is cleaved by lipoprotein lipase to make free fatty acids (FFA) and glycerol

- Some FFA taken up by cells and used for energy (muscle) or storage (fat cell)
- Remainder bound to albumin, to be taken up by other cells for use

FFA are unable to cross "blood-brain barrier" to be used to fuel the brain

Normal metabolism

Dietary carbohydrates supply glucose for brain, muscle, liver and some other organs

Dietary fats supply FFA for the muscles and some other organs

Dietary protein mostly goes to make body proteins for repair and regeneration

Fuel intake = fuel used; no extra to storage or draw-down from storage