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Does a ketogenic diet lower a very high Lp(a)? A striking experiment in a male physician

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ABSTRACT

The level of lipoprotein(a) (Lp(a)), an important cardiovascular risk factor, is considered to be genetically determined. I am a 55-year-old male physician specialised in preventive medicine and a hobby triathlete with a body mass index of 24.9 kg/m^2 and a maximum oxygen consumption (VO_2max) of ~50 mL/(kg×min), with an average of 7–10 hours of exercise per week.

I discovered my own Lp(a) at 92–97 mg/dL in 2004 and measured a maximum Lp(a) of 108 mg/dL in 2013. Surprisingly, I observed a much lower Lp(a) of 65 mg/dL in 2018. This happened after I had adopted a very-low-carb ketogenic diet for long-term endurance exercise.

My n=1 experiment in July 2020 demonstrated an increase in Lp(a) back to 101 mg/dL on a very high-carb diet within 2 weeks, and a drop back to 74 mg/dL after 3 weeks on the ketogenic diet afterwards. The observed large changes in my Lp(a) were thus reproducible by a change in carbohydrate consumption and might have clinical relevance for patients as well as researchers in the field of Lp(a).

Lipoprotein(a) (Lp(a)) is an important and causal risk factor for cardiovascular disease (CVD).[1] There are 1.43 billion people (approximately 20%–30% of the population, with some racial variations) with an elevated Lp(a) >50 mg/dL and 2%–3% with a very high Lp(a) >100 mg/dL, which translate into moderate (+80%) or strong (+300%) increase in CVD risk, respectively.[2] Due to its genetic basis, once in a lifetime measurement of Lp(a) is currently considered sufficient for risk assessment.

I am a physician specialised in preventive medicine with no family history of CVD. I discovered my own Lp(a) at 97 mg/dL in 2004 (with a maximum Lp(a) of 108 mg/dL measured in 2013). As there were no effective treatments to lower Lp(a) in 2004, I decided to start rosuvastatin 10 mg/dL, which I have taken since 2005. Low-density lipoprotein (LDL) cholesterol fell to 80–90 mg/dL on average.

From 2004 to early 2018 I consumed a Mediterranean-style diet with 200–250 g of carbohydrates (CH) per day, while exercising 7–10 hours per week. As a hobby triathlete, I learnt about the effects of a very-low-carb ketogenic diet (VLCKD) on long-term endurance.[3] In spring 2018 I went on VLCKD (50–80 g of CH=<10% enCH). In the same season I remeasured my Lp(a), which fell to 65–70 mg/dL on separate occasions (table 1).

The lab's assay (DiaSys Lp(a) 21 FS a) remained unchanged since 2004. This Lp(a) assay has high accuracy, with an intra-assay and interassay SD of 0.528–1.08 mg/dL, as reported by the manufacturer. MVZ Labor Dr Riegel is a certified German laboratory in accordance with DIN EN ISO 15189.

The observed large variation in a 'genetically determined' risk factor motivated me to do a n=1 nutrition experiment. In July 2020 I switched from VLCKD to a high-carb-low-fat (HCLF) diet with an average intake of >400 g of CH per day for 2 weeks. Nutrition protocols were documented in the nutrition app 'Ernährung Pro'. Weight was unchanged at 89 kg (body mass index 24.9 kg/m^2). Statin therapy was unchanged with 10 mg of rosuvastatin at night. Physical activity levels were kept constant at 2 hours per day on average.

As shown in table 1, Lp(a) was measured at 67 and 69 mg/dL before the change and went up to 95 and 101 mg/dL after 14 days on HCLF diet. When I went back to VLCKD, Lp(a) fell again to 80 mg/dL after 2 weeks and to 74 mg/dL after 3 weeks. While on VLCKD, mild ketosis (beta hydroxybutyrate level 0.8 mmol/L) was documented with FreeStyle Libre.

To my knowledge this is the first observation of such a large change in Lp(a) induced by dietary modification. I was unable to find any diet study done in patients with a very high Lp(a). A recent review examined the effect of dietary interventions on Lp(a),[4] but baseline Lp(a) was normal in all seven studies. The changes in Lp(a) of 10%–20% or 2–5 mg/dL, which were reported in this review in

Table 1 Lipoprotein(a), cholesterol values and glucose metabolism under different diets

Date	20 September 2004	12 October 2004	24 September 2013	11 September 2018	10 October 2018	13 July 2020	14 July 2020	29 July 2020	30 July 2020	10 August 2020	24 August 2020
Diet	High-carb 250 g	High-carb 250 g	High-carb 250 g	VLCKD (50–80 g)	VLCKD (50–80 g)	VLCKD (50–80 g)	VLCKD (50–80 g)	High-carb >400 g since 14 July 2020	High-carb >400 g since 14 July 2020	VLCKD (50–80 g) since 1 August 2020	VLCKD (50–80 g) since 1 August 2020
Lipoprotein(a)	92	97	108	65	70	67	69	95	101	80	74
Glucose	98		97	104				112	113	107	98
Insulin				3.90				6.27	8.12	4.48	3.29
HOMA index				1.00				1.7	2.3	1.2	0.8
Total cholesterol	190		213	164	181	149	158	185	185	160	147
HDL cholesterol	51		48	61	54	63	63	63	62	60	55
LDL cholesterol	127		147		92	78	83	104	108	88	81
Triglycerides	58		90	<40	173	42	58	91	77	62	57
GGT	34		27	30	36	25	27	37	36	36	32
ALT	29		37	40	68	46	47	73	74	57	51

All blood samples were drawn after an overnight fast.
ALT, Alanin Transaminase; GGT, Gamma-Glutamyl Transferase; HDL, high-density lipoprotein; HOMA, Homeostatic Model Assessment; LDL, low-density lipoprotein; VLCKD, very-low-carb ketogenic diet.

participants with normal baseline levels of Lp(a), have no clinical relevance.

On the other hand, if a very high Lp(a) of >100 mg/dL could be lowered by a dietary intervention to below 70 mg/dL as documented here, this might well translate into a significant risk reduction for CVD.

Possible mechanisms for an increase in Lp(a) on a high-carb diet include insulin mediation, as my HOMA index increased substantially while consuming high-carb diet. Insulin is a potent regulator of de-novo lipogenesis in the liver via transcription factors CHREB-P and SREB-P. It is well known that an HCLF diet compared with a Low-Carb-High-Fat (LCHF) diet will increase apo-CIII, triglycerides, very-low-densitiy lipoprotein (VLDL), apolipoprotein B and small-dense LDL particles.[5] To exclude possible confounders, physical activity levels were kept constant during the experiment, as was the average wine consumption with dinner. There were no infections present (normal high-sensitive C-reactive protein (hs-CRP)) when blood samples were taken, so it is very likely that the change in CH ingestion from <50 g/day to >400 g/day is causally related to the changes in Lp(a).

CONCLUSION

This n=1 experiment documented a reproducible reduction in Lp(a) in the range of 30–40 mg/dL with VLCKD compared with a high-carb diet in an individual with a very high baseline Lp(a) of >100 mg/dL. Controlled dietary intervention studies with VLCKD in this high-risk population seem warranted. Studies with new drugs to lower Lp(a) should monitor the diet of patients with high Lp(a), as dietary CH content might be a relevant confounder, and low-carb weight loss studies might re-examine their data with respect to participants with high baseline Lp(a) to see if they observed similar changes as reported here.

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