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

Johannes Georg Scholl

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/m² and a maximum oxygen consumption (VO₂max) 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). 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 translates into moderate (+80%) or strong (+300%) increase in CVD risk, respectively. 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. 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. I observed that 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.

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), 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...
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<tr>
<td>Diet</td>
<td>High-carb 250g</td>
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<td>High-carb 250g</td>
<td>VLCKD (50–80 g)</td>
<td>VLCKD (50–80 g)</td>
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<td>Lipoprotein(a)</td>
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<td>67</td>
<td>69</td>
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<td>Insulin</td>
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<td>6.27</td>
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<td>1.7</td>
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<tr>
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<td>54</td>
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<tr>
<td>LDL cholesterol</td>
<td>127</td>
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<td>92</td>
<td>78</td>
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<td>73</td>
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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 CHREBP and SREBP. It is well known that an HCLF diet compared with a Low-Carb-High-Fat (LCHF) diet will increase apo-CIII, triglycerides, very-low-density lipoprotein (VLDL), apolipoprotein B and small-dense LDL particles. 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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REFERENCES