Ketogenic Dietary Therapy -Effects on Cardiovascular Health

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The cardiovascular effects of the ketogenic diet therapies (KDT) in epilepsy remain an area of clinical uncertainty, with evidence demonstrating both potential benefits and recognised risks. KDT has been associated with favourable short-term cardiometabolic changes. Meta-analyses report increases in high-density lipoprotein (HDL), reductions in triglycerides (TG), improvements in blood pressure, weight, fat mass, BMI, and glycaemic control during the early stages of treatment (1,2). However, these improvements frequently occur alongside significant rises in low-density lipoprotein (LDL), total cholesterol (TC), apolipoprotein B (ApoB), and small dense LDL particles, changes strongly associated with increased cardiovascular risk, particularly when the diet is high in saturated fats. (2,3). These lipid elevations typically emerge within the first three to six months of dietary initiation and are particularly pronounced in children, where LDL levels may increase from approximately 2.33 mmol/L to 4.65 mmol/L within six months (4). Adults commencing the Modified Atkins Diet (MAD) also demonstrate significant increases in TC and LDL at three months, although some subgroups partial normalisation by twelve months is observed, particularly those with pre-existing dyslipidaemia (3,5).

Although KDT can alter lipid profiles, no direct association has been established between KDT and myocardial infarction or stroke in epilepsy populations, although the absence of evidence does not equate to long-term safety (3). Recent studies have found traditional lipid markers may not reliably predict plaque progression in non-epilepsy individuals following KDT long term, and some adults exhibit the Lean Mass Hyper-Responder (LMHR) phenotype, characterised by a very high LDL cholesterol in the absence of demonstrable vascular pathology. These findings suggest that lipid responses to carbohydrate restriction may represent a metabolically distinct pattern in which LDL elevations do not necessarily correspond to atherosclerotic change (6-8). Baseline plaque, rather than cholesterol levels, was found to predict progression, challenging the assumption that diet-induced increases in LDL cholesterol inherently raise the risk of heart disease in this specific metabolic phenotype. The authors conclude that hypercholesterolaemia associated with KDT in otherwise healthy individuals does not predict atherosclerosis, emphasising the importance of personalised cardiovascular risk assessment rather than relying solely on LDL cholesterol (6-8). Nevertheless, increases in ApoB and small dense LDL particles, both strongly linked to atherosclerotic risk, have been observed even when LDL and TC stabilise over time (3,8).

Recent population studies provide additional context for evaluating the long-term cardiovascular implications of KDT. A large longitudinal (17 year) study in the United States reported greater adherence to a ketogenic-style dietary pattern was associated with lower all-cause mortality, with no corresponding increase in cardiovascular-related mortality (9). Although this study was observational and not directly reflective of clinical KDT protocols, its findings suggest that a ketogenic diet intake does not confer excess cardiovascular risk at the population level. When considered alongside the LMHR study which found no relationship between diet-induced hypercholesterolaemia and coronary plaque progression (6), this epidemiological evidence contributes to a broader picture in which KDT may not inherently elevate cardiovascular risk (9).

Short-term vascular findings in patients treated with ketogenic dietary therapy (KDT) vary across age groups and study designs. In adults, one study reported that carotid intima–media thickness (CIMT) was higher in individuals receiving KDT, suggesting that CIMT may serve as an early biomarker of cardiovascular risk in this population (10). In paediatric cohorts, one investigation found increases in arterial stiffness, higher

augmentation index, and reduced carotid distensibility shortly after diet initiation, with partial reversibility following dietary modification (11). In contrast, another six-month study in children reported no adverse changes in CIMT, arterial elasticity, aortic dimensions, or diastolic cardiac function despite predictable rises in lipid levels (12). Overall, these findings suggest that while children may experience transient functional vascular alterations without evidence of short-term structural harm, adults may show early measurable structural changes that warrant ongoing monitoring.

Emerging evidence suggests that KDT may exert both pro-oxidative and anti-inflammatory effects, depending on the population studied and the timing of assessment. In paediatric cohorts, early increases in oxidative stress markers have been observed shortly after initiating KDT, indicating a transient pro-oxidative response during the adaptation phase, likely influenced by the high saturated-fat content of the therapy (13,14). In contrast, studies in adults following sustained nutritional ketosis consistently demonstrate reductions in inflammatory biomarkers, including C-reactive protein (CRP), suggesting that once metabolic adaptation is established, carbohydrate restriction may confer anti-inflammatory benefits despite concurrent lipid elevations (15,16). Broader reviews further support these anti-inflammatory and cardiometabolic benefits, particularly when ketogenic diets emphasise unsaturated fats (17). Collectively, these findings highlight differing physiological responses across age groups and time frames, with early oxidative changes more evident in children and anti-inflammatory effects more consistently observed in adults (13-16).

Cardiovascular outcomes appear to be strongly influenced by diet composition, with monounsaturated fatty acids (MUFA) including olive oil, rapeseed oil ,avocados, and certain nuts, and polyunsaturated fatty acids (PUFA) such as omega-3 and omega-6 fatty acids found in fish, seeds, and plant oils sunflower, corn, flaxseed, soyabean fat-based ketogenic diets producing more favourable reductions in LDL cholesterol and total cholesterol compared with saturated fat based ketogenic diets (17).

Studies using olive-oil–based (MUFA-rich) ketogenic diets suggest improved tolerability and potentially gentler metabolic effects, although direct lipid comparisons with other fat types are limited (17,18). Some Mediterranean-style ketogenic diets that emphasise olive oil as the primary fat source have reported improvements in TG, HDL, and vascular markers in adults (17). However, paediatric epilepsy studies where olive oil is also commonly used as the main fat source consistently show significant rises in TC, LDL, and TG at 1, 3, 6, and 12 months compared with baseline, despite the MUFA-rich composition of the diet. These effects have been documented in multiple longitudinal studies of children (18).

Several studies have investigated medium chain fatty acids (MCT), provided in the MCT ketogenic diet or as a supplement in the classical ketogenic diet, on lipid profiles. In animal studies, involving high fat diets, supplementation of octanoic (C8:0) MCT oil or decanoic acid (C10:0) MCT oil lowered TC and LDL (19), and in a cholesterol rich diet MCT supplementation also lowered TC and LDL and improved HDL/LDL ratio (20). In human studies, an early analysis of MCT oil supplementation of middle-aged men with mild hypercholesterolemia on a standard diet increased total cholesterol and LDL levels compared to sunflower oil supplementation (21). Similar comparative effects were confirmed in a meta-analysis (22) however overall effects of MCT supplements do not significantly alter cholesterol, LDL or HDL but trigger a small increase in TG (22). Thus, MCT may provide distinct lipid profiles to that shown following long chain fatty acid-based KDTs.

Lipid responses to ketogenic dietary therapies (KDTs) vary widely and are influenced by multiple patient specific factors, including age, genetic predisposition, baseline lipid status, obesity, and family history of cardiovascular disease (23). Clinical guidelines emphasise that the safety profile of KDTs is strongly shaped by the duration of therapy and the frequency and quality of clinical monitoring (24). Longer treatment periods increase the likelihood of metabolic and cardiovascular adverse effects, including dyslipidaemia, particularly when follow-up intervals are extended or inconsistent (25). International consensus statements recommend

structured clinical supervision with regular assessment of lipid profiles, liver enzymes, renal function, and cardiovascular risk markers to ensure early detection and management of adverse changes (24). Inadequate monitoring may allow lipid abnormalities to progress, whereas timely follow up enables clinicians to adjust macronutrient composition, modify fat sources, or introduce pharmacological therapy when required (17).

Most long-term evidence regarding the long-term cardiovascular implications of sustained ketogenic diet therapies (KDT) use comes from paediatric studies, with limited adult follow-up beyond twenty-four months, leaving uncertainty (3). Paediatric studies provide valuable insights into metabolic and lipid trajectories over prolonged therapy, but their applicability to adult populations is limited due to differences in physiology, comorbidities, and treatment. The gap highlights the need for extended adult follow-up to clarify whether the lipid and cardiovascular changes observed in short-term studies persist, attenuate, or deteriorate over time (3).

Long-term cardiovascular outcomes in individuals who previously followed a ketogenic diet, particularly those treated in childhood, remain essentially undocumented. Existing evidence focuses on current KDT adherence and short to medium term cardiometabolic effects rather than post-cessation risk, highlighting a significant gap in the literature (3).

Given these considerations, proactive cardiovascular risk management is essential when prescribing KDT. Baseline assessment should include a full lipid profile (TC, HDL, LDL and TG), ApoB, and, where available LDL particle analysis, alongside blood pressure, ECG, BMI, glucose, HbA1c, smoking status, and family history of premature cardiovascular disease (3,24,26).

Lipid monitoring is recommended at three months following initiation of KDT, with earlier specialist review if LDL rises substantially, for example exceeding 4.9 mmol/L (190 mg/dL) or with a marked relative increase and after a fasting lipid profile (24,26). For individuals who continue long-term therapy, further lipid evaluation is recommended at six months and subsequently every six to twelve months, with more frequent monitoring in those who develop persistent abnormalities (24,26). Dietary adjustments should prioritise MUFA and PUFA, increased fibre intake, and reduced saturated and trans fats, with consideration of lower-ratio ketogenic variants where clinically appropriate (17,24,26). A recent review of ketogenic dietary therapies for epilepsy and neurological diseases proposed adapting these diets to incorporate Mediterranean foods such as olive oil, nuts, and fish to enhance nutritional quality, cultural acceptability, and long-term tolerability without compromising ketosis (27). If dyslipidaemia persists despite dietary modification, stepping down to a less restrictive ketogenic therapy or initiating lipid-lowering medication may be necessary, ideally in coordination with a metabolic specialist to ensure safe prescribing (24,26).

For many individuals with drug-resistant epilepsy, the therapeutic benefits of seizure reduction may outweigh potential cardiovascular risks; however, this balance requires careful clinical assessment and clear communication. Documenting informed consent and engaging in shared decision-making with families and caregivers is essential. While short-term cardiometabolic improvements are encouraging, long-term safety remains uncertain, and clinicians should adopt an individualised, vigilant approach to monitoring and risk mitigation. Evidence gaps remain, particularly regarding long-term cardiovascular outcomes in both paediatric and adult populations. Data on vascular imaging changes during ketogenic therapy are limited, and the clinical relevance of LDL particle alterations observed in ketogenic states is still uncertain (3). Emerging studies suggest that elevated LDL cholesterol during ketogenic therapy does not necessarily predict atherosclerotic progression, and some cohorts demonstrate stable coronary plaque burden despite marked lipid elevations (6,7). Nonetheless, current data remain limited, and most cardiovascular risk assessments are derived from short to medium term follow up. Continued research is needed to clarify these uncertainties and guide future clinical practice (3,9).

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