The influence of low carbohydrate and ketogenic diets on longevity and skeletal muscle maintenance with ageing

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Background and Aim: Longevity and the maintenance of skeletal muscle mass and metabolic function with aging are very closely related. Calorie restriction (CR) has been shown to increase lifespan in many animal species and results in a shift in metabolism to increased reliance on fat oxidation and elevated biosynthesis of circulating ketone bodies. Low carbohydrate high fat (LCHF) diets are known to result in similar shifts in metabolism. Ketogenic (KETO) diets have been reported to reduce inflammation and mitochondrial dysfunction associated with aging and have been used as a therapeutic treatment for neurological disorders. Currently, little is known about the effects of LCHF or KETO diets on longevity and maintenance of skeletal muscle mass with aging. Therefore the aims of this study are to determine effect of LCHF or KETO diets on lifespan in mice and whether a metabolic shift to reliance of fat oxidation is associated with a better preservation of muscle mass and function with aging.

Methods: C57BL/6 male mice began the study at 12 months of age and were individually housed and fed 11.2 kCal/day to prevent hyperphagia and obesity. Mice were randomly assigned to a control (CON - 65% CHO, 17% fat, 18% protein), a non-ketogenic low carbohydrate (LCHF - 10% CHO, 70% fat, 18% protein) or a ketogenic diet (KETO - <1% CHO, 90% fat, 10% protein). One cohort of mice was allowed to live their natural lifespan, whereas another was tested for physiological function (muscle and cognitive) after 1 or 14 months of dietary intervention. Following testing, hindlimb muscles (TA, EDL, GAST, SOL, PLN) were weighed and collected for histological (CSA, fibre tying) and biochemical analysis (mRNA and protein levels).

Results: The KETO diet has extended median longevity by 13% and significantly increased mean survival compared to the CON diet. The LCHF diet has also reduced early mortality and increased median longevity by ~7% compared to the CON diet. Mice fed the KETO diet had significantly higher muscle function (motor coordination and grip strength) and cognition (novel object recognition) then the CON group after 14 months of dietary intervention. The GAST, PLN, SOL and TA muscle mass was significantly greater in the mice fed the KETO diet when compared to the CON group. The effect of the diet on fibre type, cross-sectional area and markers of anabolic sensitivity are actively being determined.

Conclusion: These results to date of this dietary intervention highlight that lowering dietary carbohydrates in healthy mice extends lifespan and reduces the loss of physical function with aging. These results also suggest that the combination of low dietary carbohydrate and an increase in endogenous production of ketone bodies results in an additive improvement in lifespan and function with aging. Finally, the higher muscle weights in the KETO group after 15 months of dietary intervention suggests that this diet may play a role in preserving muscle mass with aging. However, the mechanism underlying the effect of lowering carbohydrates and increasing ketone biosynthesis on muscle mass and function is still to be uncovered.