



MAY 2023

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Salted Arteries: Is High Sodium Intake Associated with Atherosclerosis?

Wuopio J, Ling YT, Orho-Melander M, Engström G, Ärnlov J. The association between sodium intake and coronary and carotid atherosclerosis in the general Swedish population. *Eur Heart J Open*. 2023 Mar 30;3(2):oead024.

Background

- There is a the strong dose-response and linear relationship between sodium and CVD outcomes that has crystallised with more recent evidence.
- However, it is known that salt exerts other effects on the cardiovascular system, for example increased left ventricular size of the heart.
- What about atherosclerosis? The present study investigated this association in a Swedish cohort.

The Study

- A cross-sectional analysis from the Swedish Cardiopulmonary bioImage Study [SCAPIS], a population-based study of men and women aged between 50–64yrs. Sodium intake was measured by taking a single urinary sample in the morning, and by using the Kawasaki formula to estimate 24 h sodium intakes in each participant. The study analysed the associations between estimated 24 h sodium and the presence of carotid artery plaques, coronary artery stenosis [i.e., a narrowing of the artery from fatty plaque build-up], and CAC scores.

Findings, Strengths & Limitations

- 10,764 participants were included in the final analysis, of which 52% were women. Average estimated 24 h sodium intake was 2,925mg and 3,642mg in women and men, respectively.
- When not adjusting for blood pressure there was 4% higher odds for the presence of plaque in the carotid arteries per 1,000mg estimated sodium.
- There were no associations between estimated sodium and either CAC scores or stenosis.
- Strengths included the assessment of atherosclerosis using imaging and ultrasound. The major limitation of the study is the use of estimated 24 h sodium intake based off a single urinary sodium “spot sample” and mathematical formula, which is highly inaccurate.

Context

- Even in this cohort of participants with relatively good blood pressure readings, it was blood pressure that explained the associations with the levels of atherosclerosis observed in the study.
- Previous research showed that over 10yrs the risk of a CVD event was twice as high in the “normal” BP range when compared to the optimal range.
- A 2011 study that used a single full 24 h urinary collection to measure sodium, which is still limited but better than a “spot sample” and formula-based guesstimate, showed an association between higher urinary sodium and carotid artery intima thickness that remained significant after adjusting for systolic blood pressure.

Application

- There is a well-established causal chain between sodium, hypertension, and CVD.
- 10% of deaths from CVD globally have been attributed to sodium intakes above 2,000mg/d.
- That said, to what extent sodium intakes may relate to atherosclerosis progression specifically remains to be established in better quality, prospective research.

Does High Morning Energy Intake Lead to Greater Weight Loss?

Young IE, Poobalan A, Steinbeck K, O'Connor HT, Parker HM. Distribution of energy intake across the day and weight loss: A systematic review and meta-analysis. *Obes Rev.* 2023 Mar;24(3):e13537..

Background

- The theory that timing of food intake could play a substantial role in bodyweight regulation and metabolic health has long existed in nutrition research.
- Human intervention trials in the early 2010's found that frontloading morning energy intake might result in significantly greater weight loss compared to the same energy intake consumed with dinner in the evening.
- Until the present study, however, no meta-analysis of this evidence had been conducted.

The Study

- The study was a systematic review and meta-analysis of studies that investigated the effects of early compared to later distribution of energy on weight loss. Trials were required to have a specified distribution of energy across the day with a proportion distributed earlier [i.e., breakfast or lunch] in the day.

Findings, Strengths & Limitations

- 9 trials were included in the meta-analysis, all of which were RCTs with a total number of participants of 485; $n = 244$ for early energy distribution and $n = 241$ for later energy distribution.
- Comparing early to later distribution of energy, the meta-analysis of all included studies showed that early energy distribution resulted in 1.23kg [95% CI 0.06 to 2.40kg] greater weight loss compared to later energy distribution. This was no longer significant [1.14kg and 95% CI range from 2.38kg weight loss to 0.11kg weight gain] upon removal of one study that compared two different timings of dinner, rather than a true early vs. later energy comparison.
- Strengths are the clear research question and exclusion of studies on intermittent fasting, time-restricted eating [TRE], or Ramadan. Limitations include the low overall power of the meta-analysis.

Context

- The most tightly controlled study to date that compared early vs. later energy distribution but with controlled diets found no difference in weight loss, but significant reductions in appetite in the early energy distribution condition.
- There is little good evidence of any enhanced energy expenditure with morning-loaded energy intake.
- The studies in the present meta-analysis were all free-living interventions without full control of diet, and therefore likely to reflect effects of energy distribution on factors like appetite and resulting lower energy intakes compared to control/evening loaded energy intakes.

Application

- Early energy intake does not, for example, enhance TEF or lead to increases in other components of energy expenditure.
- There may be some individuals who benefit from the appetite regulatory effects of eating more earlier in the day. To what extent that influences weight loss appears, on balance of evidence, to be modest.

The Plant-Based “Portfolio Diet” and Cardiovascular Disease Outcomes.

Glenn AJ, Lo K, Jenkins DJA, Boucher BA, Hanley AJ, Kendall CWC, Manson JE, Vitolins MZ, Sneltselaar LG, Liu S, Sievenpiper JL. Relationship Between a Plant-Based Dietary Portfolio and Risk of Cardiovascular Disease: Findings From the Women’s Health Initiative Prospective Cohort Study. J Am Heart Assoc. 2021 Aug 17;10(16):e021515.

Background

- In the early 2000’s, David Jenkins and colleagues at the University of Toronto developed the ‘Portfolio Diet’ pattern, a dietary pattern designed to emphasise inclusion of multiple foods with evidence for lowering blood cholesterol levels.
- The Portfolio Diet resulted in a 28.6% decrease in LDL-C compared to a 30.9% reduction with lovastatin in a 2003 RCT.
- The present study created a quantitative score for the Portfolio Diet and compared the effects of high to low adherence scores on disease outcomes in a longer-term cohort study.

The Study

- Participants from Women’s Health Initiative [WHI] RCT and prospective cohort study combined were analysed for the associations between adherence to the Portfolio Diet score and CVD outcomes over 15yrs. The primary outcomes were total CVD, coronary heart disease, and stroke.

Findings, Strengths & Limitations

- The final sample for the present analysis included 123,330 women. The highest level of adherence to the Portfolio Diet had an 11% lower risk of total CVD, and 14% lower risk of CHD. Stroke was non-significant.
- Strengths include the large sample size and number of CVD events, and the creation and use of a Portfolio Diet index provided a means of capturing the characteristics of this diet for nutritional epidemiological research. Limitations include low levels of intake of key Portfolio Diet nutrients, including plant-sourced monounsaturated fats and plant sterols, and the homogenous demographics which require some caution in generalising the findings.

Context

- The Portfolio Diet in RCTs reliably reduces the causal risk factor for CVD in LDL-C, along with other cardio-metabolic risk factors; the present study demonstrates reductions in hard CVD endpoints associated with the characteristics of the Portfolio Diet over 15yrs.
- The study thus provides an example of where RCT evidence meets long-term epidemiological research in congruence.
- It is possible that the significant effects noted for nuts are explained by the phytosterol content, which has previously been shown. Plant sterols also independently showed an association with lower risk.

Application

- The full implementation of the Portfolio Diet recommendations from the intervention trials for an average 2,000kcal/d diet include: 50g soy protein, 45g nuts, 20g viscous fibre, 2g plant sterols, 45g MUFAs, <7% energy from saturated fat and <200mg cholesterol per day.
- While this may be difficult to people to meet in total, the evidence suggests that some adherence is better than none, and more is better than less.

The Effects of Energy-Restricted Dieting on Bone Density

Villareal DT, Fontana L, Das SK, Redman L, Smith SR, Saltzman E, Bales C, Rochon J, Pieper C, Huang M, Lewis M, Schwartz AV; CALERIE Study Group. Effect of Two-Year Caloric Restriction on Bone Metabolism and Bone Mineral Density in Non-Obese Younger Adults: A Randomized Clinical Trial. *J Bone Miner Res.* 2016 Jan;31(1):40-51.

Background

- The human skeleton is not a biologically inert structure; it is a live organ tissue comprised of minerals and proteins, and is in a constant state of flux throughout the lifespan.
- While ~60–80% of bone mass is genetically determined, 20–40% is influenced by lifestyle factors, with nutrition and physical activity the two most influential factors.
- While specific nutrients are critical to bone health, energy restriction and weight loss have previously been shown to lead to lower bone mineral density [BMD].

The Study

- The present study was a secondary analysis of bone health markers from a 2yr RCT of sustained energy restriction. 118 healthy young (~37yrs) adults with a BMI of 21kg/m² at baseline completed the full 2yr study. Participants in the intervention group were prescribed a 25% reduction in energy intake to sustain over 2yrs. The control group consumed an *ad libitum* diet. No specific diet or macronutrient prescriptions were provided to any participants.

Findings, Strengths & Limitations

- At both 1yr and 2yrs of the study, BMD at each site [lumbar spine, total hip, femoral neck, and intertrochanter] decreased significantly by 1.2–1.7% in the energy restriction intervention group compared to the *ad libitum* control group. This effect did not differ between men and women.
- The analysis demonstrated that the decrease in BMD was predicted by weight loss.
- Measured levels of bone resorption [i.e., breakdown] markers increased, while bone formation markers decreased.
- Strengths include the comprehensive measures of bone and use of intention-to-treat for the statistical analysis. Limitations include the lack of achieved 25% energy reduction in the intervention group and high drop-out rate..

Context

- The bone related outcomes were not primary intended outcomes of the parent RCT and are best considered as exploratory findings.
- The study was well-executed in controlling for crucial bone health nutrients [e.g., calcium, vitamin D] thereby isolating effects of the weight loss consequent on energy restriction in the intervention group.
- Exercise may attenuate or abolish the effects of energy restriction and weight loss on BMD.
- The absolute magnitude of these changes was miniscule and would translate to <0.5% increase in risk of fractures over 10yrs in a woman ~50yrs of age.

Application

- Nutrition and physical activity – are modifiable factors, and that in population subgroups prone to BMD loss, i.e., postmenopausal women and the elderly, the boring but solid advice applies: good nutrition and exercise are what someone can look to aside from picking their parents for genes.