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CRUCIFEROUS VEGETABLES INTAKE & HEALTH BENEFITS

There is significant evidence that increasing consumption of fruit and vegetables is of benefit for maintaining health and preventing a host of diseases. But are all fruit and vegetables equal? Cruciferous vegetables, which include amongst others broccoli, cauliflower, cabbages, bok choy, kale, watercress, turnip and rocket, seem to be particularly standing out.

Three summary reports in this issue are reporting epidemiological observational studies, which show a significant inverse association between consumption of cruciferous vegetables and all-cause mortality (Mori et al.), lung cancer risk (Zhang et al.) and hardening of arteries (Blekkenhorst et al.). Interestingly, these studies report observations from different geographical locations, with notably different types of cruciferous vegetables consumed (for example, Asian populations are predominantly consuming Chinese cabbages, whereas US, Australian and European populations are predominantly consuming broccoli and cauliflower). This suggests that despite the varied structural diversity of the glucosinolates, the sulfur compounds that are unique to cruciferous vegetables, they all share common mechanistic pathways that prevent disease. Once consumed, glucosinolates are converted into bioactive isothiocyanates, which have been shown to have anti-inflammatory, anti-oxidant, and chemopreventive properties, in animal and cell models.

The time is now right to support such observational evidence for the health benefits of cruciferous vegetables with robust experimental clinical studies in humans, in order to determine whether glucosinolates are alone responsible for the benefits, or other sulfur metabolites found in these vegetables are also beneficial.

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Cruciferous vegetable intake is inversely associated with mortality

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Cruciferous vegetables are abundant sources of isothiocyanates which have been reported to suppress inflammation and oxidative stress closely linked with chronic diseases[1,2]. Isothiocyanates have also been reported to inhibit the bioactivation of procarcinogens and potentially enhance the excretion of carcinogens before they damage the DNA, thus possibly leading to cancer prevention[3,4]. Along with isothiocyanates, cruciferous vegetables contain several micronutrients (folate, vitamin C, tocopherols, and carotenoids) associated with reduced risk of mortality[5].

Study on 88 184 middle-aged Japanese

This is the first study aimed to investigate the association between cruciferous vegetables intakes with all-cause mortality and the five leading causes of death (cancer, heart disease, cerebrovascular disease, respiratory disease, and injuries) among 88 184 Japanese middle-aged (45-74 years old) men and women.

A Food Frequency Questionnaire (FFQ) was distributed at the 5-years follow-up survey to collect information on habitual dietary intake of 138 items including 8 cruciferous vegetables (cabbage, Chinese radish, komatsuna, broccoli, Chinese leaves, pak choi, leaf mustard and Swiss chard) and 3 pickled cruciferous vegetables (pickled Chinese radish, pickled rape and leaf mustard and pickled Chinese leaves). Hazard ratios (HRs) of all- and specific-cause mortality were estimated according to the quintile (Q) of cruciferous vegetables intake, Q1 being for the lowest intake and Q5 for the highest.

Profile of cruciferous vegetable consumers

Participants who consumed more cruciferous vegetables (Q5), compared with those who have the lowest intake (Q1), were:

- ***Significantly older***
(Q5: 58.4 / Q1: 54.7 years old in men and Q5: 58.1 / Q1: 55.6 years old in women)
- ***Less likely to be current smokers***
(Q5: 43% / Q1: 51.8% in men and Q5: 4.5% / Q1: 7.8% in women)
- ***More likely to consume more fruit***
(Q5: 222 g/d / Q1: 120 g/d in men and Q5: 279 g/d Q1: 184 g/d in women) ***and other vegetables***
(Q5: 180 g/d / Q1: 67 g/d in men and Q5: 196 g/d / Q1: 88 g/d in women).

Cruciferous vegetable intake and all-cause, specific-cause mortality

Compared with participants in Q1, those who consumed more cruciferous vegetables had significantly lower risk of all-cause mortality (HR= 0.86 for men and 0.89 for women) regardless of smoking status.

In men, this inverse association was predominantly associated with cancer mortality (Figure 1). The inverse association seen among smokers could possibly be because of the reduced bioactivation of procarcinogens in tobacco smoke.

In women, it was predominantly associated with heart disease (HR=0.73), cerebrovascular disease (HR=0.78) and injury-related mortality (HR=0.60) (Figure 1). This could possibly be related to anti-inflammatory properties of isothiocyanate found in cruciferous vegetables.

These findings suggest that a higher cruciferous vegetable intake is associated with reduced risk of all-cause mortality.

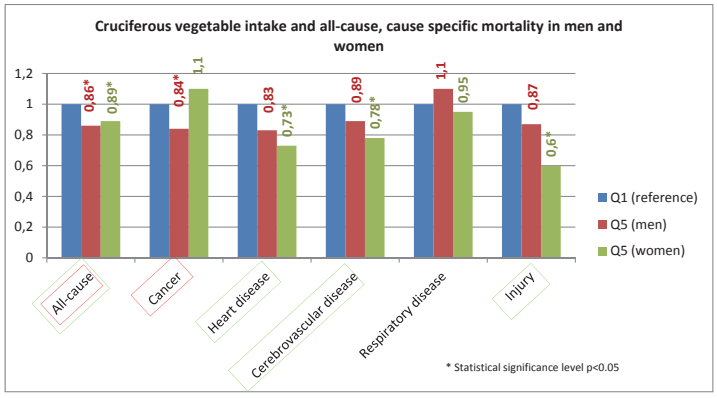

Figure 1: Cruciferous vegetable intake and all-cause, cause specific mortality in men and women

Based on: Mori N, et al., Cruciferous vegetable intake and mortality in middle-aged adults: A prospective cohort study, Clinical Nutrition (2018), https://doi.org/10.1016/j.clnu.2018.04.012

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Cruciferous vegetables and lung cancer prevention

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In the United States and around the world, lung cancer is the leading cause of cancer-related deaths. Smoking and air pollution exposures are primary factors for increasing one's risk of lung cancer. Diet may reduce one's risk of lung cancer by modifying the detoxification process of airborne carcinogenic compounds, and cruciferous vegetables are among these potential dietary factors. Once ingested, glucosinolates are hydrolyzed into various metabolites including isothiocyanates (ITCs), nitriles, indole-3-carbinoles (I3C), and oxazolidine-2-thiones[1]. I3C and ITCs have been shown to have chemopreventive properties in preclinical studies. The ITCs that we commonly consume are: sulforaphane (SFN; glucoraphanin precursor), allyl isothiocyanate (AITC), benzyl isothiocyanate (BITC), and 2-phenyl isothiocyanate (PEITC).

Review of 31 observational studies and two clinical trials

The aim of this review paper was to summarize the current evidence regarding cruciferous vegetable intake and ITCs for lung cancer prevention from 31 observational studies quantitatively and two clinical trials qualitatively.

Observational studies

Inverse association between cruciferous vegetable intake and lung cancer risk

Regarding observational studies, our meta-analysis of 31 studies found a statistically significant inverse association between cruciferous vegetable intake and lung cancer risk; the summary odds ratio/relative risk and 95% confidence intervals comparing the highest with lowest intake categories were 0.81 and 0.74-0.89.

Stratification by smoking status

There was a strong evidence of heterogeneity among studies, indicating that several factors may modify the inverse association of cruciferous vegetable intake with lung cancer risk. To examine potential sources of heterogeneity, a stratified meta-analysis by sex, smoking status, or both was conducted.

Stratification by smoking status showed a statistically significant inverse association among non-smokers with no evidence of heterogeneity, but not among past and current smokers. This suggests a strong impact of smoking on lung cancer risk.

Limitations of previous observational studies and recommendations for future research directions

The main limitations of observational studies are related to:

- Measurement errors inherent in self-reported intake;
- The use of food frequency questionnaire that may not accurately estimate cruciferous vegetable intake;
- Insufficient data concerning the source and preparation methods of cruciferous vegetables that can strongly impact ITC absorption;
- The limited availability of urinary samples to measure ITC levels that reflect intake within 24 hours (because ITCs do not accumulate in plasma or serum).

For future studies, more observational studies need to be conducted in populations that have high intake of cruciferous vegetables to investigate the association of urinary ITC concentrations with lung cancer risk.

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Clinical trials

Current evidence is limited to two phase II trials with incomplete reporting:

- **Trial 1**: 12-week placebo-controlled broccoli beverage trial in Qidong, China in 2011–2012, including 82 participants in each arm[2];
- **Trial 2**: 5-week (5-day intervention phase) cross-over PEITC trial in smokers at the University of Minnesota conducted between 2008 and 2013, including 41 participants[3].

Both trials provided standardized bioactive compounds: 600 µmol glucoraphanin and 40 µmol SFN once/day in the Qidong study, and 61 µmol PEITC 4 times/day in the Minnesota study. Given that benzene can be detected at elevated concentrations in cigarette smoke and industrial polluted air and is detoxified through the mercapturic acid metabolites, they measured urinary concentrations of mercapturic acid, a detoxification product of benzene. Both studies reported increased urinary concentrations of mercapturic acid, although they used different ITC compounds and amounts. These results are exciting; however, more short-term clinical trials (phase II) need to be conducted to investigate effects of varying amounts and many types of cruciferous vegetables on risk and efficacy biomarkers of lung cancer.

Based on: Zhang Z. et al. The Role of Cruciferous Vegetables and Isothiocyanates for Lung Cancer prevention: Current Status, Challenges, and Future Research Directions. Mol. Nutr. Food Res. 2018, 62 (18).

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Eating cruciferous vegetables may protect elderly women from hardening arteries

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Cardiovascular disease (CVD) contributes to 1 in 2 non-communicable disease deaths worldwide[1]. The main underlying cause of CVD is atherosclerosis, a multifactorial disorder of the arteries initiated by endothelial dysfunction, inflammation, and dyslipidaemia[2]. Subclinical measures of generalised atherosclerosis include common carotid artery intima-media thickness (CCA-IMT) and carotid focal plaque from B-mode carotid ultrasound[3], both associated with an increased risk of CVD events[4].

There is a broad consensus on the health benefits of a higher vegetable intake consistently associated with a reduced risk of CVD[5]. However, the associations of total and specific vegetable intake with measures of subclinical atherosclerosis remain understudied. Therefore, we sought to investigate the associations of total and specific vegetable intake with measures of subclinical atherosclerosis, including CCA-IMT and carotid focal plaque.

Study on 968 Australian elderly women

The study included 968 older Australian women aged between 70 and 85 years old with dietary measures and carotid ultrasound taken in late 1990s and early 2000s. Food frequency questionnaire developed and validated by the Cancer Council of Victoria, Australia was used to estimate total vegetable intake: 24 vegetables including cruciferous vegetables (cabbage, Brussels sprouts, cauliflower and broccoli), allium, yellow/orange/red, leafy green and legumes CCA-IMT and carotid focal plaque were assessed using high-resolution B-mode ultrasonography.

Higher intake of total vegetables is associated with lower CCA-IMT

Higher total vegetable intakes were associated with lower CCA-IMT. For each additional serving (75 g/d), there was 1.4% lower mean CCA-IMT and 1.7% lower maximum CCA-IMT after adjusting for lifestyle and CVD risk factors. Women consuming ≥225 grams per day of total vegetable intake had 4.6 to 5% lower CCA-IMT compared to those women consuming <150 grams per day.

Higher intake of cruciferous vegetables is associated with lower CCA-IMT

Intake of cruciferous vegetables was inversely associated with lower CCA-IMT. For every 10 g/d of cruciferous vegetables, there was a 0.8% lower mean and maximum CCA-IMT after adjusting for lifestyle and CVD risk factors. This relationship remained after additional adjustment for non-cruciferous vegetable intakes. There was no association for allium, yellow/orange/red, and leafy green vegetables with mean or maximum CCA-IMT.

Potential mechanisms of consuming cruciferous vegetables

Potential mechanisms that could explain the observed associations between intake of cruciferous vegetables and lower arterial wall thickening are that cruciferous vegetables contain nutrients and bioactive compounds that may be involved in antioxidant and anti-inflammatory activity[6]. Organosulfur compounds are found almost exclusively in cruciferous vegetables and only a few other vegetables, such as allium vegetables. These compounds have been extensively researched for their anticancer properties and evidence is now accumulating to suggest benefits towards cardiovascular health[7]. Isothiocyantates are a group of organosulfur compounds found exclusively in cruciferous vegetables. Sulforaphane, a compound within the isothiocyanate group, may reduce vascular damage by blocking oxidative stress, inhibiting advanced glycation end products and reducing inflammation (8). Additional research is necessary to explore these and other compounds within cruciferous vegetables and their potential benefits towards cardiovascular health.

Our findings support the need for dietary guidelines worldwide to highlight the importance of increasing cruciferous vegetable intake for protection against CVD.

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Based on: Blekkenhorst, L.C., et al. Cruciferous and total vegetable intakes are inversely associated with subclinical atherosclerosis in older adult women. J Am Heart Assoc. 2018;7(8):1-13.

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