Invited Commentary

Dietary flavonoid intake and cardiovascular mortality

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In this issue of the British Journal of Nutrition, Mursu et al.(1) have reported the association between flavonoid intake, cardiovascular mortality and ischaemic stroke among a group of participants in the Kuopio Ischaemic Heart Disease Risk Factor Study. After following up 1950 Finnish men for an average time of 15·2 years, they ascertained 102 ischaemic strokes and 153 CVD deaths. They found no significant association between total flavonoid intake and risk of ischaemic stroke and cardiovascular mortality; however, individual subclasses of flavonoids were marginally associated with reduced risk of ischaemic stroke and CVD mortality; those in the highest quartile of flavonol intakes had lower risks for ischaemic stroke and those in the highest quartile of flavanone and flavone intakes were less likely to die of CVD.

Fruit and vegetable intakes have consistently been reported to be inversely associated with cardiovascular mortality(2–4). Parts of this association might be explained by their higher content of flavonoids. Several epidemiological studies have assessed the association between flavonoid intake and cardiovascular risk(5–8), albeit with inconsistent results. Overall, available data suggest that those with higher intakes of flavonoids have modestly lower risks for CVD. However, very few studies considered all flavonoid subclasses(1,5) and most have used dietary intakes of one or two subclasses(7,8). The study by Mursu et al.(1) is the second that has used updated US Department of Agriculture databases of flavonoids. Investigators from the Iowa Women’s Heart Disease Risk Factor Study. After following up 1950 Finnish men for an average time of 15·2 years, they ascertained 102 ischaemic strokes and 153 CVD deaths. They found no significant association between total flavonoid intake and risk of ischaemic stroke and cardiovascular mortality; however, individual subclasses of flavonoids were marginally associated with reduced risk of ischaemic stroke and CVD mortality; those in the highest quartile of flavonol intakes had lower risks for ischaemic stroke and those in the highest quartile of flavanone and flavone intakes were less likely to die of CVD.

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for energy intake in some reports, and different dietary and cultural patterns across populations.

**Flavonoid intake and risk of stroke**

Inconsistent findings are available regarding flavonoid intakes and stroke. Mursu et al.\(^1\) found that dietary intakes of flavonols and less strongly flavan-3-ols were inversely associated with the risk of ischaemic stroke while total flavonoid consumption and intakes of other subclasses (namely flavones, flavanonols and anthocyanidins) were not found to be associated. In a cross-sectional report from this population, Mursu et al.\(^{14}\) have indicated that flavan-3-ols were inversely associated with common carotid artery intima-media thickness, an early marker of ischaemic stroke and atherosclerosis. They found a marginally significant inverse association between intakes of flavonols and mean common carotid artery intima-media thickness. In line with Mursu et al.\(^{11}\), two other studies\(^{12,15}\) have also reached significant inverse association between dietary intake of flavonoids and the risk of stroke. However, in a recent prospective study among postmenopausal women, neither total flavonoid intakes nor individual flavonoid subclasses were associated with the risk of stroke\(^5\). Others have also failed to find any significant association between dietary intakes of flavonols\(^{16-18}\), flavones\(^{15-18}\), flavanonones\(^{12}\) or catechins\(^{19}\) and stroke. Overall, limited data available in this field make judgement very difficult, particularly when the findings are inconsistent. Different findings could be explained by relatively low numbers of stroke incidence during follow-ups, considering different subtypes of stroke, examining stroke mortality instead of stroke incidence as an outcome variable, confinement of the study population to a specific gender or a specific group of participants (e.g. smokers) and using different tools for dietary intake assessments. Although some flavonoid-rich foods have been reported to be protective against stroke, it is not clear whether such protection is conferred by flavonoids, other nutrients and phytochemicals in flavonoid-rich foods, or the whole foods themselves\(^{20}\).

**Flavonoids and cardiovascular mortality**

The inverse association between intake of individual subclasses of flavonoids and cardiovascular mortality has been suggested by several investigators. However, others have failed to reach such conclusions. Mursu et al.\(^3\) found an inverse association between flavanone and flavone intakes, but not total flavonoid intake, and cardiovascular mortality. In the Zutphen Elderly Study, a well-known study in this field, by assessing flavonoid intake of 805 elderly men, Hertog et al.\(^{21}\) found that those in the highest tertile were 68% less likely to have CHD death compared to those in the lowest tertile. Later, these findings were confirmed in the Seven Countries Study\(^{22}\). Intake of flvanonones and anthocyanidins, but not total flavonoids, were associated with a decreased risk of CHD, CVD and all-cause mortality in a recent study among 34 489 women in the Iowa Women’s Health Study with 16 years of follow-up\(^5\). Previous reports of this cohort have shown decreased risk for CHD mortality with greater flavonol, flavone, catechins and epicatechins (flavan-3-ols) intakes\(^{16,19}\). Contrary to these studies, some data do not support the hypothesis of inverse association between flavonoids and cardiovascular mortality. In the US Health Professionals Follow-up Study, Rimm et al.\(^8\) did not find flavonoid intake (flavonols and flavones) to be associated with the risk of CHD mortality. This finding has recently been confirmed in US women\(^7\). The Caerphilly Study demonstrated an increased risk of the all-cause mortality by flavonol intakes\(^{23}\).

It seems that consumption of selected subclasses of flavonoids is more efficacious to human health than total flavonoid intake. A recent meta-analysis of prospective cohort studies showed that high dietary intakes of flavonoids might be associated with a modestly decreased risk of CHD mortality\(^{24}\). The inhibition of LDL oxidation and platelet aggregation by flavonoids\(^{20}\) suggests that higher intakes might protect against cardiovascular mortality. As mentioned earlier, some epidemiological studies have suggested an inverse relation while others demonstrated low or even no relationship between flavonoid intake and the risk of death from CHD. These contradictory findings may be due to various factors such as lifestyle in different populations, lack of control for other dietary components, limitation to estimate total flavonoid intake due to lack of complete flavonoid database etc. Therefore, in the absence of well-designed clinical trials, the possibility of decreased cardiovascular mortality by dietary flavonoids warrants further investigations.

Most investigations assessing flavonoid intakes so far have been limited in their ability to estimate total flavonoid intake due to the lack of a complete flavonoid database. The use of a new database of flavonoids released by the US Department of Agriculture\(^{25}\) might help to clearly define the association between flavonoid intake and cardiovascular mortality. Just the study by Mursu et al.\(^1\) and a recent study in American women\(^{26}\) have used these databases to assess total flavonoid intakes in relation to cardiovascular risks. Mursu et al.\(^1\) have used five subclasses while the American study has used seven subclasses\(^5\). Although some countries have assembled databases of flavonoid contents of foods, information on subclasses of flavonoids are lacking in many countries. Because of recent investigations about the health benefits of flavonoids, developing or expanding flavonoid food composition databases is warranted. Accurate and extensive food composition databases, although difficult and time-consuming, are required to clarify the relationships between consumption of flavonoids and incidence of chronic disease.

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**References**


