

Dietary epicatechin intake and 25-y risk of cardiovascular mortality: the Zutphen Elderly Study

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BACKGROUND

- + Cardiovascular disease (CVD) is the leading cause of death worldwide, accounting for ~30% of all deaths.
- + Consumption of plant-based foods rich in flavan-3-ols, a subclass of flavonoids, is inversely associated with CVD.
- + Diet is a crucial contributing factor to CVD development.
- + Cocoa, tea and apples are major dietary sources of the flavan-3-ol epicatechin.

AIM

The associations of dietary epicatechin intake with 25-year CVD mortality in elderly men were investigated.

METHODS

+ Study-design

- Prospective cohort study
- 744 elderly men, aged 65-84y, residing in Zutphen, Netherlands
- Followed up from 1985 till 2010
- 4 assessment points for epicatechin: in 1985, 1990, 1995 and 2000

+ Dietary assessment

- Participants were interviewed about their usual food-intake patterns
- Food intake data were converted into energy and nutrient data
- Flavan-3-ol contents of 120 commonly consumed plant foods and beverages were determined and used to estimate participants' intake

+ Additional data collected

Baseline:

- BMI
- Blood pressure
- Cholesterol and HDL cholesterol
- Medical history and medication
- Social economic status

Repeated intervals:

- Medical history and medication
- Smoking status
- Physical activity

+ Case ascertainment

- Participants were followed until death or censored on June 30th 2010
- Causes of death were evaluated by official death certificates
- Causes of death were coded according to the International Classification of diseases

METHODS

Data analysis

Model 1

Adjusted for age

Model 2

Adjusted for:

- Age
- Prevalence of myocardial infarction, stroke, heart failure and diabetes at baseline
- Aspirin use, antihypertensive medication, smoking status, alcohol intake, and physical activity

Model 3

As model 2 plus adjusted for intakes of total energy, saturated fat, trans-fat, n-3 fatty acids, n-6 fatty acids, dietary fiber, potassium, β -carotene, and coffee

Stratified analysis
for the prevalence of CVD
Dose-response analysis for
epicatechin from tea compared
to non-tea dietary sources

RESULTS

- + Mean epicatechin intake was 15.2 ± 7.7 mg/d and the main dietary sources were tea (51%), apples (28%), and cocoa (7%).
- + There was a strong correlation on the 5-year repeated estimate of epicatechin intake: individual epicatechin intake did not vary over time.
- + 712 men died and causes of death could be assigned to:
 - CVD (329)
 - Coronary heart disease (CHD) (148)
 - Stroke (72)
- + Risk of CHD mortality was inversely associated with epicatechin intake in all 3 models.
- + Long term risk of CHD mortality was 38% lower (model 3) in men in the highest ($\bar{x}=22$ mg/ day) vs the lowest ($\bar{x}=8$ mg/ day) tertile of epicatechin intake.

RESULTS

- + Risk of CVD mortality was inversely associated with intake of epicatechin in model 1 only (age adjusted), when top tertile was compared to bottom tertile.
- + For men with prevalent CVD, intake of epicatechin was associated with 46% lower CVD mortality risk for those in the highest vs the lowest tertile of epicatechin intake.
- + The dose-response analysis showed throughout all epicatechin sources (total epicatechin, epicatechin from tea and epicatechin from other sources) ~25% decreased risk of CVD death.
- + Epicatechin intake was inversely associated with non-CVD and all-cause mortality, but only the inverse association with all-cause mortality was significant.
- + Catechin intake was strongly correlated with that of epicatechin and was inversely related to CHD mortality. The strength of this association was similar to that of epicatechin.

CONCLUSION

“Higher epicatechin intake is associated with lower risk of long-term CHD mortality in elderly men, as well as with CVD mortality in men with prevalent CVD”.

Dietary epicatechin intake and 25-y risk of cardiovascular mortality: the Zutphen Elderly Study^{1–3}

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ABSTRACT

Background: Prospective cohort studies have shown that the consumption of cocoa and tea is associated with lower risk of cardiovascular diseases (CVDs), and cocoa and tea have been shown to improve CVD risk factors in randomized controlled trials. Cocoa and tea are major dietary sources of the flavan-3-ol epicatechin.

Objective: We investigated the associations of dietary epicatechin intake with 25-y CVD mortality in elderly Dutch men.

Design: We used data from the Zutphen Elderly Study, which was a prospective cohort study of 774 men aged 65–84 y in 1985. Epicatechin intake was estimated 4 times in 15 y with the use of the crosscheck dietary history method. Time-dependent Cox proportional hazards models were used to investigate repeated measures of epicatechin intake in relation to 25-y CVD mortality.

Results: Mean intake of epicatechin was 15.2 ± 7.7 mg/d, and the major dietary sources were tea (51%), apples (28%), and cocoa (7%). During 25 y of follow-up, 329 men died from CVD, 148 died from coronary heart disease (CHD), and 72 men died from stroke. Risk of CHD mortality was 38% lower in men in the top tertile of epicatechin intake than in men in the bottom tertile of epicatechin intake (HR: 0.62; 95% CI: 0.39, 0.98). Epicatechin intake was also significantly associated with 46% lower risk of CVD mortality in men with prevalent CVD (HR: 0.54; 95% CI: 0.31, 0.96) but not in men who were free of CVD.

Conclusions: We show, for the first time to our knowledge, that epicatechin intake is inversely related to CHD mortality in elderly men and to CVD mortality in prevalent cases of CVD. More studies are needed before conclusions can be drawn. *Am J Clin Nutr* 2016;104:58–64.

Keywords: cardiovascular disease, cocoa, epicatechin, flavan-3-ols, tea

INTRODUCTION

Cardiovascular disease (CVD)⁶ is the leading cause of death and is responsible for ~30% of all deaths worldwide (1). Diet is an important determinant of CVD (2). The consumption of plant-based foods, which are a rich source of flavan-3-ols, was inversely associated with CVD risk (3). Flavan-3-ols are a subclass of flavonoids, and cocoa (*Theobroma cacao*), tea (*Camellia sinensis*), and apples are their major dietary sources.

A meta-analysis of 7 observational studies ($n = 114,009$) showed that the highest chocolate consumption was associated

with 37% lower risk of CVD (RR: 0.63; 95% CI: 0.44, 0.90) and 29% lower risk of stroke (RR: 0.71; 95% CI: 0.52, 0.98) (4). In a meta-analysis of 14 cohort studies, the consumption of 3 cups black or green tea/d was associated with 13% lower risk of stroke (RR: 0.87; 95% CI: 0.81, 0.94) (5). A meta-analysis of 5 additional observational studies ($n = 35,808$) showed that individuals who drank 1–3 cups green tea/d had 36% lower risk of stroke (OR: 0.64; 95% CI: 0.47, 0.86) (6). Black tea consumption was not associated with CHD (7).

Clinical trials have shown that chocolate and cocoa improved endothelial function, blood pressure (BP), and insulin resistance (8). Likewise, meta-analyses of tea trials have shown that black or green tea consumption improved endothelial function (9), and black (10) and green tea reduced BP (11). Randomized controlled trials (RCTs) have also shown that green tea reduced fasting glucose and insulin concentrations (12), thereby reducing insulin resistance, which is an important risk factor for type 2 diabetes and CVD (13–15). Indeed, a meta-analysis of prospective cohort studies showed that consumption of >3–4 cups was related to 15% lower risk of incident type 2 diabetes (RR: 0.84; 95% CI: 0.73, 0.94) (16).

Epicatechin is the most-abundant flavan-3-ol in cocoa. Black and green teas are also rich in epicatechin, and contribute ~40% of the epicatechin intake in European populations (17). Recently, we showed that a supplement of 10 mg pure epicatechin/d decreased soluble endothelial selectin, which is a marker of

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³Supplemental Figure 1 and Supplemental Tables 1–3 are available from the “Online Supporting Material” link in the online posting of the article and from the same link in the online table of contents at <http://ajcn.nutrition.org>.

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⁶Abbreviations used: BP, blood pressure; CHD, coronary heart disease; CVD, cardiovascular disease; ECg, epicatechin gallate; EGCG, epigallocatechin gallate; MET, metabolic equivalent tasks; RCT, randomized controlled trial.

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