

Can tea consumption reduce the risk of CVD? A discussion paper of a recently published cohort study

Sofia - Panagiota Giannakopoulou, Demosthenes Panagiotakos
*Department of Nutrition – Dietetics, School of Health Science and Education,
Harokopio University*

Abstract

Cardiovascular disease is the leading cause of death globally. Tea contains high amounts of bioactive compounds which exert cardioprotective role through many proposed mechanisms such as regulation of glucose control, lipid metabolism, platelet aggregation, vasodilation and inflammation. In the present article, a prospective cohort study that aimed to investigate the effect of daily tea consumption on the risk of ischemic heart disease is discussed. The analysis of the results showed that there are benefits from daily tea consumption. Although, there is cumulative evidence that tea consumption is associated with reduced risk of CVD, more studies should be conducted in order to establish causal relationship and to better evaluate the impact of tea consumption on cardiovascular health.

Key words: tea; cardiovascular disease; polyphenols; flavonoids; catechins; ischemic heart disease

1. Introduction

Cardiovascular disease (CVD) is one of the greatest public health challenges worldwide. According to

World Health Organization (WHO), CVD is globally the leading cause of death and is expected to account for >22.2 million deaths by 2030 [1]. Apart from the cost

SUBMISSION: 17/07/2018 | ACCEPTANCE: 29/09/2018

Citation

Giannakopoulou SP, Panagiotakos D. Can tea consumption reduce the risk of CVD? A discussion paper of a recently published cohort study. *Hell J Atheroscler* 2018; 9: 104-110

*Corresponding author: Prof Demosthenes B Panagiotakos
Harokopio University, 176 71 Athens, Greece
Tel. +30 210-9549332
Email: dbpanag@hua.gr

to the patient and his/her family, CVD is a great economic burden for healthcare services and the society, as well. According to recent reports, the CVD cost to the EU economy is estimated €210 billion a year [2]. Taking into consideration the substantial clinical and economic cost of CVD, emphasis was put on its prevention.

2. Dietary habits, beverages and atherosclerotic disease

Healthy lifestyle patterns can be regarded as cornerstone for both primary and secondary prevention of atherosclerotic disease and particular CVD [3]. Diet has revealed as an important component of a healthy lifestyle. Healthy dietary habits have protective role in CVD primarily via effects on various risk factors, such as cholesterol, blood pressure (BP), body weight and diabetes mellitus (DM). A cardio-protective diet is characterized by low intake of saturated and trans fatty acids (<10% and <1% of total energy intake respectively), reduction of salt intake (<5g/d), adequate intake of fruit (≥ 200 g/d), vegetables (≥ 200 g/d), fiber (30-45g/d), fish (1-2 times/week) and nuts (30g/d, unsalted), limited consumption of alcoholic beverages (≤ 20 g/d alcohol for men and ≤ 10 g/d for women) and discouragement of sugar-sweetened drinks consumption [4]. All these characteristics characterize a very well-known and studied dietary pattern, the Mediterranean diet, which has been associated with decreased CVD risk [5, 6] but also with reduced risk of all-cause mortality in healthy subjects [7]. Beverages are consumed in every human culture and, as a major part of the new diet of affluence, can either influence health status. Tea, next to water, is the cheapest beverage humans consume. Drinking the beverage tea has been considered a health-promoting habit since ancient times [8].

In this paper, the results of a recently published prospective cohort study [9] that aimed to investigate the effect of daily tea consumption on the risk of ischemic heart disease (IHD), is discussed. The study consisted of 487375 Chinese participants, with no history of cancer, heart disease and stroke at baseline. Participants were enrolled during 2004-2008 and followed up until 31 December 2013. Data were obtained from China Kadoorie Biobank (CKB) study [10, 11]. In order to assess tea consumption, a qualitative food frequency questionnaire (FFQ) was used at baseline. All study partic-

ipants were asked to self-report their tea consumption for the last 12 months. For this reason, the questionnaire provided five frequency categories. For the participants who declared weekly tea consumption, there were additional questions about days consuming in a typical week, amount of tea, grams of tea added each time, times of changing tea leaves, type of tea used as well as the age in which the weekly tea consumption was started. However, as authors mentioned, the questions concerning tea consumption were not directly validated, and this may reveal an issue for serious bias in results interpretation. Moreover, the paper lacks information about stirring and brewing methods used for the preparation of tea. All participants divided into three groups based on their tea consumption frequency (i.e., never, less than daily, daily), while the daily consumers were additionally grouped, according to rounded quartiles. In order to assess covariates, information about socio-demographic characteristics, lifestyle, personal and family medical history was obtained. Regarding the personal medical history and specifically prevalent hypertension and diabetes, the authors mention that the diagnosis could be either self-reported or measurement-based, which means variation in the diagnosis method. The dietary information obtained from the participants included only intake of alcohol, red meat, fresh fruits and vegetables. However, authors do not justify the reason of obtaining partial and not detailed dietary information. Also, they do not define the methods that were used to select the three food groups finally used in the questionnaire. The primary outcomes were: (a) major coronary events (MCEs) included fatal IHD and non-fatal myocardial infarction (b) a broader spectrum of IHD, mostly chronic IHD. The data analysis showed that the participants who reported daily tea consumption had 8% lower relative risk for ischemic heart disease (IHD) and 10% lower risk for major cardiovascular events (MCE). In particular, the 26.3% of the participants (n=128280), reported at baseline almost daily tea consumption, while the most common type of tea was green. During the median follow-up (7.2 years), a number of 24665 IHD cases and 3959 MCEs cases were reported. A Cox proportional hazard model was used for the estimation of the hazard ratio (HR) and 95% confidence interval (CI). The multivariable-adjusted HRs and 95% CIs for less than daily and daily

tea consumers were 0.97 (0.94 to 1.00) and 0.92 (0.88 to 0.95) for IHD, 0.92 (0.85 to 1.00) and 0.90 (0.82 to 0.99) for MCE. Also, for daily consumers, tests for linear trend with amount of tea consumption as continuous variable were conducted but were not significant ($P_{\text{linear}} > 0.05$). Further associations based on the tea type and years of tea consumption were made, all as compared with those who reported no tea consumption for the last 12 months. No difference observed between green tea and non-green tea consumers, regarding IHD and MCE. The effect of tea consumption on risk for IHD was greater to those who reported long-term tea consumption. The researchers also conducted subgroup analysis according to age, region, smoking, alcohol consumption, physical activity, BMI, hypertension and diabetes at baseline. The CVD risk in the subgroup analysis was differentiated by the region of residence in favor to rural – underlying a potential diet – environmental interaction-, by BMI category in favor to $< 24 \text{ kg/m}^2$ and by diabetes status in favor to absence, at baseline.

Despite the limitations observed in the study design and discussed here, the reported findings may suggest that daily tea consumption may be used as a potential supplementary nutritional mean for CVD prevention.

3. The role of tea consumption in atherosclerotic disease prevention

In addition to solid foods, beverages are an important part of daily nutrition. Tea is after water, the second most consumed beverage worldwide [12]. Tea is an infusion of the leaves of the *Camellia sinensis* plant and according to fermentation method used, can be divided into four types, green tea, white tea, black tea and oolong tea [13]. Green tea is produced by non-fermented leaves; oolong tea is made from partially fermented leaves while black tea is derived from fully fermented leaves. Tea leaves are high in antioxidant content. About 30% of the dry substance, are polyphenols mainly flavonoids. The main class of flavonoids in tea are flavanols and flavonols. The leading flavanol compounds are catechins such as epicatechin (EC), epigallocatechin (EGC), epicatechin gallate (ECG), and epigallocatechin gallate (EGCG), whereas the main flavonols in tea are quercetin and kaempferol. The fermentation process affects the antioxidant content in each tea type. During the processing complex condensation and po-

lymerization products are derived from flavanols, such as theaflavins and thearubigins [14]. Therefore, green tea is mainly constituted from catechins (80-90%) and less condensed flavanols (theaflavins and thearubigins) (10%), whereas black tea is high in theaflavins (50-60%) than in catechins (20-30%) due to fermentation process [15, 16]. Tea, especially green, contains also vitamins and minerals. Thus, a tea consumption of five cups per day may contribute up to 10% in the requirements of riboflavin, niacin, folic acid and pantothenic acid, up to 45% of manganese, up to 25% of potassium and up to 5% of magnesium [12]. Tea contains also caffeine but in lower amounts than coffee (16). A cup (200 mL) of green tea contains approximately about 142 mg EGCG, 65 mg EGC, 28 mg ECG, 17 mg EC, and 76 mg caffeine [17] while black tea infusions contain 17-25 mg/L quercetin, 13-17 mg/L kaempferol and about 3 mg/L myricetin [18].

Due to high frequency of tea intake it is important to evaluate its effect on CVD risk. Evidence from observational, epidemiological and experimental studies, suggest that tea consumption is associated with improved cardiovascular function [12, 19, 20]. Tea exerts pleiotropic effects through several possible mechanisms in numerous aspects of CVD (**Figure 1**). One of the main characteristics of CVD is impaired lipid metabolism [21]. It is also suggested that tea catechins can reduce intestinal lipid absorption, promote cholesterol fecal excretion and inhibit hepatic enzymes involved in cholesterol synthesis [22]. CVD is also a state of oxidative stress [21] and there is evidence that tea catechins may have radical-scavenging ability [23]. Tea compounds such as catechins and quercetin may prevent the oxidation of LDL, leading to reduced risk of CVD [22, 24]. Results from a meta-analysis of randomized controlled trials showed that green tea consumption significantly lowered total cholesterol concentration by 7.20 mg/dL and LDL-cholesterol by 2.19 mg/dL [25]. Furthermore, tea flavonoids, and more specifically theaflavin, are proposed to have anti-inflammatory effects through inhibition of tumor necrosis factor-alpha (TNF- α) mediated interleukin-8 (IL-8) gene expression [26]. CVD is characterized by impaired endothelial function and increased blood pressure [21]. Tea consumption results in improved endothelial function as assessed with flow-mediated dilatation (FMD) of the brachial artery

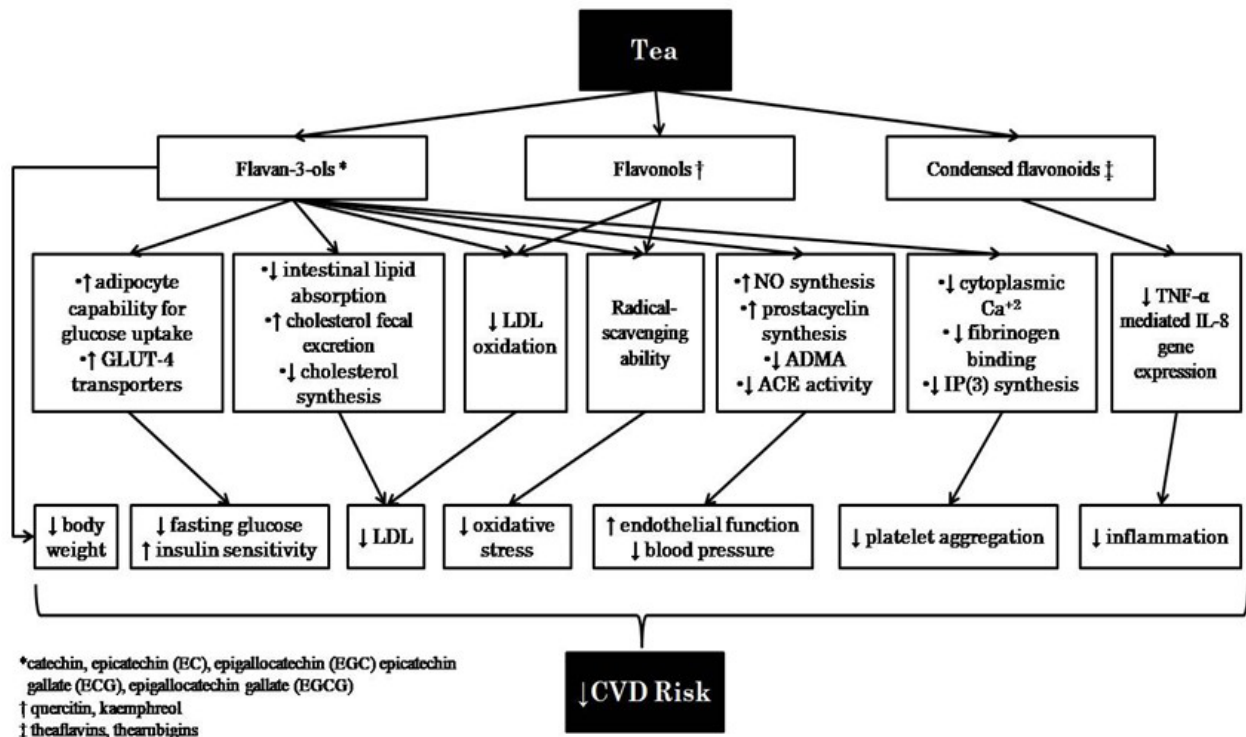


Figure 1: Some of the proposed mechanisms by which tea components exert cardioprotective effect.

[27]. The proposed mechanisms for this effect include the impact of tea catechins to the promotion of nitric oxide (NO) and prostacyclin synthesis which are vasodilators and the reduction of asymmetric dimethylarginine (ADMA), which inhibits the NO production. Tea catechins also seem to suspend the angiotensin-converting enzyme (ACE) activity, achieving vasodilatory effect [23]. In vitro analyses have found that tea catechins can inhibit platelet aggregation and also protect platelets from peroxidative stress through inhibition of cytoplasmic calcium (Ca²⁺) increase which results to the inhibition of fibrinogen binding and IP[3] synthesis [28]. In addition, tea via its catechins may enhance the adipocyte capability for glucose uptake by increasing glucose transporter-4 (GLUT-4) content in adipocytes. In this way, tea consumption can promote insulin sensitivity and result to decreased fasting glucose [29, 30]. Finally, catechins seem to decrease body weight but also helping weight loss maintenance [31].

The half-life of polyphenols in plasma is short (2-3h), so maintenance of high plasma concentration is achieved with regular consumption, and specifical-


ly with close together repeated intakes, because otherwise plasma concentrations fluctuate and accumulation failure is observed [32]. The results of the present study also suggest that protective effect is strongly related to the consistency and chronicity of the consumption. So, repeated exposure seems to be essential in order tea consumption to be beneficial. The protective effect was observed to participants with BMI < 24 kg/m². Role in this differentiation may have the altered gut microbiota of obese people.

Although total polyphenol content is similar among all tea types, the polyphenol concentration in the extract varies, depending on the preparation process [15]. It is known that stirring and brewing methods affect the quality of the final product. The catechin to caffeine ratio is determined by brewing time. Polyphenols are more difficult to extract than caffeine which means that longer brewing time is associated with higher catechin to caffeine ratio [16]. However in the present study, information about tea extract production was not acquired. The study was also lacking the information about the parallel consumption of known confound-

ers, such as coffee. As authors state, due to lack of detailed dietary information, generalization of the results to other population cannot be made. Also individuals with CVD related conditions might have changed their tea consumption before baseline thus reverse causality is possible, despite the fact that participants with major diseases were excluded at baseline.

4. Conclusion

There is cumulative evidence that tea consumption is associated with reduced risk of CVD. However, a causal relationship and the elucidation of the mechanisms by

which tea consumption influences CVD risk have not been established, yet. Also consideration must be taken into the potential side effects of great tea consumption on patients with comorbidities, such as kidney diseases which are closely interrelated with CVD. Nevertheless, tea drinking is a flavorful way of getting enough fluid into body each day, that also seems to protect against heart diseases, as well as possibly even helping to stave off cancer. 

Conflict of interest

There is no conflict of interest.

Περίληψη

Μπορεί η κατανάλωση τσαγιού να μειώσει τον κίνδυνο καρδιαγγειακής νόσου; Ένα άρθρο συζήτησης μιας πρόσφατα δημοσιευμένης μελέτης κοορτής.

Σοφία - Παναγιώτα Γιαννακοπούλου, Δημοσθένης Β. Παναγιωτάκος

Τμήμα Επιστήμης Διαιτολογίας - Διατροφής, Χαροκόπειο Πανεπιστήμιο, Αθήνα, Ελλάδα

Η καρδιαγγειακή νόσος είναι η κύρια αιτία θανάτου παγκοσμίως. Το τσάι περιέχει μεγάλες ποσότητες βιοδραστικών ενώσεων που ασκούν καρδιοπροστατευτικό ρόλο μέσω πολλών προτεινόμενων μηχανισμών όπως ρύθμισης του ελέγχου της γλυκόζης, του μεταβολισμού των λιπιδίων, της συσσωμάτωσης των αιμοπεταλίων, της αγγειοδιαστολής και της φλεγμονής. Στο παρόν άρθρο συζητείται μια προοπτική μελέτη κοορτής, η οποία είχε στόχο τη διερεύνηση της επίδρασης της καθημερινής κατανάλωσης τσαγιού στον κίνδυνο ισχαιμικής καρδιοπάθειας. Η ανάλυση των αποτελεσμάτων έδειξε ότι υπάρχουν οφέλη από την καθημερινή κατανάλωση τσαγιού. Παρόλο που υπάρχουν σωρευτικές ενδείξεις ότι η κατανάλωση τσαγιού συνδέεται με μειωμένο κίνδυνο καρδιαγγειακής νόσου, πρέπει να διεξαχθούν περισσότερες μελέτες προκειμένου να καθοριστεί η αιτιώδης σχέση και να αξιολογηθεί καλύτερα ο αντίκτυπος της κατανάλωσης τσαγιού στην καρδιαγγειακή υγεία.

Λέξεις ευρητηρίου: τσάι, καρδιαγγειακή νόσος, πολυφαινόλες, φλαβονοειδή, κατεχίνες, ισχαιμική καρδιακή νόσος

References

1. WHO. Global Status Report on Noncommunicable Diseases 2014. Geneva, Switzerland 2014
2. Wilkins E, Wilson L, Wickramasinghe K, Bhatnagar P, Leal J, Luengo-Fernandez R, et al. European Cardiovascular Disease Statistics 2017. Brussels: 2017
3. Notara V, Panagiotakos DB, Pitsavos CE. Secondary prevention of acute coronary syndrome. Socio-economic and lifestyle determinants: a literature review. *Cent Eur J Public Health* 2014 ;22: 175-182
4. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Eur Heart J* 2016; 37: 2315-2381
5. Williams CM, Lovegrove JA, Griffin BA. Dietary patterns and cardiovascular disease. *Proc Nutr Soc* 2013; 72: 407-411
6. Panagiotakos DB, Georgousopoulou EN, Pitsavos C, Chrysohoou C, Skoumas I, Pitaraki E, et al. Exploring the path of Mediterranean diet on 10-year incidence of cardiovascular disease: the ATTICA study (2002-2012). *Nutr Metab Cardiovasc Dis* 2015; 25: 327-335
7. Prinelli F, Yannakoulia M, Anastasiou CA, Adorni F, Di Santo SG, Musicco M, et al. Mediterranean diet and other lifestyle factors in relation to 20-year all-cause mortality: a cohort study in an Italian population. *Br J Nutr* 2015; 113: 1003-1011
8. Sumpio BE, Cordova AC, Berke-Schlessel DW, Qin F, Chen QH. Green tea, the "Asian paradox," and cardiovascular disease. *J Am Coll Surg* 2006; 202(5): 813-825
9. Li X, Yu C, Guo Y, Bian Z, Si J, Yang L, et al. Tea consumption and risk of ischaemic heart disease. *Heart* 2017; 103: 783-789
10. Chen Z, Lee L, Chen J, Collins R, Wu F, Guo Y, et al. Cohort profile: the Kadoorie Study of Chronic Disease in China (KSCDC). *Int J Epidemiol* 2005; 34: 1243-1249
11. Chen Z, Chen J, Collins R, Guo Y, Peto R, Wu F, et al. China Kadoorie Biobank of 0.5 million people: survey methods, baseline characteristics and long-term follow-up. *Int J Epidemiol* 2011; 40: 1652-1666
12. Hartley L, Flowers N, Holmes J, Clarke A, Stranges S, Hooper L, et al. Green and black tea for the primary prevention of cardiovascular disease. *Cochrane Database Syst Rev* 2013; : CD009934
13. Namal Senanayake SPJ. Green tea extract: Chemistry, antioxidant properties and food applications – A review. *J Funct Foods* 2013; 5: 1529-1541
14. V. Chemical composition of tea. *Food Reviews International*. 1995; 11: 435-456
15. Deka A, Vita JA. Tea and cardiovascular disease. *Pharmacol Res* 2011; 64: 136-145
16. Bohn SK, Ward NC, Hodgson JM, Croft KD. Effects of tea and coffee on cardiovascular disease risk. *Food Funct* 2012; 3: 575-591
17. Shukla Y. Tea and cancer chemoprevention: a comprehensive review. *Asian Pac J Cancer Prev* 2007; 8: 155-166
18. Hertog MGL, Hollman PCH, van de Putte B. Content of potentially anticarcinogenic flavonoids of tea infusions, wines, and fruit juices. *J Agric Food Chem* 1993; 41: 1242-1246
19. Pang J, Zhang Z, Zheng TZ, Bassig BA, Mao C, Liu X, et al. Green tea consumption and risk of cardiovascular and ischemic related diseases: A meta-analysis. *Int J Cardiol* 2016; 202: 967-974
20. Kuriyama S. The relation between green tea consumption and cardiovascular disease as evidenced by epidemiological studies. *J Nutr* 2008; 138: 1548S-1553S
21. Serafini M, Del Rio D, Yao DN, Bettuzzi S, Peluso I. Health Benefits of Tea. In: nd, Benzie IFF, Wachtel-Galor S, editors. *Herbal Medicine: Biomolecular and Clinical Aspects*. Boca Raton (FL) 2011
22. Kim A, Chiu A, Barone MK, Avino D, Wang F, Coleman CI, et al. Green tea catechins decrease total and low-density lipoprotein cholesterol: a systematic review and meta-analysis. *J Am Diet Assoc* 2011; 111: 1720-1729
23. Moore RJ, Jackson KG, Minihane AM. Green tea (*Camellia sinensis*) catechins and vascular function. *Br J Nutr* 2009; 102: 1790-1802
24. Hollman PC, Katan MB. Absorption, metabolism and

- health effects of dietary flavonoids in man. *Biomed Pharmacother* 1997; 51: 305-310
25. Zheng XX, Xu YL, Li SH, Liu XX, Hui R, Huang XH. Green tea intake lowers fasting serum total and LDL cholesterol in adults: a meta-analysis of 14 randomized controlled trials. *Am J Clin Nutr* 2011; 94: 601-610
 26. Aneja R, Odoms K, Denenberg AG, Wong HR. Theaflavin, a black tea extract, is a novel anti-inflammatory compound. *Crit Care Med* 2004; 32: 2097-2103
 27. Alexopoulos N, Vlachopoulos C, Aznaouridis K, Baou K, Vasiliadou C, Pietri P, et al. The acute effect of green tea consumption on endothelial function in healthy individuals. *Eur J Cardiovasc Prev Rehabil* 2008; 15: 300-305
 28. Kang WS, Chung KH, Chung JH, Lee JY, Park JB, Zhang YH, et al. Antiplatelet activity of green tea catechins is mediated by inhibition of cytoplasmic calcium increase. *J Cardiovasc Pharmacol* 2001; 38: 875-884
 29. Liu K, Zhou R, Wang B, Chen K, Shi LY, Zhu JD, et al. Effect of green tea on glucose control and insulin sensitivity: a meta-analysis of 17 randomized controlled trials. *Am J Clin Nutr* 2013; 98: 340-348
 30. Polychronopoulos E, Zeimbekis A, Kastorini CM, Papairakleous N, Vlachou I, Bountziouka V, et al. Effects of black and green tea consumption on blood glucose levels in non-obese elderly men and women from Mediterranean Islands (MEDIS epidemiological study). *Eur J Nutr* 2008; 47: 10-16
 31. Hursel R, Viechtbauer W, Westerterp-Plantenga MS. The effects of green tea on weight loss and weight maintenance: a meta-analysis. *Int J Obes (Lond)* 2009; 33: 956-961
 32. Manach C, Scalbert A, Morand C, Remesy C, Jimenez L. Polyphenols: food sources and bioavailability. *Am J Clin Nutr* 2004; 79: 727-747