

## Introduction

There has been considerable interest in the possible medicinal benefits of tea and the topic has been widely studied. Because it is consumed ubiquitously, even small benefits of tea could have far reaching benefits. In fact, the LDL cholesterol antioxidant properties of polyphenolic flavonoids present in tea, especially black and green tea, has made it a promising inhibitor of cardiovascular disease (CVD) (1). Tea consumption has also been shown to have protective effects against elements associated with CVD such as atherosclerosis, vascular dysfunction, and thrombus formation (2,3,4). In light of this evidence it seems optimistic that drinking tea can protect against heart disease.

Despite the recent evidence, don't go out and buy shares of Lipton stock just yet. The jury is still out on just how tea exerts many of its effects. There is even evidence that tea may not be beneficial for preventing CVD (5,6). To date, there has not been a large-scale, long-term randomized trial on the effects of tea on cardiovascular outcomes, so we cannot be sure that tea is the heart disease-fighting ambrosia that it appears to be. In addition, bias towards publishing studies that show protective effects of tea raises further caution in interpreting the results of studies regarding the cardiovascular benefits of drinking tea (7). Clearly, we are just beginning to understand the relationship between tea and cardiovascular disease.

## Consumption of tea reverses endothelial dysfunction

Disruption in endothelial function has been established as a predictor of CVD progression (9-12). Therefore, it stands to reason that if endothelial function can be improved, CVD could be decreased. Two recent studies have examined the effect of tea consumption on endothelial function.

In the most recent of these studies by Hodgson et al., it was found that regular ingestion of black tea improves vascular function in subjects with elevated serum cholesterol and triglycerides. The study employed a randomized, controlled, parallel design with 21 subjects randomly assigned to either a 4-week course of 5-250 ml cups of hot water or black tea per day. Changes from baseline in endothelium-dependent and endothelium-independent brachial artery vasodilator function were assessed using ultrasonography (US). The study found a 41% improvement in endothelium dependent vasodilation (2.3%;  $P=.008$ ). Interestingly, the researchers also found a significant increase in endothelium independent vasodilatation (4.2%;  $P=.03$ ), which suggests that improvements in brachial artery vasodilator function cannot be solely attributed to an effect of tea on endothelial function (8). The researchers found no effect on vasodilator function with ingestion of hot water. In another study by Duffy et al., researchers investigated the effect of short- and long-term tea consumption on brachial artery, flow-mediated dilation in those with coronary artery disease. In the study, 66 patients with coronary artery disease were randomized to water or tea consumption first with endothelial function assessed by US after short and long term tea and hot water consumption. Duffy et al also looked at the effect of an equivalent amount of caffeine on flow-mediated dilation. Compared to baseline both short-term (1 serving of 450mL) and long-term (900 mL per day for 4 weeks) tea consumption significantly improved endothelium-dependent brachial artery flow-mediated dilatation with no effect for hot water ( $P<.001$ ) (3). Caffeine was not found to affect the short-term effects of tea.

These two studies suggest that the demonstrated protective effects of tea may be due to improved vasodilator function in arteries such as the coronary arteries, using the brachial artery as a proxy. Both authors suggest that flavonoid-induced increases in the bioavailability of nitric oxide may be one mechanism by which tea exerts this effect (3,8). There are several limitations, however that could confound their results. First, lifestyle differences such as diet and physical activity were not taken into account and such lifestyle factors have been associated with CVD (13). Concurrent medication usage was not well controlled for in the Duffy et al study and this could have had some influence on the results. Randomized assignment to treatment groups in these studies is likely to have minimized the effects of potential confounders, however. The small sample size of the Hodgson et al study raises questions about the power of the study to detect a clinically relevant difference in vasodilator function among the treatment groups. The influence of caffeine was not controlled for at all in the Hodgson et al study and although Duffy et al concluded that caffeine did not influence the short-term effects of tea, it is unknown how caffeine may have influenced the long-term effects.

### Regular tea consumers have fewer heart attacks

What might all of this mean in terms of tangible health outcomes? Well, according to a study published last year by Geleijnse et al, drinking tea may actually protect against the incidence of myocardial infarction (MI). In the study, 4807 healthy participants over the age of 55 participating in the Rotterdam study were followed for an average of 5.6 years. The researchers found that tea drinkers had a reduced risk of suffering a MI, especially fatal events, among those who consumed at least 375 mL of tea per day (RR: 0.57; 95%CI: 0.33, 0.98) compared to non tea drinkers. This data was obtained after adjustment for the following factors: body mass index, smoking status, alcohol usage, educational level, and dietary factors. When they looked at the effect of dietary flavonoids alone, the authors found that they were almost significantly related to a reduction in risk of MI (RR: 12.7%; P=.07) per 10 mg increase in tea intake. After adjustment for the factors mentioned above this effect was attenuated to a 9 % risk reduction (2). The results of this study are strengthened by the fact that lifestyle and dietary factors were adjusted for. However, a major flaw in this study is the fact that physical activity, which has been found to be strongly associated with CVD, was not taken into account (13). Also, from this study we are not sure what kind of tea was consumed- whether black, green, herbal or other so no conclusions can be drawn regarding the effects of a particular type of tea.

It is important to mention that there are two recent epidemiological studies that seem to contradict the findings of Geleijnse et al. In the Caerphilly Study by Hertog et al, a protective effect of tea against ischemic heart disease was not found among men aged 45-79 years (5). Moreover, in the Health Professionals Follow-up study by Rimm et al, no association between tea and ischemic heart disease was found (6). These studies have drawbacks of their own, however, because they did not control for dietary factors, nor did they account for physical activity as potential confounders.

Evidence that the conclusions regarding a protective effect of tea against MI may be at least overestimated comes from a study by Peters et al. In a meta-analysis of 17 studies published from 1966 to 2000, Peters et al found a bias toward the publication of studies that show a protective effect of tea against MI and stroke. Peters et al is careful to mention that the publication bias does not disprove the possibility of a protective effect, but that the overall strength of the effect might be attenuated if all unpublished results were brought to light (7). The

fact that there has been only two epidemiological studies published within the last seven years that have results inconsistent with a protective effect, may be proof that this bias is ongoing.

### Tea drinkers have better survival after a heart attack

Because tea consumption has been shown to have protective effects against endothelial dysfunction and incidence of MI, there has been a question regarding whether tea drinkers fare better than their non tea-drinking counterparts after a heart attack. As part of the Determinants of Myocardial Infarction Onset Study by Mukamal et al, 1900 patients hospitalized after suffering an acute MI were interviewed regarding tea consumption during the previous year. Tea consumption was categorized as heavy (>14 cups per week), moderate (<14 cups per week), or none. After an average of 3.8 years, age- and sex-adjusted cardiovascular and non-cardiovascular mortality was lower in moderate and heavy tea drinkers (hazard ratio: 0.69; 95% CI: 0.53, 0.89 & hazard ratio: 0.61; 95% CI 0.42, 0.86 respectively) versus non-tea drinkers. Adjustment for additional factors such as: previous MI, diabetes mellitus, hypertension, non cardiac co-morbidity, medication use, smoking status, body mass index, use of thrombolytic therapy, usual exercise frequency, alcohol use, income, education, and complications of congestive heart failure or ventricular tachycardia while hospitalized, did not greatly alter the results for moderate and heavy tea drinkers (hazard ratio 0.56; 95% CI: 0.37, 0.84 & hazard ratio: 0.72; 95% CI: 0.55, 0.94) (14). Non-tea caffeine intake was assessed in a similar manner and was not found to be associated with subsequent mortality. The fact that non-cardiovascular mortality was also decreased among tea drinkers suggests that tea drinkers may be different from non-tea drinkers in some other factor(s) that affect mortality.

One strength of this study is the fact that the presence of possible confounders was well thought out and considered in the analysis of the data. As with other studies, however, the study by Mukamal et al did not elucidate whether black tea differs from green tea in producing the study results. Also, dietary differences among those with higher versus lower mortality was not considered. Differences in diet may help explain the differences that the researchers found in overall mortality between tea drinkers and non-drinkers. Since this is the only study that has examined the effect of tea consumption on mortality after a heart attack, further studies on the subject are warranted.

### Conclusion

Studies have recently demonstrated that drinking tea can protect against CVD by reversing endothelial dysfunction thereby decreasing the risk of having a heart attack, and improving mortality after a heart attack. Although the evidence seems convincing that tea has at least some protective effects against CVD, there is so much that we still do not know about the topic. For example: if tea really does have a protective effect, how much must be consumed to realize any benefits?; what are the mechanisms by which tea exerts its protective effects?; is there a dose-response relationship between tea and severity of CVD?; do black tea and green tea differ in their effects?; does adding sugar and cream influence the effect?; etc. These questions demonstrate the need for further research. Future research, however, must be well designed in order to clearly establish an association between tea and CVD. Furthermore, researchers should submit- and peer-reviewed journals should publish studies with disregard to the findings. Learning more about the effect of this relaxing and fragrant beverage on the leading cause of mortality in industrialized societies is an exciting and important prospect.

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