Letters to the Editor

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Safety and efficacy concerns regarding elective coronary artery surgery in patients with prior coronary stents

Recent data have raised concerns about the safety of drug-eluting stents. Stents are used in over 70% of percutaneous coronary interventions (PCIs) because they reduce the risk of acute major complications of PCI and long-term restenosis. Despite the low procedural morbidity afforded by stenting, coronary artery bypass graft (CABG) surgery offers significantly greater freedom from angina, repeat revascularization, myocardial infarction, stroke, and death in the treatment of multivessel ischaemic heart disease. Stenting has, however, become first line treatment in increasing numbers of patients that are surgical candidates. Many of these patients eventually require coronary artery surgery: in the UK over 5% of patients undergoing CABG have a history of previous PCI.

Surgeons suspect that prior stenting may have a negative impact on outcome after elective coronary surgery for several reasons. In-stent restenosis is associated with a higher risk of early venous graft failure. The presence of coronary stents means that grafts are anastomosed more distally, and endarterectomy may be required. Anti-platelet medication adds to increased morbidity and potential mortality, resulting from excess post-operative bleeding, and stopping this medication has been associated with stent thrombosis in off-pump CABG patients.

Pathophysiological processes associated with stenting may adversely affect surgical outcomes. Stenting causes prolonged endothelial dysfunction and local and systemic inflammatory syndromes, more profound than after balloon angioplasty, because of persistent radial mechanical strain, vessel wall rupture, and the presence of an intra-vascular foreign body. The local inflammatory response is stimulated by disruption of the coronary endothelium, and is characterized by a florid macrophage response that does not occur after balloon angioplasty. Six months after PCI endothelium-dependent vasomotor function has been shown to be more abnormal in stented coronaries compared with those undergoing balloon angioplasty. Two years after stenting a chronic inflammatory response surrounds the stent, characterized by non-occlusive mural thrombi. Drug-eluting stents induce this inflammatory response, most prominently at the edges of the stent, but also where endothelialization is delayed leaving the intima exposed to metal within the stent. Troponin release is higher in patients receiving stents compared with those undergoing angioplasty alone, and is associated with increased peri-procedural mortality, rates of myocardial infarction, and repeat revascularization.

UK data suggest that patients with previous PCI had higher mortality after CABG than patients without prior PCI, even when patients undergoing salvage CABG for failed PCI are excluded from the analysis. Unfortunately, the timing of PCI in 90% of the remaining patients, and the proportion of PCIs that involve stenting are unknown. We propose a prospective longitudinal multicentre study to evaluate the effect of previous stenting on clinical outcomes after elective coronary surgery, using peak oxygen consumption (VO2) as the primary outcome. For 80% power to detect a difference of 1.5 mL/kg/min in VO2 at the 5% two-tailed significance level, we would need 176 patients in each group. Secondary outcome measures include major adverse clinical events, quality-of-life adjusted years, and perfusion imaging with a 5-year follow-up.

References

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Addition of milk prevents vascular protective effects of tea

The paper of Lorenz et al., concludes that milk may counteract the favourable health effect of tea on vascular function. Impaired vasodilation is one of the mechanisms underlying hypertension. We agree with the authors in that all dietary components should be considered, and that potential interactions should be examined when interpreting effects.

We, however, would like to address two major aspects. That there was a significant positive effect of a large serving of tea on vasodilation is plausible considering what we know about the biological function of tea ingredients and phenolic compounds in other foods. It was, however, minor in absolute terms, just 3.5% above the control response. It is open how long the effect would last and what it could mean for the vasodilatory response throughout a whole day.

The authors then assumed that the inhibitory effect (or rather non-stimulatory) effect of tea if consumed together with milk might be caused by casein complexing the tea catechins. If such a complex is formed in the intestinal tract, would catechins remain complexed once casein is broken down to amino acids and peptides? We doubt this. Casein is a well-digestible protein. But casein forms a curd in the stomach. Release into the small intestine is delayed in comparison with other proteins, like whey proteins. When milk was fed to miniature pigs, whose gastrointestinal...
physiology is reasonably close to that of humans, the majority of proteins consumed was still in the stomach after 2 h of intake. Milk processing influenced the degree of retention. Therefore, complexed tea catechins might also remain in the stomach for an extended time, but would probably be released and absorbed later on, influence vasodilation at a later time post-prandially, and last longer. Of note, milk does not necessarily delay catechin absorption. When 25% milk was added to coffee, up to 40% of chlorogenic acid were bound to milk proteins, but these interactions tended to decrease during in vitro gastric and intestinal digestion. When ingested with a regular breakfast, there was no different appearance of catechins in blood between tea alone and tea with 100 ml of milk. Lorenz et al. served tea or tea plus milk with a croissant. We advise to perform repeated tests of the post-prandial vasodilatory response to tea and tea plus milk, at least up to 6 h. We would also suggest to perform an additional test with milk alone (plus water) as a control.

A major focus of research is on the health effects of dietary fats. Dietary fats mostly impair post-prandial vasodilation, but a number of substances, for example polyphenols from olive oil have the potential to prevent this impaired response or even improve vasodilation above the fasting level. Concurrent consumption of soy protein or casein did also prevent the fat-induced impaired vasodilation. In experiments of our group, a fat-rich mixed meal containing casein did not impair post-prandial vasodilatation (unpublished results). In fact, milk products seem to have beneficial effects of their own. A number of epidemiological studies observed an inverse correlation between consumption of milk and milk products and hypertension, and several intervention studies demonstrated a reduction of blood pressure with consumption of milk and milk products. Milk is rich in calcium and other minerals and low in sodium, and vasoactive peptides are encrypted in milk proteins. A trial within the so-called DASH programme (Dietary Approach to Stop Hypertension) showed that a diet rich in fruits, vegetables, and low-fat milk products reduces blood pressure significantly better than a fruit and vegetable diet alone, in individuals with both optimal and elevated blood pressure. Inclusion of dairy products nearly doubled inflow-mediated dilation (FMD) after volunteers had consumed the tea the evening before measurements.

The authors further doubt whether complexes between catechins and casein, if formed at all in the intestinal tract, would remain once the catechins are broken down to amino acids and peptides. As we have shown in Table 2 of our paper, tea catechins become complexed as soon as milk is added to tea. Whether these complexes are broken down during digestion of the caseins and whether the catechins are subsequently released and absorbed later on represent interesting questions. We are also aware of the study by van het Hof et al., who did not observe a difference in plasma catechin concentrations after consumption of black tea with or without milk. This observation needs to be further investigated. A plausible explanation of the fact that we observed an impairment of FMD response after addition of milk to tea may be that the catechins, owing to the longer retention period in the digestive tract, could have been modified and thus rendered physiologically inactive. The suggestion by the authors to measure the vasodilatory response at later time points is an important issue that should be addressed in future studies.

The remarks of the authors on the beneficial effects of milk products, including casein, on blood pressure are interesting. At no point, however, are we questioning these effects, nor did we intend to investigate the effects of milk alone on vasodilatory responses. We merely attempted to study the interaction of milk with tea and to determine whether milk could have an adverse effect on the well-known positive vasodilatory effects of tea.

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Addition of milk prevents vascular protective effects of tea: reply

We appreciate the interesting comments of Pfeuffer and Schrezenmeir regarding our paper. The authors state that the increase in flow-mediated dilation (FMD) after consumption of black tea in our study was just 3.5% above the control response. However, this value lies within the physiological range in the increase in FMD after consumption of beverages or food. Similar increases in FMD were observed after consumption of a high-flavanol cocoa drink as well as after oral ingestion of epicatechin, after consumption of dark chocolate, drinking of white and red wine, and consumption of black tea.

We measured FMD after 2 h, according to maximal flavonoid bioavailability. Chronic tea consumption for 4 weeks improved FMD after volunteers had consumed the tea the evening before measurements.

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