Meal fatty acids and postprandial vascular reactivity

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Abstract
With increasing recognition of the pivotal role of vascular dysfunction in the progression of atherosclerosis, the vasculature has emerged as an important target for dietary therapies. Recent studies have indicated that chronic fatty acid manipulation alters vascular reactivity, when measured after an overnight fast. However, individuals spend a large proportion of the day in the postprandial (non-fasted) state. Several studies have shown that high fat meals can impair endothelial function within 3–4 h, a time period often associated with peak postprandial lipoaemia. Although the impact of meal fatty acids on the magnitude and duration of the postprandial lipaemic response has been extensively studied, very little is known about their impact on vascular reactivity after a meal.

Introduction
Vascular tone/reactivity/elasticity is defined as the balance between vasorelaxing and vasoconstricting mechanisms in the environment of the vascular smooth muscle cells, the muscle group which determines vascular tone. Reductions in the bioavailability of nitric oxide, an endothelial-derived vasorelaxant, due to decreased synthesis, enhanced degradation and/or inactivation by an excess generation of reactive oxygen species in the subendothelial space, have been shown to contribute to endothelial dysfunction [1]. Impaired vascular reactivity/tone has been associated with the accelerated progression of atherosclerosis and serves as a marker for general vascular dysfunction [2]. Recent studies have highlighted the prognostic value of measures of vascular reactivity of both the coronary and peripheral arteries in predicting future coronary events [3].

Meal fat content, composition and vascular reactivity
Evidence is emerging in the literature that mechanisms involved in the control of vascular tone are influenced by dietary factors, with dietary fat emerging as a potentially important modulator. In general, diets rich in SFAs (saturated fatty acids) have been shown to negatively affect fasting endothelial function. Reductions in the bioavailability of nitric oxide, an endothelial-derived vasorelaxant, due to decreased synthesis, enhanced degradation and/or inactivation by an excess generation of reactive oxygen species in the subendothelial space, have been shown to contribute to endothelial dysfunction [1]. Impaired vascular reactivity/tone has been associated with the accelerated progression of atherosclerosis and serves as a marker for general vascular dysfunction [2]. Recent studies have highlighted the prognostic value of measures of vascular reactivity of both the coronary and peripheral arteries in predicting future coronary events [3].

Over the last decade a number of studies have examined the impact of meal fat quantity on vascular reactivity measured 2–8 h after a meal, but inconsistent findings have been reported. Although some studies have observed no relationship, a greater number have indicated that increasing the total fat content of a test meal reduces both cardiac and peripheral vascular reactivity [4]. In general, high fat meals (50–105 g) have been shown to impair endothelium-dependent vasodilation compared with low fat meals (less than 10 g). Several studies have suggested that acute hypertriglyceridaemia is responsible for this effect [5–7]. This raises the question as to whether reported differences in postprandial TAG (triacylglycerol) responses following meals of different fatty acid composition [8] could also contribute to dietary-induced differences in endothelial function.

Of the studies conducted in healthy subjects, the majority show a decrease in vascular reactivity 3–4 h after the high fat meals, regardless of meal fatty acid composition. However, a recent investigation in a male cohort has indicated that addition of fish oil fatty acids to a standard test meal improved vascular tone compared with baseline measurements [9] (Table 1). Only two other studies have examined the impact of fish oil fatty acids on postprandial vascular tone [6,7], with a significant impact of EPA (eicosapentaenoic acid)/DHA (docosahexaenoic acid) only observed by Vogel and co-workers [6]. In this study, the consumption of a meal containing canned red salmon or canola oil was shown to decrease FMD (flow-mediated dilatation) to a lesser extent than extra-virgin olive oil. Unlike the study of Armah et al. [9], an increase in vascular reactivity was not observed with the canned red salmon even though similar amounts of n–3 PUFAs were consumed. Differences in the food matrix (i.e. oil or whole food), total fat and EPA/DHA content of the meals may have contributed to the effects observed on vascular reactivity. In addition, it has been proposed that DHA, but not EPA supplementation, improves vascular tone [10], a finding which warrants further investigation within an acute setting.
Table 1 | Recent studies comparing the effects of meal fatty acid composition on postprandial vascular reactivity
Mixed meal refers to a combination of foods used in the test meal (e.g. milkshake containing test oil with toast and jam). ACh, acetylcholine; ALNA, α-linolenic acid; FBF, forearm blood flow; HC, hypercholesterolaemic; LDI, laser Doppler iontophoresis; PWA, pulse wave analysis; PWV, pulse wave velocity; SNP, sodium nitroprusside; VOP, venous occlusion plethysmography. 1 kcal = 4.184 kJ.

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Study group</th>
<th>Test meal</th>
<th>Vascular assessment method measurements</th>
<th>Significant results compared with baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raitakari et al. [18]</td>
<td>2000</td>
<td>Twelve healthy men and women (18–45 years)</td>
<td>Mixed meal (1030 kcal) containing 61 g of fat rich in SFAs or MUFAs</td>
<td>VOP and brachial artery FMD at 0, 3 and 6 h</td>
<td>↑ Brachial artery diameter, resting FBF and postischaemic hyperaemia after both meals; no changes in FMD with either meal</td>
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<td>Vogel et al. [6]</td>
<td>2000</td>
<td>Ten healthy men and women (28–56 years)</td>
<td>Mixed meal (900 kcal) containing 50 g of olive oil or canola oil or 420 g of canned red salmon (6 g of n-3 PUFAs)</td>
<td>Brachial artery FMD at 0 and 3 h</td>
<td>↓ FMD at 3 h with olive oil (31 %); this reduction was greater than for the canola (10 %) and fish oil (2 %) meals</td>
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<tr>
<td>Ng et al. [19]</td>
<td>2001</td>
<td>Ten healthy men (mean age 22 years)</td>
<td>Mixed meal (900 kcal) containing 50 g of fat consisting of a Western or an Asian high-fat meal</td>
<td>Brachial artery FMD at 0 and 4 h</td>
<td>↓ FMD 4 h after both meals (7.7–8.6 %)</td>
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<tr>
<td>Williams et al. [20]</td>
<td>2001</td>
<td>Fourteen healthy men (23–53 years)</td>
<td>Mixed meal (900 kcal) containing 60 g of olive oil or safflower oil</td>
<td>Brachial artery FMD at 0 and 4 h</td>
<td>No change in FMD with either meal</td>
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<td>De Roos et al. [21]</td>
<td>2002</td>
<td>Twenty-one healthy men (≥35 years)</td>
<td>Mixed meal (1178 kcal) containing palm kernel oil or partially hydrogenated soya bean oil (0.9–1.0 g/kg of body mass)</td>
<td>Brachial artery FMD at 0 and 3 h</td>
<td>No change in FMD with either meal</td>
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<tr>
<td>Armah et al. [9]</td>
<td>2005</td>
<td>Twenty healthy men (18–70 years)</td>
<td>Mixed meal (800 kcal) containing 40 g of palm olein/soya bean oil or 31 g of palm olein/soya bean oil and 9 g of fish oil</td>
<td>LDI in response to ACh and SNP at 0 and 4 h</td>
<td>↑ Vasodilatory response to SNP (46.8 %) 4 h after 31 g of palm olein/soya bean oil and 9 g of fish oil</td>
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<tr>
<td>West et al. [7]</td>
<td>2005</td>
<td>Eighteen Type 2 diabetic men and women (mean age 55 years)</td>
<td>Milk-based drink (625 kcal) rich in MUFAs, ALNA and MUFAs or EPA/DHA and MUFAs, total fat content 50 g</td>
<td>Brachial artery FMD at 0 and 4 h</td>
<td>No change in FMD with any meal [↑ FMD (17 %) in the group when data for all meals combined]</td>
</tr>
<tr>
<td>Berry et al. [13]</td>
<td>2006</td>
<td>Seventeen healthy men (18–40 years)</td>
<td>Mixed meal (749 kcal) containing 50 g of shea butter or high oleic sunflower oil</td>
<td>PWV, PWA and brachial artery FMD at 0 and 3 h</td>
<td>↓ FMD 3 h after high oleic sunflower oil; difference in FMD between meals at 3 h; ↓ PWA (%) 3 h after both meals</td>
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<td>Cortés et al. [12]</td>
<td>2006</td>
<td>Twelve healthy men and women and 12 HC patients</td>
<td>A saturated fat meal with 25 g of olive oil or 40 g of walnuts; fat content of meal 80 g (1200 kcal)</td>
<td>Brachial artery FMD at 0 and 4 h</td>
<td>↓ FMD with olive oil (17 %) in healthy subjects; ↓ FMD with olive oil (36 %) and ↑ FMD with walnuts (24 %) in HC patients</td>
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<tr>
<td>Nicholls et al. [22]</td>
<td>2006</td>
<td>Fourteen healthy men (18–40 years)</td>
<td>Mixed meal containing safflower oil or coconut oil (1 g/kg of body mass)</td>
<td>VOP and brachial artery FMD at 0, 3 and 6 h</td>
<td>↑ Post-hyperaemic blood flow 3 h after safflower oil (45 %) and coconut oil (21 %); ↓ FMD (2.2 %) 3 h following coconut oil</td>
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<tr>
<td>Reuda-Clausen et al. [23]</td>
<td>2007</td>
<td>Ten healthy men (18–23 years)</td>
<td>Vegetable soup (600 kcal) with 60 ml of soya bean, olive or palm oil</td>
<td>Brachial artery FMD at 0 and 3 h</td>
<td>↓ FMD (27–34 %) 3 h after each meal</td>
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</table>
In Type 2 diabetics, an increase in vascular reactivity was also observed with the addition of both marine and plant sources of $n-3$ PUFAs to a MUFA meal, but this association was only observed when the data for the study group were analysed with respect to fasting TAG concentration [7]. Lower postprandial TAG concentrations after the $n-3$ PUFA meals were inversely correlated with the increase in FMD in the subjects with higher fasting TAG levels. Conversely, a decrease in FMD was observed with the addition of fish oil to the MUFA meal in the low fasting TAG level group. This finding emphasizes the significance of the postprandial TAG response as a predictor of post-meal changes in endothelial-dependent vasodilation and may provide an explanation for the more exaggerated effects of meal fatty acids observed in hyperlipidaemic patients compared with healthy controls [11,12]. As exaggerated postprandial lipaemia is the central lipid defect in the increasingly prevalent metabolic syndrome, a better understanding of the relationship between lipaemia and vascular reactivity and the impact of meal fat composition on these processes is clearly needed.

**Meal fatty acids and vascular reactivity: underlying mechanisms**

Interestingly, of the studies highlighted in Table 1, oleic acid-rich oils appear to consistently impair endothelial function compared with baseline measurements and it appears that this change is directly related to the greater postprandial TAG response following MUFA-rich oils [6,7,13]. Several studies have suggested that the mechanism through which high fat meals inhibit vascular reactivity is via the induction of a temporary state of fat-induced oxidative stress. In agreement with this, Vogel et al. [6] found that addition of vitamins (C and E) or balsamic vinegar and salad to an olive oil meal reduced the impairment in endothelial function induced by the olive oil alone. Recent studies have also shown that consumption of a meal rich in virgin olive oil with a high phenolic content improves endothelial-dependent vasodilation as a result of the decrease in oxidative stress [14] and increase in nitric oxide metabolites [15]. Therefore oleic acid-rich oils may have differential effects on endothelial function depending on the phytochemical content of the oils.

The extent of the postprandial lipaemic response may in part mediate these differential effects of meal fatty acid composition on postprandial vascular tone, with SFA and MUFA meals increasing the magnitude and duration of the postprandial TAG response compared with $n-6$ and $n-3$ PUFA meals [8]. Studies have also shown that meal fatty acids can influence the lipid and apolipoprotein composition of TAG-rich lipoproteins and influence their interaction with endothelial cells [16]. Differences in the length of exposure of endothelial cells to TAG-rich lipoproteins (chylomicrons and very low density lipoproteins) and their remnants during the postprandial period may also contribute to the changes observed in vascular reactivity.

Inclusion of fish oil fatty acids in a high-fat meal was shown to have the potential to improve postprandial vascular tone in both healthy [6,9] and Type 2 diabetic subjects [7], a finding consistent with the impact of chronic fish oil supplementation. With respect to the impact of fish oils, it is predicted that these beneficial effects may be in part mediated by a direct effect of EPA/DHA on endothelial metabolism, in addition to their influence on the postprandial lipaemic response. One of the mechanisms may be via a reduction in tissue oxidative stress and induction of antioxidant enzyme activity [17]. Both EPA and DHA have been recognized as ligands for PPARγ (peroxisome-proliferator-activated receptor γ), the transcriptional regulator of both superoxide dismutase and nicotinamide adenine dinucleotide phosphate oxidase. However, the effects of fish oil fatty acids on PPARγ activity and cellular redox status during the postprandial state are currently unknown and worthy of investigation.

**References**


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