

Dietary saturated and unsaturated fats as determinants of blood pressure and vascular function

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The amount and type of dietary fat have long been associated with the risk of CVD. Arterial stiffness and endothelial dysfunction are important risk factors in the aetiology of CHD. A range of methods exists to assess vascular function that may be used in nutritional science, including clinic and ambulatory blood pressure monitoring, pulse wave analysis, pulse wave velocity, flow-mediated dilatation and venous occlusion plethysmography. The present review focuses on the quantity and type of dietary fat and effects on blood pressure, arterial compliance and endothelial function. Concerning fat quantity, the amount of dietary fat consumed habitually appears to have little influence on vascular function independent of fatty acid composition, although single high-fat meals postprandially impair endothelial function compared with low-fat meals. The mechanism is related to increased circulating lipoproteins and NEFA which may induce pro-inflammatory pathways and increase oxidative stress. Regarding the type of fat, cross-sectional data suggest that saturated fat adversely affects vascular function whereas polyunsaturated fat (mainly linoleic acid (18 : 2*n*-6) and *n*-3 PUFA) are beneficial. EPA (20 : 5*n*-3) and DHA (22 : 6*n*-3) can reduce blood pressure, improve arterial compliance in type 2 diabetics and dyslipidaemics, and augment endothelium-dependent vasodilation. The mechanisms for this vascular protection, and the nature of the separate physiological effects induced by EPA and DHA, are priorities for future research. Since good-quality observational or interventional data on dietary fatty acid composition and vascular function are scarce, no further recommendations can be suggested in addition to current guidelines at the present time.

Saturated fatty acids: Unsaturated fatty acids: Blood pressure: Vascular function

Introduction

Dietary fat has long been implicated in the aetiology of CVD. The majority of research into the role of dietary fat in CVD has focused on the effects of dietary fats on lipoprotein metabolism, due to the well-characterised association between blood cholesterol levels and cardiovascular mortality⁽¹⁾. The strength of the evidence enabled the prediction of changes in blood cholesterol, LDL-cholesterol, HDL-cholesterol and TAG that would occur on diets varying in their total fat content and fatty acid composition in a meta-analysis of sixty studies⁽²⁾. Clearly the field of nutritional science has made great inroads into our understanding of how dietary fats may affect cardiovascular risk through their effects on lipoprotein metabolism. Recommendations for dietary fat intake by the UK government are based on this evidence; it appears that the average British diet is edging closer to the dietary fat

guidelines but there is still a need for a reduction in population intake of SFA, and an increase in some unsaturated fats (Table 1). In addition to lipoprotein metabolism, dietary fats may also exert effects on less well-researched components of cardiovascular risk such as insulin sensitivity, haemostasis or vascular function. The purpose of the present review is to offer a new perspective on the role that the amount of dietary fat, as well as the fatty acid composition (SFA, PUFA and MUFA), may have in the maintenance of normal blood vessel tone.

Vascular function and cardiovascular risk factors

The ability of the vascular tree to respond and adapt to the demands placed upon it is critical to the lifelong development of atherosclerosis and eventual CVD. Vascular function is a general term used to describe the regulation of

Abbreviations: ALA, α -linolenic acid; DVP, digital volume pulse; eNOS, endothelial NO synthase; FMD, flow-mediated dilatation; LA, linoleic acid; LCP, long-chain PUFA; PGI, prostacyclin; PWV, pulse wave velocity.

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Table 1. UK dietary reference values for fat in adults

	Average intake (% total food energy intake) ⁽¹⁷⁴⁾		Recommended intake (% total food energy intake) ^(175,176)
	Men	Women	
Total fat	35.8	34.9	< 35 (< 33 % of total energy intake including alcohol)
SFA	13.4	13.2	< 11 (< 10 % of total energy intake including alcohol)
<i>Trans</i> -fatty acids	1.2	1.2	< 1
<i>n</i> -6 PUFA	5.4	5.3	6.5 (6 % of total energy intake including alcohol) total (<i>n</i> -6 plus <i>n</i> -3) PUFA*
<i>n</i> -3 PUFA	1.0	1.0	Individual minimum 1.0 linoleic acid and 0.2 ALA (0.45 g <i>n</i> -3 PUFA from oily fish per d (equivalent to one portion per week)†
MUFA	12.1	11.5	13 (12 % of total energy intake including alcohol)‡

* Recommended population average intake for total PUFA is 6.5 % of total food energy, with an individual maximum intake of 10 % energy intake, and an *n*-6:*n*-3 PUFA ratio of 5:1.

† Only 27 % of the UK population consumes oily fish, so the majority of the population will have intakes below the population average.

‡ If other guidance is followed, average population intake should be 13 % of total food energy.

blood flow, arterial pressure, capillary recruitment and filtration and central venous pressure, all of which are controlled by a multitude of intrinsic mechanisms (for example, NO, prostacyclin (PGI), adenosine, histamine, the stretch-activated Bayliss myogenic response, etc) and extrinsic mechanisms (sympathetic and parasympathetic innervation, adrenaline, angiotensin, vasopressin and insulin). Components of vascular function, such as hypertension, arterial stiffness and endothelium-dependent vasodilation, are associated with cardiovascular mortality^(3–5), and are therefore important risk factors that may be targeted with dietary modification.

Endothelial function measurements

The function of conduit (muscular) and terminal (resistance) arteries can be assessed by methods designed to measure vasodilation and vasoconstriction, mainly determined by endothelial mechanisms. Endothelial dysfunction (comprising increased permeability, reduced vasodilation, and activation of thrombotic and inflammatory pathways) is a crucial factor in the early stages of atherosclerosis⁽⁶⁾. Prolonged activation of vascular mechanisms for protecting against adverse stimuli (inflammatory response, procoagulation and vasoconstriction) can lead to endothelial dysfunction. Endothelium-dependent vasodilation is mainly mediated by NO, which is released from the endothelium following activation of the enzyme endothelial NO synthase (eNOS), causing the underlying smooth muscle to relax⁽⁷⁾. Other endothelium-dependent vasodilatory factors include PGI and endothelium-derived hyperpolarising factor⁽⁷⁾. The endothelium also secretes vasoconstricting factors, the major vasoconstrictor being the peptide endothelin-1. Figure 1 illustrates some of the endothelium-dependent mechanisms that are known to mediate arterial vasodilation and vasoconstriction.

Flow-mediated dilatation (FMD) of the brachial artery is now regarded as the most reliable assessment of endothelium-dependent vasodilation and as a surrogate measure of NO production⁽⁸⁾. It uses ultrasound to record images of the endothelium-dependent dilatatory responses of the brachial artery caused by reactive hyperaemia (FMD)⁽⁹⁾.

Another method involves venous occlusion plethysmography to measure forearm blood flow in peripheral resistance vessels following infusion of acetylcholine⁽¹⁰⁾. A third method uses laser Doppler imaging to measure peripheral microvascular endothelial function, a technique that assesses the response of cutaneous blood vessels to transdermal delivery of endothelium-dependent (for example, acetylcholine) and endothelium-independent (for example, sodium nitroprusside) vasoactive agents by iontophoresis⁽¹¹⁾. These methods have been widely adopted and shown to be reasonable prognostic indicators of cardiovascular events in patients with vascular diseases^(12–16).

Arterial stiffness and compliance measurements

Arterial stiffness (the inverse of arterial compliance) is mainly a consequence of changes in arterial wall composition in the systemic elastic arteries (loss of integrity of the elastin and increased collagen formation) and therefore can be quantified as a measure of ageing, hypertension and development of arteriosclerosis in the large central elastic arteries⁽¹⁷⁾. Muscular arteries are unaffected by these kinds of age- and hypertension-related changes, and drugs that are designed to reduce blood pressure by vasodilation have only indirect effects on the central elastic arteries via alteration of wave reflection amplitude and timing^(18,19). However, endothelial dysfunction of the conduit and terminal arteries may exacerbate arterial stiffness by increasing peripheral resistance due to an imbalance in vasodilators and vasoconstrictors⁽¹⁷⁾. Measurements of arterial compliance are commonly used as an indicator of arterial stiffening or ageing, but they are also indicative of endothelial function to a limited extent, since peripheral arterial compliance is partly dependent on endothelium-dependent vasodilation⁽¹⁸⁾. Information about the elasticity of arteries and peripheral vasodilation can be gleaned from arterial pulse wave analysis. Following ventricular ejection, the pulse pressure wave begins in the aorta. Stroke volume and the elasticity of the central aorta determine the peak pressure of the initial pulse wave during systole. Aortic compliance (the ability of the walls of the aorta to expand to accommodate the increase in blood

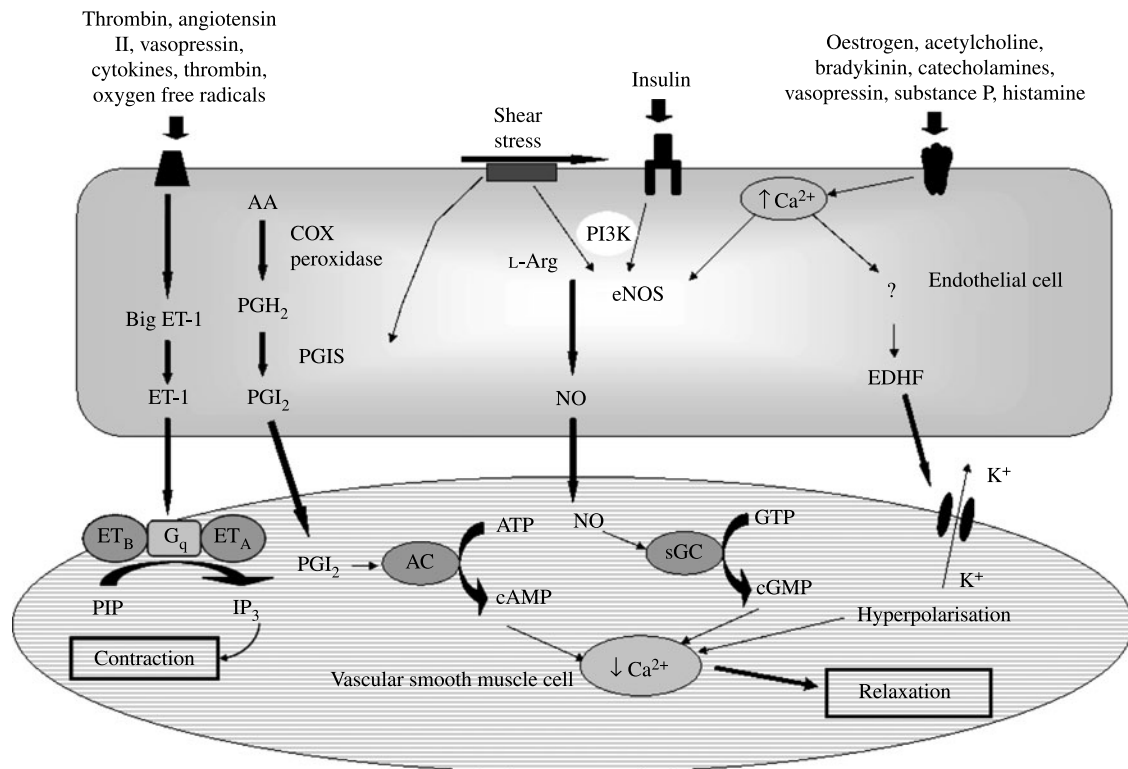


Fig. 1. Outline of major mechanisms for vascular smooth muscle cell relaxation and contraction mediated by the endothelial cell. Shear stress arising from blood flow increases intracellular Ca^{2+} levels. A rise in endothelial Ca^{2+} triggers the production of three relaxing factors: NO, prostacyclin (PGI_2) and endothelium-derived hyperpolarising factor (EDHF) which diffuse to the smooth muscle cell leading to relaxation. Increased intracellular Ca^{2+} activates endothelial NO synthase (eNOS), which then converts L-arginine (L-Arg) to L-citrulline, and NO is released. NO diffuses to the vascular smooth muscle cell where it activates soluble guanylate cyclase (sGC), causing an increase in cGMP production and consequently a decrease in smooth muscle intracellular Ca^{2+} and relaxation. PGI_2 interacts with the PGI_2 receptor, elevating cAMP levels and decreasing intracellular Ca^{2+} , leading to relaxation of the smooth muscle. EDHF is a vasorelaxant that has not been definitively identified and which can cause vasorelaxation by hyperpolarising vascular smooth muscle cells. Stimulation of endothelin-1 (ET-1) production by stress stimuli occurs in the endothelial cell. ET-1 binds to endothelin receptor A (ET_A) and endothelin receptor B (ET_B) receptors on the vascular smooth muscle cell, activating the phosphatidylinositol 4,5-bisphosphate–inositol 1,4,5-trisphosphate (PIP– IP_3) pathway and triggering contraction by increasing intracellular Ca^{2+} levels. AA, arachidonic acid; COX, cyclo-oxygenase; PI3K, phosphoinositide-3 kinase; PGH_2 , PG H_2 ; PGIS, prostacyclin synthase; G_q , Gq protein; AC, adenyllyl cyclase.

volume) is therefore directly related to pulse pressure. As the pulse pressure wave travels beyond the aorta, through smaller conduit and muscular arteries, and then arterioles, a second reflected pressure wave occurs as the blood flow passes bifurcations in the arterial tree and encounters increased resistance⁽²⁰⁾.

Pulse wave velocity (PWV) is a common method for assessing arterial stiffness⁽⁴⁾, is associated with all-cause mortality and cardiovascular outcomes⁽²¹⁾ and is regarded as a 'gold standard' measurement⁽²²⁾. PWV involves applanation tonometry (alternatively MRI or Doppler ultrasound) to measure the pressure wave of the carotid and femoral arteries commonly, although other sites can be used. PWV is usually measured as the delay between the initial upstrokes of the initial pulse pressure peak at the carotid and femoral pulse sites (adjusted for anatomical distance)⁽¹⁷⁾. The smaller the delay between the corresponding points on the upstroke of the initial wave (therefore the higher the velocity) the stiffer the arteries. An analogous measure of arterial stiffness, requiring minimal training of the observer, can be produced using the digital volume pulse (DVP) method, whereby finger photoplethysmography yields the

digital pulse pressure waveform in order to calculate a stiffness index⁽²³⁾. Further methodological techniques and considerations in the measurement of arterial stiffness are reviewed in detail elsewhere^(17,21,22,24). The radial or carotid artery pressure waves can also be used to calculate the augmentation index: the ratio of the magnitude of the reflected wave to the initial wave⁽²⁵⁾. This is an indirect measure of arterial stiffness and is mainly determined by the timing of return of the reflected wave, since an earlier return will increase the amplitude of the reflected wave by occurring in systole rather than diastole. However, it is also affected by changes in vascular tone in the muscular arteries (itself determined by release of vasodilators such as NO and vasoconstrictors such as endothelin-1), and can vary independently of PWV⁽¹⁸⁾. The equivalent measure using the DVP is the reflection index and is thought to represent changes in vascular tone in the periphery⁽²⁶⁾.

Blood pressure measurements

Although changes in arterial stiffening are the most accurate method to monitor the effects of ageing, systolic and

diastolic blood pressure measurements have been a valuable routine tool for many years in the monitoring of vascular changes and prediction of cardiovascular risk. Mean arterial pressure is determined by cardiac output and total peripheral resistance, and systolic and diastolic blood pressures depend on the size of the oscillation in pressure either side of mean arterial pressure⁽²⁰⁾. Systolic blood pressure is the peak arterial pressure during systole and depends on peripheral wave reflection, arterial stiffness and stroke volume, whereas diastolic blood pressure is the lowest pressure during cardiac relaxation and is primarily influenced by the tone of small arteries and arterioles⁽²⁰⁾. Many other factors regulate blood pressure, including the sympathetic nervous system and the kidneys, but since hypertension leads to vascular dysfunction, as well as being a function of arterial tone, it is a key parameter for vascular function. The latest British Hypertension Society classification of blood pressure levels is given in Table 2⁽²⁷⁾. Blood pressure measurements were traditionally carried out using a mercury sphygmomanometer, but they are now usually carried out with a semi-automatic oscillometric electronic blood pressure monitor for clinic and home measurements. Ambulatory blood pressure measurement has been shown to be a good predictor of cardiovascular risk and avoids a number of sources of error that occur with clinic measurements⁽²⁸⁾. In particular, ambulatory blood pressure monitoring gives a more accurate overview of blood pressure since there are many repeat measurements and they are taken over a range of different activities, giving a true picture of average 24 h, day-time and night-time blood pressure. Furthermore, ambulatory blood pressure monitoring reduces the risk of artificial values due to influences such as white-coat hypertension⁽²⁸⁾. Slightly different classifications are adopted when interpreting data from ambulatory blood pressure monitors (Table 2).

Dietary fat and vascular function

Although it is generally accepted that salt, alcohol and fruit and vegetable intakes can modulate blood pressure, the effects of dietary fatty acids on vascular function are less well characterised in the literature. The remainder of the present review will evaluate the nature and the strength of evidence for the chronic and acute influence of total fat on blood pressure, arterial compliance and endothelial function, and will then consider the differential effects of saturated and unsaturated fatty acids from observational and both chronic and acute intervention studies. The *n-3* long-chain PUFA (LCP) EPA and DHA have been investigated more extensively and appear to have distinct mechanisms of action upon the vasculature, and therefore the evidence for EPA- and DHA-modulated effects on arterial function will be examined in a separate section.

Total fat

Epidemiological and chronic intervention studies. Total fat as a proportion of energy intake does not seem to have a strong effect on the risk of CHD when other dietary variables are adjusted for, according to the results of the Nurses' Health Study, which reported incidence of CHD in

Table 2. Guidelines for classification of clinic and ambulatory blood pressure levels (mmHg)*

Category	European Society of Hypertension classification of ambulatory blood pressure levels ⁽¹⁷⁷⁾					
	British Hypertension Society classification of clinic blood pressure levels ⁽²⁷⁾		Day-time		Night-time	
	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)
Optimal blood pressure	< 120	< 80	< 130	< 80	< 115	< 65
Normal blood pressure	< 130	< 85	< 135	< 85	< 120	< 70
High-normal blood pressure	130–139	85–89				
Grade 1 hypertension (mild)	140–159	90–99				
Grade 2 hypertension (moderate)	160–179	100–109				
Grade 3 hypertension (severe)	≥ 180	≥ 110	> 140	> 90	> 125	> 75
Abnormal blood pressure						

* If clinic systolic blood pressure and diastolic blood pressure fall into different categories, the higher value should be taken for classification. No classification is given to differentiate between mild, moderate and severe hypertension using ambulatory blood pressure monitoring due to lack of evidence to base recommendations upon.

80 082 women 14 and 20 years after baseline assessment^(29,30). In fact, a number of studies showed that blood pressure may actually be reduced by a high-fat diet (specifically high-MUFA) compared with a high-carbohydrate diet, in populations at risk of CVD^(31–33). Evidence showing low-fat diets to be beneficial for the regulation of blood pressure may reflect the reduction in SFA rather than total dietary fat *per se* (Table 3). Two diets with similar MUFA content, a high-fruit-and-vegetable/high-fat diet, and a high-fruit-and-vegetable/low-fat diet, were compared with a control diet using ambulatory blood pressure monitoring in the Dietary Approaches to Stop Hypertension (DASH) trial⁽³⁴⁾. Both diets reduced blood pressure but the low-fat diet had a greater effect, possibly due to reduced SFA content, although other dietary components such as increased intake of wholegrain foods and Ca may have also played a part. The overall picture for high-fat *v.* low-fat diets affecting blood pressure is muddled by the failure to keep the type of fat constant, and the few studies that have attempted to control for fatty acid composition report no differences^(35–37). Few studies have been conducted with regards to other measures of vascular function. Cross-sectional analysis of a cohort of children aged 10 years suggested that total fat intake was associated with arterial stiffness, independently of dietary fatty acid composition, suggesting that the total amount of fat in the diet may influence arterial integrity from an early stage in life⁽³⁸⁾. However, high-fat *v.* low-fat dietary intervention studies (also differing in type of fat) had no differential effect on arterial stiffness or endothelial function^(39–41). Overall, the evidence suggests that total fat *per se* does not have a strong effect on vascular function and that dietary fatty acid composition may have a more important bearing.

Acute intervention studies. Studies of postprandial responses to dietary fat are more straightforward and less time-consuming to conduct compared with chronic dietary intervention studies. Furthermore, single-meal interventions are not beset by problems such as non-compliance to dietary advice. Possibly for these reasons, there are now at least fifteen studies that have investigated the acute effects of high-fat meals^(42–56), and at least eight studies reporting the relative acute effects of saturated and unsaturated fat on endothelial function^(57–63). These studies provide information about the stress imposed on the endothelium by everyday postprandial exposure to increased TAG and NEFA, and allow us to discover the optimum fatty acid composition of a meal in order to reduce any adverse effects on vascular function, ultimately protecting against long-term arterial damage.

In general, high-fat meals have been shown to impair endothelium-dependent vasodilation, mostly using FMD methodology^(42,44,45,49–51,54–56,64), but also forearm blood flow^(46,48). Furthermore, high-fat meals may impair systemic arterial compliance⁽⁶⁵⁾. In contrast to these findings, Djousse *et al.*⁽⁴³⁾ did not report impaired FMD after a meal of burger and chips, possibly due to the added effect of the protein in the meal, which has been shown to prevent dietary fat-induced endothelial dysfunction⁽⁵¹⁾. An Australian group, using venous occlusion strain-gauge plethysmography to measure forearm blood flow^(47,61),

stand alone in reporting increased endothelium-dependent vasodilation following a high-fat meal, possibly due to methodological differences. Interestingly, Skilton *et al.* showed that the increase in forearm blood flow after a high-fat meal (61 g fat, providing 53% of total energy) was diminished with age, but unaffected by insulin sensitivity⁽⁴⁷⁾. Further confusion is added by the fact that Williams *et al.* demonstrated impaired FMD after a high-fat meal (64 g fat) using deep-fried cooking oil (obtained from a restaurant), but not a high-fat meal using unheated cooking oil⁽⁵²⁾, but in a second paper they reported no impairment in FMD following 78 g of either heated (used to deep-fry potato chips) or unheated safflower-seed and olive oils⁽⁵³⁾. Rueda-Clausen *et al.* compared three types of oils at two levels of deep-frying and showed that all the heated and unheated fats induced a reduction in FMD of approximately 32%⁽⁶²⁾. Clearly there is little evidence so far that deep-frying oil can acutely affect endothelial function over and above the effect of the total amount of fat, although the longer-term effects of habitual consumption on arterial health are unknown.

Dietary saturated v. unsaturated fatty acids

Altering the fatty acid composition of the diet necessarily involves the manipulation of more than one component. For example, reduction of SFA in the diet will require replacement with another type of fatty acid or another macronutrient in order to avoid the confounding effect of energy deficits. Therefore, it is more useful to consider the influence of the dietary fatty acid profile as a whole (SFA, MUFA and PUFA) rather than each type of fatty acid in isolation. Since *n*-3 LCP have been studied more extensively and may have distinct mechanisms of action, current knowledge on their vascular effects will be examined in a separate section.

Cross-sectional studies. Table 4 summarises a selection of cross-sectional studies that have investigated potential associations between dietary fatty acid intake (estimated from dietary assessment methods or by using biomarkers of intake) and vascular function. Cross-sectional studies assessing dietary intake via food records^(66,67) have shown that PUFA intake is inversely related to blood pressure whereas SFA intake is positively related to blood pressure, with some studies finding no relationship⁽⁶⁸⁾. Dietary fat intake as assessed by 24 h recall or dietary records from relatively small sample sizes probably do not provide reliable estimates of associations with vascular function due to well-documented methodological constraints⁽⁶⁹⁾. However, since dietary fatty acid intake is a major determinant of tissue fatty acid profile, serum, plasma, erythrocyte or adipose tissue fatty acid composition data can be used as biomarkers of dietary fatty acid intake. The strength of the relationship between dietary and tissue fatty acid composition depends on the tissue type, and indeed the fatty acid type. Fatty acids that are synthesised endogenously and that make up a large proportion of the tissue fat, such as oleic acid and SFA, do not show close associations between dietary intake and tissue composition. However, fatty acids that are not synthesised in the body and are not present in

Table 3. Dietary intervention studies on chronic and acute effects of total fat intake on blood pressure (BP) or vascular function

Reference	Subjects	n	Study design	Duration of study (PAL) or intervention arm (CO)	Dietary intervention	Amount of fat: average % energy (chronic) or amount in g and % energy per meal (acute)	Vascular measurements	Difference	Outcome
Chronic									
Brussard <i>et al.</i> (1981) ⁽³⁵⁾	Healthy, M and W, aged 18–30 years	60	PAL	5 weeks	Moderate fat (H-PUFA) v. LF (L-PUFA) v. HF (L-PUFA) v. HF (H-PUFA)	Moderate fat 30 %; LF (L-PUFA) 22 %; HF (L-PUFA) 39 %; HF (H-PUFA) 40 %	Clinic BP	No	No differences
Mensink <i>et al.</i> (1988) ⁽³⁷⁾	Healthy, M and W, aged 18–59 years	47	PAL	36 d	HF (H-SFA) baseline diet, then HF (H-MUFA*) or LF (H-CHO)	HF (H-MUFA) 41 %; LF (H-CHO) 22 %	Clinic BP	No	BP ↓ equally after both diets relative to baseline diet
Rasmussen <i>et al.</i> (1993) ⁽³²⁾	T2D, M and W, aged 57 (sd 2) years	15	CO	3 weeks	H-MUFA* v. H-CHO	50 v. 30 %	ABP	Yes	H-MUFA ↓ BP compared with H-CHO
Nielsen <i>et al.</i> (1995) ⁽¹⁷⁸⁾	T2D, M and W, aged 50–75 years	10	CO	3 weeks	H-MUFA* v. H-CHO	H-MUFA 50 %; H-CHO 30 %	ABP	No	No difference
Moore <i>et al.</i> (1999) ⁽³⁴⁾	Healthy, M and W, aged 45 (sd 10) years	345	PAL	8 weeks	Control v. H-F&V v. combination (H-F&V, LF, L-GI)	Control 36 %; F&V 36 %; combination 26 %	ABP	Yes	BP ↓ after F&V and combination diets; effect was greater after combination diet
Ashton <i>et al.</i> (2000) ⁽³⁹⁾	Healthy, M, aged 48 (sd 6) years and healthy, postmenopausal W, aged 55 (sd 3) years	14 M and 14 W	CO	4 weeks	LF (H-CHO) v. HF (H-MUFA)	LF (H-CHO): 22–25 %; HF (H-MUFA): 40–42 %	Clinic BP Arterial elasticity	No	No differences
Clifton <i>et al.</i> (2004) ⁽³⁶⁾	Overweight, W, aged 47 (sd 11) years	62	PAL	12 weeks	Weight-loss diet: HF (H-MUFA) v. VLF	H-MUFA 35 %; VLF 12 % SFA similar	Clinic BP	No	No differences
Appel <i>et al.</i> (2005) ⁽³¹⁾	Pre-HT and stage 1 HT, M and W, aged 54 (sd 11) years	164	CO	6 weeks	H-MUFA v. H-protein v. H-CHO	MUFA 37 %; Protein 27 %; CHO 27 % SFA: 6 % all diets	Clinic BP	Yes	MUFA diet ↓ BP more than CHO diet
Shah <i>et al.</i> (2005) ⁽³³⁾	T2D, M and W, aged 58 (sd 10) years	42	CO	6 week (subset 14 weeks, n 21)	H-MUFA v. H-CHO	45 v. 30 %	Clinic	Yes	No difference at 6 weeks; small ↑ BP in subset who had H-CHO diet for 14 weeks compared with H-MUFA
Keogh <i>et al.</i> (2008) ⁽⁴¹⁾	Overweight and obese, M and W, aged 24–64 years	99	PAL	8 weeks	Weight-loss diet: HF (H-SFA) v. LF (H-CHO)	61 v. 30 % SFA differed	Clinic BP PWV FMD	No	No changes in FMD. PWV improved with both diets
Sanders <i>et al.</i> (2009) ⁽¹⁰¹⁾	Healthy, M and W, aged 30–70 years	110	PAL	6 months	H-SFA v. H-MUFA v. LF (H-CHO)	38 v. 38 v. 28 %	PWV DVP FMD	No	No difference in BP, FMD or PWV between diets. ↓ DVP-SI after LF (H-CHO) compared with H-SFA and H-MUFA
Acute†									
Vogel <i>et al.</i> (1997) ⁽⁵⁴⁾	Healthy, M and W, aged 39 (sd 10) years	10	CO	6 h	HF v. LF	50 v. 0 g 50 v. 0 %	FMD	Yes	FMD ↓ after HF compared with LF

Dietary fats and vascular function

Table 3. Continued

Reference	Subjects	n	Study design	Duration of study (PAL) or intervention arm (CO)	Dietary intervention	Amount of fat: average % energy (chronic) or amount in g and % energy per meal (acute)	Vascular measurements	Difference	Outcome
Ong <i>et al.</i> (1999) ⁽⁴⁴⁾	Healthy, M, aged 30 (SD 5) years	16	CO	3 h	H-MUFA v. LF	50 v. 5 g 59 v. 6%	FMD	Yes	FMD ↓ after H-MUFA meal
Williams <i>et al.</i> (1999) ⁽⁵²⁾	Healthy, M, aged 34–52 years	10	CO	4 h	LF v. HF v. deep-fried HF	64.4 v. 18.4 g 65 v. 34 %	FMD	Yes	FMD ↓ after deep-fried HF, but not after HF or LF
Nestel <i>et al.</i> (2001) ⁽⁶⁵⁾	Healthy, M and W, aged 51 (SD 10) years	36	PAL	6 h	LF v. HF (mixed meals)	6 v. 50 g 8 v. 67 %	Systemic arterial compliance	Yes	Systemic arterial compliance ↓ after HF
Bae <i>et al.</i> (2003) ⁽⁴²⁾	Healthy, M, aged 26 (SD 1) years	10	CO	6 h	HF meal (rice, Korean barbeque, egg, milk, oil, mayonnaise, vegetables), LF meal (rice, vegetable soup, vegetables, orange juice, apple, kimchi)	53.4 v. 3 g 60 v. 3 %	Clinic BP FMD	Yes	No difference in BP FMD ↓ after HF meal at 3 and 4 h
Steer <i>et al.</i> (2003) ⁽⁴⁸⁾	Healthy, M and W, aged 20–30 years	26	PAL	2 h	HF v. MF v. LF	Fat g depended on body weight 34 v. 20 v. 3 %	FBF	Yes	EDV ↑ after LF and ↓ after HF
Westphal <i>et al.</i> (2005) ⁽⁵¹⁾	Healthy, M and W, aged 19–23 years	16	CO	8 h	HF v. HF + soya protein v. HF + caseinate protein	0.99 g fat/kg body weight	FMD	Yes	FMD ↓ after HF at 2, 3 and 4 h. Prevented ↓ by addition of protein
Padilla <i>et al.</i> (2006) ⁽⁴⁵⁾	Healthy, M and W, aged 26 (SD 1) years	8	CO	4 h	LF (cereal and skimmed milk meal) v. HF (fast food)	0 v. 48 g 0 v. 46 %	FMD	Yes	FMD ↓ after HF meal
Shimabukuro <i>et al.</i> (2007) ⁽⁴⁶⁾	Healthy, M and W, aged 36 (SD 1) years	12	CO	4 h	H-CHO v. HF v. standard meal	0 v. 30 v. 17 g 0% of 300 kcal/100 g food v. 35% of 342 kcal/100 g food v. 33% of 478 kcal/100 g food‡	FBF	Yes	Peak FBF ↓ after HF but not H-CHO or standard meal

PAL, parallel design; CO, cross-over design; M, men; W, women; H-PUFA, high-PUFA; LF, low-fat; L-PUFA, low-PUFA; HF, high-fat; H-SFA, high-SFA; H-MUFA, high-MUFA; T2D, type 2 diabetics; H-CHO, high in carbohydrate; ABP, ambulatory blood pressure; L-GI, low glycaemic index; H-F&V, high in fruit and vegetables; VLF, very low-fat; HT, hypertensive; PWV, pulse wave velocity; FMD, flow-mediated dilatation; DVP, digital volume pulse; DVP-SI, stiffness index measured by the DVP; MF, medium fat; FBF, forearm blood flow; EDV, endothelium-dependent vasodilation.

* Source: olive oil.

† Single-meal (uncontrolled) studies excluded.

‡ 300 kcal = 1255 kJ; 342 kcal = 1431 kJ; 478 kcal = 2000 kJ.

Table 4. Cross-sectional studies on dietary saturated and unsaturated fatty acids (FA) intake and blood pressure (BP) and vascular function

Reference	Subjects	n	Methods	Association	Outcome
Blood pressure					
Oster <i>et al.</i> (1979) ⁽⁷³⁾	Germany, M, aged 20–40 years	650	Clinic BP Adipose tissue FA	Yes	Inverse association with LA
Miettinen <i>et al.</i> (1982) ⁽⁷⁸⁾	Finland, M, aged 40–55 years	64	Clinic BP Serum FA	Yes	Inverse association with LA and positive association with PA, AA and EPA
Berry & Hirsch (1986) ⁽⁷⁹⁾	USA, M, aged 20–78 years	399	Clinic BP Adipose tissue FA	Yes	Inverse association with ALA only
Riemersma <i>et al.</i> (1986) ⁽⁷⁵⁾ ; Rubba <i>et al.</i> (1987) ⁽⁷⁴⁾ ; Ciocca <i>et al.</i> (1987) ⁽⁷⁶⁾	Scotland, Finland and Italy, M, aged 40–49 years Italy, W, aged 20–69 years	390 839	Clinic BP Adipose tissue FA Clinic BP Erythrocyte FA	Yes No	Inverse association with LA in one Finnish centre only; positive association with SFA in Italian centre only No associations
Williams <i>et al.</i> (1987) ⁽⁶⁶⁾	USA, M, aged 30–55 years	76	Clinic BP 3 d food records	Yes	Inverse association with MUFA and PUFA intake
Cambien <i>et al.</i> (1988) ⁽⁸⁰⁾	France, M, aged 20–60 years	3348	Clinic BP Plasma cholesteryl ester FA	Yes	Positive association with POA in alcohol drinkers only
Salonen <i>et al.</i> (1988) ⁽⁶⁷⁾	Finland, M, aged 54 years exactly	722	Clinic BP 4 d food records	Yes	Positive association with SFA and negative association with ALA
Simon <i>et al.</i> (1996) ⁽⁷¹⁾	USA, M, aged 35–57 years	156	Clinic BP Serum FA	Yes	Inverse association with SA and positive association with POA, ETA and DGLA
Grimsgaard <i>et al.</i> (1998) ⁽⁷²⁾	Norway, M, aged 40–42 years	4033	Clinic BP Plasma phospholipid FA	Yes	Inverse association with LA and positive associations with PA, POA, OA and DGLA
Zheng <i>et al.</i> (1999) ⁽⁷⁷⁾	USA, M and W, aged 45–64 years	3081	Clinic BP Plasma cholesteryl ester FA	Yes	Inverse association with LA and positive association with PA, POA and GLA
Dauchet <i>et al.</i> (2007) ⁽⁶⁸⁾	France, M and W, aged 35–63 years	4652	Clinic BP 24 h food record	No	No associations
Miura <i>et al.</i> (2008) ⁽⁸¹⁾	Japan, China, UK, USA, M and W, aged 40–59 years	4680	Clinic BP 24 h dietary recalls	Yes	Inverse association with LA
Arterial stiffness and endothelium-dependent vasodilation					
Sarabi <i>et al.</i> (2001) ⁽⁸³⁾ ; Lind <i>et al.</i> (2002) ⁽⁸²⁾	Sweden, M and W, aged 20–69 years	56	FBF by venous occlusion plethysmography Serum cholesteryl ester FA	Yes	EFI had an inverse association with PA and POA and positive association with LA. ALA was positively associated with EDV and EIDV
Steer <i>et al.</i> (2003) ⁽⁸⁴⁾	Sweden, M and W, aged 20–30 years	74	FBF by venous occlusion plethysmography Serum FA	Yes	EFI inverse association with total SFA, positive association with ALA (M). DGLA inversely associated with EDV. EPA and DHA positively associated with EIDV. Total PUFA positively associated with basal FBF
Schack-Nielsen <i>et al.</i> (2005) ⁽³⁸⁾	Denmark, male and female children, aged 10 years exactly	87	PWV (radial to femoral) 7 d food record	No	No associations

M, men; LA, linoleic acid; PA, palmitic acid; AA, arachidonic acid; ALA, α -linolenic acid; W, women; POA, palmitoleic acid; SA, stearic acid; ETA, eicosatrienoic acid; DGLA, dihomo- γ -linolenic acid; OA, oleic acid; GLA, γ -linolenic acid; FBF, forearm blood flow; EFI, endothelial function index; EDV, endothelium-dependent vasodilation; EIDV, endothelium-independent vasodilation; PWV, pulse wave velocity.

large amounts in the diet, such as *n*-3 PUFA, *trans*-fatty acids and linoleic acid (LA) make for better predictors when measured in plasma or tissue⁽⁷⁰⁾. Serum cholesteryl ester fatty acid data from the Multiple Risk Factor Intervention Trial (MRFIT) study⁽⁷¹⁾, plasma phospholipid fatty acid data from the Nordland Health study⁽⁷²⁾, and adipose tissue fatty acid data^(73–75) all yielded fatty acid-specific associations with blood pressure in men, although there were no associations with erythrocyte fatty acids in women⁽⁷⁶⁾. In the MRFIT study, cholesteryl ester stearic acid (18:0) was higher when blood pressure was lower but palmitic acid (16:0) was not related⁽⁷¹⁾, unlike the majority of studies that showed that palmitic acid was positively associated with blood pressure^(72,74,77,78). Oster *et al.* demonstrated an inverse relationship between adipose tissue LA (18:2*n*-6) and blood pressure⁽⁷³⁾, which agreed with subsequent serum phospholipid data in a subgroup of a cohort of middle-aged men⁽⁷⁸⁾, but not adipose tissue analysis in middle-aged American men where it was shown that α -linolenic acid (ALA; 18:3*n*-3), not LA, was inversely associated with blood pressure⁽⁷⁹⁾. The Paris Prospective Study 2 found that palmitoleic acid (16:1*n*-7) was the only fatty acid related to blood pressure in men; this positive relationship was only apparent in alcohol drinkers⁽⁸⁰⁾. Overall, the evidence for associations between biomarkers of dietary fat intake and blood pressure is confusing, and the lack of consistency may reflect the variety of tissues and subfractions of serum or plasma used. Recently a large cross-sectional study (INTERNational collaborative of MAcronutrients and blood Pressure; INTERMAP) attempted to clarify the relationship with LA intake by using four \times twenty-four dietary recalls and eight \times clinic blood pressure measurements over 3 weeks in seventeen populations in Japan, China, UK and USA (*n* 4680)⁽⁸¹⁾. Multiple regression analyses showed there was an inverse relationship between dietary LA intake and blood pressure, which was strongest in the subgroup that was not receiving any prescribed or non-prescribed nutritional or medical intervention and had no history of CVD or diabetes.

Cross-sectional analyses using other markers of vascular function demonstrate a potential relationship between serum fatty acid levels and endothelial function^(82–84). Both palmitic acid (16:0) and palmitoleic acid (in cholesteryl esters and phospholipids) were inversely associated with an index of endothelial function derived from forearm blood flow measurements (ratio of endothelium-dependent vasodilation to endothelium-independent vasodilation) in predominantly middle-aged men and women, whereas phospholipid oleic acid (18:1*n*-9) and cholesteryl ester LA were positively associated⁽⁸³⁾. The same study showed that phospholipid ALA was positively associated with both endothelium-dependent and endothelium-independent vasodilation, suggesting that the protective effects of this fatty acid were exerted through different mechanisms to those of oleic acid and LA⁽⁸³⁾. Some of these relationships were also present in younger men (SFA inversely associated with endothelial function index, and ALA positively associated with endothelium-dependent vasodilation), but not in younger women⁽⁸⁴⁾. Despite the influence of total dietary fat intake on arterial stiffness (PWV) in children, no associations were found with dietary fatty acid composition⁽³⁸⁾.

Longitudinal studies. The Nurses' Health Study, a prospective cohort study carried out in over 80 000 women, showed that there is a greater risk of CHD with increasing intake of SFA, and that PUFA, and to a lesser extent MUFA, are protective⁽²⁹⁾. There are few of these types of prospective epidemiological studies that have investigated the incidence of hypertension and none to the author's knowledge on arterial stiffness or endothelial dysfunction. Studies that have estimated dietary fat intakes at baseline and related to blood pressure at follow-up have produced mixed results^(68,85,86). There were no associations between total fat, SFA or PUFA intake at baseline and risk of hypertension during 4 years of follow-up⁽⁸⁵⁾. In agreement with this, no associations were shown between intake of dairy products or Key's score at baseline with change in blood pressure at follow-up (median 5.4 years) in the Supplémentation en Vitamines et Minéraux Antioxydants (SU.VI.MAX) study⁽⁶⁸⁾. However, the Multiple Risk Factor Intervention Trial (MRFIT) study group reported that the average dietary intake of PUFA over 6 years, as recorded by 24 h recalls, was inversely related to average blood pressure over 6 years, with further positive associations shown for SFA intake and the Key's score⁽⁸⁶⁾. Furthermore, plasma cholesteryl ester SFA was positively related and PUFA was inversely related to systolic blood pressure in the Atherosclerosis Risk in Communities (ARIC) 6 years follow-up study⁽⁷⁷⁾.

Chronic intervention studies: blood pressure. Randomised controlled trials that have used methodology to measure arterial compliance and/or endothelial function in order to compare saturated and unsaturated fats (for example, SFA *v.* MUFA, or MUFA *v.* *n*-6 PUFA) are scarce (Table 5). There is some evidence in the literature regarding relative effects of dietary fats on blood pressure⁽⁸⁷⁾, but the evidence base is limited by issues such as non-randomisation^(88,89), small sample size⁽⁹⁰⁾, and reliance on clinic measures of blood pressure rather than ambulatory blood pressure monitoring, which is a more reliable measure of true blood pressure over a 24 h period. There was a trend towards reduced blood pressure following a 4-week MUFA intervention compared with SFA in eight overweight or obese men⁽⁹⁰⁾, supported by a larger study in healthy subjects where blood pressure was reduced following a 3-month high-MUFA diet compared with a high-SFA diet, but only in those who consumed <37% fat (*n* 40)⁽⁹¹⁾. Blood pressure was increased following a high-SFA diet compared with a high-MUFA diet but the study design involved non-randomised consecutive 5-week phases of SFA, MUFA, *n*-6 PUFA, *n*-6 PUFA plus *n*-3 PUFA, with no washout periods, and therefore may have been subject to bias⁽⁸⁹⁾. Others have found no differential effects on blood pressure of diets differing in their SFA and PUFA content^(92,93), or SFA and MUFA content (The RISCK Study Group, unpublished results).

From a public health point of view it would be useful to be able to recommend the relative proportion of MUFA and *n*-6 PUFA that should be consumed, if saturated fat is less than or equal to the recommended 11% of food energy intake. There are few examples in the literature where *n*-6 PUFA has been compared with MUFA with respect to clinic or ambulatory blood pressure or arterial tone. A number of

Table 5. Dietary intervention studies on chronic and acute effects of saturated and unsaturated fatty acids (FA) on blood pressure (BP) and vascular function

Reference	Subjects	n	Study design	Duration of study (PAL) or intervention arm (CO)	Dietary intervention	Amount of fat	Type of fat: % energy	Vascular measurements	Difference	Outcome
Chronic										
Iacono <i>et al.</i> (1983) ⁽⁸⁸⁾	Healthy, M and W, aged 40–49 years	59	Consecutive diet phases (NR)	1 week → 6 weeks → 6 weeks	Baseline diet (Con) → LF/L-SFA/H-PUFA → Con	39% → 24% → 36%	Baseline Con: 22% SFA, 12% MUFA, 3% PUFA LF/L-SFA/H-PUFA: 8% SFA, 6% MUFA, 9% PUFA Con: 20% SFA, 12% MUFA, 3% PUFA	Clinic BP	Yes	↓ BP on LF/L-SFA/H-PUFA diet*
Margetts <i>et al.</i> (1985) ⁽¹⁷⁹⁾	Healthy, M and W, aged 20–59 years	54	CO	6 weeks	Low PUFA:SFA ratio v. high PUFA:SFA ratio	43%	Low PUFA:SFA ratio: 18% SFA, 16% MUFA, 6% PUFA High PUFA:SFA ratio: 14% SFA, 12% MUFA, 15% PUFA	Clinic BP	No	No difference between diets
Puska <i>et al.</i> (1985) ⁽¹⁸⁰⁾	Healthy, M and W, aged 35–49 years	84	PAL	12 weeks	Baseline HF/H-SFA then LF with either PUFA:SFA ratio of 0.9 or 0.4	Baseline 38% then 24% both diets	Baseline: 20% SFA, 13% MUFA, 4% PUFA 0.9 PUFA:SFA ratio: 9% SFA, 6% MUFA, 8% PUFA 0.4 PUFA:SFA ratio: 11% SFA, 8% MUFA, 5% PUFA	Clinic BP	No	↓ BP following both LF/L-SFA diets
Sacks <i>et al.</i> (1987) ⁽⁹³⁾	HT, M and W, aged 26–63 years	21	CO	6 weeks	H-SFA v. H-PUFA v. H-CHO	38, 27 and 28%	H-SFA: 16% SFA, 5% PUFA, 13% MUFA H-PUFA: 10% SFA, 14% PUFA, 11% MUFA H-CHO: 11% SFA, 5% PUFA, 10% MUFA	Clinic and home BP	No	No difference between diets
Sacks <i>et al.</i> (1987) ⁽⁹⁷⁾	Healthy, M and W, aged 35 (sd 10) years	17	CO	4 weeks	LA v. OA	Not specified	Safflower-seed oil either high in LA or OA (23 g/d)	Clinic BP	No	No difference
Mensink <i>et al.</i> (1990) ⁽⁹⁵⁾	Healthy, M and W, M aged 25 (sd 7) years, W aged 24 (sd 6) years	58	PAL	5 weeks	H-MUFA† (olive oil) v. H-PUFA (sunflower-seed oil)	36%	H-MUFA: 13% SFA, 15% MUFA, 8% PUFA H-PUFA: 13% SFA, 11% MUFA, 13% PUFA	Clinic BP	No	No difference between diets
Mutanen <i>et al.</i> (1992) ⁽⁹⁴⁾	Healthy, M and W, aged 18–65 years	59	CO	3.5 weeks	H-MUFA v. H-PUFA	38%	H-PUFA: 13% PUFA H-MUFA: 16% MUFA	Clinic BP	No	Minor effects on BP
Uusitupa <i>et al.</i> (1994) ⁽⁸⁷⁾	Healthy, M and W, aged 23–58 years	159	PAL	6 months	H-SFA v. AHA (L-SFA, H-PUFA) v. H-MUFA (L-SFA, H-MUFA) v. LF	35 v. 32 v. 34 v. 30%	Fat energy ratio (SFA:MUFA:PUFA): H-SFA: 14:10:4 AHA: 10:8:8 H-MUFA: 11:11:5 LF: 12:8:3 H-MUFA: 10% SFA, 30% MUFA, 7% PUFA H-PUFA: 9% SFA, 10% MUFA, 27% PUFA	Clinic BP	Yes	↓ SBP following AHA and ↓ BP following H-SFA in M only
Thomsen <i>et al.</i> (1995) ⁽⁹⁸⁾	T2D, M and W, aged 59 (sd 7) years	16	CO	3 weeks	H-MUFA† v. H-PUFA	49%	H-MUFA: 10% SFA, 30% MUFA, 7% PUFA H-PUFA: 9% SFA, 10% MUFA, 27% PUFA	ABP	Yes	↓ BP after H-MUFA compared with H-PUFA

Table 5. Continued

Reference	Subjects	n	Study design	Duration of study (PAL) or intervention arm (CO)	Dietary intervention	Amount of fat	Type of fat: % energy	Vascular measurements	Difference	Outcome
Lahoz <i>et al.</i> (1997) ⁽⁸⁹⁾	Healthy, M and W, 45 (sd 16) years	42	Consecutive diet phases (NR)	5 weeks	H-SFA → H-MUFA† → H-PUFA → H-PUFA + n-3 FA	35 %	H-SFA: 17% SFA, 14% MUFA, 4% PUFA H-MUFA: 9% SFA, 21% MUFA, 4% PUFA H-PUFA: 10% SFA, 12% MUFA, 13% PUFA H-PUFA + n-3 FA: 9% SFA, 12% MUFA, 13% PUFA, including 1.6% n-3 PUFA	Clinic BP	Yes	BP differed according to diet: H-SFA > H-MUFA, H-MUFA < H-PUFA, H-PUFA + n-3 FA < H-PUFA, H-PUFA + n-3 FA > MUFA
Storm <i>et al.</i> (1997) ⁽¹⁰³⁾	T2D, M and W, aged 53 (sd 9) years	15	CO	3 weeks	H-SFA (SA) v. H-SFA (PA) v. H-CHO	45 v. 45 v. 29 %	H-SFA (SA): 13% SA, 19% SFA, 17% MUFA, 6% PUFA H-SFA (PA): 16% PA, 21% SFA, 16% MUFA, 6% PUFA H-CHO: 9% SFA, 11% MUFA, 5% PUFA	ABP	No	No difference between diets
Aro <i>et al.</i> (1998) ⁽⁹⁶⁾	Healthy, M and W, aged 40–65 years	87	PAL	8 weeks	Three low-fat diets: Con v. H-MUFA v. H-PUFA	Con 20%, H-MUFA 26% and H-PUFA 26%	Con: 7.9% SFA, 7.8% MUFA, 3% PUFA H-MUFA: 7.3% SFA, 14.1% MUFA, 3.2% PUFA H-PUFA: 7.5% SFA, 8.2% MUFA, 8.1% PUFA	Clinic BP	No	No difference
De Roos <i>et al.</i> (2001) ⁽¹⁸¹⁾	Healthy, M and W, aged 30 (sd 16) years	29	CO	4 weeks	H-SFA v. trans-MUFA	H-SFA 37%, trans-MUFA 41 %	H-SFA: 23% SFA, 0.4% MUFA trans, 9% MUFA cis, 7% PUFA Trans-MUFA: 13% SFA, 9% MUFA trans, 9% MUFA cis, 5% PUFA	FMD	Yes	↓ FMD after trans-MUFA compared with H-SFA
Fuentes <i>et al.</i> (2001) ⁽¹⁰⁰⁾	HC, M, aged 41 (sd 15) years	22	CO	4 weeks (H-SFA) then 4 weeks (Mediterranean or NCEP-1) then 4 weeks (Mediterranean or NCEP-1)	Baseline diet (Con: H-SFA) → Mediterranean (H-MUFA) v. NCEP-1 (LF, H-CHO)	38% (H-SFA) → 38% (Mediterranean) v. 28% (NCEP-1)	H-SFA: 20% SFA, 12% MUFA, 6% PUFA Mediterranean: < 10% SFA, 22% MUFA, 6% PUFA NCEP-1: < 10% SFA, 12% MUFA, 6% PUFA	FMD	Yes	↓ FMD on H-SFA compared with Mediterranean. No difference between NCEP-1 and H-SFA
Piers <i>et al.</i> (2003) ⁽⁹⁰⁾	Overweight and obese, M, aged 24–49 years	8	CO	4 weeks	H-SFA v. H-MUFA†	40 %	H-SFA: 24% SFA, 13% MUFA, 3% PUFA H-MUFA: 11% SFA, 23% MUFA, 6% PUFA	Clinic BP	No	Trend towards ↓ DBP and MAP following H-MUFA compared with H-SFA
Ambring <i>et al.</i> (2004) ⁽¹⁸²⁾	Healthy, M and W, aged 43 (sd 1) years	22	CO	4 weeks	Mediterranean v. Swedish diet	Mediterranean 34%, Swedish 36 %	Mediterranean: 8% SFA, 14% MUFA Swedish: 36% SFA, 12% MUFA	Clinic BP Carotid artery elasticity, echo-tracking FBF	No	No difference

Keogh <i>et al.</i> (2005) ⁽¹⁰²⁾	Healthy, M and W, aged 56 (sd 11) years	40	CO	3 weeks	LF (H-CHO) v. HF (H-SFA), H-MUFA or H-PUFA	LF: 18%, HF 37%	LF: 7% SFA, 6% MUFA, 3% PUFA H-PUFA: 9% SFA 15%, 10% MUFA, PUFA H-MUFA: 8% SFA, 7%, 19% MUFA, PUFA H-SFA: 19% SFA, 12% MUFA, 4% PUFA	PWV FMD	Yes	↓ FMD after H-SFA compared with other three diets. No difference between LF, H-PUFA and H-MUFA
Rasmussen <i>et al.</i> (2006) ⁽⁹¹⁾	Healthy, M and W, aged 30–65 years	162	PAL	3 months	H-SFA v. H-MUFA	37%	H-MUFA: 8% SFA, 23% MUFA, 6% PUFA H-SFA: 17% SFA, 14% MUFA, 6% PUFA	Clinic BP	Yes	↓ BP in H-MUFA compared with H-SFA in individuals who consumed <37% energy as fat
Sanders <i>et al.</i> (2009) ⁽¹⁰¹⁾	Healthy, M and W, aged 30–70 years	110	PAL	6 months	H-SFA v. H-MUFA v. H-CHO	38 v. 38 v. 28%	H-SFA: 16.9% SFA, 12.2% MUFA, 6.3% PUFA H-MUFA: 10.1% SFA, 16.9% MUFA, 7.1% PUFA H-CHO: 9.4% SFA, 10.4% MUFA, 5.8% PUFA	PWV DVP FMD	No	No difference in BP, FMD or PWV between diets. ↓ DVP-SI after H-CHO compared with H-SFA and H-MUFA
Acute										
Raitakari <i>et al.</i> (2000) ⁽⁶¹⁾	Healthy, M and W, aged 18–45 years	10	Consecutive meals (NR)	6 h	SFA v. MUFA	53% (sausage, muffins, hash brown in tallow fat v. similar meal with MUFA (not specified))	H-SFA: 25% SFA, 21% MUFA, 4% PUFA H-MUFA: 5.3% SFA, 45% MUFA, 2.7% PUFA	MAP FBF FMD	No	No differences between meals
Vogel <i>et al.</i> (2000) ⁽⁶³⁾	Healthy, M and W, aged 28–56 years	10	CO	3 h	H-MUFA v. H- <i>n</i> -3 PUFA	50% (olive oil + bread v. rapeseed oil + bread v. salmon + crackers)	Not specified	FMD	Yes	↓ FMD following H-MUFA but not H- <i>n</i> -3 PUFA
Williams <i>et al.</i> (2001) ⁽⁵³⁾	Healthy, M, aged 23–53 years	14	CO	4 h	MUFA v. PUFA	70% (milkshake containing either MUFA (olive oil) v. heated MUFA (olive oil) v. PUFA (safflower-seed oil) v. heated PUFA (safflower-seed oil))	H-MUFA: 16% SFA, 36% MUFA, 9% PUFA	FMD	No	No differences between meals
De Roos <i>et al.</i> (2002) ⁽⁵⁹⁾	Healthy, M, aged ≥35 years	21	CO	3 h	Palm kernel fat (H-SFA) v. partially hydrogenated soyabean oil (H- <i>trans</i> -FA)	60% (milkshake, bread, spread, preserves)		FMD	No	No difference between meals
Cortes <i>et al.</i> (2006) ⁽⁵⁸⁾	Healthy, M and W, aged 32 (sd 8) years and HC, M and W, aged 45 (sd 13) years	24 (12 healthy, 12 HC)	CO	4 h	Olive oil v. walnuts added to a HF meal	63% (mixed meal)	Olive oil meal: 35% SFA, 25% MUFA, 5% PUFA Walnut meal: 35% SFA, 15% MUFA, 15% PUFA	Clinic BP FMD	Yes	Walnuts ↑ FMD, olive oil ↓ FMD
Nicholls <i>et al.</i> (2006) ⁽⁶⁰⁾	Healthy, M and W, aged 18–40 years	14	CO	6 h	Coconut oil (H-SFA) v. safflower-seed oil (H-PUFA)	1 g fat/kg body weight (in carrot cake and milkshake)	Safflower-seed oil composition (8.8% SFA, 13.6% MUFA, 75% PUFA); coconut oil composition (89.6% SFA, 5.8% MUFA, 1.9% PUFA)	FBF FMD	No	Weak trend towards beneficial effects of PUFA compared with SFA

Table 5. Continued

Reference	Subjects	n	Study design	Duration of study (PAL) or intervention arm (CO)	Dietary intervention	Amount of fat	Type of fat: % energy	Vascular measurements	Difference	Outcome
Rueda-Clausen <i>et al.</i> (2007) ⁽⁶²⁾	Healthy, M, aged 18–23 years	10	CO	3 h	SFA v. MUFA v. PUFA	91% (soyabean v. olive v. palm oil added to potato soup)	Soyabean oil meal: 14.8% SFA, 22.2% MUFA, 48% PUFA Olive oil meal: 13% SFA, 70.8% MUFA, 6% PUFA Palm oil meal: 39.7% SFA, 42.2% MUFA, 9.1% PUFA	MAP FMD	No	↓ FMD all meals – no difference between meals
Berry <i>et al.</i> (2009) ⁽⁶⁷⁾	Healthy, M, aged 27 (sd 5) years	17	CO	3 h	SFA v. MUFA (shea butter rich in SA) v. high-oleic sunflower-seed oil)	53% (in muffin and milkshake)	Shea butter: 28% SA, 17.5% OA, 4.7% LA High-oleic sunflower-seed oil: 0.8% SA, 44.8% OA, 4.2% LA	Clinic BP Alx FMD	Yes	↓ FMD following high-oleic sunflower-seed oil compared with shea butter. No difference in Alx or BP

M, men; W, women; NR, not randomised; PAL, parallel design; CO, cross-over design; Con, control treatment; LF, low-fat; L-SFA, low-SFA; H-PUFA, high-PUFA; HF, high-fat; H-SFA, high-SFA; HT, hypertensive; H-CHO, high-carbohydrate; LA, linoleic acid; OA, oleic acid; H-MUFA, high-MUFA; AHA, American Heart Association diet; SBP, systolic blood pressure; T2D, type 2 diabetes; ABP, ambulatory blood pressure; SA, stearic acid; PA, palmitic acid; FMD, flow-mediated dilatation; HC, hypercholesterolaemic; NCEP-1, National Cholesterol Education Program-1 diet; low in fat and saturated fat; DBP, diastolic blood pressure; DVP-SI, stiffness index measured by the digital volume pulse; MAP, mean arterial pressure; FBF, forearm blood flow; PWV, pulse wave velocity; DVP, digital volume pulse; Alx, augmentation index.

*Energy intake was also lower on this diet.

†Source: olive oil.

studies found that high-MUFA and high-PUFA diets had no differential effects on clinic blood pressure^(94–97). In contrast, ambulatory blood pressure was reduced, mainly during the day-time, following 3-week high-MUFA diets compared with high-PUFA diets in type 2 diabetics⁽⁹⁸⁾. These conflicting results may be due to differing methodology for measuring blood pressure or it may be that MUFA is more beneficial than PUFA in the insulin-resistant state only. It has been hypothesised that an increase in ALA intake would decrease blood pressure, since ALA is a precursor of *n*-3 LCP (known to exert blood pressure-lowering effects). A meta-analysis of ALA and blood pressure studies (total *n* 348) showed no hypotensive effect, although this was based on three studies only⁽⁹⁹⁾. Overall, the results of these studies tend to show that blood pressure is minimally affected by the extent of fatty acid saturation, if at all; however, no firm recommendations can be made with respect to saturated or unsaturated fats and blood pressure until more data from randomised controlled trials with adequate statistical power, using appropriate methodology, are available.

Chronic intervention studies: arterial compliance and endothelial function. There is some evidence in hypercholesterolaemic subjects that changing from a high-SFA diet to a high-MUFA diet can improve FMD, although the dietary MUFA happened to be part of a Mediterranean diet and therefore the role of MUFA *per se* is unclear⁽¹⁰⁰⁾. The RISCK (Reading University, Imperial College London, Surrey University, MRC Human Nutrition Research Cambridge and King's College London) study also investigated the effects of SFA and MUFA on arterial stiffness (PWV) and endothelium-dependent and endothelium-independent vasodilation (FMD) in a subgroup and, again, no diet-dependent differences were demonstrated. However, arterial stiffness (measured by the DVP method) was marginally reduced following the low-fat diet compared with the high-SFA and high-MUFA diets. Although stiffness index measured by the DVP correlates with PWV (which is mainly a measure of arterial elasticity and age), it is also sensitive to changes in vascular reactivity, suggesting that in this study total fat intake influenced large arterial tone, whereas the dietary fatty acid composition had little influence on vascular function⁽¹⁰¹⁾. It is important to note that the RISCK study also investigated the role of high-*v*. low-glycaemic index diets, and all the comparisons described above were between high-glycaemic index diets. Therefore, it is unknown whether there would have been a difference between SFA and MUFA if a low-glycaemic index diet had been followed.

Keogh *et al.* reported different findings from their randomised, controlled cross-over trial (*n* 40) in healthy adults. Comparisons of 3-week diets high in carbohydrate, SFA, MUFA and PUFA showed a marked decrease in FMD following the high-SFA diet compared with the carbohydrate, MUFA and PUFA diets, with no differences observed between the diets high in carbohydrate, MUFA and PUFA⁽¹⁰²⁾. The difference in findings between these two studies^(101,102) may lie in the duration (3 weeks *v*. 6 months) and type of dietary manipulation that was administered: Keogh *et al.*⁽¹⁰²⁾ supplemented the SFA diet with butter

only (which is highest in oleic acid, followed by myristic acid (14:0) > palmitic acid > stearic acid), whereas Sanders *et al.* (101) supplied a range of cooking oils, baking fats, spreads and salad creams which were high in stearic acid, palmitic acid and lauric acid (12:0). Although there is currently little evidence that different SFA may differ in their effects on blood pressure (103), this is a relatively unexplored area and until more randomised controlled trials have been carried out in this area, studies that have used different sources of saturated fat may not be strictly comparable.

Acute intervention studies: saturated v. unsaturated fatty acids. With regard to the relative postprandial effects of high-fat meals rich in SFA, MUFA or *n*-6 PUFA, differences in the source of fat and the type of meal administered in relevant studies published to date preclude any firm conclusions. A high-SFA meal (using shea butter, rich in stearic acid) did not significantly impair FMD after 3 h, whereas a high-MUFA meal (using high-oleic acid sunflower-seed oil) did reduce FMD (57). The observed reduction in FMD following a MUFA-rich meal was in agreement with previous studies (44,58,63). It should be noted, however, that shea butter induces a diminished postprandial lipaemia and oxidative stress compared with high-oleic acid sunflower-seed oil (57,104). Raitakari *et al.* also compared a high-SFA meal with a high-MUFA meal, showing no differences in forearm blood flow or FMD between meals; this study is difficult to interpret, however, since the meals were complex (sausages, hash browns and muffins), were not administered in a randomised order, and the MUFA source was not specified (61). Another study compared safflower-seed oil (PUFA-rich) and coconut oil (SFA-rich), showing possible impairment in endothelial function following SFA compared with PUFA, but endothelium-dependent vasodilation differences between fat types were small (60). In summary, acute studies of postprandial vascular response to dietary fat show that a high-fat meal can impair endothelial function, but this is dependent on the other components of the meal, such as protein (51), soluble fibre (105) or antioxidants (64,105–108); MUFA-rich meals appear to impair endothelium-dependent vasodilation in the brachial artery but the relative effects of different types of fat are still unclear.

Dietary n-3 long-chain polyunsaturated fatty acids: blood pressure, arterial compliance and endothelial function

Consumption of *n*-3 LCP derived from oily fish has been extensively investigated in relation to CVD risk. A reduction in cardiovascular events and mortality occurs with increased consumption of oily fish (109) or following *n*-3 LCP supplementation (110,111). The cardioprotective effects of *n*-3 LCP have been attributed to a number of mechanisms, including effects on blood TAG levels, coagulation, vascular inflammation, heart rate variability, endothelium-dependent vasodilation, arterial tone, eicosanoid balance, blood pressure, cardiac arrhythmia and the stability of the atherosclerotic plaque.

Blood pressure. The blood pressure-lowering effects of *n*-3 LCP are well established (112), and the epidemiological evidence for an inverse relationship between *n*-3 LCP intake and blood pressure (113) is supported by data from dietary trials. Blood pressure can be reduced by an average of 2.3 mmHg (systolic blood pressure) and 1.5 mmHg (diastolic blood pressure) following increased *n*-3 LCP intake, as shown in a meta-analysis of thirty-six randomised trials that had administered fish oil to hypertensives and non-hypertensives, with doses ranging from 0.2 to 15 g/d (median 3.7 g/d) (114). The reduction in blood pressure was more pronounced in older subjects. It is not known whether this effect is attributable to EPA and DHA together, or just one of them, but a recent study showed that a moderate dose of 0.7 g DHA/d lowered diastolic blood pressure by 3.3 mmHg (115), whereas EPA does not seem to be effective in reducing blood pressure (116,117).

Arterial compliance and endothelial function. Arterial stiffness is reduced in populations that have increased intakes of *n*-3 LCP (118). Supplementation with *n*-3 LCP at doses of 1.8–3 g/d for 6 weeks to 12 months improved arterial compliance and PWV in type 2 diabetics and dyslipidaemics (119–121). However, supplementation with 0.7 g DHA/d had no effects on the arterial stiffness index or the reflected wave using DVP (115), suggesting either that higher doses are required to have a physiological effect or that EPA is the bioactive component of fish oil which improves the elasticity of the artery. The evidence for differential effects of EPA and DHA on blood pressure is conflicting. EPA supplementation (1.8 g/d, approximately 2 years) reduced arterial stiffness in type 2 diabetics, probably by improving arterial integrity since carotid intima-media thickness was also reduced, although no changes in blood pressure were observed (122). Tomiyama *et al.* also detected a beneficial effect on arterial stiffness over 12 months with EPA only, and it was suggested that this fatty acid may reduce PWV by modulating eicosanoid metabolism (121). However, despite a slightly greater increase in systemic arterial compliance following 3 g EPA/d compared with DHA (36 v. 27 % respectively), there was no significant difference between the two treatments (120). A dose–effect threshold and/or duration of treatment are possibly stronger determinants of the effects of chronic *n*-3 LCP intake on arterial stiffness, rather than the type of fatty acid.

Early studies using animal models demonstrated that endothelial function could be modulated by feeding EPA and DHA (123–125). Cross-sectional evidence indicated that dietary EPA and DHA intakes are positively associated with endothelial function in young smokers (but not non-smokers) and young adults at greater metabolic risk (126). Estimates of dietary *n*-3 LCP intake are also inversely associated with markers of endothelial activation, for example, cell adhesion molecules (127). Supplementation with *n*-3 LCP (EPA plus DHA) for periods ranging from 2 weeks up to 8 months improved endothelium-dependent vasodilation, prevented vasoconstriction or augmented exercise-induced blood flow at doses ≥ 0.5 g/d (128–136). A moderately low dose of DHA alone did not have much effect on salbutamol-induced changes in reflection index

measured by the DVP, but this may be due to methodological problems in detecting endothelium-dependent vasodilatory responses using the digital pulse contour analysis technique⁽¹¹⁵⁾.

Recently, a handful of studies have addressed the acute mechanisms whereby *n*-3 LCP may influence arterial tone. Large arterial tone was reduced following two sequential high-fat meals when the initial meal contained 5 g EPA compared with high-fat control meals, possibly due to NO-independent mechanisms, since it was also observed that plasma NO metabolite (NOx) concentrations were not influenced by EPA consumption⁽¹³⁷⁾. Consumption of tinned red salmon or rapeseed oil (containing 6 and 5 g *n*-3 PUFA respectively) resulted in no postprandial change in FMD, whereas an olive oil meal containing an equal amount of fat significantly impaired FMD⁽⁶³⁾; this could be interpreted as a prevention of impaired NO production by *n*-3 LCP following the salmon meal, although it is equally as likely to be the presence of protein⁽⁵¹⁾. FMD was improved postprandially when the meal contained *n*-3 PUFA (either EPA/DHA or ALA) in type 2 diabetics who had high fasting plasma TAG but not in type 2 diabetics with normal fasting TAG^(138,139). Other researchers demonstrated an acute effect of fish oil on endothelium-independent vasodilation in the microvasculature using laser Doppler iontophoresis but no significant change in endothelium-dependent vasodilation⁽¹⁴⁰⁾, possibly indicating differential mechanisms for *n*-3 LCP-induced postprandial vasodilation according to the size and location of the blood vessel. The lack of studies that have investigated acute effects of *n*-3 PUFA on arterial tone precludes any clear idea of the relative dose-related effects of EPA and/or DHA on vascular function. However, it may be tentatively suggested that these fatty acids may induce vasorelaxation postprandially, potentially via both endothelium-dependent and endothelium-independent routes.

Mechanisms for modulation of vascular function and blood pressure by dietary fatty acids

The key findings from the review of the epidemiological and intervention studies can be summarised simply: (1) long-term total dietary fat intake probably does not influence vascular function or blood pressure independently of the saturated fat content; (2) biomarkers of dietary saturated fat intake are positively associated with blood pressure, although a causal effect has not been confirmed by robustly designed randomised controlled trials; (3) high-fat meals may impair postprandial endothelial function, particularly high-MUFA meals; however, there is no evidence that long-term consumption of high-MUFA diets have any adverse effect on blood pressure or vascular function; (4) higher levels of dietary LA and ALA intake are associated with improved blood pressure but there is not enough randomised controlled trial evidence to draw definite conclusions; and (5) chronic studies suggest that *n*-3 LCP can reduce blood pressure, improve arterial compliance in type 2 diabetics and dyslipidaemics, and augment endothelium-dependent vasodilation, but few studies have investigated acute effects.

Although there is not yet enough evidence from human trials regarding the effects of fatty acid saturation and vascular function, there is evidence in the rat that a

high-SFA diet increases systolic blood pressure, with the opposite effect induced by a high-LA diet⁽¹⁴¹⁾. The possible mechanisms for the opposing effects of dietary SFA and *n*-6 PUFA intake are not yet clear. Studies *in vitro* have shown that incubation of cultured human coronary artery endothelial cells and smooth muscle cells with palmitate caused an increased expression of the inflammatory cytokine, IL-6; this did not occur when linoleate was added⁽¹⁴²⁾. The increase in IL-6 expression was especially marked in the endothelial cells, suggesting that dietary palmitic acid may increase blood pressure by a pro-inflammatory mechanism within the endothelium. It has been clearly demonstrated that elevated circulating levels of NEFA are associated with higher blood pressure⁽¹⁴³⁾ and can induce endothelial dysfunction of conduit arteries^(144,145). Circulating NEFA reflect dietary fatty acid composition to some extent, so it seems likely that a high dietary palmitic acid intake, especially in obese or insulin-resistant individuals (who are likely to have elevated circulating NEFA), could impair vascular function and raise blood pressure. Elevated SFA-rich NEFA may cause concomitant endothelial dysfunction and insulin resistance by inhibition of the common insulin-mediated cell-signalling pathway that activates eNOS in endothelial cells and triggers GLUT-4 translocation in skeletal muscle cells^(146,147). In addition to their potential pro-inflammatory effects, SFA may also impair vascular function by increasing oxidative stress within the endothelium, as evidenced by the reduction in SFA-induced impairment in endothelium-dependent vasodilation of rat resistance arteries and rabbit aorta by the addition of ascorbic acid or superoxide dismutase^(148,149). Furthermore, the latter study showed that the SFA-induced impairment of endothelium-dependent vasodilation occurred acutely (within 15 min) and was associated with NO production⁽¹⁴⁹⁾.

The impact of high-fat meals on postprandial vascular function has often been suggested to be linked with postprandial lipaemia. The size of the increase in postprandial TAG is inversely associated with the decrease in endothelial function^(55,138,150), and a greater impairment in FMD following a high-fat meal is observed in hypertriglycerolaemics compared with normolipidaemics⁽¹⁵¹⁾. Postprandial TAG-rich lipoproteins up-regulated the expression of cell adhesion molecules, monocyte chemoattractant protein-1 and IL-6 when incubated *ex vivo* with endothelial cells, indicating a probable endothelial inflammatory response to high-fat meals *in vivo*⁽¹⁵¹⁾, especially those isolated following a high-SFA meal⁽¹⁵²⁾. The acute effect of postprandial lipaemia on endothelial function is clearly somehow linked to increased oxidative stress^(42,49,50,105,106,108,150,153), but the precise mechanisms remain to be discovered. One theory proposes that remnant TAG-rich lipoproteins induce production of reactive oxygen species within the endothelium, reducing the bioavailability of NO. Remnant TAG-rich lipoproteins isolated from hyperlipidaemic subjects impaired endothelium-dependent relaxation in rabbit aortic strips⁽¹⁵⁴⁾ and levels of remnant TAG-rich lipoproteins were associated with impaired dilation of coronary arteries in human subjects, linked to NO bioavailability⁽¹⁵⁵⁾. Some recent research using artificial chylomicron remnant-like particles has helped to resolve the

molecular mechanisms that mediate postprandial effects on the endothelium, showing that these particles inhibit NO production from cultured endothelial cells, induce cyclo-oxygenase-2 activity, and increase expression of inflammatory molecules and antioxidant enzymes⁽¹⁵⁶⁾.

The likely mechanisms for the beneficial effects of *n*-3 LCP on the arterial wall are numerous and may differ for DHA and EPA. *In vitro* studies have been employed to investigate the effects of different fatty acids on endothelial cells but differences in experimental conditions make the evidence extremely difficult to interpret, as outlined by Shaw *et al.* in a recent attempt to compare the effects of a wide range of fatty acids on endothelial function in human umbilical vein endothelial cells⁽¹⁵⁷⁾. However, broad patterns that emerge from this literature indicate that DHA has a greater effect than EPA in reducing endothelial inflammation. DHA tends to inhibit markers of endothelial function, such as inflammatory cell adhesion molecules and monocyte chemoattractant protein-1 gene and protein expression, and the adhesion of leucocytes to the endothelium, whereas EPA either up-regulated gene expression of monocyte chemoattractant protein-1 or was a weaker inhibitor of cell adhesion molecules than DHA^(157–161).

Interestingly, the extent of inhibition of vascular cell adhesion molecule-1 by DHA was directly related to the increase in incorporation of DHA into the total endothelial cell lipids, possibly into the phospholipids of the inner plasma membrane⁽¹⁵⁸⁾. One of the mechanisms by which EPA and DHA are believed to improve vascular tone are by increasing endothelial cell membrane fluidity, and in fact DHA appears to be the more effective of the two in increasing plasma membrane fluidity of vascular endothelial cells⁽¹⁶²⁾. In addition, DHA treatment increases the total *n*-3 LCP content of caveolae (invaginations of the plasma membrane where eNOS is located when it is inactivated) in cultured endothelial cells, and displaces the protein caveolin-1, which is responsible for securing eNOS in the caveolae region, from the caveolae⁽¹⁶³⁾. This suggests that DHA may influence endothelial function by incorporation into the cell membrane, including caveolae, leading to an increase in eNOS activity and an inhibition of intracellular signalling pathways that may activate the inflammatory response⁽¹⁶⁴⁾. In fact the relationship between DHA and caveolin-1 and eNOS distribution in the endothelial cell membrane was also demonstrated with EPA⁽¹⁶⁵⁾, and incubation with both EPA and DHA can induce eNOS translocation and NO production in cultured endothelial cells^(163,165–167).

Another mechanism whereby EPA and DHA may influence vascular tone is via modulation of the eicosanoid pathway. EPA and DHA inhibit cyclo-oxygenase-1 protein and gene expression in cultured endothelial cells, thereby inhibiting the conversion of arachidonic acid to PG, some of which is eventually converted to thromboxane, a vasoconstrictor, and some to PGI₂, a vasodilator^(168,169). However, incubation with EPA and DHA increases PGI₂ and PGI₃ production *in vitro* and *in vivo*^(170,171), PGI₃ being an EPA-derived PGI which acts as a vasodilator similarly to PGI₂. EPA-derived epoxyeicosatrienoic acids, which can be synthesised in the endothelium by P450-dependent

epoxygenation of EPA instead of arachidonic acid, and are thought to be an endothelium-derived hyperpolarising factor, may influence vascular tone via modulation of Ca-activated K channels in vascular smooth muscle cells⁽¹⁷²⁾. Finally, the oxidation of EPA to F₃-isoprostanes may also result in reduced oxidative stress and increased vasorelaxation⁽¹⁷³⁾.

Summary and conclusions

In summary, consideration of the epidemiological evidence suggests an adverse effect of SFA and a beneficial effect of LA and ALA on vascular function, but the quantity and quality of the experimental evidence is not sufficient to support this convincingly. Reports of differential effects of saturated and unsaturated fatty acids on blood pressure and vascular function are patchy and inconclusive, and it would be premature to make any recommendations based on the literature to date. Large, well-powered randomised controlled trials are required to determine the differential effects of dietary fatty acid composition on blood pressure, arterial compliance and endothelial function in men and women, both in the healthy state and with metabolic or vascular complications. The strength of evidence that high-fat meals transiently impair shear stress-induced endothelium-dependent vasodilation is overwhelming, but the exact intracellular events that mediate these effects are not fully understood. Currently the impairment in endothelium-dependent vasodilation during postprandial lipaemia appears to be associated with an induction of pro-inflammatory pathways and oxidative stress, with elevated NEFA and postprandial TAG-rich lipoproteins being potential mediators in this process. These acute effects on arterial function should not be underestimated, as a lifetime of high-fat meals and transient endothelial injury could ultimately accumulate into major arterial damage, and much remains to be understood regarding the differential acute effects of saturated and unsaturated fatty acids. The role of *n*-3 LCP in vascular health is well known and the quality of the evidence for an effect of EPA and DHA on blood pressure, arterial compliance and endothelial function is much stronger than that for SFA, MUFA, ALA and *n*-6 PUFA. However, more studies investigating the differential effects of EPA and DHA, following both long-term consumption and acute doses, will shed more light on the mechanisms for their beneficial effects, and will furnish health professionals and nutritionists with a greater knowledge base from which to make recommendations to the general public.

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