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Ernährungsphysiologie

The effects of fat amount and fatty acid composition on postprandial metabolic events in older adults with a risk phenotype for cardiometabolic diseases

Dissertation

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List of abbreviations

Acety-CoA	Acetyl coenzyme A
AIx	Augmentation index
AIx_{75}	Augmentation index standardized to a heart rate of 75 bpm
ALA	Alpha-linolenic acid (α-linolenic acid)
ANOVA	Analysis of variance
ApoB	Apolipoprotein B
AUC	Area under the curve
BMI	Body mass index
BP	Blood pressure
BW	Body weight
CAD	Coronary artery disease
CCK	Cholesystokinin
CE	Cholesteryl ester
CHO	Carbohydrate
CM	Chylomicron
C_{max}	Maximum concentration
CRP	C-reactive protein
CVD	Cardiovascular disease
DHA	Docosahexaenoic acid
DNA	Deoxyribonucleic acid
ECLIA	Electrochemiluminescence immunoassay
EFSA	European Food Safety Authority
ELISA	Enzyme-linked immunosorbent assay
EN%	Energy percentage
eNOS	Endothelial nitric oxide synthase
EPA	Eicosapentaenoic acid
ESC	European Society of Cardiology
FA	Fatty acid
FLI	Fatty liver index
FMD	Flow-mediated dilation

GI	Glycemic index
GIP	Glucose-dependent insulinotropic polypeptide
GL	Glycemic load
GLP-1	Glucagon-like peptide-1
HDL	High-density lipoprotein
HFM	High-fat meal
HOMA-IR	Homeostasis model assessment for insulin resistance
HOMA-β	Homeostasis model assessment of beta-cell function
HPLC	High performance liquid chromatography
iAUC	Incremental area under the curve
IL	Interleukin
LC	Long chain
LCFA	Long-chain fatty acid
LCT	Long-chain triglyceride
LDL	Low-density lipoprotein
LFM	Low-fat meal
LPL	Lipoprotein lipase
MAG	Monoglyceride
MAP	Mean arterial pressure
MCFA	Medium-chain fatty acid
MCT	Medium-chain triglyceride
MUFA	Monounsaturated fatty acid
N/A	Not available
nd	Not detectable
net AUC	Net incremental area under the curve
NEFA	Non-esterified fatty acid
NF-κB	Nuclear factor kappa-light-chain-enhancer of activated B cells
NO	Nitric oxide
OXM	Oxyntomodulin
PL	Phospholipid
PP	Pancreatic polypeptide

PUFA	Polyunsaturated fatty acid
PWV	Pulse wave velocity
PWV_{c-f}	Carotid-femoral pulse wave velocity
PYY	Peptide tyrosine tyrosine
RCT	Randomized controlled trial
RNS	Reactive nitrogen species
RONS	Reactive oxygen/nitrogen species
ROS	Reactive oxygen species
SCFA	Short-chain fatty acid
SCT	Short-chain triglyceride
SD	Standard deviation
SEM	Standard error of the mean
SFA	Saturated fatty acid
T1DM	Type 1 diabetes mellitus
T2DM	Type 2 diabetes mellitus
tAUC	Total area under the curve
TEAC	Trolox equivalent antioxidative capacity
TG	Triglyceride
t_{max}	Time taken to reach maximum concentration
TNF-α	Tumor necrosis factor-α
TRL	Triglyceride-rich lipoprotein
VLDL	Very low-density lipoprotein
wt%	Weight percentage

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1. General introduction

After ingestion of food, the human body enters the so-called postprandial period, which involves the digestion and absorption of nutrients (1). The postprandial state is a dynamic and complex physiological process that affects almost every organ and tissue in the body (1, 2). Although food is essential for humans (3), nutrient intake is an "exogenous stressor" to which the organism must develop an adaptive response (4). The aim is to overcome the short-term metabolic disruption and to regain homeostasis (2). In modern societies, most people are exposed to the fed state for approximately 18 h a day due to frequent food intake (5). Consequently, the fasting state is only reached for a limited period of time at night. The main metabolic events that occur after ingestion of food are lipemia, glycemia, and insulinemia (2), meaning that blood concentrations of lipids, glucose, and insulin increase acutely (6).

1.1 Overview of the main postprandial metabolic processes

Postprandial lipemia, which occurs after the ingestion of fat, is primarily characterized by the release of intestinal and hepatic triglyceride-rich lipoproteins (TRLs; namely chylomicrons [CMs] and very low-density lipoproteins [VLDLs]) into the circulation (7, 8). This leads to an increase in blood triglyceride (TG) concentration (6). After the peak TG concentration, which is usually reached 2–4 h postprandially (9, 10), the concentration of TGs decreases as a result of their elimination from the blood (6). This TG clearance is achieved through the interaction of CMs with the lipoprotein lipase (LPL) on the surface of endothelial cells, especially in muscle and adipose tissue (11, 12). The enzyme LPL hydrolyses TGs into monoglycerides and fatty acids (FAs), which are primarily oxidized (mainly in muscle) or stored (mainly in adipose tissue) (11). FAs that are not taken up by tissue bind to albumin and are transported through the bloodstream as non-esterified FAs (NEFAs), which can be taken up by the liver (12). After hydrolysis by LPL, the modified CM particle, the so-called CM remnant, is also taken up by the liver (12, 13). In the liver, FAs derived from the NEFA plasma pool and the TGs of CM remnants are incorporated into VLDLs (12). The incorporation of TGs containing FAs from the NEFA plasma pool into VLDLs is a fast process, whereas the repackaging of TGs from the CM remnant into VLDLs is slow. VLDLs are released from the liver into the circulation, and like CMs, they undergo hydrolysis by LPL (5, 13). **Figure 1-1** provides an overview of the postprandial TG metabolism.

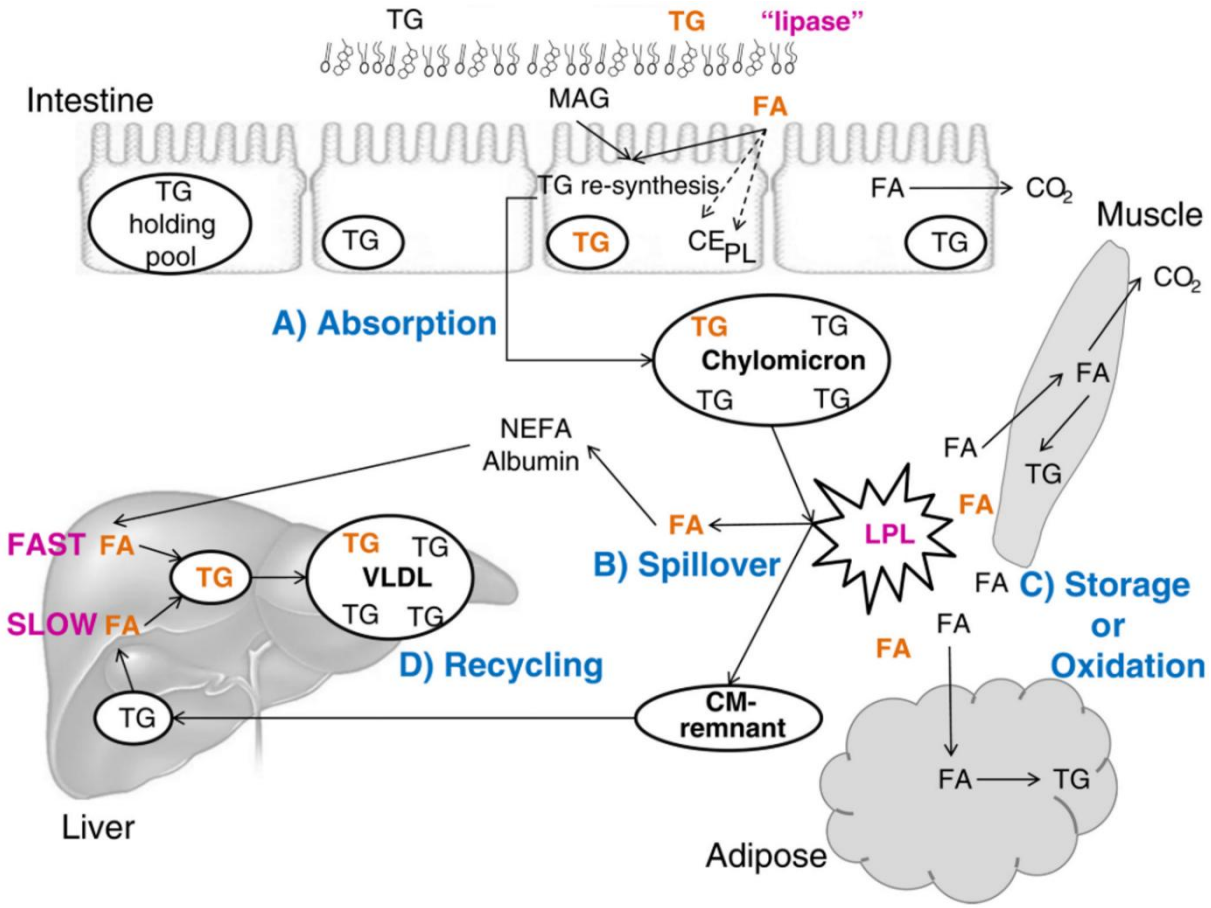

Figure 1-1 Overview of the postprandial triglyceride metabolism. Figure modified from (12). CE, cholesteryl ester; CM, chylomicron; FA, fatty acid; LPL, lipoprotein lipase; MAG, monoglyceride; NEFA, non-esterified fatty acid; PL, phospholipid; TG, triglyceride; VLDL, very low-density lipoprotein.

Because the concentration of TGs remains elevated for 5–8 h after intake of a high-fat meal, the digestive system is regularly confronted with the next meal before the TG level has returned to baseline (14). **Figure 1-2A** illustrates the typical concentration-time profile of plasma TGs in response to a mixed meal. As shown in this figure, the TG concentration rises rapidly after the intake of a fat-containing meal. Because of this immediate increase during the postprandial period, the TG concentration is considered the most appropriate parameter to assess lipemia (15). It is used as a biomarker for TRLs and their remnants in the blood circulation (16).

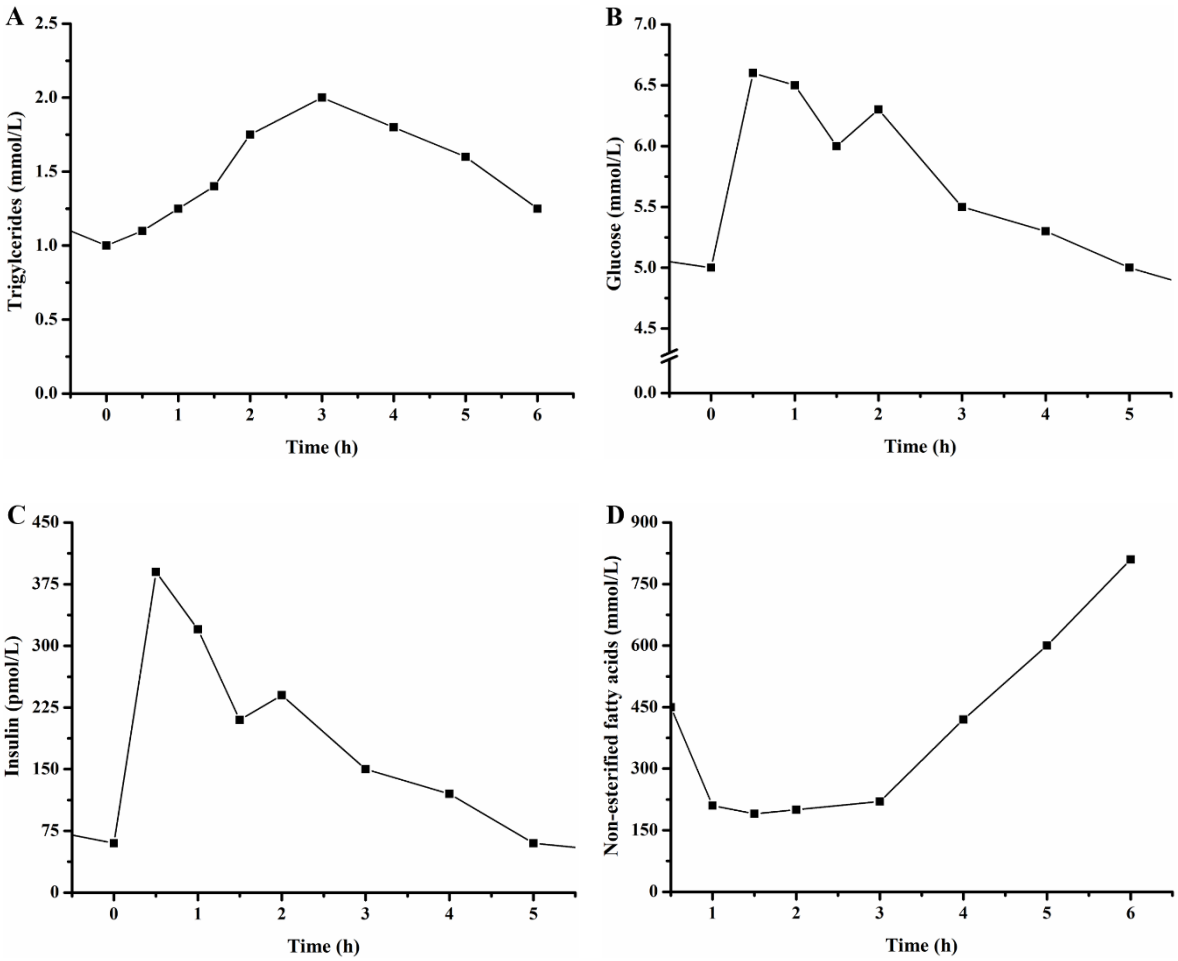

Figure 1-2 Typical concentration-time profiles of triglycerides (A), glucose (B), insulin (C), and non-esterified fatty acids (D) in plasma in response to a mixed meal. Figure modified from (6).

Compared to the prolonged TG response after fat ingestion, the rise in glucose level after carbohydrate (CHO) ingestion occurs over a shorter period of time (**Figure 1-2B**) (6, 14). After the enzymatic cleavage of CHOs, such as starch and disaccharides, into glucose in the gastrointestinal tract, the plasma glucose concentration increases within the first 2 h after meal ingestion (17). The rise in glucose level is accompanied by a rapid increase in insulin concentration in response to CHO intake (**Figure 1-2C**) (6). One of the key metabolic effects of insulin is the stimulation of glucose uptake by muscles, the liver, and adipocytes (18). Insulin is secreted in two phases: an initial, rapid release, followed by a second, sustained release (19, 20). Therefore, both glucose and insulin concentrations typically peak in a biphasic manner following food intake (**Figures 1-2B and 1-2C**) (6). As a result of insulin suppressing intracellular lipases, the concentration of NEFAs decreases postprandially (**Figure 1-2D**). The concentration-time profile of NEFAs often shows a rebound effect during the late postprandial period, because not all FAs are absorbed by tissues after LPL hydrolysis, and spill over into the plasma (**Figure 1-1**) (6, 12).

In addition to glycemia itself, pancreatic glucose-dependent insulin secretion is stimulated by the release of the two incretins glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) from the gut (17, 21). GLP-1 reduces the postprandial rise in glucose concentration not only by amplifying the release of insulin from the pancreas, but also by slowing gastric emptying; this effect is associated with reduced hunger and desire to eat in the postprandial period (22). GLP-1 is therefore classified as an anorexigenic (satiety) hormone, along other hormones such as peptide tyrosine tyrosine (PYY), pancreatic polypeptide (PP), cholecystokinin (CCK), and oxyntomodulin (OXM) (23). As an antagonist, ghrelin acts as orexigenic (hunger) hormone (23, 24). These gut peptides are released postprandially from the stomach (ghrelin), the pancreas (PP), the small intestine (CCK, GLP-1, PYY, OXM), and the colon (GLP-1, PYY, OXM) (25, 26). They either transmit signals by activating neural pathways or enter the bloodstream to act as hormones (26).

1.2 Factors influencing the postprandial response

Postprandial metabolic processes are influenced by numerous meal-dependent and meal-independent factors (4, 13, 27), some of which are presented in **Table 1-1**.

Table 1-1 Selected meal-dependent and meal-independent factors influencing postprandial metabolic processes (4, 13, 27)

Meal-dependent factors	Meal-independent factors
• Energy content • Carbohydrate and fat content • Fiber content • Glycemic index • Fatty acid composition • Selected secondary plant products (e.g., polyphenols) • Food matrix/structure (e.g., liquid, solid)	• Lifestyle factors (e.g., physical activity, smoking) • Physiological factors (e.g., age, gender) • Pathological conditions (e.g., obesity, hypertriglyceridemia) • Genetic factors (e.g., polymorphisms in apolipoproteins or enzymes)

The acute metabolic response to food intake is largely influenced by dietary factors, especially energy content (4) and macronutrient composition (13) of the ingested meal. In this context, a meta-analysis showed that a modest replacement of CHOs with fats in mixed meals significantly reduces the glucose and insulin responses, while significantly increasing the TG response (28). Another recent meta-analysis showed that in adults without type 1 (T1DM) or type 2 (T2DM) diabetes mellitus, adding dairy or plant protein to a CHO-containing meal

results in a dose-dependent decrease in the glucose response and a dose-dependent increase in the insulin response (29). In addition to the CHO content of a meal, postprandial glucose and insulin responses are decisively influenced by its glycemic index (GI) and glycemic load (GL) (30). The GI is defined as the area under the curve (AUC) of blood glucose concentration for a food relative to the AUC after ingesting an equivalent amount of CHOs as glucose (31). The GI of an individual food determines several attributes of the glucose response curve, such as the peak response (32). Additionally, a meal with a higher GI (white bread, GI: 70) has been shown to induce a more pronounced inflammatory response than a meal with a lower GI (cooked pasta, GI: 35) (33). The GL is an extension of the GI which considers both the quality and quantity of CHOs (34). Compared to the content of available CHOs, the GL is superior at predicting the glycemic and insulinemic responses to single foods and mixed meals (35). In the context of GI and GL as relevant determinants of postprandial metabolism, several meta-analyses showed that the intake of whole grain foods can significantly attenuate glycemic and insulinemic responses compared to the intake of refined foods (e.g., white wheat bread or pasta) (36-38). This effect is partially attributed to the higher dietary fiber content of whole grain products. Regarding postprandial lipemia, the acute TG response has been shown to be lowered by soluble fiber, but not by insoluble fiber (39).

With respect to postprandial lipemia, the amount of fat in a meal is considered the most important determinant (40). The postprandial TG concentration increases in a dose-dependent manner with the amount of fat ingested (9, 10). In addition to the fat dose, the FA composition of a meal can have a substantial impact on the acute TG response. The generally accepted concept is that saturated FAs (SFAs) induce the strongest lipemic response, followed by monounsaturated FAs (MUFAs) and polyunsaturated FAs (PUFAs) (13). This assumption is supported by a meta-analysis that reported that the TG response to PUFAs was significantly lower than to SFAs (41). The authors observed this effect with observation periods of 8 and 2 h, but not with observation periods of 6 and 4 h. Additionally, comparing SFAs and MUFAs revealed no significant differences regarding the TG response. Another meta-analysis found that the incremental area under the curve (iAUC) of TGs was lower after an SFA-rich meal than after a meal rich in unsaturated FAs when observed 4–7 h postprandially (42). In contrast, the iAUC of TGs was higher after an SFA-rich meal than after a meal rich in unsaturated FAs when observed more than 8 h postprandially. Taken together, evidence regarding the acute effects of the FA composition of a meal on the lipemic response is highly inconclusive. Research suggests that in addition to the FA composition of an acutely ingested meal, the FA composition of the habitual diet also influences the postprandial TG response to acute fat ingestion. Here, a similar

order is assumed as for the acute influence of the FA composition on postprandial TGs (SFAs > MUFAs = n-6 PUFAs > n-3 PUFAs) (13).

In addition to the degree of saturation of FAs, the extent of postprandial lipemia is also influenced by the FA chain length. Long-chain FAs (LCFAs), such as oleic acid (C18:1 n-9) found in olive oil (43) and canola oil (44), are incorporated into CMs and released into the circulation via the lymphatic system (45). This process results in postprandial lipemia (**Figures 1-1 and 1-2A**). In contrast, medium chain FAs (MCFAs) and short-chain FAs (SCFAs) are absorbed directly into the portal vein and rapidly transported to the liver, where they are oxidized (7, 45, 46). Therefore, the TG response to a meal enriched with MCFAs is significantly lower than to a meal enriched with LCFAs (47). **Figure 1-3** illustrates the different transport pathways of SCFAs, MCFAs, and LCFAs. The classification of FAs based on their chain length is partly inconsistent, especially with regard to lauric acid (C12:0). Particularly in the context of food chemistry, food technology, and food industry, lauric acid is classified as an MCFA (48-51). However, from a physiological point of view, considering its biological actions and metabolic effects, lauric acid should be classified as an LCFA (52-55).

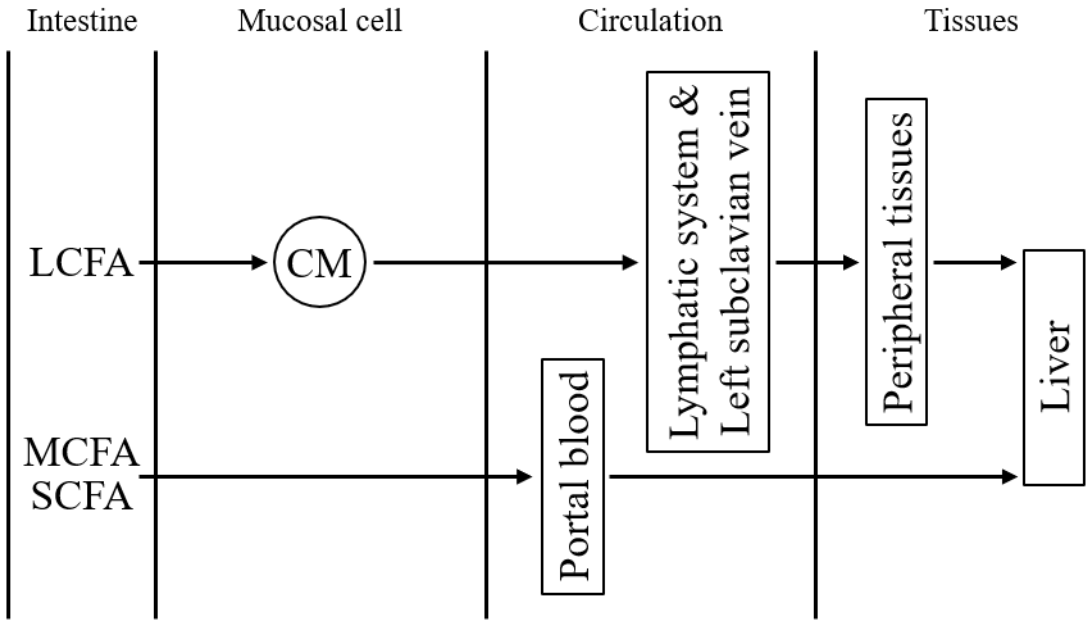

Figure 1-3 Transport pathways of long-chain, medium-chain, and short-chain fatty acids. While short-chain fatty acids and medium-chain fatty acids are transported to the liver via the portal vein, long-chain fatty acids are incorporated into chylomicrons and enter the circulation via the thoracic duct. Figure modified from (45). CM, chylomicron; LCFA, long-chain fatty acid; MCFA, medium-chain fatty acid; SCFA, short-chain fatty acid.

In addition to meal-dependent factors, several meal-independent factors influence postprandial metabolic processes (**Table 1-1**). For example, lifestyle factors, such as physical activity, are considered relevant determinants of the postprandial metabolic response. Numerous meta-analyses confirmed that physical exercise can reduce the postprandial TG, glycemic, and insulinemic responses (56-61). One example of a physiological factor that enhances the metabolic response is age (13, 62-64). Both aspects, physical activity and age, were combined in a study by Emerson et al. (65), which showed that the decline in metabolic capacity that occurs with increasing age can be mitigated by physical activity.

Among pathological factors, central obesity, elevated fasting TGs, and insulin resistance/T2DM have been shown to enhance the postprandial metabolic response (13). It was found that in overweight and obese adults, among several predictor variables (e.g., aerobic exercise frequency, homeostasis model assessment for insulin resistance [HOMA-IR]), visceral adiposity was the strongest predictor of the TG iAUC and the postprandial TG magnitude (66). Other authors observed that the iAUC of plasma interleukin(IL)-6 was significantly higher in obese women than in lean women after the ingestion of five different mixed meals, and that the waist circumference as a measure of central adiposity was a significant determinant of the magnitude of postprandial IL-6 change (67).

1.3 Postprandial metabolic events as a cardiovascular disease risk factor

According to the leading scientific model, a chronic excessive metabolic response to fat- and CHO-rich meals promotes the development of several diseases (e.g., atherosclerosis, metabolic syndrome) (2). In prospective studies, the postprandial TG level showed a strong independent association with the incidence of cardiovascular events in both women and men (68, 69). In addition, it has been observed that only the postprandial glucose level, but not the fasting glucose level, is predictive of cardiovascular events (70, 71). Therefore, postprandial dysmetabolism, meaning abnormal increases in lipid and glucose concentrations during the postprandial phase, is considered an independent predictor of future cardiovascular events (72). In particular, the dietary patterns of modern societies, characterized by an overconsumption of processed, energy-dense foods and foods with a high GI, contribute to the postprandial dysmetabolism and associated chronic diseases (73). Frequent excessive food intake, a characteristic of modern Western eating behavior, leads to exaggerated and prolonged metabolic, oxidative and immune imbalances (known as "postprandial oxidative stress"), accompanied by low-grade inflammation and impaired endothelial function (74). These main

mechanisms by which postprandial dysmetabolism is thought to promote cardiovascular diseases (CVDs) are addressed in the following sections.

The term oxidative stress generally describes "an imbalance that favors the production of ROS over antioxidant defenses" (ROS = reactive oxygen species) (75). Examples of ROS include superoxide (O_2^-) and the hydroxyl radical (OH) (76). Complexes I and III of the mitochondrial respiratory chain are considered to be the primary intracellular source of ROS (75). Under conditions of nutrient overload, the production of acetyl coenzyme A (acetyl-CoA) increases excessively due to an overloaded tricarboxylic acid cycle (77). This overproduction of acetyl-CoA stimulates the mitochondrial production of superoxide from oxygen, most of which is converted to hydrogen peroxide (H_2O_2) and then to a highly reactive hydroxyl radical. In addition to ROS, reactive nitrogen species (RNS) are products of cellular metabolism (78). Although the moderate generation of reactive oxygen/nitrogen species (RONS) is essential for the body's physiological functions, a redox imbalance, resulting from an increased RONS production or impaired antioxidant defenses, can damage surrounding biomolecules (79). Oxidative damage caused by ROS (e.g., to cellular lipids, deoxyribonucleic acid [DNA]) and nitrosylation reactions induced by RNS (e.g., to proteins) inhibit the normal function of cell structures (78). Therefore, redox imbalances are involved in the development of CVDs (80, 81).

The postprandial pro-oxidative state is considered to be closely associated with a transient impairment of normal endothelial function (82). Here, the molecule nitric oxide (NO) plays a central role (15). NO is released by the endothelium and mediates basic endothelial functions, including vasodilation, inhibition of platelet aggregation, and inhibition of mononuclear cell adhesion to the endothelium (83). The intense mitochondrial production of superoxide during the postprandial phase reduces the bioavailability of NO by scavenging NO to form peroxynitrite ($ONOO^-$) and by impairing NO production (15). Inadequate production and activity of NO is considered a main component of endothelial dysfunction (84). The term endothelial dysfunction describes a functional impairment of the endothelium associated with reduced vasodilation, a pro-inflammatory state, and prothrombotic properties (85). Endothelial dysfunction occurs in the early, preclinical stage of atherosclerosis (84, 85). All of the aforementioned radicals have been associated with the induction or progression of CVDs (80).

The pro-inflammatory state is another main component in the development of CVDs through postprandial dysmetabolism (73). The oxidative imbalance and pro-inflammatory processes that occur during the postprandial period are closely related. The accumulation of ROS in the cytoplasm under conditions of nutrient overload is associated with a change in the redox state,

which activates redox-sensitive transcription factors such as nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) (77). NF-κB in turn induces the expression of several genes, including pro-inflammatory cytokines (e.g., tumor necrosis factor-α [TNF-α], IL-6), chemokines (e.g., IL-8), adhesion molecules (e.g., E-selectin, intercellular adhesion molecule-1), and inflammatory enzymes (e.g., cyclooxygenase-2) (86, 87). Activation of NF-κB plays a central role in atherosclerosis and related manifestations (e.g., myocardial infarction, stroke), not only by mediating inflammation, but also by regulating cell survival, cell differentiation, and cell proliferation (88).

Postprandial oxidative processes trigger inflammatory cascades via NF-κB-mediated cell signaling pathways (77, 89). However, the activation of the innate immune system during the postprandial period can also occur independently of pro-oxidative processes, for example by the activation of toll-like receptor 4 by SFAs (1, 90). Compared to classic inflammatory diseases, the transient inflammatory processes during the postprandial period are less intense (4). This so-called low-grade inflammation is even considered a physiological phenomenon, with the idea of protecting the healthy body from potentially harmful effects of macronutrients (1). Within a moderate range of pro-oxidative and pro-inflammatory processes during the postprandial period, the body successfully adapts to the meal-induced stress and recovers from the metabolic disturbance, but when the metabolic stress exceeds normal levels, the inflammatory response becomes exaggerated and prolonged; this impaired homeostasis results in dysmetabolism, vascular endothelial dysfunction, and CVDs (4). It is hypothesized that immunological cascades, activated by prolonged excessive nutrient intake, inhibit metabolic pathways and contribute to a backlog of nutrients in the system (91). Chronic systemic low-grade inflammation plays a central role in pathologies such as obesity, T2DM, and cancer (73). In the context of obesity, chronic low-grade inflammation mediated by metabolic cells (e.g., adipocytes) in response to excessive nutrient and energy intake is referred to as "metaflammation" (91).

In addition to the aforementioned mechanisms, lipoprotein particle penetration of the arterial wall has been linked to cardiovascular damage caused by postprandial dysmetabolism (92). Small TRLs, which accumulate in plasma after the lipolysis of CMs and VLDLs, infiltrate the subendothelial space of the arterial wall, where they are phagocytosed by macrophages (93). The transformation of these macrophages into "foam cells" is a characteristic of early and late atherosclerotic lesions (94).

1.4 Canola oil

The original oil from *Brassica napus* contained a high level of erucic acid, which has shown toxic effects in various animal models, including rats and monkeys (95). Additionally, the presence of glucosinolates limited its use as an edible oil (96). In 1974, the first cultivated variety of *Brassica napus* with lower levels of erucic acid and glucosinolates was developed in Canada (97), which eliminated the potential health risks associated with ingesting the oil (96). Today, the modified oil, known as canola oil, is one of the world's most important edible plant oils, with the third highest global production after palm oil and soybean oil (98). As shown in **Table 1-2**, canola oil is rich in MUFAs (~63 g/100 g) and PUFAs (~25 g/100 g), with oleic acid (C18:1 n-9, ~60 g/100 g), linoleic acid (C18:2 n-6, ~18 g/100 g) and α-linolenic acid (ALA; C18:3 n-3, ~8 g/100 g) accounting for the majority of FAs (44).

The ratio of n-6 FAs to n-3 FAs and the ratio of unsaturated FAs to SFAs in canola oil are considered favorable from a nutritional perspective (99). Canola oil contains a very low proportion of SFAs, but a considerable amount of the essential FA ALA (**Table 1-2**) (44). ALA can be converted into longer-chain n-3 FAs (especially eicosapentaenoic acid [EPA]) to a limited extent via the elongase-desaturase system (100). A recent meta-analysis reported that, compared with placebo, ALA supplementation significantly reduced inflammatory biomarkers (C-reactive protein [CRP], TNF-α), serum TGs, and systolic blood pressure (BP) in overweight and obese participants (101). Regular intake of canola oil has been associated with several health benefits, including reduced levels of total and low-density lipoprotein (LDL) cholesterol, as well as increased insulin sensitivity and glucose tolerance (102). A recent umbrella review confirmed the beneficial effects of canola oil on cardiometabolic risk by reporting that its regular intake reduces concentrations of apolipoprotein B (apoB), total cholesterol, and LDL cholesterol (103). A meta-analysis indicates that canola oil provides the greatest benefit to cardiometabolic risk factors (total and LDL cholesterol, TGs) when ~15% of total energy intake from other edible oils (e.g., olive oil, sunflower oil) is replaced with canola oil (104). Cohort studies suggest that an increase in ALA intake of 1 g/day (~1 tablespoon of canola oil) is associated with a 5% lower risk of all-cause and CVD mortality (105). Additional evidence indicates that intake of canola oil improves parameters of lipid metabolism (total, LDL cholesterol) particularly in adults over 50 years of age and when ingested for more than 30 days (106). The effects of canola oil on lipid metabolism are mainly attributed to its replacement of other dietary fat sources. This is because the independent effects of FAs cannot be investigated in studies due to the lack of a suitable placebo, as FAs provide a substantial

proportion of daily energy intake (107). In this context, a comprehensive multiple regression analysis showed that replacing energy intake from SFAs with an equivalent amount of MUFAs or PUFAs significantly reduces total and LDL cholesterol (108). Due to its high MUFA and PUFA content and the associated cardiovascular benefits, regular intake of canola oil is recommended in dietary guidelines (109-111). The European Food Safety Authority (EFSA) Panel on Dietetic Products, Nutrition and Allergies assumes that the LDL cholesterol-lowering effect of canola oil, compared to most other dietary fats, is due to its relatively high content of linoleic acid and ALA, combined with its low SFA content (112).

Table 1-2 Contents of selected fatty acids and vitamin E in canola oil and coconut oil (44, 113)

	Canola oil	**Coconut oil**
SFAs (g/100 g)	6.61	82.5
C8:0	No data provided	6.8
C10:0	No data provided	5.39
C12:0	No data provided	41.8
C14:0	0.05	16.7
C16:0	3.86	8.64
C18:0	1.66	2.52
MUFAs (g/100 g)	62.6	6.31
C18:1 n-9	60.3	6.25
PUFAs (g/100 g)	25.3	1.7
C18:2 n-6	17.8	1.68
C18:3 n-3	7.45	0.02
Vitamin E (mg/100 g)		
α-tocopherol	17.3	0.11
β-tocopherol	0	0.6
γ-tocopherol	41.3	0
δ-tocopherol	1.48	0.18
α-tocotrienol	0	2.17
β-tocotrienol	8.07	0.13
γ-tocotrienol	0	0.36
δ-tocotrienol	0	0.25

MUFAs, monounsaturated fatty acids; PUFAs, polyunsaturated fatty acids; SFAs, saturated fatty acids.

In contrast to the long-term metabolic effects, the postprandial metabolic effects of canola oil are less well studied and inconclusive. Pedersen et al. (114) observed no significant differences in TG, lipoprotein, apolipoprotein, NEFA, and glucose responses to a breakfast (~359 kcal) and lunch (~1,338 kcal) enriched with canola oil, sunflower oil, or palm oil (breakfast: 15 g, lunch: 55 g) in healthy young men. However, 30 min after both meals, the insulin response to sunflower oil was significantly lower than to canola oil. Nielsen et al. (115) reported no significant difference in the TG response to mixed meals (~1,362 kcal, 41 E% fat) enriched with canola oil, sunflower oil, olive oil, palm oil, or butter in healthy men. In contrast, Manning et al. (67) observed a significantly lower TG iAUC in obese, but not in lean women in response to a meal (~850 kcal based on mean body weight [BW] for obese women) enriched with canola oil (0.6 g/kg BW) compared to a meal enriched with cream (SFA-rich, 1.6 g/kg BW). Another meal enriched with olive oil (0.6 g/kg BW) did not induce a significantly different TG response compared to the other two meals, and other parameters of the postprandial metabolic response (e.g., glucose, insulin, NEFAs, IL-6, IL-8, TNF-α) were not affected by the fat type in either lean or obese women.

1.5 Coconut oil

In various tropical and subtropical regions, coconut products are an essential part of daily life, used not only in the diet, but also for other purposes such as hair treatment and folk medicine (55, 116, 117). The Philippines, Indonesia, and India are the world's leading coconut-producing countries (117). Botanically, the coconut tree (*Cocos nucifera*, also called the "tree of life") belongs to the family Arecaceae (55, 116, 117). The coconut fruit is considered a drupe, despite its name containing the word "nut" (55, 116). Inside the drupe is the kernel from which most coconut products (e.g., coconut milk, coconut oil) are made (116). Coconut oil, which is actually a fat rather than an oil, is the main product derived from coconuts. At temperatures of 30°C and above, coconut oil is colorless and liquid, but at 25°C, it solidifies and turns white (118). As shown in **Table 1-2**, coconut oil is characterized by a high SFA content (~83 g/100 g), dominated by lauric acid (C12:0, ~42 g/100 g) and myristic acid (C14:0, ~17 g/100 g) (113), making it resistant to oxidation and suitable for cooking (119).

Despite various health promises (55, 116, 117), international professional societies such as the American Heart Association advise against the regular intake of coconut oil, mainly because coconut oil has been shown to significantly increase LDL cholesterol levels (120). This effect can be attributed to the high amounts of lauric, myristic, and palmitic acid in coconut oil. These FAs strongly increase LDL cholesterol levels (108), primarily by inhibiting LDL receptor

activity (121). In contrast, unsaturated FAs increase LDL receptor activity and reduce the production rate of LDL cholesterol, thereby decreasing the LDL cholesterol level (121, 122). It is therefore recommended to replace coconut oil with non-tropical liquid plant oils rich in unsaturated FAs (**Figure 1-4**) (52, 109). In addition to its unfavorable effect on cholesterol metabolism (103), a meta-analysis reported that long-term intake of coconut fat (mainly coconut milk and oil) significantly increased HOMA-IR without affecting fasting glucose, insulin, or homeostasis model assessment of beta-cell function (HOMA-β) (123).

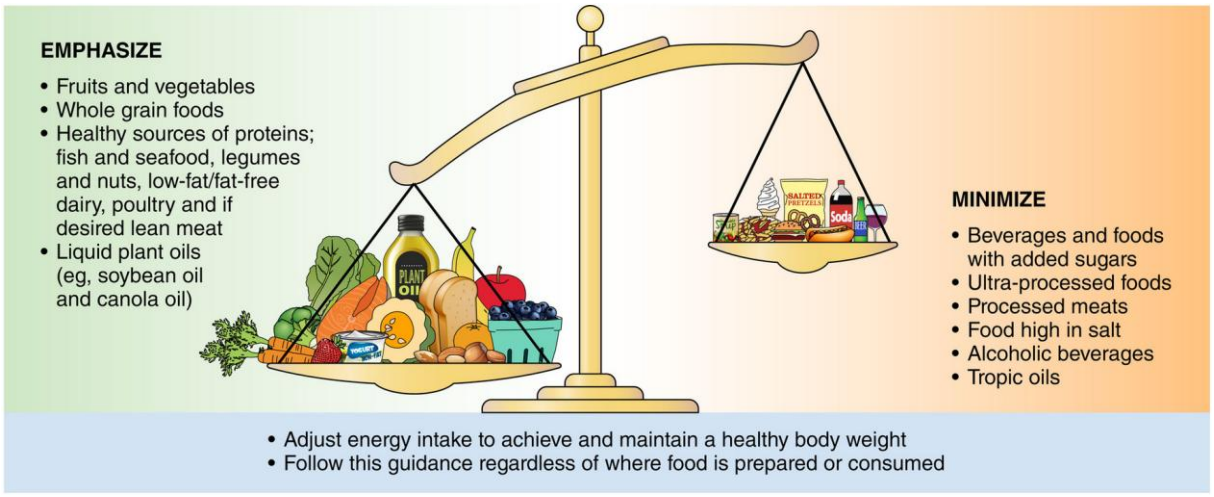

Figure 1-4 The American Heart Association recommends using liquid plant oils (e.g., canola oil) instead of tropical oils (e.g., coconut oil), animal fats (e.g., butter), and partially hydrogenated fats to promote cardiovascular health. Figure from (109).

Several studies compared the acute metabolic effects of coconut oil with those of fat sources rich in unsaturated FAs. Metin et al. (124) reported no significantly different effects of mixed meals (~550 kcal) enriched with coconut oil or olive oil (25 g test oil) on postprandial responses of TGs, glucose, insulin, and PYY in normal-weight and obese men who were metabolically healthy. Consistent with this, the ingestion of bread containing coconut oil (~450 kcal, 50 E% total fat) did not elicit significantly different glucose and insulin responses than bread containing butter, grapeseed oil, or olive oil in healthy men (125). Narverud et al. (126) observed that chocolate cakes enriched with coconut oil, coconut and linseed oil, or coconut, linseed, and cod liver oil (~690–710 kcal, 67–70 E% total fat) did not induce significantly different postprandial changes of CCK, PYY, GIP, amylin, or insulin in healthy lean women. In contrast, in women with excess body fat, Valente et al. (127) reported a significant meal effect on insulin and HOMA-IR after the ingestion of mixed meals (~118 kcal) enriched with coconut oil or olive oil (25 mL test oil). However, the meal × time interaction did not reach statistical significance. There were no significant differences in the TG, total cholesterol, high-density lipoprotein (HDL) cholesterol, LDL cholesterol, and glucose responses to the test

meals. Irawati et al. (128) investigated the metabolic response to mixed meals (~741 kcal) enriched with coconut oil, palm oil, or rice bran oil (40 g test oil) in normolipidemic subjects. They found that hyper-responders had a significantly higher plasma TG iAUC after palm oil compared to coconut oil and rice bran oil, and a significantly higher plasma apoB-48 iAUC after palm oil compared to coconut oil. Hyper-responders were defined as subjects with plasma TGs greater than 1.7 mmol/L 4 h after ingestion of the palm oil-enriched meal. Another study investigated the metabolic response to mixed meals (~668 kcal, 33.5 g fat) enriched with coconut oil, fish oil, coconut and fish oil, or placebo (placebo for coconut oil: tallow, placebo for fish oil: olive oil) in healthy adults (129). The TG iAUC was significantly higher after coconut oil than after the mixture of coconut oil and fish oil. No significant differences were observed between treatments for AUC and iAUC of total cholesterol, HDL cholesterol, LDL cholesterol, and total cholesterol to HDL cholesterol ratio. Another study reported that in healthy young women, the TG iAUCs after meals (~430 kcal) enriched with coconut oil or a mixture of medium-chain TG (MCT) oil and palm oil (30 g test oil) were significantly lower compared to a meal enriched with soybean oil, canola oil, and palm oil (long-chain triglyceride [LCT] meal), while the iAUCs of ketone bodies were significantly higher (47). The iAUCs of VLDL cholesterol and intermediate-density lipoprotein cholesterol were significantly lower only after the coconut oil-containing meal compared to the LCT meal. There were no significant differences between meals regarding the iAUCs of NEFAs and CM cholesterol. Lyte et al. (130) found that in healthy adults, the responses of TG, IL-6, IL-8, IL-10, and TNF-α after a porridge meal enriched with coconut oil (25 % of participants' estimated daily energy requirement, 35 E% total fat) were not significantly different from the response after meals enriched with fish oil or grapeseed oil. However, the NEFA concentrations were significantly higher after coconut oil compared to the other test oils. A meta-analysis reported that coconut fat intake (primarily coconut milk and oil) significantly increased glucose iAUC and decreased insulin iAUC compared to control meals (e.g., with olive oil) (123).

Very few studies compared the postprandial metabolic effects of canola oil and coconut oil. Rather than providing a comprehensive analysis of the postprandial response to canola oil and coconut oil, the few available studies analyzed basic metabolic parameters such as TGs, glucose, or LDL cholesterol. There is a lack of studies comprehensively comparing the postprandial metabolic responses to canola oil and coconut oil, including basic parameters as well as more specific aspects, such as parameters of pro-oxidative and pro-inflammatory processes. Additionally, there is limited data on plasma/serum FA kinetics in postprandial protocols, which is why the FA kinetics after canola oil and coconut oil intake remain unclear.

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2. Objectives

Human data regarding the short-term metabolic responses to canola oil and coconut oil intake are scarce and conflicting. Thus, the overall aim of this thesis was to investigate the acute metabolic and vascular effects of canola oil and coconut oil in the context of a randomized controlled crossover trial (RaKo study, **Chapter 5**). Canola oil was studied because it contains high amounts of unsaturated FAs and is known for its beneficial effects on cardiometabolic risk parameters, such as its LDL cholesterol-lowering effect (1, 2). Coconut oil was chosen as a comparator for canola oil because this tropical fat source is rich in SFAs and is increasingly consumed (3), although regular intake of coconut oil raises the levels of total and LDL cholesterol (3-5). It is of high practical relevance to investigate the postprandial responses to these two plant oils, as there is a lack of well-designed studies on the postprandial effects of plant oils traditionally consumed in Europe compared to those of tropical fat sources. Choosing canola oil and coconut oil as fat sources in the RaKo study not only enabled a comparison of the postprandial effects of FAs with different degrees of saturation (canola oil: rich in MUFAs and PUFAs; coconut oil: rich in SFAs), but also a comparison of the postprandial effects of FAs with different chain lengths (canola oil: rich in oleic acid [C18:1 n-9], linoleic acid [C18:2 n-6], and ALA [C18:3 n-3]; coconut oil: rich in lauric acid [C12:0]; **Table 1-2**).

In addition to the two fat sources, the meals in the RaKo study contained different amounts of fat (25 or 50 g), since the ingested fat dose is known as relevant determinant of postprandial metabolic events (6, 7). The combination of the different amounts and types of fat resulted in four meals: canola high-fat meal (HFM), containing 50 g of canola oil; coconut HFM, containing 50 g of coconut oil; canola low-fat meal (LFM), containing 25 g of canola oil; and coconut LFM, containing 25 g of coconut oil. This strategy enabled the investigation of the effects of both fat type and fat amount on the postprandial response. The meals were designed to contain a variety of commercially available foods rather than shakes or liquid meal components in order to increase the practical relevance of the study results.

The postprandial TG concentration was chosen as the primary outcome of the RaKo study, because it is the most appropriate parameter to assess lipemia (8). Additionally, concentrations of total cholesterol, LDL cholesterol, HDL cholesterol, and NEFAs were measured to further investigate the postprandial lipemic response to the test meals. In order to analyze the impact of fat amount and FA composition on glucose metabolism, glucose and insulin concentrations were analyzed, and HOMA-IR and the insulin-glucose ratio were calculated. Additionally,

concentration of IL-6 and trolox equivalent antioxidative capacity (TEAC) were measured to address postprandial pro-inflammatory and pro-oxidative processes. Furthermore, postprandial arterial stiffness was determined by assessing carotid-femoral pulse wave velocity ($PWV_{c\text{-}f}$) and augmentation index (AIx) to analyze the effects of fat amount and FA composition on vascular function. A special highlight of the RaKo study was the characterization of the kinetics of postprandial plasma α- and γ-tocopherol levels, as well as postprandial serum FA profiles (in total 29 individual FAs). The characterization of FA profiles is particularly relevant because there is very little data on FA kinetics from postprandial protocols, meaning the kinetics of FAs in response to meal ingestion are largely unknown. In addition to the listed parameters, the subjective feeling of hunger and satiety, as well as hunger- and satiety-associated gut hormones (ghrelin, PYY), and neuropsychological parameters (attention, memory) were investigated. The latter data are reported by Diekmann et al. (9) and are not included in this thesis.

In the RaKo study, older adults (60–80 years of age) with a risk phenotype for cardiometabolic diseases were included, because age and certain pathological conditions (e.g., obesity, hypertriglyceridemia) intensify the postprandial metabolic response (6, 7). Compared to healthy individuals, the effects of a dietary intervention may be more pronounced in metabolically impaired subjects (10). Additionally, modifying the postprandial response to influence CVD-related biomarkers through fat exchange is particularly important for this population.

Before conducting the RaKo study, literature searches were performed with the aim to systematically analyze the effects of fat amount and FA composition on postprandial lipemia and vascular function in metabolically healthy adults and subjects with increased CVD risk in the context of two review articles. The first systematic review (**Chapter 3**) focused on postprandial TG concentration as a marker of the lipemic response, because elevated non-fasting TG concentrations are associated with an increased CVD risk (11-15). The second systematic review (**Chapter 4**) centered on flow-mediated dilation (FMD), AIx, and pulse wave velocity (PWV), three important markers of vascular function, all of which are independent predictors of cardiovascular events and all-cause mortality (16-19).

After presenting the two review articles and the RaKo study (**Chapter 5**), the main results are discussed in the context of the current literature. Additionally, the RaKo study data are reanalyzed in the relation to several characteristics of the study population associated with CVD risk, such as body mass index (BMI) and fasting TG concentration (**Chapter 6**).

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3. Review on postprandial lipemia

Impact of Meal Fatty Acid Composition on Postprandial Lipemia in Metabolically Healthy Adults and Individuals with Cardiovascular Disease Risk Factors: A Systematic Review

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ABSTRACT

Consuming fat results in postprandial lipemia, which is defined as an increase in blood triglyceride (TG) concentration. According to current knowledge, an excessively elevated postprandial TG concentration increases the risk of cardiovascular disease (CVD). It is well known that meal-dependent (e.g., nutrient composition) as well as meal-independent factors (e.g., age) determine the magnitude of the lipemic response. However, there is conflicting evidence concerning the influence of fatty acid (FA) composition on postprandial TG concentration. The FA composition of a meal depends on the fat source used; for example, butter and coconut oil are rich in SFAs, while olive oil and canola oil have a high content of unsaturated FAs. To investigate the influence of meals prepared with fat sources rich in either SFAs or unsaturated FAs on postprandial lipemia, we carried out a systematic literature search in PubMed, Scopus, and the Cochrane Library. Randomized crossover studies were analyzed and the AUC of postprandial TG concentration served as the primary outcome measure. To examine the influence of health status, we differentiated between metabolically healthy individuals and those with CVD risk factors. In total, 23 studies were included. The results show that, in metabolically healthy adults, the FA composition of a meal is not a relevant determinant of postprandial lipemia. However, in individuals with CVD risk factors, SFA-rich meals (>32 g SFA/meal) often elicited a stronger lipemic response than meals rich in unsaturated FAs. The results suggest that adults with hypertriglyceridemia, an elevated BMI (≥30 kg/m^2), and/or who are older (>40 y) may benefit from replacing SFA sources with unsaturated FAs. These hypotheses need to be verified by further studies in people with CVD risk factors using standardized postprandial protocols. This review was registered in PROSPERO as CRD42021214508 (https://www.crd.york.ac.uk/prospero/).

STATEMENT OF SIGNIFICANCE

To the best of our knowledge, this is one of the first reviews highlighting the effects of the fatty acid composition of mixed meals enriched with natural fat sources on postprandial lipemia using a food-based approach. A unique aspect of this review is the investigation of both metabolically healthy subjects and adults with CVD risk factors.

INTRODUCTION

In developed societies, the modern lifestyle is characterized by excessive and regular food intake. As a result, many individuals spend the majority of their waking hours in the postprandial state (1). This postprandial phase is characterized by increases in blood lipids (lipemia), glucose (glycemia), and insulin (insulinemia) (2). These metabolic processes are accompanied by postprandial "oxidative stress" and low-grade inflammation, which are associated with impaired endothelial function (2). Scientific interest in postprandial metabolic events as risk factors for cardiovascular disease (CVD) is therefore increasing.

Postprandial metabolic processes are dynamic, and the magnitude and duration of change are influenced by both meal-independent and -dependent factors. Age, health status, and pathological conditions (e.g., type 2 diabetes) are examples of meal-independent factors (3). Meal-dependent factors include the energy content and nutrient composition of meals, especially the fat content and composition (4, 5). Due to the intake of multiple meals, the degree of lipemia fluctuates during the day (3). Epidemiological studies have found that postprandial lipemia, particularly a high triglyceride (TG) concentration, is associated with increased CVD risk (6–10). Thus, attenuating postprandial lipemia by dietary modification may lower CVD risk.

The fatty acid (FA) composition of a meal is determined by the main source of fat. Major dietary sources of SFAs include butter and cream (both 64% of total fat as SFAs) and coconut oil (83% of total fat as SFAs) (11). Olive oil and canola oil are rich in MUFAs (73% and 63% of total fat as MUFAs, respectively), whereas other plant oils are rich in n–6 PUFAs [e.g., sunflower oil, 66% of total fat as linoleic acid (18:2n–6)] and/or n–3 PUFAs [e.g., linseed oil, 14% of total fat as linoleic acid, and 53% as α-linolenic acid (18:3n–3)] (11).

The effects of different FAs on fasting lipid profiles are well described (12), and these have been incorporated into evidence-based dietary guidelines for CVD prevention (9). SFAs are commonly judged to have a negative health impact since they lead to increased concentrations of LDL cholesterol (13). By contrast, unsaturated FA intake has beneficial effects on blood lipid profile due to their role in inhibiting cholesterol synthesis and lowering LDL cholesterol by triggering the expression of hepatic LDL receptor (14). Thus, one well-accepted dietary strategy to improve the blood lipid profile is to replace food rich in SFAs with food rich in unsaturated FAs, especially MUFAs (12). However, it is essential that unsaturated FAs are mainly supplied by plant oils like canola or olive oil, and not by foods that are simultaneously

rich in SFAs. A recent comprehensive meta-regression analysis demonstrated that, for each 1% of dietary energy as SFAs replaced with an equivalent amount of PUFAs or MUFAs, there was a significant decrease in fasting TGs and total and LDL cholesterol (12).

Compared with fasting lipid profiles, less is known about the importance of FA composition and different FA food sources on postprandial lipemia. Two recent meta-analyses examined the postprandial TG response after fat challenges containing different types of FAs. In contrast to fasting lipid responses, both meta-analyses found no difference in overall TG response between SFA and unsaturated FA intake in their primary analyses (15, 16). However, secondary analyses revealed that when fat tolerance tests lasted for over 8 h, there was a lower TG response to meals rich in PUFAs (15). Neither review differentiated between subjects without metabolic disorders, and therefore considered metabolically healthy, and individuals with CVD risk factors in the form of metabolic disorders (e.g., metabolic syndrome, hypertriglyceridemia). It has been shown that certain pathological conditions such as obesity, hypertriglyceridemia, and insulin resistance promote an exaggerated postprandial lipemic response (3, 17). We hypothesized that due to a more extensive metabolic reaction in subjects at risk of CVD (18–21), differences in the postprandial lipemic response after ingestion of meals with different FA compositions become more visible than in metabolically healthy participants. Thus, it might be useful to consider the metabolic health status when analyzing the metabolic reaction to different FA compositions. In addition, the primary focus of both meta-analyses was on classifying FAs according to their degree of saturation, and less on the food source of different FAs (e.g., SFAs from butter vs. SFAs from coconut oil), or on SFAs of different chain lengths (15, 16). However, these characteristics may affect the impact of SFAs on fasting lipid profile and postprandial lipemic response (12, 22, 23).

Therefore, our aim was to systematically review and critically evaluate existing evidence from acute studies comparing meals rich in SFAs and unsaturated FAs on postprandial lipemia. We chose to specifically focus on complete breakfast meals, prepared with natural, commercially available foods rather than fat tolerance tests administered as liquid meals or shakes, because the results of complete breakfast meals have a more practical relevance. In addition, we investigated whether the lipemic response differs between metabolically healthy subjects and individuals with established CVD risk factors.

METHODS

A systematic literature search in the PubMed database (https://pubmed.ncbi.nlm.nih.gov) was conducted between October and December 2020. The search term "postprandial lipemia AND triglycerides AND dietary fatty acids AND meal" was used to identify suitable studies. A second literature search, using the same search term, was conducted in the Cochrane Library (https://www.cochranelibrary.com) and in the Scopus database (https://www.scopus.com). Additional studies were detected by computer-assisted manual searches. Both authors independently reviewed the identified papers and compared them with the inclusion and exclusion criteria (**Table 3-1, Figure 3-1**). The main inclusion criteria were as follows: studies were of a randomized, crossover design and measured postprandial responses in humans; study participants consumed at least one SFA-rich meal and one meal rich in unsaturated FAs, both prepared with natural fat sources such as plant oils or high-fat dairy products; postprandial TG concentrations were measured periodically at regular intervals; and the paper was written in English. Studies were excluded if the test meals were served as liquid meals or shakes, or if meals were enriched with isolated FAs or modified TGs (e.g., inter-esterified synthetic fats or structured TGs containing specific FAs). Different types of the AUC of postprandial TG concentration [e.g., the incremental, total, or net AUC (iAUC, tAUC, net AUC, respectively)] served as the primary outcome measure. This review was registered in PROSPERO (CRD42021214508).

Table 3-1 Inclusion and exclusion criteria[1]

Inclusion criteria	Exclusion criteria
1. Randomized human study	1. In vitro studies
2. Crossover design	2. Animal studies
3. Adult participants (≥ 18 years)	3. Consumption of liquid meals or shakes
4. Consumption of at least 2 mixed meals containing carbohydrates, proteins, and either a high amount of SFAs or unsaturated FAs	4. Consumption of meals enriched with isolated FAs or modified TGs
5. Preparation of meals with natural, commercially available ingredients (e. g., pasta, bread, plant oils, dairy products)	
6. Measurement of postprandial TG concentrations in blood samples periodically at regular intervals	
7. Days of intervention separated by a wash-out phase	
8. Paper in English language	

[1]FA, fatty acid.

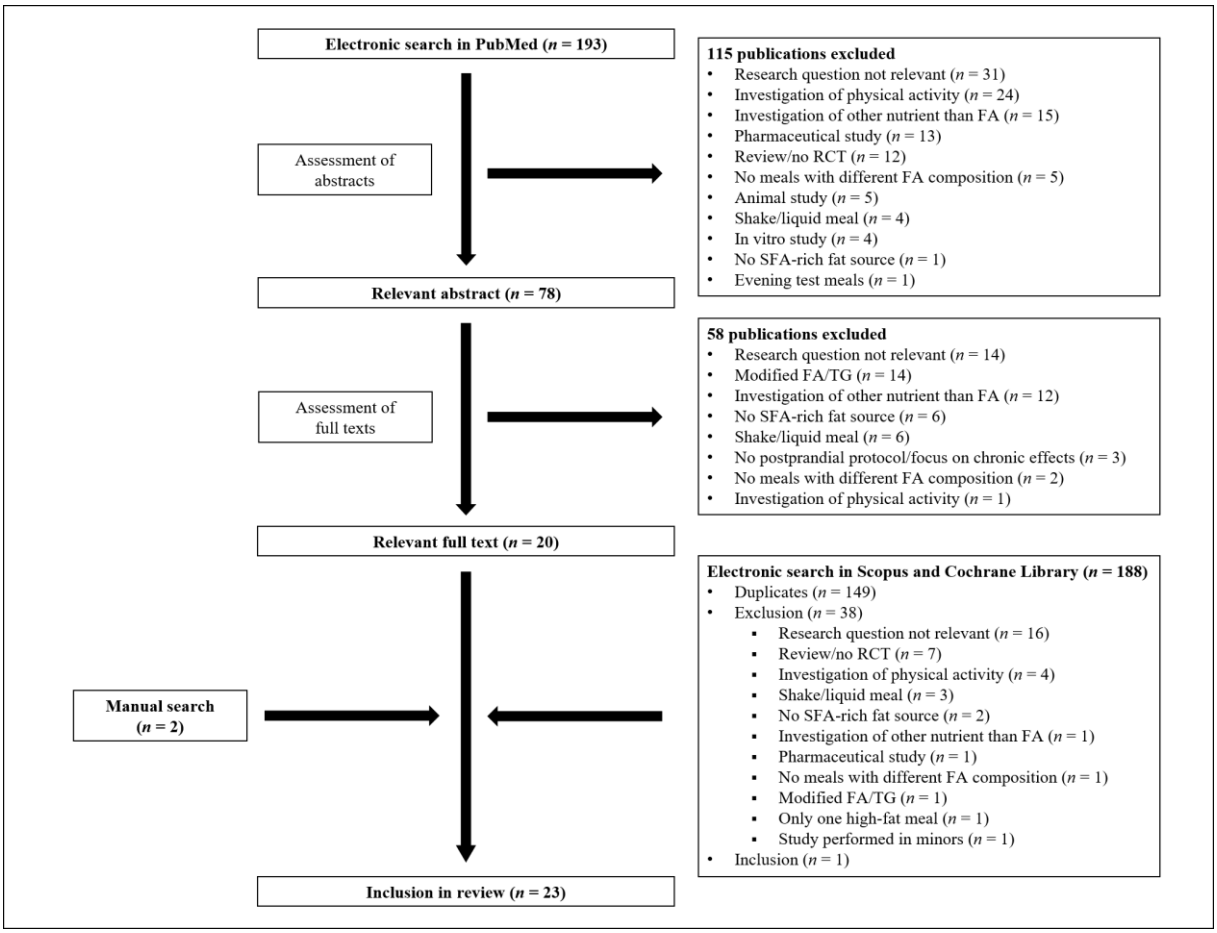

Figure 3-1 Flowchart of article search and selection process. FA, fatty acid; RCT, randomized controlled trial.

RESULTS

The systematic literature search in the PubMed database identified 193 publications. Of these, 115 studies were excluded after screening the abstracts because they did not fulfil the inclusion criteria and/or fulfilled at least one exclusion criterion (**Table 3-1**). After examining the full texts of the remaining 78 studies, 20 publications were rated as suitable for this review. The systematic literature searches in the Scopus database and in the Cochrane Library revealed 111 and 77 publications, respectively. After removing duplicates and screening the articles, 1 publication was included in the analysis. In addition, 2 studies were identified during the manual search. In total, 23 articles were included (**Figure 3-1**).

15 studies were performed in metabolically healthy subjects (**Tables 3-2 and 3-5**) and 4 studies included individuals with CVD risk factors (**Table 3-3**). In 4 studies, data from metabolically healthy subjects and individuals with CVD risk factors were obtained (**Table 3-4**). CVD risk factors included an elevated fasting TG concentration, hypercholesterolemia, being overweight, or combinations of several CVD risk factors (e.g., hypertension, elevated plasma glucose).

The meals of 20 studies compared SFA content with unsaturated FA content (**Tables 3-2–3-4**). Butter was used as the main source of SFAs, while olive oil served as the primary source of unsaturated FAs. In 3 studies, fats composed predominantly of SFAs of different origins were used to achieve a specific FA composition in meals (**Table 3-5**).

Impact of fat dose on postprandial lipemia

In 3 studies, participants received a fat-free control meal in addition to high-fat mixed meals (24–26) (**Tables 3-2 and 3-3**). Data revealed that fat-free meals did not increase TG concentration postprandially. By contrast, all high-fat meals provoked an increase in postprandial TG concentration. In addition to postprandial TG concentration, fat dose also influenced the time taken to reach maximum TG concentration (t_{max}). In protocols with very high fat doses (50 g/m^2 body surface/meal, 79 g/meal), the TG concentration peaked 2 h after meal consumption (25, 27), whereas in studies with lower fat doses (35 g, 40 g), the maximum TG concentration (C_{max}) was reached 3–4 h postprandially (28, 29).

Influence of FA composition on postprandial lipemia: metabolically healthy subjects

In metabolically healthy subjects, 11 of 16 studies investigated the effect of FA composition on lipemia by calculating the AUC of postprandial TG concentration (**Tables 3-2 and 3-4**).

SFAs vs. unsaturated FAs

In comparison with meals rich in unsaturated FAs, 2 studies reported a higher TG concentration after the consumption of a SFA-rich meal. Austin et al. (30) found that coconut oil provoked a higher $iAUC_{0–5\ h}$ than a blend of coconut and fish oils. In addition, compared with control meals (tallow and olive oil), they reported a lower $AUC_{0–5\ h}$ after the consumption of meals enriched with a blend of coconut and fish oils or with only fish oil (**Table 3-2**). Bermudez et al. (31) demonstrated that the consumption of butter led to a higher postprandial TG $iAUC_{0–8\ h}$ than the consumption of oils with a larger proportion of unsaturated FAs. Reference fat sources were olive oil, high-palmitic sunflower oil, and a blend of vegetable and fish oils (**Table 3-4**).

In 2 studies at least one meal rich in unsaturated FAs provoked a significantly greater TG AUC than a SFA-rich meal (**Table 3-2**); the SFA-rich meals of both studies were prepared with butter (24, 28). Sun et al. (28) observed that olive oil triggered a stronger postprandial lipemic response than butter, whereas Mekki et al. (24) made the same observation and additionally reported a greater TG $iAUC_{0–7\ h}$ after the consumption of a meal enriched with sunflower oil.

8 studies reported no significant differences in the AUC of postprandial TG concentration between SFA-rich meals and meals rich in unsaturated FAs (**Tables 3-2 and 3-4**). Most meals contained butter as the SFA source (26–29, 32, 33), whereas others were enriched with coconut oil (32, 34), palm oil (34), or with a blend of coconut and palm oil (35). Sources of unsaturated FAs were olive oil (26, 27, 29, 32, 33), canola oil (32), grapeseed oil (28), rice bran oil (34), and walnuts (33). Other meals were prepared with a blend of sunflower and canola oils (35), a blend of linseed and canola oils (29), or a blend of olive and fish oils (27).

Studies using an alternative parameter of postprandial lipemia

In 5 studies, the AUC of postprandial TG concentration was not measured (**Table 3-2**). When comparing alternative parameters of postprandial lipemia (e.g., total TG concentration, median % change from baseline), no significant differences between meals were found in 4 studies. Sources of SFAs were butter (36), dairy products (37), palm oil (38), and cocoa butter (39). Meals rich in unsaturated FAs were prepared with walnuts (36), soy products (37), olive oil (36, 39), and canola and sunflower oils (38). Only Perez-Martinez et al. (40) reported differences in the lipemic responses to high-fat meals. Compared with butter and walnuts,

a meal rich in olive oil resulted in a higher TG concentration in the early postprandial phase and in an earlier decrease to the preprandial TG concentration.

Comparisons of SFAs

In 3 studies, all meals contained SFA-rich fat sources (**Table 3-5**). Metabolically healthy subjects were investigated and postprandial TG AUC was calculated. Every study reported at least one nonsignificant comparison between 2 meals with different SFA profiles. Specifically, there were no significant differences in the lipemic response between palm olein and a blend of coconut and corn oils (41), butter and lard (23), and milk fat, coconut oil, and tallow (42). 2 studies observed significant differences in the AUC of the postprandial TG concentration between meals. Karupaiah et al. (41) observed a lower lipemic response after the consumption of palm olein and a blend of coconut and corn oils than after the intake of a blend of cocoa butter and corn oil. In addition, Panth et al. (23) reported a higher net $AUC_{0–6\ h}$ in response to butter and lard than to coconut oil.

Influence of FA composition on postprandial lipemia: individuals with CVD risk factors

In every study that included patients with increased CVD risk, the AUC of postprandial TG concentration served as the parameter for lipemia (**Tables 3-3 and 3-4**). When comparing meals rich in SFAs with those rich in unsaturated FAs, 5 studies reported a higher postprandial TG AUC after the consumption of a SFA-rich meal. Bermudez et al. (31) showed that, in subjects with a high fasting TG concentration, a meal enriched with butter provoked a greater TG $iAUC_{0–8\ h}$ than meals rich in unsaturated FAs. Reference oils were high-palmitic sunflower oil, refined olive oil, and a blend of vegetable and fish oils. Likewise, Lopez et al. (25) reported a stronger lipemic response after the consumption of butter than of olive oil in subjects with hypertriglyceridemia. Irawati et al. (34) defined hyper-responders as subjects whose TG concentration exceeded 1.7 mmol/L 4 h after the consumption of a palm oil–enriched meal; the TG concentration of normal-responders remained below this threshold. Hyper-responders had a greater TG $iAUC_{0–8\ h}$ after the consumption of palm oil than of rice bran oil. By contrast, in normal-responders, the lipemic responses to the palm oil–enriched and the rice bran oil–enriched meals were comparable. Diekmann et al. (43) and Schönknecht et al. (44) focused on dietary pattern rather than fat sources. Compared with a Mediterranean diet meal, Diekmann et al. (43) observed a greater TG $iAUC_{0–4.5\ h}$ after consumption of a Western diet meal. Schönknecht et al. (44) observed a similar effect; a Western diet, high-fat meal provoked a stronger lipemic response than a Mediterranean diet meal. None of the

studies reported a higher postprandial TG AUC after a meal rich in unsaturated FAs than after a SFA-rich meal (**Tables 3-3 and 3-4**).

In 4 studies, no significant differences were observed when comparing the AUC of postprandial TG concentration between a SFA-rich meal and an unsaturated FA-rich meal. Meals contained coconut or rice bran oil (34), palm olein, or a blend of palm olein with soy or canola oil (45). Other studies compared a blend of palm and coconut oils with a blend of sunflower and canola oils (35), as well as meals prepared with butter, olive oil, and walnuts (33) (**Tables 3-3 and 3-4**).

Table 3-2 Acute test-meal studies comparing the effects of SFA-rich meals and meals rich in unsaturated FAs on postprandial lipemia in metabolically healthy subjects[1]

Reference	Age and BMI of subject group (*n*)	Study design	Energy, kcal	Meal composition	Amount of fat source	Fat source/ meal pattern	FA composition	Blood collection, h	Results[2]
Austin et al. (30)	54 y, 26 ± 1 kg/m^2 (*n* = 15)	Crossover, double-blind	667	34 g fat, 17 g protein, 71 g CHO	0 g	Control (tallow for coconut oil; olive oil for fish oil)	15 g SFA, 15 g MUFA, 2 g PUFA[3]	0, 2, 3, 3.5, 4, 4.5, 5	$AUC_{0\text{-}5h}$ control > fish oil and fish oil and coconut oil (*P* = 0.0125 and *P* = 0.0186) $iAUC_{0\text{-}5h}$ coconut oil > fish oil and coconut oil (*P* = 0.0480)
			667	34 g fat, 17 g protein, 71 g CHO	6 g	Fish oil	15 g SFA, 11 g MUFA, 6 g PUFA[3]		
			667	34 g fat, 17 g protein, 71 g CHO	19 g	Extra virgin coconut oil	23 g SFA, 7 g MUFA, 1 g PUFA[3]		
			667	34 g fat, 17 g protein, 71 g CHO	6 g, 19 g	Fish oil, Extra virgin coconut oil	22 g SFA, 3 g MUFA, 6 g PUFA[3]		
Bellido et al. (36)	Age and BMI not stated (*n* = 8)	Crossover, 4 wk of Western diet before study	50–66% of daily intake	60 EN% fat, 15 EN% protein, 25 EN% CHO	1 g/kg body mass	Butter	35 EN% SFA, 22 EN% MUFA, 4 EN% PUFA[3]	0, 3, 6, 9	No calculation of AUC of postprandial TG concentration. No significant difference in alternative parameter.
						Olive oil	22 EN% SFA, 38 EN% MUFA, 4 EN% PUFA[3]		
						Walnuts	20 EN% SFA, 24 EN% MUFA, 16 EN% PUFA[3]		

Meikle et al. (37)	53 ± 5 y, 30 ± 6 kg/m^2 (n = 16)	Crossover	745 786	54 g fat, 29 g protein, 37 g CHO 54 g fat, 29 g protein, 47 g CHO	Not stated	Dairy products Soy products	67 g SFA, 23 g MUFA, 5 g PUFA[4] 37 g SFA, 40 g MUFA, 24 g PUFA[4]	0, 1, 2, 3, 4	No calculation of AUC of postprandial TG concentration. No significant difference in alternative parameter.
Mekki et al. (24)	20–29 y, 22 ± 1 kg/m^2 (n = 10)	Crossover	Not stated	Not stated	0 g 40 g	No fat Butter Olive oil Sunflower oil	Not stated 54 g/100 g SFA: 14 g/100 g C4:0–C12:0, 11 g/100 g C14:0, 30 g/100 g C16:0, 11 g/100 g C18:0, 25 g/100 g C18:1[4] 11 g/100 g C16:0, 76 g/100 g C18:1, 9 g/100 g C18:2[4] 21 g/100 g C18:1, 67 g/100 g C18:2[4]	0, 1, 2, 3, 4, 5, 6, 7	$iAUC_{0\text{-}7h}$ butter < other meals (P < 0.05)
Pederson et al. (38)	24 y, 23 kg/m^2 (n = 12)	Crossover, double-blind	Breakfast, 358 Lunch, 1337	17 g fat, 9 g protein, 43 g CHO 64 g fat, 32 g protein, 153 g CHO	15 g 55 g	Palm oil Canola oil Sunflower oil	39% SFA, 47% MUFA, 14% PUFA[4] 7% SFA, 63% MUFA, 30% PUFA[4] 11% SFA, 21% MUFA, 68% PUFA[4]	Every 15 min for 1.5 h after breakfast, every 30 min for 2.5 h after lunch, hourly until 9 h postprandially	No calculation of AUC of postprandial TG concentration. No significant difference in alternative parameter.

Perez-Martinez et al. (40)	22 ± 2 y, 25 ± 3 kg/m^2 (n = 20)	Crossover, 4 wk of diet matching the FA composition of the postprandial protocol before study	50–66% of daily intake	60 EN% fat, 15 EN% protein, 25 EN% CHO	1 g/kg body mass	Butter	35 EN% SFA, 22 EN% MUFA, 4 EN% PUFA[3]	0, 1, 2, 3, 4, 5, 6, 8.5, 11	No calculation of AUC of postprandial TG concentration. Olive oil: greater TG concentration in early postprandial phase and earlier decrease to preprandial TG concentration (P = 0.002 and P = 0.012).
						Olive oil	20 EN% SFA, 36 EN% MUFA, 4 EN% PUFA[3]		
						Walnuts	20 EN% SFA, 24 EN% MUFA, 16 EN% PUFA[3]		
Sanders et al. (27)	23 ± 4 y, 23 ± 3 kg/m^2 (n = 9)[5]	Crossover, 3 wk of diet matching the FA composition of the postprandial protocol before study	1846	79 g fat, 54 g protein, 238 g CHO	Not stated	Butter	46 wt% SFA, 33 wt% MUFA, 12 wt% PUFA[4]	0, 1, 2, 4, 6	No significant difference
						Olive oil	22 wt% SFA, 55 wt% MUFA, 18 wt% PUFA[4]		
						Olive oil and fish oil	20 wt% SFA, 52 wt% MUFA, 19 wt% PUFA[4]		
Sciarillo et al. (32)	24 ± 1 y, 26 ± 7 kg/m^2 (n = 10)	Crossover	13 kcal/kg body mass (mean 995 kcal)	61 EN% fat, 7 EN% protein, 32 EN% CHO	Individual (mean 65 g)	Unsalted butter	Not stated	0, 1, 2, 3, 4, 5, 6	No significant difference
						Native coconut oil			
						Native olive oil extra			
						Canola oil			

					48 g (40 g fat)	Unsalted butter	24 g SFA, 8 g MUFA, 8 g PUFA[3]		
Sun et al. (28)	27 ± 6 y, 23 ± 3 kg/m^2 (n = 20)	Crossover, single-blind	Not stated	Not stated	44 g (40 g fat)	Refined olive oil	6 g SFA, 31 g MUFA, 3 g PUFA[3]	0, 0.25, 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 3.5, 4	$iAUC_{0\text{-}4h}$ butter < olive oil (P < 0.01)
					40 g	Refined grape seed oil	4 g SFA, 8 g MUFA, 28 g PUFA[3]		
					42 g (35 g fat)	Butter	75 mol% SFA (C4:0–C18:0), 20 mol% MUFA, 2 mol% PUFA[4]		
Svensson et al. (29)	34 ± 8 y, 23 ± 3 kg/m^2 (n = 19)	Crossover, single-blind	786	47 g fat, 23 g protein, 69 g CHO	35 g	Native olive oil	15 mol% SFA (C4:0–C18:0), 69 mol% MUFA, 16 mol% PUFA[4]	0, 1, 3, 5, 7	No significant difference
					35 g	Linseed oil and canola oil	7 mol% SFA (C4:0–C18:0), 39 mol% MUFA, 55 mol% PUFA[4]		
Tholstrup et al. (39)	38 ± 11 y, 21 ± 1 kg/m^2 (n = 10)	Crossover, single-blind	621 kcal/ 100 g	76 EN% fat, 3 EN% protein, 21 EN% CHO	1 g/kg body mass (mean 62 g)	Cocoa butter	48 EN% SFA, 26 EN% MUFA, 2 EN% PUFA[3]	0, 4, 6	No calculation of AUC of postprandial TG concentration. No significant difference in alternative parameter.
						Olive oil	12 EN% SFA, 57 EN% MUFA, 8 EN% PUFA[3]		

Thomsen et al. (26)	23 ± 2 y, 21 ± 2 kg/m^2 (n = 10)	Crossover, single-blind	Not stated	Not stated	0 g	No fat	Not stated	0, 1, 2, 3, 4, 5, 6, 7, 8	No significant difference
					100 g	Butter	72% SFA[4]		
					80 g	Olive oil	74% MUFA[4]		

[1]Age and BMI are given as mean ± SD. Numbers are rounded to whole numbers. CHO, carbohydrate; EN%, energy percentage; FA, fatty acid; iAUC, incremental AUC; wt%, weight percentage.
[2]Referring to comparisons between AUC of postprandial TG concentration (plasma, serum, capillary blood) after SFA-rich meals and meals rich in unsaturated FAs.
[3]Referring to the content of SFA, MUFA, and PUFA in the meal.
[4]Referring to the content of SFA, MUFA, and PUFA in the fat source.
[5]Age and BMI referring to all 26 study participants.

Table 3-3 Acute test-meal studies comparing the effects of SFA-rich meals and meals rich in unsaturated FAs on postprandial lipemia in subjects with risk factors for CVD[1]

Reference	Health condition	Age and BMI of subject group (*n*)	Study design	Energy, kcal	Meal composition	Amount of fat source	Fat source/ meal pattern	FA composition	Blood collection, h	Results[2]
Diekmann et al. (43)	Characteristics of metabolic syndrome	70 ± 5 y, 30 ± 2 kg/m^2 (*n* = 26)	Crossover	1014	59 g fat, 26 g protein, 94 g CHO	Not stated	Western diet	32 g SFA, 20 g MUFA, 4 g PUFA[3]	0, 1.5, 3, 4.5	$iAUC_{0\text{-}4.5h}$ Western diet meal > Mediterranean diet meal ($P < 0.001$)
				1015	40 g fat, 26 g protein, 133 g CHO		Mediterranean diet	5 g SFA, 20 g MUFA, 11 g PUFA[3]		
Karupaiah and Sundram (45)	Cholesterol fasting 5.26 ± 0.78 mmol/L	36 ± 5 y, 22 ± 2 kg/m^2 (*n* = 15)	Crossover, 1 wk before intervention 50 g/d of fat source of post-prandial protocol	1010	53 g fat, 32 g protein, 101 g CHO	50 g	Palm olein	42% SFA, 45% MUFA, 11% PUFA[4] 42 EN% SFA, 46 EN% MUFA, 12 EN% PUFA[3]	0, 1.5, 3.5, 5.5, 7	No significant difference
							Palm olein and soy oil	26% SFA, 40% MUFA, 32% PUFA[4] 27 EN% SFA, 41 EN% MUFA, 30 EN% PUFA[3]		
							Palm olein and canola oil	14% SFA, 58% MUFA, 26% PUFA[4] 18 EN% SFA, 56 EN% MUFA, 24 EN% PUFA[3]		

Lopez et al. (25)	TG fasting > 2.26 mmol/L	33 ± 7 y, 24 ± 5 kg/m^2 (n = 14)	Crossover, single-blind	10 kcal/kg body weight (mean 800 kcal)	Not stated	0 g	No fat	Not stated	
					72% fat, 6% protein, 22% CHO	50 g/m^2 body surface	Butter	65% SFA, 31% MUFA, 3% PUFA[4]	0, 1, 2, 3, 4, 5, 6, 7, 8	iAUC$_{0\text{-}8h}$ butter > olive oil (P < 0.05)
							Olive oil	15% SFA, 81% MUFA, 4% PUFA[4]		
Schön-knecht et al. (44)	Characteristics of metabolic syndrome	70 ± 5 y, 31 ± 3 kg/m^2 (n = 60)	Crossover	1010	59 g fat, 26 g protein, 94 g CHO	Not stated	High-fat Western diet	32 g SFA, 20 g MUFA, 4 g PUFA[3]	0, 1, 2, 3, 4, 5	iAUC$_{0\text{-}5h}$ High-fat Western diet meal > other meals (P < 0.001)
				1013	34 g fat, 26 g protein, 145 g CHO		Low-fat Western diet	19 g SFA, 11 g MUFA, 2 g PUFA[3]		
				1012	40 g fat, 26 g protein, 133 g CHO		Mediterranean diet	6 g SFA, 24 g MUFA, 9 g PUFA[3]		

[1]Age and BMI are given as means ± SDs. Numbers are rounded to whole numbers. CHO, carbohydrate; CVD, cardiovascular disease; EN%, energy percentage; FA, fatty acid; iAUC, incremental AUC.
[2]Referring to comparisons between AUC of postprandial TG concentration (plasma, serum, capillary blood) after SFA-rich meals and meals rich in unsaturated FAs.
[3]Referring to the content of SFA, MUFA, and PUFA in the meal.
[4]Referring to the content of SFA, MUFA, and PUFA in the fat source.

Table 3-4 Acute test-meal studies investigating the effects of high-fat meals with different FA composition on postprandial lipemia in subjects with risk factors for CVD and metabolically healthy controls[1]

Reference	Health condition	Age and BMI of subject group (*n*)	Study design	Energy, kcal	Meal composition	Amount of fat source	Fat source/ meal pattern	FA composition	Blood collection, h	Results[2]
Bermudez et al. (31)	TG fasting > 2.24 mmol/L	Age not stated, 24 ± 5 kg/m^2 (*n* = 14)	Crossover, double-blind	Not stated	Not stated	50 g/m^2 body surface	Butter	65% SFA, 31% MUFA, 3% PUFA[3]	0, 1, 2, 3, 4, 5, 6, 7, 8	Both groups: iAUC$_{0\text{-}8h}$ butter > other meals (P < 0.05)
							Refined olive oil	15% SFA, 81% MUFA, 4% PUFA[3]		
							High-palmitic sunflower oil	27% SFA, 66% MUFA, 7% PUFA[3]		
	Metabolically healthy	Age not stated, 24 ± 2 kg/m^2 (*n* = 14)					Vegetable oils and fish oils	11% SFA, 75% MUFA, 14% PUFA[3]		
Irawati et al. (34)	Hyper-responder	43 ± 6 y, 29 ± 1 kg/m^2 (*n* = 10)	Crossover, single-blind	740	43 g fat, 14 g protein, 69 g CHO	40 g	Coconut oil	92% SFA, 8% MUFA, 0% PUFA[3]	0, 4, 8	Hyper-responder: iAUC$_{0\text{-}8h}$ palm oil > other meals (P = 0.001)
	Normo-responder	39 ± 4 y, 24 ± 1 kg/m^2 (*n* = 16)					Palm oil	60% SFA, 31% MUFA, 9% PUFA[3]		Palm oil: iAUC$_{0\text{-}8h}$ hyper-responder > normo-responder (P < 0.01)
							Rice bran oil	28% SFA, 40% MUFA, 32% PUFA[3]		

Lozano et al. (33)	Lower-weight subjects Higher-weight subjects	23 ± 2 y, 26 kg/m^2 (n = 21)	Crossover, 4 wk of Western diet before study	50–66% of daily intake	60% fat, 15% protein, 25% CHO	1 g/kg body mass	Butter	35% SFA, 22% MUFA, 4% PUFA[4]	0, 1, 2, 3, 4, 5, 6, 8.5, 11	No significant difference
							Olive oil	22% SFA, 38% MUFA, 4% PUFA[4]		
							Walnuts	20% SFA, 24% MUFA, 16% PUFA[4]		
Øyri et al. (35)	Familial hypercho-lesterolemia	25 y, 23 kg/m^2 (n = 13)	Crossover, double-blind	764	61 g fat, 7 g protein, 48 g CHO	Not stated	Palm oil and coconut oil	36 g SFA, 19 g MUFA, 5 g PUFA[4]	0, 2, 4, 6	No significant difference
	Metabolically healthy	25 y, 22 kg/m^2 (n = 14)		768	63 g fat, 6 g protein, 45 g CHO		Sunflower oil and canola oil	8 g SFA, 21 g MUFA, 34 g PUFA[4]		

[1]Age and BMI are given as means ± SDs. Numbers are rounded to whole numbers. CHO, carbohydrate; CVD, cardiovascular disease; FA, fatty acid; iAUC, incremental AUC.
[2]Referring to comparisons between AUC of postprandial TG concentration (plasma, serum, capillary blood) after SFA-rich meals and meals rich in unsaturated FAs.
[3]Referring to the content of SFA, MUFA, and PUFA in the fat source.
[4]Referring to the content of SFA, MUFA, and PUFA in the meal.

Table 3-5 Acute test-meal studies comparing the effects of different SFA-rich meals on postprandial lipemia in metabolically healthy subjects[1]

Reference	Age and BMI of subject group (*n*)	Study design	Energy, kcal	Meal composition	Amount of fat source	Fat source/ meal pattern	FA composition	Blood collection, h	Results[2]
Karupaiah et al. (41)	30 ± 8 y, 23 ± 4 kg/m^2 (n = 20)	Crossover, single-blind, 1 wk before intervention 50 g/d of fat source of postprandial protocol	960	50 g fat, 29 g protein, 98 g CHO	50 g	Coconut oil and corn oil	75% SFA, 21% MUFA, 12% PUFA[3] 17 EN% SFA, 5 EN% MUFA, 3 EN% PUFA[4]	0, 2, 4, 5, 6, 8	$AUC_{0\text{-}8h}$ cacao butter and corn oil > other meals (P = 0.016)
						Cacao butter and corn oil	59% SFA, 35% MUFA, 12% PUFA[3] 14 EN% SFA, 9 EN% MUFA, 3 EN% PUFA[4]		
						Palm olein	44% SFA, 45% MUFA, 12% PUFA[3] 11 EN% SFA, 12 EN% MUFA, 3 EN% PUFA[4]		
Panth et al. (23)	18–45 y, 24 ± 3 kg/m^2 (n = 16)	Crossover, single-blind	666	41 g fat, 7 g protein, 64 g CHO	40 g	Butter	27 g SFA, 8 g MUFA, 1 g PUFA[4]	0, 2, 3, 4, 6	Net $AUC_{0\text{-}6h}$ butter, lard > coconut oil (P < 0.05)
			659	39 g fat, 7 g protein, 66 g CHO		Lard	20 g SFA, 14 g MUFA, 2 g PUFA[4]		
			659	39 g fat, 7 g protein, 66 g CHO		Coconut oil	35 g SFA, 1 g MUFA, 1 g PUFA[4]		

Poppitt et al. (42)	27 ± 9 y, 23 ± 2 kg/m^2 (n = 18)	Crossover, single-blind	Breakfast, 792 Lunch, ad libitum	52 g fat, 19 g protein, 64 g CHO Individual	Not stated Individual	Soft-fraction milk fat	3 g SCT, 7 g MCT, 42 g LCT[4]	0, 0.5, 2, 3	No significant difference
						Tallow	0 g SCT, 0 g MCT, 52 g LCT[4]		
						Coconut oil	0 g SCT, 10 g MCT, 42 g LCT[4]		

[1]Age and BMI are given as means ± SDs. Numbers are rounded to whole numbers. CHO, carbohydrate; EN%, energy percentage; FA, fatty acid; LCT, long-chain triglycerides; MCT, medium-chain triglycerides; SCT, short-chain triglycerides.
[2]Referring to comparisons between AUC of postprandial TG concentration (plasma, serum, capillary blood) after several SFA-rich meals.
[3]Referring to the content of SFA, MUFA, and PUFA in the fat source.
[4]Referring to the content of SFA, MUFA, and PUFA in the meal.

DISCUSSION

The aim of this review was to investigate the influence of mixed meals enriched with fat sources with different FA compositions on postprandial lipemia. We focused on a food-based approach and distinguished between metabolically healthy adults and individuals with CVD risk factors.

Metabolically healthy subjects

Most studies in metabolically healthy subjects did not report a significant difference in the AUC of postprandial TG concentration after the consumption of fat sources rich in SFAs or unsaturated FAs (**Tables 3-2 and 3-4**). Therefore, for metabolically healthy humans, the SFA content of meals does not seem to be a relevant determinant of postprandial lipemia.

It should be noted that the assumption, that in a state of metabolic health the FA composition of a meal has no effect on lipemia, is based on comparisons between certain fat sources. For example, 10 studies compared the effects of meals prepared with butter or olive oil on postprandial TG concentration (24, 26–29, 31–33, 36, 40), whereas only 1 study compared pure coconut oil with canola oil (32). There is a particular lack of evidence concerning fat sources with potential health-promoting effects, such as coconut oil and hemp seed oil. Since these fat sources are increasingly used in modern kitchens, more studies are required to determine their effect on postprandial metabolism.

A lack of significant effects of SFA-rich meals on postprandial lipemia has recently been described by Yao et al. (16). Although they hypothesized a beneficial effect of unsaturated FAs on postprandial TG and cholesterol response, their meta-analysis of 17 studies, including 13 studies in metabolically healthy subjects, did not reveal any significant differences in these parameters.

However, in our analysis, 2 studies reported a significantly higher postprandial TG AUC after the consumption of a SFA-rich meal (30, 31), both of which used a blend of plant and fish oils as the reference fat source (**Tables 3-2 and 3-4**). In the study of Austin et al. (30), lower lipemic responses to fish oil–containing meals were found although they had a similar fat and SFA content as comparison meals (olive oil, coconut oil); thus, the addition of fish oil to a mixed meal may attenuate the postprandial lipemic response to high-fat meals. There is also well-described evidence that long-term supplementation with fish oil lowers fasting and postprandial TG in metabolically healthy, normolipidemic subjects. Brown and Roberts (46)

reported that, in comparison to olive oil, 6 wk of fish oil intake led to a significantly lower postprandial TG concentration in response to a standardized high-fat meal. Park and Harris (47) confirmed this observation by showing that supplementation with marine n–3 FAs for 4 wk reduced postprandial TG concentration by 16%. It has been suggested that marine n–3 PUFAs lower postprandial lipemia by diminishing endogenous production of VLDLs (48). Additionally, EPA and DHA accelerate the clearance of chylomicrons by upregulating lipoprotein lipase activity (47). α-linolenic acid from plant foods (e.g., linseed oil) may serve as an alternative source of long-chain n–3 FAs, but further studies are needed to determine its effects on lipoprotein production and clearance.

In most of the studies analyzed, participants received butter or olive oil (24, 26–29, 31–33, 36, 40); however, comparison of postprandial TG AUC between meals revealed contradictory results (**Tables 3-2 and 3-4**). One reason may be differences in the FA composition of the same fat source. For example, the butter in the study of Sun et al. (28) contained 50% SFAs, whereas Thomsen et al. (26) used butter with 72% SFAs. When evaluating the results of several studies, variations in FA profiles of similar fat sources should be considered.

The role of chain length of SFAs

According to Karupaiah et al. (41) and Panth et al. (23), coconut oil provokes a weaker postprandial lipemic response than cocoa butter, butter, and lard (**Table 3-5**). All of these fat sources are rich in SFAs, but differ in their SFA composition. Coconut oil is dominated by lauric acid (12:0, 42 g/100 g) and myristic acid (14:0, 17 g/100 g), whereas the content of palmitic acid (16:0, 8.6 g/100 g) and stearic acid (18:0, 2.5 g/100 g) is low (11). Compared with coconut oil, butter (24), cocoa butter, and lard (11) have a higher content of palmitic acid (30, 25, and 24 g/100 g, respectively) and stearic acid (11, 33, and 14 g/100 g, respectively). Thus, the chain length of the SFAs may influence the magnitude of the postprandial lipemic response. However, conflicting results should be noted. Poppitt et al. (42) did not find any significant differences when comparing the $AUC_{0–3\ h}$ of postprandial TG concentration after meals enriched with coconut oil, tallow, and milk fat (**Table 3-5**). Likewise, in the study of Karupaiah et al. (41), a blend of coconut oil and corn oil did not provoke a different lipemic response than palm olein. There were also no differences between meals enriched with butter or lard (23). To better understand the impact of SFA chain length on postprandial lipemia, systematic investigations with standardized amounts of FAs are required.

Subjects with CVD risk factors

In nearly every study of subjects with CVD risk factors, a SFA-rich meal provoked a higher postprandial TG AUC than a meal rich in unsaturated FAs (**Tables 3-3 and 3-4**). Most meals with a high content of SFAs contained butter; thus, individuals with CVD risk factors may benefit from replacing butter with fat sources rich in unsaturated FAs such as canola or olive oil. The recent meta-analysis of Yao et al. (16) of 17 studies, including 4 studies in people with CVD risk factors, did not reveal significant differences in the AUCs of postprandial TG concentration between SFA-rich meals and meals enriched with unsaturated FAs. The authors did not differentiate between metabolically healthy subjects and individuals with a CVD risk profile. A meta-analysis including studies solely in people with CVD risk factors may provide clarity concerning the effects of FA composition on postprandial lipemia in these individuals.

The role of the type of CVD risk factors

Our analysis illustrates that investigations of postprandial lipemia require consideration of the CVD risk factors of participants. In studies with significant differences in the AUC of postprandial TG concentration, subjects had hypertriglyceridemia (25, 31), elevated postprandial TG concentrations (34), or several characteristics of the metabolic syndrome (43, 44). By contrast, investigations in subjects with mild or familial hypercholesterolemia did not reveal significant differences between meals rich in SFAs or unsaturated FAs (35, 45). In addition, subjects in studies with significant differences in the lipemic response were older and had a higher BMI than those in studies without significant differences (**Tables 3-3 and 3-4**). Thus, impaired TG metabolism (especially hypertriglyceridemia), advanced age (≥40 y), and elevated BMI appear to promote an exaggerated postprandial lipemic response to SFA-rich meals. It should be noted that in the study of Lozano et al. (33), meals with different FA compositions did not provoke significant differences in the postprandial TG iAUC in plasma of lower-weight subjects and higher-weight subjects; however, all subjects had a BMI (in kg/m^2) <30. Therefore, a threshold of 30 may be required for detection of significant differences in lipemic responses to meals with different FA compositions.

Other investigations confirm the assumption that certain CVD risk factors increase the extent of postprandial lipemia. Jackson et al. (49) reported that, as the number of metabolic syndrome components increases, the $AUC_{0–8\ h}$ and the $iAUC_{0–8\ h}$ of postprandial TG concentration also increase. In several investigations, a correlation between BMI and the magnitude of the postprandial TG response was observed (32, 50). Couillard et al. (51)

showed that men responded with a greater postprandial TG $iAUC_{0–8\ h}$ than women. However, the gender difference disappeared after matching for visceral adipose tissue, since there was a significant association between visceral adipose tissue and postprandial lipemia in both genders. In the study of Madhu et al. (52), men with type 2 diabetes responded to a fat-rich meal with a greater postprandial TG $AUC_{0–8\ h}$ and $iAUC_{0–8\ h}$ than metabolically healthy controls. In addition, diabetic subjects showed a higher TG peak. Emerson et al. (53) observed that advanced age promotes an exaggerated postprandial lipemic response to a high-fat meal. Younger, active adults (mean age, 25 y) showed a significantly lower $tAUC_{0–6\ h}$ of postprandial TG concentration, as well as a lower TG peak, than both older active and inactive older adults. Furthermore, older active adults (mean age, 67 y) responded to the meal with a lower lipemic response than older inactive adults (mean age, 68 y). Further studies are required to confirm the finding that older inactive subjects with characteristics of metabolic syndrome benefit from exchanging SFAs (e.g., butter) with unsaturated FAs (e.g., canola oil and olive oil).

Influence of the fat dose on magnitude and time course of postprandial lipemia

At the end of the last century, a dose–response relation between the fat content of meals and postprandial TG concentration was described (54, 55). Cohen et al. (54) demonstrated that the magnitude of lipemia was proportional to the fat content of high-fat meals. Dubois et al. (55) observed a stepwise increase in serum TG concentration after the consumption of meals with graded amounts of fat. Likewise, current reviews reported increasing lipemia with increasing fat intake (56, 57). Our analysis did not focus on the effect of fat dose on postprandial lipemia, in part because none of the included studies were performed with gradually increasing amounts of fat. Meals contained high fat doses and, in some investigations, an additional meal without fat was consumed (24–26). Comparing the lipemic responses to fat-free meals with those to high-fat meals suggests a positive dose–response relation, although this association remains to be confirmed.

It is well known that, in response to a mixed meal, TG concentration increases rapidly until C_{max}, which is usually reached between the second and third hour postprandially (54, 55). After reaching a plateau between the third and fourth hour, the TG concentration remains elevated until 6 h after meal intake (57). Data indicate that, compared with a moderate fat load (e.g., 35 g), a high fat load (e.g., 79 g) triggers an earlier C_{max} of TGs. However, this observation was not based on studies with graded fat loads but on comparisons between studies (**Tables 3-2 and 3-3**). Due to variations in study protocols, it remains uncertain

whether variation in the quantity of fat in meals was responsible for differences in the TG time course. Previous investigations with graded fat loads do not clearly confirm an influence of fat dose on the t_{max} of postprandial TG concentration (54, 55). Thus, in addition to the fat content of meals, other factors that influence postprandial lipemia should be considered when analyzing lipemic responses.

Strengths and limitations

A strength of this analysis is the investigation of both metabolically healthy subjects and individuals with CVD risk factors. In addition, the focus on natural, commercially available fat sources means the results have a practical application. This review helps to develop nutritional recommendations to reduce postprandial lipemia. Considering that a high postprandial TG concentration is associated with increased risk of CVD, the conclusions from our analysis may contribute to lowering CVD risk, especially of individuals with CVD risk factors.

One limitation of this analysis is that meals were categorized into those rich in SFAs and those rich in unsaturated FAs. Especially in meals rich in unsaturated FAs, this categorization may not have been specific enough to capture differences between unsaturated FA composition. Fat sources dominated by MUFAs (e.g., olive oil) or PUFAs (e.g., grapeseed oil, fish oil) can have different effects on postprandial lipemia (28, 30, 58). This limitation may also affect SFAs, which include several subgroups such as medium-chain SFAs (23, 41). Therefore, it would be useful for further analysis to consider the differences in the FA profiles of SFAs and unsaturated FAs.

Due to the high heterogeneity of population, intervention, comparison, and outcome measurement of included studies, we did not perform meta-analysis. Considering the limited number of comparable studies (e.g., administering the same fat sources, or having the same length of observational period), we decided not to attempt meta-analysis with subsequent subgroup analyses. As a result, our findings have an increased risk of exaggerating effects and should be interpreted carefully. Standardization of the designs of postprandial protocols (**Table 3-6**) would enable meaningful meta-analyses verifying our findings.

Table 3-6 Recommendations for designs of future postprandial studies[1]

	Recommendations
Subject group	• Adult participants (≥18 y) • CVD risk phenotype (e. g., advanced age, obesity, characteristics of metabolic syndrome)
Study design	• Randomized controlled crossover study • Adequate wash-out phase
Behavior before intervention days	• Avoidance of intense physical activity and alcohol • Overnight fasting
Type of meal	• Breakfast • Preparation with natural, commercially available food (e. g., pasta, bread, plant oils, dairy products) • Characterized nutrient profile (e.g., energy content, total fat and individual FAs, protein and carbohydrate content)
Fat dose	• 35–50 g per meal • Absolute dosage or relative to the body mass
Meal consumption and postprandial period	• Consumption of the meal within a standardized time period (e.g., 20 min) • Postprandial observation period of 6–8 h • Blood collection every 1–1.5 h
Primary parameter of postprandial lipemia	• iAUC of postprandial TG concentration • Analyzed in blood plasma or serum
Examples for additional parameters of postprandial lipemia	• Maximum TG concentration (C_{max}) • Time to reach the maximum TG concentration (t_{max}) • TG concentration in TG-rich lipoproteins • Analyze of specific lipoprotein subfractions

[1]CVD, cardiovascular disease; FA, fatty acid; iAUC, incremental AUC.

Conclusions

This review revealed 3 main findings. First, in metabolically healthy subjects, the FA composition of a mixed meal is not a relevant determinant of the magnitude of postprandial lipemia. Second, in subjects with CVD risk factors, a high SFA content (>32 g SFA/meal) often provokes a greater lipemic response than unsaturated FAs. Subjects with hypertriglyceridemia, an elevated BMI (≥30 kg/m^2), and/or who are older (≥40 y) may benefit from replacing SFAs with unsaturated FAs. To verify this suggestion, further postprandial protocols should concentrate on subjects with CVD risk factors rather than metabolically healthy adults. Third, because of the dose–response relation between fat load and the magnitude of postprandial lipemia, lowering the fat content of meals has a greater impact on postprandial lipemia than modifying the FA composition.

Future directions

This analysis revealed a lack of standardized procedures in postprandial protocols (**Tables 3-2–3-5**). Marked differences were noted in the fat dose, the length of the observational period (3–11 h), the number of postprandial blood sample collections (2–15), and the parameter of lipemia (e.g., iAUC, mmol/L × 6 h). To increase the comparability of study results, standardized procedures for postprandial protocols are required (57). To reliably induce lipemia while maintaining the physiological relevance and applicability of results, a moderate fat load (35–50 g/meal) is recommended. A postprandial observational period of 6–8 h with regular collection of blood samples (every 1–1.5 h) ensures that fluctuations in lipemia are fully captured. With regard to lipemia parameters, measuring the iAUC of postprandial TG concentration is most advisable. Because the AUC does not allow any analysis of time course, differences in lipemia may be missed when focusing only on the AUC of postprandial TG concentration. To avoid misinterpretations, further analysis should include parameters of the time course such as t_{max} (overview of recommendations in **Table 3-6**).

Attenuating the lipemic response is an effective strategy to lower CVD risk through nutritional recommendations. The postprandial TG concentration in blood plasma or serum is one of several parameters considered to be an independent predictor of CVD. In some studies, despite nonsignificant differences in plasma TG, meals with different FA compositions did provoke significant differences in TG concentration in specific lipoprotein fractions—for example, in small TG-rich lipoproteins (33) or in the chylomicron-rich fraction (26).

Therefore, to comprehensively evaluate the influence of fat sources on cardiovascular health, it would be useful to analyze a broader spectrum of postprandial lipemia parameters. In addition, further metabolic processes, such as glycemia, insulinemia, and low-grade postprandial inflammation, should be considered when evaluating the influence of meal composition on CVD risk parameters.

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4. Review on postprandial vascular function

A Systematic Review of the Impact of Fat Quantity and Fatty Acid Composition on Postprandial Vascular Function in Healthy Adults and Patients at Risk of Cardiovascular Disease

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ABSTRACT

Atherosclerosis is a key risk factor for developing cardiovascular diseases (CVDs). Flow-mediated dilation (FMD), which reflects vascular reactivity, as well as pulse wave velocity (PWV) and augmentation index (AIx), both markers of arterial stiffness, have emerged as noninvasive, subclinical atherosclerotic markers for the early stages of altered vascular function. In addition to the long-term effects of diet, postprandial processes have been identified as important determinants of CVD risk, and evidence suggests an acute effect of fat quantity and fatty acid (FA) composition on vascular function. However, robust analyses of this association are lacking, especially concerning parameters of arterial stiffness. Therefore, we carried out a systematic literature search in PubMed, Scopus, and the Cochrane Library to investigate the impact of fat quantity and FA composition of meals on postprandial vascular function. Postprandial studies measuring FMD, PWV, and/or AIx in healthy adults and subjects with increased CVD risk (e.g., those with hypercholesterolemia or metabolic syndrome) were analyzed. In total, 24 articles were included; 9 studies focused on the effect of high-fat meals compared with control; and 15 studies investigated the effects of different fat sources. We found that consumption of a high-fat meal causes a reduction in FMD (decrease in vasodilation) and AIx (decrease in arterial stiffness). For eicosapentaenoic acid/docosahexaenoic acid (from fish oil), postprandial assessment (FMD and AIx) indicates a beneficial effect on vascular function. There is limited evidence of an influence of CVD risk on the vascular response to meals with varying fat doses or FA composition. However, meaningful conclusions were difficult to draw because of the large heterogeneity of the studies. Inconsistent results regarding both the impact of fat dose and FA composition on postprandial vascular function should be noted. We propose standardized methods for postprandial protocols to improve data quality in future studies. This review was registered in PROSPERO as CRD42022352986.

INTRODUCTION

In the past few decades, the number of global, cardiovascular disease (CVD)-related deaths has steadily increased, from 12.1 million in 1990 to 18.6 million in 2019 [1]. According to the American Heart Association, an estimated 19.1 million people worldwide died in 2020 because of CVDs, with the highest age-standardized mortality rates in Eastern Europe and Central Asia [2]. Alongside increases in mortality, CVD-attributable disability-adjusted life years, years of life lost, and years lived with disability have increased considerably [1]. Atherosclerosis plays a critical role in the development of CVDs, including as an underlying cause of myocardial infarction and stroke [3]. During atherogenesis, an initially reversible fatty streak forms into a fibrous fatty lesion that becomes an atheroma [4]. Over time, this atherosclerotic plaque can rupture or erode, resulting in a cardiovascular event. The early stage of atherosclerosis is characterized by endothelial dysfunction [5,6]. Endothelial dysfunction describes a functional impairment of the endothelium. Characteristics include a decreased vasodilatation, a proinflammatory state, and prothrombotic properties [7]. Evidence also suggests an association between atherosclerosis and arterial stiffness [8,9]. Arterial stiffness is influenced by age and increased blood pressure [10], and structural alterations (e.g., fragmentation of elastic lamellae, increased collagen and calcium content) play a central role in its development [11].

In developed societies, humans spend ~18 h of the day in a postprandial state [12] with continuously fluctuating diurnal lipemia [13]. Evidence suggests that postprandial lipemia leads to temporary, low-grade endothelial dysfunction mediated by local oxidative stress [14–17]. According to current hypotheses, this enhanced oxidative stress reduces the availability of nitric oxide (NO) by increasing breakdown and reducing production [14]. NO plays an essential role in vasodilation, and reduced NO availability, resulting from either decreased production or activity, can cause endothelial dysfunction and contribute to atherosclerosis [18]. Thus, postprandial hypertriglyceridemia in response to a high-fat meal (HFM) may result in endothelial dysfunction, a marker of early stage of atherosclerosis, mediated by local oxidative stress and reduced NO availability.

There is convincing evidence that a dose–response relationship exists between total fat intake and postprandial triglyceride (TG) response [19]. In addition, 2 recent meta-analyses demonstrated that the fatty acid (FA) composition of a test meal influences the extent of postprandial lipemia [20,21]. Considering the detrimental effect of postprandial TGs on endothelial function, impaired vascular function is likely influenced by the amount and

composition of fat ingested. Previous reviews on the acute effects of single HFMs on vascular function focused mainly on flow-mediated dilation (FMD) [22,23], revealing evidence of a marked decrease in FMD in the postprandial state compared with baseline values [23] and low-fat meals (LFMs) [22]. Concerning FA composition, evidence suggests an adverse effect of MUFAs [22] and a beneficial effect of long-chain n–3 (ω-3) PUFAs [24] on postprandial FMD. However, the overall evidence regarding the acute effects of FA composition on vascular function remains inconclusive [22,25].

In a recently published meta-analysis, Fewkes et al. [23] concluded that the effect size of an HFM on postprandial FMD is influenced by several factors, including age and BMI. Previously, we found that meals rich in SFAs provoke greater postprandial lipemia than meals with high amounts of unsaturated FA, especially in older subjects and/or subjects with elevated BMI [19]. These results suggest that especially in adults with certain CVD risk factors (e.g., obesity), high-fat doses and, in particular, SFA-rich meals, may have detrimental effects on postprandial vascular function.

Given this background, we aimed to systematically review and critically evaluate the existing evidence on the acute effects of fat dose and FA composition on vascular function assessed by FMD, pulse wave velocity (PWV), and augmentation index (AIx). An additional aim was to investigate whether acute changes in vascular function differ between metabolically healthy individuals and participants with increased CVD risk (e.g., those with obesity, metabolic syndrome, and hypertriglyceridemia). In addition, to maximize practical relevance, we focused on mixed meals.

METHODS

Measurement of FMD, PWV, and AIx

Our analysis included noninvasive, yet reliable, measures of vascular function (FMD, PWV, and AIx) as outcome measures [26–29]. Although FMD is the most well-established method to characterize endothelial function and reactivity [30], vessel stiffness is assessed by PWV and AIx [22]. FMD, PWV, and AIx are all independent predictors of cardiovascular events (e.g., fatal strokes) and all-cause mortality [31–33].

The FMD test was developed in 1992 by Celermajer et al. [34] and measures the endothelial-dependent vessel diameter change in response to blood flow-associated shear stress after a cuff occlusion period (recommended for 5 min) [26]. There are significant correlations between FMD and invasive measures of coronary artery changes [35] and brachial FMD and future cardiovascular events [36].

Likewise, PWV is an independent predictor of CVD risk and cardiovascular events [27]. $PWV_{c–f}$ is calculated by dividing the distance between the common carotid artery and the common femoral artery by the transit time of the pulse wave between these points [28]. A higher PWV indicates a higher arterial stiffness [27]. In the 2018 European Society of Cardiology/European Society of Hypertension Guidelines for the management of arterial hypertension, the cut-off value for an influence of $PWV_{c–f}$ on CVD risk was set at 10 m/s [37]. According to the European Network for Noninvasive Investigation of Large Arteries, $PWV_{c–f}$ is regarded as the gold standard measurement of arterial stiffness [28].

Similar to the PWV, AIx serves as a surrogate parameter of arterial stiffness and these parameters correlate strongly [38]. The AIx is determined during pulse wave analysis [29]. It is a measure of wave reflection during systole and is usually adjusted to the heart rate by which it is influenced [27]. AIx correlates significantly with several CVD risk scores [29]. All 3 parameters of vascular function (FMD, PWV, and AIx) are reproducible [35,39].

Literature search

To identify suitable studies, the databases of PubMed (https://pubmed.ncbi.nlm.nih.gov/), Scopus (https://www.scopus.com), and the Cochrane Library (https://www.cochranelibrary.com) were searched using the search term "postprandial AND fat AND meal AND (arterial stiffness OR flow mediated dilatation OR pulse wave velocity OR pulse wave analysis)". The initial database searches were conducted between July and August 2022, and the last update

was made in June 2023. Both authors independently reviewed the identified papers and compared them with the inclusion and exclusion criteria. The main inclusion criteria (**Table 4-1**) were as follows: human intervention trial; adult participants; preparation of meals with fat sources (e.g., plant oils and dairy products); periodic measurement of postprandial FMD, PWV, and/or AIx; and paper written in English. To investigate the impact of HFMs on postprandial vascular function, studies were included if ≥1 HFM and 1 LFM were served or if ≥1 HFM meal was served and participants fasted as a control. To analyze the impact of the FA composition on postprandial vascular function, studies were included if the participants consumed ≥2 HFMs with varying FA compositions (e.g., SFA-rich compared with PUFA-rich). Articles were excluded if a tolerance test (e.g., fat tolerance test) was performed, or if chronic effects of total fat intake or FA composition were investigated. Furthermore, pilot studies and conference papers were excluded (**Table 4-1**). Studies were selected by consensus of both the authors (**Figure 4-1**). This review was registered in PROSPERO (CRD42022352986).

Table 4-1 Inclusion and exclusion criteria

Inclusion criteria	**Exclusion criteria**
1. Human intervention trial	1. In vitro studies
2. Adult participants (≥18 y)	2. Animal studies
3. Preparation of meals with natural fat sources (e.g., plant oils)	3. Pilot studies
4. At least 1 of the following comparisons was included:	4. Conference papers
a. HFM vs. LFM	5. Chronic protocols
b. HFM vs. fasting control	6. Tolerance tests (e.g., lipid or glucose tolerance tests)
c. HFM vs. HFM with different FA compositions	
5. Periodic measurement of postprandial FMD, PWV, and/or AIx	
6. Paper in the English language	

Abbreviations: AIx, augmentation index; FA, fatty acid; FMD, flow-mediated dilation; HFM, high-fat meal; LFM, low-fat meal; PWV, pulse wave velocity.

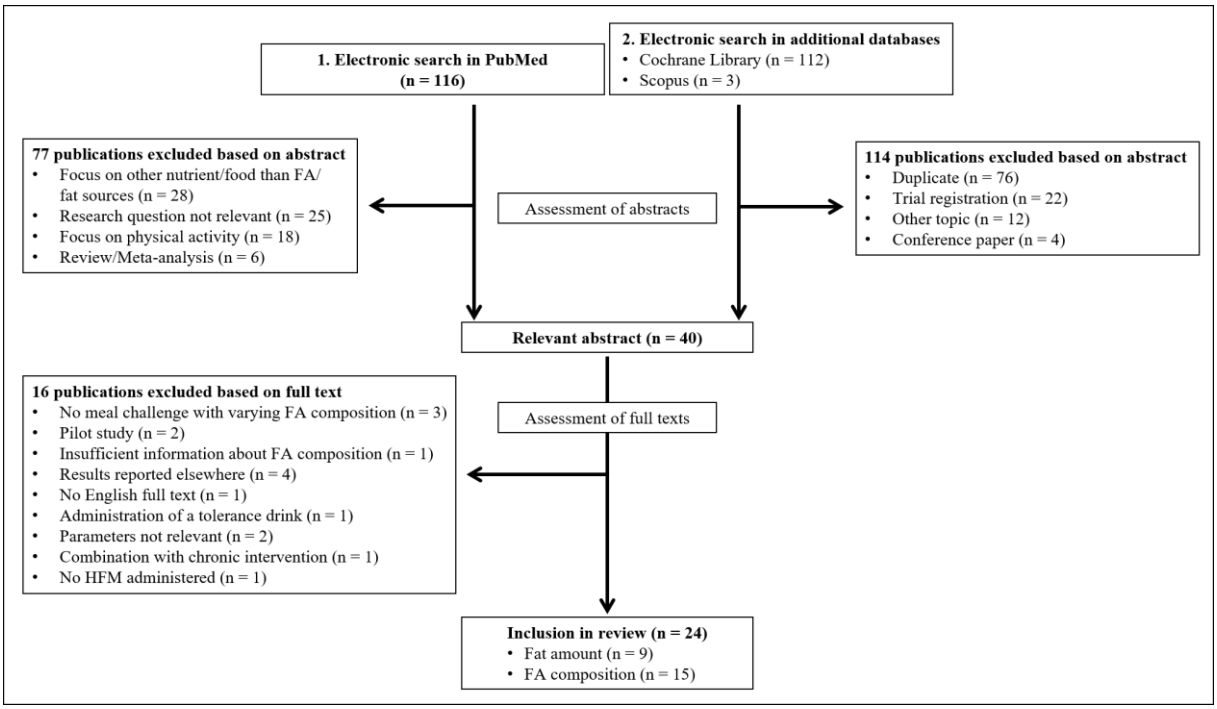

Figure 4-1 Flowchart of the article search and selection process. FA, fatty acid; HFM, high-fat meal.

RESULTS

Using the search string, 116 articles were identified during the systematic literature search in PubMed. On the basis of these abstracts, 77 publications were excluded because they did not fulfill the inclusion criteria and/or fulfilled ≥1 exclusion criterion (**Table 4-1**). The remaining 39 full texts were screened, of which 23 articles were rated as suitable for this review and thus included in the analysis. Using the same search string, literature searches in the Cochrane Library and Scopus were performed, revealing 112 and 3 publications, respectively. On the basis of the titles and abstracts, 76 duplicates were removed, and an additional 38 articles were excluded according to the inclusion and exclusion criteria (in total, 114 excluded abstracts). The remaining full text was assessed and rated as suitable for this review. In total, 24 publications were included in this analysis (**Figure 4-1**), which were published between 1999 and 2021.

The impact of fat dose on postprandial vascular function

In the majority of studies that investigated the impact of fat dose on vascular function (**Tables 4-2–4-4**), FMD (%) was the assessment measure used [40–47]. Two studies provided data on AIx (%) [43,48], none measured PWV (m/s). In 7 trials, only healthy adults were investigated [40,42–47], 1 study included subjects with coronary artery disease (CAD) [41], and 1 investigated lean adults, adults with obesity, and adults with type 2 diabetes mellitus (T2DM) [48]. Test meals were served as mixed meals consisting of commercially available foods (e.g., muffins, croissants, and milk) [40,41,44–46,48] or as shakes [42,43,47] (**Tables 4-2–4-4**). The amount of fat administered via test meals varied between studies from 0 to 18.4 g for the LFMs and from 50 to 95 g for the HFMs.

The effect of fat dose on FMD in healthy adults and those with CVD risk factors

In 7 studies, FMD (%) was measured in metabolically healthy adults [40,42–47] (**Table 4-2**). In 5 of these, interventions consisted of an HFM and an LFM [40,42–44,47]. Esser et al. [43] reported a small but significant decrease in FMD (%) from baseline 3 h after ingestion of the HFM (95 g fat) and LFM (14.5 g fat), without significant differences between the 2 meals. Bae et al. [40] and Benson et al. [42] observed a significant decrease in FMD (%) from preprandial values in response to the HFM (fat content: 53.4 g, 1 g/kg body weight [BW]), but did not detect a significant change in FMD (%) after consumption of the LFM (fat content: 3 g, 0.04 g/kg BW). In contrast, Poitras et al. [44] and Williams et al. [47] found no effect of either an HFM (fat content: 54 g, 64.4 g) or LFM (fat content: 0 g, 18.4 g) on

postprandial FMD (%) (**Table 4-2**). In 2 studies [45,46], FMD (%) was measured after consumption of 1 or 2 consecutive HFMs and on a different day during a fasting period (**Table 4-2**). Tushuizen et al. [45] reported a significant decrease in FMD (%) from baseline after a fat-rich lunch that was ingested 4 h after a fat-rich breakfast (each meal: 50 g fat). The difference in FMD (%) at the equivalent time point during the fasting protocol tended toward statistical significance ($P = 0.051$). Patik et al. [46] observed that 2 h postprandially, a fat-rich, fast-food meal (55 g fat) led to a significant decrease in FMD (%) from baseline compared with the fasting protocol; however, 2 h later, there was no significant difference in FMD (%) change from baseline between conditions. In both studies, the fasting state had no influence on FMD (%) (**Table 4-2**).

The literature search revealed one study in which the effects of an HFM (53.4 g fat) and an LFM (3 g fat) on FMD (%) were measured in participants with enhanced CVD risk (**Table 4-3**). Bae et al. [41] reported no significant effects of the test meals on postprandial FMD (%) in adults with CAD.

The effect of fat dose on AIx and PWV in healthy adults and those with CVD risk factors

Two studies investigated the impact of an HFM on AIx (%) [43,48] (**Tables 4-2 and 4-4**). In healthy adults, Esser et al. [43] observed a significant decrease in heart rate corrected AIx (%) from baseline after eating both an HFM (95 g fat) and an LFM (14.5 g fat), with no significant difference between groups (**Table 4-2**). Phillips et al. [48] reported that in lean adults, non diabetic adults with obesity, and individuals with T2DM, AIx (%) decreased from baseline after consumption of an HFM (57.5 g fat) but remained unchanged during the fasting period (**Table 4-4**).

No studies investigating the effects of fat dose on vascular function measured PWV (m/s).

The impact of FA composition on postprandial vascular function

In total, 15 studies were included that analyzed the impact of FA composition on vascular function (**Tables 4-5–4-7**). Seven were performed in healthy adults [49–55] and 6 in adults with CVD risk factors [56–61]. The remaining 2 studies [62,63] included both healthy adults and adults with increased CVD risk. Berry et al. [49] measured all 3 parameters of vascular function (FMD [%], PWV [m/s], and AIx [%]), Lithander et al. [50] and McManus et al. [57] determined AIx (%) and PWV (m/s), and Kendall et al. [56] and Chong et al. [55] only

measured AIx (%). Most studies supplied data on FMD (%) but not AIx (%) or PWV (m/s) [51–54,58–63]. In many papers, the meals consisted of a shake or drink (e.g., a chocolate drink), either entirely [50, 60] or partially [49,51,55,57–59]. The test meals were enriched with a pure fat source (e.g., olive oil [50,61–63]), an oil blend (e.g., palm/soy bean oil mixture [55,57]), or they contained fat-rich foods (e.g., burger and French fries [52], various dairy products [58]) (**Tables 4-5–4-7**). The fat amount consumed via the test meals ranged from 29 to 80 g.

The effect of FA composition on FMD in healthy adults and those with CVD risk factors

The literature search revealed 7 studies investigating the impact of FA composition on FMD (%) in healthy adults [49, 51–54,62,63] (**Tables 4-5 and 4-7**). Of these, 3 found that a HFM led to a decrease in FMD (%) from baseline, while another meal, enriched with a different vegetable fat source, had no influence on postprandial FMD (%) [49,51,62]. Specifically, Berry et al. [49] reported a decrease in FMD (%) from baseline after a meal enriched with high-oleic sunflower oil (**Table 4-5**), whereas Cortés et al. [62] reported similar results after a meal enriched with olive oil (also rich in oleic acid) (**Table 4-7**). By contrast, meals enriched with a shea butter blend (refined shea butter blended with sunflower oil, rich in stearic acid) or shelled walnuts (rich in linoleic acid) had no influence on postprandial FMD (%) [49,62]. Nicholls et al. [51] reported a significant decrease in FMD (%) from baseline 3 h after consumption of a SFA-rich meal (enriched with coconut oil) but not in response to a PUFA-rich meal (enriched with safflower oil) (**Table 4-5**); responses were not significantly different between meals. After 6 h, the effect of the SFA-rich meal on FMD (%) was no longer significantly different compared with the baseline. Rudolph et al. [52] observed that 3 fast-food meals administered with varying FA profiles (providing different amounts of SFAs and trans FAs) provoked significant reductions in FMD (%) from baseline without significant differences between meals (**Table 4-5**). The remaining 3 studies did not detect significant postprandial changes in FMD (%) subsequent to test meals [53,54,63] (**Tables 4-5 and 4-7**). Meals contained SFA- and MUFA-rich foods [53], SFA- and PUFA-rich foods [54], or butter (SFA-rich) and olive oil (MUFA-rich) as fat sources [63].

In addition to healthy adults, 2 of the above-mentioned studies also included hypercholesterolemic individuals [62] and subjects with type 1 diabetes mellitus (T1DM) [63] (**Table 4-7**). In hypercholesterolemic individuals, Cortés et al. [62] reported a decrease in FMD (%) from baseline in response to a meal enriched with olive oil (rich in oleic acid), whereas FMD (%) increased from baseline after ingestion of the meal with shelled walnuts

(rich in linoleic acid). Cutruzzolà et al. [63] found that compared with a meal enriched with butter (rich in SFAs, especially lauric acid), FMD (%) was significantly higher after a meal containing extra virgin olive oil (predominantly composed of MUFAs) (**Table 4-7**). Four further studies, including adults with CVD risk factors were analyzed [58–61] (**Table 4-6**).

Three did not detect significant differences in FMD (%) after ingestion of meals enriched with refined bleached deodorized palm olein or olive oil [61], a breakfast and lunch containing conventional dairy products or FA-modified dairy products (decreased SFA amount and increased MUFA amount) [58], or meals enriched with fat sources consisting mainly of SFAs (butter), MUFAs (refined olive oil and olive oil and canola oil-blended spread), or n–6 PUFAs (safflower oil and spread) [59] (**Table 4-6**). West et al. [60] included adults with T2DM and differentiated between individuals with high- and low fasting TGs. In the group with low fasting TGs, FMD (%) did not change significantly in response to test meals rich in MUFAs (fat source: high-oleic safflower oil, canola oil), MUFAs + α-linolenic acid (ALA) (fat sources: canola oil, high-oleic safflower oil, and safflower oil), or MUFAs + EPA/DHA (fat sources: high-oleic safflower oil, safflower oil, and sardine oil). In the group with high fasting TGs, there was no change in FMD (%) following the MUFA meal, but FMD (%) showed a significant increase from baseline 4 h after ingestion of the MUFA + ALA and the MUFA + EPA/DHA meal, leading to a significant treatment–group interaction (**Table 4-6**).

The effect of FA composition on AIx in healthy adults and those with CVD risk factors

The literature search revealed 3 studies that investigated the effects of FA composition on AIx (%) in healthy subjects [49,50, 55] (**Table 4-5**). Berry et al. [49] reported a significant decrease in central and peripheral AIx (%) from baseline in response to test meals enriched with shea butter blend (refined shea butter blended with sunflower oil, rich in stearic acid) and high-oleic sunflower oil (**Table 4-5**); there was no significant difference between test meals. Similarly, Lithander et al. [50] observed a significant reduction in AIx (%) and AIx_{75} (%, standardized to a heart rate of 75 bpm) from baseline after a SFA-rich meal (fat sources: double cream, sunflower oil; rich in palmitic acid) and a MUFA-rich meal (fat source: olive oil; rich in oleic acid) (**Table 4-5**). The effect on AIx_{75} (%) remained significant after adjustment for mean arterial pressure (MAP), whereas the effect on AIx (%) was no longer significant when adjusted for increases in heart rate and MAP. There was no significantly different effect of MUFA-rich meal compared with SFA-rich meal on AIx or AIx_{75} (%). Chong et al. [55] found that following a postprandial AIx_{75} (%) reduction in response to both

meals, the AIx_{75} (%) increased to a lower extent after a meal enriched with EPA and DHA compared with a control meal (fat source: palm olein and soybean oil) (**Table 4-5**).

Two publications investigated the effects of FA composition on AIx (%) in adults with CVD risk factors [56,57] (**Table 4-6**). Kendall et al. [56] reported that in response to white bread, butter, and cheese (high SFA content), as well as to white bread and pistachios (high MUFA and PUFA content), AIx (%) decreased from baseline in subjects with metabolic syndrome (**Table 4-6**). However, the change from fasting was not significantly different between meals. McManus et al. [57] observed that compared with a meal enriched with palm and soy bean oil (control meal), the decrease in AIx (%) was significantly greater when subjects with CVD risk factors consumed a meal enriched with palm oil, soy bean oil, and DHA (palm and soybean oil mixture partly replaced by DHA-rich oil). Compared with the control meal, a meal enriched with palm oil, soy bean oil, and EPA (palm and soybean oil mixture partly replaced by EPA-rich oil) tended to cause a greater decrease in AIx (%, $P = 0.06$) (**Table 4-6**).

The effect of FA composition on PWV in healthy adults and those with CVD risk factors

In 2 of the above-mentioned studies, PWV (m/s) was measured to analyze the effect of FA composition on arterial stiffness in healthy subjects [49,50] (**Table 4-5**). Compared with baseline values, Berry et al. [49] reported no changes in $PWV_{c–f}$ (m/s) measured 3 h after ingestion of meals enriched with high-oleic sunflower oil or shea butter blend (refined shea butter blended with sunflower oil, rich in stearic acid) (**Table 4-5**). Regardless of the FA composition of test meals (SFA meal rich in palmitic acid compared with MUFA meal rich in oleic acid), Lithander et al. [50] observed a significant increase in $PWV_{c–f}$ (m/s) from baseline in the postprandial state; however, this effect was no longer significant when adjusted for the increase in MAP. Furthermore, FA composition (SFA-rich meal compared with MUFA-rich meal) had no influence on $PWV_{c–f}$ (m/s) (**Table 4-5**).

The only study measuring PWV (m/s) in subjects with increased CVD risk factors reported no influence of FA composition (control meal compared with EPA-rich meal compared with DHA-rich meal) on postprandial $PWV_{c–f}$ (m/s) [57] (**Table 4-6**).

Table 4-2 Postprandial studies investigating the effects of fat dose on vascular function in healthy adults[1]

Refe-rence	Study design	Age and BMI of subject group (*n*)	Meal components	Energy[2] (kcal)	Macro-nutrient composition	FA composition	Parameter of vascular function (h)	Results
Bae et al. [40]	Parallel	HFM group 56 ± 6 y BMI N/A *n* = 11 (4 M, 7 F) LFM group 56 ± 12 y BMI N/A *n* = 9 (6 M, 3 F)	HFM 110 g rice 100 g Korean barbecue 20 g egg, 200 mL milk 8 g oil 25 g mayonnaise 50 g vegetable LFM 312 g rice 100 g vegetable soup 200 g vegetable 190 mL orange juice 400 g apple 50 g kimchi	HFM 803 LFM 802	HFM 53.4 g (59.9 E%) fat 30.7 g protein 50 g CHO LFM 3 g (3.4 E%) fat 15.7 g protein 178 g CHO	Both meals N/A	FMD (%) Ultrasound, brachial artery (0, 2 h)	HFM: significant decrease in FMD from baseline ($P < 0.005$) LFM: no significant postprandial change in FMD HFM, 2 h: significantly lower FMD compared with LFM ($P = 0.037$)
Benson et al. [42]	Crossover	26 ± 3 y 24.7 ± 3.9 kg/m^2 *n* = 10 (10 M, 0 F)	HFM Milkshake (no further specification) LFM Low-fat, isoenergetic meal (no further specification)	Both meals 11.6 kcal/ kg BW	HFM 1 g/kg BW fat 0.15 g/kg protein 0.5 g/kg BW CHO LFM 0.04 g/kg BW fat 0.28 g/kg BW protein 2.54 g/kg BW CHO	Both meals N/A	FMD (%, controlled for BMI) Ultrasound, brachial artery (0, 4 h)	HFM: significant decrease in FMD from baseline ($P = 0.005$) LFM: no significant postprandial change in FMD HFM: significantly greater FMD change compared with LFM ($P < 0.05$, meal x time interaction $P = 0.046$)

Esser et al. [43]	Crossover Randomized Double-blind	22 ± 2 y 22.7 ± 2.4 kg/m^2 *n* = 20 (20 M, 0 F)	<u>HFM (500 mL)</u> 53% fresh cream 3% sugar 44% water <u>LFM (500 mL)</u> 43% full-cream milk 48% full-cream yogurt 4% lemonade 4% fantomalt 1% wheat fiber	<u>HFM</u> 954 <u>LFM</u> 400	<u>HFM</u> 95 g fat 6 g protein 22 g CHO <u>LFM</u> 14.5 g fat 17 g protein 49.5 g CHO	<u>HFM</u> 54 g SFA <u>LFM</u> 9 g SFA	<u>FMD (%)</u> Ultrasound, brachial artery (0, 3, 6 h) <u>AIx (%, corrected for heart rate)</u> Applanation tonometry, radial artery (SphygmoCor) (0, 3, 6 h)	<u>Both meals, 3 h</u>: significant decrease in FMD from baseline (P = 0.004); no significant group difference <u>Both meals, 6 h</u>: FMD returned to baseline <u>Both meals</u>: significant decrease in AIx from baseline (P = 0.012); no significant group difference
Patik et al. [46]	Crossover Randomized	24 ± 3 y 24.3 ± 3.8 kg/m^2 *n* = 10 (10 M, 0 F)	<u>HFM</u> 1 egg muffin 1 sausage muffin 2 hash browns 591 mL water <u>Fasting state</u> 591 mL water	<u>HFM</u> 990 <u>Fasting state</u> No energy intake	<u>HFM</u> 55 g (50 E%) fat 35 g (14 E%) protein 89 g (36 E%) CHO <u>Fasting state</u> No macronutrient intake	<u>HFM</u> 19 g SFA <u>Fasting state</u> No fat intake	<u>FMD (%)</u> Ultrasound, brachial artery (0, 2, 4 h)	<u>HFM, 2 h</u>: significant decrease from baseline compared with fasting condition (2 h: P = 0.002, 4 h: P = 0.004) and compared with HFM, 4 h (P = 0.001) <u>FMD change from baseline, 4 h</u>: no significant difference between conditions

Poitras et al. [44]	Crossover[3] Researcher analyzing images was blinded	23.2 ± 3.3 y 24.4 ± 2.4 kg/m^2 *n* = 10 (10 M, 0 F)	HFM 1 egg muffin 1 sausage muffin 2 hash browns Water LFM 160 g frosted flakes 500 mL skimmed milk 500 g orange juice	HFM 1000 LFM 990	HFM 54 g fat 32 g protein 94 g CHO LFM 0 g fat 23 g protein 209 g CHO	HFM 16 g SFA 1 g trans fat LFM 0 g SFA 0 g trans fat	FMD (%) Ultrasound, brachial artery (0, 1, 2, 3, 4 h)	No significant effect of meal or time on FMD
Tushui-zen et al. [45]	Crossover Randomized	25.4 ± 3 y 23.6 ± 1.8 kg/m^2 *n* = 17 (17 M, 0 F)	HFM: breakfast (0 h) 1 egg muffin 1 croissant with butter and marmalade 200 mL milk 20 mL cream HFM: lunch (4 h) 1 hamburger 1 croissant with butter 200 mL milk Fasting state Water (restricted to a maximum of 50 mL/h)	HFM (each meal) 900 Fasting state No energy intake	HFM (each meal) 50 g fat 30 g protein 55 g CHO Fasting state No macronutrient intake	HFM (each meal) 60 % SFA (of total fat) Fasting state No fat intake	FMD (%) Ultrasound, brachial artery (0, 2, 4, 6, 8 h)	After lunch, 6 h: significant decrease in FMD from baseline ($P < 0.05$) Difference in FMD between interventions at 6 h: $P = 0.051$

			HFM (shake) LFM enriched with 46 g unused cooking fat	HFM 897	HFM 64.4 g fat 20.5 g protein 62.5 g CHO	HFM 30 g SFA 4 g PUFA		
Williams et al. [47]	Crossover[4] Randomized	38 ± 6 y 24.6 ± 2.9 kg/m^2 *n* = 10 (10 M, 0 F)	LFM (shake) 100 g ice cream 200 mL trim milk 50 mL evaporated milk 10 g yogurt 50 g tinned apricots (without syrup) 12 g egg yolk 30 g egg white Chocolate flavor	LFM 483	LFM 18.4 g fat 20.5 g protein 62.5 g CHO	LFM 8 g SFA 2 g PUFA	FMD (%) Ultrasound, brachial artery (0, 4 h)	Both meals: no significant postprandial changes in FMD

Abbreviations: AIx, augmentation index; BW, body weight; CHO, carbohydrate; E%, energy percentage; FA, fatty acid; FMD, flow-mediated dilation; HFM, high-fat meal; LFM, low-fat meal; N/A, not available.

[1] Age and BMI are given as mean ± SD.

[2] Data on energy intake in MJ or kJ were converted to kcal (1 kcal = 4.184 kJ = 0.004184 MJ).

[3] On 2 additional occasions, participants passed mental stress tasks; methods and results are not stated here.

[4] A third test meal was enriched with used cooking fat; meal composition and results are not stated here.

Table 4-3 Postprandial studies investigating the effects of fat dose on vascular function in adults with CVD risk factors[1]

Refe-rence	Study design	Age and BMI of subject group (*n*)	Meal components	Energy (kcal)	Macro-nutrient composition	FA composition	Parameter of vascular function (h)	Results
Bae et al. [41]	Parallel[2]	HFM group (CAD) 59 ± 11 y BMI N/A *n* = 9 (6 M, 3 F)	HFM 110 g rice 100 g Korean barbecue 20 g egg 200 mL milk 8 g oil 25 g mayonnaise 50 g vegetable	HFM 803	HFM 53.4 g (59.9 E%) fat 30.7 g protein 50 g CHO	Both meals N/A	FMD (%) Ultrasound, brachial artery (0, 2 h)	Both meals: no significant postprandial changes in FMD
		LFM group (CAD) 57 ± 11 y BMI N/A *n* = 9 (8 M, 1 F)	LFM 312 g rice 100 g vegetable soup 200 g vegetable 190 mL orange juice 400 g apple 50 g kimchi	LFM 802	LFM 3 g (3.4 E%) fat 15.7 g protein 178 g CHO			

Abbreviations: CHO, carbohydrate; E%, energy percentage; FA, fatty acid; FMD, flow-mediated dilation; HFM, high-fat meal; LFM, low-fat meal; N/A, not available.

[1] Age and BMI are given as mean ± SD.

[2] Two additional groups received angiotensin-converting enzyme inhibition and fibrates in addition to HFM; methods and results are not stated here.

Table 4-4 Postprandial studies investigating the effects of fat dose on vascular function in healthy adults and adults with CVD risk factors[1]

Refe-rence	Study design	Age and BMI of subject group (*n*)	Meal components	Energy[2] (kcal)	Macro-nutrient composition	FA composition	Parameter of vascular function (h)	Results
Phillips et al. [48]	Crossover Randomized	Lean adults 46.4 ± 10.7 y 23.2 (21.3, 24.2) kg/m^2 *n* = 8 (8 M, 0 F)	HFM 1 bacon muffin 1 egg muffin 2 hash browns 1 caramel-flavored milk drink	HFM 989	HFM 57.5 g fat 35 g protein 83 g CHO	HFM 19.8 % SFA	AIx, AIx75 (%) Applanation tonometry, radial artery (SphygmoCor) (first h every 10 min, second h every 15 min, until 6 h every 30 min)	HFM, time course: decrease in AIx from baseline in all 3 groups (P value N/A) Fasting state, time course: no postprandial change in AIx in all 3 groups HFM, AIx iAUC: T2DM and lean subjects > obese subjects (obese vs. T2DM subjects $P < 0.005$; obese vs. lean subjects $P < 0.05$); difference across groups remained statistically significant when corrected for heart rate (75 bpm) HFM, AIx T2DM subjects: significant delay in time to return to baseline compared with lean subjects ($P < 0.05$)
		Adults with obesity 40.9 ± 9.8 y 38.2 (31.8, 40.5) kg/m^2 *n* = 10 (10 M, 0 F)						
		Adults with T2DM 56.3 ± 9.5 y 27.1 (26.5, 28.7) kg/m^2 *n* = 10 (10 M, 0 F)	Fasting state Water (50 mL/h)	Fasting state No energy intake	Fasting state No macronutrient intake	Fasting state No fat intake		

Abbreviations: AIx, augmentation index; CHO, carbohydrate; FA, fatty acid; HFM, high-fat meal; iAUC, incremental AUC; N/A, not available; T2DM, type 2 diabetes mellitus.

[1] Age and BMI are given as mean ± SD or median (interquartile range).

[2] Data on energy intake in MJ or kJ were converted to kcal (1 kcal = 4.184 kJ = 0.004184 MJ).

Table 4-5 Postprandial studies investigating the effects of FA composition on vascular function in healthy adults[1]

Refe-rence	Study design	Age and BMI of subject group (*n*)	Meal components	Energy[2] (kcal)	Macro-nutrient composition	Fat source(s)	FA composition	Parameter of vascular function (h)	Results
Berry et al. [49]	Crossover Randomized	27.1 ± 5.3 y 24.3 ± 3.0 kg/m^2 *n* = 17 (17 M, 0 F)	Both meals 2 muffins (each containing 25 g test fat) 1 milkshake	Both meals 853	Both meals 50 g fat 15 g protein 89 g CHO	Meal rich in stearic acid Shea butter blend (refined shea butter blended with small amount of sunflower oil)	Meal rich in stearic acid 26.7 g C18:0 16.6 g C18:1 n–9 4.5 g C18:2 n–6	FMD (%) Ultrasound, brachial artery (0, 3 h)	Significant meal x time interaction for FMD (P = 0.039) High-oleic sunflower oil: significant decrease from baseline (P < 0.001) Shea butter blend: no significant postprandial change in FMD Change in FMD, 3 h: significant difference between meals (P < 0.05)
						Meal rich in oleic acid High-oleic sunflower oil	Meal rich in oleic acid 0.8 g C18:0 42.5 g C18:1 n–9 4.0 g C18:2 n–6	$PWV_{c–f}$ (m/s) Applanation tonometry, carotid and femoral artery (SphygmoCor) (0, 3 h)	Both meals: no significant postprandial changes in $PWV_{c–f}$

							AIx (%) Applanation tonometry, radial artery (SphygmoCor) (0, 3 h)	Significant time effect (decrease after both meals) for central AIx ($P = 0.019$) and peripheral AIx ($P < 0.001$) Changes in central AIx and peripheral AIx, 3 h: no significant differences between meals
Chong et al. [55]	Crossover Randomized Single-blind	48 ± 18 y 24.7 ± 3.2 kg/m^2 $n = 25$ (12 M, 13 F)	Both meals[3] Chocolate milkshake (containing 30 g test fat) 3 slices white bread Strawberry jam	Both meals N/A	Both meals 33.3 g fat 23 g protein 138 g CHO	Control meal Palm olein and soybean oil (4:1) LC n–3 PUFA-rich meal 23.2 g control oil, 6.8 g fish oil (2.0 g EPA, 2.7 g DHA)	Both meals N/A	AIx$_{75}$ (%) Applanation tonometry, radial artery (SphygmoCor) (0, 0.5, 1, 1.5, 2, 3, 4 h)	Significant treatment and time effects (both: $P = 0.02$) LC n–3 PUFA: attenuating effect on AIx$_{75}$ compared with control (more moderate increase toward baseline subsequent to AIx$_{75}$ reduction)

Lithander et al. [50]	Crossover Randomized Single-blind	38.7 ± 14.4 y 24.1 ± 2.3 kg/m^2 *n* = 20 (20 M, 0 F)	SFA-rich meal (shake) Whole milk Skimmed milk powder Instant drink powder (strawberry flavor) Water Double cream Sunflower oil 400 ml water	SFA-rich meal 747	SFA-rich meal 57.6 g fat 18.8 g protein 41.1 g CHO	SFA-rich meal Double cream Sunflower oil	SFA-rich meal 33.84 g SFA (5.31 g C14:0 14.29 g C16:0 5.9 g C18:0) 14.64 g MUFA 4.18 g PUFA	AIx, AIx_{75} (%) Applanation tonometry, radial artery (SphygmoCor) (0, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4 h)	Significant decrease in AIx and AIx_{75} from baseline (time effect for both $P < 0.01$); AIx no longer significant after adjustment for heart rate and MAP increase; AIx_{75} significant after adjustment for MAP increase ($P < 0.05$) No significant differential effects of meal type
			MUFA-rich meal (shake) Whole milk Skimmed milk powder Instant drink powder (strawberry flavor) Water Olive oil 400 ml water	MUFA-rich meal 712	MUFA-rich meal 54.5 g fat 17.4 g protein 39.7 g CHO	MUFA-rich meal Olive oil	MUFA-rich meal 11.7 g SFA 36.42 g MUFA (35.4 g C18:1 n–9) 3.97 g PUFA	PWV_{c-f} (m/s) Applanation tonometry, carotid and femoral artery (SphygmoCor) (0, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4 h)	Significant increase in PWV_{c-f} from baseline (time effect $P < 0.05$); no longer significant after adjustment for MAP increase No significant differential effects of meal type

Nicholls et al. [51]	Crossover Randomized Single-blind (investigator)	29.5 ± 2.3 y 23.6 ± 0.8 kg/m^2 *n* = 14 (8 M, 6 F)	Both meals Slice of carrot cake Milkshake	Both meals N/A	Both meals 1 g/kg BW fat	PUFA-rich meal Safflower oil SFA-rich meal Coconut oil	PUFA-rich meal 8.8 % SFA 13.6 % MUFA 75 % PUFA SFA-rich meal 89.6 % SFA 5.8 % MUFA 1.9 % PUFA	FMD (%) Ultrasound, brachial artery (0, 3, 6 h)	FMD, 3 h: significant decrease from baseline following coconut oil ($P < 0.05$); no significant postprandial change following safflower oil Change in FMD: no significant group difference FMD, 6 h, both meals: no significant change in FMD from fasting values
Raitakiri et al. [53]	N/A	33 ± 7 y 24.3 ± 3.1 kg/m^2 Meal 1 *n* = 12 (7 M, 5 F) Meal 2 *n* = 10 (re-studied, sex N/A)	Meal 1, SFA-rich 1 sausage 2 muffins 2 hash browns (cooked in 61 g fresh tallow) Meal 2, MUFA-rich Similar constituents, fat content and energy amount (not further specified) Different FA composition	SFA-rich meal 1030	SFA-rich meal N/A	SFA-rich meal Fresh tallow	SFA-rich meal 48 % SFA 40 % MUFA 7.4 % PUFA 4.6 % trans FA MUFA-rich meal 10 % SFA 85 % MUFA 5 % PUFA	FMD (%) Ultrasound, brachial artery (0, 3, 6 h)	Both meals: no significant postprandial changes in FMD

Rudolph et al. [52]	Crossover Randomized Single-blind (observer)	32 ± 11 y 24 ± 5 kg/m^2 *n* = 24 (10 M, 14 F)	Beef burger meal 211 g beef burger 152 g French fries 20 mL Ketchup 500 mL soft drink	Beef burger meal 1245	Beef burger meal 49 g fat 33 g protein 158 g CHO	Beef burger meal Burger French fries	Beef burger meal 13.1 g SFA 7.8 g trans FA	FMD (%) Ultrasound, brachial artery (0, 2, 4 h)	All meals: significant decrease in FMD from baseline over time (time effect $P < 0.001$); no significant differences between meals (no significant meal type effect)
			Vegetarian burger meal 1 203 g vegetarian burger 152 g French fries 20 mL ketchup 500 mL soft drink	Vegetarian burger meal 1 1216	Vegetarian burger meal 1 49 g fat 17 g protein 167 g CHO	Vegetarian burger meal 1 Burger French fries	Vegetarian burger meal 1 5.0 g SFA 6.9 g trans FA		
			Vegetarian burger meal 2 203 g vegetarian burger 90 g salad 30 mL dressing 306 g yogurt (fruit) 500 mL orange juice	Vegetarian burger meal 2 1057	Vegetarian burger meal 2 31 g fat 25 g protein 161 g CHO	Vegetarian burger meal 2 Burger Dressing Yogurt	Vegetarian burger meal 2 4.0 g SFA 0.3 g trans FA		

Volpe et al. [54]	Crossover[4] Randomized Single-blind (observer)	40 ± 11 y 26 ± 4 kg/m^2 *n* = 18 (18 M, 0 F)	<u>SFA-rich meal</u> 3 ounces of bacon 1 slice of processed cheese 2 servings of egg substitute 5 large black olives 1 bagel 1.3 tbsp yogurt-based margarine 0.75 cup canned pears in water 8 oz milk (1% fat) <u>PUFA-rich meal</u> 5 oz salmon 1 bagel 2.25 tbsp yogurt-based margarine 1 tbsp cashew butter 0.5 tbsp parmesan cheese 1.5 tbsp walnuts 0.25 cup canned peaches in water 8 oz mineral water	<u>Both meals</u> 700	<u>SFA-rich meal</u> 29 g fat 43 g protein 65 g CHO <u>PUFA-rich meal</u> 29 g total fat 44 g protein 65 g CHO	<u>SFA-rich meal</u> Various foods (SFA-rich) <u>PUFA-rich meal</u> Various foods (PUFA-rich)	<u>SFA-rich meal</u> 10 g SFA <u>PUFA-rich meal</u> 5 g SFA 4 g n–3-FA	<u>FMD (%)</u> Ultrasound, brachial artery (0, 3 h)	<u>Both meals</u>: no significant postprandial changes in FMD

Abbreviations: AIx, augmentation index; BW, body weight; CHO, carbohydrate; E%, energy percentage; FA, fatty acid; FMD, flow-mediated dilation; LC, long chain; N/A, not available; PWV, pulse wave velocity.

[1] Age and BMI are given as mean ± SD.

[2] Data on energy intake in MJ or kJ were converted to kcal (1 kcal = 4.184 kJ = 0.004184 MJ).

[3] Test meals were consumed 5 h after a low-fat, standard breakfast (400 kcal, 2.1 g of fat).

[4] In addition to healthy adults, HIV-infected adults with and without antiretroviral therapy were studied; methods and results are not stated here.

Table 4-6 Postprandial studies investigating the effects of FA composition on vascular function in adults with CVD risk factors[1]

Refe-rence	Study design	Age and BMI of subject group (*n*)	Meal components	Energy[2] (kcal)	Macro-nutrient composition	Fat source(s)	FA composition	Parameter of vascular function (h)	Results
Kendall et al. [56]	Crossover[3] Randomized	54 ± 8 y 37.5 ± 7.9 kg/m^2 *n* = 20 (8 M, 12 F) Metabolic syndrome	SFA-rich meal 110 g white bread 19 g butter 80 g cheese MUFA-/ PUFA-rich meal 85 g white bread 85 g pistachios	SFA-rich meal 704.3 MUFA-/ PUFA-rich meal 705.4	SFA-rich meal 42.3 g fat 29.3 g protein 50.0 g available CHO MUFA-/ PUFA-rich meal 41.9 g fat 29.1 g protein 50.1 g available CHO	SFA-rich meal Butter Cheese MUFA-/ PUFA-rich meal Pistachios	SFA-rich meal 26.8 g SFA 11.7 g MUFA 1.6 g PUFA MUFA-/ PUFA-rich meal 5.1 g SFA 21.9 g MUFA 12.7 g PUFA	AIx (%) Pulse amplitude tonometry (Endo-PAT) (0, 1, 3 h)	Both meals: significant decrease in AIx from baseline (*P* value N/A); no significant group differences
Markey et al. [58]	Crossover Randomized Double-blind	53 ± 2 y 25.9 ± 0.5 kg/m^2 *n* = 52 (31 M, 21 F) Moderate CVD risk	Breakfast 75 g white bread 32.6 g cheddar cheese 29.4 g butter (control meal) 32.6 g butter (modified meal) 38 g cornflakes 195 g milk Milkshake (330 g milk, 19 g strawberry sauce)	Control breakfast 980 Control lunch 598	Control breakfast 49.9 g fat 39.7 g protein 101.4 g CHO Control lunch 30.3 g fat 19.6 g protein 63.3 g CHO	Control meals Various conventional dairy products	Control breakfast 31.7 g SFA 12.3 g MUFA 2.8 g PUFA 2.2 g trans FA Control lunch 19.1 g SFA 7.4 g MUFA 1.8 g PUFA 1.4 g trans FA	FMD (%) Ultrasound, brachial artery (0, 3, 5, 7 h)	No significant effect on FMD (time-course profile, overall treatment) or difference in FMD between meal types (AUC, iAUC)

			Lunch 60 g white bread 15 g cheddar cheese 18.6 g butter (control meal) 19.8 g butter (modified meal) Milkshake (control: 350 g milk, modified: 352 g milk, both: 27 g strawberry sauce)	Modified breakfast 1028 Modified lunch 621	Modified breakfast 50.6 g fat 36.1 g protein 105.9 g CHO Modified lunch 30.6 g fat 20.9 g protein 64.6 g CHO	Modified meals Various dairy products with modified FA composition[4]	Modified breakfast 24.5 g SFA 20.0 g MUFA 2.9 g PUFA 3.9 g trans FA Modified lunch 14.8 g SFA 12.1 g MUFA 1.8 g PUFA 2.6 g trans FA		
McMa-nus et al. [57]	Crossover Randomized Double-blind	45 ± 5 y 27.4 ± 3.3 kg/m^2 n = 26 (26 M, 0 F) Increased CVD risk	All test meals Milk shake (40 g test fat 150 g skimmed milk 15 g chocolate-flavored powder 15 g skimmed milk powder 2 g peppermint oil extract) 73 g white bread 30 g jam	All test meals 748	All test meals 51.0 E% (42.4 g) fat 9.5 E% protein 39.5 E% CHO	Control meal 4:1 palm oil and soybean oil mixture EPA-containing meal 6.94 g of oil mixture replaced by EPA-rich oil	Control meal N/A EPA-containing meal 4.16 g EPA (not further specified)	AIx (%) Oscillo-metric device, brachial artery (Vicorder) (0, 4 h)	Significant time effect (P < 0.010) and time x treatment interaction (P = 0.005) Post hoc analysis: significantly greater reduction in AIx after DHA-containing meal compared with control meal (P = 0.047); comparison of EPA-containing meal and control meal reached borderline signifi-cance (P = 0.06)

						DHA-containing meal 8.33 g of oil mixture replaced by DHA-rich oil	DHA-containing meal 4.16 g DHA (not further specified)	PWV_{c-f} (m/s) Oscillo-metric device, carotid and femoral artery (Vicorder) (0, 4 h)	All meals: no significant postprandial changes in PWV
Rathna-yake et al. [59]	Crossover Randomized Double-blind	58 ± 1 y 25.9 ± 0.7 kg/m^2 *n* = 32 (0 M, 32 F) Postmenopausal women	SFA breakfast Chocolate drink (containing 42 g test fat) Toast with strawberry jam and test fat (20 g)	SFA breakfast 908	SFA breakfast 53.7 g fat 19.6 g protein 98.4 g CHO	SFA breakfast Butter (62 g)	SFA breakfast 32.9 g SFA 13.3 g MUFA 1.8 g n–6 PUFA 0.6 g n–3 PUFA 1.95 g trans FA	FMD (%) Ultrasound, brachial artery (0, 3, 5, 7 h)	No significant effect on FMD (time-course profile, overall treatment) or difference in FMD between meal types (AUC, iAUC)
			SFA lunch Chocolate drink (containing 15 g test fat) Toast with strawberry jam and test fat (20 g)	SFA lunch 717	SFA lunch 31.8 g fat 19.5 g protein 98.2 g CHO	SFA lunch Butter (35 g)	SFA lunch 19.1 g SFA 7.7 g MUFA 1.3 g n–6 PUFA 0.3 g n–3 PUFA 1.12 g trans FA		

MUFA breakfast Chocolate drink (containing 36 g test fat) Toast with strawberry jam and test fat (17 g)	MUFA breakfast 908	MUFA breakfast 53.1 g fat 19.2 g protein 98.0 g CHO	MUFA breakfast Refined olive oil (17 g) Olive oil and rapeseed oil-blended spread (36 g)	MUFA breakfast 9.4 g SFA 35.2 g MUFA 5.1 g n–6 PUFA 0.9 g n–3 PUFA 0.13 g trans FA
MUFA lunch Chocolate drink (containing 15 g test fat) Toast with strawberry jam and test fat (15 g)	MUFA lunch 717	MUFA lunch 31.1 g fat 19.2 g protein 98.0 g CHO	MUFA lunch Refined olive oil (15 g) Olive oil and rapeseed oil-blended spread (15 g)	MUFA lunch 6.1 g SFA 19.4 g MUFA 3.4 g n–6 PUFA 0.6 g n–3 PUFA 0.12 g trans FA
n–6 PUFA breakfast Chocolate drink (containing 36 g test fat) Toast with strawberry jam and test fat (17 g)	n–6 PUFA breakfast 908	n–6 PUFA breakfast 53.1 g fat 19.2 g protein 98.0 g CHO	n–6 PUFA breakfast Safflower oil (17 g) Safflower oil spread (36 g)	n–6 PUFA breakfast 7.6 g SFA 6.7 g MUFA 36.2 g n–6 PUFA 0.1 g n–3 PUFA 0.12 g trans FA
n–6 PUFA lunch Chocolate drink (containing 14 g test fat) Toast with strawberry jam and test fat (17 g)	n–6 PUFA lunch 717	n–6 PUFA lunch 31.1 g fat 19.2 g protein 98.0 g CHO	n–6 PUFA breakfast Safflower oil (17 g) Safflower oil spread (14 g)	n–6 PUFA breakfast 5.4 g SFA 4.1 g MUFA 20.0 g n–6 PUFA 0.1 g n–3 PUFA 0.12 g trans FA

Stone-house et al. [61]	Crossover Randomized Double-blind	56.8 (53.7, 59.8) y 30.0 (28.7, 31.3) kg/m^2 *n* = 28 (28 M, 0 F) Overweight and obese	Both meals 200 g chicken (fried in 40 g of test oil) Fried white bread Small salad (20 g lettuce, 10 g tomato, 10 g cucumber)	Both meals 667	Both meals 44 g (58 E%) fat 40 g (30 E%) protein 21 g (11 E%) CHO	SFA-rich meal Refined bleached deodorized palm olein MUFA-rich meal Olive oil	SFA-rich meal 41.9 % SFA (36.2 % C16:0) 46.8 % MUFA (46.1 % C18:1 n–9) 11.5 % PUFA (11.3 % C18:2 n–6) MUFA- rich meal 16.6% SFA (11.7% C16:0) 76.2% MUFA (74.1% C18:1 n–9) 7.25% PUFA (6.8% C18:2 n–6)	FMD (%) Ultrasound, brachial artery (0, 1, 2, 3, 4, 5 h)	Both meals: no significant postprandial changes in FMD No difference in FMD response between meals
West et al. [60]	Crossover Randomized Double-blind	T2DM, low TGs 51.4 ± 2.3 y 29.6 ± 1.4 kg/m^2 *n* = 10 (80 % M, 20 % F)	All test meals 473 mL skimmed milk 50 g test oil Ice Flavorings	All test meals 625	All test meals 50 g (72 E%) fat 20 g (13 E%) protein 24 g (15 E%) CHO	MUFA meal High-oleic safflower oil (90%) Canola oil (10%)	MUFA meal 4.5 g SFA 32.6 g MUFA 9.8 g PUFA (9.2 g C18:2 n–6 0.5 g C18:3 n–3)	FMD (%) Ultrasound, brachial artery (0, 4 h)	T2DM, low TGs All meals: no significant postprandial changes in FMD

		MUFA + ALA meal Canola oil (70%) High-oleic safflower oil (20%) Safflower oil (10%)	MUFA + ALA meal 3.5 g SFA 31.2 g MUFA 12.8 g PUFA (9.2 g C18:2 n–6 3.3 g C18:3 n–3)	T2DM, high TGs MUFA meal: no significant postprandial change in FMD MUFA + ALA meal and MUFA + EPA/DHA meals: significant increases in FMD from baseline ($P \leq 0.04$) FMD change: significant treatment x group interaction ($P < 0.03$)
T2DM, high TGs 59.6 ± 3.2 y 28.6 ± 0.8 kg/m^2 *n* = 8 (62 % M, 38 % F)		MUFA + EPA/DHA meal High-oleic safflower oil (60%) Safflower oil (25%) Sardine oil (15%)	MUFA + EPA/DHA meal 5.0 g SFA 30.7 g MUFA 11.8 g PUFA (6.1 g C18:2 n–6 4.8 g n–3 FA 0.2 g C18:3 n–3 2.76 g C20:5 n–3 1.16 g C22:6 n–3)	

Abbreviations: AIx, augmentation index; CHO, carbohydrate; CVD, cardiovascular disease; E%, energy percentage; FA, fatty acid; FMD, flow-mediated dilation; iAUC, incremental AUC; N/A, not available; PWV, pulse wave velocity; T2DM, type 2 diabetes mellitus.

[1] Age and BMI are given as mean ± SD or mean (95 % CI).

[2] Data on energy intake in MJ or kJ were converted to kcal (1 kcal = 4.184 kJ = 0.004184 MJ).

[3] Three additional test meals consisted of white bread (12 and 50 g available CHO) and pistachios; the nutrient composition and results of these meals are not stated here.

[4] SFA content was decreased and MUFA content was increased by a "high-oleic sunflower oil dairy-cow feeding strategy".

Table 4-7 Postprandial studies investigating the effects of FA composition on vascular function in healthy adults and adults with CVD risk factors[1]

Refe-rence	Study design	Age and BMI of subject group (*n*)	Meal components	Energy (kcal)	Macro-nutrient composition	Fat source(s)	FA composition	Parameter of vascular function (h)	Results
Cortés et al. [62]	Crossover Randomized	Healthy control 32 ± 8 y 24.7 ± 3.0 kg/m^2 *n* = 12 (9 M, 3 F) Hyper-cholesterolemic 45 ± 13 y 26.3 ± 3.5 kg/m^2 *n* = 12 (11 M, 1 F)	Both meals 100 g white bread 75 g salami 50 g fatty cheese 125 g yogurt (10%) Water ad libitum In addition Olive oil or walnuts	Both meals 1200	Both meals 63% fat (80 g total fat) 15% protein 22% CHO	Olive oil meal 25 mL olive oil Walnut meal 40 g shelled walnuts	Olive oil meal 35% SFA 38 % MUFA (olive oil: 78% C18:1 n–9) 7% PUFA Walnut meal 35% SFA 23% MUFA 23% PUFA (5.4 g C18:3 n–3)	FMD (%) Ultrasound, brachial artery (0, 4 h)	Healthy control Olive oil: decrease in FMD from baseline (–17%) Walnut meal: no postprandial change in FMD Hyper-cholesterolemic Olive oil: decrease in FMD from baseline (–36%) Walnut meal: increase in FMD from baseline (+24%)

Cutruz-zolà et al. [63]	Crossover Randomized Sonographer was blinded to meal type	<u>Healthy control</u> 25 ± 3 y 22.3 ± 1.8 kg/m^2 *n* = 6 (6 M, 0 F) <u>T1DM</u> 28 ± 8 y 24.2 ± 3.0 kg/m^2 *n* = 10 (7 M, 3 F)	<u>Both meals</u> 80 g white rice 200 g potatoes 140 g lean beef 100 mL water <u>In addition</u> Butter or extra virgin olive oil	<u>Both meals</u> 900	<u>Butter meal</u> 39.7 g (40%) fat 40.9 g (17%) protein 100.5 g (43%) CHO <u>Olive oil meal</u> 41.1 g (40%) fat 38.5 g (17%) protein 100.1 g (43%) CHO	<u>Butter meal</u> 40 g butter <u>Olive oil meal</u> 35 g extra virgin olive oil	<u>Butter meal</u> 21.7 g SFA 11.6 g MUFA 2.6 g PUFA <u>Olive oil meal</u> 7.7 g SFA 28.0 g MUFA 4.6 g PUFA	<u>FMD (%)</u> Ultrasound, brachial artery (0, 1, 3, 5 h)	<u>Healthy control</u> No significant postprandial changes in FMD <u>T1DM</u> Significantly higher FMD after olive oil meal compared with butter meal (*P* = 0.007)

Abbreviations: CHO, carbohydrate; CVD, cardiovascular disease; FA, fatty acid; FMD, flow-mediated dilation; T1DM, type 1 diabetes mellitus.
[1] Age and BMI are given as mean ± SD.

DISCUSSION

In this review, we aimed to summarize and analyze the existing evidence on the impact of dietary fat dose and FA composition on vascular function in metabolically healthy adults and individuals with increased CVD risk, measured by postprandial changes in FMD, PWV, and AIx. We specifically focused on studies that fed commercially available foods.

The impact of fat dose on vascular function

Studies showed that after an overnight fast of 10.0–12.5 h, a further extension of the fasting period did not affect FMD [45,46] or AIx [48]. By contrast, consumption of an HFM (breakfast or lunch) resulted in a reduction in FMD [45,46] and AIx [48] from baseline. The energy and fat content of the HFMs were comparable between studies (**Tables 4-2 and 4-4**).

Six trials compared the impact of HFMs and LFMs on vascular function [40–44,47], providing inconsistent results (**Tables 4-2–4-4**). Bae et al. [40] and Benson et al. [42] reported that the HFM but not the LFM affected FMD in healthy adults, resulting in a significant group difference between meals. Both trials demonstrated strong methodical quality by feeding isoenergetic meals with a strongly varying fat content (53.4 g compared with 3 g; 1 g/kg BW compared with 0.04 g/kg BW). This observation agrees with Jackson et al. [64] who report that compared with meals containing <10 g fat, meals with a higher fat content (50–105 g) impair vascular reactivity. In a recent review, Zhao et al. [65] described 3 main mechanisms by which postprandial lipemia triggers endothelial dysfunction and atherosclerosis. First, postprandial increases in TGs and TG-rich lipoproteins result in direct damage to endothelial function; this is closely linked to an imbalance in vasodilator and vasoconstrictor factors. The vasodilator decrease mainly results from decreased NO and increased oxidative stress. The second factor impairing vascular function is increased oxidative stress and decreased antioxidant capacity induced by postprandial lipemia. During postprandial lipemia, the antioxidant enzymes glutathione peroxidase and superoxide dismutase decrease, whereas the excretion of oxidative stress markers 8-external prostaglandin F2 and free 8-iso-prostaglandin $F_{2\alpha}$ increases; production of reactive oxygen species is also intensified during the postprandial state. Third, consumption of an HFM induces transient, low-grade inflammation with impairment of the endothelial barrier. In this process, proinflammatory genes are upregulated in endothelial cells, leukocyte activation marker expression is increased, and the proinflammatory complement system is involved [65]. Considering that, in the above-mentioned studies, the LFMs had no influence on FMD; these LFMs may not have

contained enough fat (3 g, 0.04 g/kg BW) to trigger sufficient postprandial lipemia with subsequent endothelial dysfunction [40,42]. This assumption is supported by the fact that in both studies, only consumption of the HFMs but not of the LFMs resulted in a significant increase in TGs compared with baseline values.

Consistent with the findings of Bae et al. [40] and Benson et al. [42], Esser et al. [43] also observed an effect of an HFM (95 g fat) on vascular function in healthy adults, which resulted in significantly lower postprandial FMD and AIx compared with baseline values (**Table 4-2**). One mechanism by which an HFM may induce a postprandial AIx reduction is a decrease in central systolic and diastolic blood pressure following meal intake, caused by transient relaxation of arterial smooth muscles in the general circulation [66]. However, contrary to Bae et al. [40] and Benson et al. [42], Esser et al. [43] also reported a significant reduction in FMD and AIx from baseline subsequent to the LFM (14.5 g fat), without significant group differences between the HFM and LFM. The significant decrease in FMD 3 h after consumption of the LFM is surprising, especially given the results from Williams et al. [47], where a similar LFM (18.4 g fat) exerted no influence on FMD in healthy adults.

In addition to Williams et al. [47], 2 further studies detected no effect of either the HFM or the LFM on vascular function determined by FMD [41,44]. There are several reasons to explain the lack of change in FMD subsequent to the consumption of an HFM. For example, certain factors, such as physical activity determine an individual's capacity to tolerate acute triggers that impair vascular function (e.g., an HFM) [67]. Combined with small samples sizes (often only ~10 participants), low susceptibility to fat-induced modulation of vascular function might have prevented alterations in endothelial function following HFM consumption. Furthermore, short postprandial periods (e.g., 2 h), a small number of measurement time points (e.g., baseline and only 1 postprandial measurement), large time intervals between measurements (e.g., 4 h) may have meant that significant effects on vascular function were not detected in the postprandial period. Regarding the fact that an increase in TGs was observed during the postprandial period but no effect on vascular function was detected, Williams et al. [47] and Poitras et al. [44] noted that a rise in TGs may not consistently impair endothelial function. However, in 3 studies, the postprandial increase in TGs was correlated with the decrease in FMD assessed 2 h postprandially [40,41,46].

The impact of FA composition on vascular function

Most of the studies that investigated the impact of FA composition on AIx showed no differential effect of meal FA composition [49,50,56] (**Tables 4-5 and 4-6**). However, 2 studies showed a beneficial effect of a meal enriched with DHA [57] or EPA and DHA [55] on vascular function assessed by AIx. The favorable effect of marine n–3 PUFAs (EPA/DHA) on the endothelium is widely described, including a reduction of proatherogenic and prothrombotic factors (e.g., reduced expression of endothelial adhesion molecules and proinflammatory cytokines) [68,69].

The data on the impact of FA composition on FMD is highly inconsistent (**Tables 4-5–4-7**). Six studies reported no postprandial change in FMD after consumption of meals with varying FA compositions in healthy adults [53,54,63] or adults with CVD risk factors [58,59,61]. However, Rudolph et al. [52] reported that several burger meals resulted in a decrease in FMD compared with baseline, but without significant group differences. Nicholls et al. [51] found no significant group differences in FMD change from baseline after consumption of meals with 2 different fat sources; in this study, only the SFA-rich meal (coconut oil) and not the PUFA-rich meal (safflower oil) led to a significant reduction in FMD from baseline. Mechanistic studies suggest differential effects of FAs on vascular function at the molecular level. Although in human aortic endothelial cells, incubation with oleic acid promoted signal transduction via the PI3K/Akt/endothelial nitric oxide synthase (eNOS) pathway [70], palmitic acid inhibited the Akt/eNOS pathway in human umbilical vein endothelial cells, leading to a decrease in NO production by inhibition of eNOS activity [71]. On the level of FA classes, incubation of human aortic endothelial cells with SFAs and n–3 PUFAs resulted in greater downregulation of the PI3K/Akt pathway than with SFAs alone [70]. The assumption that the dietary FA composition acts as a modulator of vascular function is supported by 4 of the included studies, all of which reported a differential effect of meal FA composition on postprandial FMD [49,60,62,63]. Berry et al. [49] observed that in healthy adults, a MUFA-rich meal (high-oleic sunflower oil) led to a significantly greater postprandial reduction in FMD than the SFA-rich meal (shea butter blend). Meanwhile, Cutruzzolà et al. [63] reported that in T1DM subjects, the SFA-rich meal (butter) resulted in a significantly lower FMD than the MUFA-rich meal (olive oil). Cortés et al. [62] also fed a MUFA-rich meal enriched with olive oil, but compared the effects on FMD with those of a walnut-rich meal, reporting a decrease in FMD from baseline after an olive oil-rich meal in both healthy and hypercholesterolemic adults. Furthermore, FMD in healthy adults remained unchanged

from baseline after the walnut meal, whereas FMD increased in hypercholesterolemic subjects. By showing an increase in FMD from baseline when enriching a MUFA-rich meal with ALA or EPA and DHA, West et al. [60] provided evidence for a favorable effect of n–3 PUFAs on vascular function in T2DM subjects with high fasting TGs.

The role of health status

One study that focused on the impact of fat dose on vascular function included healthy, lean adults and adults with obesity or T2DM (**Table 4-4**) [48]. Lean subjects and those with T2DM had a higher AIx incremental AUC after consuming an HFM than obese participants. In addition, T2DM subjects showed a delay in time to return to baseline AIx values than lean individuals. Besides, in 2 different trials, Bae et al. [40,41] used the same HFM and LFM in healthy adults and CAD patients. Although in healthy adults, consumption of the HFM resulted in a significantly lower FMD than the LFM, no effect was observed in CAD subjects (**Tables 4-2 and 4-3**).

Concerning FA composition, 2 studies included healthy subjects and adults with hypercholesterolemia [62] and T1DM [63] (**Table 4-7**). Cortés et al. [62] reported that only in hypercholesterolemic patients but not in healthy adults, a walnut meal led to an increase in FMD. Likewise, in the study of Cutruzzolà et al. [63], FMD was unaffected by meals enriched with butter or olive oil in healthy adults, whereas in subjects with T1DM, FMD postprandially increased following the olive oil meal compared with the butter meal. In addition, West et al. [60] investigated patients with T2DM, with and without high fasting TGs. Only in subjects with high fasting TGs did enrichment of a MUFA-containing meal with ALA or EPA and DHA result in a postprandial increase in FMD (**Table 4-6**).

Strengths and limitations

To our knowledge, this is the first review to systematically investigate the effects of fat dose and FA composition on various subclinical markers of atherosclerosis in healthy adults and CVD risk patients. The inclusion of 3 diagnostic parameters of vascular function (FMD, PWV, and AIx) enabled us to evaluate both vascular reactivity and arterial stiffness. In addition, we increased the practical application of our findings by using a food-based approach, focusing on fat sources and their FA composition from whole foods. Nevertheless, because of our focus on fat dose and FA composition, a possible influence of other meal characteristics (e.g., content of energy, carbohydrates, and antioxidants) on vascular function that might contribute to the heterogeneity of study results was not considered. The high

heterogeneity of the study results was certainly also influenced by the broad range of fat amount administered via the LFMs (0–18.4 g) and HFMs (29–95 g). Because of the high variation of meal compositions (e.g., energy content and fat source), study protocols (e.g., time points of measurements and time period of protocols), and study populations and comparisons, we did not perform a meta-analysis. To obtain convincing results and more consistent evidence on the effects of meal composition on vascular function, standardization of postprandial protocols is required (**Table 4-8**). To provide a more comprehensive view of the influence of meal composition on vascular function, in addition to the diagnostic parameters presented in this review, other target systems such as inflammatory processes associated with the postprandial state and postprandial endothelial activation should be investigated. Because vascular function is multifactorially determined, and atherosclerotic processes are too complex to be reduced to just a few mechanisms (e.g., atherosclerosis caused by HFM intake), in addition to analyzing the acute influence of meal intake, other elements (e.g., habitual diet and psychologic influences) should be considered in the research on precipitating and protective factors on endothelial dysfunction and atherosclerosis.

Conclusion

This review revealed 3 main findings. First, evidence suggests that meal consumption results in decreases in FMD and AIx; specifically, higher fat doses appear to impair vascular reactivity measured by FMD more strongly than lower fat doses. Second, concerning FA composition, most studies indicate no clinically relevant or contradictory effects on subclinical atherosclerosis markers (FMD, PWV, and AIx). One exception might be marine n–3 PUFAs (EPA and DHA), as data from 3 studies suggest a beneficial effect on acute vascular function. Third, some studies found differences in the vascular response to meals with varying fat doses or FA composition between metabolically healthy subjects and subjects with CVD risk factors, but based on the analyzed literature with highly heterogenic populations, the specific effects could not be deduced. Our current findings of the impact of meal total fat content and FA composition on postprandial vascular function assessed by FMD, PWV, and AIx are based on meal studies in which a variety of fat sources (e.g., virgin or refined vegetable oils, milk fat, and butter) was used in different amounts and meal recipes. At this time, it cannot be concluded which fat source in which amount and meal composition has beneficial effects on postprandial vascular function.

Further directions

To enhance the meaningfulness of systematic reviews and to allow valid meta-analyses concerning the effects of meal composition on vascular function, we strongly recommend standardization of postprandial protocols. In **Table 4-8**, we provide an overview of fundamental aspects concerning study design. The recommendations mainly refer to the test meal and postprandial period. Meals should be fed as breakfast after an overnight fast (≥10 h). To enhance practical applications, and possibly derive subsequent dietary recommendations, the use of commercially available foods is advisable. With respect to the assumed connection between postprandial lipemia and alterations in vascular function, we recommend a fat amount of ≥50 g/meal to induce reliable lipemia. To allow synthesis and comparison of data from different studies, nutrient and FA profiles should be characterized. Finally, noninvasive measurement of vascular function should be performed after a resting period in a supine position by trained personnel.

Table 4-8 Recommendations for the design of future postprandial studies on vascular function

	Recommendations
Subject group	• Adult participants (≥18 y)
Study design	• Randomized • Crossover • Blinded (at least single-blinded, if possible) • Wash-out phase of 1–2 wk
Pre-intervention days	• Avoidance of intense physical activity and alcohol consumption • Overnight fast (last meal ≥10 h before first measurement)
Meal characteristics	• Breakfast • Preparation with natural, commercially available foods (e.g., pasta, bread, plant oils, and dairy products) • Characterized nutrient profile (energy content; total protein, carbohydrates, and fat; SFA, MUFA, and PUFA; dietary fiber; other nutrients, if applicable)
Fat dose	• ≥50 g/meal • Given as absolute dose or relative to body mass
Meal consumption	• Consumption within a standardized time period (e.g., 20 min) • Consumption under supervision of study personnel
Standardization before examination of vascular function	• Sufficiently long resting time in supine position (e.g., 10 min) • Rest in a quiet and climatized room • Protocol starting at the same time (an effect of circadian rhythm has been described) • No consumption of coffee or tea on the day of the examination • Standardized intake of vasoactive drugs (e.g., all vasoactive drugs should not be taken the evening before or on the day of the examination)
Measurement of vascular function	• Measurement of FMD (vascular response to hyperemia) or of PVW and AIx (arterial stiffness) • Performed by trained and blinded personnel

Abbreviations: AIx, augmentation index; FMD, flow-mediated dilation; PWV, pulse wave velocity.

AUTHOR CONTRIBUTIONS

The authors' responsibilities were as follows – HFK, SE: literature search, study selection and evaluation; HFK: preparation of the first draft of the manuscript; HFK, SE: finalization of the manuscript in close collaboration; and both authors: read and approved the final manuscript and declare responsibility for its final content.

CONFLICT OF INTEREST

The authors report no conflicts of interest.

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DATA AVAILABILITY

All data generated or analyzed during this study are included in this published article.

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5. RaKo study

Postprandial Responses to Meals Enriched With Canola or Coconut Oil in Men and Women With a Risk Phenotype for Cardiometabolic Diseases: A Randomized Crossover Trial

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ABSTRACT

We investigated the metabolic response to meals with canola or coconut oil (rich in unsaturated vs. rich in saturated fatty acids [FAs]). Although the longer-term metabolic effects of these fats are well evidenced, their postprandial effects remain inconclusive. In this randomized crossover trial, 29 participants with increased cardiometabolic risk consumed four isoenergetic meals containing 25 or 50 g (low-fat meals [LFMs], high-fat meals [HFMs]) of canola or coconut oil. Blood samples for analysis of triglycerides (TGs), glucose, insulin, non-esterified FAs (NEFAs), IL-6, and individual FAs were collected in the fasting state and 6 h postprandially (every 0.5–1 h). The incremental areas under the curves (iAUCs) of TGs and IL-6 were higher after canola than after coconut oil. Concentrations of lauric and myristic acid were higher after coconut oil, while concentrations of oleic, linoleic, and α-linolenic acid were higher after canola oil. The TG iAUC was higher after HFMs than after corresponding LFMs. NEFAs decreased more after LFMs than after HFMs. The glucose and insulin iAUCs were higher after LFMs than after HFMs. Canola and coconut oil induced different metabolic responses. The manner and strength of the postprandial effects differed depending on the parameter.

INTRODUCTION

Current dietary guidelines and specialized societies (e.g., the American Heart Association) recommend that dietary saturated fatty acids (SFAs) are replaced by unsaturated fatty acids (FAs) to lower the incidence of cardiovascular diseases (CVDs) [1–3]. A versatile fat source rich in unsaturated FAs is canola oil, which has a high content of monounsaturated fatty acids (MUFAs; ~63 g/100 g) and polyunsaturated fatty acids (PUFAs; ~25 g/100 g, ~7.5 g/100 g α-linolenic acid) [4]. Mainly due to its FA composition, canola oil effectively lowers CVD-related risk factors; for example, a regular consumption of canola oil reduces fasting concentrations of total and LDL cholesterol [5–9]. Furthermore, canola oil-based diets have been shown to improve glucose tolerance and insulin sensitivity [5]. In contrast, regular consumption of coconut oil increases fasting concentrations of total and LDL cholesterol [1, 10, 11], an effect attributed to its high content of SFAs (~83 g/100 g [12]), especially of lauric, myristic, and palmitic acid (per 100 g coconut oil: ~42, 17, and 9 g [12]) [13–16]. These three FAs inhibit LDL receptor activity, enhance LDL cholesterol production, and increase the concentration of LDL cholesterol in mechanistic studies [17].

Variations in the dietary FA composition influence blood parameters associated with cardiovascular risk immediately after food intake [18]. Among acute risk markers, the postprandial triglyceride (TG) concentration plays a central role because non-fasting TGs are an independent risk factor for coronary artery disease and cardiovascular events [19–21]. Two meta-analyses showed that the postprandial TG response to meals enriched with unsaturated FAs is lower than that to SFA-rich meals, at least if the postprandial phase lasts 8 h [18, 22]. In this context, studies comparing the acute effects of coconut oil with MUFA- and/or PUFA-rich meals on the TG concentration provide inconsistent results [23–30]. The aim of this study was to compare the acute effects of canola and coconut oil in adults with increased cardiometabolic risk (e.g., abdominal obesity and advanced age), because these individuals have a more pronounced postprandial metabolic response [31–36]. In addition to our primary outcome TG concentration, we analyzed several further metabolic parameters and vascular function by measuring arterial stiffness to comprehensively understand the postprandial effects of canola and coconut oil. Both plant oils were administered in mixed meal challenges to increase the practical applicability.

EXPERIMENTAL SECTION

Participants

This study was conducted at the Institute of Nutritional and Food Science, Nutritional Physiology at the University of Bonn. Volunteers were recruited from Bonn (Germany) and the surrounding area via advertisement in the local newspaper, posters, and flyers. Out of 209 individuals who participated in telephone anamnesis, 86 volunteers attended a screening (**Figure 5-1**). This 1-h screening session comprised (1) fasting blood sampling, analyzed for serum creatinine, total bilirubin, gamma-glutamyl transferase, alanine transaminase, aspartate transaminase, lipase, serum lipids and lipoproteins, plasma glucose, serum C-reactive protein (CRP), and blood count; (2) survey of the participant's medical history and dietary habits; and (3) physical assessments, including measurement of height and weight, waist and hip circumference, fat and fat-free mass, resting blood pressure (BP), and heart rate.

The following inclusion criteria were applied to identify individuals at increased cardiometabolic risk: 60–80 years; overweight or obesity (BMI 27–34.9 kg/m^2); visceral adiposity (waist circumference ≥ 94 cm for men and ≥ 80 cm for women); two or more of the four characteristics of metabolic syndrome, namely, dyslipidemia (serum TGs ≥ 1.7 mmol/L and/or serum HDL cholesterol < 1.03 mmol/L for men and < 1.29 mmol/L for women), increased resting BP (systolic BP ≥ 130 mmHg and/or diastolic BP ≥ 85 mmHg), and increased plasma glucose (≥ 5.6 mmol/L) [37]. Metabolic syndrome refers to the simultaneous occurrence of several cardiometabolic risk factors that increase the risk of CVD and Type 2 diabetes mellitus [38].

The exclusion criteria were smoking, malabsorption syndromes, untreated thyroid diseases, impaired kidney function, myocardial failure, insulin-treated diabetes mellitus, chronic inflammatory diseases, cancer, alcohol or drug abuse, epilepsy, anemia, immunosuppression, long-term intake of certain supplements (especially marine n-3 FAs and vitamin E), and participation in another intervention study within the last 30 days.

Figure 5-1 shows a flowchart of the participants from the first screening to the final analysis. This study was conducted in accordance with the Declaration of Helsinki, and the study protocol was approved by the ethics committee of the Medical Faculty of the Rheinische Friedrich Wilhelms-University of Bonn (Germany) under the identifier 420/21. All participants were informed in detail about the procedures and provided written informed

consent. The study was registered in ClinicalTrials.gov (https://clinicaltrials.gov/) under the identifier NCT05208346.

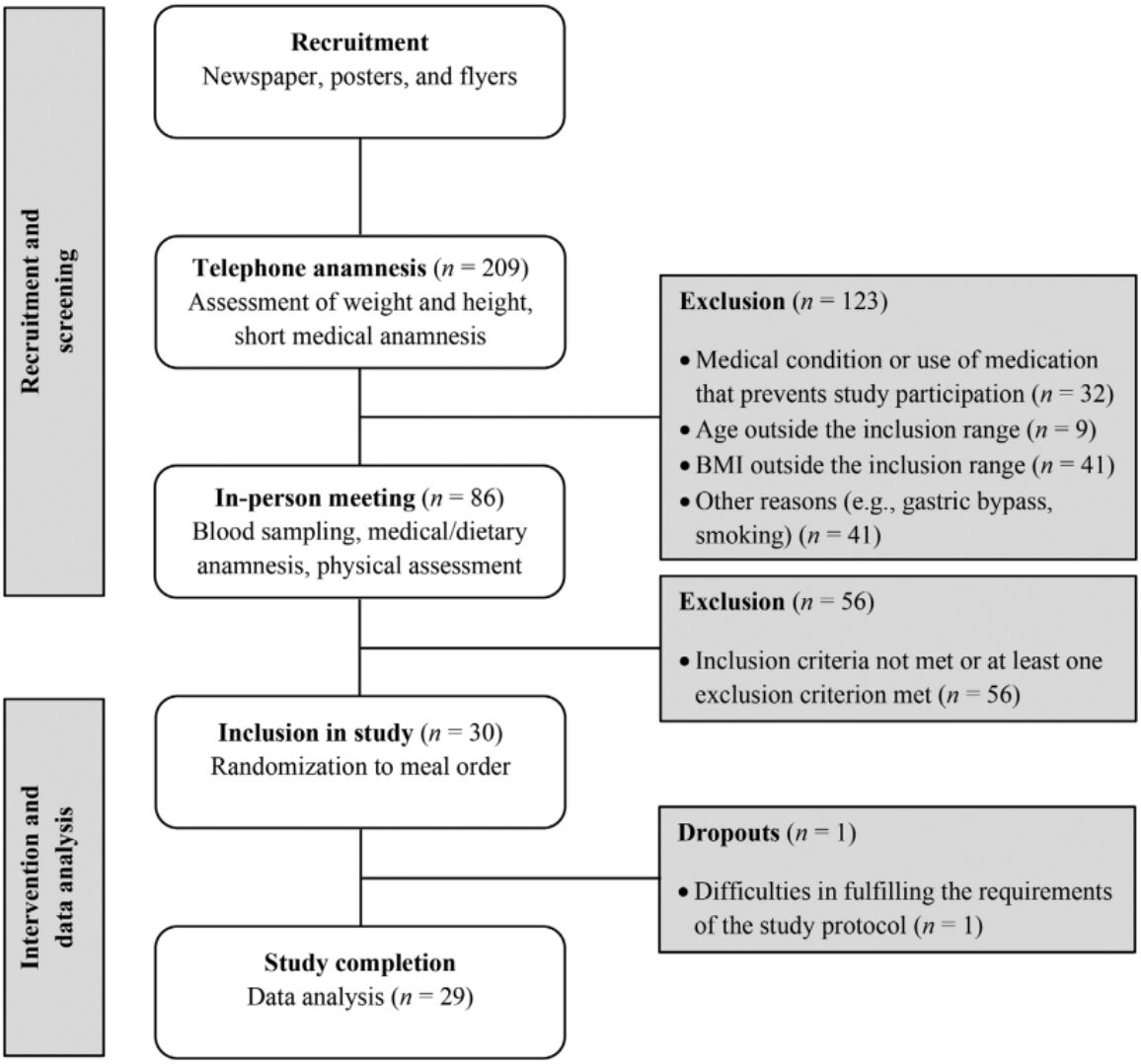

Figure 5-1 Flowchart of inclusion and exclusion of participants.

Study design

Before the first study day, the meal order for each subject was randomized via Williams design by the cooperating biometrician. Participants were not informed about the order of the four meals (**Table 5-1**) they received. Separated by wash-out phases of about 14 days, the participants attended four study visits on which they received one of four different test meals. Each treatment condition lasted 6.0 h, from morning until afternoon. The meals were provided in the morning after a 10-h overnight fast. Venous blood samples were collected before breakfast (0 h) and 0.5, 1.0, 1.5, 2.0, 3.0, 4.0, 5.0, and 6.0 h after meal ingestion. Carotid-femoral pulse wave velocity ($PWV_{c\text{-}f}$) and augmentation index (AIx) were determined in the fasting condition (0 h) and at 2.0, 4.0, and 6.0 h postprandially.

Throughout the entire study period, participants were instructed to maintain their habitual diet, level of physical activity, lifestyle, and weight. Participants were asked to standardize their dinner and to refrain from alcohol consumption and intensive physical activity on the day before each study visit. Participants taking antihypertensive agents (n = 20), lipid-lowering drugs (n = 11), inhibitors of platelet aggregation (n = 9), thyroid therapy (n = 7), and antidiabetic medication (n = 3) were instructed to continue taking their medication without changes.

Test meal composition

Four isoenergetic (~4200 kJ) and isonitrogenous (26.6 g protein) mixed meals (challenges) with different fat amounts and FA composition were administered on separate occasions. Each meal contained 25 or 50 g (here referred to as low-fat meals [LFMs] or high-fat meals [HFMs]) canola oil (Brölio canola oil; Brökelmann + Co, Hamm, Germany; rich in unsaturated FAs) or coconut oil (virgin cold pressed coconut oil; Schneekoppe, Buchholz/Nordheide, Germany; rich in SFAs). **Table 5-2** provides an overview of the analyzed FA composition of the used plant oils and their analyzed α- and γ-tocopherol content. The main FAs in canola oil were oleic acid (62.3%), linoleic acid (19.2%), and α-linolenic acid (7.2%). Coconut oil consisted mainly of lauric acid (52.5%), myristic acid (20.1%), palmitic acid (8.4%), and capric acid (5.8%). Although 30 mg α-tocopherol and 40 mg γ-tocopherol were present in 100 g canola oil, neither was detectable in coconut oil.

Besides the test oils, the main components of the meals were a homemade vegetable soup and other commercially available foods such as baguettes, yoghurt, jam, and fruit juice. **Table 5-1** presents the nutrient compositions of the four test meals (canola oil-containing HFM, canola

oil-containing LFM, coconut oil-containing HFM, and coconut oil-containing LFM). All meals were specifically designed for the present study, and their energy content and nutrient composition were calculated using the computer-based nutrient calculation program EBISpro (University of Hohenheim, Stuttgart, Germany), based on the German Nutrient Database Bundeslebensmittelschlüssel (Max Rubner-Institut, Karlsruhe, Germany). The meals were prepared by study personnel at the study site on the morning of each intervention day according to a standardized protocol, which involved weighing the food to the exact gram. The participants were requested to completely ingest the meal within 20 min under the supervision of study personnel.

Table 5-1 Energy content and nutrient composition of the four test meals.

	Canola oil-containing HFM	**Coconut oil-containing HFM**	**Canola oil-containing LFM**	**Coconut oil-containing LFM**
Energy (kJ)	4187	4202	4192	4200
Carbohydrates (g)	85.5	85.5	144.1	144.1
Carbohydrates (EN%)	35	35	59	59
Mono- and disaccharides (g)	39.9	39.9	73.2	73.2
Polysaccharides (g)	45.3	45.3	68.1	68.1
Ratio of polysaccharides to mono- and disaccharides	1.14	1.14	0.93	0.93
Dietary fiber (g)	6.6	6.6	11.2	11.2
Protein (g)	26.6	26.6	26.6	26.6
Protein (EN%)	11	11	11	11
Total fat (g)	60.9	60.5	33.6	33.4
Total fat (EN%)	54	54	30	30
SFAs (g)	8.2	45.7	5.9	24.6
SFAs (EN%)	7.3	40.2	5.2	21.7
Lauric acid (12:0) (g)	0.2	21.1	0.2	10.7
Myristic acid (14:0) (g)	0.6	8.8	0.5	4.8
Palmitic acid (16:0) (g)	4.6	6.8	3.0	4.0
MUFAs (g)	35.5	7.0	18.4	4.2
MUFAs (EN%)	31.4	6.2	16.2	3.7
Oleic acid (18:1n-9) (g)	34.2	6.5	17.6	3.8
PUFAs (g)	15.8	2.5	8.4	1.8
PUFAs (EN%)	14.0	2.2	7.4	1.6
Linoleic acid (18:2n-6) (g)	10.9	2.2	5.8	1.4
α-linolenic acid (18:3n-3) (g)	4.8	0.3	2.6	0.3
Cholesterol (mg)	210	210	15	15
Vitamin E[a)] (mg)	14.5	2.5	8.2	2.2
Vitamin C (mg)	43.6	43.6	60.0	60.0

Abbreviations: EN%, energy percentage; HFM, high-fat meal; LFM, low-fat meal.
[a]α-tocopherol equivalents.

Table 5-2 Fatty acid composition and α- and γ-tocopherol content of the test oils.

Component	**Canola oil**	**Coconut oil**
Fatty acids	*% of total fatty acids*	
Caprylic acid (8:0)	nd	4.68
Capric acid (10:0)	0.01	5.82
Lauric acid (12:0)	0.01	52.53
Myristic acid (14:0)	0.05	20.06
Palmitic acid (16:0)	4.38	8.42
Stearic acid (18:0)	1.46	3.14
Oleic acid (18:1n-9)	62.27	4.36
Linoleic acid (18:2n-6)	19.15	0.71
α-linolenic acid (18:3n-3)	7.24	nd
Tocopherols	*mg/100 g*	
α-tocopherol	30	nd
γ-tocopherol	40	nd

Abbreviation: nd, not detectable.

Measurements

Anthropometrics

Weight and height were measured using a stadiometer with an integrated scale (seca 704; Seca, Hamburg, Germany) to the nearest 0.05 kg and 0.1 cm, respectively. Waist and hip circumferences were measured in duplicate with the participants in an upright position using a flexible tape to an accuracy of 0.1 cm. Waist circumference was measured midway between the lowest rib and the iliac crest while participants were breathing calmly. Hip circumference was measured at the level of the maximum circumference above the pubic bone. Body composition (fat and fat-free mass) was determined by air-displacement plethysmography using the BOD POD body composition system (Cosmed, Rome, Italy) according to the instruction manual.

BP and Heart Rate

Systolic and diastolic BP as well as heart rate were determined using an automatic BP measurement device (Boso Carat Professional; Bosch + Sohn GmbH, Jungingen, Germany) in a sitting position. The measurements were performed in duplicate under standardized conditions and according to international guidelines [39].

Blood Sample Processing and Analysis

Fasting and postprandial blood samples were collected via an indwelling venous cannula (Vasofix Safety; B. Braun Melsungen AG, Melsungen, Germany) and drawn into tubes containing EDTA, fluoride, or a coagulation activator (SARSTEDT AG & Co. KG, Nümbrecht, Germany). Plasma and serum were obtained by centrifugation at 3000 × g for 15 min at 8°C. Screening blood parameters as well as TGs, total cholesterol, LDL cholesterol, HDL cholesterol, insulin, and glucose on the study days were assayed within 4 h after blood draw. Plasma and serum aliquots for quantification of non-esterified FAs (NEFAs), IL-6, and α- and γ-tocopherol, as well as for determination of trolox equivalent antioxidative capacity (TEAC) and FA profiles, were immediately frozen in cryovials and stored at −80°C until analysis.

Serum TGs, total cholesterol, LDL cholesterol, and HDL cholesterol were analyzed by fully automated photometric methods and the plasma glucose by the hexokinase method on a cobas c702 analyzer (Roche Diagnostics, Mannheim, Germany). Serum insulin concentrations were analyzed by fully automated electrochemiluminescence immunoassays (ECLIA, Elecsys tests)

on a cobas e801 analyzer (Roche Diagnostics). Homeostasis model assessment for insulin resistance (HOMA-IR) was calculated using the following formula: (insulin concentration [mU/L] × glucose concentration [mg/dL])/405. The insulin–glucose ratio was determined by dividing the insulin concentration (pmol/L) by the glucose concentration (mmol/L).

Serum CRP concentrations were measured using a turbidimetric immunoassay (cobas c702, Roche Diagnostics). Blood count parameters were analyzed by fluorescence flow cytometry, the resistance measurement technique, and photometry using a hematology analyzer (Sysmex XN9000 and Sysmex XN1000; Sysmex, Kobe, Japan). Serum gamma-glutamyl transferase, alanine transaminase, aspartate transaminase, lipase, total bilirubin, and creatinine were measured by fully automated photometric methods (cobas c702, Roche Diagnostics).

An in vitro enzymatic colorimetric method assay (NEFA-HR(2); FUJIFILM Wako Chemicals Europe GmbH, Neuss, Germany) was used to measure the serum NEFA concentration in duplicate. The plasma concentration of IL-6 was analyzed in duplicate using a commercially available ELISA (R&D Systems, Minneapolis, USA). Plasma concentrations of α- and γ-tocopherol were determined via HPLC as described previously [40]. Serum FA profiles were determined in duplicate by gas chromatography as described previously [41]. The plasma total antioxidant capacity was determined using the TEAC method developed by Miller et al. [42].

Parameters of Arterial Stiffness

$PWV_{c\text{-}f}$ and AIx were determined using a Vicorder device (SMT Medical Technology GmbH, Würzburg, Germany). Before starting the measurement, the participants rested in a quiet and well-tempered examination room for 2 min in a supine position on an examination bed with the headboard angled at 30°. In the first step, one of the inflatable cuffs was attached centrally on the upper arm to conduct pulse wave analysis, which includes the determination of AIx. After an initial BP measurement, pulse wave analysis was performed. In the second step, the inflatable cuff was attached around the upper thigh to determine $PWV_{c\text{-}f}$. After measuring the distance between the cuff and the jugulum using a special compass to adjust for the convexity of the torso, a neck cuff was tightly attached at the level of the carotid artery. The mean value of two measurements was used for statistical analysis of the two arterial stiffness markers.

Self-Reported Physical Activity and Dietary Intake of Energy and Nutrients

Participants were instructed to complete a 1-day food diary and physical activity log on the day before each study visit to identify possible variations in food intake and physical activity. The food diaries were analyzed using the computer-based nutrient calculation program EBISpro (University of Hohenheim, Stuttgart, Germany). Each subject additionally completed a 3-day food diary once before the start of the study to assess their habitual diet.

Statistical Analyses

The postprandial TG concentration was used as the primary outcome to determine the sample size. The calculation was based on data from previous postprandial studies of the study group with comparable study designs [43, 44] and anticipated postprandial changes of the TG concentration in the four treatment conditions (one-factor analysis of variance [ANOVA], $p < 0.05$). The calculation indicated that a sample size of 24 participants allowed detection of a difference of 0.14 mmol/L in the TG concentration with a power of 80%, assuming an SD of 0.23 mmol/L. Considering possible drop-outs, 30 participants were included in the study. Drop-outs were to be replaced using the same sequence of meals for the newly enrolled subject.

All statistical analyses were performed using the IBM SPSS statistical software package, version 28 (IBM, Armonk, NY, USA). Data were analyzed according to a prespecified analysis plan, which was finalized before outcome data were available. The significance level was set at 0.05. Baseline characteristics of men and women were compared using the unpaired Student's *t* test. Data of the 1-day food diaries and physical activity logs were compared between the four pretreatment days using a one-factor ANOVA.

The effects of the interventions (fat type: coconut oil and canola oil; fat amount: low-fat and high-fat), time points (fasting and 0.5, 1.0, 1.5, 2.0, 3.0, 4.0, 5.0, and 6.0 h postprandially), and their interactions (fat amount × fat type, fat amount × time, fat type × time, and fat amount × fat type × time) on all postprandial parameters were tested using a linear mixed model with repeated measures; time within a subject and period was treated as repeated effect. The interventions, time points, and their interactions were set as fixed factors, as were the visit, but without interaction with the previous ones. The subject identifier was included as a random variable, and the fasting value was included as a covariate. When there was no significant interaction between the factors, the linear mixed model was repeated without the respective interaction term. To assess the adequacy of the statistical tests, the residuals

resulting from the analysis were assessed for a normal distribution. When there were non-normally distributed residuals, the linear mixed model was rerun with log-transformed data.

Additionally, for each parameter, the incremental area under the curve (iAUC) was calculated using the linear trapezoidal rule and analyzed using the linear mixed model. Here, fat type, fat amount, and their interaction as well as the visit were set as fixed factors. The subject identifier was included as a random variable.

RESULTS

Baseline Characteristics

In total, 30 participants were included in this study. **Table 5-3** provides an overview of the baseline characteristics of the 29 participants (age, 70.0 ± 5.3 years; BMI, 30.2 ± 2.6 kg/m^2) who completed all study days. One woman dropped out during the intervention period due to difficulties in fulfilling the requirements of the study protocol. Height ($p < 0.001$), weight ($p = 0.008$), waist circumference ($p = 0.045$), the waist-to-hip ratio ($p < 0.001$), and fat mass ($p < 0.001$) significantly differed between men and women.

Table 5-3 Baseline characteristics of subjects who completed the study.

	Total (*n* = 29)	**Men (*n* = 18)**	**Women (*n* = 11)**	***p* value**
Age (year)	70.0 ± 5.3	69.0 ± 5.4	71.7 ± 4.8	0.179
Height (cm)	171.6 ± 8.3	176.6 ± 5.0	163.5 ± 5.7	< 0.001
Weight (kg)	89.1 ± 10.1	92.8 ± 8.8	83.0 ± 9.3	0.008
BMI (kg/m^2)	30.2 ± 2.6	29.8 ± 2.5	31.0 ± 2.7	0.217
Waist circumference (cm)	107.1 ± 7.9	109.4 ± 7.2	103.4 ± 7.9	0.045
Hip circumference (cm)	107.6 ± 6.6	105.9 ± 5.5	110.5 ± 7.6	0.066
Waist-to-hip ratio	0.997 ± 0.069	1.034 ± 0.051	0.937 ± 0.048	< 0.001
Fat mass (%)	39.2 ± 8.3	33.7 ± 4.3	48.3 ± 3.9	< 0.001
Systolic BP (mmHg)	150.7 ± 18.3	154.9 ± 14.7	143.8 ± 22.0	0.113
Diastolic BP (mmHg)	87.4 ± 9.7	88.9 ± 11.4	84.9 ± 5.7	0.284
Pulse (min^{-1})	64.7 ± 8.8	65.4 ± 9.8	63.5 ± 7.0	0.563
Serum triglycerides (mmol/L)	1.83 ± 0.77	1.89 ± 0.87	1.74 ± 0.60	0.633
Serum total cholesterol (mmol/L)	5.58 ± 1.22	5.60 ± 1.27	5.55 ± 1.20	0.907
Serum HDL cholesterol (mmol/L)	1.45 ± 0.47	1.37 ± 0.53	1.58 ± 0.34	0.250
Serum LDL cholesterol (mmol/L)	3.51 ± 1.02	3.60 ± 1.02	3.36 ± 1.06	0.551
Plasma glucose (mmol/L)	5.88 ± 1.05	5.97 ± 1.20	5.74 ± 0.78	0.572
Serum CRP (mg/L)	2.05 ± 1.52	1.82 ± 1.33	2.39 ± 1.78	0.344

Data are shown as mean ± SD. All blood parameters were measured at the screening visit in fasting samples. Values of men and women were compared using the unpaired Student's *t* test. Abbreviations: BP, blood pressure; CRP, C-reactive protein.

Dietary Intake and Physical Activity on Pretreatment Days

Based on 1-day food diaries and physical activity logs, participants maintained their habitual dietary pattern and level of physical activity throughout the entire study phase. Total energy and macronutrient intake and the physical activity level did not significantly differ between the four pretreatment days. Additionally, habitual energy and macronutrient intake, assessed by 3-day food diaries, did not differ from the intake on pretreatment days (data not shown).

Analysis of Fasting and Postprandial Parameters in Plasma/Serum

Serum Lipids, Lipoproteins, and NEFAs

In response to all meals, the TG concentration increased up to 3.0 h postprandially and then decreased (time effect $p < 0.001$) (**Figure 5-2**). At the end of the observation period, the TG concentration was still above the preprandial level for all meals. A significant fat type effect ($p = 0.013$) and a significant fat type × time interaction ($p = 0.035$) were observed, meaning that canola oil provoked stronger lipemia than coconut oil. Additionally, HFMs provoked more extensive lipemia, indicated by a significant effect of fat amount ($p = 0.004$). iAUC data confirmed the effect of fat type (canola vs. coconut 47.9 ± 15.2 mmol/L × min, $p = 0.002$) and fat amount (HFM vs. LFM 45.2 ± 15.2 mmol/L × min, $p = 0.004$) on the postprandial TG concentration (**Table 5-4, Figure 5-3**).

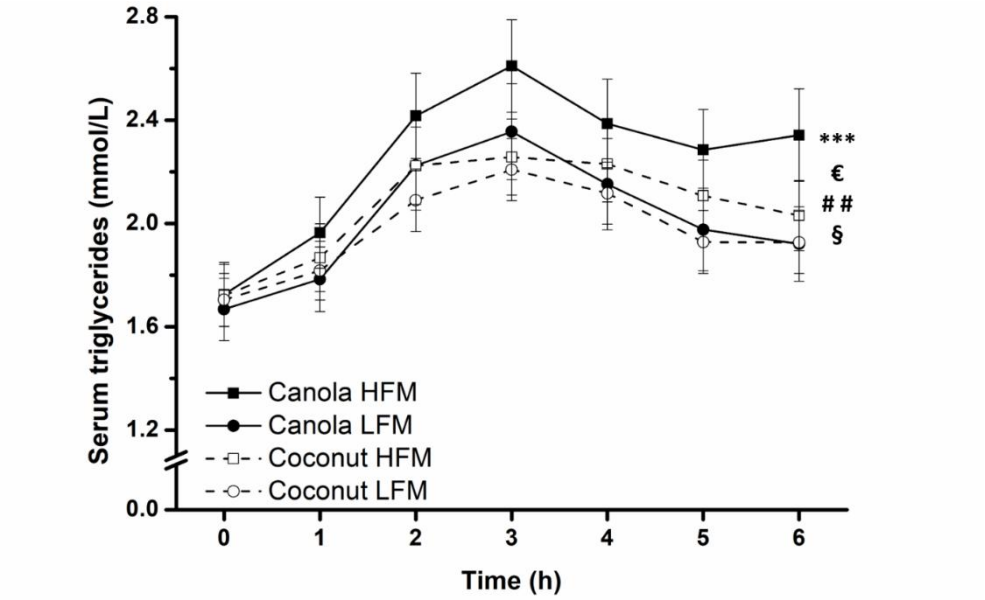

Figure 5-2 Fasting and postprandial concentrations of serum triglycerides in response to test meals in adults with increased cardiometabolic risk. Canola oil consumption resulted in a higher triglyceride concentration than coconut oil consumption. Data are shown as mean ± SEM (n = 29). A linear mixed model with repeated measures was used to test for effects of interventions, time points, and their interactions. ***$p < 0.001$ for fixed factor time, €$p < 0.05$ for fixed factor fat type, ##$p < 0.01$ for fixed factor fat amount, §$p < 0.05$ for fat type × time interaction. Abbreviations: HFM, high-fat meal; LFM, low-fat meal.

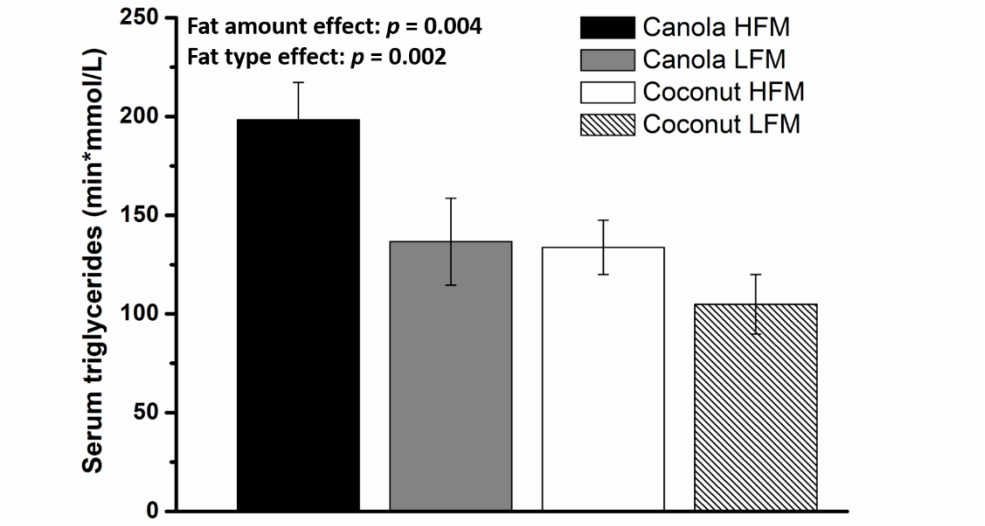

Figure 5-3 Effects of test meals on postprandial concentrations of serum triglycerides shown by incremental area under the curve. Data are shown as mean ± SEM (n = 29). A linear mixed model was used to test for effects of interventions, time points, and their interactions. Abbreviations: HFM, high-fat meal; LFM, low-fat meal.

Table 5-4 Postprandial responses shown by the incremental area under the curve for blood parameters of participants with a risk phenotype for cardiometabolic diseases.

	Canola oil-containing HFM	**Canola oil-containing LFM**	**Coconut oil-containing HFM**	**Coconut oil-containing LFM**	***p* value (fat amount)**	***p* value (fat type)**
Lipid and glucose metabolism						
Triglyceride iAUC (mmol/L × min)	198.4 ± 18.9	136.7 ± 22.0	133.8 ± 13.8	105.0 ± 15.1	0.004	0.002
NEFA iAUC (mmol/L × min)	-62.9 ± 6.3	-90.8 ± 10.0	-67.5 ± 13.8	-89.0 ± 9.6	0.002	0.835
Total cholesterol iAUC (mmol/L × min)	-49.5 ± 10.9	-64.7 ± 11.4	-36.8 ± 9.1	-73.3 ± 15.3	0.019	0.870
HDL cholesterol iAUC (mmol/L × min)	-17.3 ± 3.3	-15.2 ± 3.4	-14.6 ± 3.3	-18.0 ± 3.3	0.820	0.970
LDL cholesterol iAUC (mmol/L × min)	-53.9 ± 8.7	-49.5 ± 9.6	-33.4 ± 6.00	-53.8 ± 6.8	0.252	0.261
Glucose iAUC (mmol/L × min)	60.7 ± 33.5	173.6 ± 44.7	29.1 ± 43.5	164.2 ± 53.7	< 0.001	0.617
Insulin iAUC (nmol/L × min)	100.6 ± 16.4	146.5 ± 26.7	102.3 ± 18.1	144.9 ± 22.5	< 0.001	0.990
Inflammation and oxidation						
IL-6 iAUC (pg/mL × min)	355.6 ± 91.8	280.2 ± 59.2	178.7 ± 51.4	183.9 ± 61.9	0.574	0.047
TEAC iAUC (mmol trolox equivalent/L × min)	1.9 ± 4.5	-16.8 ± 6.7	-10.1 ± 5.9	0.1 ± 7.4	0.468	0.713
α-tocopherol iAUC (µg/mL × min)	-124.4 ± 54.4	-228.0 ± 49.5	-114.5 ± 44.6	-171.5 ± 108.6	0.195	0.617
γ-tocopherol iAUC (µg/mL × min)	24.4 ± 6.6	1.8 ± 6.5	-18.3 ± 3.5	-21.3 ± 8.6	0.020	< 0.001

Data are shown as mean ± SEM (n = 29). A linear mixed model was used to test for effects of interventions, time points, and their interactions. Abbreviations: HFM, high-fat meal; iAUC, incremental area under the curve; LFM, low-fat meal; NEFA, non-esterified fatty acid; TEAC, trolox equivalent antioxidative capacity.

Concentrations of HDL, LDL, and total cholesterol decreased postprandially, resulting in a significant time effect (all $p < 0.001$) (**Figure 5-4**). A significant fat type × fat amount interaction was observed for LDL cholesterol in time-course profiles ($p = 0.032$), but not in iAUC data. For total cholesterol, a significant fat amount effect ($p = 0.014$) and a significant fat amount × time interaction ($p = 0.007$) were observed. The effect of fat amount on total cholesterol was also observed in iAUC data (LFM vs. HFM −25.8 ± 10.8 mmol/L × min, $p = 0.019$), indicating total cholesterol decreased more after LFMs than after HFMs (**Table 5-4**).

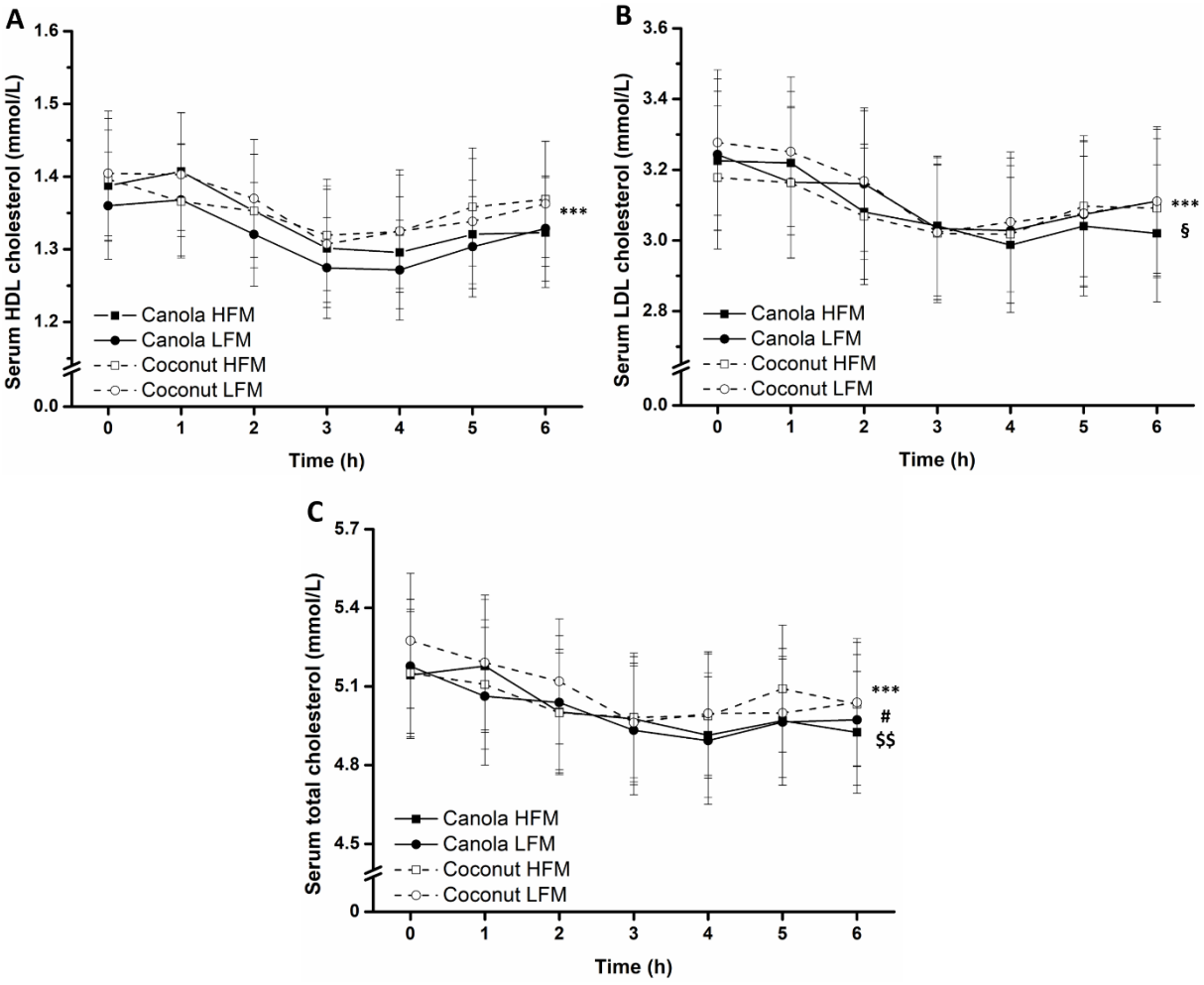

Figure 5-4 Fasting and postprandial serum concentrations of serum HDL cholesterol (A), serum LDL cholesterol (B), and serum total cholesterol (C) in response to test meals. Data are shown as mean ± SEM ($n = 29$). A linear mixed model with repeated measures was used to test for effects of interventions, time points, and their interactions. ***$p < 0.001$ for fixed factor time, #$p < 0.05$ for fixed factor fat amount, §$p < 0.05$ for fat type x time interaction, $$$p < 0.01$ for fat amount x time interaction. Abbreviations: HFM, high-fat meal; LFM, low-fat meal.

After all meals, the NEFA concentration decreased up to 2.0 h postprandially and then increased (time effect $p < 0.001$) (**Figure 5-5**). Throughout the entire postprandial period, NEFA concentrations were significantly lower after LFMs, resulting in a significant effect of fat amount ($p < 0.001$) and a significant fat amount × time interaction ($p = 0.007$). The effect of fat amount on the NEFA concentration was confirmed by analysis of iAUC data (LFM vs. HFM −24.6 ± 7.5 mmol/L × min, $p = 0.002$) (**Table 5-4, Figure 5-6**).

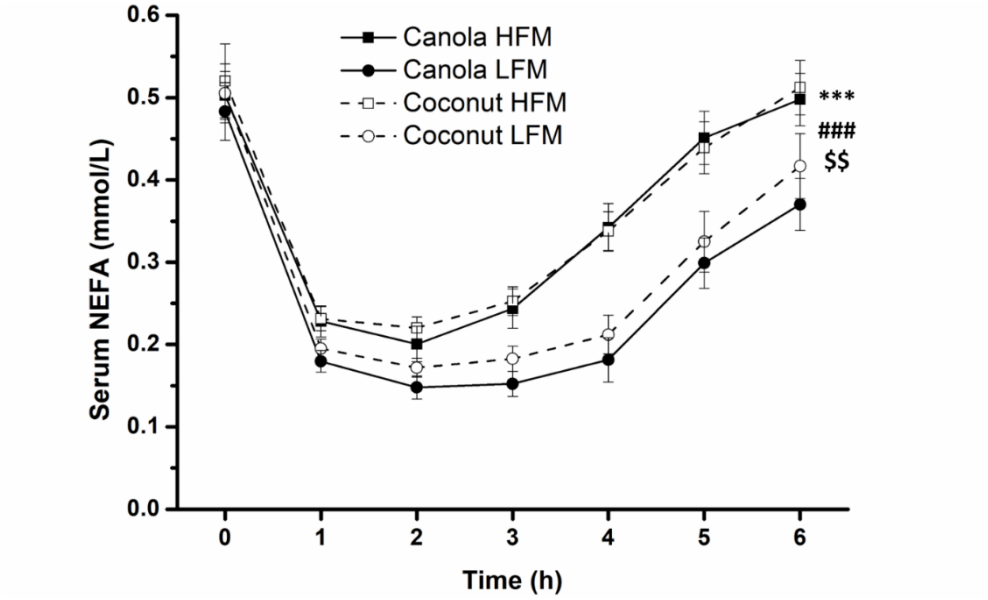

Figure 5-5 Fasting and postprandial concentrations of serum non-esterified fatty acids in response to test meals in adults with increased cardiometabolic risk. Low-fat meal consumption resulted in a lower NEFA concentration than high-fat meal consumption. Data are shown as mean ± SEM ($n = 29$). A linear mixed model with repeated measures was used to test for effects of interventions, time points, and their interactions. ***$p < 0.001$ for fixed factor time, ###$p < 0.001$ for fixed factor fat amount, $$$p < 0.01$ for fat amount × time interaction. Abbreviations: HFM, high-fat meal; LFM, low-fat meal; NEFA, non-esterified fatty acid.

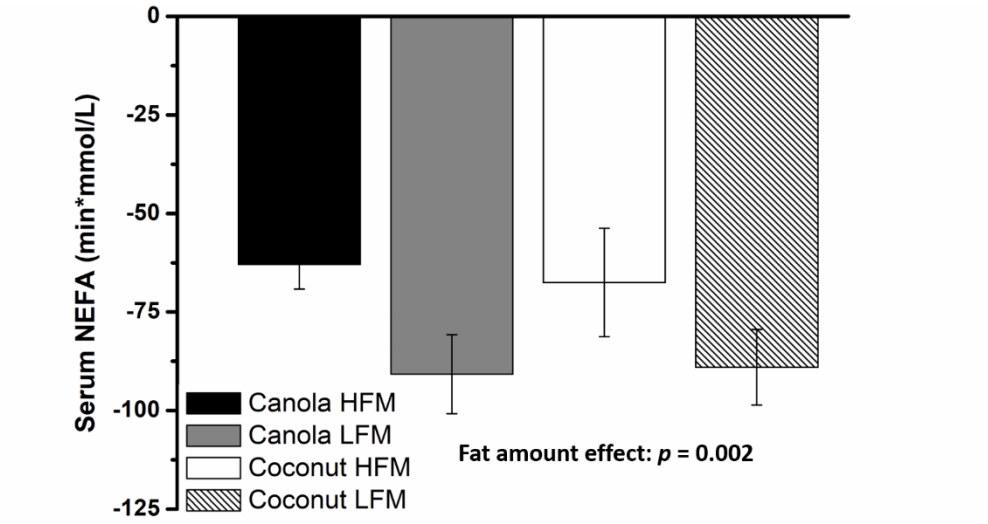

Figure 5-6 Effects of test meals on postprandial concentrations of serum non-esterified fatty acids shown by incremental area under the curve. Data are shown as mean ± SEM (n = 29). A linear mixed model was used to test for effects of interventions, time points, and their interactions. Abbreviations: HFM, high-fat meal; LFM, low-fat meal; NEFA, non-esterified fatty acid.

Serum FA Profiles

Analysis of FA time-course profiles showed a significant time effect for lauric, myristic, oleic, and α-linolenic acid (all $p < 0.001$) (**Figure 5-7**). Concentrations of lauric and myristic acid were higher after coconut oil consumption, while concentrations of oleic, linoleic, and α-linolenic acid were higher after canola oil consumption. This was reflected in a significant fat type effect and a significant fat type × time interaction for lauric, myristic, oleic, and α-linolenic acid (all $p < 0.001$). For linoleic acid, only a significant fat type effect was observed ($p = 0.005$) (**Figure 5-7**).

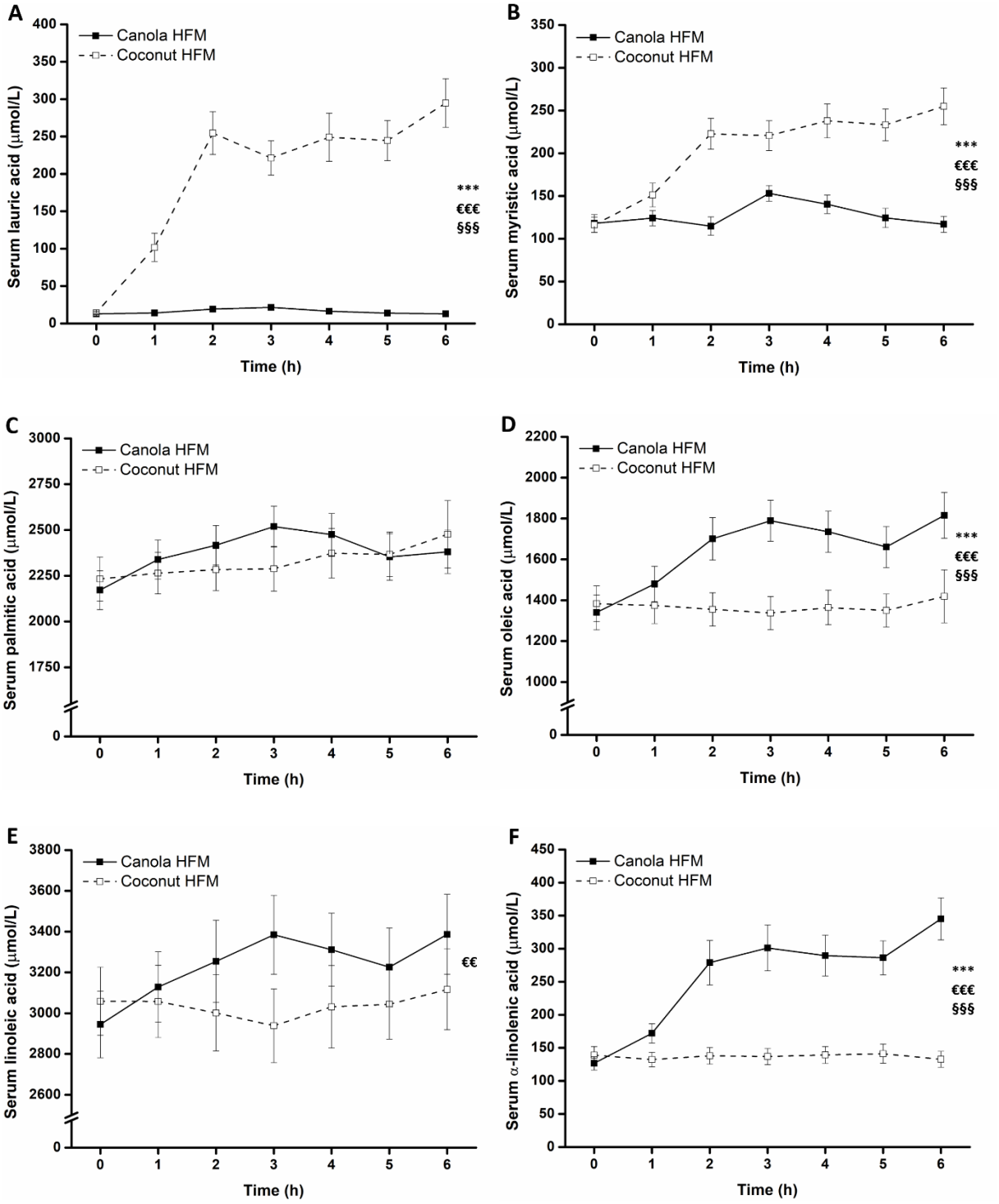

Figure 5-7 Fasting and postprandial serum concentrations of lauric acid (A), myristic acid (B), palmitic acid (C), oleic acid (D), linoleic acid (E), and α-linolenic acid (F) in response to test meals. Data are shown as mean ± SEM (n = 29). A linear mixed model with repeated measures was used to test for effects of interventions, time points, and their interactions. ***$p < 0.001$ for fixed factor time, €€$p < 0.01$ for fixed factor fat type, €€€$p < 0.001$ for fixed factor fat type, §§§$p < 0.001$ for fat type x time interaction. Abbreviation: HFM, high-fat meal.

Plasma Glucose, Serum Insulin, HOMA-IR, and the Insulin–Glucose Ratio

In response to all meals, the glucose concentration increased from baseline, peaked at 0.5 h postprandially, and gradually decreased to below the baseline at 6.0 h postprandially (time effect $p < 0.001$). Likewise, the insulin concentration increased, plateaued between 0.5 and 2.0 h postprandially, and subsequently decreased (time effect $p < 0.001$) (**Figure 5-8**). LFMs provoked stronger glycemic and insulinemic responses, reflected in significant fat amount effects ($p = 0.016$ and $p < 0.001$) and fat amount × time interactions (both $p < 0.001$). Similar effects as those in the glucose and insulin time-course profiles were observed for HOMA-IR and the insulin–glucose ratio (**Figure 5-9**). Analysis of iAUC data confirmed the significant effect of fat amount on glucose and insulin (LFM vs. HFM 127.9 ± 31.8 mmol/L × min, $p < 0.001$; LFM vs. HFM 43.7 ± 6.7 nmol/L × min, $p < 0.001$) (**Table 5-4, Figure 5-10**).

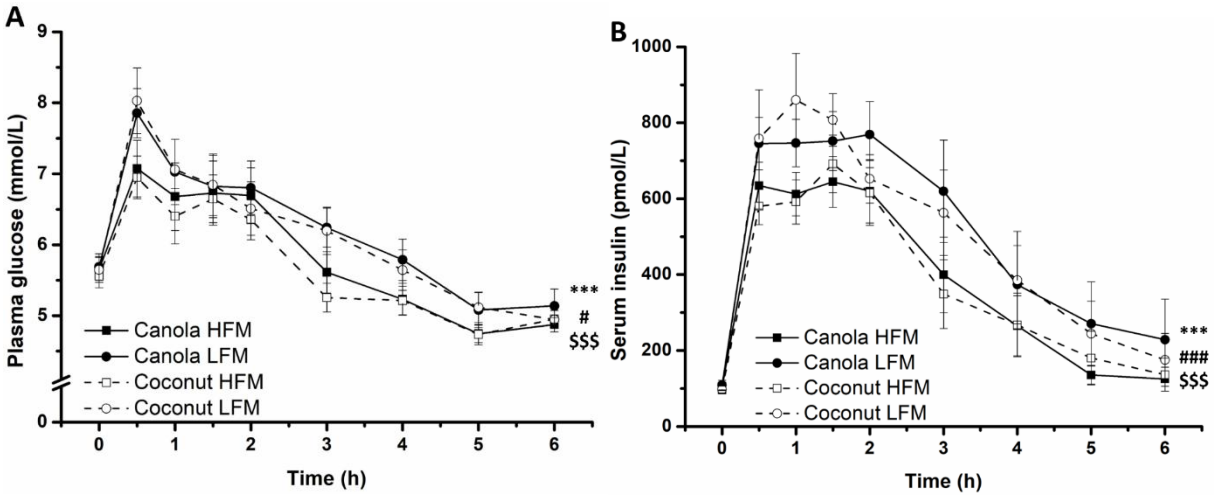

Figure 5-8 Fasting and postprandial concentrations of plasma glucose (A) and serum insulin (B) in response to test meals in adults with increased cardiometabolic risk. Low-fat meal consumption resulted in higher glucose and insulin concentrations than high-fat meal consumption. Data are shown as mean ± SEM ($n = 29$). A linear mixed model with repeated measures was used to test for effects of interventions, time points, and their interactions. ***$p < 0.001$ for fixed factor time, #$p < 0.05$ for fixed factor fat amount, ###$p < 0.001$ for fixed factor fat amount, $$$$p < 0.001$ for fat amount × time interaction. Abbreviations: HFM, high-fat meal; LFM, low-fat meal.

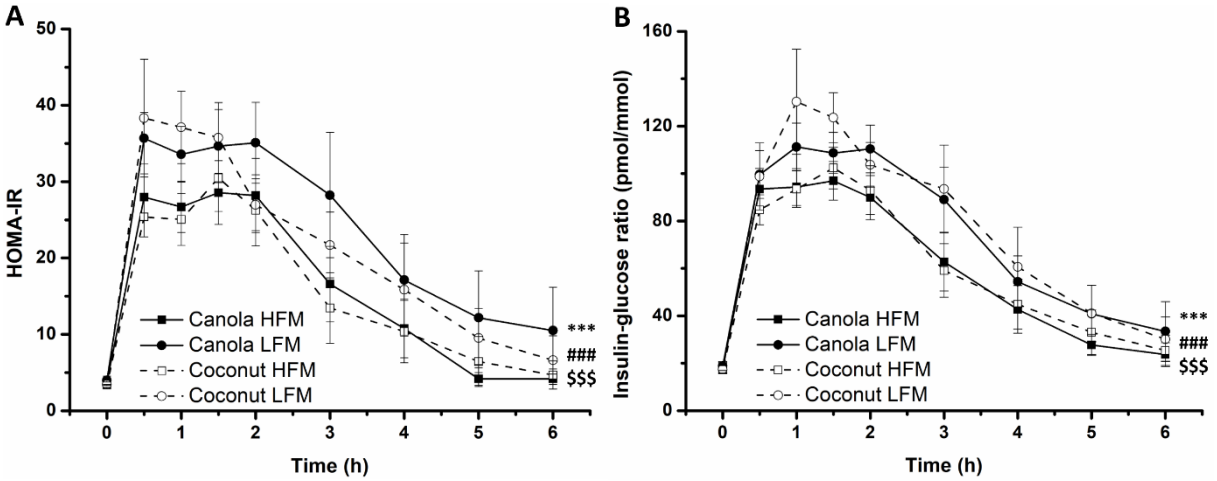

Figure 5-9 Fasting and postprandial values of homeostasis model assessment for insulin resistance (A) and insulin-glucose ratio (B) in response to test meals. Data are shown as mean ± SEM (n = 29). A linear mixed model with repeated measures was used to test for effects of interventions, time points, and their interactions. ***$p < 0.001$ for fixed factor time, ###$p < 0.001$ for fixed factor fat amount, $$$$p < 0.001$ for fat amount x time interaction. Abbreviations: HFM, high-fat meal; HOMA-IR, homeostasis model assessment for insulin resistance; LFM, low-fat meal.

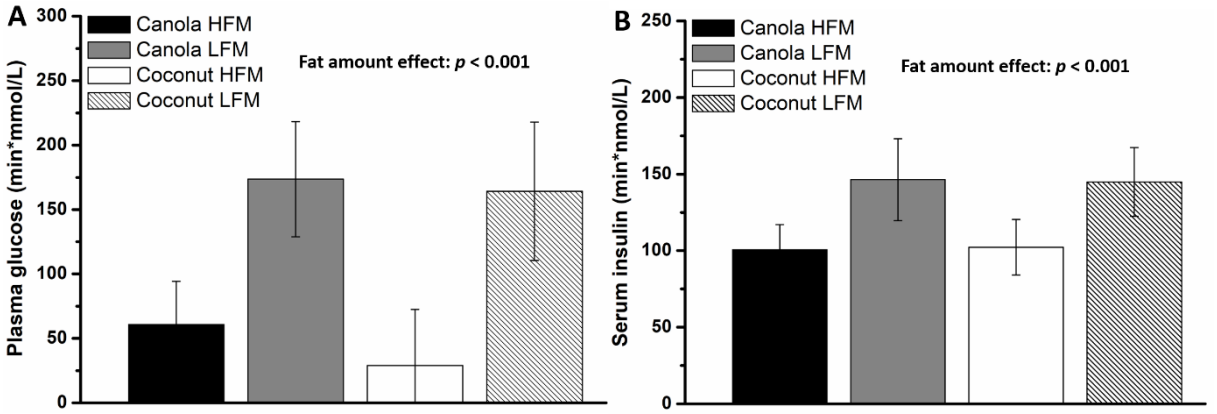

Figure 5-10 Effects of test meals on postprandial concentrations of plasma glucose (A) and serum insulin (B) shown by incremental area under the curve. Data are shown as mean ± SEM (n = 29). A linear mixed model was used to test for effects of interventions, time points, and their interactions. Abbreviations: HFM, high-fat meal; LFM, low-fat meal.

Plasma IL-6, α- and γ-Tocopherol, and TEAC

The concentration of IL-6 significantly increased after all meals (time effect $p < 0.001$) and was higher after canola oil consumption (fat type effect $p = 0.025$) (**Figure 5-11**). This significant fat type effect was confirmed by iAUC data (canola vs. coconut 131.1 ± 65.0 pg/mL × min, $p = 0.047$) (**Table 5-4, Figure 5-12**). The iAUC data of TEAC showed a significant fat type × fat amount interaction ($p = 0.023$), which was not observed in time-course profiles (data not shown). There were no effects of fat type or fat amount on TEAC (**Table 5-4**).

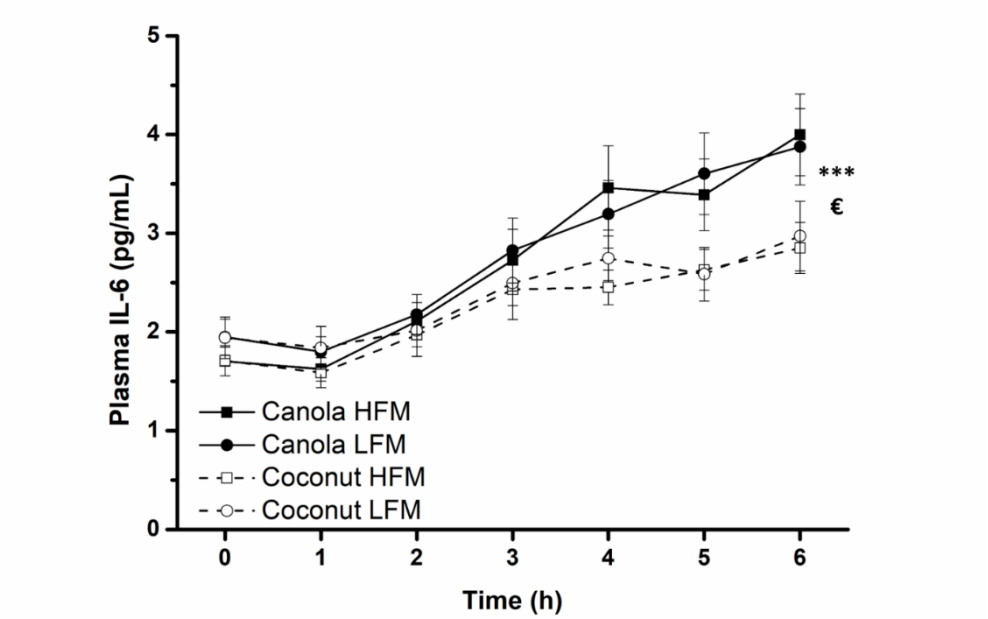

Figure 5-11 Fasting and postprandial concentrations of plasma IL-6 in response to test meals in adults with increased cardiometabolic risk. Canola oil consumption resulted in a higher IL-6 concentration than coconut oil consumption. Data are shown as mean ± SEM (n = 29). A linear mixed model with repeated measures was used to test for effects of interventions, time points, and their interactions. ***$p < 0.001$ for fixed factor time, €$p < 0.05$ for fixed factor fat type. Abbreviations: HFM, high-fat meal; LFM, low-fat meal.

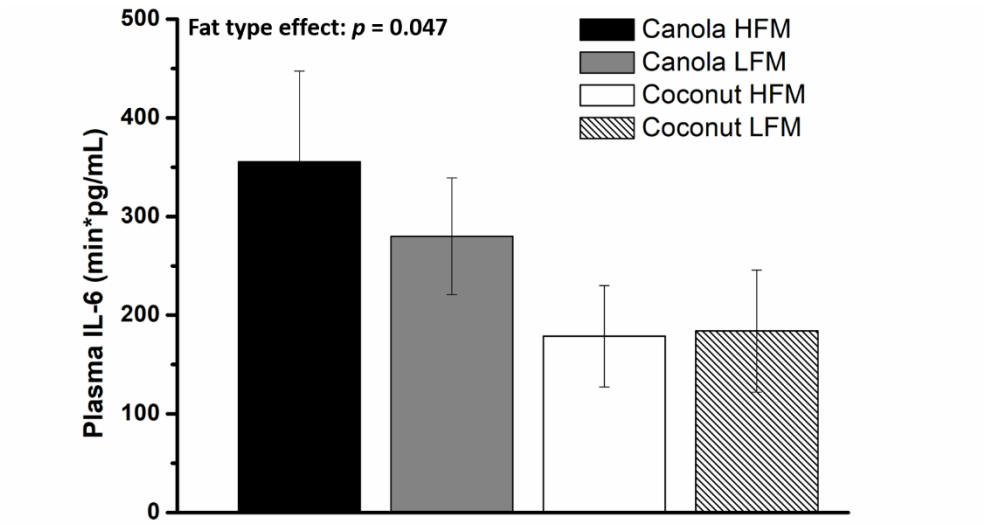

Figure 5-12 Effects of test meals on postprandial concentrations of plasma IL-6 shown by incremental area under the curve. Data are shown as mean ± SEM (n = 29). A linear mixed model was used to test for effects of interventions, time points, and their interactions. Abbreviations: HFM, high-fat meal; LFM, low-fat meal.

Time-course profiles of α-tocopherol showed a significant time effect ($p < 0.001$) and a significant fat amount × time interaction ($p = 0.039$) (**Figure 5-13A**). In addition to a significant time effect ($p < 0.001$), concentrations of γ-tocopherol were significantly higher after canola oil consumption, indicated by a significant fat type effect and fat type × time interaction (both $p < 0.001$) (**Figure 5-13B**). Although iAUC data revealed no effect of fat amount or fat type on α-tocopherol, both factors significantly influenced the iAUC of γ-tocopherol (HFM vs. LFM 13.2 ± 5.6 µg/mL × min, $p = 0.020$; canola vs. coconut 32.9 ± 5.5 µg/mL × min, $p < 0.001$) (**Table 5-4, Figure 5-14**).

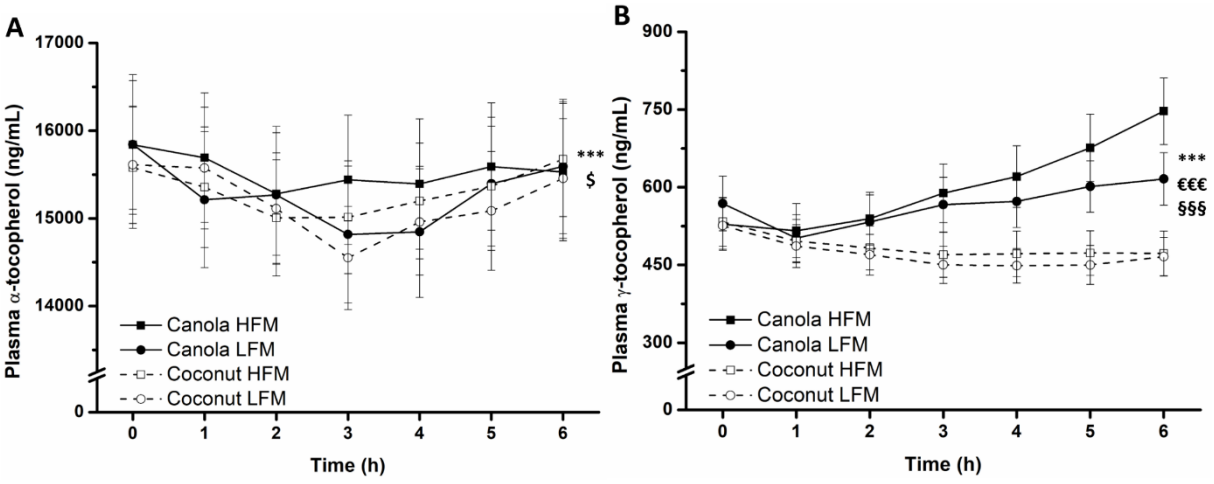

Figure 5-13 Fasting and postprandial concentrations of plasma α-tocopherol (A) and plasma γ-tocopherol (B) in response to test meals in adults with increased cardiometabolic risk. Canola oil consumption resulted in a higher γ-tocopherol concentration than coconut oil consumption. Data are shown as mean ± SEM ($n = 29$). A linear mixed model with repeated measures was used to test for effects of interventions, time points, and their interactions. ***$p < 0.001$ for fixed factor time, €€€$p < 0.001$ for fixed factor fat type, §§§$p < 0.001$ for fat type × time interaction, \$$p < 0.05$ for fat amount × time interaction. Abbreviations: HFM, high-fat meal; LFM, low-fat meal.

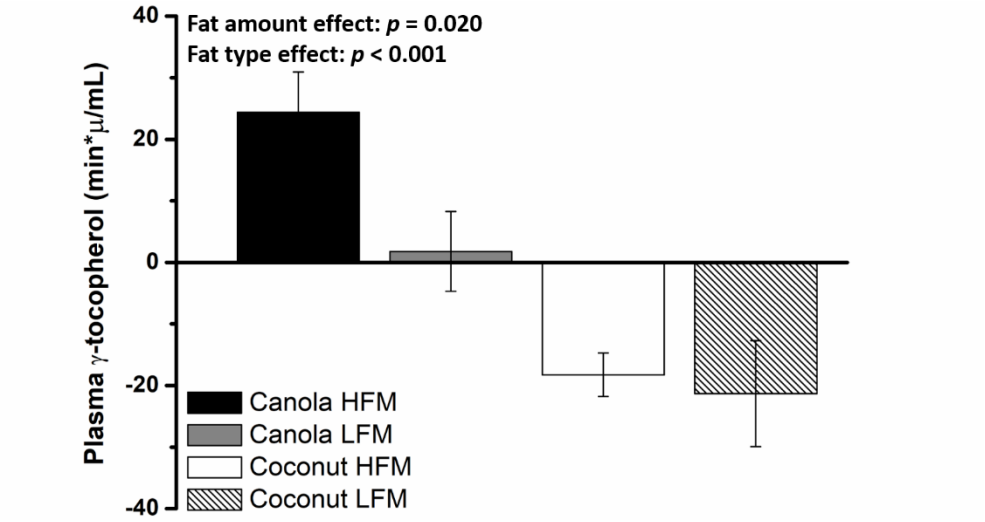

Figure 5-14 Effects of test meals on postprandial concentrations of plasma γ-tocopherol shown by incremental area under the curve. Data are shown as mean ± SEM (n = 29). A linear mixed model was used to test for effects of interventions, time points, and their interactions. Abbreviations: HFM, high-fat meal; LFM, low-fat meal.

Parameters of Arterial Stiffness

$PWV_{c\text{-}f}$ and AIx values postprandially decreased until 2.0 h and then increased. At the end of the observation period, AIx values were below the baseline. A significant time effect was observed for both $PWV_{c\text{-}f}$ and AIx (both $p < 0.001$). No effect of fat amount or fat type was detected in the time-course profiles of $PWV_{c\text{-}f}$ and AIx (**Figure 5-15**).

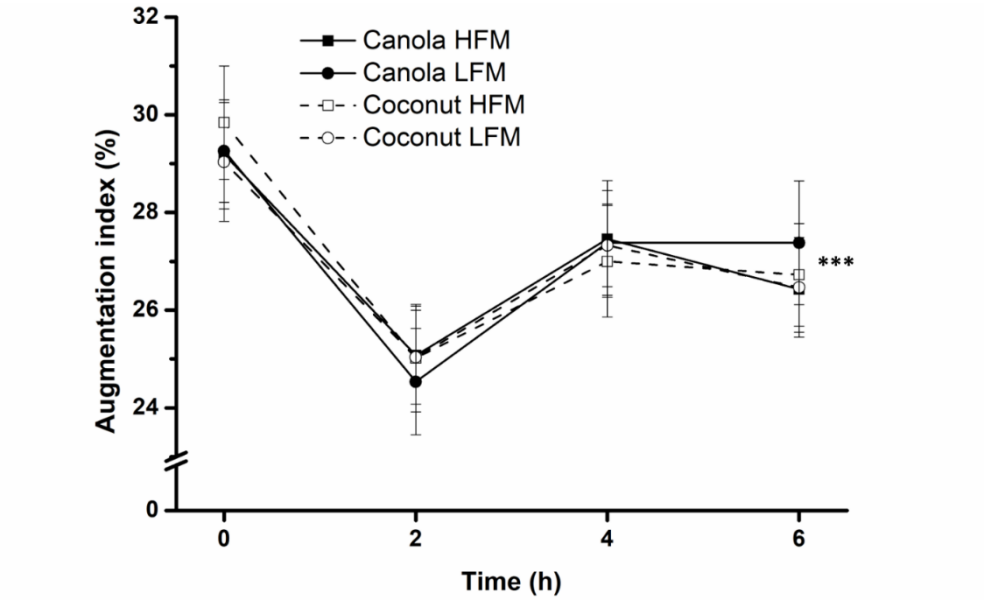

Figure 5-15 Fasting and postprandial values of augmentation index in response to test meals. Data are shown as mean ± SEM (n = 29). A linear mixed model with repeated measures was used to test for effects of interventions, time points, and their interactions. ***$p < 0.001$ for fixed factor time. Abbreviations: HFM, high-fat meal; LFM, low-fat meal.

DISCUSSION

This randomized controlled postprandial trial aimed to investigate the acute effects of four mixed meals enriched with 25 or 50 g canola or coconut oil on the metabolic response and parameters of arterial stiffness in overweight and obese older adults with a risk phenotype for cardiometabolic diseases. To the best of our knowledge, this is the first randomized controlled trial on canola and coconut oil that analyzed a wide range of parameters addressing the metabolic response and arterial stiffness as well as the postprandial FA profile.

Our major finding was that consumption of canola oil resulted in a stronger TG response than consumption of coconut oil. The strong increase of the TG concentration observed after canola oil consumption may be attributed to the fact that canola oil consists almost entirely of FAs with a chain length of at least 16 carbon atoms, which are incorporated into chylomicrons and released into the systemic circulation via the lymphatic system [45, 46]. The lower TG response after coconut oil consumption indicates that specific FAs, mainly caprylic and capric acid (which together account for approximately 10.5% of the total FA content of coconut oil), were directly transported via the portal vein to the liver. The marked increase in the TG concentration after coconut oil consumption and the high concentrations of lauric acid found in postprandial serum supports the assumption that lauric acid was metabolized as a long-chain FA. The transport of lauric acid via chylomicrons was additionally confirmed by the similar time-course profiles of lauric acid and long-chain FAs analyzed in blood serum (e.g., oleic and α-linolenic acid).

Another reason for the observed effect of fat type on the TG concentration may be possible differences in the degradation behavior of chylomicrons with varying compositions because it has been suggested that FA classes influence the composition of TG-rich lipoproteins [47]. With regard to the present trial, this means that chylomicrons rich in lauric acid would have been degraded faster than chylomicrons rich in oleic acid. Future studies regarding the influence of different dietary fats on postprandial lipemia should measure the concentration and composition of chylomicrons to investigate the lipid response to test meals in more detail.

In addition to the differential effect of fat type on the lipemic response, we found a robust effect of fat amount on lipemia, meaning that the higher fat dose of a plant oil (HFMs, 50 g test oil) triggered a stronger TG response than the corresponding meal with the lower fat dose (LFMs, 25 g test oil). This finding is consistent with the well-established concept that the TG response gradually increases with an increasing dietary fat dose [48, 49]. The observation

that the TG concentration peaked 3 h postprandially is also consistent with other trials in which fat-containing meals were administered [43, 44, 50, 51].

In the present study, ingestion of all four meals induced glycemia and insulinemia as well as significant increases in the derived parameters HOMA-IR and the insulin–glucose ratio. The intensive insulin secretion between 0.5 and 2.0 h postprandially caused a rapid decline of the glucose concentration to values below the baseline after it had peaked at 0.5 h after meal consumption. The more extensive glycemic and insulinemic response after LFMs can be attributed to their higher contents of carbohydrates (LFMs: 144.1 g vs. HFMs: 85.5 g) and mono- and disaccharides (LFMs: 73.2 g vs. HFMs: 39.9 g) than HFMs. This is consistent with a recent meta-analysis describing the attenuating effect on acute glucose and insulin responses by exchanging carbohydrates for fats in mixed meals [52]. Concerning the test oils, the results of our trial suggest that the FA composition of a meal does not influence the postprandial concentrations of glucose and insulin. This assumption is confirmed by other acute studies that observed no differential effect of meals high in SFAs, MUFAs, or PUFAs on glucose or insulin levels [53–56].

Insulin is a potent inhibitor of intracellular lipases [57]. For example, insulin reduces the activity of hormone-sensitive lipase, which is required for complete hydrolysis of triacylglycerol and release of NEFAs [58]. Hence, the increase in the insulin concentration observed in the early postprandial phase is closely linked to the rapid decrease of the NEFA concentration within the first 2 h after meal intake. Given this inverse relationship between insulin and NEFA concentrations, it stands to reason that consumption of LFMs not only triggered a stronger insulinemic response than consumption of HFMs but also resulted in a greater decrease of NEFAs. At the end of the postprandial period, the NEFA concentration typically increases above the preprandial values [57]. It can be assumed that due to the strong decrease of the NEFA concentration in the early postprandial period and its gradual increase in the later phase, our postprandial observation period of 6 h might have been too short to capture the rebound of the NEFA concentration above postabsorptive values. A postprandial observation period of 8 h would have been useful to capture the rebounding effect of NEFAs [59].

In a comprehensive review of the inflammatory response to single HFMs, Emerson et al. [60] concluded that of five common inflammatory markers, only IL-6 consistently increased postprandially. Accordingly, in our trial, the IL-6 concentration significantly increased after all four test meals. This distinct time effect has also been demonstrated in two former trials of

our study group [43, 44]. In addition, there is mechanistic evidence that the postprandial increase in IL-6 results from activation of inflammatory signaling cascades, in particular increased DNA-binding activity of the transcription factor nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) and increased degradation of the inhibitory protein IκB-α [61]. In the context of assessing inflammatory markers in postprandial protocols, it should be considered that the inflammatory response after meal consumption is regarded as a physiological phenomenon [62], and the body is able to successfully adapt to this meal-induced "stress" [63]. Regarding the fact that canola oil induced a stronger IL-6 response than coconut oil, a connection with its stronger TG response may be assumed because changes in the TG concentration are associated with changes in markers of postprandial inflammation [64, 65]. However, no association between TGs and IL-6 in response to canola oil-containing meals was observed in our data, neither in the correlation analysis for repeated measures (canola HFM $r = -0.05$, canola LFM $r = -0.12$) nor in the mediation analysis assessing whether the IL-6 response to canola oil-containing meals was mediated by TGs (indirect effect $ab = -11.18$, 95% CI [−73.37, 32.56]). The proinflammatory state after HFMs may result from leukocyte activation induced by chylomicron remnants [66]. In general, it appears that patterns and clusters of inflammatory markers may be more robust than single markers to comprehensively characterize the inflammatory response [67].

After ingestion of HFMs, we observed significant increases in serum concentration of FAs derived from oils, meaning that the concentrations of lauric and myristic acid strongly increased in response to the coconut oil-containing HFM, while the concentrations of oleic, linoleic, and α-linolenic acid markedly increased after the canola oil-containing HFM. Analogous to the serum FA profile, we were able to depict the postprandial change in γ-tocopherol. The concentration increased most after the canola oil-containing HFM (20 mg γ-tocopherol/50 g canola oil), followed by the canola oil-containing LFM (10 mg γ-tocopherol/25 g canola oil). No increment was observed after the coconut oil-containing meals due to the fact that γ-tocopherol could not be detected in this oil. The absence of an increase in the α-tocopherol level during the postprandial period can be explained by a relatively high α-tocopherol concentration at baseline, especially compared to γ-tocopherol, and a rather low α-tocopherol intake via the test meals.

In this study, consumption of all meals significantly decreased AIx, which is in accordance with the results of our recently published review [68]. Similarly, $PWV_{c\text{-}f}$ values significantly decreased postprandially regardless of the fat amount and the FA composition of the meal.

Little research has been conducted on the effects of the fat amount and FA composition of mixed meals on $PWV_{c\text{-}f}$, and the available evidence is inconsistent [68–70]. Due to substantial deviations in the study protocols (e.g., study groups and test oils), it would be questionable to compare our data with these trials. It remains unclear whether the decreases in AIx and $PWV_{c\text{-}f}$ are attributable to the consumption of the test meals or to the circadian rhythm. Since both AIx and $PWV_{c\text{-}f}$ are largely determined by BP [71, 72], there may be a connection between the postprandial decreases in AIx and $PWV_{c\text{-}f}$ and the physiological decreases in systolic and diastolic BP, which occur after food intake due to the activation of the parasympathetic system [73].

Strengths and Limitations

The main strengths of this study are the randomized crossover design, controlled setting, and high treatment compliance. Strong deviations in the environmental conditions would have been apparent and could have been considered in the data analysis by monitoring nutrient intake and physical activity on pretreatment days. The well-planned protocol enabled us to analyze a great variety of metabolic parameters and the vascular response. Short time intervals between blood collections allowed us to continuously monitor postprandial responses, which is beneficial with regard to the rapid changes in metabolic parameters such as glucose and insulin levels. The determination of the postprandial serum FA profile in addition to common metabolic parameters enabled us to better understand the effects of the two test oils on the TG response. Compared with previous studies [43, 44, 69, 74, 75], in this trial, we chose a prolonged observation period of 6 h to capture metabolic responses in the late phase of digestion. This trial helps to clarify the metabolic effects of tropical fats that are increasingly used in modern cuisine by analyzing the postprandial effects of coconut oil in comparison with those of canola oil. This study administered complete meals with commercially available foods instead of liquid tolerance test meals, which further enhances its practical relevance.

Despite the prolonged observation period, the TG concentration was still above the preprandial level after 6 h. A further extension of the observation period would have allowed us to describe the metabolic response in even greater detail, but would have placed too great a burden on the study participants. When interpreting the significant effects of fat amount (e.g., on glucose, insulin), it should be noted that the variation in fat content between HFMs and LFMs was accompanied by a variation in carbohydrate content, as the meals were intended to be isoenergetic and isonitrogenous. Another potential limitation of this study is

that the results are of limited transferability to other populations (e.g., metabolically healthy individuals); however, especially for the vulnerable group of participants with increased cardiometabolic risk, attenuating the postprandial metabolic response by dietary FA modification might be an effective strategy to reduce the CVD risk [76]. The organization of the study did not allow double-blinding in full, meaning that only measurements (blood drawing and analyses, measurement of arterial stiffness parameters) but not the serving of meals occurred in a double-blinded manner. Nevertheless, we assume that the lack of full double-blinding had no effect on our data, especially because statistical analyses were conducted without knowledge of the randomization protocol. It should be noted that our study analyzed the acute effects of canola and coconut oil on metabolism. For a further nutritional-physiological evaluation of both oils, their long-term effects on CVD-related parameters should also be considered. In this context, canola oil has a beneficial effect on several cardiometabolic risk markers [5, 6], while coconut oil is associated with increased LDL cholesterol levels [1, 9, 77].

In conclusion, our results show that in adults with a risk phenotype for CVDs, both the meal fat amount and its FA composition affect cardiometabolic risk factors. Canola and coconut oil induced different metabolic responses, and the manner and strength of the effects differed depending on the parameter. For the further physiological evaluation of dietary fats, more well-designed and highly standardized studies on the acute and longer-term metabolic effects of plant oils used in modern cuisine are needed. Future studies should consider the following aspects in particular: postprandial period of at least 6–8 h, randomized crossover design, well-characterized intervention (e.g., analyzed composition of test meals), further studies with different study populations (e.g., metabolically healthy individuals, risk phenotype, or risk genotype for CVDs), and measurement of a wide range of physiological and immunological parameters.

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AUTHOR CONTRIBUTIONS

HFK, CD, RN, and SE designed the study; HFK, CD, TS, CW, CK, MC, and SE conducted the study; BSW, HFK, and CK analyzed blood samples; HFK, CD, and RN performed statistical analysis; HFK wrote the first draft of the manuscript, which was finalized in close collaboration with CD and SE; and all authors declare responsibility for the final content and have read and approved the final manuscript.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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DATA AVAILABILITY STATEMENT

Data described in the manuscript can be made available upon request pending application and approval.

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6. General discussion

This doctoral thesis primarily aimed to investigate the effects of canola oil and coconut oil on postprandial metabolism and arterial stiffness parameters in men and women at increased risk for cardiometabolic diseases (**Chapter 2**). Before conducting a randomized controlled crossover trial (RaKo study, **Chapter 5**) to specifically investigate canola oil and coconut oil, systematic literature searches were performed to comprehensively analyze the influence of fat amount and FA composition of mixed meals on postprandial lipemia (**Chapter 3**) and postprandial vascular function (**Chapter 4**) in the context of two review articles.

According to the 2023 Atlas of Cardiovascular Disease Statistics published by the European Society of Cardiology (ESC), CVDs are the leading cause of death in ESC member countries (e.g., Austria, France, Germany, Greece, Spain), causing >1.6 million deaths in women and >1.5 million deaths in men (1). In 2021, the global prevalence of CVDs was 621 million, accounting for 20.5 million deaths (2). Prospective studies show that the postprandial concentrations of TGs and glucose predict cardiovascular events (3-5). Additionally, arterial stiffness, as measured by PWV or AIx, is recognized as an independent predictor of cardiovascular risk, cardiovascular events, and all-cause mortality (6-8). Therefore, developing dietary strategies that reduce postprandial metabolic events (e.g., postprandial TG response) and arterial stiffness could contribute to reducing the individual cardiovascular risk and thus the overall societal burden of CVDs. Such efforts are particularly relevant for populations at increased cardiometabolic risk.

The review on postprandial lipemia (**Chapter 3**) suggested that in subjects at increased CVD risk, SFA-rich meals often provoke a greater TG response than meals rich in unsaturated FAs. In contrast, in the RaKo study (**Chapter 5**), canola oil (rich in unsaturated FAs) induced a more pronounced TG response than coconut oil (rich in SFAs). This discrepancy may be due to the fact that most of the studies included in the results section of the review on individuals with CVD risk factors used SFA-rich fat sources other than coconut oil (mainly butter). The literature search identified only two studies on the effects of coconut oil on postprandial lipemia in subjects at increased CVD risk that met the inclusion criteria. In one study, the SFA-rich meal was enriched with pure coconut oil (9), and in the other study, a blend of palm oil and coconut oil was used (10). Since lauric acid by far accounts for the largest proportion of FAs in coconut oil (per 100 g: 82.5 g SFAs, 41.8 g lauric acid; **Table 1-2**) (11), the effects of coconut oil on postprandial lipemia are mainly determined by lauric acid. From a physiological

perspective, lauric acid is classified as an LCFA, because it is primarily transported via the lymphatic system (~70–75 %) (12-15). Compared to coconut oil, butter, on which most of the comparisons in the review on postprandial lipemia were based, has a much lower content of SFAs and lauric acid (per 100 g: 50.5 g SFAs, 2.6 g lauric acid) (16). Although coconut oil and butter are both categorized as SFA-rich fat sources, they differ considerably in their FA composition (11, 16) and the induced lipemic response as meal components (17). The chain length of the contained SFAs appears to be the key factor for the divergent effects of SFA-rich fat sources on postprandial lipemia, since despite conflicting results, meals enriched with SFAs of different chain lengths (e.g., butter, lard, palm oil) can induce different lipemic responses (17-19). Therefore, the conclusion of the review on postprandial lipemia, which was based mainly on studies using butter as an SFA-rich fat source, cannot be unreservedly transferred to the RaKo study, in which coconut oil served as the source of SFAs.

As described above, the acute metabolic response to meals enriched with different SFA-rich fat sources can differ. Nevertheless, the traditional classification of fat sources according to their degree of saturation (SFAs, MUFAs, and PUFAs), as used in the review on postprandial lipemia, can still be considered useful for evaluating their nutritional physiological properties. This categorization enables the prediction of the metabolic response to one class of fat source, particularly with regard to the long-term metabolic effects, and allows practical dietary recommendations to be provided to consumers (e.g., limitation of dietary SFA intake). However, when investigating a particular fat source for its nutritional physiological properties, in addition to the degree of saturation of the contained FAs, their chain length should also be considered (19).

Besides the fact that the literature analysis in the review on postprandial lipemia was based primarily on studies investigating SFA-rich fat sources other than coconut oil, none of the studies with participants at increased CVD risk used pure canola oil as a fat source rich in unsaturated FAs. Only two studies investigated canola oil blended with palm olein (20) and sunflower oil (10). The lack of studies on meals enriched with pure canola oil has likely contributed to the discrepancy between the results of the RaKo study and the conclusion of the review on postprandial lipemia that in adults at increased CVD risk, SFA-rich fat sources often induce a stronger postprandial lipemia than fat sources rich in unsaturated FAs.

The type of administered fat source is one of many methodological aspects that vary widely among postprandial studies. It is a common problem in reviews and meta-analyses of the effects of FA composition on postprandial lipemia that the included intervention studies are difficult to compare due to strong methodological differences (21-26). In some cases, it is even impossible to draw a clear conclusion (22-24). Two main areas related to the standardization of postprandial protocols are aspects regarding the interventions (e.g., fat dose, length of postprandial observation period) and pre-test conditions (27). An overview of recommendations for designing future postprandial studies can be found in both reviews (**Tables 3-6 and 4-8**). Regarding the pre-test conditions, it is advisable to standardize the dinners in order to account for the "second meal effect". This effect describes that the composition of a previous meal influences the metabolic response to the following meal (28). In this context, Robertson et al. (29) observed that a high-fat dinner resulted in higher plasma glucose concentrations during an oral glucose tolerance test than a high-CHO dinner, whereas a high-CHO dinner induced higher plasma TG concentrations during an oral fat tolerance test than a high-fat dinner. In addition to standardized dinners, participants should avoid intense physical activity—not only in the mornings before the start of the intervention days, but also throughout the entire pre-treatment days—since physical exercise lowers the postprandial TG response on the following day (30). It is advisable to use 1-day food diaries and physical activity logs to verify that participants adhere to the dinner standardization and the restriction on intensive physical activity. The absence of significant differences in physical activity on pre-treatment days and intakes of energy, macronutrients, and dietary fiber during the dinners indicates that the "metabolic status" of the participants was similar at the beginning of all four intervention days in the RaKo study, meaning that the confounding effect of external factors on the postprandial response was considerably reduced. Despite conflicting results (31-33), studies suggest that the menstrual cycle influences the acute metabolic response (34, 35). In the RaKo study, possible influences of the menstrual cycle were avoided by only including postmenopausal women.

The review on postprandial lipemia (**Chapter 3**) suggested that lowering the fat content of meals has a greater impact on the postprandial TG response than modifying the FA composition. The RaKo study (**Chapter 5**) revealed both, a robust fat amount effect and a robust fat type effect. The mean differences for the iAUC comparisons of fat amount (HFM vs. LFM 45.2 ± 15.2 mmol/L × min, $p = 0.004$) and fat type (canola oil vs. coconut oil 47.9 ± 15.2 mmol/L × min, $p = 0.002$) were comparable. This observation does not support the assumption that modifying the amount of fat in a meal has a greater effect on postprandial lipemia than exchanging the fat source. This disagreement can be attributed to several aspects.

First, the conclusion of the review on postprandial lipemia that lowering the fat content of meals has a greater effect on the postprandial TG response than modifying the FA composition was not based on studies conducted with gradually increasing amounts of fat while controlling for the FA composition. The administered meals contained high doses of fat with variations in the FA composition, and in some studies, an additional fat-free meal was consumed (36-38). The review on postprandial lipemia did not focus on the amount of fat, and assumptions about the fat dose were not based on solid data. Second, the LFMs of the RaKo study contained a considerable amount of fat (~34 g), as both the HFMs (~61 g fat) and the LFMs were designed to induce a robust postprandial lipemia, which can be observed with a meal fat content of about 30 g (39). In studies that focused on the acute effects of different fat doses without considering the FA composition, the LFMs contained considerably less fat, for example 3 g (vs. HFM 53.4 g fat) (40, 41) or 0 g (vs. HFM 54 g fat) (42). It can be hypothesized that if the LFMs in the RaKo study had contained as little fat as those in the cited studies, the fat amount effect would have been stronger than the fat type effect. However, the postprandial metabolic effects of the fat type would have been difficult or impossible to analyze in the case of a very low fat content in the LFMs. Third, the difference in the lipemic response to canola oil and coconut oil in the RaKo study was very pronounced. It can be speculated that if other fat sources with less variations in the FA composition had been compared, the fat type effect of would have been weaker than the fat amount effect.

Evidence suggests that pathological metabolic conditions, such as elevated fasting TG concentration, central obesity, and insulin resistance, amplify the postprandial metabolic response (23, 24, 43). Among several physiological and lifestyle factors, visceral adiposity emerged as the strongest predictor of the TG iAUC in overweight and obese adults (44). Jackson et al. (45) found a positive relationship between the number of metabolic syndrome traits and the magnitude of the postprandial TG and glucose responses. Additionally, the review on postprandial lipemia indicated that the lipemic response to meals with different FA compositions varies depending on the health status. This assumption is supported by the meta-analysis of Lee et al. (46) where, contrasted against SFAs, all other fats had a significantly lowering effect on postprandial TGs (iAUC) in the metabolically impaired population but not in the healthy population. In contrast, a TG elevating effect (AUC) only occurred in the metabolically healthy population. Against this background, it appears likely that the participants of the RaKo study show differences in the postprandial metabolic response depending on the baseline values of cardiometabolic risk factors. Therefore, the postprandial TG response to the four test meals (canola HFM, canola LFM, coconut HFM, coconut LFM) was analyzed in

subgroups defined based on selected baseline characteristics of the participants. The following subgroup analyses were performed on relatively small sample sizes and should therefore be considered as exploratory data analyses.

In the subgroup of participants with baseline values of BMI, fat mass, and waist circumference below the median, the fat type, but not the fat amount, showed a significant effect on the TG response (**Figures 6-1A–6-1C**). Similar to the analysis of the entire study group, canola oil induced a stronger TG response than coconut oil in these subgroups. The significant effect of fat type did not occur among participants whose baseline values of BMI, fat mass, and waist circumference were above the median. However, an effect of fat amount on the TG response was observed in these subgroups, meaning that the HFMs induced a stronger TG response than the LFMs, regardless of the fat type (**Figures 6-1A–6-1C**). These data suggest that adults with less elevated BMI (27.0–30.13 kg/m^2), fat mass (women: 40.9–48.2 %, men: 25.2–33.2 %), and waist circumference (women: 94.75–100.25 cm, men: 99.25–107.75 cm) are sensitive to changes in the FA composition of a meal with respect to the postprandial TG response. In contrast, the data indicate that adults with greater increases in BMI (> 30.13–34.9 kg/m^2), fat mass (women: > 48.2–55.3 %, men: > 33.2–41.8 %), and waist circumference (women: > 100.25–117.25 cm, men: > 107.75–124.25 cm) are more sensitive to changes in the fat content of a meal.

The review on postprandial lipemia (**Chapter 3**) suggested that the BMI threshold at which differences in the acute lipemic response to meals with different FA compositions can be observed may be 30 kg/m^2. In the RaKo study (**Chapter 5**), an effect of fat type on the postprandial TG concentration was observed only in the subgroup with a BMI below the median (≤ 30.13 kg/m^2), but not in the subgroup with a BMI above the median (**Figure 6-1A**). Regarding this apparent contradiction, it should be noted that the study from which the 30 kg/m^2 threshold was derived (47), included a different study group than the RaKo study (healthy young adults, BMI < 30 kg/m^2 vs. older adults with increased cardiometabolic risk, BMI 27.0–34.9 kg/m^2). Additionally, the meals were enriched with different fat sources (butter, olive oil, and walnuts vs. canola oil and coconut oil). These methodological differences may explain why the RaKo study could not confirm the hypothesis of a BMI threshold of 30 kg/m^2 for observing differences in the lipemic response to meals with different FA compositions.

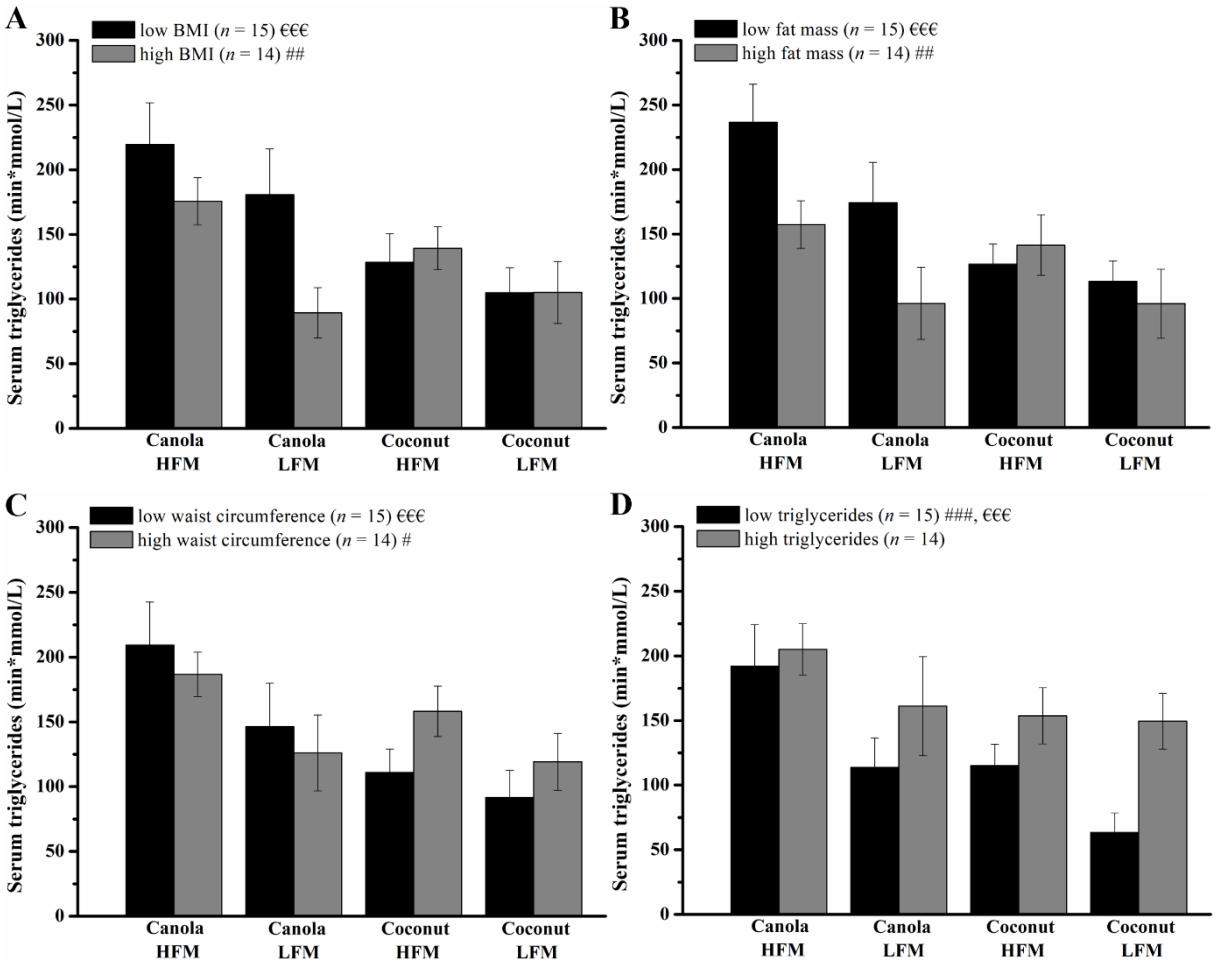

Figure 6-1 Subgroup analyses of the effects of test meals on postprandial serum triglyceride concentration as shown by incremental area under the curve. Data are presented as mean ± SEM. Participants were divided into subgroups below and above the median for baseline values of (A) body mass index (median: 30.13 kg/m^2), (B) fat mass (median women: 48.2 %, median men: 33.2 %), (C) waist circumference (median women: 100.25 cm, median men: 107.75 cm), and (D) serum triglyceride concentration (median: 1.6 mmol/L). A linear mixed model was used to test for effects of interventions, time points, and their interactions. €€€$p < 0.001$ for fixed factor fat type, #$p < 0.05$ for fixed factor fat amount, ##$p < 0.01$ for fixed factor fat amount, ###$p < 0.001$ for fixed factor fat amount. Abbreviations: BMI, body mass index; HFM, high-fat meal; LFM, low-fat meal.

When the participants were subgrouped according to their baseline TG levels, significant effects of fat amount and fat type occurred only in the group with TGs below the median (**Figure 6-1D**). This suggests that adults with lower fasting TGs (≤ 1.6 mmol/L [140 mg/dL]) are more sensitive to changes in fat amount and FA composition of a meal compared to adults with higher fasting TGs (> 1.6 mmol/L). The reason why the lipemic response to different test meals was less differentiated in subjects with higher baseline TG levels than in those with lower levels remains unclear. Additionally, subgroup analysis by baseline TGs showed that, after all four test meals, participants with baseline TGs above the median experienced a greater TG response compared to those with baseline TGs below the median (**Figure 6-1D**). The more pronounced

TG response in participants with higher baseline TGs was also evident when the TG iAUCs were averaged over all four test meals (**Figure 6-2**). This observation confirms that elevated fasting TGs intensify the postprandial TG response (24).

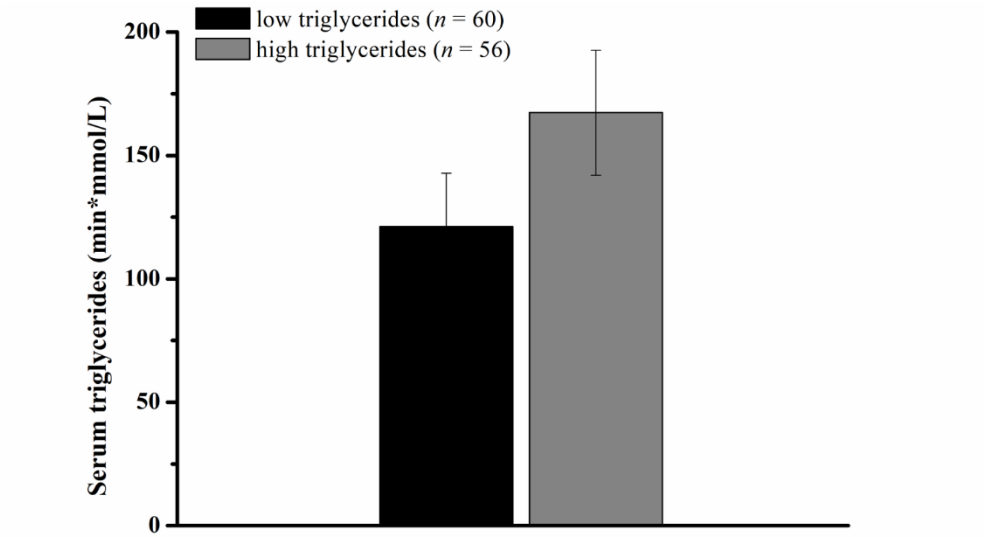

Figure 6-2 Effect of baseline serum triglyceride concentration on the postprandial triglyceride response, regardless of meal type. Data are presented as mean ± SEM. Participants were divided into subgroups below and above the median for baseline serum triglyceride concentration (median: 1.6 mmol/L). The triglyceride incremental areas under the curves were averaged over all four test meals. The unpaired Student's *t* test was used to test for differences in the triglyceride response between groups. The triglyceride response was more pronounced in participants with triglycerides above the median compared to participants with triglycerides below the median ($p = 0.013$).

Subgroup analyses based on baseline values of BMI, fat mass, waist circumference, and plasma glucose level were performed in order to test for differences in the postprandial glucose response according to these baseline characteristics (**Figures 6-3A–6-3D**). Similar to the analysis of the entire study group, a robust effect of fat amount on the postprandial glucose response was observed in nearly all subgroups, meaning that the meals with higher content of CHOs (LFMs: 144.1 g vs. HFMs: 85.5 g) and mono- and disaccharides (LFMs: 73.2 g vs. HFMs: 39.9 g) induced a stronger postprandial glucose response. The fat amount effect was missing only in the subgroup with a fat mass above the median (women: > 48.2–55.3 %, men: > 33.2–41.8 %) (**Figure 6-3B**). Notably, the magnitude of the glucose response to coconut HFM and coconut LFM was comparable in this subgroup, despite considerable differences in meal composition, particularly in terms of CHO, monosaccharide, and disaccharide content. Regarding baseline BMI, participants with values above the median (> 30.13–34.9 kg/m^2) showed a greater glucose response to all four test meals than participants with values below the median (27.0–30.13 kg/m^2) (**Figure 6-3A**).

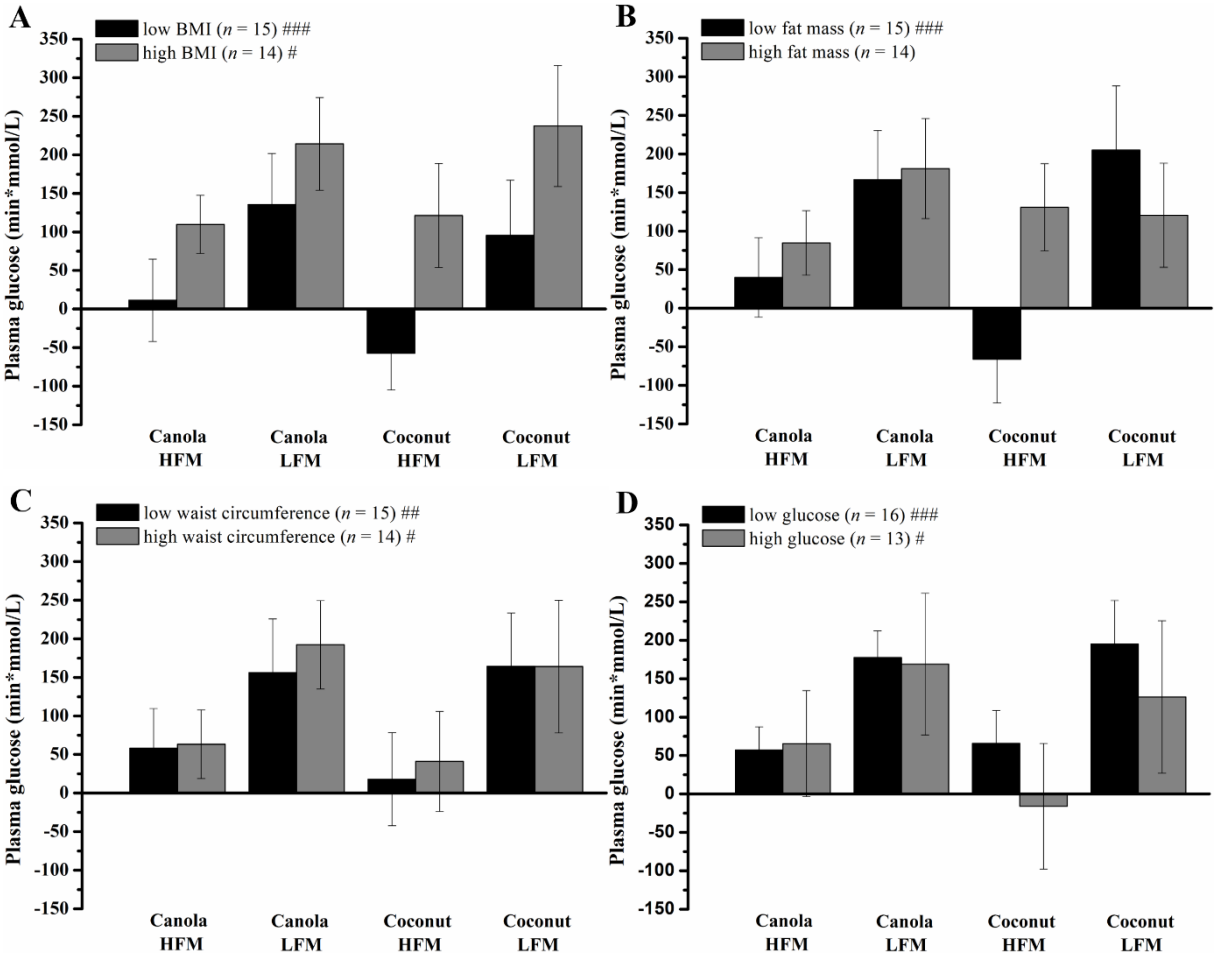

Figure 6-3 Subgroup analyses of the effects of test meals on postprandial plasma glucose concentration as shown by incremental area under the curve. Data are presented as mean ± SEM. Participants were divided into subgroups below and above the median for the baseline values of (A) body mass index (median: 30.13 kg/m2), (B) fat mass (median women: 48.2 %, median men: 33.2 %), (C) waist circumference (median women: 100.25 cm, median men: 107.75 cm), and (D) plasma glucose concentration (median: 5.6 mmol/L). A linear mixed model was used to test for effects of interventions, time points, and their interactions. #$p < 0.05$ for fixed factor fat amount, ##$p < 0.01$ for fixed factor fat amount, ###$p < 0.001$ for fixed factor fat amount. Abbreviations: BMI, body mass index; HFM, high-fat meal; LFM, low-fat meal.

In contrast to the TG response, which was amplified by a high baseline TG concentration (**Figures 6-1D and 6-2**), the glucose response was not more pronounced in subjects with fasting glucose levels above the median (> 5.6 mmol/L [101 mg/dL]) than in subjects with fasting glucose levels below the median (≤ 5.6 mmol/L) (**Figure 6-3D**).

Subgroup analyses of the IL-6 response were conducted based on baseline values of CRP and fatty liver index (FLI, calculated according to (48)) to test for a relationship between basal inflammatory status or the likelihood of fatty liver disease and the postprandial inflammatory response. The FLI estimates the risk of fatty liver disease, calculated from BMI, waist circumference, fasting TG level, and gamma-glutamyl transferase level. Values < 30 rule out

hepatic steatosis, while values ≥ 60 indicate its presence, as detected by ultrasonography (48). None of the participants in the RaKo study had an FLI < 30, a minority (n = 4) had an FLI between 30 and 59, and the majority (n = 25) had an FLI ≥ 60. Analysis of the entire RaKo study group revealed that the fat type significantly affected both the concentration-time profile and the iAUC of the IL-6 response, indicating that the magnitude of the postprandial IL-6 increase was higher following canola oil intake than following coconut oil intake. In the subgroup analyses (**Figures 6-4A–6-4D**), the significant effect of fat type was only observed in the concentration-time profile of participants with an FLI below the median (≤ 76.6) (**Figure 6-4C**). The reason why the fat type effect on the IL-6 response could not be reproduced in most subgroup analyses remains unclear. The data suggest that the postprandial increase in IL-6 was mainly caused by energy intake itself, rather than by the amount of fat or the FA composition of the test meals. Subgroup analyses of the IL-6 response also showed that compared to participants with CRP and FLI below the median, those with values above the median had slightly higher IL-6 concentrations throughout the entire postprandial period, though the differences were not statistically significant (**Figures 6-4A and 6-4C**). The IL-6 concentrations increased in all subgroups simultaneously, and subjects with CRP and FLI above the median did not exhibit an amplified postprandial inflammatory response. These data are consistent with a previous trial conducted by Schönknecht et al. (49), in which the postprandial IL-6 concentrations increased equally in high and low inflammation groups.

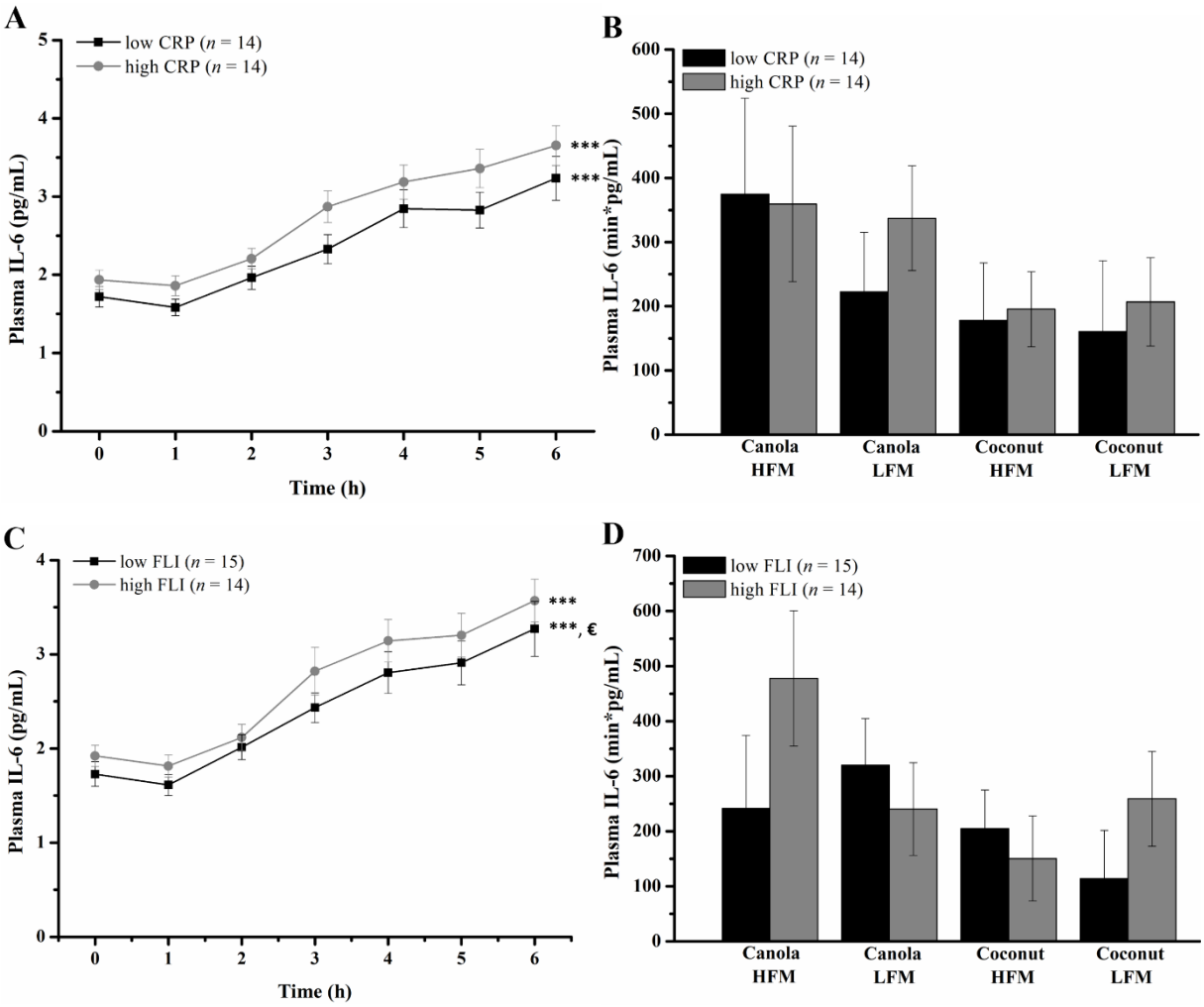

Figure 6-4 Subgroup analyses of the effects of test meals on postprandial plasma interleukin-6 concentration as shown by concentration-time profile (A, C) and incremental area under the curve (B, D). Data are presented as mean ± SEM. Participants were divided into subgroups below and above the median for baseline values of C-reactive protein (median: 1.37 mg/L) and fatty liver index (median: 76.6). A linear mixed model was used to test for effects of interventions, time points, and their interactions. ***$p < 0.001$ for fixed factor time, €$p < 0.05$ for fixed factor fat type. Abbreviations: CRP, C-reactive protein; FLI, fatty liver index; HFM, high-fat meal; IL-6, interleukin-6; LFM, low-fat meal.

The second review, which focused on the influence of fat amount and FA composition of meals on the postprandial vascular function (**Chapter 4**), showed that the AIx decreases in response to meal intake, mostly independent of the FA composition. The decreasing effect of meal intake on AIx was also observed in the RaKo study (**Chapter 5**). Here, the AIx decreased postprandially and then increased again, with the change in AIx over time occurring independent of the fat type. Similar effects were observed for the $PWV_{c\text{-}f}$ values. Thus, the RaKo study confirmed the assumption of the review on postprandial vascular function that the FA composition of a meal has no significant effect on parameters of acute arterial stiffness. As reported in the review, long-chain n-3 PUFAs from fish oil (EPA, docosahexaenoic acid

[DHA]) may be an exception, as data suggest a greater postprandial reduction in AIx (50) and a lesser re-increase in AIx (51) compared to control meals.

The BP is known to follow a circadian rhythm, with two peaks during the day, a higher peak in the morning (~8–10 am) and a lower peak in the evening (~7–9 pm) (52). Under normal conditions, the BP drops during the night, a phenomenon referred to as "dipping". The AIx, which can be calculated as the quotient of augmentation (describes the influence of the reflected pressure wave on the arterial BP) and pulse pressure (BP amplitude; difference between systolic and diastolic BP), is largely determined by the BP (53). The BP has also been identified as a relevant factor that affects PWV. To avoid an influence of circadian rhythm of the BP on AIx and $PWV_{c\text{-}f}$ values, the measurements of arterial stiffness in the RaKo study were performed according to a standardized time schedule.

Studies show that aging and several CVD risk factors (e.g., obesity, metabolic syndrome) are associated with increased arterial stiffness (54). Additionally, Phillips et al. (55) reported that the time taken for the AIx to return to baseline after the postprandial decline was significantly longer in subjects with T2DM than in lean subjects, indicating that the metabolic health status influences the postprandial AIx response. Therefore, analyses were performed based on the RaKo study data to test for correlations between selected baseline characteristics of the participants (age, BMI, waist circumference, percentage of body fat, number of cardiometabolic risk factors, plasma concentrations of α-/γ-tocopherol, and serum concentrations of EPA/DHA) and postprandial arterial stiffness parameters (AIx, $PWV_{c\text{-}f}$; fasting values and postprandial changes). A positive correlation was observed between percentage of body fat and fasting AIx value (0.586; $p < 0.001$) (**Figure 6-5A**). Additionally, a positive correlation was found between waist circumference and the degree of postprandial AIx change 2 and 4 h after ingestion of the test meals (0.379; $p = 0.043$ and 0.520; $p = 0.004$) (**Figures 6-5B and 6-5C**). None of the participants' baseline characteristics that were tested showed a significant correlation with the fasting $PWV_{c\text{-}f}$ or the postprandial $PWV_{c\text{-}f}$ response. It can be speculated that the study group was too homogeneous in terms of the cardiometabolic risk profile to reveal more significant correlations between baseline characteristics and parameters of postprandial arterial stiffness.

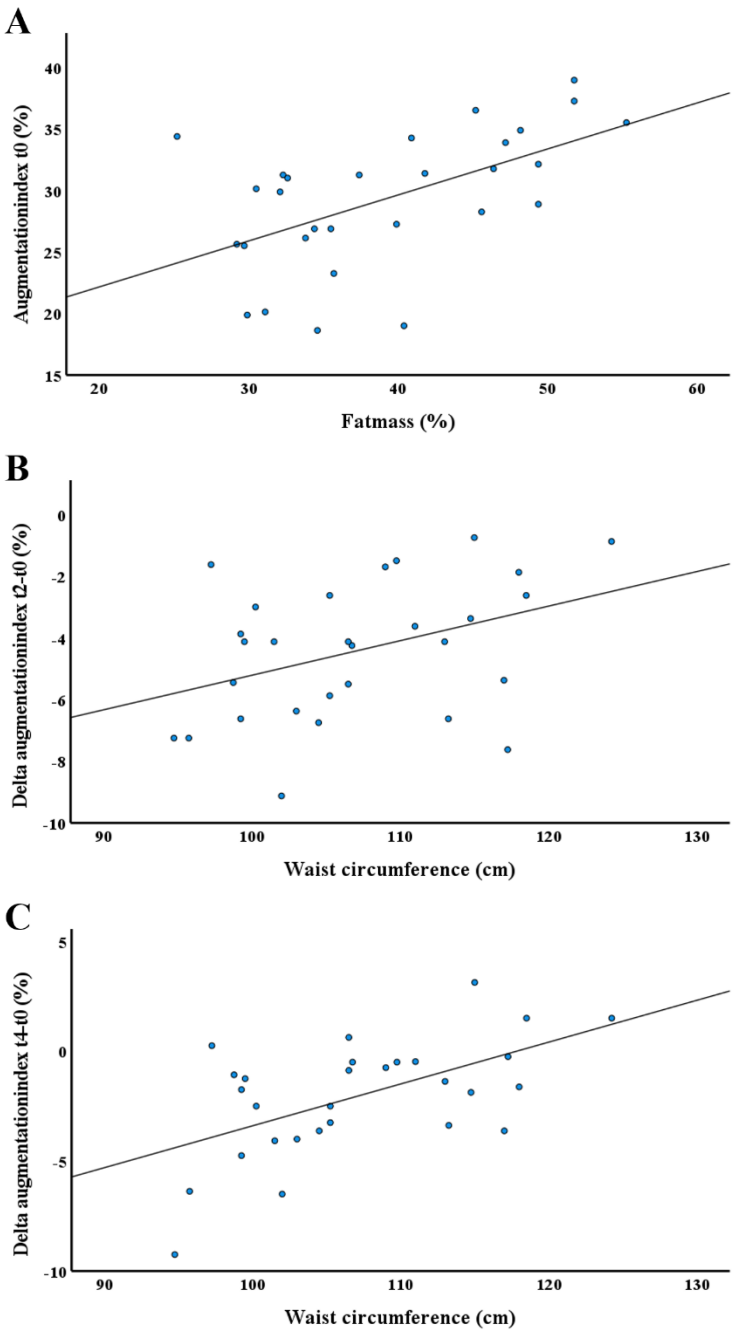

Figure 6-5 Correlations between participants' baseline characteristics and augmentation index. Scatter plots show positive correlations between (A) body fat mass and fasting value of augmentation index (0.586; $p < 0.001$), (B) waist circumference and postprandial change of augmentation index at 2 h postprandial (0.379; $p = 0.043$), and (C) waist circumference and postprandial change of augmentation index at 4 h postprandial (0.520; $p = 0.004$).

A very limited number of human studies compared the effects of canola oil and coconut oil on postprandial metabolic parameters. In young adults, Sciarillo et al. (56) found no significant meal × time interaction or meal effect with regard to the responses of TGs, glucose, metabolic load index (sum of postprandial TG and glucose concentrations), LDL cholesterol, HDL cholesterol, or total cholesterol to mixed meals (13 kcal/kg BW, 61 E% fat; for 60 kg BW: ~780 kcal, 54 g fat) enriched with canola oil, olive oil, coconut oil, or butter. Meals did also not

induce significant differences in peak, time to peak, total AUC (tAUC), or iAUC of these metabolic parameters. Gradek et al. (57) reported that in participants with arteriosclerotic vascular disease, HDL and LDL cholesterol concentrations did not change in response to test meals (~736 kcal) enriched with coconut oil, canola oil, or safflower oil (50.1 g test oil), but that the postprandial TG increase was greater after canola oil and safflower oil compared with coconut oil. However, no statistical test was performed to determine whether the difference in the TG response between meals reached a statistically significant level. The RaKo study complements previous research by providing a thorough analysis of the postprandial responses to canola oil and coconut oil, addressing lipemia and glycemia, as well as parameters of pro-oxidative and pro-inflammatory processes, parameters of arterial stiffness, and serum FA kinetics. Instead of focusing on a specific aspect of the postprandial metabolic response, the RaKo study applied a holistic approach by measuring a wide range of parameters. In particular, the strong TG response to canola oil was a surprising finding, as it contrasts with the numerous cardioprotective effects associated with long-term intake of canola oil (58-61). In light of this interesting result, it would be useful to conduct a follow-up study in order to better understand the mechanisms of the TG response to meals enriched with canola oil and coconut oil. This study could be performed on metabolically healthy individuals and should focus on the postprandial lipid metabolism. In addition to the TG concentration, further parameters that characterize postprandial lipemia should be measured, such as postprandial changes in apoB-48 or apoB-100 in blood samples. These apolipoproteins are the major protein components of CMs secreted from the intestine after fat ingestion (apoB-48) and VLDLs synthesized in the liver (apoB-100) (62). Because each CM and VLDL particle contains a single apoB-48 or apoB-100 molecule, respectively (63, 64), these apolipoproteins could be used to quantify TRLs during the postprandial period. To further characterize postprandial lipemia, the CM size could be determined; it is larger with a higher lymph TG concentration and smaller with a lower concentration (65). It can be assumed that the stronger serum TG response to canola oil intake compared to coconut oil intake is associated with CMs of a larger size. The metabolism of CMs and remnants has been shown to be regulated by both size and particle number, basically with slower plasma clearance for smaller particles and higher particle number (65, 66). Investigating the CM clearance after intake of canola oil and coconut oil by measuring CM-related parameters could therefore also be relevant in the context of a follow-up study. The FA composition of CM TGs reflects the FA composition of a test meal (67). Therefore, the FA composition of TGs in postprandial TRLs could additionally be analyzed to strengthen the impressive characterization of the postprandial kinetics of individual serum FAs in the RaKo

study. Similar to the strong TG response to canola oil, it was likewise unexpected that canola oil (rich in unsaturated FAs) induced a more pronounced IL-6 response than coconut oil (rich in SFAs), since especially SFAs are known as potent triggers of the postprandial inflammatory response (43). However, n-6 PUFAs likewise promote postprandial inflammatory processes, whereas n-3 PUFAs mitigate them. In order to better understand the differences in the postprandial inflammatory response between canola oil and coconut oil, it would be useful to investigate the activation status of immune cells in a follow-up study. This could be realized by isolating T cells and monocytes from blood in the postprandial state and measuring cytokine secretion (e.g., IL-6, IL-1β) after stimulation with phytohemagglutinin or lipopolysaccharide. For the further analysis of the postprandial inflammatory response, performing such in vitro tests would be more useful than measuring various inflammatory markers in the blood, because most common parameters, except IL-6, do not increase postprandially (e.g., IL-8, CRP) (68).

There is clear evidence that regular intake of canola oil decreases total and LDL cholesterol levels (58-61), whereas regular intake of coconut oil increases levels of both (13, 59, 69). Such superior effects of canola oil on endogenous lipid metabolism were not observed in the acute design of the RaKo study, in which the short-term TG response to fat intake was stronger after canola oil intake than after coconut oil intake, and cholesterol metabolism was largely unaffected by the type of fat. Because the FA composition of the habitual diet affects the postprandial lipemic response to acute fat ingestion (24), it would be interesting to investigate the metabolic effects of combining chronic and acute study protocols, whereby both the habitual diet and acute test meals are enriched with canola oil and coconut oil. This could be achieved by conducting a further randomized crossover study in which participants integrate a specified amount of either canola oil or coconut oil into their diets for several weeks (e.g., 50 g/day for 6 weeks). Providing further specifications regarding the energy content or macronutrient and FA compositions of the intervention diets would increase the standardization of the intervention diets, but it would require a considerable additional effort from the participants and study personnel. Before and after the chronic intervention phase, selected metabolic parameters (e.g., TGs, total and LDL cholesterol, glucose, insulin, and HOMA-IR) should be measured to analyze the long-term effects of canola oil and coconut oil intake. Immediately following the chronic intervention phase, a postprandial protocol should be performed to investigate the effects of enriching the habitual diet with canola oil or coconut oil on the postprandial response. In the postprandial protocol, two test meals with similar energy and macronutrient composition should be used, consisting of the same meal components except for the added test oil (canola oil or coconut oil, depending on the chronic phase). The HFMs from the RaKo study (**Table 5-**

1), which contained 50 g of either canola oil or coconut oil, would be suitable for such a postprandial test meal challenge. The crossover design involves each subject undergoing two intervention phases (chronic and subsequent acute protocols), one based on canola oil and one based on coconut oil; the two phases should be separated by a sufficiently long washout phase (e.g., 6 weeks). To increase the comparability of the RaKo study results and those of this further postprandial protocol, it would be reasonable to select a subject group similar to the one in the RaKo study (60–80 years of age, metabolic syndrome traits). A comparison of the RaKo study data and the data obtained in this further protocol would reveal how the chronic intake of canola oil and coconut oil influences the postprandial metabolic response to an acute test meal challenge enriched with the same fat source as the study diet of the chronic intervention.

Conclusion and future perspective

The amount of fat in a meal and its FA composition are two important factors that determine the postprandial metabolic response, particularly among individuals at increased CVD risk. This was confirmed in the RaKo study by showing that meals enriched with a higher fat amount (HFMs, 50 g of test fat) and canola oil (rich in unsaturated FAs) induced a stronger lipemic response than meals with a lower fat amount (LFMs, 25 g of test fat) and coconut oil (rich in SFAs). Besides, the meals with higher content of CHOs (LFMs: 144.1 g vs. HFMs: 85.5 g) and mono- and disaccharides (LFMs: 73.2 g vs. HFMs: 39.9 g) induced stronger postprandial glucose and insulin responses as well as a stronger decrease in NEFA concentration. Additional differences in the postprandial metabolic response to the test meals were observed, such as a stronger IL-6 response after canola oil intake compared to coconut oil intake. The marked increase in the TG concentration and the kinetics of lauric acid in postprandial serum samples after coconut oil intake confirm that lauric acid acted biologically as an LCFA and should therefore not be classified as an MCFA from a physiological point of view. Independent of fat amount and FA composition of the meals, measures of arterial stiffness ($PWV_{c\text{-}f}$, AIx) decreased postprandially, which is largely consistent with the results of the review on postprandial vascular function.

Subgroup analyses of the RaKo study data suggest that regarding the TG response, participants with less severe cardiometabolic risk manifestations responded sensitive to variations in the meal FA composition, while those with more severe manifestations responded sensitive to variations in the meal fat amount. Regarding the glucose response, participants were sensitive to changes in CHO content, largely independent of baseline characteristics. Results from

subgroup analyses need to be confirmed by studies specifically designed to compare the postprandial responses to meals with different FA compositions in groups of participants with varying cardiometabolic risk characteristics and severity.

The review on postprandial lipemia suggested that in subjects with CVD risk factors, meals enriched with SFAs often induce a stronger lipemic response than meals enriched with unsaturated FAs. The opposite effect was observed in the RaKo study, which arises mainly from the fact that the review primarily comprised studies that investigated sources of fat other than canola oil and/or coconut oil. In general, strong methodological differences in protocols of postprandial studies make it difficult to compare their results.

With its holistic approach, the RaKo study provides a comprehensive insight into the postprandial responses to canola oil and coconut oil. Particularly with regard to the strong differences in the TG response to the two test oils, it would be desirable for future studies to investigate further parameters characterizing the lipemic response (e.g., apoB-48, CM size). Additionally, it would be interesting to investigate the postprandial metabolic effects of canola oil and coconut oil in a further randomized crossover study with two chronic intervention phases prior to the postprandial meal challenges, during which canola oil and coconut oil are consumed daily in a defined quantity as part of the habitual diet.

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7. Summary

The modern human spends the majority of the day in the postprandial state, which is a dynamic period following food intake and is characterized by alterations in the concentration of various metabolic parameters in the blood. The major postprandial metabolic events are acute increases in concentrations of triglycerides (TGs), glucose, and insulin (lipemia, glycemia, and insulinemia). The postprandial metabolic response is influenced by various meal-dependent and meal-independent factors, including the amount of fat in the meal, its fatty acid (FA) composition, and the individual health status. According to the current state of knowledge, frequent excessive food intake increases the risk of cardiovascular diseases (CVDs), primarily through exaggerated and prolonged metabolic, oxidative and immune imbalances, accompanied by low-grade inflammation and impaired endothelial function. Therefore, strategies that mitigate the postprandial metabolic response could contribute to reducing both the individual cardiovascular risk and the societal burden caused by CVDs.

The core of this thesis was a randomized controlled crossover trial investigating the postprandial metabolic and vascular effects of canola oil (rich in unsaturated FAs) and coconut oil (rich in saturated FAs [SFAs]) in individuals with a risk phenotype for cardiometabolic diseases. In the so-called RaKo study, 29 participants (70.0 ± 5.3 y; 30.2 ± 2.6 kg/m^2) consumed four isoenergetic (~4,200 kJ) and isonitrogenous (~27 g protein) meals that were enriched with either 25 or 50 g of canola oil or coconut oil. The combination of different fat amounts and fat sources resulted in four test meals: canola low-fat meal (LFM), coconut LFM, canola high-fat meal (HFM), coconut HFM. In the fasting state and at 1, 2, 3, 4, 5 and 6 h after meal intake blood samples for analysis of TGs, total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, non-esterified fatty acids (NEFAs), individual FAs, glucose, insulin, homeostasis model assessment for insulin resistance (HOMA-IR), insulin-glucose ratio, interleukin-6 (IL-6), α- and γ-tocopherol, as well as trolox equivalent antioxidative capacity (TEAC) were collected. Parameters of glucose metabolism were additionally measured 0.5 and 1.5 h postprandially. Besides, carotid-femoral pulse wave velocity ($PWV_{c\text{-}f}$) and augmentation index (AIx), both parameters of arterial stiffness, were determined in the fasting state and 2, 4, and 6 h postprandially. The main findings were that canola oil induced a stronger serum TG incremental area under the curve (iAUC) and plasma IL-6 iAUC than coconut oil. Besides, the iAUC of plasma γ-tocopherol was significantly higher after canola oil intake than after coconut oil intake. Consistent with the FA composition of the test oils, serum concentrations of

lauric and myristic acid were higher after coconut oil intake, while serum concentrations of oleic, linoleic, and α-linolenic acid were higher after canola oil intake. The kinetics of serum TGs and lauric acid in response to coconut oil intake support the recommendation that lauric acid should not be classified as an MCFA from a physiological point of view, since it biologically acts as an LCFA. Regarding the effects of fat amount on the postprandial response, the HFMs induced a stronger serum TG iAUC than the corresponding LFMs. Besides, plasma glucose, serum insulin, HOMA-IR, and the insulin-glucose ratio increased stronger after the LFMs than after the HFMs, and serum NEFAs decreased more after the LFMs than after the HFMs. These effects are primarily attributed to the higher content of carbohydrates (LFMs: 144.1 g vs. HFMs: 85.5 g) and mono- and disaccharides (LFMs: 73.2 g vs. HFMs: 39.9 g) in the LFMs. Additionally, iAUC data indicated that serum total cholesterol decreased more after the LFMs than after the HFMs. The canola HFM induced a stronger increase in plasma γ-tocopherol than the canola LFM. No effect of fat type or fat amount was observed in the iAUC data of serum LDL cholesterol, serum HDL cholesterol, plasma TEAC and plasma α-tocopherol. $PWV_{c\text{-}f}$ and AIx decreased postprandially, independent of fat amount and FA composition of the test meals.

In addition to the RaKo study, two literature searches were conducted as part of this doctoral thesis. The first review systematically investigated the impact of fat amount and FA composition of mixed meals on postprandial lipemia in metabolically healthy adults and individuals with CVD risk factors. The main finding of this analysis was that in individuals with increased CVD risk, SFA-rich meals often induced a stronger lipemic response than meals rich in unsaturated FAs. This appears to contradict the RaKo study, in which canola oil (rich in unsaturated FAs) induced a stronger postprandial TG response than coconut oil (rich in SFAs). The discrepancy is mainly attributable to two aspects. First, the review included mainly studies investigating fat sources other than canola oil and coconut oil, which limits the transferability of the results to the RaKo study. Second, fat sources categorized in the same class (e.g., SFA-rich) can differ considerably in their FA composition with regard to chain length and the induced postprandial metabolic response. Therefore, when investigating the postprandial metabolic effects of a specific fat source, the chain length of the contained FAs should be considered. Besides the main finding, the review confirmed the relevant influence of fat amount on lipemia.

The second review systematically investigated the impact of fat amount and FA composition on postprandial vascular function in healthy adults and individuals at increased CVD risk. The main findings were that flow-mediated dilation (FMD) and AIx decreased postprandially, and that the FA composition did not influence the postprandial vascular function in most studies. This is in accordance with the RaKo study, where parameters of arterial stiffness decreased, irrespective of FA composition of the test meals.

The RaKo study provides a comprehensive overview of the postprandial responses to meals enriched with canola oil and coconut oil. In conclusion, the results show that the amount of fat in a meal and its FA composition affect cardiometabolic risk factors in adults with a risk phenotype for CVDs. Canola oil and coconut oil induced different metabolic responses, and the strength and manner of their effects depended on the parameter. For a further physiological evaluation of dietary fats, more well-designed, highly standardized studies on the acute and longer-term metabolic effects of plant oils, conducted with different populations, are needed. Future studies should include the measurement of a wide range of physiological and immunological parameters.

8. Zusammenfassung

Der moderne Mensch verbringt den größten Teil des Tages im postprandialen Zustand, einem dynamischen Zeitraum nach der Nahrungsaufnahme, der durch Veränderungen in der Konzentration verschiedener Stoffwechselparameter im Blut gekennzeichnet ist. Die wichtigsten postprandialen Stoffwechselereignisse sind akute Anstiege der Konzentrationen an Triglyzeriden (TG), Glukose und Insulin (Lipämie, Glykämie und Insulinämie). Die postprandiale Stoffwechselreaktion wird durch verschiedene mahlzeitabhängige und mahlzeitenunabhängige Faktoren beeinflusst, darunter der Fettgehalt und die Fettsäurenzusammensetzung (FS-Zusammensetzung) der Mahlzeit sowie der individuelle Gesundheitszustand. Nach derzeitigem Kenntnisstand erhöht eine häufige übermäßige Nahrungsaufnahme das Risiko für Herz-Kreislauf-Erkrankungen (HKEs), primär durch übermäßige und andauernde metabolische, oxidative und immunologische Ungleichgewichte, einhergehend mit einer geringgradigen Entzündung und einer beeinträchtigten endothelialen Funktion. Daher könnten Strategien, welche die postprandiale Stoffwechselreaktion abmildern, dazu beitragen, sowohl das individuelle HKE-Risiko als auch die hierdurch verursachte soziale Belastung zu verringern.

Im Mittelpunkt dieser Arbeit stand eine randomisierte kontrollierte Crossover-Studie, in der die postprandialen metabolischen und vaskulären Auswirkungen von Rapsöl (reich an ungesättigten FS) und Kokosöl (reich an gesättigten Fettsäuren [SAFAs]) bei Personen mit einem Risikophänotyp für kardiometabolische Erkrankungen untersucht wurden. In der sogenannten RaKo-Studie verzehrten 29 Teilnehmer (70,0 ± 5,3 Jahre; 30,2 ± 2,6 kg/m^2) vier isoenergetische (∼4.200 kJ) und isonitrogene (∼27 g Protein) Mahlzeiten, die entweder mit 25 oder 50 g Rapsöl oder Kokosöl angereichert waren. Die Kombination verschiedener Fettmengen und Fettquellen resultierte in vier Testmahlzeiten: Rapsöl mit niedrigem Fettgehalt (LFM, von englisch *low-fat meal*), Kokosöl LFM, Rapsöl mit hohem Fettgehalt (HFM, von englisch *high-fat meal*), Kokosöl HFM. Im nüchternen Zustand und 1, 2, 3, 4, 5 sowie 6 Stunden nach der Nahrungsaufnahme wurden Blutproben zur Analyse von TG, Gesamtcholesterin, Low-Density-Lipoprotein-Cholesterin (LDL-Cholesterin), High-Density-Lipoprotein-Cholesterin (HDL-Cholesterin), nicht veresterten Fettsäuren (NEFAs), spezifischen FS, Glukose, Insulin, Homöostase-Modell zur Abschätzung der Insulinresistenz (HOMA-IR), Insulin-Glukose-Verhältnis, Interleukin-6 (IL-6), α- und γ-Tocopherol sowie der antioxidativen Kapazität (TEAC) entnommen. Die Parameter des Glukosestoffwechsels wurden zusätzlich 0,5 und 1,5 Stunden postprandial gemessen. Außerdem wurden die Karotis-Femoral-

Pulswellengeschwindigkeit (PWV_{c-f}) und der Augmentationsindex (AIx), beides Parameter der arteriellen Steifigkeit, im nüchternen Zustand und 2, 4 sowie 6 Stunden postprandial bestimmt. Die wesentlichen Ergebnisse waren, dass Rapsöl hinsichtlich Serum-TG und Plasma-IL-6 eine größere inkrementelle Fläche unter der Kurve (iAUC) auslöste als Kokosöl. Außerdem war die iAUC von Plasma-γ-Tocopherol nach Rapsölverzehr signifikant größer als nach Kokosölverzehr. Übereinstimmend mit der FS-Zusammensetzung der Testöle waren die Serumkonzentrationen von Laurin- und Myristinsäure nach Kokosölverzehr höher, während die Serumkonzentrationen von Öl-, Linol- und α-Linolensäure nach Rapsölverzehr höher waren. Die Kinetiken der Serum-TG und der Laurinsäure nach Kokosölverzehr unterstützen die Empfehlung, Laurinsäure aus physiologischer Sicht nicht als MCFA einzustufen, da sie biologisch als LCFA wirkt. Hinsichtlich der Auswirkungen der Fettmenge auf die postprandiale Antwort induzierten die HFMs eine stärkere Serum-TG-iAUC als die jeweiligen LFMs. Außerdem stiegen Plasmaglukose, Seruminsulin, HOMA-IR und das Insulin-Glukose-Verhältnis nach den LFMs stärker an als nach den HFMs, und die Serum-NEFAs sanken nach den LFMs stärker als nach den HFMs. Diese Effekte sind primär auf den höheren Gehalt an Kohlenhydraten (LFMs: 144,1 g vs. HFMs: 85,5 g) und Mono- und Disacchariden (LFMs: 73,2 g vs. HFMs: 39,9 g) in den LFMs zurückzuführen. Darüber hinaus zeigten die iAUC-Daten, dass das Serum-Gesamtcholesterin nach den LFMs stärker sank als nach den HFMs. Die Rapsöl HFM bewirkte einen stärkeren Anstieg von Plasma-γ-Tocopherol als die Rapsöl LFM. Es wurde kein Einfluss der Fettart oder der Fettmenge auf die iAUC-Daten von Serum-LDL-Cholesterin, Serum-HDL-Cholesterin, Plasma-TEAC und Plasma-α-Tocopherol beobachtet. PWV_{c-f} und AIx sanken postprandial, unabhängig von der Fettmenge und FS-Zusammensetzung der Testmahlzeiten.

In Ergänzung zur RaKo-Studie wurden im Rahmen dieser Dissertation zwei Literaturrecherchen durchgeführt. In der ersten Übersichtsarbeit wurden die Auswirkungen der Fettmenge und FS-Zusammensetzung von gemischten Mahlzeiten auf die postprandiale Lipämie bei stoffwechselgesunden Erwachsenen und Personen mit HKE-Risikofaktoren systematisch untersucht. Das zentrale Ergebnis dieser Analyse war, dass bei Personen mit erhöhtem HKE-Risiko SAFA-reiche Mahlzeiten häufig eine stärkere lipämische Reaktion hervorrufen als Mahlzeiten, die reich an ungesättigten FS sind. Dies scheint im Widerspruch zur RaKo-Studie zu stehen, in der Rapsöl (reich an ungesättigten FS) eine stärkere postprandiale TG-Antwort auslöste als Kokosöl (reich an SAFAs). Diese Diskrepanz ist hauptsächlich auf zwei Aspekte zurückzuführen. Erstens wurden in der Übersichtsarbeit hauptsächlich Studien berücksichtigt, die andere Fettquellen als Rapsöl und Kokosöl untersuchten, was die

Übertragbarkeit der Ergebnisse auf die RaKo-Studie einschränkt. Zweitens können sich Fettquellen, die in dieselbe Kategorie (z. B. SAFA-reich) eingeordnet werden, in ihrer FS-Zusammensetzung hinsichtlich der Kettenlänge und der induzierten postprandialen metabolischen Reaktion erheblich unterscheiden. Daher sollte bei der Untersuchung der postprandialen metabolischen Auswirkungen einer bestimmten Fettquelle die Kettenlänge der enthaltenen FS berücksichtigt werden. Neben dem zentralen Ergebnis bestätigte die Übersichtsarbeit den relevanten Einfluss der Fettmenge auf die Lipämie.

Die zweite Übersichtsarbeit untersuchte systematisch die Auswirkungen der Fettmenge und FS-Zusammensetzung auf die postprandiale Gefäßfunktion bei gesunden Erwachsenen und Personen mit erhöhtem HKE-Risiko. Die zentralen Ergebnisse waren, dass die flussvermittelte Vasodilatation (FMD) und der AIx postprandial sanken und dass die FS-Zusammensetzung in den meisten Studien keinen Einfluss auf die postprandiale vaskuläre Funktion hatte. Dies steht im Einklang mit der RaKo-Studie, in der die Parameter der arteriellen Steifigkeit sanken, unabhängig von der FS-Zusammensetzung der Testmahlzeiten.

Die RaKo-Studie bietet einen umfassenden Überblick über die postprandialen Antworten auf mit Rapsöl und Kokosöl angereicherte Mahlzeiten. Zusammenfassend zeigen die Ergebnisse, dass die Fettmenge und die FS-Zusammensetzung einer Mahlzeit kardiometabolische Risikofaktoren bei Erwachsenen mit einem Risikophänotyp für HKEs beeinflussen. Rapsöl und Kokosöl lösten unterschiedliche Stoffwechselreaktionen aus, wobei die Stärke und die Art der Effekte vom jeweiligen Parameter abhängig waren. Für eine weitere physiologische Bewertung von Nahrungsfetten sind mehr sorgfältig konzipierte, hoch standardisierte Studien zu den akuten und längerfristigen metabolischen Auswirkungen von Pflanzenölen erforderlich, die mit unterschiedlichen Bevölkerungsgruppen durchgeführt werden sollten. Künftige Studien sollten die Messung eines breiten Spektrums physiologischer und immunologischer Parameter umfassen.

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