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REVIEW

Dietary Monounsaturated Fatty Acids Are Protective Against Metabolic Syndrome and Cardiovascular Disease Risk Factors

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Abstract Over 50 years of research has sought to define the role dietary fat plays in cardiovascular disease (CVD) risk. Although optimal dietary fat quantity has been keenly pursued over past decades, attention has recently centered on the value of dietary fat quality. The purpose of the present review is to provide a critical assessment of the current body of evidence surrounding efficacy of dietary monounsaturated fatty acids (MUFA) for reduction of traditional risk factors defining metabolic syndrome (MetS) and CVD. Due to existing and emerging research on health attributes of MUFA rich diets, and to the low prevalence of chronic disease in populations consuming MUFA rich Mediterranean diets, national dietary guidelines are increasingly recommending dietary MUFA, primarily at the expense of saturated fatty acids (SFA). Consumption of dietary MUFA promotes healthy blood lipid profiles, mediates blood pressure, improves insulin sensitivity and regulates glucose levels. Moreover, provocative newer data suggest a role for preferential oxidation and metabolism of dietary MUFA, influencing body composition and ameliorating the risk of obesity. Mounting epidemiological and human clinical trial data continue to demonstrate the cardioprotective activity of the MUFA content of dietary fat. As the debate on the optimal fatty acid composition of the diet continues, the benefit of increasing MUFA intakes, particularly as a substitute for dietary SFA, deserves considerable attention.

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Abbreviations

ALA	Alpha-linolenic acid
BMI	Body mass index
CHD	Coronary heart disease
CHO	Carbohydrate
CVD	Cardiovascular disease
DM	Diabetes mellitus
HDL-C	High-density lipoprotein cholesterol
LF	Lower fat
LNA	Linoleic acid
LDL-C	Low-density lipoprotein cholesterol
MetS	Metabolic syndrome
MF	Moderate fat
MUFA	Monounsaturated fatty acids
OLA	Oleic acid
PUFA	Polyunsaturated fatty acids
SFA	Saturated fatty acids
STA	Stearic acid
TAG	Triglyceride
TC	Total cholesterol
TFA	Trans fatty acids

Introduction

Considerable scientific interest has focused on the impact of dietary fat in the development of metabolic disorders, leading to cardiovascular disease (CVD) [1, 2]. The complications associated with metabolic syndrome (MetS) are the primary foundation of CVD morbidity and

mortality. Dyslipidemia, hypertension, hyperglycemia, insulin resistance and obesity, namely abdominal obesity, are critical factors contributing to MetS. As MetS is a combination of modifiable risk factors, dietary intervention is targeted in primary prevention and secondary treatment therapies. Cumulative scientific evidence suggests that dietary monounsaturated fatty acids (MUFA) effect reductions in key risk factors for MetS [3–5]. Dietary MUFA promote a healthy blood lipid profile, mediate blood pressure, and favorably modulate insulin sensitivity and glycemic control. Conversely, the detrimental effects of diets rich in saturated fatty acids (SFA) have been widely recognized [6, 7]. Thus, national dietary guidelines with a primary focus on cardiovascular health have emphasized the need to reduce consumption of SFA as compared to a decrease in total dietary fat. With emerging research on the health attributes of MUFA rich diets, and the low prevalence of chronic disease in populations consuming MUFA rich Mediterranean diets [8], recommendations have been made to replace SFA intakes with unsaturated fats [9]. However, questions still remain as to the optimal dietary replacement for SFA, comparing MUFA intakes to those of polyunsaturated fatty acids (PUFA) and carbohydrates (CHO). Despite PUFA numerous cardiovascular benefits, intakes have been limited to $\leq$10% of energy due to potential adverse effects, including reduction of high-density lipoprotein cholesterol (HDL-C) levels and increased susceptibility of low-density lipoprotein (LDL) to oxidation [4, 10]. Furthermore, the replacement of dietary SFA with CHO may result in challenges in glucose metabolism and insulin resistance, as well as blood triglyceride (TAG) and HDL-C levels [11, 12]. Thus, potential health attributes of increasing MUFA intakes, particularly at the expense of dietary SFA, deserve careful attention. In light of the recent attention challenging the cardioprotective benefits of MUFA [13, 14], professional organizations continue to recommend dietary MUFA for the prevention of CVD [15, 16]. The purpose of the present review, therefore, is to critically assess the current evidence from human clinical trials surrounding the efficacy of dietary MUFA in the reduction of risk factors for MetS, ultimately targeting a reduction in CVD.

Metabolic Syndrome; Definition and Prevalence

The rising prevalence of chronic disease is related to unhealthy lifestyle choices, including atherogenic diets and lack of physical activity. Metabolic syndrome is defined by a collection of metabolic disorders occurring in an individual and associates with an increased risk of developing type 2 diabetes mellitus (DM-II) and CVD [17–19]. The primary clinical endpoint of MetS is CVD morbidity and mortality. Since the term was first classified by Reaven [20], the definition has evolved to include specific diagnostic criteria by several professional organizations. Recently, the National Cholesterol Education Program's Adult Treatment Panel III (NCEP ATP III) defines MetS as an individual possessing any three or more of the following five risk factors; elevated TAG [$\geq$150 mg/dL (1.7 mmol/L)], reduced HDL-C [<40 mg/dL (1.03 mmol/L) in men or <50 mg/dL (1.29 mmol/L) in women], elevated fasting glucose [$\geq$100 mg/dL (5.6 mmol/L)], hypertension ($\geq$130/85 mmHg or drug treatment), or obesity [waist circumference $\geq$102 cm (40 in) in men or $\geq$88 cm (35 in) in women] [20], with ethnicity specific values for waist circumference outlined by the International Diabetes Federation [21]. Furthermore, emerging risk factors for MetS include a proinflammatory and prothrombotic state [20]. Initially it was hypothesized that insulin resistance was the main risk factor for MetS [22], however, recent definitions propose abdominal obesity to be the predominate risk factor underlying MetS [20, 21, 23, 24]. The prevalence of MetS ranges worldwide [25], impacted by cultural differences associated with population dietary and lifestyle patterns. For example, the prevalence of MetS in the United States (34.5%) is approximately threefold that of Mediterranean countries [25–27]; predominated by the epidemic growth of obesity in the United States [28]. Currently, approximately 66% of the United States population are classified as overweight (BMI > 25 kg/m^2) and 33% obese (BMI > 30 kg/m^2) [29]. The components of the Mediterranean diet are fundamental to the lower prevalence of MetS [30]. Although the Mediterranean diet is complex in nature, rich in fruits, vegetables, and whole-grains, the MUFA content of Mediterranean diets accounts for 16–29% of energy [4], with olive oil providing 15–30% of energy [8]. Therefore, incorporating MUFA into Western dietary patterns, particularly at the expense of SFA, may target a reduction in risk for MetS and CVD.

Monounsaturated Fat; Structure and Sources

Monounsaturated fatty acids are classified as fatty acid chains containing one double bond. Monounsaturated fatty acids possess higher melting points than PUFA, which contain two or more double bonds. Both MUFA and PUFA are liquid at room temperature, whereas MUFA exist as semi-solids or solids when refrigerated. Conversely, SFA contain no double bonds and are solid at room temperature. Structurally, the common MUFA, palmitoleic acid (16:1n-7) and oleic acid (OLA; 18:1n-9), are both *cis* isomers of MUFA. The major dietary *trans* isomer of MUFA is elaidic

acid (*trans*18:1n-9). Oleic acid is the predominate MUFA in the diet, representing ~92% of *cis*MUFA [4]. Table 1 outlines the fatty acid content of food rich in MUFA. Of the MUFA rich dietary oils, the most commonly consumed are olive and canola oil. Furthermore, over the last decade an increase has occurred in commercial production of high OLA modified dietary oils with increased stability for the use in food processing, as a replacement to dietary oils rich in SFA and *trans* fatty acids (TFA) [31].

Current and Recommended Intakes of Dietary Fatty Acids

The total fat intake from Western diets is similar to that of the Mediterranean diet (Table 2), however, the type of dietary fat, specifically MUFA, differs vastly. In the United States, MUFA intakes are 13–14% of energy, SFA intakes are in excess at 11–12% of energy, and PUFA intakes are ≤7% of energy, of which 85–89% of PUFA intakes are

Table 1 Fatty acid composition of oils, nuts, seeds and fruit high in monounsaturated fat

	Calories (kcal)	Total fat (g)	SFA (g)	MUFA (g)	PUFA (g)	n-6 PUFA (g)	n-3 PUFA (g)
Vegetable oil							
Almond oil	884	100	8.2	69.9	17.4	17.4	0.0
Apricot oil	884	100	6.3	60.0	29.3	29.3	0.0
Avocado oil	884	100	11.6	70.6	13.5	12.5	1.0
Canola oil	884	100	7.4	63.3	28.1	19.0	9.1
Hazelnut oil	884	100	7.4	78.0	10.2	10.1	0.0
Olive oil	884	100	13.8	73.0	10.5	9.8	0.7
High-oleic canola oil	884	100	6.5	72.0	17.1	14.5	2.6
High-oleic safflower oil	884	100	6.2	74.6	14.4	14.4	0.0
High-oleic sunflower oil	884	100	9.7	83.6	3.8	3.6	0.2
Mid-oleic sunflower oil	884	100	9.0	57.3	29.0	29.0	0.0
Nuts and seeds[a]							
Almonds	597	52.8	4.0	33.7	12.6	12.6	0.0
Cashews	574	46.4	9.2	27.3	7.8	7.7	0.2
Hazelnuts	646	62.4	4.5	46.6	8.4	8.4	0.1
Macadamia nuts	718	76.1	11.9	59.3	1.5	1.3	0.2
Mixed nuts	594	51.5	6.9	31.4	10.8	10.5	0.2
Peanuts	585	49.7	6.9	24.6	15.7	15.7	0.0
Peanut butter (smooth)	588	50.4	10.3	23.7	13.9	13.8	0.1
Pistachios	571	46.0	5.6	24.2	13.9	13.6	0.3
Pecans	710	74.3	6.3	44.0	20.6	19.6	1.0
Sesame seeds	565	48.0	6.7	18.1	21.0	20.7	0.4
Tahini (sesame butter)	595	53.8	7.5	20.3	23.6	23.1	0.4
Walnuts (black)	618	59.0	3.4	15.0	35.1	33.1	2.0
Walnuts (English)	654	65.2	6.1	8.9	47.2	38.1	9.1
Fruit							
Avocado, raw	160	14.7	2.1	9.8	1.8	1.7	0.1
Olives, ripe	481	10.7	1.4	7.9	0.9	0.8	0.1
Selected animal products							
Ground beef, regular 100 g	259	16.3	5.7	7.5	0.6	0.5	0.1
Chicken breast, boneless skinless 100 g	690	3.57	1.0	1.2	0.8	0.7	0.1
Egg, large whole 50 g	324	5.3	1.6	2.0	0.7	0.6	0.1
Fried bacon, 3 slices	529	9.6	3.2	4.3	1.1	1.0	0.1

Source: USDA National Nutrient Database for Standard Reference. United States Department of Agriculture Website (http://www.nal.usda.gov/fnic/foodcomp/search/) Accessed 18 August 2009

MUFA monounsaturated fatty acids, *PUFA* polyunsaturated fatty acids, *SFA* saturated fatty acids

[a] All nuts and seeds are dry roasted, without salted added

Table 2 Current nutrient intakes in the Mediterranean and United States as compared to the recommended intakes outlined by health professional organizations

	Current Intakes			Recommended intakes					
	Mediterranean (%)[a]	United States (%)[a,b]	United States (g)[c]	Dietary guidelines (%)[a]	ADA and DC (%)[a]	NCEP ATP III (%)[a]	USDA's MyPyramid (g)[c]	NHLBI's dash eating plan (g)[c]	Harvard health eating pyramid (g)[c]
Total fat	33–40	33	83–87	20–35	20–35	25–35	64.8	41.1	69.0
SFA	<8	11–12	28–30	<10	<10	<7	17.3	10.0	12.8
MUFA	16–29	13–14	32–33	–	≤25	≤20	23.5	15.0	24.8
PUFA	<7	<7	17–18	–	≤10	≤10	19.6	12.6	25.7

ADA American Dietetic Association, *DASH* Dietary Approaches to Stop Hypertension, *DC* Dietitians of Canada, *MUFA* monounsaturated fatty acid, *NCEP ATPIII* National Cholesterol Education Program Adult Treatment Panel III, *NHLBI* National Heart, Lung, and Blood Institutes, *PUFA* polyunsaturated fatty acids, *SFA* saturated fatty acids, *USDA* United States Department of Agriculture

– Not specified, however supports recommendations by other expert organizations

[a] Percent of daily energy

[b] Means of United States male and females (ages 20–59) from the NHANES, 1999–2000

[c] Based on a ~2,000 kcal/day

omega-6 PUFA, principally linoleic acid (LNA) [4, 32, 33]. Conversely, the majority of total fat intake (33–40% of energy) in the Mediterranean diet is represented by MUFA, ranging from 16 to 29% of energy, with olive oil as the principal fat [4, 34, 35]. The high MUFA intake of the Mediterranean diet is at the expense of SFA, with intakes of SFA <8% of energy. Thus, an inverse relationship between the Mediterranean diet and coronary heart disease (CHD) risk has been substantiated in both epidemiological studies and randomized clinical trails [1].

Cardiovascular disease, the clinical outcome of MetS, remains the leading cause of mortality in the Western population [29] and therefore, several professional health organizations have outlined target fatty acid intakes to reduce MetS, DM and CVD risk (Table 2) [9, 36–41]. Recently, the recommendations focus on dietary fat quality versus fat quantity with less emphasis on high CHO diets. The American Diabetes Association (ADA) have modified their previous dietary recommendations for individuals with diabetes, which consisted of high CHO intakes and restricted total fat to ≤30% of energy, with SFA, MUFA, and PUFA at ≤10% of energy [42]. The ADA currently recommends that 60–70% of total calories in diets of those affected with DM-I and -II should be obtained from MUFA and CHO, emphasizing individualization of macronutrients by healthcare professionals [43, 44]. Moreover, the most recent position statement on dietary fatty acids from the ADA and Dietitians of Canada allows for total fat between 20 and 35% of energy, enhancing MUFA intakes up to 25% of energy [36]. The upper limit of total fat at 35% of energy is to minimize intakes of SFA, as well as an upper limit of PUFA intake at 10% of energy due to inconclusive scientific evidence supporting higher intakes of LNA for individuals with DM. Furthermore, the NCEP ATP III, endorsed by the American Heart Association (AHA), has recommended dietary guidelines for primary and secondary prevention of CHD with emphasis on monitoring total dietary fat and targeting a reduction in SFA. Similar to the ADA, earlier recommendations by the AHA, NCEP Step I and II diets, limited total fat intake to ≤30% and MUFA intake to ≤15% of energy [45]. However, in 2001 the NCEP released revisions to the ATP III guidelines [9] increasing total fat to 25–35% of energy, allowing a specific increase in MUFA intakes of up to 20% of energy, with a recommendation for replacing CHO with unsaturated fats for individuals with DM or MetS. Of interest, the current NCEP ATP III recommendations mirror the dietary fat profile of the Mediterranean diet (Table 2) [4, 34, 35]. Recently, the Joint FAO/WHO Expert Consultation on Fats and Fatty Acids in Human Nutrition recommended that MUFA intakes be 15–20% of energy, according to total fat intakes [46]. Unlike other fatty acids with a recommended limit, MUFA intakes should be determined by calculating the difference, i.e. MUFA (% energy) = Total Fat (% of energy) − SFA (% of energy) − PUFA (% of energy) − TFA (% of energy). Thus, MUFA intakes will range with respect to the total fat and fatty acid composition of the diet.

As mentioned, olive oil is the predominate fat in the Mediterranean diet, and although olive oil use is not as common in Western diets, MUFA rich canola oil use in the United States has increased 5.5-fold from 1985 to 1994 [32]. Canola oil, originally naturally bred from rapeseed oil and low in erucic acid, has grown to become the third largest consumed vegetable oil in the world and, next to soybean oil, canola oil is the second most consumed

vegetable oil in the United States. Canola oil can be regarded as one of the most healthy consumed vegetable oils with an attractive fatty acid profile distinctively low in SFA, and rich in MUFA and n-3 PUFA α-linolenic acid (ALA) (Table 1). Consequently, in 2006 the United States Food and Drug Administration (FDA) authorized a qualified health claim stating that canola oil (~19 g daily) may reduce the risk of CHD due its unsaturated fat content, recommending direct caloric replacement of dietary SFA with canola oil [47]. A recent dietary modeling study revealed that replacing common dietary fats in the United States with canola oil and canola-based spreads would increase the percentage of Americans complying with current dietary intake recommendations for fatty acids, namely SFA, MUFA, and ALA, but not for LNA [48]. More specifically, a 50% substitution of fats with canola oil would decrease SFA intakes by 4.7%, whereas a 100% substitution would decrease SFA and LNA intakes by 9.4 and 44.9%, respectively, while increasing MUFA and ALA intakes by 27.6 and 73.0%, respectively. Based on the emphasis of increasing the intakes of MUFA in the diet, particularly at the expense of SFA, it is timely and appropriate to explore the efficacy of MUFA rich diets in the prevention of MetS and CVD.

Monounsaturated Fat and Blood Lipids

Numerous randomized controlled trials have investigated the impact of dietary intervention on changes in circulating lipids [49–52]. The NCEP ATP III guidelines have outlined risk factors that increase CHD risk over a 10 year period. Traditionally, elevated LDL-C [>100 mg/dL (2.6 mmol/L)] remains the strongest primary factor in predicting CHD and therefore is a primary target of therapy [53]. However, as circulating TAG and HDL-C concentrations are critical risk factors in MetS, the TC:HDL-C ratio has been considered a more valuable marker in determining CHD risk [52]. Although the hypolipidemic effect of reducing dietary SFA is well-known and remains the primary target of dietary intervention [7], the debate as to whether MUFA, PUFA or CHO should replace SFA in the diet continues.

Effects of Monounsaturated Fat Compared with Saturated Fat

Evidence from randomized controlled trials has substantiated the deleterious effects of dietary SFA on circulating lipids and lipoproteins [49–51]. When MUFA isocalorically replace SFA in the diet there are improvements in the TC:HDL-C ratio, namely associated with a decrease in serum LDL-C levels and preservation of HDL-C levels. Recently, attention has focused on the lipidemic effects of individual SFA, as stearic acid (STA, 18:0) is considered to have neutral or hypolipidemic effects on circulating lipids compared with other SFA, namely lauric (12:0), myristic (14:0) and palmitic (16:0) acids [52, 54]. Although only a few studies have directly compared OLA to STA intakes, Hunter et al. [54] collectively showed that when OLA replaced STA, LDL-C levels decreased by 5–13% in 3 of 8 studies, however, had no effect in 5 other studies. HDL-C levels increased in one study between 5 and 7%, with no effect in 7 of 8 studies. Triglycerides decreased 20–37% in 2 studies; with no effect in 6 other studies. Finally, an estimated directional decrease in TC:HDL-C ratio was observed in 6 of the 8 studies when OLA replaced STA. Overall compared to OLA, STA tended to increase LDL-C and TAG levels, lower HDL-C levels, and resulted in an increase in the TC:HDL-C ratio. Thus, novel modified dietary oils with a high OLA content have been developed by agricultural and food industries to replace partially hydrogenated oils rich in TFA and SFA for use in food preparation, including frying, baking, and blending with other fats [31]. However, as there are specific food applications that require a solid fat (i.e. shortenings and baked goods), a high STA fat may provide an alternative to fat-containing TFA [54].

Dietary Monounsaturated Fat Versus Carbohydrate for Replacement of Saturated Fat

The effects on CHD risk with substitution of SFA by other macronutrients continue to be a primary focus of public health agendas [14, 52, 55]. Diets rich in CHO, PUFA and MUFA have been compared to those rich in SFA in assessing the ability of each dietary strategy to favorably alter plasma lipids. In studies conducted with healthy subjects comparing high MUFA diets to high CHO diets, those on high MUFA diets showed significant reductions in TAG levels [56–58]. Likewise, overweight and obese subjects [59], those with DM-II [5, 60, 61], and MetS [62] also benefitted from the substitution of MUFA rich diets, as compared to CHO rich diets, in improving plasma TAG levels. One of the main cardioprotective activities of high MUFA diets is the ability of MUFA to either preserve or increase HDL-C levels when compared to CHO rich diets which mostly produce decreases in HDL-C levels [5, 56, 60, 62, 63]. As compared to high CHO diets, high MUFA diets more favorably affect the TC:HDL-C ratio, emphasized by a reduction in LDL-C and TAG levels, while increasing HDL-C levels [52]. Recently, Cao et al. [64] conducted a meta-analysis of 30 controlled-feeding studies in subjects with and without diabetes, comparing moderate fat (MF) (30.2–50% of energy; mean MUFA intake 23.6%

of energy) versus lower fat (higher CHO) diets (LF) (18.3–30.2% of energy; mean MUFA intake 11.4% of energy). In all subjects, reductions in LDL-C levels were similar between the MF and LF diets. However, the MF diet increased HDL-C levels (2.28 mg/dL; 95% CI 1.66–2.90 mg/dL) and decreased TAG levels (−9.36 mg/dL; 95% CI −12.16 to −6.08 mg/dL) versus the LF diet. Moreover, in subjects with diabetes, a further decrease in TAG levels (−24.79 mg/dL) was observed after the MF diet, as well as a decrease in the TC: HDL-C ratio (−0.62) and non-HDL-C (−5.39%) versus the LF diet. The authors concluded that MF diets reduced predicted CHD risk by 6.37% in men and 9.34% in women, including subjects with diabetes, compared with the LF diet. Therefore, MUFA versus CHO replacement for SFA may be more beneficial for individuals predisposed to MetS or with DM-II [5, 53].

Dietary Monounsaturated Fat Versus Polyunsaturated Fat for Replacement of Saturated Fat

Comparison studies and reviews have also examined the action of PUFA rich versus MUFA rich diets on plasma lipid modulation [4, 52, 65–67]. Evidence supports the notion that MUFA rich diets have slightly less or comparable TC and LDL-C lowering effects to those of PUFA rich diets. Whereas n-3 PUFA rich diets may additionally reduce serum TAG [68], MUFA rich diets have more favorable effects on HDL-C concentrations. The ability to effectively target an increase in plasma HDL-C is critical in patients with MetS, DM-II and the prevention of CVD [69, 70]. When PUFA and MUFA rich diets were compared for replacement of dietary SFA in healthy adult subjects, those consuming MUFA rich diets demonstrated a preservation of HDL-C levels to a greater extent with only a 4% decrease in HDL-C levels compared to those consuming PUFA rich diets, which decreased HDL-C levels by 14% [71]. Thus, due to the preservation of HDL-C with MUFA versus PUFA rich diets, effects on the TC:HDL-C ratio where comparable when either MUFA or PUFA replaced dietary SFA [52, 71].

Dietary Monounsaturated Fat and Blood Pressure

Evidence from human clinical studies have shown that dietary MUFA either have neutral or hypotensive effects when compared to diets rich in CHO, n-6 or n-3 PUFA, notably reporting consistent reductions in blood pressure when MUFA are compared to SFA rich diets (Table 3). A study comparing hypertensive subjects consuming MUFA and PUFA rich diets revealed that virgin olive oil high in OLA resulted in significant decreases in total blood pressure [72]. The hypotensive effect of MUFA also alleviated the need of anti-hypertensive drug therapy by 48%, whereas all subjects on a PUFA rich diet required further drug therapy. In contrast, a study conducted by Mutanen et al. [73] failed to observe hypotensive effects of either MUFA or PUFA rich diets in normotensive subjects. Among the studies comparing MUFA and PUFA rich diets, hypotensive benefits of MUFA rich diets are observed in individuals predisposed to MetS in 2 clinical trials, whereas 4 of 5 clinical trials observed no difference between MUFA and PUFA diets in healthy individuals (Table 3).

The effects of MUFA versus CHO rich diets on blood pressure were compared in a meta-analysis by Shah et al. [74]. Of the 10 intervention trials assessed, MUFA rich diets were associated with a slight reduction in blood pressure, specifically systolic blood pressure, compared to the CHO rich diets. Similarly, in this review, 3 of 6 clinical trials observed hypotensive benefits with MUFA rich diets compared to CHO rich diets in individuals predisposed to MetS (Table 3). Muzio et al. [75] compared consumption of high MUFA diets to high CHO diets in 100 obese subjects with MetS over 5 months. At study cessation, while both groups showed significant reductions in all components of MetS, only the diet high in MUFA produced a significantly lower systolic blood pressure, as well as lowered heart rate. In the large randomized, crossover Omni Heart Trial, 164 subjects with prehypertension or stage-1 hypertension consumed diets varying in dietary fats for 6 weeks to determine their subsequent risk of hypertension [76]. Compared to a high CHO diet, consumption of high protein and MUFA diets produced significant reductions in systolic blood pressure and additional benefits in TAG and HDL-C levels.

Considering prospective cohort studies, the SUN (Seguimiento Universidad de Navarra) study of nearly seven thousand subjects reported that high intake of olive oil for an average of 28.5 months was associated with a decrease in the incidence of hypertension in men, but not women [77]. Similarly, in the Greek EPIC (European Prospective Investigation into Cancer and Nutrition) study, olive oil consumption was a primary dietary factor in the Mediterranean diet preventing hypertension [78]. More specifically, a reduction in both systolic and diastolic blood pressure was noted with olive oil consumption, even after controlling for vegetable intake. Alongside, there was an inverse relationship between blood MUFA:SFA ratio and arterial blood pressure. Indeed, olive oil in Mediterranean diets has potent hypotensive effects [79]. However, the OLA content of olive oil, independent of its other components, has been shown to be directly associated with a reduction in blood pressure [80]. As such, strong support can be obtained from clinical trials of the blood pressure

Table 3 Human clinical trials investigating the effects of monounsaturated fat and hypertension

Reference	Subject characteristics	Study design/ duration	Diets	Outcome
Individuals predisposed to metabolic syndrome				
Gulseth et al. [125]	MetS subjects ($n = 486$)	Randomized, parallel 12 weeks	MUFA 39% fat; 10% SFA, 19% MUFA, 7% PUFA SFA 40% fat; 18% SFA, 13% MUFA, 6% PUFA H-CHO 30% fat; 9% SFA, 12% MUFA, 6% PUFA H-CHO + n-3 PUFA 29% fat; 9% SFA, 11% MUFA, 6% PUFA, 1.6 g/d EPA + DHA	No difference in systolic BP or diastolic BP between diets ↓ Pulse pressure with MUFA vs. SFA in men
Brehm et al. [94]	Overweight or obese with DM-II subjects ($n = 124$)	Randomized, parallel 12 months	MUFA 38% fat; 14% MUFA H-CHO 28% fat; 8% MUFA	No difference in diastolic BP between diets
Muzio et al. [75]	Hypercholesterolemic obese subjects with MetS ($n = 100$)	Randomized 5 months	H-CHO 22% fat; 5% SFA, 14% MUFA, 3% PUFA MUFA 33% fat; 9% SFA, 21% MUFA, 4% PUFA	↓ Systolic BP and HR with MUFA vs. H-CHO
Appel et al. [76]	Pre-HT or HT (stage 1) subjects ($n = 164$)	Randomized, crossover 6 weeks	H-CHO 27% fat; 6% SFA, 13% MUFA, 8% PUFA Protein 27% fat; 6% SFA, 13% MUFA, 8% PUFA MUFA 37% fat; 6% SFA, 21% MUFA, 10% PUFA	↓ Systolic and diastolic BP with MUFA and protein vs. CHO in all subjects
Shah et al. [126]	DM-II subjects ($n = 41$)	Randomized, crossover 6 weeks, then 14 weeks	H-CHO 30% fat; 10% SFA, 10% MUFA, 10% PUFA MUFA 45% fat; 10% SFA, 25% MUFA, 10% PUFA	No difference in BP between diets at 6 weeks ↑ Diastolic BP and heart rate at 14 weeks with H-CHO vs MUFA
Piers et al. [106]	Overweight or obese men ($n = 8$)	Randomized, crossover 4 weeks	SFA 40% fat; 24% SFA, 13% MUFA, 3% PUFA MUFA 40% fat; 11% SFA, 22% MUFA, 7% PUFA	↓ Mean arterial pressure and diastolic BP with MUFA vs. SFA
Ferrara et al. [72]	HT subjects ($n = 23$)	Randomized, crossover 6 months	MUFA 27% fat; 6% SFA, 17% MUFA, 4% PUFA PUFA 27% fat; 6% SFA, 11% MUFA, 11% PUFA	↓ Systolic and diastolic BP with MUFA vs. PUFA ↓ HT drug treatment with MUFA but not PUFA

Table 3 continued

Reference	Subject characteristics	Study design/ duration	Diets	Outcome
Thomsen et al. [127]	DM-II subjects ($n = 16$)	Randomized, crossover 3 weeks	MUFA 49% fat; 10% SFA, 30% MUFA, 7% PUFA PUFA 49% fat; 9% SFA, 10% MUFA, 27% PUFA	↓ Arterial BP with MUFA vs. PUFA
Walker et al. [128]	DM-II subjects ($n = 24$)	Randomized, crossover 12 weeks	H-CHO 23% fat; 9% SFA, 10% MUFA, 4% PUFA MUFA 36% fat; 11% SFA, 20% MUFA, 5% PUFA	No differences in BP between diets
Healthy individuals				
Rasmussen et al. [129]	Healthy subjects ($n = 162$)	Randomized, parallel 3 months	SFA 37% fat; 17% SFA, 14% MUFA, 6% PUFA MUFA 37% fat; 8% SFA, 23% MUFA, 6% PUFA Further randomization with n-3 PUFA (fish oil): 3.6 g/d	↓ Systolic and diastolic BP with MUFA from baseline ↔ BP with SFA from baseline ↓ Diastolic BP with MUFA vs. SFA ↔ BP with addition of fish oil supplementation
Aro et al. [130]	Healthy subjects ($n = 87$)	Randomized, parallel 8 weeks	Control 20% fat; 8% SFA, 8% MUFA, 3% PUFA MUFA 26% fat; 7% SFA, 14% MUFA, 3% PUFA PUFA 26% fat; 8% SFA, 8% MUFA, 8% PUFA	No differences in BP between diets
Lahoz et al. [131]	Healthy subjects ($n = 42$)	4 Consecutive diet phases 5 weeks	SFA 35% fat; 17% SFA, 14% MUFA, 4% PUFA MUFA 35% fat; 9% SFA, 21% MUFA, 4% PUFA n-6 PUFA 35% fat; 10% SFA, 12% MUFA, 13% PUFA n-3 PUFA 35% fat; 9%SFA, 12% MUFA, 13% PUFA (1.6% n-3 PUFA)	↓ Systolic BP with MUFA vs. SFA and n-6 PUFA

Table 3 continued

Reference	Subject characteristics	Study design/ duration	Diets	Outcome
Uusitupa et al. [132]	Healthy subjects ($n = 159$)	Randomized, parallel 6 months	SFA 35% fat; 14:19:4 SFA:MUFA:PUFA AHA diet 32% fat; 10:8:8 SFA:MUFA:PUFA MUFA 34% fat; 11:11:5 SFA:MUFA:PUFA Low-fat 30% fat; 12:8:3 SFA:MUFA:PUFA	↓ Systolic BP with AHA only ↑ BP with SFA in men only
Mutanen et al. [73]	Healthy subjects ($n = 59$)	Randomized, crossover 3.5 weeks	MUFA 38% fat; 13% PUFA PUFA 38% fat; 16% MUFA	No differences in BP between diets
Mensink et al. [133]	Healthy subjects ($n = 58$)	Randomized, parallel 5 weeks	MUFA 36% fat; 13% SFA, 15% MUFA, 8% PUFA PUFA 36% fat; 13% SFA, 11% MUFA, 13% PUFA	No differences in BP between diets
Mensink et al. [134]	Healthy subjects ($n = 47$)	Randomized, parallel 5 weeks	H-CHO 22% fat; 7% SFA, 9% MUFA, 5% PUFA MUFA 41% fat; 10% SFA, 24% MUFA, 5% PUFA	No differences in BP between diets

Direction of effect on biomarkers of hypertension (↑ increased; ↓ decreased; ↔ no effect)

AHA American Heart Association, *BP* blood pressure, *CHO* carbohydrate, *DM-II* Diabetes Mellitus-II, *H-CHO* high-carbohydrate, *HT* hypertensive, *HR* heart rate, *MetS* metabolic syndrome, *MUFA* monounsaturated fatty acids, *PUFA* polyunsaturated fatty acids, *SFA* saturated fatty acids, *vs* versus

lowering effects of MUFA rich diets in both normotensive and hypertensive individuals.

Monounsaturated Fats, Insulin Resistance and Diabetes Mellitus-II

With the rising prevalence of DM worldwide [81], MUFA have gained attention for their ability to regulate glycemic response and improve insulin sensitivity. Similar to the detrimental effects on circulating lipids, SFA have been shown to impair glycemic control and insulin sensitivity [12], specifically in skeletal muscle cells [82]. Therefore, clinical trials replacing dietary SFA with MUFA have noted improvements in insulin sensitivity and glycemic response in individuals predisposed to insulin resistance [83–86], as well as healthy people [87–91] (Table 4). The KANWU (Kuopio, Aarhus, Naples, Wollongong and Uppsala) Study of 162 healthy subjects reported a reduction in insulin sensitivity following consumption of a SFA rich diet for 3 months, and that replacement of SFA with a MUFA rich diet improved insulin sensitivity [89]. More specifically, when total daily fat intake was <37% of energy, an 8.8% increase in insulin sensitivity was observed with the MUFA rich diet, whereas the SFA rich diet decreased insulin sensitivity by 12.5%. However, these effects were not observed when total daily fat intakes exceeded 37% of energy. In the development of DM-II, pancreatic β-cells that secrete insulin to counteract postprandial rises in blood glucose become overwhelmed and as a result, fail to effectively provide the necessary insulin to regulate glucose levels [92]. Recently, MUFA was shown to have a direct action on β-cell function and lower

Table 4 Human clinical trials investigating the effects of monounsaturated fat on glucose and insulin responses

Reference	Subject characteristics	Study design/ duration	Diets	Outcome
Individuals predisposed to metabolic syndrome				
Brehm et al. [94]	Obese and overweight subjects with DM-II ($n = 124$)	Randomized 1 year	H-CHO 28% fat; 7–9% MUFA MUFA 38% fat; 14–15% MUFA	No differences in glucose and insulin sensitivity between groups
Due et al. [83]	Nondiabetic obese subjects ($n = 46$)	Randomized, parallel 6 months	SFA 32% fat; 15% SFA, 10% MUFA, 4% PUFA MUFA 39% fat; 7% SFA, 20% MUFA, 8% PUFA Low-fat 23% fat; 8% SFA, 8% MUFA, 5% PUFA	↓ Fasting glucose, insulin, and insulin resistance score with MUFA vs. other diets ↓ HOMA-IR with MUFA vs. other diets
Paniagua et al. [84]	Obese DM-II subjects ($n = 11$)	Randomized, crossover 28 days	SFA 38% fat; 23% SFA, 9% MUFA, 6% PUFA MUFA 38% fat; 9% SFA, 23% MUFA, 6% PUFA H-CHO 20% fat; 6% SFA, 8% MUFA, 6% PUFA	↓ Fasting glucose with MUFA and H-CHO vs. SFA ↑ Insulin sensitivity (↓ HOMA-IR) with MUFA vs. other diets ↑ Postprandial GLP-1 with MUFA vs. H-CHO
Shah et al. [85]	DM-II subjects ($n = 11$)	Randomized, crossover 15 days	SFA 50% fat; 26% SFA, 20% MUFA, 5% PUFA MUFA 50% fat; 7% SFA, 39% MUFA, 5% PUFA n-6 PUFA 50% fat; 4% SFA, 8% MUFA, 39% PUFA n-3 PUFA 50% fat; 9% SFA, 15% MUFA, 44% PUFA	↓ Postprandial insulin response with MUFA and n-3 PUFA vs. SFA and n-6 PUFA ↔ Postprandial glucose response between diets
Vega-Lopez et al. [135]	Hyperlipidemic subjects ($n = 15$)	Randomized, crossover 5 weeks	TFA 30% fat; 9% SFA, 10% MUFA, 8% PUFA, 4% TFA SFA 30% fat; 15% SFA, 11%MUFA, 4% PUFA MUFA 32% fat; 6% SFA, 15% MUFA, 9% PUFA PUFA 28% fat; 7% SFA, 8% MUFA, 12% PUFA	No difference in fasting insulin, fasting glucose, or HOMA between diets

Table 4 continued

Reference	Subject characteristics	Study design/ duration	Diets	Outcome
Gerhard et al. [136]	DM-II subjects ($n = 11$)	Randomized, crossover 6 weeks	Low-fat 20% fat; 4% SFA, 8% MUFA, 6% PUFA MUFA 40% fat; 6% SFA, 25% MUFA, 6% PUFA	No difference in fasting glucose, glycemic control or insulin sensitivity between diets
Thomsen et al. [137]	Overweight subjects with DM-II ($n = 12$)	Randomized, crossover $\geq$1 week	SFA MUFA	↔ Glucose or insulin responses between diets ↑ GLP-1 responses with MUFA vs. SFA
Lovejoy et al. [138]	Healthy, normal and overweight subjects ($n = 25$)	Randomized, crossover 4 weeks	SFA 28% fat; 9% SFA MUFA 28% fat; 9% MUFA TFA 28% fat; 9% TFA	↔ Insulin sensitivity between diets ↓ Insulin sensitivity with SFA vs. MUFA for overweight subjects
Lauszus et al. [139]	Pregnant women with gestational DM-II ($n = 27$)	Randomized From 33rd gestational week for 5 weeks	H-CHO 30% fat; 13% SFA, 11% MUFA, 6% PUFA MUFA 37% fat; 10% SFA, 22% MUFA, 5% PUFA	No difference in fasting insulin and glucose, insulin sensitivity between diets
Rodriguez-Villar et al. [140]	DM-II subjects ($n = 12$)	Randomized, crossover 12 weeks	CHO 29% fat; 6% SFA, 12% MUFA, 5% PUFA MUFA 40% fat; 8% MUFA, 25% MUFA, 5% PUFA	No differences in fasting or postprandial glucose and insulin between diets
Luscombe et al. [141]	DM-II subjects ($n = 21$)	Randomized, crossover 4 weeks	CHO (high GI diet) 21% fat; 8% SFA, 7% MUFA, 4% PUFA CHO (low GI diet) 23% fat; 8% SFA, 7% MUFA, 4% PUFA MUFA (high GI diet) 35% fat; 8% SFA, 18% MUFA, 7% PUFA	No difference in fasting insulin and glucose between diets
Christiansen et al. [86]	DM-II and obese subjects ($n = 16$)	Randomized, crossover 6 weeks	SFA 30% fat; 20% SFA, 5% MUFA, 5% PUFA MUFA 30% fat; 5% SFA, 20% MUFA, 5% PUFA TFA 30% fat; 5% SFA, 20% TFA, 5% PUFA	↔ Glycemic control or postprandial glycemic response between diets ↓ Postprandial insulinemia with MUFA vs. SFA and TFA

Table 4 continued

Reference	Subject characteristics	Study design/ duration	Diets	Outcome
Sarkkinen et al. [142]	IGM subjects ($n = 22$)	Randomized 8 weeks	SFA 37% fat; 18%SFA, 11% MUFA, 5% PUFA MUFA 40% fat; 11% SFA, 19% MUFA, 8% PUFA PUFA 34% fat; 11% SFA, 10% MUFA, 10% PUFA	↓ Fasting glucose with MUFA vs. SFA ↔ Fasting glucose with PUFA vs. SFA ↑ Glucose effectiveness with MUFA vs. PUFA
Parillo et al. [143]	DM-II subjects ($n = 10$)	Randomized 15 days	H-CHO 20% fat MUFA 40% fat	↓ Fasting glucose and insulin with MUFA vs. H-CHO
Bonanome et al. [144]	DM-II subjects ($n = 19$)	Consecutive diets 2 months	H-CHO 25% fat; 10% SFA, 10% MUFA, 5% PUFA MUFA 40% fat; 10% SFA, 25% MUFA, 5% PUFA	↔ Fasting glucose or insulin response between diets
Garg et al. [60]	DM-II subjects ($n = 10$)	Randomized 28 days	H-CHO 25% fat MUFA 50% fat; 33% MUFA	↓ Plasma glucose and insulin requirements with MUFA vs. H-CHO
Healthy individuals				
Lopez et al. [87]	Healthy men ($n = 14$)	Randomized, crossover Single meal 8 h	NCEP Step-I diet 29% fat Butter diet 38% fat; 0.48 MUFA:SFA High-palmitic sunflower oil diet 38% fat; 2.42 MUFA:SFA Refined olive oil diet 38% fat; 5.43 MUFA:SFA Vegetables/fish oil diet 38% fat; 7.08 MUFA:SFA	↑ Postprandial β-cell function and insulin sensitivity with an increase in the MUFA to SFA ratio of dietary fats
Perez-Jimenez et al. [88]	Healthy subjects ($n = 59$)	Randomized, crossover 28 days	SFA 20% SFA, 12% MUFA, 6% PUFA H-CHO 28% fat; 10% SFA, 12% MUFA, 6% PUFA MUFA 38% fat; 10% SFA, 22% MUFA, 6% PUFA	↑ Fasting insulin and mean glucose for the SFA vs. MUFA and H-CHO Improvement in insulin sensitivity with MUFA and H-CHO vs. SFA

Table 4 continued

Reference	Subject characteristics	Study design/ duration	Diets	Outcome
Vessby et al. [89]	Healthy subjects ($n = 162$)	Randomized 3 months	SFA 37% fat; 18% SFA, 13% MUFA, 5% PUFA MUFA 37% fat; 10% SFA, 21% MUFA, 5% PUFA	↓ Insulin sensitivity with SFA vs. MUFA ↔ Insulin secretion between diets
Salas et al. [90]	Healthy men ($n = 41$)	Consecutive diets 4 weeks	SFA 38% fat; 20% SFA MUFA 38% fat; 22% MUFA NCEP Step-I 47% CHO, 28% fat	↑ Insulin on SFA diet ↓ Fasting glucose and insulin with MUFA vs. NCEP Step-I diet
Thomsen et al. [95]	Healthy subjects ($n = 16$)	Randomized, crossover 4 weeks	H-CHO 28% fat; 9% SFA, 8% MUFA, 7% PUFA MUFA 42% fat; 9% SFA, 24% MUFA, 6% PUFA	↔ Insulin sensitivity between diets ↔ Fasting blood glucose between diets
Thomsen et al. [145]	Healthy subjects ($n = 10$)	Randomized Single meal 8 h	CHO SFA MUFA	↔ Postprandial glucose or insulin response between diets ↑ GLP-1 and GIP responses with MUFA vs. SFA
Louheranta et al. [146]	Healthy women ($n = 15$)	Randomized, crossover 4 weeks	SFA 39%fat; 19% SFA, 12% MUFA, 6% PUFA MUFA 41% fat; 13% SFA, 19% MUFA, 6% PUFA	↔ Glucose or insulin responses between diets ↔ Insulin sensitivity between diets
Joannic et al. [147]	Healthy men ($n = 8$)	Randomized, crossover Single meal 3 h	MUFA 47% fat; 4.3 MUFA:PUFA PUFA 47% fat; 0.4 MUFA:PUFA	↓ Postprandial glucose and insulin responses with PUFA vs. MUFA
Uusitupa et al. [91]	Healthy subjects ($n = 10$)	Randomized, crossover 3 weeks	SFA 39% fat; 20% SFA, 12% MUFA, 4% PUFA MUFA 40% fat; 9% SFA, 19% MUFA, 10% PUFA	↓ Glucose AUC with MUFA vs. SFA ↑ Glucose disappearance rate with MUFA vs. SFA

Direction of effect on biomarkers of glucose and insulin responses (↑ increased; ↓ decreased; ↔ no effect)

AUC area under curve, *CHO* carbohydrate, *DM-II* diabetes mellitus-II, *GI* glycemic index, *GIP* gastric inhibitory polypeptide, *GLP-1* glucagon-like peptide-1, *H-CHO* high-carbohydrate, *HOMA-IR* homeostasis model assessment of insulin resistance, *IGM* irregular glucose metabolism, *MUFA* monounsaturated fatty acid, *NCEP* National Cholesterol Education Program, *PUFA* polyunsaturated fatty acids, *SFA* saturated fatty acids, *TFA* trans fatty acids, *vs* versus

insulin resistance in a study of 14 healthy men using a randomized, crossover design [87]. Data revealed that MUFA improved insulin sensitivity and β-cell function when compared with SFA. With the incremental substitution of MUFA for SFA, direct linear decreases in insulin resistance were observed.

As a replacement for dietary SFA, high MUFA diets have been compared to high CHO diets for preventing insulin resistance and DM-II risk [3, 5]. An earlier meta-analysis of 10 randomized controlled trials by Garg [5], assessing the effects of high MUFA diets in patients with either DM-I or DM-II, reported improvements in glycemic control, as well as lipoprotein profiles, as compared to high CHO diets. Ros [3] reviewed the evidence on dietary MUFA and metabolic control in DM-II following the comprehensive meta-analysis by Garg [5] and observed similar beneficial metabolic effects of MUFA rich diets. Following these analyses, Paniagua et al. [84, 93] demonstrated that compared to SFA or CHO rich diets, insulin resistant subjects consuming a MUFA rich diet exhibited improvements in insulin sensitivity, as well as other hormonal and metabolic parameters. Similarly, when compared to high CHO and high SFA diets, diets high in MUFA have been shown to significantly decrease fasting glucose by 3% and insulin by 9.4%, and improve insulin sensitivity by 12.1% [83]. In contrast, clinical trials with healthy subjects have observed no difference between MUFA and CHO rich diets in markers of glucose–insulin homeostasis [88, 94, 95]. However, due to other metabolic abnormalities associated with high CHO diets, such as the deleterious effects on plasma TAG and HDL-C levels [11] high MUFA diets may be more beneficial for ameliorating the risk of DM-II. Taken together, evidence from prospective cohort studies have reported that dietary MUFA are not associated with increased risk of DM-II in men [96] or women [97] after adjustment for other dietary fats, age and BMI.

Monounsaturated Fat in Weight Maintenance and Obesity

There is a perception that fat, rich in calories as compared to CHO or protein, is associated with body weight gain leading to obesity [98]. However, a strong argument also exists that dietary fat is not the primary cause of the high prevalence of obesity [99, 100]. Moreover, fat quality may have a stronger correlation to weight gain than fat quantity [101]. Considering fat quality and specific effects of dietary fatty acids for risk of obesity, evidence from prospective cohort studies have reported that MUFA intake is not associated with increases in waist circumference or body weight gain [101, 102]. In the Health Professionals Study of 16,587 men over a 9 year period, replacement of 2% energy of PUFA or CHO with MUFA was not associated with any change in waist circumference, whereas replacement with TFA or SFA led to an increase [102]. Similarly, in the Nurses' Health Study, consumption of MUFA, as well as PUFA, was not associated with an increase in body weight, while TFA and SFA positively correlated with weight gain after 8 years [101]. Large prospective cohort studies in the Mediterranean region have revealed that high intakes of olive oil [103] or nuts [104], both rich sources of MUFA, or adherence to a Mediterranean diet [105] were not associated with an increase in weight or risk of obesity over the longer term [103, 104].

With respect to human clinical trials, Paniagua et al. [93] have demonstrated that compared to CHO rich diets, insulin resistant subjects consuming a MUFA rich diet showed significantly increased fat oxidation rates and decreased abdomen-to-leg adipose ratios, thus preventing central body fat distribution [93]. This finding has important implications for those at risk for MetS since the increase in central adiposity was associated with a reduction in adiponectin expression and insulin sensitivity following the CHO rich diet as compared to the MUFA rich diet. An inverse relationship has been shown between circulating adiponectin levels and body fat percentage as well as central body fat accumulation, specifically visceral adiposity. Similarly, Piers et al. [106] substituted a SFA rich diet with MUFA for 4 weeks in eight overweight and obese men using a randomized crossover design to determine the effects on body weight and composition. Assessment of body composition by dual energy X-ray absorptiometry (DEXA) revealed a significant decrease in body mass (-2.1 ± 0.4 kg; $p = 0.0015$) and fat mass (-2.6 ± 0.6 kg; $p = 0.0034$) following the MUFA compared to the SFA rich diet, albeit no differences in total energy or fat intake were noted between diets. Furthermore, the changes in body mass and fat mass were accompanied with a decrease in waist-to-hip ratio after the MUFA rich versus the SFA rich diets. The favorable modifications in body composition and amelioration of weight gain after consumption of MUFA compared to SFA have also been observed in healthy subjects [107].

Of interest and as extensively reviewed by Bergouignan et al. [82], MUFA is the primary fat composing adipose tissue, however, there appears to be no direct relation between MUFA intake and MUFA levels in adipose. Rather SFA intake seems to be more closely associated with endogenous MUFA levels [108, 109]. Bergouignan et al. [82] hypothesized that in vivo desaturation of SFA may be related to an increase in MUFA versus SFA in adipose tissue. Furthermore, OLA preferentially accumulates in subcutaneous fat versus visceral fat, whereas the reverse exists with palmitate [110, 111]. Thus, since a direct correlation exists between visceral fat and risk factors for metabolic syndrome [112], OLA concentrating in subcutaneous fat versus visceral fat may be less atherogenic. Moreover, dietary MUFA may be preferentially oxidized as compared to other dietary fatty acids, as the degree of fatty acid chain length and unsaturation may

contribute to the partitioning of dietary fat to energy expenditure versus energy storage [107, 113–116]. Furthermore, the metabolism of dietary fat stimulates behavioral changes in food intake preference [117]. Indeed, evidence suggests that different dietary fats may elicit varying effects on satiety and total energy intake [118]. Taken together, dietary MUFA consumption is associated with maintenance of body weight and favorable shifts in reducing central body fat adiposity, potentially ameliorating obesity risk.

Monounsaturated Fats and Cardiovascular Risk; Epidemiological Evidence

As effects on risk markers may not directly translate into effects on clinical outcomes of disease, it is thus critical to assess effects of dietary MUFA on the primary clinical endpoint of MetS, that is CVD morbidity and mortality. Randomized controlled trials are considered the gold standard for evaluating the causal relationship between dietary intervention and chronic disease endpoints in humans; however, to date no randomized controlled trials have investigated dietary MUFA on CVD morbidity and/or mortality as the clinical endpoint [1]. Consequently, Rudel et al. [119] have challenged the cardioprotective effects of MUFA, observing equal coronary artery atherosclerotic effects between dietary MUFA and SFA in nonhuman primates. However, it is acknowledged that results from experimental animal models may not always extrapolate to humans. Considering the substantial evidence presently reviewed supporting the beneficial effects of dietary MUFA on risk factors for MetS and CVD, additional evidence is needed to uncover the discrepancy between human epidemiological evidence and experimental animal models. The following literature discusses the evidence from ecological and prospective cohort studies on effects of MUFA and CVD risk.

Ecological Studies

In a landmark epidemiological trial of 11,579 men aged 40–59 in the Seven Countries study, Keys et al. [8] presented important data revealing that areas consuming a Mediterranean diet rich in OLA from olive oil, even though higher in total fat (33–40% of energy), exhibited lower incidence of CHD mortality. Indeed, in this 15 year follow-up trial, data continued to emphasize the strong inverse relationship between dietary MUFA, as well as the ratio of dietary MUFA to SFA, and incidence of CHD mortality. Conversely, Hegsted and Ausman [120] reported a positive correlation between dietary MUFA and CHD mortality in men aged 35–74 from 18 countries. It is important, however, to note the authors emphasized a rather high correlation between MUFA and SFA intakes and stated that SFA as a confounding variable compromised conclusions linking dietary MUFA with increase risk of CHD.

Prospective Cohort Studies

Large prospective cohort studies are considered to be the strongest source of evidence of the observational studies. Recently, a systematic review of 507 prospective cohort studies confirmed the relationship between a Mediterranean diet and decreased risk of CHD (RR = 0.66; 95% CI 0.57–0.75), evidence that was further confirmed as effective through pooled analysis of 94 randomized control trials [1]. Of interest, analysis of the prospective cohort studies revealed strong evidence of an inverse relationship between dietary MUFA and CHD risk (RR = 0.81; 95% CI 0.68–0.93). Conversely, Mente et al. also identified that consumption of foods high in TFA and glycemic load were attributed to increased CHD risk (RR = 1.32; 95% CI 1.16–1.48; and RR = 1.33; 95% CI 1.13–1.52, respectively). In a 14 year follow-up of 80,082 women in the Nurses' Health Study, a 5% increase in energy intake from MUFA was associated with a relative risk of CHD of 0.81 (95% CI 0.65–1.00) [121]. Furthermore, it was estimated that a 5 or 2% energy replacement of SFA or TFA with MUFA decreased risk of CHD by approximately 30 and 50%, respectively, whereas a 5% energy replacement of MUFA with CHO increased risk of CHD by approximately 25%. Results of the Finnish ATBC (Alpha-Tocopherol, Beta-Carotene) Cancer Prevention Study revealed that after adjustment for vitamin E, C, and β-carotene intakes, an inverse association existed between MUFA intakes and CHD mortality (RR between the extreme quintiles = 0.73; 95% CI 0.56–0.95) [122]. Conversely, a pooled analysis of 11 American and European cohort studies conducted by Jakobsen et al. [14] failed to identify a causal link between MUFA intake and decreased CHD risk. These authors reported that a 5% energy substitution of MUFA for SFA resulted in a hazard ratio of 1.19 (95% CI 1.00–1.42) for CHD events and 1.01 (95% CI 0.73–1.41) for CHD deaths. The authors, however, discussed that the association of MUFA intakes with CHD risk may be confounded by incomplete adjustments for TFA intakes, as MUFA intakes in Westernized diets are primarily from meat, dairy and hydrogenated oils [123]. Moreover, data from the Nurses' Health Study reported a strong correlation between MUFA intakes and SFA ($r = 0.81$) and TFA ($r = 0.55$) [121]. Taken together, observational evidence supports dietary MUFA for

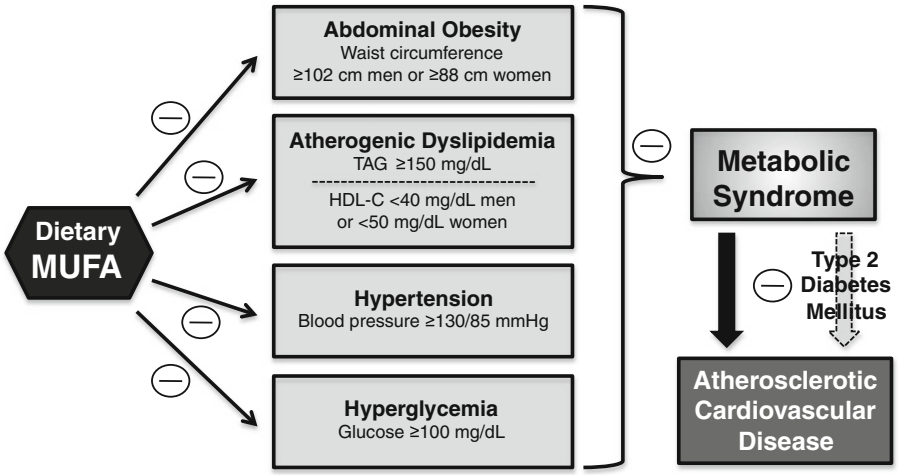

Fig. 1 Dietary monounsaturated fats for the prevention of metabolic syndrome and atherosclerotic cardiovascular disease risk

reduction of CVD risk, however, results from large randomized controlled trials are crucial to substantiate the cardioprotective effects of dietary MUFA.

Conclusion

As dietary intervention remains the primary strategy for the prevention of CVD risk, professional organizations continue to ascertain the optimal fatty acid profile for population intake recommendations. This critical assessment of randomized controlled trials demonstrates that dietary MUFA prevent or ameliorate MetS and CVD risk by favorably modulating blood lipids, blood pressure and insulin sensitivity. Moreover, MUFA preferential oxidation and metabolism influence body composition and potentially ameliorate the risk of obesity (Fig. 1). Considering dietary replacement of SFA, as compared to CHO, MUFA are effective at preserving HDL-C levels, lowering TAG levels, and improving insulin sensitivity; benefits which are especially important in individuals with MetS and DM. As compared to PUFA, MUFA have slightly less or comparable plasma LDL-C and TC lowering effects, however, ameliorate reductions in HDL-C levels, and potentially provide hypotensive effects. The majority of epidemiological data favor the cardioprotective activity of dietary MUFA. More specifically, strong evidence from prospective cohort studies suggests that dietary MUFA are associated with a 20% reduced risk in CHD events [1]. It has also been well established that the intake of a Mediterranean diet rich in MUFA contributes to reducing CHD in both healthy adults and those with established chronic disease.

In North America, where consumption of SFA and TFA are in excess, a dietary movement is occurring to reduce the content of these deleterious fats from commercial production of foods. With the escalating use of MUFA rich canola oil, replacing common dietary fats with canola oil and canola-based spreads would increase the percentage of North Americans complying with current dietary intake recommendations for fatty acids [48]. Consumer awareness of the health implication of dietary fats is increasing [124] and there is a demand for modified dietary oils with a high OLA content for the use in cooking and food preparation in replace of partially hydrogenated oils rich in TFA and SFA [31]. Novel dietary oils rich in OLA with enhanced oxidative stability, such as high-oleic canola oil, provide an attractive healthful alternative to increase dietary MUFA and reduce SFA in commercial food use. With epidemiological and human clinical research substantiating the cardioprotective value of dietary MUFA, increasing population consumption of MUFA, specifically as a substitute for SFA, will embark beneficial implication for MetS, CVD and overall health.

Conflict of interest The authors have no conflict of interest to declare.

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