Maturitas 108 (2018) 45–52

Contents lists available at ScienceDirect

Maturitas

journal homepage: www.elsevier.com/locate/maturitas

Review

# Dietary management of dyslipidaemias. Is there any evidence for cardiovascular benefit?

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ARTICLE INFO

*Keywords:*
Dyslipidaemia
Hypercholesterolaemia
Hypertriglyceridaemia
Mediterranean diet
Sterols
Red yeast rice

ABSTRACT

Specific dietary strategies are the mainstay of management in most cases of dyslipidaemia, prior to or simultaneously with the initiation of a lipid-lowering agent. The exact approach differs according to the type of dyslipidaemia. In particular, a reduction in carbohydrates (mainly foods with a high glycaemic index) and their substitution with mono- and polyunsaturated fatty acids is the main strategy in patients with high levels of triglycerides (Tg) and/or low levels of high-density lipoprotein cholesterol (HDL-c). A reduction in saturated and trans fatty acids, combined with an increased intake of specific dietary components, such as plant sterols, soy protein and red yeast rice, constitutes the more efficacious dietary approach in cases where levels of total cholesterol and low-density lipoprotein cholesterol (LDL-c) are elevated. A reduction in excessive body weight is beneficial in every type of dyslipidaemia, whereas increased physical activity is mostly effective in cases with low HDL-c and high Tg levels. With respect to the potential cardiovascular benefit of these dietary interventions, there is currently evidence for the Mediterranean diet. Potential benefit may derive also from single dietary components of that diet, such as legumes, fruits, vegetables, nuts and omega-3 fatty acids, although to a lesser extent than with that general dietary pattern. The purpose of this review is to outline current knowledge regarding the recommended specific dietary pattern according to the type of dyslipidaemia and the evidence for the potential cardiovascular benefits of such approaches.

## 1. Introduction

Dyslipidaemia is a well-established and prominent cause of cardiovascular morbidity and mortality worldwide [1–3]. This term is used to describe a composite of disorders in lipid metabolism, including high concentrations of low-density lipoprotein cholesterol (LDL-c) and/or triglycerides (Tg) and/or low concentrations of high-density lipoprotein cholesterol (HDL-c), either as mixed or pure disorders. Dyslipidaemias are generally classified into primary and secondary disorders. Primary dyslipidemias are mainly genetically determined and are further subdivided into hyperchylomicroneamia, familial hypercholesterolaemia (FH), mixed hyperlipidaemia, familial hypertriglyceridaemia and familial reduction in HDL-c levels [2]. A dyslipidaemia is characterized as "secondary", when a specific disease [such as diabetes mellitus (DM), hypothyroidism, Cushing's syndrome, acromegaly, chronic kidney disease (CKD) or nephrotic syndrome, human immunodeficiency virus (HIV) infection, cirrhosis and alcohol abuse] or drug (such as estrogen and oral contraceptives, androgen, tamoxifene, progestagen, corticosteroids, cyclosporine, β-blockers, thiazide diuretics) is implicated in its pathogenesis [1–3].

Except for the cases of elevated Tg (> 500 mg/dl), the main target should be LDL-c. This target is set after categorizing the patient according to his/her 10-year risk of cardiovascular death, according to the recent European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS) guidelines for the management of dyslipidaemias [1] and national societies, such as the Hellenic Atherosclerosis Society [2]. In "low" (when the calculated SCORE is < 1% for 10-year risk of fatal CVD) and "moderate risk" (when the SCORE is ≥1% and < 5%) individuals, the LDL-c goal is < 115 mg/dl. In "high risk" patients [when the calculated SCORE is ≥5% and < 10% or single risk factors are markedly elevated, such as in FH or CKD] the LDL-c target is < 100 mg/dl, whereas an LDL-c goal < 70 mg/dl is recommended for very high risk patients, such as those with established coronary heart disease (CHD) or CHD equivalents, such as type 2 DM

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https://doi.org/10.1016/j.maturitas.2017.11.011
Received 29 October 2017; Received in revised form 9 November 2017; Accepted 13 November 2017

(T2DM) [1,2]. Recent guidelines released by the American Association of Clinical Endocrinologists (AACE) identify an additional CVD risk category, termed "extreme risk", which includes those with progressive atherosclerotic CVD (unstable angina in patients after achieving an LDL-c < 70 mg/dl), premature CVD (males < 55 yrs, females < 65 yrs) or established CVD in patients with DM, CKD or heterogyzous FH. The LDL-c target for this category is < 55 mg/dl [3]. Additional target, especially in high-risk patients, is non-HDL-c levels. The calculation formula for the latter is by adding 30 mg/dl to the LDL-c target [1–3].

The approach to the patient's CVD risk according to a specific LDL-c target has been adopted by most scientific societies. On the contrary, the American College of Cardiology/American Heart Association (ACC/AHA) guidelines propose a ≥50% reduction in LDL-c in high CVD risk patients (recommending high-intensity statin therapy) or a 30–50% reduction in LDL-c in those with moderate CVD risk (recommending moderate-intensity statins) [4]. This approach could significantly expand the number of patients receiving statins if implemented in the European population (nearly all men and two-thirds of women older than 65 years) [5]. It also leads to suboptimal treatment of patients in specific categories, such as those with FH [4].

Epidemiological evidence shows improvement in total cholesterol (TC) and LDL-c concentrations in the general population, mainly due to the increased use of lipid-lowering agents (statins). However, there still remains a significant proportion with lipid profile above targets, mainly attributed to the dietary pattern [3]. Although total CVD risk reduction should be individualized, lifestyle intervention remains the first-line approach, before initiation of lipid-lowering treatment in all risk categories, except for very high risk patients with LDL-c concentrations > 70 mg/dl [2]. It is also the most cost-effective option for CVD risk reduction [3]. However, a general dietary pattern does not fit all categories of dyslipidemias and, thus, a tailored approach is suggested. Except for the well-recognized benefits of the Mediterranean diet and its individual components, there is also evidence for specific functional foods, such as plant sterols or stanols. What is of outmost importance, is whether these approaches confer an independent benefit on CVD risk reduction [1,2].

The purpose of this narrative review was to provide current knowledge regarding the dietary approach and management according to the type of dyslipidaemia and, more remarkably, the existing evidence for cardiovascular benefit of each approach.

## 2. Methods

We searched PubMed for English language publications until September 2017, under the following terms: "diet" OR "dietary" AND ("dyslipidaemia" OR "dyslipidaemias" OR "hyperlipidaemia" OR "hyperlipidaemias" "hypercholesterolaemia" OR "hypertriglyceridaemia" OR ""dyslipidemia" OR "dyslipidemias" OR "hyperlipidemia" OR "hyperlipidemias" "hypercholesterolemia" OR "hypertriglyceridemia"] AND ("cardiovascular disease" OR "cardiovascular death" OR "cardiovascular events" OR "cardiovascular mortality" OR "cardiovascular morbidity"). Additionally, we included references from the reviewed articles in order to widen our search. On the top, a manual search of key journals and abstracts from the major annual meetings in the field of Endocrinology and Lipidiology was conducted. Special attention was paid to guidelines or original papers focusing on the management of patients with dyslipidaemias.

This review collected, analyzed and qualitatively re-synthesized information regarding: (1) the classification of dyslipidaemias, (2) the general dietary approach (3) the dietary management according to the type of dyslipidaemia, (4) the cardiovascular benefit of the Mediterranean diet and its components separately.

## 3. General dietary approach to the patient with dyslipidaemia

The first step is to exclude secondary causes of dyslipidaemias. Afterwards, the patient's lipid profile should be categorized according to the classification used for primary dyslipidaemias, as described before. General and well-balanced rules include a reduction of initial body weight by 5–10% (in overweight and obese patients) with a comprehensive lifestyle intervention, which leads to amelioration in most of CVD risk factors [5]. According to expert guidelines, this is achieved generally by adopting an energy deficit of 500–750 kcal/d or 30% of daily calorie intake (which is usually translated to 1200 to 1500 kcal/d for women and 1500 to 1800 kcal/d for men) [5]. After the maximum weight loss is achieved at six months, this is usually followed by a plateau and gradual regain over time. To avoid this phenomenon, further strategies, such as frequent self-weighing, consumption of a reduced calorie diet and physical activity of at least 200 min/week are suggested [5].

Various dietary patterns have been proposed for weight loss. Debate still exists with regard to the most efficacious strategy on weight loss, comparing low fat (LF) with low carbohydrate (LC) diets. Many studies have been published on this concept retrieving conflicting results. A recent *meta*-analysis of randomized-controlled trials (RCTs) showed that LC diets lead to a greater reduction in body weight [weighted mean difference (WMD): −2.17 kg; 95% Confidence Interval (CI): −3.36, −0.99] compared with LF diets [6]. However, two older *meta*-analyses of RCTs showed that the preponderance in body weight by LC diets was evident only at six months (WMD: −3.3 kg; 95% CI: −5.3–−1.4 kg) [7] and −4.02 (95% CI: −4.54–−3.49) kg [8]. LC was equally effective with LF diet after one year (WMD: −1.05 kg; 95% CI: −2.09–−0.01 kg) [8] and −1.0 kg; 95% CI: −3.5–1.5 kg) [7].

Another general rule is to reduce saturated fat acids (SFA) to < 10% of daily calorie consumption and to avoid *trans*-fatty acids (TFA). Reduction of SFA intake is associated with a reduction in CVD events by 17% [risk ratio (RR): 0.83; 95% CI: 0.72, 0.96], including mainly the risk of fatal and non-fatal myocardial infarction (MI) (RR: 0.90; 95% CI: 0.80, 1.01), but without effect on all-cause or CVD mortality. Notably, this benefit is evident when SFA are substituted by poly-unsaturated (PUFA) [9]. Mono-unsaturated fatty acids (MUFA) and PUFA should constitute at least 10% of daily energy intake. Furthermore, cholesterol intake should be restricted to < 300 mg/d [1–3].

TFA are unsaturated fatty acids, the structure of which is characterized by the presence of at least one unsaturated, non-conjugated double bond located in the trans (rather than the usual cis) configuration [10]. They are found in foods containing hydrogenated oils, such as baked goods, snacks (potato, corn and tortilla chips), fried foods, creamer and margarine. TFA seem to adversely affect cardiovascular health, via their detrimental effect on lipid profile, insulin sensitivity, systemic inflammation and endothelial dysfunction [10]. If TFA are preferred instead of carbohydrates or SFA, this leads to a 24% and 20% higher risk for MI and CHD death, respectively, for every 2% of isocalorically daily intake [10]. This CVD risk is stronger with *trans*-18:1 (produced by light hydrogenation or deodorization) isomers than *trans*-16:1 isomers and with industrial TFA, compared with ruminant ones [10,11]. It is recommended that TFA should not exceed 1% of total calorie intake [1–3]. Higher TFA intake (≥1% of energy) is associated with both increased CHD (HR: 1.28, 95% CI: 1.09–1.50) and all-cause mortality (HR: 1.34, 95% CI: 1.16–1.56) [11].

Carbohydrates [1–3] should account for 45–50% of the total calorie intake, mainly deriving from whole grain food (25–40 g/d, including at least 7–13 g of soluble fibre) [1–3]. Smoking cessation and modest alcohol consumption (two units/d for men and one unit/d for women) are also encouraged, as a part of a lifestyle intervention to reduce CVD risk [1–3].

## 4. Dietary management according to the type of dyslipidaemia

### 4.1. Hypertriglyceridaemia

High Tg concentrations have been independently associated with