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REVIEW

Obesity and Dyslipidemia

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Abstract

Purpose of Review This article sumarizes pathopysiological consequencies between obesity and dyslipidemia and aims to bring some practical approach.

Recent Findings Dyslipidemia is often present in individuals with obesity and simultaneusly, many obese individuals have lipid metabolism disorders. Especially the abdominal obesity increases the cardiometabolic risk because of the presence of atherogenic dyslipidemia while the total low density lipoprotein cholesterol (LDL-C) may be normal. LDL-C is the primary goal in dyslipidemia treatment. Apoliprotein B (Apo B) and non – high density lipoprotein cholesterol (non-HDL-C) should be estimated to precise the cardiovascular risk and represents the secondary goal in treatment. Weight loss either with diet or antiobestic medication induces the decrease in triglycerides (TG) and LDL-C and the increase in HDL-C. Composition of nutrients, esp. fatty acids, influences lipid levels. Bariatric surgery is efficient in weight loss and has a significant effect on serum lipids.

Summary Dyslipidemia and obesity present common diseases that must be managed to decrease the cardiovascular risk and the risk of obesity-related complications.

Keywords Visceral obesity · Dyslipidemia · Metabolic syndrome · Cardiovascular risk · Lifestyle · Hypolipidemic treatment

Introduction

Obesity is defined as a body mass index (BMI) > 30 kg/m^2 according to the defnition of the World Health Organisation [1]. The prevalence of obesity is inceasing worldwide. E.g. in the United States it is estimated that 43% of men and 41.9% of women are obese [2]. In Europe, the prevalence of obesity in men ranges from 4.0% to 28.3% and in women from 6.2% to 36.5% with a higher prevalence in Central, Eastern, and Southern Europe than in Western and Northern Europe [3]. Additionally, approximately 1/3 of the population is overweight defined as a BMI between 25 and 30 kg/m^2 [2]. Obesity has emerged as a leading global health concern. Overweight and obesity increase the risk for many health problems, such as type 2 diabetes, arterial hypertension, heart disease, stroke, joint problems, liver disease, gallstones, some types of cancer, and sleep and breathing disorders, among other conditions [4•, 5]. Approximately 60–70% of obese individuals have dyslipidemia [6•].

One has to distinguish that obesity does not mean hypercholesterolemia/dyslipidemia automatically. Hypercholesterolemia, i.e. elevated LDL-C has frequently the same prevalence in obese and non-obese individuals or is only slightly elevated in obese individuals [6•]. The typical dyslipidemia in individuals with abdominal (visceral) obesity is the atherogenic (insulinresistant) dyslipidemia characterized by moderately elevated triglycerides (TG), very low density lipoprotein (VLDL), Apo B, and non-HDL-C levels. The non-HDL-C presents the atherogenic part of the plasma. By contrast, HDL-C and apolipoprotein A-I (Apo A-I) levels are typically low [6•, 7, 8]. Atherogenic dyslipidemia belongs to the conditions of the metabolic syndrome. The presence of 3 of the following 5 factors is establishing the presence of metabolic syndrome: abdominal obesity (highly correlated with insulin resistence), elevated TG, reduced HDL-C, elevated blood pressure, and impaired fasting glucose or

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impaired glucose tolerance or type 2 diabetes mellitus. In the absence of atherosclerotic cardiovascular disease (ASCVD) or diabetes, the metabolic syndrome is a predictor of these conditions. The definition of metabolic syndrome is the Table 1 [9].

Dyslipidemia in Visceral Obesity

The fat tissue distribution in an obese individual plays a key role in further cardiometabolic consequencies. Waist circumferences of at least 102 cm (approximately 40 in.) in men and of at least 88 cm (approximately 35 in.) in women indicate abdominal obesity, which is associated with increased risk for adiposity-related disease. Lower thresholds (eg, ≥ 94 cm [≈ 37 in.] in men and ≥ 80 cm [≈ 32 in.] in women) are used outside of the United States; specific thresholds regarding region and ethnicity also may be used. For instance, in patients of South Asian, Southeast Asian, and East Asian heredity, waist circumference of at least 85 cm (≈ 34 in) in men and at least 74 cm to 80 cm (29–32 in.) in women should be used to identify abdominal obesity [10, 11].

In the Dallas Heart Study sample, the presence of visceral adipose tissue compared to subcutaneus adipose tissue was significantly associated with the homeostasis model assessment of insulin resistance (HOMA-IR), lower adiponectin, small LDL and HDL particle size, large VLDL size, and increased LDL and VLDL particle number ($p < 0.001$ for each). Visceral adipose tissue was also associated with prevalent diabetes, metabolic syndrome, hepatic steatosis, and aortic plaque ($p < 0.001$ for each). Visceral adipose tissue was independently associated with C-reactive protein. In contrast, subcutaneus adipose tissue was associated with leptin and inflammatory biomarkers, but not with dyslipidemia or atherosclerosis. These findings suggest that abdominal fat distribution defines distinct obesity sub-phenotypes with heterogeneous metabolic and ASCVD risk [12].

In contrast to elevated TG, Apo B and non-HDL-C and low HDL-C, LDL-C levels are frequently in the normal to slightly elevated range. The normal LDL-C level in atherogenic dyslipidemia is a false friend and must be further examined and taken in account, especially when Apo B elevated. Individuals with abdominal obesity often present an increase in small dense LDL resulting in an increased number of LDL particles [6•, 7, 8]. Small dense LDL particles are regarded as more pro-atherogenic than large LDL particles. On the other hand small dense HDL particles are less anti-atherogenic.

Elevated TG levels are independently associated with increased incidence of cardiovascular events, even in patients treated effectively with statins (s.c. residual cardiovascular risk). Elevated TG-rich lipoproteins in the postprandial state were assessed as a source of residual risk for ASCVD; remnant cholesterol was signed as a causal risk factor. The evidence from the large Copenhagen General Population Study suggests that non-HDL-C, the sum of the total cholesterol carried by atherogenic lipoproteins (including LDL, triglyceride-rich lipoprotein [TRL] and TRL remnants), provides a better indication of cardiovascular disease risk than LDL-C, particularly in patients with hypertriglyceridemia [13]. The last analysis of the Copenhagen studies shows unexpectedly, that elevated measured LDL-TG were significantly associated with an increased relative risk of ASCVD; but does not explain the causal relationship between LDL-TG and ASCVD [14•].

Table 1 Criteria for Clinical Diagnosis of the Metabolic Syndrome [9]

Risk factor of metabolic syndrome	Cut Points
Abdominal obesity	
Waist circumference	> 102 cm in males > 88 cm in females
Atherogenic dyslipidemia	
Elevated TG/drug treatment for elevated TG	≥ 1.7 mmol/L (150 mg/dL)
Reduced HDL-C/drug treatment for reduced HDL-C	< 1.0 mmol/L (40 mg/dL) in males < 1.3 mmol/L (50 mg/dL) in females
Elevated blood pressure	
Elevated blood pressure/antihypertensive medication	Systolic ≥ 130 and/or diastolic ≥ 85 mm Hg
Glucose metabolism disorder	
Impaired fasting glucose Or impaired glucose tolerance/drug treatment of glucose metabolism disorder/type 2 diabetes mellitus	≥ 5.6 mmol/L (100 mg/dL)

Waist circumference can vary due to population- and country-specific definitions [10, 11]

TG – triglycerides, HDL-C – high density lipoprotein cholesterol

How to Manage Dyslipidemia and Obesity

There are several possibilities to influence the prognosis and quality of life in an obese individual with dyslipidemia. The lifestyle recommendations are the cornerstone of every intervention. Also pharmacotherapy of dyslipidemia or obesity can be used when indicated. Subjects with normal (healthy) weight (BMI, 18.5 to < 25 kg/m^2) should be counseled on the health benefits of avoiding weight gain. Those whose genetics, biomarkers, family history, ethnicity, cultural practices, or individual behaviors put them at high risk for overweight or obesity should be counseled to avoid weight gain and educated in healthy meal planning and physical activity [10, 11]. In general all patients with overweight or obesity achieve the realistic and meaningful goal of 5% to 10% weight loss within 6 months. A structured and comprehensive lifestyle intervention, an in-person, high-intensity program (≥ 14 sessions in 6 months) is recommended as the most effective behavioral treatment for overweight or obesity. [10, 11]. Dyslipidemia has to be managed according to current guidelines. Primarily the total cardiovascular risk has to be estimated and further treatment with target lipid values suggested while obesity counts to risk factors increasing the total cardiovasvular risk [15•, 16]. Also the other additional risk factors have to be influenced by pharmacotherapy such as arterial hypertension or glucose impairment.

Physical Activity

Physical activity is important in weight reduction and dyslipidemia and other present risk factors management. Nevertheless, physical acitivity alone without diet was shown not to be sufficient to induce any significant weight loss but it is essential for weight loss maintenance [17, 18]. Physical activity has to be combined with diet to facilitate the weight loss and to decrease the risk of the muscle mass loss during weight loss [17]. The decrease in LDL-C levels follows weight loss and varies between 4 and 7% in a large metaanalysis [19]. Nevertheless some authors refer some increase of LDL-C during weight loss and exercise. This may be explained by the change of LDL particles size and quality and by the transformation of small dense atherogenic particles to a larger size [19]. The effect of exercise on HDL-C level is well known but it requires a regular and more intensive physical activity [18, 19]. The decrease of TG levels and its variability is high, betweeen 4 – 37% (24% in average) [18, 20]. Changes in HDL-C and TG levels during physical activity are observed independently of the weigt loss while indurance training has a greater benefit than resistance training [13]. Physical activity reduces the risk of many adverse health outcomes and risk factors in all ages and both sexes. There is an inverse relationship between moderate-to-vigorous physical activity and all-cause mortality, cardiovascular morbidity and as well as incidence of type 2 diabetes mellitus [21]. E.g. according to the European Society of Cardiology Guidelines on cardiovascular disease prevention in clinical practice, it is recommended for adults of all ages to strive for at least 150—300 min a week of moderate-intensity or 75—150 min a week of vigorous intensity aerobic physcal activity, or an equivalent combination thereof, to reduce all-cause mortality, cardiovascular mortality, and morbidity. Adults who cannot perform 150 min of moderate-intensity physical activity a week should stay as active as their abilities and health condition allow. It is recommended to reduce sedentary time to engage in at least light activity throughout the day to reduce all-cause and cardiovascular mortality and morbidity. Performing resistance exercise, in addition to aerobic activity, is recommended on 2 or more days per week to reduce all-cause mortality. Lifestyle interventions, such as group or individual education, behaviour-change techniques, telephone counselling, and use of consumer-based wearable activity trackers, should be considered to increase pfysical activity participation. Most important is to encourage activity that people enjoy and/or can include in their daily routines, as such activities are more likely to be sustainable [15•]. The quidelines of the American College of Cardiology/American Heart Association on primary cardiovascular prevention postpone a nearly similar recommendation [16].

Diet

Diet is essential in weight loss and dyslipidemia management. Both weight loss and the composition of nutrients influence the final lipid levels. Diet and weight loss have to be combined with physical activity for a better efficiency and to maintain body muscle [15•]. In a metanalysis of 30 randomized controlled trials with more than 2 000 subjects was demonstrated that lifestyle change (diet and/or exercise) was followed by a 4 mg/dL (0.05 mmol/l) decrease in TG, a 1.28 mg/dL (0.03 mmol/l) decrease in LDL-C, and 0.46 mg/dL (0.01 mmol/l) increase in HDL-C per 1 kg weight loss after 1 year [22]. The degree of decrease in serum TG levels is related to baseline TG levels with higher levels typically demonstrating a greater reduction with weight loss. Nevertheless, the variability of lipidogram changes between individuals is huge [23]. There is a continuous debate on which composition of the diet regarding the intake of fat, protein and carbohydrates is the most beneficial. While comparing certain types of diets in more than 800 individuals in a

time period longer than 2 years, there was no difference in weight loss. The main problem was to maintain the reduced weight and compliance after 6 months of the beginning of the study [24]. Up to date, low-carb and ketogenic diets are very modern and trending. In a meta-analysis comparing ketogenic diets (eg. very-low in carbohydrates) with low-fat diets was demonstrated a greater decrease in TG and increase in HDL-C levels with the ketogenic than with the low-fat diet. Nevertheless, the ketogenic diet increased LDL-C levels so the ketogenic diet in ASCVD prevention is rather doubtful [25]. Consistent evidence from epidemiological studies indicates that higher consumption of fruit, non-starchy vegetables, nuts, legumes, fish, vegetable oils, yoghurt, and wholegrains, along with a lower intake of red and processed meats, foods higher in refined carbohydrates, and salt, is associated with a lower incidence of CV events [26]. Moreover, it indicates that the replacement of animal fats, including dairy fat, with vegetable sources of fats and polyunsaturated fatty acids (PUFAs) may decrease the risk of ASCVD, rather than to decrease the fat comsumption at all [27]. Trans fatty acids are naturally present in diary products, but also formed during industrial processing of fats. They have unfavourable effects on total cholesterol (TC) (increase) and HDL-C (decrease). On average, a 2% increase in energy intake from trans fatty acids is associated with a 23% higher ASCVD risk. When guidelines to lower saturated fat intake are followed, in dietary cholesterol intake follow [28]. Alcohol intake has a major impact on TG levels, particularly in individuals with hypertriglyceridemia. The detrimental effects of a high-carbohydrate diet on TGs occur mainly when refined carbohydrate-rich foods are consumed, while they are much less prominent if the diet is based largely on fibre-rich, low-glycaemic index foods. This applies particularly to people with diabetes mellitus and/or metabolic syndrome, i.e. also those with visceral obesity/overweight [29•].

Smoking Cessation, Lipids and Obesity

Smoking cessation is one of the most important topics in cardiovascular prevention [15•, 16]. Smokers who try to quit smoking often postpone the topic of weight gain after smoking cessation and may question the benefit of smoking cessation. In a cohort of a total 16 663 participants followed for 8 years was found that smoking cessation was accompanied by a substantial weight gain by aprox. 3.4 kg and a BMI gain by 0,82 $kg.m^{-2}$ compared to continuing smokers; however, this was not associated with an increased risk of chronic diseases or an attenuation of the mortality benefit of cessation [30]. Visceral adiposity index (VAI), a sex-specific calculated index, based on waist circumference, BMI, triglycerides, and HDL cholesterol, indirectly expressing visceral fat function is becoming increasingly popular in the detection of cardiometabolic risks in several disorders and general population [31]. It was measured in subjects after quitting smoking in an experiment. Although weight, waist circumference, BMI, and HDL-C levels increased, VAI levels were found to decrease significantly at the 3rd month [32]. Despite some weight gain, smoking cessation improves HDL-C, especially in women. Increases in HDL may mediate part of the reduced ASCVD risk observed after smoking cessation [33]. In conclusion, quitting smoking brings uncomparable benefits although there can be some weight gain.

Bariatric/Cardiometabolic Surgery as a Possibility to Improve Cardiometabolic Risk

Metabolic surgery was originally performed to treat hypercholesterolemia. Today, the major indication is severe obesity. A meta-analysis shows results in more than 25 000 subjects (preoperative BMI 45.5 ± 4.8 kg/m^2) who underwent one of the methods of bariatric surgery (Roux-en-Y gastric bypass [RYGBP], adjustable gastric banding, biliopancreatic diversion, or sleeve gastrectomy) at 1 year. In patients undergoing any bariatric surgery, compared with baseline, there were significant reductions in TC (-28.5 mg/dL [0.74 mmol/L]), LDL-C (-22.0 mg/dL [0.57 mmol/L]), TG (-61.6 mg/dL [0.7 mmol/L]), and a significant increase in HDL-C (6.9 mg/dL [0.18 mmol/L]) at 1 year ($P < 0.00001$ for all). The magnitude of this change was significantly greater than that seen in nonsurgical control patients (another group of cca 27 000 patients, eg LDL-C; -22.0 mg/dL [0.57 mmol/L]vs -4.3 mg/dL [0.11 mmol/L]). When assessed separately, the magnitude of changes varied greatly by surgical type (P interaction < 0.00001; eg, LDL-C: biliopancreatic diversion -42.5 mg/dL [1.1 mmol/L], RYGBP -24.7 mg/dL [0.64 mmol/L], adjustable gastric banding -8.8 mg/dL [0.23 mmol/L], sleeve gastrectomy -7.9 mg/dL [0.2 mmol/L]). In the cases of adjustable gastric banding (TC and LDL-C) and sleeve gastrectomy (LDL-C), the response at 1 year following surgery was not significantly different from nonsurgical control patients. Contemporary bariatric surgical techniques produce significant improvements in serum lipids, but changes vary widely, likely due to anatomic alterations unique to each procedure. These differences may be relevant in deciding the most appropriate technique for a given patient [34].

Effect of Antiobesitic Medication on Obesity and Lipids

Medication for weight loss is mostly available on medical prescription only. An older antiobesitic drug is the phenteramine + topiramate combination (USA) or phentermine

(Europe). This drug acts as an anorectic and is known for a lot of adverse effects. The weight decrease in combination with a program of diet and exercise was 10% to 11% of the body weight compared to 1% to 2% for those who received placebo [35, 36]. Treatment with phenteramine + topiramate led to progressively greater reductions in TG and greater increases in HDL-C than did placebo, despite the fact that the placebo group required a markedly greater net increase in the number of lipid-lowering medications used compared with the phenteramine + topiramate group. There was no significant effect on LDL-C levels. Nevertheless, the changes in TG and HDL-C seem likely to be weight – related [37].

Another older antiobesitic drug is orlistat, a lipase inhibitor that decreases fat absorption. Thirty-three studies were included in a meta-analysis (5522 and 4210 participants in the orlistat therapy and control groups, respectively). Orlistat reduced body weight (weighted mean difference: -2.12, $p < 0.001$), TC (weighted mean difference: -5.4. mg/dL [0.14 mmol/L], $p < 0.001$), LDL-C (weighted mean difference: -4.9 mg/dL [0.13 mmol/L], $p < 0.001$), HDL-C (weighted mean difference: -0.6 mg/dL [0.02 mmol/L], $p < 0.001$) and TG (weighted mean difference: -1.6 mg/dL [0.02 mmol/L], $p < 0.001$) concentrations, while no effect on lipoprotein(a) was observed. Total- and LDL-C lowering were associated negatively with duration of orlistat treatment and positively with body weight changes. In conclusion, orlistat treatment slightly reduces cholesterol and TG levels, but not lipoprotein(a) levels. Total- and LDL-C levels reductions are more consistent in patients with greater body weight reduction and shorter duration of orlistat treatment [38]. Another studies have shown that the levels of small dense LDL are reduced and the average LDL particle size increased with orlistat [39].

A combination of an opioid antagonist naltrexone and an antidepressant bupropion is widely used as an antiobesitic medication. In large randomized control trials naltrexone + bupropion decreased TG levels by approx. 8–12%, decreased LDL-C by 0–6%, and increased HDL-C by 3–8%. No aditional effect on lipid levels is suspected except the effect from weight loss. [40, 41]. A new drug group of the GLP-1 agonists is aproved for the treatment of diabetes and also of obesity. Liraglutide and semaglutide have shown to reduce postprandial TG by reducing circulating chylomicrons due to decreasing intestinal lipoprotein production [40]. Liraglutide has shown some reductions in TG (9%) and LDL-C levels (2.4%) and also increases in HDL-C (1.9%) [42]. Semagludite has shown a LDL-C decrease by 7 mg/dL (0.18 mmol/L) and a more marked TG decrease by 17 mg/dL (0.19 mmol/L) while HDL-C was increased by 1.5 mg/dL (0.04 mmol/L) [43]. It was concluded that the lipids changes are mostly driven by weigt loss. In conclusion, except for orlistat, the effect of weight loss drugs on fasting lipid levels seems to be caused by the weight loss.

Hypolipidemic Treatment Focused on Atherogenic Dyslipidemia in Clinical Practise

Dyslipidemia has to be treated according current guidelines to decrease the risk of all ASCVD and to prolong life with a good quality of life [15•, 16, 29•]. First of all, the total 10-year CVD risk has to be evaluated according to age, sex, blood lipids, blood pressure, smoking habits, presence of diabetes mellitus and kidney function impairment, history of ASCVD and other modifying factors like social status, psychiatric and rheumatic disorders etc. Obesity increases the risk of ASCVD [15•, 16, 29•]. Blood lipids examination in an obese individual should include the value of total cholesterol, LDL-C, HDL-C, TG, but also calculated nonHDL-C (total cholesterol – HDL-C) as the atherogenic part of the plasma, Apo B to exclude the false normal LDL-C value as mentioned above, and Apo A and lipoprotein (a) [29•]. Depending on total risk of ASCVD, target levels of LDL-C should be estimated. Subjects with low risk should have their LDL-C < 3 mmol/L (116 mg/dL), with an intermediate risk < 2.6 mmol/L (< 100 mg/dL), with a high risk < 1.8 mmol/L (< 70 mg/dL) and with a very high risk < 1.4 mmol/L (< 54 mg/dL) or with an extreme risk < 1 mmol/L (cca 40 mg/dL) In subjets with high/very high risk or extreme risk of ASCVD, LDL-C should be lowered by 50% of the basic value, aditionally [29•].

Non-HDL-C or ApoB are good markers of TRLs and remnants, and are a secondary objective of therapy. Non-HDL-C < 2.6 mmol/L (< 100 mg/dL) and Apo B < 80 mg/dL are desirable in those at high-risk, and non-HDL-C < 2.2 mmol/L (< 85 mg/dL) and Apo B < 65 mg/dL in those at very high-risk. For those at very high-risk with recurrent ASCVD events, a goal of non-HDL-C < 1.8 mmol/L (< 70 mg/dL) and Apo B < 55 mg/dL may be considered [29•].

Statins are the drug of the first choice, including atherogenic dyslipidemia. Statins decrease plasma concentrations of LDL- and other ApoB-containing lipoproteins, including TG-rich particles. As for the atherogenic dyslipidemia, statins usually reduce TG levels by 10–20% from baseline values [44]. Statins should be uptitirated to maximal/tolerated doses to reach the target values od LDL-C. More potent statins (atorvastatin, rosuvastatin, and pitavastatin) demonstrate robust lowering of TG levels, especially at high doses and in patients with elevated TG, in whom the absolute risk, and therefore the absolute risk reduction, is larger [29•]. The mechanism of the TG-lowering effect has not been fully elucidated, but it seems to be partly independent of the LDLR pathway. It may involve the upregulation of VLDL uptake by hepatocytes,

as well as a reduction of the production rate of VLDLs; these effects seem to be dependent on pre-treatment VLDL concentrations [45]. Patients on statin treatment have been shown to exhibit an increased risk of dysglycaemia and development of type 2 diabetes mellitus. Overall, the absolute reduction in the risk of ASCVD in high-risk patients clearly outweighs the possible adverse effects of a small increase in the incidence of diabetes [46].

Ezetimibe inhibits intestinal uptake of dietary and biliary cholesterol at the level of the brush border of the intestine. A meta-analysis that included over 2700 people showed an 18.5% reduction in LDL-C as compared with placebo. In addition, there was a significant 3% increase in HDL-C, a significant 8% reduction in TG, and a 13% reduction in total cholesterol with ezetimibe as compared with placebo [47]. Ezetimibe lowers LDL-C by ~24% and, when added to statin therapy, decreases the risk of major vascular events [48]. The relative risk reduction in major vascular events is proportional to the absolute degree of LDL-C lowering and consistent with the relationship seen for statins. The subset of patients with DM in IMPROVE-IT had, as expected, a higher rate of major vascular events than patients without diabetes (46 vs. 31% 7 year Kaplan–Meier rate in the placebo arm). Ezetimibe appeared particularly efficacious in patients with diabetes, with a relative risk reduction of 15% (95% CI 6–22%) and an absolute risk reduction of 5.5% [49]. Ezetimibe used as second-line therapy in association with statins when the therapeutic goal is not achieved at the maximal tolerated statin dose, or in cases where a statin cannot be prescribed [29•].

Fibrates are agonists of peroxisome proliferator-activated receptor-α (PPAR-α), acting via transcription factors regulating, among other things, various steps in lipid and lipoprotein metabolism. As a consequence, fibrates have good efficacy in lowering fasting TG levels, as well as post-prandial TG and TRL remnant particles. Fibrates cause 50% reduction of the TG level, a ≤ 20% reduction of the LDL-C level (but a paradoxical small LDL-C increase may be observed with high TG levels), and an increase of the HDL-C level of ≤ 20% [50]. Although fibrates are efficient in TG lowering, statins are the first drugs of choice in hypertriglyceridemia treatment in subjects with a high risk of ASCVD and TG > 2.3 mmol/l (200 mg/dl) [29•]. When such subjects with high ASCVD or subjects in primary prevention are at goal of LDL-C and still do not reach TG < 2.3 mmol/L, fibrates may be considered for combination with statins (class of recommendation IIb) [29•, 51•].

A new approach in (very) high risk patients in with elevated TG to 1.5–5.6. mmol/L (135 – 499 mg/dL) despite statin treatment are the PUFAs – polyunsaturated fatty acids. The REDUCE-IT trial demonstrated that in statin-treated patients with high CV risk with fasting TG levels between 135–499 mg/dL (1.52–1.63 mmol/L), high-dose icosapent ethyl 2 × 2 g/day, significantly reduced the risk of ischaemic events, including CV death, by about one-quarter over a median follow-up of 4.9 years. This approach is recommended by guidelines [29•, 52].

A new drug group of proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors is involved in an increase of LDL receptors number. Their potential to lower LDL-C is around 60%, to lower TG by 26% and and lipoprotein (a) by 20%, and raise HDL-C and ApoA-I by 9 and 4% [53, 54]. Further investigation in subjects with higher TG is needed. Small interfering RNA (siRNA) way working inclisiran that interferes with the synthesis of PCSK9, decreases LDL-C by aprox 50%, TG by 15%, liporoptein (a) by 20%, and increases HDL-C by 7% [55]. Bempedoic acid which is a newly marketed adenosine triphosphate citrate lyase (ACL) inhibitor, that inhibits the synthesis of LDL-C, decreases LDL-C by aprox 25%, inreases HDL-C by 7.5% and has no significat effect on TG [56]. Drugs to increase HDL-C in terms of cardiovascular prevention failed [29•].

Conclusion and a Practical Approach

Dyslipidemia and obesity present a consequent health topic, although not all obese patients are dyslipidemic. The most dangerous dyslipidemic feature in obese individuals with visceral obesity is the atherogenic dyslipidemia. While LDL-C is a primary aim of dyslipidemia treatment, apo B or non-HDL-C should be evaluated as a secondary aims especially in patients with high TG level. Both dyslipidemia and obesity should be treated with care to reduce cardiovascular risk and obesity-related complication. Lifestyle changes, behavioral interventions and pharmacotherapy should be applied when the total cardiovascular risk is high or very high.

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