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專題報導

Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in High-Risk Adults: The Current Guidelines and New Drugs

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Abstract

Statins have been the main treatment for patients with dyslipidemia and for prevention of clinical atherosclerotic cardiovascular disease (ASCVD). According to the 2013 American College of Cardiology / American Heart Association (ACC/AHA) lipid guideline, four statin benefit groups were issued, including patients with clinical ASCVD, low-density lipoprotein cholesterol (LDL-C) ≥190 mg/dL, diabetes mellitus (DM), or with 10-year ASCVD risk of ≥7.5%. Although the ACC/AHA guideline suggested the intensity of statin treatment for patients with different risk categories, it did not recommend the specific target levels of LDL-C. The 2016 European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS) guideline suggested the SCORE system for risk assessment. For very high-risk, high-risk, and moderate-risk patients, the treatment goals of LDL-C were <70 mg/dL, <100 mg/dL, and <115 mg/dL, respectively. The 2017 Taiwan lipid guidelines clearly defined the high-risk patients and the treatment goals of LDL-C. For patients with peripheral arterial disease (PAD), cerebrovascular disease, DM, and familial hypercholesterolemia (FH), the LDL-C <100 mg/dL is suggested, whereas LDL-C <70 mg/dL is suggested for patients with acute coronary syndrome (ACS) or stable coronary artery disease (CAD). For diabetic patients with ACS, LDL-C should be <55 mg/dL. Several novel agents have become available as adjunctive treatment of FH to reduce LDL-C levels. For example, mipomersen is an antisense oligonucleotide (ASO) inhibitor of apolipoprotein B (Apo B). Lomitapide can inhibit the microsomal triglyceride transfer protein (MTP). Evolocumab, alirocumab, and bococizumab are proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors. Further studies are necessary to confirm the effects of these aforementioned agents on clinical outcomes. (J Intern Med Taiwan 2017; 28: 223-231)

Key Words: Atherosclerotic cardiovascular disease, Statin, Familial hypercholesterolemia

Introduction

High levels of low-density lipoprotein cholesterol (LDL-C) are associated with an increased risk of atherosclerotic cardiovascular disease (ASCVD). Based on evidence from randomized clinical trials (RCT), the American College of Cardiology (ACC) and the American Heart Association (AHA) issued a revolutionary guideline in 2013 that addressed the treatment of statins to reduce the risk of ASCVD in

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adults, and focused on four statin benefit groups[1]. However, the ACC/AHA guideline did not provide recommendations of specific LDL-C target levels for patients in each of the four categories. On the other hand, the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS) published the guidelines for the management of dyslipidemia in 2016 that described the risk assessment system for fatal cardiovascular disease (CVD) and the treatment targets for patients with different risk categories[2]. Recently, the 2017 Taiwan lipid guidelines have been issued and clearly addressed the treatment goals of LDL-C for high-risk patients[3]. In this article, we would like to briefly review the current ACC/AHA and ESC/EAS guidelines of statin treatment in adults, provide the information of LDL-C goals for high-risk patients suggested by the 2017 Taiwan lipid guidelines, and introduce the new pharmacological agents.

An Overview of the 2013 ACC/AHA Guideline for Statin Treatment to Reduce Atherosclerotic Cardiovascular Risk

Four Statin Benefit Groups

Before initiating statin therapy, the patient's medical history and clinical evidence of ASCVD should be evaluated carefully. Clinical ASCVD includes acute coronary syndromes (ACS), history of myocardial infarction (MI), stable or unstable angina, coronary or other arterial revascularization, stroke, transient ischemic attack (TIA), or peripheral arterial disease (PAD) presumed to be of atherosclerotic origin[1]. Additionally, the 10-year risk of ASCVD should be estimated to identify high-risk patients who will benefit from statin therapy. The Pooled Cohort Equations developed by the Risk Assessment Work Group are recommended to calculate the estimated 10-year ASCVD risk (http://my.americanheart.org/cvriskcalculator and http://www.cardiosource.org/en/Science-And-Quality/Practice-Guidelines-and-Quality-Standards/2013-Prevention-Guideline-Tools.aspx).

Four statin benefit groups were addressed in the 2013 ACC/AHA guideline: (1) patients with clinical evidence of ASCVD; (2) patients with LDL-C levels of ≥190 mg/dL; (3) patients without clinical ASCVD but with diabetes mellitus (DM) who are 40 to 75 years of age and have LDL-C levels of 70 to 189 mg/dL; and (4) patients without clinical ASCVD or DM who have LDL-C levels of 70 to 189 mg/dL and an estimated 10-year ASCVD risk of ≥7.5%.

Brief Principles of Statin Treatment in the 2013 ACC/AHA Guideline

Table 1 listed the brief principles of statin treatment for patients with different categories. For patients who have clinical ASCVD or LDL-C ≥190 mg/dL, high-intensity statin therapy should be initiated. For patients in whom high-intensity statin therapy is contraindicated, or patients with characteristics predisposing to statin-associated adverse effects, moderate-intensity statins should be considered. For patients without clinical ASCVD but with DM and LDL-C 70-189 mg/dL, moderate-intensity statin therapy should be initiated for patients of 40 to 75 years of age. In those with estimated 10-year ASCVD risk of ≥7.5%, high-intensity statin therapy is considered unless contraindicated. For patients without clinical ASCVD or DM but with LDL-C 70-189 mg/dL, 10-year ASCVD risk should be calculated carefully for this set of patients to decide the intensity of statin treatment. In patients of 40 to 75 years of age with an estimated 10-year ASCVD risk of ≥7.5%, moderate- to high-intensity statin therapy should be suggested. If the 10-year risk of ASCVD is 5% to 7.5%, moderate-intensity statin is suggested. For patients with LDL-C <190 mg/dL who do not fall into an aforementioned benefit group or for whom risk-based treatment is uncertain, other factors may be considered to facilitate the decision of statin treatment. These factors may include primary LDL-C ≥160 mg/dL, evidence of genetic hyperlipidemia, family history of premature ASCVD (onset

before 55 years of age in a first-degree male relative or before 65 years of age in a first-degree female relative), high-sensitivity C-reactive protein ≥2 mg/L, and coronary artery calcium score ≥300 Agatston units. Statin therapy may be considered after evaluating for potential benefits, adverse events, drug-drug interactions, and patient preferences (Table 1). Furthermore, there are no recommendations on initiating or discontinuing statin therapy in patients with New York Heart Association class II through IV ischemic systolic heart failure or in patients on maintenance hemodialysis[1].

Intensity of Statin Therapy

In the 2013 ACC/AHA guideline, the intensity of statin treatment was derived from the systematic reviews for RCTs and defined on the basis of the average expected LDL-C response to a specific statin and dose[1]. For example, there was a high level of evidence that high-intensity statin therapy with atorvastatin 40 mg to 80 mg reduced ASCVD risk more than moderate-intensity statin therapy with atorvastatin 10 mg, pravastatin 40 mg, or simvastatin 20 mg to 40 mg twice daily (Table 1).

Treatment Targets

There are no recommendations for specific target levels for LDL-C in the primary or secondary prevention of ASCVD in the 2013 ACC/AHA guideline[1]. Generally, high-intensity statin therapy on average lowers LDL-C by approximately ≥50%, moderate-intensity statin therapy lowers LDL-C by approximately 30% to 50%, and low-intensity statin therapy lowers LDL-C by <30% (Table 1).

Table 1. Principles of statin treatment for patients with different categories and the intensity of statin therapy suggested by 2013 ACC/AHA guidelines

Patients with different risk categories	Principles of statin treatment
(1) Patients with clinical evidence of ASCVD	High-intensity statin therapy
(2) Patients with LDL-C levels of ≥190 mg/dL	High-intensity statin therapy
(3) Patients with DM who are 40 to 75 years of age with LDL-C levels of 70 to 189 mg/dL but without clinical ASCVD	Moderate-intensity statin therapy (High-intensity statin therapy for those who have the 10-year ASCVD risk of ≥7.5%)
(4) Patients without clinical ASCVD or DM who have LDL-C levels of 70 to 189 mg/dL and an estimated 10-year ASCVD risk of ≥7.5%	Moderate- to high-intensity statin therapy (Moderate-intensity statin therapy for those who have the 10-year risk of ASCVD is 5% to 7.5%)
(5) Patients with LDL-C <190 mg/dL who do not fall into an aforementioned group or for whom risk-based treatment is uncertain	Other factors may be considered to facilitate the decision of statin treatment, including primary LDL-C ≥160 mg/dL, evidence of genetic hyperlipidemia, family history of premature ASCVD with onset before 55 years of age in a first-degree male relative or before 65 years of age in a first-degree female relative, high-sensitivity C-reactive protein ≥2 mg/L, and coronary artery calcium score ≥300 Agatston units. Statin therapy may be considered after evaluating for potential benefits, adverse events, drug-drug interactions, and patient preferences.

Levels of statin intensity	High-intensity	Moderate-intensity	Low-intensity
Suggested LDL-C reduction on daily dose	Approximately ≥50%	Approximately 30-50%	Approximately <30%
Statin / Dosage	Atorvastatin 40-80 mg Rosuvastatin 20-40 mg	Atorvastatin 10-20 mg Rosuvastatin 5-10 mg Simvastatin 20-40 mg Pravastatin 40-80 mg Lovastatin 40 mg Fluvastatin XL 80 mg Pitavastatin 2-4 mg	Simvastatin 10 mg Pravastatin 10-20 mg Lovastatin 20 mg Pitavastatin 1 mg

Abbreviation: ASCVD=atherosclerotic cardiovascular disease; DM=diabetes mellitus; LDL-C=low-density lipoprotein cholesterol.

An Overview of the 2016 ESC/EAS Guideline for the Management of Dyslipidemias to Prevent CVD

Assessment of Cardiovascular Risk and Risk Categories

Based on large, representative European cohort datasets, the 2016 ESC/EAS guidelines[2] suggested to adopt the SCORE system[4] as an assessment tool to estimate the 10-year cumulative risk of a first fatal atherosclerotic event, including heart attack, stroke or sudden cardiac death. The risk categories stratified by the SCORE system and the patient's clinical conditions are as follows[2,4]:

(1) Very high-risk: Patients with documented CVD, including previous MI, ACS, coronary revascularization (percutaneous coronary intervention (PCI), coronary artery bypass graft surgery (CABG)) and other arterial revascularization procedures, stroke, TIA, and PAD. Patients with unequivocally documented CVD on imaging that has been shown to be strongly predisposed to clinical events, such as significant plaque on coronary angiography or carotid ultrasound. Patients with DM and target organ damage such as proteinuria or with a major risk factor such as smoking, hypertension or dyslipidemia. Patients with severe CKD (GFR < 30 mL/min/1.73 m^2). Patients with a calculated SCORE ≥ 10% for 10-year risk of fatal CVD.

(2) High-risk: Patients with markedly elevated single risk factor, in particular total cholesterol > 310 mg/dL or blood pressure ≥180/110 mmHg. Patients with moderate CKD (GFR 30–59 mL/min/1.73 m^2). Patients with a calculated SCORE ≥5% and <10% for 10-year risk of fatal CVD.

(3) Moderate-risk: Patients with a calculated SCORE ≥1% and <5%.

(4) Low-risk: Patients with a calculated SCORE <1%.

Brief Principles of Intervention Strategy for Patients with Specific Risk Categories According to the 2016 ESC/EAS Guideline

The 2016 ESC/EAS guidelines suggested intervention strategies as a function of total CV risk and LDL-C level based on evidence from multiple meta-analyses and RCTs. Generally, no lipid intervention is needed for low-risk patients with a LDL-C level <190 mg/dL, moderate-risk patients with a LDL-C

Table 2. Intervention strategies stratified by total CV risks and LDL-C levels according to 2016 ESC/EAS guidelines

Total CV risk (SCORE) %	LDL-C level				
	≥190 mg/dL	155 to <190 mg/dL	100 to <155 mg/dL	70 to <100 mg/dL	<70 mg/dL
≥10 or Very high-risk	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention, consider drug
≥5 to <10, or High-risk	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention, consider drug if uncontrolled	No lipid intervention
≥1 to <5 Moderate-risk	Lifestyle intervention, consider drug if uncontrolled	Lifestyle intervention, consider drug if uncontrolled	Lifestyle intervention, consider drug if uncontrolled	No lipid intervention	No lipid intervention
<1 Low-risk	Lifestyle intervention, consider drug if uncontrolled	No lipid intervention	No lipid intervention	No lipid intervention	No lipid intervention

Abbreviation: CV=cardiovascular; LDL-C=low-density lipoprotein cholesterol; SCORE=Systematic Coronary Risk Estimation.

level <100 mg/dL, and high-risk patients with a LDL-C level <70 mg/dL. On the other hand, life style intervention and concomitant drug intervention are suggested for very high-risk patients with a LDL-C level ≥70 mg/dL, high-risk patients with a LDL-C level ≥100 mg/dL. For other patients who do not fall into the aforementioned conditions, drug intervention is considered if uncontrolled after life style intervention (Table 2)[2].

Treatment Targets

In the 2016 ESC/EAS guideline, the targeted approach to lipid management is primarily aimed at reducing LDL-C. For very high-risk patients, the goal is LDL-C <70 mg/dL. For high-risk patients, the goal is LDL-C level <100 mg/dL. At least a 50% reduction from baseline should be achieved for very high-risk and high-risk patients. In moderate-risk patients, the LDL-C goal is <115 mg/dL. For patients at low-risk, drug intervention is considered if LDL-C >190 mg/dL[2].

Current Consensus of Treatment Goals for High-risk Patients in Taiwan

Statin is the First Line Therapy for Patients with High Risk

Here we provided a brief overlook for the 2017 Taiwan lipid guidelines for patients with high risk that was reported by Li[3]. Patients with high risk are referred to persons with ACS, DM, coronary artery disease (CAD), PAD, ischemic stroke, TIA, symptomatic carotid stenosis or intracranial arterial stenosis, chronic kidney disease (CKD) stage 3-5, and familial hypercholesterolemia (FH). In addition to LDL-C, the treatment goals of high-density lipoprotein cholesterol (HDL-C) and triglyceride (TG) for high-risk patients were also provided in the 2017 Taiwan lipid guidelines[3]. Lifestyle modification, including weight reduction, regular physical exercise, DASH diet, and limitation of alcohol intake, is the first step to control lipid. Lipid-lowering drugs include statins, cholesterol absorption inhibitors (ezetimibe), proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, nicotinic acids (niacin), fibric acids derivatives (fibrates), and long-chain omega-3 fatty acids. Among the aforementioned drugs, statin is usually the first line therapy.

Primary Targets of LDL-C for Adult High-risk Patients Suggested by the 2017 Taiwan Lipid Guidelines

Table 3 summarized the primary targets of LDL-C for adult patients with high risk suggested by current Taiwan lipid guideline. For patients with

Table 3. Primary target of LDL-C and secondary target for adult patients with high risk suggested by 2017 Taiwan lipid guideline

Disease category	LDL-C target
ACS	<70 mg/dL
ACS + DM	<55 mg/dL
Stable CAD	<70 mg/dL
PAD	<100 mg/dL
Ischemic stroke / TIA Symptomatic carotid stenosis / intracranial arterial stenosis	<100 mg/dL
DM	<100 mg/dL
DM + CV disease	<70 mg/dL
CKD (stage 3–5; GFR < 60 mL/min/1.73m^2)	Statin therapy should be initiated if LDL-C >100 mg/dL
FH	<100 mg/dL
FH + CV disease	<70 mg/dL
Disease category	**Secondary target**
ACS, Stable CAD, PAD with TG > 200 mg/dL	Non-HDL-C <100 mg/dL
DM	TG <150 mg/dL; HDL-C: >40 mg/dL in men >50 mg/dL in women

Abbreviation: ACS=acute coronary syndrome; CAD=coronary artery disease; CKD=chronic kidney disease; CV disease= cardiovascular disease; DM=diabetes mellitus; FH=familial hypercholesterolemia; GFR=glomerular filtration rate; LDL-C=low density lipoprotein-cholesterol; PAD=peripheral arterial disease; TIA=transient ischemic attack.
(Adapted from Li et al. 2017 Taiwan lipid guidelines for high risk patients. J Formos Med Assoc 2017; 116: 217-248)

ACS and stable CAD, LDL-C <70 mg/dL is the major target. A strict target of LDL-C <55 mg/dL can be considered in diabetic patients with ACS. For patients with PAD, a target of LDL-C <100 mg/dL should be suggested. After achieving LDL-C target, non-HDL-C can be considered as a secondary target for patients with TG > 200 mg/dL. The suggested non-HDL-C target is <100 mg/dL in patients with ACS, stable CAD, and PAD. For patients with ischemic stroke, TIA, and symptomatic carotid stenosis or intracranial arterial stenosis, LDL-C should be lowered to <100 mg/dL. Statin is necessary for DM patients with aforementioned cardiovascular diseases and the LDL-C target is <70 mg/dL. For DM patients with additional one of the cardiovascular risk factors, the LDL-C target should be lowered to < 70 mg/dL. After achieving LDL-C target, combination of other lipid-lowering agents with statin is considered for DM patients to attain the secondary target of TG <150 mg/dL and HDL-C >40 in men and >50 mg/dL in women. In adults with glomerular filtration rate (GFR) <60 mL/min/1.73m^2 without chronic dialysis (CKD stage 3–5), statin therapy should be initiated if LDL-C ≥100 mg/dL (Table 3)[4]. Mutations in LDL receptor (LDLR), apolipoprotein B (Apo B) and PCSK9 genes are the common causes of FH. Family history, clinical history of premature CAD, physical findings of xanthoma or corneal arcus and high levels of LDL-C are essential clues for the diagnosis of FH. In addition to conventional therapies, adjunctive treatment with mipomersen, lomitapide, or PCSK9 inhibitors are recommended to further reduce LDL-C in patients with FH.

New Pharmacologic Treatment to Decrease Circulating LDL-C

Several novel agents have become available as adjunctive treatment of FH: mipomersen, lomitapide, and PCSK9 inhibitors (evolocumab, alirocumab). These agents lead to additive LDL-C lowering when combined with other lipid-lowering drugs or procedures such as statins, ezetimibe, and apheresis. As a result, these novel agents should be considered for the treatment of FH and for those patients who cannot achieve LDL-C targets with conventional therapy. Mipomersen and lomitapide reduce the production of very low density lipoprotein (VLDL), whereas the PCSK9 inhibitors result in an increased catabolism of LDL-C via upregulating LDLR. Table 4 summarized the properties, indication, dosage, administration, and effect on lipid profiles of these agents.

Table 4. Summary of recent new pharmacological agents to decrease circulating LDL-C

Agent	Mechanism	Approved indication	Dosage and administration	Effect on lipid profiles
Mipomersen	ASO inhibitor of Apo B-100 synthesis	Adjunctive therapy in HoFH	200 mg s.c. once weekly	LDL-C↓: near 40% TG↓: 15-40% HDL-C↑: no effect
Lomitapide	MTP inhibitor	Adjunctive therapy in HoFH	initiate at 5 mg/d, titrating to maximum of 60 mg/d	LDL-C↓ >40% TG↓ >40% HDL-C↑: no effect
Evolocumab	PCSK9 inhibitor	Adjunctive therapy in HeFH and HoFH	HeFH: 140 mg s.c. every 2 wk or 420 mg s.c. once monthly HoFH: 420 mg s.c. once monthly	LDL-C↓: >40% TG↓: near 15% HDL-C↑: near 15%
Alirocumab	PCSK9 inhibitor	Adjunctive therapy in HeFH	HeFH: 75-150 mg s.c. every 2 wk	

Abbreviation: Apo=apolipoprotein; ASO= antisense oligonucleotide; d = day; HDL-C=high-density lipoprotein cholesterol; HeFH = hetereozygous familial hypercholesterolemia; HoFH = homozygous familial hypercholesterolemia; LDL-C=low-density lipoprotein cholesterol; MTP= microsomal triglyceride transfer protein; PCSK9 = proprotein convertase subtilisin/kexin type 9; s.c.=subcutaneous; TG=triglyceride.
(Adapted from Li et al. 2017 Taiwan lipid guidelines for high risk patients. J Formos Med Assoc 2017;116:217–248.

Mipomersen

Mipomersen was approved by the United States Food and Drug Administration (FDA) in 2013 for the treatment of patients with homozygous familial hypercholesterolemia (HoFH), based on the data derived in a phase III study in which a 24.7% LDL-C reduction was observed in 34 patients with HoFH treated by mipomersen. Other studies have also demonstrated similar efficacy of mipomersen in patients with hetereozygous familial hypercholesterolemia (HeFH) when added to conventional lipid-lowering therapy[5]. Mipomersen is an antisense oligonucleotide (ASO) inhibitor of Apo B that inhibits the protein translation at the mRNA level, thereby ultimately reducing LDL-C levels[5,6].

A meta-analysis including 8 trials and 462 patients with dyslipidemia showed mean LDL-C and TG reductions of approximately 32% and 36%, respectively[7]. Common adverse events with mipomersen included flu-like reactions, injection site reactions, and elevations in alanine aminotransaminase levels[8].

Lomitapide

The microsomal triglyceride transfer protein (MTP) is a major mediator of the assembly and secretion of VLDL from the liver, and chylomicrons from the intestine. By binding directly to MTP, lomitapide inhibits the synthesis of chylomicrons in the intestine and VLDL in the liver, with a marked reduction in plasma LDL-C. Lomitapide has been approved by the FDA for the treatment of HoFH. In a phase III study that enrolled 29 patients with HoFH who received lomitapide (median dose was 40 mg) in addition to their usual lipid-lowering therapy, the mean LDL-C reductions were approximately 50% after 26 weeks of treatment. Besides, Apo B and TG levels were significantly reduced by 49% and 45%, respectively. The most common adverse events were gastrointestinal disorders, manifested as diarrhea, nausea, dyspepsia, and vomiting, accumulation of liver fat and elevation of liver transaminases. The accumulation of fat appears to be reversible after discontinuation of lomitapide[9,10].

PCSK9 Inhibitors

The major effect of PCSK9 is to bind and target LDLR for degradation in lysosomes, and prevent normal recycling of LDLR back to the cell surface, thereby increasing plasma LDL-C concentrations. Therefore, inhibition of PCSK9 can prevent PCSK9-mediated LDLR degradation, permit LDLR to recycle back to the liver cell surface, and result in decreasing LDL-C from circulation. There are two PCSK9 inhibitors (i.e., evolocumab, and alirocumab) that are monoclonal antibodies and now available for treatment of patients with FH. Some meta-analyses have demonstrated that a mean LDL-C reduction of approximately 48%-62% could be achieved by PCSK9 inhibitors[11,12]. In a RCT involving 27,564 patients with ASCVD and LDL-C levels of $\geq$ 70 mg/dL who were receiving statin therapy, inhibition of PCSK9 with evolocumab could significantly lower LDL-C levels and reduce the risk of adverse cardiovascular events[13]. Another RCT showed that there was a reduced risk of cardiovascular events for high-risk patients treated with alirocumab in addition to statin therapy[14]. The most common adverse events among those receiving PCSK9 inhibitors were upper respiratory tract infection, influenza, gastroenteritis, and nasopharyngitis[3].

Conclusions

Statins have been the main treatment for patients with dyslipidemia and for prevention of clinical ASCVD. Before initiating statin therapy, the patient's medical history, clinical evidence of ASCVD, and the 10-year risk of ASCVD should be evaluated carefully to identify high-risk patients who will benefit from statin therapy. The current Taiwan lipid guidelines have clearly addressed the treatment goals of LDL-C for patients with high risk

(i.e., patients with ACS, DM, CAD, PAD, ischemic stroke, TIA, symptomatic carotid stenosis or intracranial arterial stenosis, CKD, and FH). In addition to conventional therapies, adjunctive treatment with mipomersen, lomitapide, or PCSK9 inhibitors are considered to further reduce LDL-C in patients with FH. Adherence to both medication and lifestyle regimens are required for ASCVD risk reduction.

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治療膽固醇與降低動脈粥樣硬化心血管風險：簡介目前的治療指引與新穎藥物

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摘 要

他汀 (statin) 類藥物一直是血脂異常患者和預防動脈粥樣硬化性心血管疾病 (ASCVD) 的主要治療方法。針對預防 ASCVD 的 statin 治療，2013 年美國心臟病學會 / 美國心臟協會 (ACC / AHA) 的血脂治療準則提出了四大受益族群，包括：已有臨床 ASCVD 病人，低密度膽固醇 (LDL-C) ≥190 mg/dL，糖尿病，以及預測 10 年 ASCVD 風險 ≥7.5% 者。此外，2013 年 ACC / AHA 血脂治療準則也建議使用不同的 statin 劑量強度來治療不同風險類別的病人，但卻沒有提出建議的 LDL-C 治療目標。2016 年歐洲心臟學會 (ESC) 和歐洲動脈粥樣硬化協會 (EAS) 的血脂治療準則提出了 SCORE 風險評估系統。對於非常高風險 (very high-risk)，高風險 (high-risk) 和中度風險 (moderate-risk) 的患者，LDL-C 的治療目標分別為 <70 mg/dL，<100 mg/dL 和 <115 mg/dL。而 2017 年台灣血脂治療準則明確界定了高危病人和 LDL-C 的治療目標。對於周邊動脈疾病 (PAD)，腦血管疾病，DM 和家族性高膽固醇血症 (FH) 患者，建議 LDL-C 須 <100 mg/dL，而急性冠心症 (ACS) 或穩定性冠狀動脈疾病 (CAD) 病人則建議 LDL-C 須 <70 mg/dL。對於 ACS 且合併 DM 之病人，LDL-C 應 <55 mg/dL。目前已有幾種新型藥物用於 FH 的輔助治療，與 statin 類藥物併用，進一步降低血液中的 LDL-C。Mipomeren 是載脂蛋白 (Apo B) 的反寡核苷酸 (ASO) 抑製劑。Lomitapide 可抑制微粒體甘油三酯轉運蛋白 (MTP)。Evolocumab，alirocumab 和 bococizumab 是前蛋白轉化酶枯草桿菌蛋白酶 / kexin 9 型 (PCSK9) 抑製劑。上述新型藥物是否可以預防臨床不良心血管事件仍待進一步的研究。