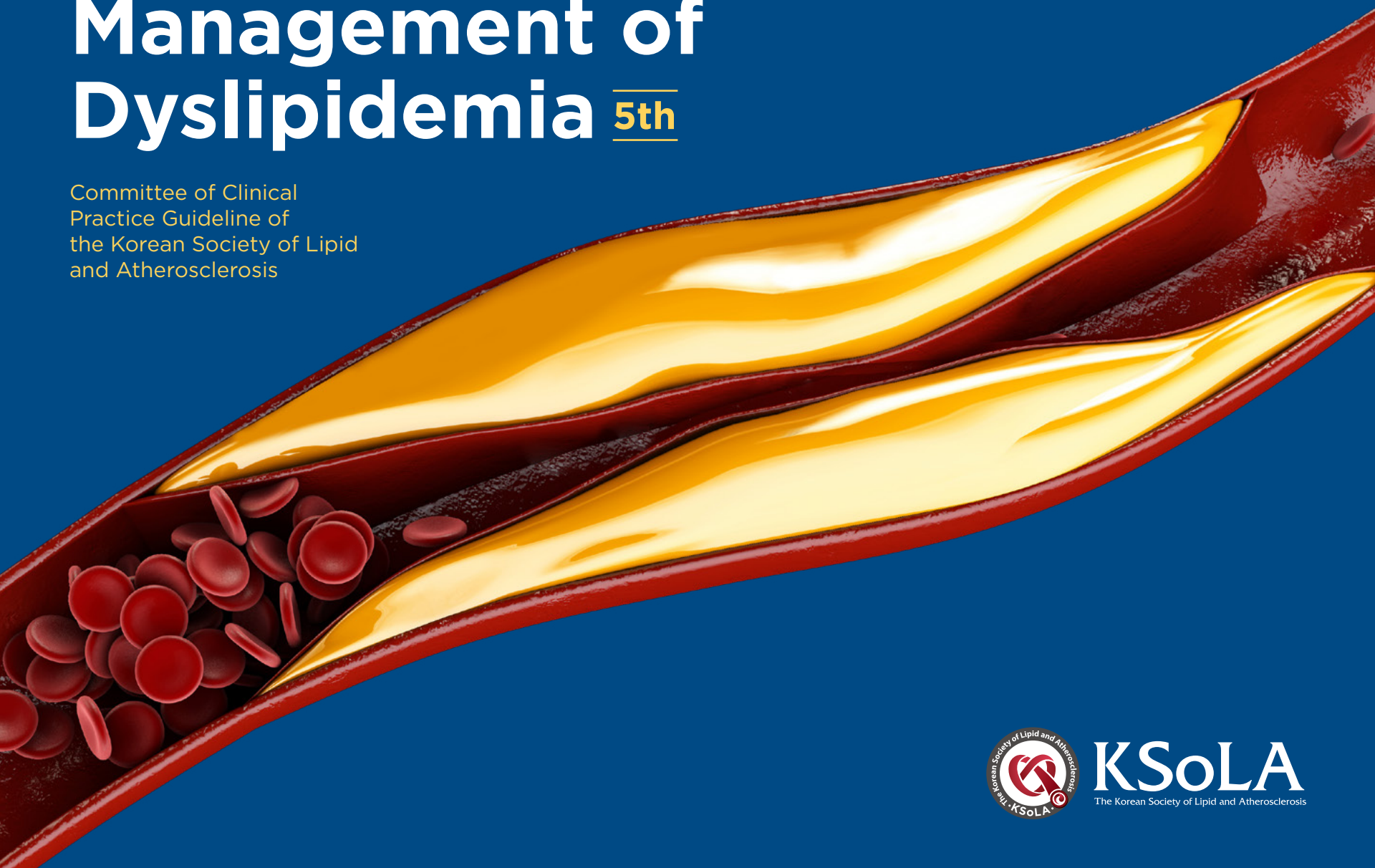
Korean Guidelines for the Management of Dyslipidemia 5th

Committee of Clinical Practice Guideline of the Korean Society of Lipid and Atherosclerosis



KSoLA
The Korean Society of Lipid and Atherosclerosis

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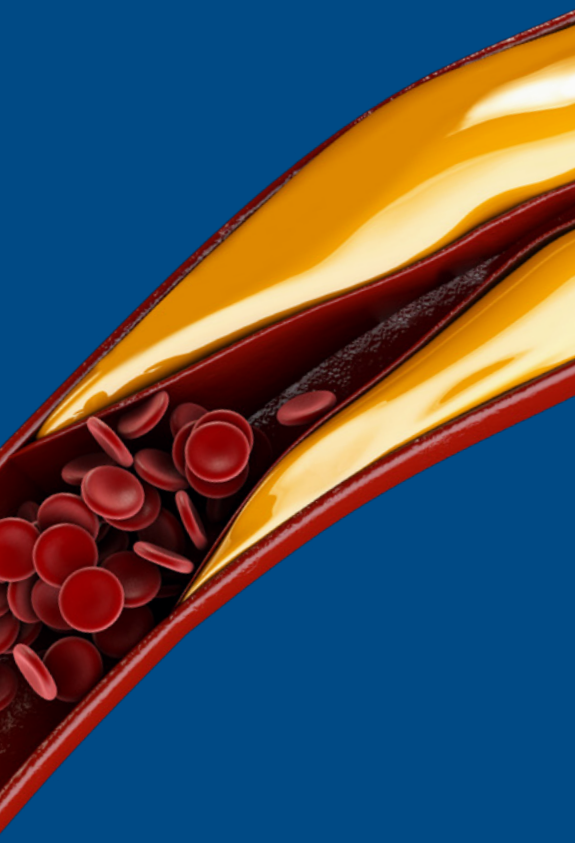


Contents

Criteria for the classification of dyslipidemia

Unit: mg/dL

Risk	Total Cholesterol
High	≥ 240
Border-line	200~239
Optimal	< 200

Risk	LDL Cholesterol
Very High	≥ 190
High	160~189
Border-line	130~159
Normal	100~129
Optimal	< 100

Risk	Triglyceride
Very High	≥ 500
High	200~499
Border-line	150~199
Optimal	< 150

Risk	HDL Cholesterol
Low	< 40
High	≥ 60

LDL, low-density lipoprotein ; HDL, high-density lipoprotein.

Major risk factors of atherosclerotic cardiovascular disease other than LDL-C[1)]

Age
(men ≥ 45; women ≥ 55 years)

Family history of premature coronary artery disease
If any of the parents or siblings(men < 55; women < 65 years) has coronary artery disease

Hypertension
(blood pressure ≥ 140/90 mmHg or on antihypertensive medication)

Smoking

Low HDL cholesterol level
(< 40 mg/dL)

1) High HDL cholesterol level (≥ 60 mg/dL) is considered as a protective factor, and one factor is excluded from the total number of risk factors

LDL-C, low-density lipoprotein cholesterol ; HDL-C, high-density lipoprotein cholesterol.

Recommendations for treatment goals of LDL-C and non-HDL-C

Risk category	LDL-C (mg/dL)	non-HDL-C (mg/dL)
Coronary artery disease[1)*]	< 55	< 85
Atherosclerotic stroke and transient ischemic attack* Carotid artery disease* Peripheral artery disease* Abdominal aortic aneurysm* Diabetes mellitus (duration ≥ 10 years or major risk factor[†] or target organ damage)[2)]	< 70	< 100
Diabetes mellitus (duration < 10 years and no major risk factors[†])	< 100	< 130
Moderate risk (major risk factors[†] ≥ 2)	< 130	< 160
Low risk (major risk factors[†] ≤ 1)	< 160	< 190

*It is also recommended to reduce LDL-C by ≥ 50% from the baseline level.
†Age (men ≥ 45 years, women ≥ 55 years), family history of premature ASCVD, hypertension, smoking, and low HDL cholesterol level (< 40 mg/dL).

1) In patient with acute myocardial infarction, statin is recommended irrespective of LDL-C level.
2) In diabetes mellitus with target organ damage (albuminuria, nephropathy, retinopathy, neuropathy, left ventricular hypertrophy) or major risk factors[†] ≥ 3: target LDL-C < 55 mg/dL (optional)

LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.

Treatment strategies according to risk categories and LDL-C

Risk category	LDL-C (mg/dL)					
	<55	55-69	70-99	100-129	130-159	≥ 160
Coronary artery disease[1]*	Lifestyle modification and cosider drug	Lifestyle modification and concomitant drug internvention	Lifestyle modification and concomitant drug internvention	Lifestyle modification and concomitant drug internvention	Lifestyle modification and concomitant drug internvention	Lifestyle modification and concomitant drug internvention
Atherosclerotic stroke and transient ischemic attack* Carotid artery disease* Peripheral artery disease* Abdominal arotic aneurysm* Diabetest mellitus (duration ≥ 10 years or major risk factor† or target organ damage)[2]	Lifestyle modification	Lifestyle modification and cosider drug	Lifestyle modification and concomitant drug internvention	Lifestyle modification and concomitant drug internvention	Lifestyle modification and concomitant drug internvention	Lifestyle modification and concomitant drug internvention
Diabetes mellitus (duration < 10 years and no major risk factors*)	Lifestyle modification	Lifestyle modification	Lifestyle modification and cosider drug	Lifestyle modification and concomitant drug internvention	Lifestyle modification and concomitant drug internvention	Lifestyle modification and concomitant drug internvention
Moderate risk[3] (major risk factors* ≥ 2)	Lifestyle modification	Lifestyle modification	Lifestyle modification	Lifestyle modification and cosider drug	Lifestyle modification and concomitant drug internvention	Lifestyle modification and concomitant drug internvention
Low risk[3] (major risk factors* ≤ 1)	Lifestyle modification	Lifestyle modification	Lifestyle modification	Lifestyle modification	Lifestyle modification and cosider drug	Lifestyle modification and concomitant drug internvention

*It is also recommended to reduce LDL-C by ≥ 50% from the baseline level.
†Age (men ≥ 45 years, women ≥ 55 years), family history of premature ASCVD, hypertension, smoking, and low HDL cholesterol level (< 40 mg/dL).

1) In patient with acute myocardial infarction, statin is recommended irrespective of LDL-C level.
2) In diabetic patients with target organ damage (albuminuria, nephropathy, retinopathy, neuropathy, left ventricular hypertrophy) or major risk factors ≥ 3 (optional)
3) In groups with moderate and low risk, statin is considered when LDL-C is consistently high even after several weeks or months of lifestyle modification.

LDL-C, low-density lipoprotein cholesterol.

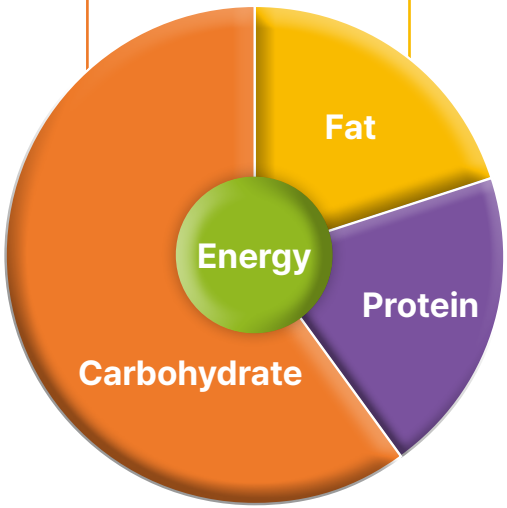
Dietary recommendation

Carbohydrate

- Total carbohydrate: ≤ 65% of energy intake
- Total sugars: < 10~20% of energy intake
- Dietary fiber: ≥ 25g

Alcohol

- Limit (≤ 1~2 drinks)

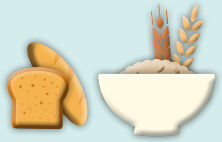


Fat

- Total fat: ≤ 30% of energy intake
- Saturated fatty acids: < 7% of energy intake
- Replace saturated fatty acids with mono- or polyunsaturated fatty acids
- Trans fatty acids: avoid
- Reduce cholesterol intake for patients with hypercholesterolemia

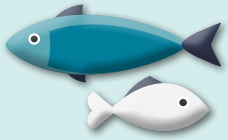
Consume energy intake to maintain a healthy weight

Consume a healthy dietary pattern with a focus on whole grains, legumes, vegetables, and fish



Consume whole grains as a staple food

Consume plenty of vegetables



Consume fish, lean meat, or legumes rather than red and processed meat

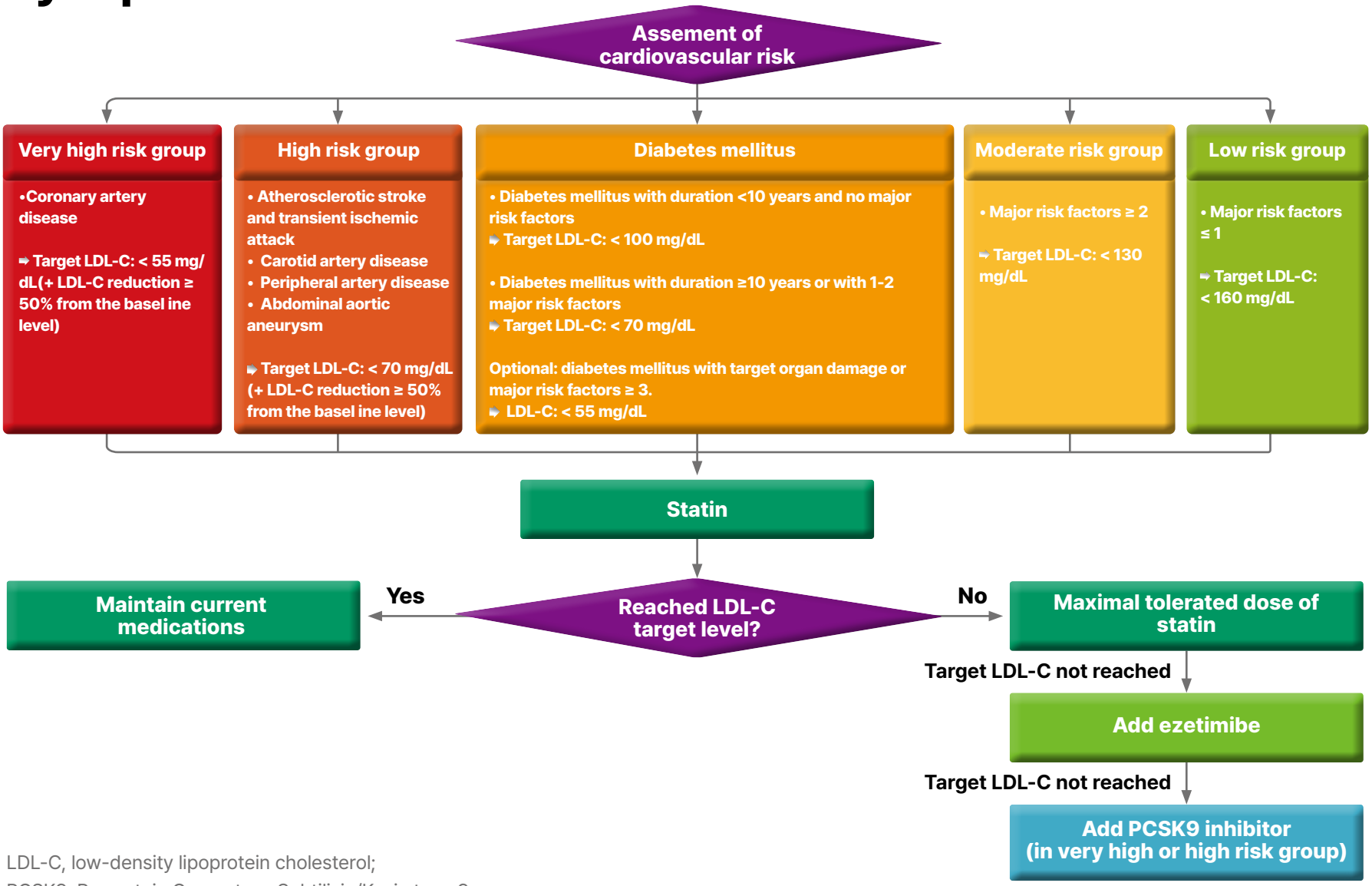
Consume fresh fruits

Exercise prescription for patients with dyslipidemia

	Aerobic exericse	Resistenace exercise	Stretching exercise
Frequency	5 or more days a week to maximize calorie consumption	2-3 days a week	2-3 days or more a week
Intensity	Moderate to high intensity, 40-75% of heart rate reserve[1,2)]	Moderate (50-69% of 1 RM[3)]) to high (70-85% of 1 RM[3)]) intensity for muscle strengthening	To the extent that the stretched area feels tight or slightly uncomfortable
Duration	30-60 minutes a day (50-60 minutes a day for weight reduction)	For muscle strength improvement: 2-4 sets, 8-12 reps; for muscle endurance improvement: 2 sets or less, 12-20 reps	10-30 seconds, 2-4 reps
Example	Continuous and rhythmic activities that use the large muscles (walking, cycling, swimming, etc.)	Use of resistance exercise equipment, full-body resistance training, free weight exercise, etc.	Static and dynamic stretching exercise

1) Heart rate reserve = maximal heart rate – resting heart rate
2) How to calculate target heart rate = (220-age-resting heart rate) x exercise intensity (0.40~0.75) + resting heart rate
3) 1 RM (repetition maximum) = intensity/weight that can be performed once with the maximum effort of the individual

Evidence-guided approach algorithm of dyslipidemia treatment



LDL-C, low-density lipoprotein cholesterol;
PCSK9, Proprotein Convertase Subtilisin/Kexin type 9.

Secondary causes of hypercholesterolemia or hypertriglyceridemia

	Elevated LDL cholesterol	Elevated Triglyceride
Diet	• Intake of saturated fatty acid • Intake of trans fatty acid • High caloric intake	• Alcohol drinking • High caloric intake • High carbohydrate intake
Drugs	• Diuretics • Glucocorticoid • Amiodarone • Cyclosporine	• Oral estrogen • Bile acid sequestrant • Retinoic acid • Sirolimus • Tamoxifen • Thiazide diuretics • Glucocorticoid • Protease inhibitor • Anabolic steroid • Raloxifen • Beta-blocker
Disease	• Obstructive liver disease • Nephrotic syndrome • Anorexia nervosa	• Chronic kidney disease • Nephrotic syndrome • Sepsis
Abnormal meta-bolism	• Obesity • Pregnancy • Hypothyroidism	• Obesity • Pregnancy • Uncontrolled diabetes

LDL, low-density lipoprotein.

Lipid-lowering efficacy and pharmacologic characteristics of statins

		Lovastatin	Pravastatin	Simvastatin	Atorvastatin	Fluvastatin	Rosuvastatin	Pitavastatin
Daily dose (mg)		20~40	10~40[1]	20~40	10~80	20~80	5~20[2]	1~4
LDL-C reduction (%)	24~28	20	20			40		1
	30~36	40	40	20	10	80		2
	39~45	80		40	20		5~10	4
	46~52				40~80		20	
Metabolism		CYP3A4	Sulfonation	CYP3A4	CYP3A4	CYP2C9	CYP2C9	Glucuronidation (Partial CYP2C9)
Protein binding (%)		> 95	43~67	95~98	98	98	88	> 99
Half-life (h)		2~4	2~3	1~3	13~30	0.5~3	19	12
Hydrophilicity		-	+	-	-	-	+	-
Elimination		Hepatobiliary	Hepatobiliary	Hepatobiliary	Hepatobiliary	Hepatobiliary	Hepatobiliary	Hepatobiliary
Renal elimination fraction (%)		10	20	13	< 2	< 6	28	15

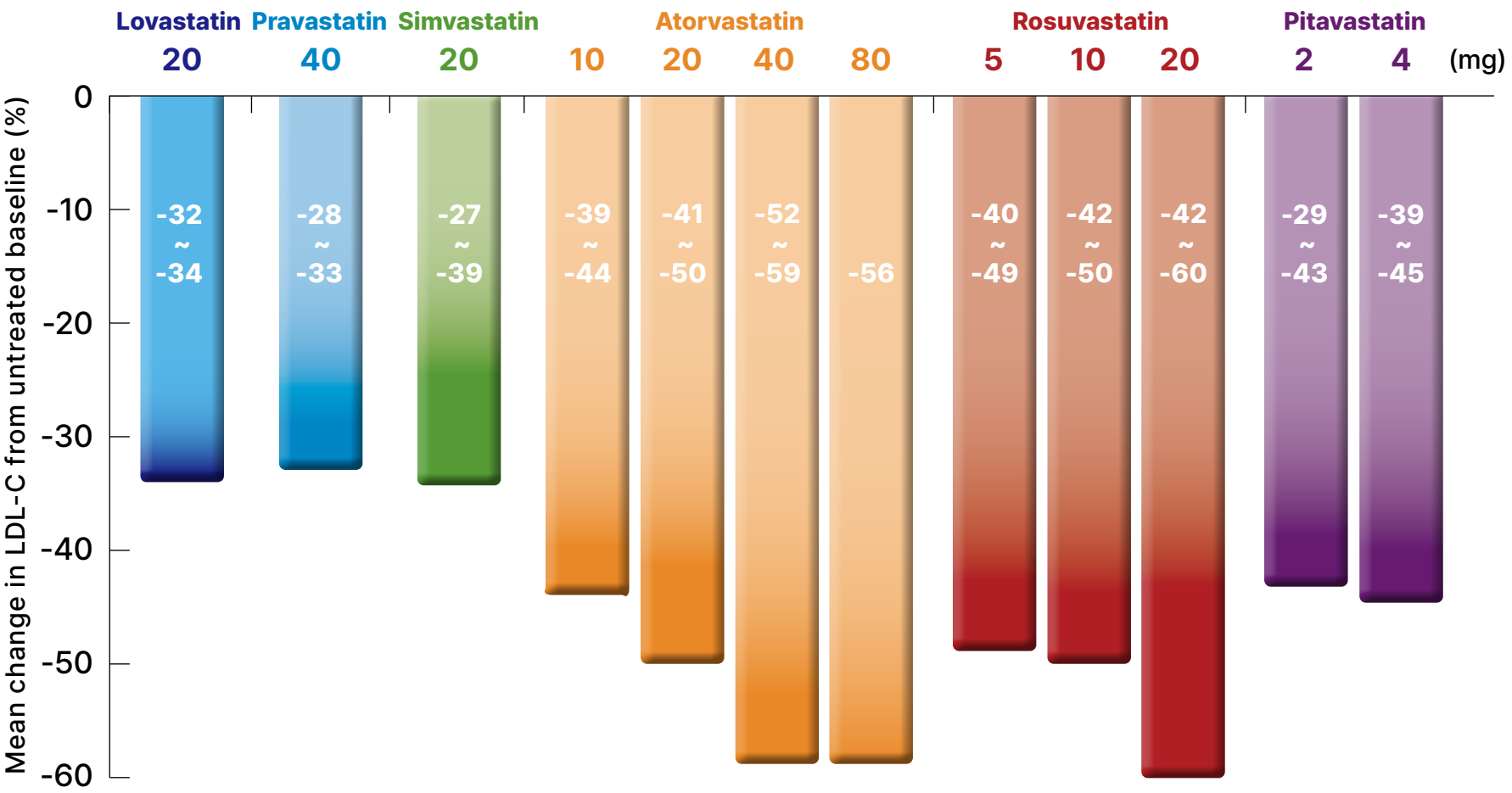
1) 40~80 mg in Caucasian countries
2) 5~40 mg in Caucasian countries

Summary of statin use

Statin: HMG-CoA reductase inhibitor

Dosing	Lovastatin	20-80 mg once daily, take with dinner
	Pravastatin	10-40 mg once daily, more effective to take it in the evening
	Simvastatin	20-40 mg once daily, more effective to take it in the evening
	Fluvastatin	20-80 mg once daily, more effective to take it in the evening
	Atorvastatin	10-80 mg once daily, not significantly affected by the time taken
	Rosuvastatin	5-20 mg once daily, not significantly affected by the time taken
	Pitavastatin	1-4 mg once daily, not significantly affected by the time taken
Monitoring		Lipid profiles, liver function test and muscle enzyme (in case of unexplained myalgia or muscle weakness)
Adverse effect		Dyspepsia, epigastric soreness, abdominal pain, hepatotoxicity, myopathy and diabetes mellitus
Contraindication		It is absolutely contraindicated in pregnant or lactating women and active or chronic liver disease. It is relatively contraindicated when co-administered with other drugs such as cyclosporin, macrolide antibiotics, antifungals, and cytochrome P-450 inhibitors.

LDL-C lowering effect of statins in Koreans



LDL-C, low-density lipoprotein cholesterol.

Dutch lipid clinic network criteria for familial hypercholesterolemia

Criteria		Points
1) Family history	1st-degree relative with known premature (men < 55 years; women < 60 years) coronary or vascular disease, or 1st-degree relative with known LDL-C > 95th percentile	1
	1st-degree relative with tendinous xanthoma and/or arcus cornealis, or children < 18 years with LDL-C > 95th percentile	2
2) Clinical history	Patient with premature CAD	2
	Patient with premature cerebral or peripheral vascular disease	1
3) Physical examination	Tendon xanthoma	6
	Arcus cornealis at age <45 years	4
4) LDL-C (without treatment)	> 8.5 mmol/L (325 mg/dL)	8
	6.5-8.4 mmol/L (251-325 mg/dL)	5
	5.0-6.4 mmol/L (191-250 mg/dL)	3
	4.0-4.9 mmol/L (155-190 mg/dL)	1
5) DNA analysis	Functional mutation in the LDLR, APOB, or PCSK9 genes	8

Choose only one score per group, the highest applicable, diagnosis is based on the total number of points
'definite' FH: ≥ 9 points / 'probable' FH: 6-8 points / 'possible' FH: 3-5 points

Simon Broome diagnostic criteria for familial hypercholesterolemia

Definite FH	**Cholesterol criteria : < 16 years: total cholesterol > 260 mg/dL or LDL-C > 155 mg/dL** **≥ 16 years: total cholesterol > 290 mg/dL or LDL-C > 190 mg/dL** **Plus at least one of the two:** **1. Tendon xanthomas in patient, or in first-[1] or in second-degree[2] relative** **2. DNA-based evidence of an *LDLR* mutation, familial defective apoB-100, or a PCSK9 mutation**
Possible FH	**Cholesterol criteria : < 16 years: total cholesterol > 260 mg/dL or LDL-C > 155 mg/dL** **≥ 16 years: total cholesterol > 290 mg/dL or LDL-C > 190 mg/dL** **Plus at least one of the two:** **1. Family history of myocardial infarction : aged ≤ 60 years in first-degree[1] relative or aged ≤ 50 years in second-degree[2] relative** **2. Family history of raised total cholesterol :** **> 290 mg/dL in adult first- or second-degree relative or** **> 260 mg/dL in child, brother or sister aged < 16 years**

1) First-degree relative: parents, siblings or children
2) Second-degree relative: grandparents, siblings of parents

FH, familial hypercholesterolemia ; LDL-C, low-density lipoprotein cholesterol ; LDL-R, low-density lipoprotein receptor ; apoB, apolipoprotein B.

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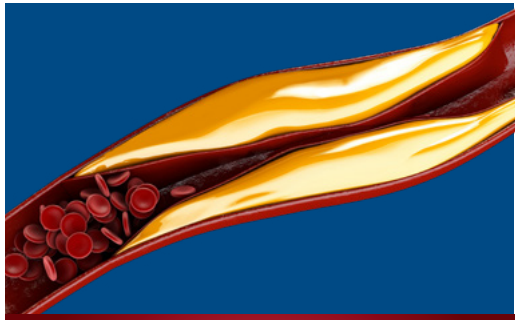

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