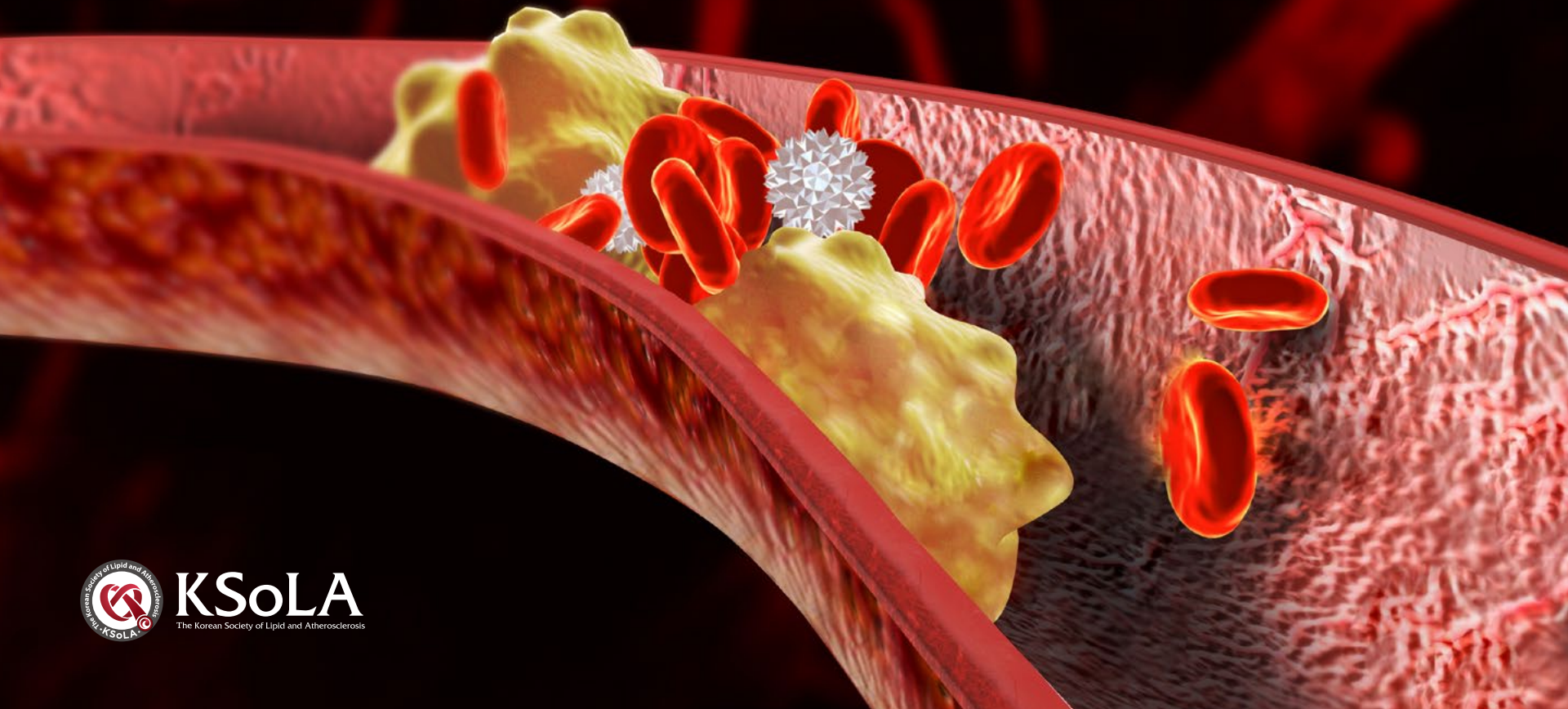


Korean Guidelines for the Management of Dyslipidemia ^{4th Ed}

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



KSoLA
The Korean Society of Lipid and Atherosclerosis

Korean Guideline for the Management of Dyslipidemia ^{4th Ed}

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Criteria for the diagnosis of dyslipidemia¹⁾ in Korea



Unit: mg/dL

Risk	Total Cholesterol	Risk	LDL Cholesterol	Risk	Triglyceride	Risk	HDL Cholesterol
High	≥ 240	Very High	≥ 190	Very High	≥ 500	Low	< 40
Border-line	200~239	High	160~189	High	200~499	High	≥ 60
Optimal	< 200	Border-line	130~159	Border-line	150~199		
		Normal	100~129	Optimal	< 150		
		Optimal	< 100				

1) Dyslipidemia is defined as total cholesterol ≥ 240 mg/dL or one or more of the followings: LDL cholesterol ≥ 160 mg/dL, triglyceride ≥ 200 mg/dL, or HDL cholesterol < 40 mg/dL

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

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



Risk categories		LDL-C (mg/dL)	non-HDL-C (mg/dL)
Very high risk	Coronary artery disease	< 70	< 100
	Atherosclerotic Stroke and transient ischemic attack		
	Peripheral artery disease		
High risk	Carotid artery disease ¹⁾	< 100	< 130
	Abdominal aortic aneurysm		
	Diabetes mellitus ²⁾		
Moderate risk	Major risk factors ³⁾ ≥ 2	< 130	< 160
Low risk	Major risk factors ³⁾ ≤ 1	< 160	< 190

1) In case of significant carotid artery stenosis (which has been shown to be strongly predisposed to clinical events)

2) Target goal can be lowered in patients who have target organ damage or major cardiovascular risk factors.

3) Age (men ≥ 45 years, women ≥ 55 years), family history of premature ASCVD, hypertension, smoking, and low HDL cholesterol level

LDL-C, low-density lipoprotein cholesterol ; non-HDL-C, non-high-density lipoprotein cholesterol ; ASCVD, atherosclerotic cardiovascular disease

Recommendations for treatment goals of LDL-C and non-HDL-C in extreme risk group



Risk category		LDL-C (mg/dL)	non-HDL-C (mg/dL)	ApoB (mg/dL)
Extreme risk	<ol style="list-style-type: none"> 1) Progressive ASCVD including unstable angina in patients after achieving an LDL-C < 70 mg/dL 2) Established clinical cardiovascular disease in patients with DM, 3) Established clinical cardiovascular disease in patients with stage 3 or 4 CKD, 4) Established clinical cardiovascular disease in HeFH 5) History of premature ASCVD (< 55M, < 65F) 	< 55	< 80	< 70

ASCVD, Atherosclerotic cardiovascular disease ; LDL-C, low-density lipoprotein cholesterol ; non-HDL-C, non-high-density lipoprotein cholesterol ; DM, diabetes mellitus ; CKD, chronic kidney disease ; HeFH, Heterozygous familial hypercholesterolemia

The LDL-C goal < 55 mg/dL is recommended for extreme risk category as above in 2017 American Association of Clinical Endocrinologists and American College of Endocrinology guidelines for management of dyslipidemia and prevention of cardiovascular disease.

This recommendation is currently under discussion in The Korean Society of Lipid and Atherosclerosis.

Treatment strategies according to risk categories and LDL-C



Risk categories		LDL-C (mg/dL)					
		< 70	70~99	100~129	130~159	160~189	≥ 190
Very high risk¹⁾	Coronary artery disease	Lifestyle modification and consider drug	Lifestyle modification and concomitant drug intervention	Lifestyle modification and concomitant drug intervention	Lifestyle modification and concomitant drug intervention	Lifestyle modification and concomitant drug intervention	Lifestyle modification and concomitant drug intervention
	Atherosclerotic Stroke and transient ischemic attack						
	Peripheral artery disease						
High risk	Carotid artery disease²⁾	Lifestyle modification	Lifestyle modification and consider drug if uncontrolled	Lifestyle modification and concomitant drug intervention	Lifestyle modification and concomitant drug intervention	Lifestyle modification and concomitant drug intervention	Lifestyle modification and concomitant drug intervention
	Abdominal aortic aneurysm						
	Diabetes mellitus³⁾						
Moderate risk⁴⁾	Major risk factors ≥ 2	Lifestyle modification	Lifestyle modification	Lifestyle modification and consider drug if uncontrolled	Lifestyle modification and concomitant drug intervention	Lifestyle modification and concomitant drug intervention	Lifestyle modification and concomitant drug intervention
Low risk⁴⁾	Major risk factors ≤ 1	Lifestyle modification	Lifestyle modification	Lifestyle modification	Lifestyle modification and consider drug if uncontrolled	Lifestyle modification and concomitant drug intervention	Lifestyle modification and concomitant drug intervention

- 1) In patient with acute myocardial infarction, statin is recommended irrespective of LDL cholesterol level.
In very high-risk group except for patients with acute myocardial infarction, statin can be considered even if LDL cholesterol level is < 70 mg/dL.
- 2) In case of significant carotid artery stenosis (which has been shown to be strongly predisposed to clinical events)
- 3) Risk category in patients who have target organ damage or major cardiovascular risk factors could be raised to higher level.
- 4) In groups with moderate and low risk, statin is considered when LDL cholesterol is consistently high even after several weeks or months of lifestyle modification.

LDL-C, low-density lipoprotein cholesterol

Major risk factors of atherosclerotic cardiovascular disease other than LDL-C¹⁾



Age

(men \geq 45; women \geq 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 \geq 140/90 mmHg or on antihypertensive medication)



Smoking

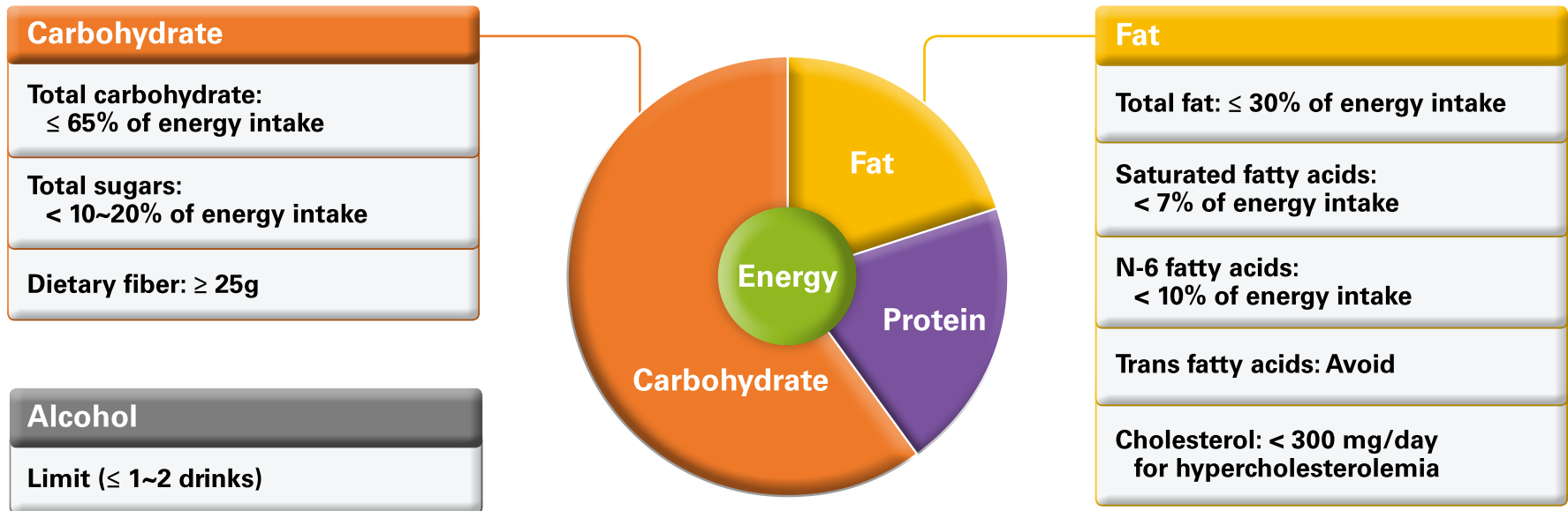


Low HDL cholesterol level

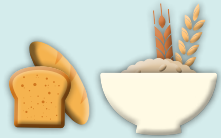


(< 40 mg/dL)

¹⁾ High HDL cholesterol level (\geq 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, high-density lipoprotein cholesterol

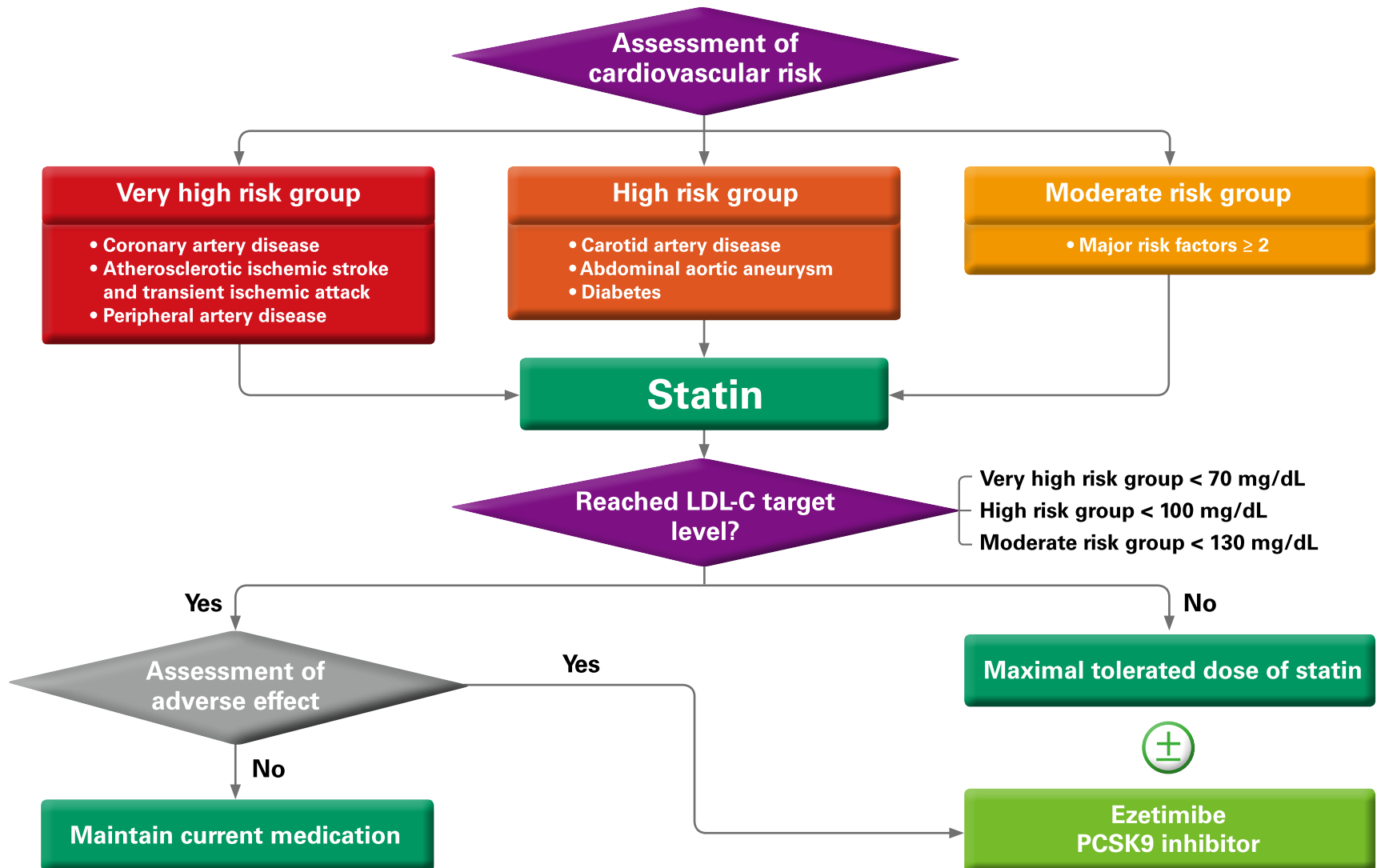
Dietary recommendation



 **Consume energy intake to maintain a healthy weight**

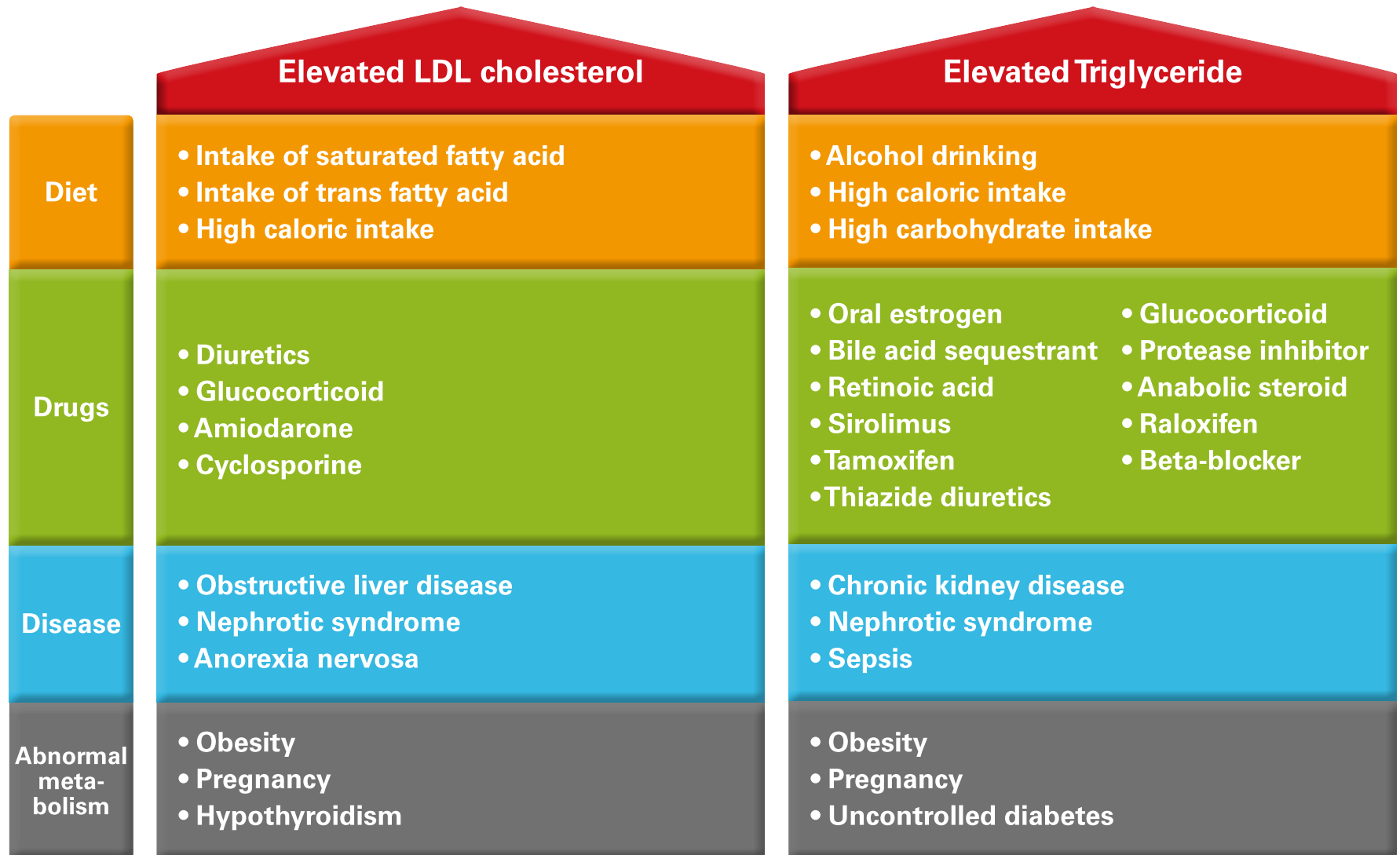
Consume a healthy dietary pattern with a focus on whole grains, vegetables & fish				
	Consume whole grains ($2/3\sim 1$ serving/meal)	Consume plenty of vegetables ($2.5\sim 3$ serving/meal)	Consume fish, lean meat, eggs, or beans ($1\sim 2$ serving/meal) & include fatty fish $2\sim 3$ times/week	Consume fresh fruits ($1\sim 2$ serving/day)

Evidence-guided approach algorithm of dyslipidemia treatment



LDL-C, low-density lipoprotein cholesterol

Secondary causes of hypercholesterolemia or hypertriglyceridemia



LDL, low-density lipoprotein

Lipid-lowering drugs for dyslipidemia



Drugs	Major indication	Pharmacologic mechanism	Major adverse effect
Statin	LDL-C ↑ High CV risk group	Cholesterol synthesis ↓ Hepatic LDL-R ↑ ↓VLDL production	Myalgia, arthralgia, elevated transaminases, dyspepsia
Ezetimibe	LDL-C ↑	Intestinal cholesterol absorption ↓ LDL-R ↑	Elevated transaminases
Bile acid sequestrant	LDL-C ↑	Bile acid excretion ↑ LDL-R ↑	Bloating, constipation, elevated TG
PCSK9 inhibitor	LDL-C ↑	Hepatic LDL-R ↑	Itching at the injection site, flu-like symptoms
Fibric acid derivative	TG ↑	LPL ↑ VLDL synthesis ↓	Dyspepsia, myalgia, gallstones, elevated transaminases
Omega-3 fatty acid	TG ↑	TG catabolism ↑	Dyspepsia, diarrhea, fishy odor to breath

LDL-C, low-density lipoprotein cholesterol ; CV, cardiovascular ; LDL-R, low-density lipoprotein receptor ; VLDL, very low-density lipoprotein ; LPL, lipoprotein lipase ; TG, triglyceride

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

Recommended daily doses of statin in adults with chronic kidney disease¹⁾



Statin	eGFR G1-G2	eGFR G3a-G5, including patients on dialysis or with a kidney transplant
Lovastatin	GP ²⁾	nd ³⁾
Pravastatin	GP	40
Simvastatin	GP	40
Simvastatin /ezetimibe	GP	20/10
Atorvastatin	GP	20
Fluvastatin	GP	80
Rosuvastatin	GP	10
Pitavastatin	GP	2

(mg/day)

1) KDIGO, Kidney Disease-Improving Global Outcomes (2013)

2) GP, any dose approved for general population

3) nd, not done or not studied

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-degree²⁾ 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-degree¹⁾ relative or aged ≤ 50 years in second-degree²⁾ 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

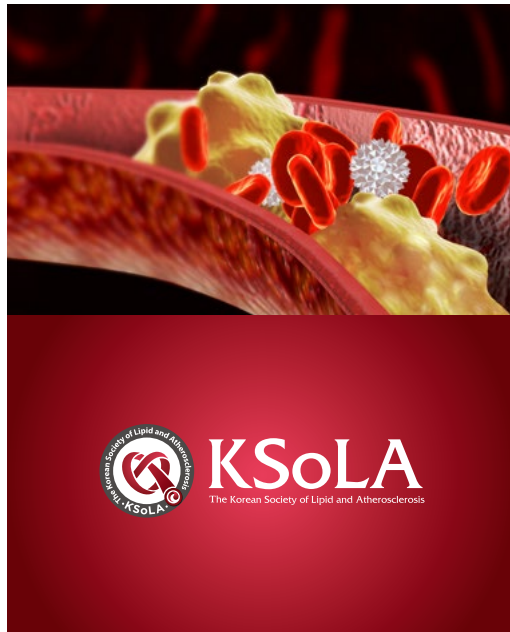
FH, familial hypercholesterolemia ; LDL-C, low-density lipoprotein cholesterol ; LDL-R, low-density lipoprotein receptor ; apoB, apolipoprotein B

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