Training series on "Screening and Evaluation of Comprehensive Intervention for Groups at High Risk of Cardiovascular Disease

Treatment of Hyperlipidemia

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- **Principles of treatment for dyslipidemia**
- **Therapeutic lifestyle recommendations**
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Assessment of Overall Cardiovascular Risk

Key Point

Interventions of different intensities according to the risk of ASCVD are the core strategy for the prevention and treatment of dyslipidemia.

Overall cardiovascular risk assessment is the basis for treatment decisions for dyslipidemia; and the risk of cardiovascular disease should be a concern for those younger than 55 years of age.

Diagnosed with ASCVD - classified as very high risk.

Those who meet one of the following conditions are directly classified as high-risk.

(1) LDL-C ≥ 4.9 mmol/L (190 mg/dl).

(2) 1.8 mmol/L (70 mg/dl) ≤ LDL-C < 4.9 mmol/L (190 mg/dl) in patients with diabetes mellitus, ≥40 years of age.

ASCVD risk stratification by number of risk factors was not required for the very high risk and high risk groups meeting the above criteria.

Assessment of Overall Cardiovascular Risk

- **Individuals who do not have any of the above conditions should be evaluated for 10-year ASCVD risk**

Number of risk factors *		Serum Cholesterol Levels (mmol/L)		
		3.1 ≤ TC <4.1(or) 1.8 ≤ LDL-C <2.6	4.1 ≤ TC <5.2(or) 2.6 ≤ LDL-C <3.4	5.2 ≤ TC <7.2(or) 3.4 ≤ LDL-C <4.9
Without HTN	0-1	Low risk (<5%)	Low risk (<5%)	Low risk (<5%)
	2	Low risk (<5%)	Low risk (<5%)	Intermediate risk (5%~9%)
	3	Low risk (<5%)	Intermediate risk (5%~9%)	Intermediate risk (5%~9%)
With HTN	0	Low risk (<5%)	Low risk (<5%)	Low risk (<5%)
	1	Low risk (<5%)	Intermediate risk (5%~9%)	Intermediate risk (5%~9%)
	2	Intermediate risk (5%~9%)	High risk (≥ 10%)	High risk (≥ 10%)
	3	High risk (≥ 10%)	High risk (≥ 10%)	High risk (≥ 10%)

Age <55 & Intermediate risk, evaluate residual risk

Individuals with ≥ 2 of the following risk factors are defined as high risk.

- **SBP ≥ 160 mmHg or DBP ≥ 100 mmHg**
- **BMI ≥ 28 kg/m²**
- **Non-HDL-C ≥ 5.2 mmol/L (200 mg/dl)**
- **Smoking**
- **HDL-C < 1.0 mmol/L (40 mg/dl)**

***: smoking, low HDL-C men ≥ 45 years or women ≥ 55 years.**

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Principles of treatment for dyslipidemia

- **LDL-C levels are the primary target of intervention, and non-HDL-C can be a secondary target.**
- **Target values: LDL-C <1.8 mmol/L for very high risk; LDL-C <2.6 mmol/L for high risk; LDL-C <3.4 mmol/L for intermediate and low risk.**
- **For those with high LDL-C baseline values who cannot reach the target value, LDL-C should be reduced by at least 50%. For very high-risk patients with LDL-C baseline within target values, LDL-C should still be reduced by about 30%.**
- **Statins are the first choice for lipid-lowering therapy. It is reasonable to start with moderate-strength statins.**

LDL-C/non-HDL-C targets

Risk Stratification	LDL-C	nom -HDL-C
Low & Intermediate	<3.4mmol/L (130 mg/dl)	<4.1mmol/L (160 mg/dl)
High	<2.6 mmol/L (100 mg/dl)	<3.4 mmol/L (130 mg/dl)
Very High	<1.8mmol/L (70 mg/dl)	<2.6 mmol/L (100 mg/dl)

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Therapeutic lifestyle changes

Quit smoking

Balanced Diet

Exercise

Weight Control

If dyslipidemia has occurred, regardless of the severity and whether or not medication is required**,** **lifestyle interventions should be started immediately** and maintained long after lipids have returned to normal to avoid rebound of lipid levels.

Therapeutic lifestyle changes

- The intensity of exercise varies from person to person, and the heart rate should be kept at (220-age) *60%~85%.
- Aerobic physical activity 3-5 sessions per week, 30-60 minutes per session.
- Walking, jogging, Taiji, gateball, and other aerobic exercises.

Patients should consume a dietary pattern that emphasizes intake of vegetables, fruits, whole grains, legumes, healthy protein sources (low-fat dairy products, low-fat poultry (without the skin), fish/seafood, and nuts), and nontropical vegetable oils; and limits intake of sweets, sugar-sweetened beverages, and red meats.

- Reduce weight to effectively blood lipid levels.
- A body mass index (BMI) of less than 24 is recommended. BMI= weight (kg)/height (m) ^{2}.
- "eat less and move more". Diet pills are not recommended.

中国胆固醇教育计划血脂异常防治建议专家组. 中国慢性疾病防治基层医院诊疗手册——血脂异常防治问答[J]. 中华健康管理学杂志, 2014, 8(5):293-295.

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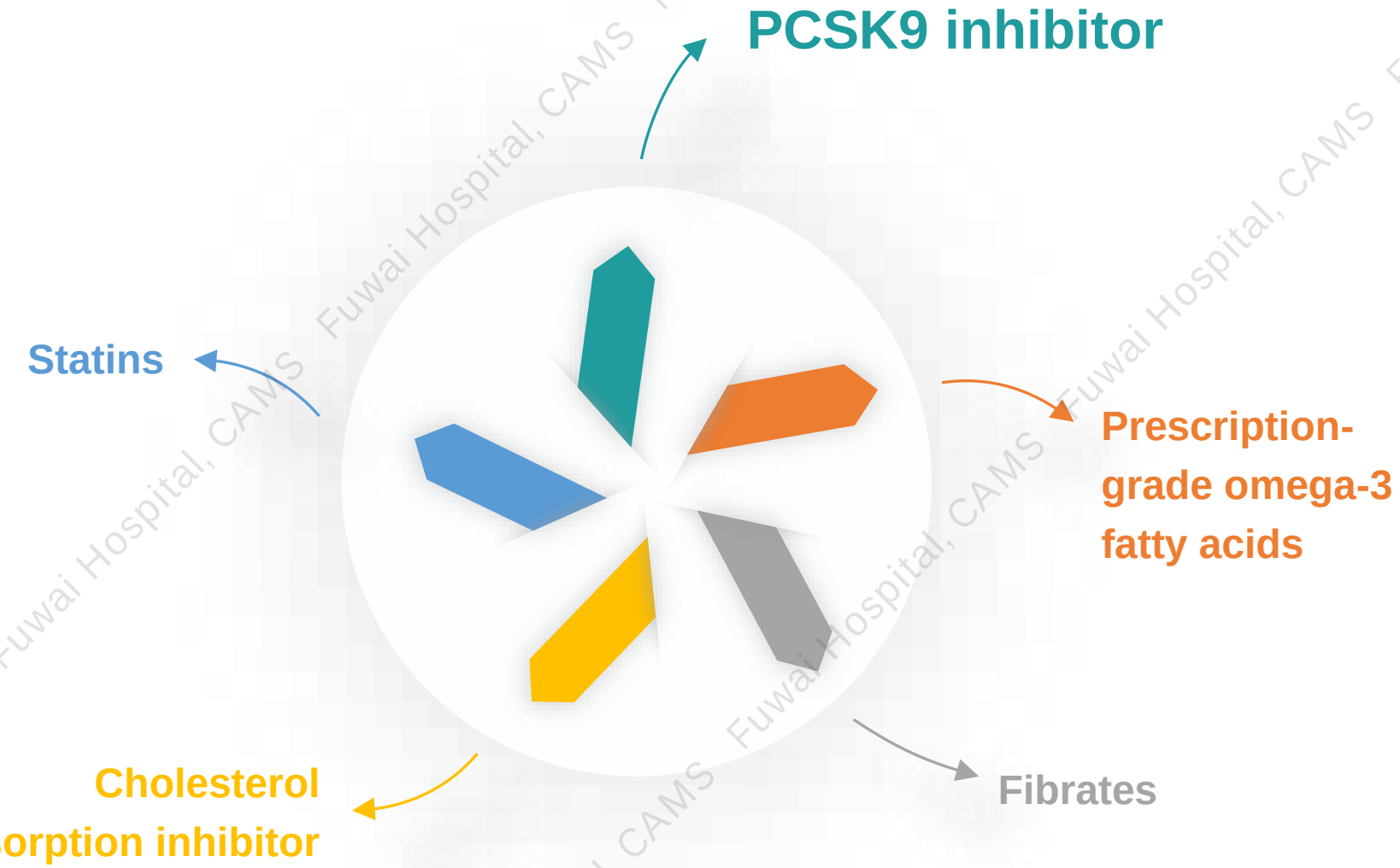
Lipid-Lowering Drugs



Statin Therapy

- **Statins inhibit the synthesis of the rate-limiting enzyme HMG-CoA reductase, decrease cholesterol synthesis, and upregulate LDL receptor, thus, accelerate the serum LDL catabolism. Statins significantly reduce serum TC, LDL-C and Apo B levels, decrease serum TG levels and slightly increase HDL-C levels.**
- **When statin dose was doubled, LDL-C was further reduced by only about 6%. Statins decrease TG level by 7% ~ 30% and increase HDL-C level by 5% ~ 15%.**

High-, Moderate-, and Low-Intensity Statin Therapy

	High Intensity	Moderate Intensity	Low Intensity
LDL-C lowering†	≥50%	30%–49%	<30%
Statins	Atorvastatin (40 mg‡) 80 mg Rosuvastatin 20 mg (40 mg)	**Atorvastatin 10 mg** (20 mg) **Rosuvastatin** (5 mg) **10 mg** **Simvastatin 20–40 mg**§	Simvastatin 10 mg
	…	**Pravastatin 40 mg** (80 mg) **Lovastatin 40 mg** (80 mg) Fluvastatin XL 80 mg **Fluvastatin 40 mg BID** Pitavastatin 1–4 mg	**Pravastatin 10–20 mg** **Lovastatin 20 mg** Fluvastatin 20–40 mg

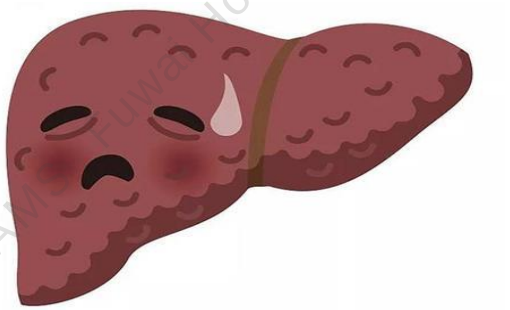
Major adverse effects of statins

Liver dysfunction:

- **Elevated transaminase, the incidence of about 0.5%~3.0%, in a dose-dependent manner. Patients with elevation of serum ALT and/ AST more than 3 ULN and with elevation of total bilirubin should reduce dosage or stop taking the drug.**
- **Decompensated cirrhosis and acute liver failure are contraindications for statins.**

Statin-associated muscle symptoms

- **Including myalgia, myositis, and rhabdomyolysis. Statin dose should be reduced or discontinued in patients with muscle discomfort and/or weakness. Creatine kinase (CK) should be tested**



Liver dysfunction

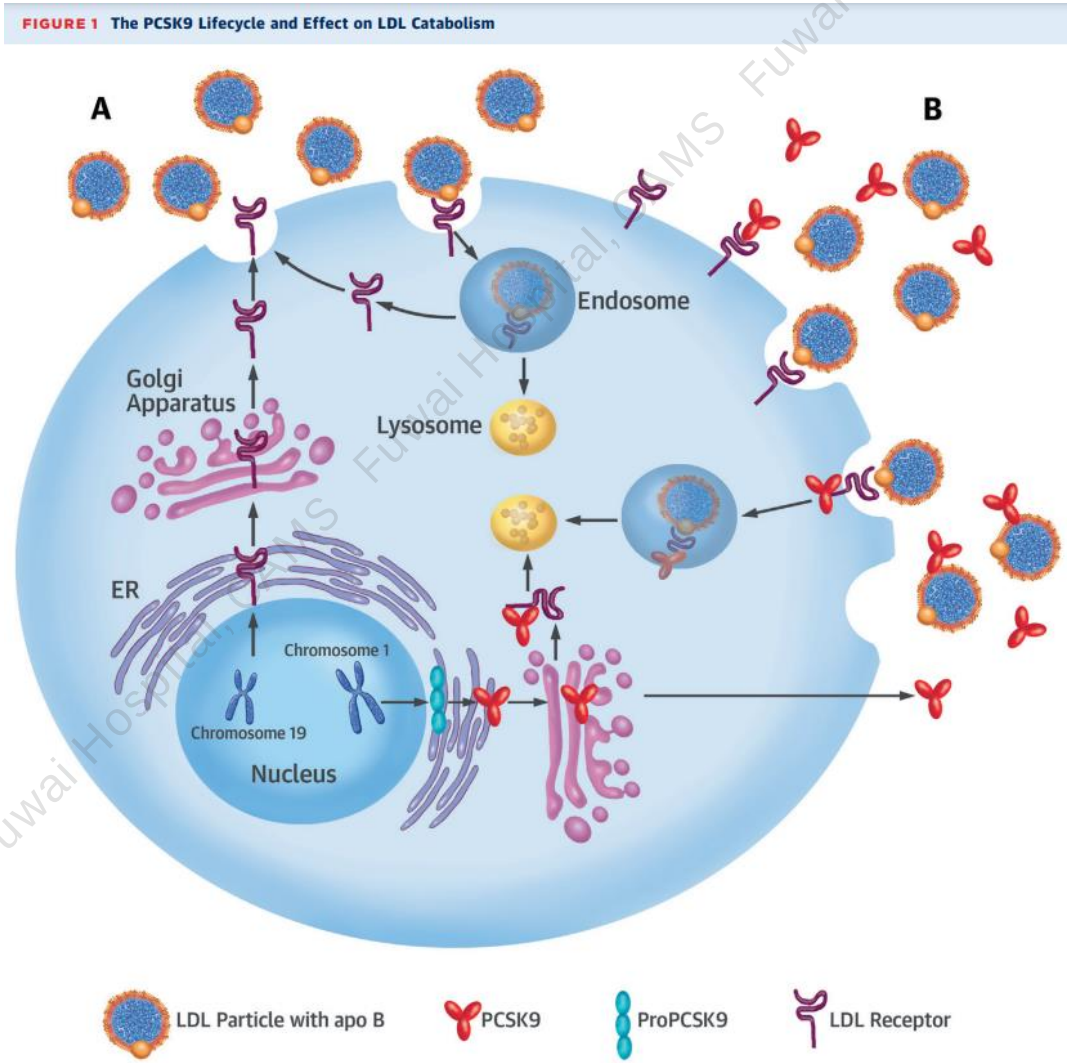
Rhabdomyolysis

Cholesterol absorption inhibitor

- **Ezetimibe effectively inhibits the absorption of cholesterol in the intestinal tract。**
- **IMPROVE-IT: Ezetimibe + Simvastatin in patients with ACS could further reduce CVD events.**
- **SHARP study: ezetimibe + Simvastatin in patients with CKD showed improved prognosis.**
- **Dose 10 mg/d.**
- **Good safety and tolerability. Side effects such as increased transaminase and myalgia may also occur when used in combination with statin. Do not use during pregnancy and lactation.**

PCSK9 inhibitors- Evolocumab & Alirocumab

- **PCSK9 is secreted by hepatocytes and binds to the LDL receptor, thus prevents the conformational change in the LDL receptor, and the LDL receptor then travels together with LDL to the lysosome, where it is destroyed.**
- **Monoclonal antibodies targeting PCSK9 can lower plasma LDL-cholesterol (LDL-C) levels by approximately 40%~70%.**
- **In dedicated cardiovascular outcome trials, PCSK9 inhibitors significantly reduced the risk of major adverse cardiovascular events.**
- **No offsetting safety concerns were reported in these trials over the timeframes studied.**



J Am Coll Cardiol. 2018 Jul 17;72(3):314-329.

Triglyceride-lowering drugs- fibrates & niacin

- Fibrates are generally considered the most potent triglyceride-lowering agents, with reductions of 45 to 55%.
- May also mildly lower LDL-C levels in patients with normal triglycerides.
- They may be useful in some patients with severe hypertriglyceridemia, but in the present document they are not listed as LDL-lowering drugs.
- No significant effect on cardiovascular death, fatal myocardial infarction or stroke.

Combined use of lipid-lowering drugs

Statins + Ezetimibe

- **Moderate/low intensity statin + ezetimibe may be considered for patients with unmet target or intolerable cholesterol levels treated with moderate intensity statin alone.**

Statins +Fibrates

- **Decreased LDL-C and TG levels and increased HDL-C levels. Combined use increases the risk of myositis and myopathy.**

Statins + PCSK9 inhibitors

- **Greater reductions in LDL-C than any single drug therapy. Statins + Ezetimibe + PCSK9 inhibitors can be considered.**

Monitoring of lipid-lowering therapy

- For diet and lifestyle therapy, serum lipid levels should be tested 3 to 6 months after treatment initiation. If lipid levels reach the recommended target, non-drug treatment should be continued, but lipid test every 6 months to 1 year is still required.
- Blood lipids, transaminases and creatine kinase should be tested within 6 weeks after the first use of lipid-lowering drugs. If the blood lipid reach the target value and there is no adverse drug reaction, the frequency of visit should be gradually expand to once every 6 to 12 months. If the blood lipid does not meet the target and there is no adverse drug reaction, monitoring once every 3 months. If the blood lipid still fails to reach the target value after 3-6 months of treatment, the dose or type of lipid-lowing drugs should be adjusted, or the combination of lipid-regulating agents with different mechanisms of action should be used for treatment.

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Summary

- **Setting lipid control targets based on cardiovascular risk;**
- **Life style change combined with lipid-lowering therapy is recommended.**
- **Statins are the foundation of LDL-C reduction;**
- **For patients with statin intolerance or very high cholesterol level or severe mixed hyperlipidemia, combined use of lipid-lowering drugs should be considered.**
- **Close monitoring of adverse drug reactions is necessary during lipid-lowering pharmacological therapy.**

Thank you!