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Supplementary information

Lp(a) in severe peripheral artery disease: Pilot implementation using LILAC framework

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A Simple Guide of Lp(a) for Health Care Professionals

- Lipoprotein(a), or Lp(a), is an atherogenic particle that carries bad cholesterol in the blood.
- Elevated Lp(a) is a common risk factor for ischaemic heart disease, myocardial infarction, stroke, calcific aortic valve stenosis, heart failure, peripheral artery disease and cardiovascular death.
- The blood level of Lp(a) is strongly influenced by genetics, meaning that there is a 50% chance of family members to have high Lp(a).

Whom to test?

International guidelines have highly recommended that anyone who is at high risk or very high risk of having a cardiovascular event should have Lp(a) tested once in their life. This includes patients with:

(i) History of ischaemic heart disease, myocardial infarction, calcific aortic valve stenosis, ischaemic stroke, transient ischaemic event, and heart failure.

(ii) At high risk of developing any cardiovascular event, e.g. diabetes mellitus, by using the Singapore Framingham Risk Score, or positive family history.

(iii) Features suggestive of familial hypercholesterolemia (FH) e.g LDL>5.5 mmol/l, tendon xanthoma

(iv) Family history of very high Lp(a) or premature ischaemic heart disease

(v) Subclinical atherosclerosis (imaging positive)

A minimum one-time Lp(a) testing is integrated into the care of patients in AMI pathway, IHD, stroke and PAD admissions. It is essential that Lp(a) level is checked at least once in their life.

How to test?

Blood test can be done at any time. Type Lp(a) to order. Fasting not required. Food, exercise, and medications to be continued as per normal. Most people only need to be tested **once** in adult lifetime.

How to interpret and What to do?

HI

OK

Lp(a) >**200** nmol/L is very high. (>80 mg/dL) → Refer to Lipid Clinic CGH.

Lp(a) >**120** nmol/L is CV risk factor. (>50 mg/dL) → Refer to Lipid Clinic **if** suspected FH or premature CVD (<60 yo or family history of premature CVD or unsure how to manage. → Use **LILAC** to help you counsel patient.

Lp(a) 70-120 nmol/L is grey zone. (30-50 mg/dL) → Can repeat much later when well. Use **LILAC** to help you counsel patient.

Lp(a) <70 nmol/L is normal. → No need to repeat for life.

Don't Forget!

Key in ICD Diagnosis Code:
Lipoprotein(a) Hyperlipoproteinemia

Note: Lp(a) may be falsely lowered during acute heart attack and stroke. Please recheck in few months. Secondary causes that increase Lp(a) include hypothyroidism, renal impairment, and hypogonadism.

How to manage high Lp(a)? → Think LILAC

L = **L**p(a) > 120 nmol/L is a CV **risk enhancer**: Use Lp(a) to improve CV risk prediction & management. [e.g. high Lp(a) may shift decision to start statin in people with intermediate CV risk]

I = **I**mprove overall risk by healthy diet and BMI, no smoking, exercise, control diabetes, lipids, and BP.

L = **L**owering LDL is essential ,e.g. healthy diet, statin, ezetimibe, agents of PCSK9 inhibition. [how low for LDL depends on CV risk, the lower the better. In patients with CVD: **aim LDL<1.4** or lower.] **L**p(a)-lowering treatment to be discussed in specialist clinic for very high Lp(a).

A = **A**ssess for Lp(a) related conditions e.g, **A**therosclerosis, **A**ortic Stenosis. **A**spirin may be considered for primary prevention if multiple CV risk factors or subclinical **A**therosclerosis (imaging) after a risk-benefit discussion with the patient.

C = **C**ascade testing of first-degree family members if the index has very high Lp(a) level. [Lipid clinic]

AMI: acute myocardial infarction; CV: cardiovascular; BP: blood pressure; PAD: peripheral artery disease FH: familial hypercholesterolemia. Agents of PCSK9 inhibition are evolocumab, inclisiran and alirocumab.

Updated as of June 2025. For feedback, please contact Clinical Assistant Professor Dr Loh Wann Jia, Senior Consultant Endocrinologist, Lipid Clinic, Department of Endocrinology, Changi General Hospital.

Figure S1. A one-page guide for healthcare professionals on the testing and management of Lp(a) using the LILAC-for-Lp(a) framework.