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Newsletter

PATHOLOGISTS LANCET Kenya

LIPOPROTEIN

What is Lipoprotein(a)

Lipoprotein (a) also referred to as Lp (a) is structurally similar to LDL- C with the exception of the presence of apolipoprotein (a) or apo (a) moiety attached to its apo B component1. Apo(a) shares homology with the fibrin binding domain of plasminogen leading to impaired conversion to its active form plasmin. In addition, Lp (a) is associated with infiammation through pathological interaction with monocytes and endothelial cells2. High levels of Lp(a) are therefore both procoagulant and pro-infiammatory leading to reduced fibrinolysis, increased foamy macrophage formation and interference with normal endothelial function2. Consequently, high Lp(a) is proatherogenic and is associated with a high risk of myocardial infarction, coronary heart disease and ischemic stroke3. This causal relationship is independent of the traditional risk factors including elevated serum LDL-C4.

Lipoprotein and CHD Risk

Evidence from reviewed publications indicate lipoprotein(a):

- is independently associated with CHD
- is a risk factor for premature CHD in persons < 50 years of age and in the elderly (older than 70 years)
- if elevated, increases risk for CHD in combination with other CHD

risk factors.

High lipoprotein(a) concentration has been shown to predict risk of angina and the risk is substantially increased with concomitant high LDL-cholesterol concentration.

Broadly speaking, there are 4 major categories of lipid abnormalities in humans:

- elevated low-density lipoprotein cholesterol (LDL-C)
- low high-density lipoprotein cholesterol (HDL-C)
- elevated triglycerides
- elevated lipoprotein(a) [Lp(a)]

LDL-C, HDL-C and triglyceride levels are affected by diet. By contrast, Lp(a) plasma levels are mediated largely by the LPA gene locus present on chromosome 6q2223, with small-to-negligible effects of diet.

Metabolism

Unlike LDL which is mopped up by the LDL receptor in the liver, Lp(a) is not bound by the LDL receptor2. It is postulated that Lp (a) is catabolized by hepatic and renal pathways which are not efficient enough to govern serum levels. Serum Lp (a) levels are predominantly (80 – 90%) determined by the synthetic rate which is subject to genetics (LPA gene)5. The levels of Lp(a) are consequently minimally affected by lifestyle modifications5.

Laboratory Analysis

Reference ranges of Lp (a) vary and depend on the assay and reporting laboratories. Lp (a) assays are yet to be subjected to a standardization traceable to a reference material4. Several types of Lp(a) assays are currently available. Prominent among these assays are sandwich enzyme-linked immunosorbent assay (ELISA), non- competitive ELISA, latex immunoassay, immunonephelometric assay, immunoturbidometric assay and fiuorescence assay.

Lp(a) is reported in mg/L or nmol/L. Conversion between mg/L and nmol/L is discouraged because unlike other lipoproteins, the different isoforms of Lp (a) have varying molecular weights4.

Whom to screen

- Lp (a) measurement in individuals with a family history of premature ASCVD5
- Primary severe hypercholesterolemia or suspected familial hypercholesterolemia4
- In patients aged 40 to 75 with borderline (5 to 7.4 percent) 10-year ASCVD risk to assess the need for statin therapy4,7.
- To identify a possible cause for a less than optimal LDL-C lowering therapy4
- For secondary prevention in patients with:
- Personal history of premature ASCVD4
- Progressive or recurrent ASCVD despite optimal lipid lowering therapy4
- Familial hypercholesterolemia with ASCVD4

The European cardiac society however recommends that Lp(a) measurement should be considered at least once in each adult person's lifetime to identify those with very high inherited Lp(a) levels >180 mg/dL (>430 nmol/L) who may have a lifetime risk of ASCVD equivalent to the risk associated with heterozygous familial hypercholesterolaemia7.

LASSA guidelines adopted from the European Consensus Guidelines, 2010

The use of novel biomarkers of cardiovascular disease (e.g. hsCRP) and imaging technologies are not recommended routinely and should be reserved to refine risk assessment in patients considered to be at moderate risk where there is uncertainty about whether to initiate drug therapy.

It should be noted that hsCRP is a nonspecific infiammatory marker that may be elevated from many causes (e.g. acute infections or non-infectious infiammatory disorders). Measuring Lp(a) is only appropriate in HIGH CVD risk subjects and/or when there is a family history of premature CVD. When Lp(a) is used as a risk marker, the cut-off value is >50 mg/dl

Lipoprotein(a) measurement at Lancet Laboratories

Principle of method: Immunoturbidimetry Specimen
Requirements: Serum
TAT: Contact your nearest PLK branch

References

1. *Evidence that Lp[a]contains one molecule of apo[a]and one molecule of apoB: evaluation of amino acid analysis data. Albers JJ, Kennedy H, Marcovina SM J Lipid Res. 1996;37(1):192.*
2. *Lipoprotein(a) and infiammation in human coronary atheroma: association with the severity of clinical presentation. Dangas G, Mehran R, Harpel PC, Sharma SK, Marcovina SM, Dube G, Ambrose JA, Fallon JT J Am Coll Cardiol. 1998;32(7):2035.*
3. *Lipoprotein(a) Concentration and Risks of Cardiovascular Disease and Diabetes.Gudbjartsson DF, Thorgeirsson G, Sulem P, Helgadottir A, Gylfason A, Saemundsdottir J, Bjornsson E, Norddahl GL, Jonasdottir A, Jonasdottir A, Eggertsson HP, Gretarsdottir S, Thorleifsson G, Indridason OS, Palsson R, Jonasson F, Jonsdottir I, Eyjolfsson GI, Sigurdardottir O, Olafsson I, Danielsen R, Matthiasson SE, Kristmundsdottir S, Halldorsson BV, Hreidarsson AB, Valdimarsson EM, Gudnason T, Benediktsson R, Steinthorsdottir V, Thorsteinsdottir U, Holm H, Stefansson K J Am Coll Cardiol. 2019;74(24):2982. Epub 2019 Dec 9.*
4. *Use of Lipoprotein(a) in clinical practice: A biomarker whose time has come. A scientific statement from the National Lipid Association. Wilson DP, Jacobson TA, Jones PH, Koschinsky ML, McNeal CJ, Nordestgaard BG, Orringer CE J Clin Lipidol. 2019;13(3):374. Epub 2019 May 17*
5. *Apolipoprotein(a) gene accounts for greater than 90% of the variation in plasma lipoprotein(a) concentrations.Boerwinkle E, Leffert CC, Lin J, Lackner C, Chiesa G, Hobbs HH J Clin Invest. 1992;90(1):52.*
6. *2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines.Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, Braun LT, de Ferranti S, Faiella-Tommasino J, Forman DE, Goldberg R, Heidenreich PA, Hlatky MA, Jones DW, Lloyd-Jones D, Lopez-Pajares N, Ndumele CE, Orringer CE, Peralta CA, Saseen JJ, Smith SC Jr, Sperling L, Virani SS, Yeboah J Circulation. 2019;139(25):e1046. Epub 2018 Nov 10.*
7. *2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, Badimon L, Chapman MJ, De Backer GG, Delgado V, Ference BA, Graham IM, Halliday A, Landmesser U, Mihaylova B, Pedersen TR, Riccardi G, Richter DJ, Sabatine MS, Taskinen MR, Tokgozoglu L, Wiklund O, ESC Scientific Document Group Eur Heart J. 2020;41(1):111.*

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