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Apolipoprotein B (ApoB)

Refining Cardiovascular Risk Management and LDL Treatment Decisions

Low-density lipoprotein (LDL) particles cause atherosclerotic cardiovascular disease (ASCVD).¹ Apolipoprotein B (ApoB) is the primary protein component of LDL and triglyceride-rich lipoprotein (TRL) particles.² The cholesterol content of these atherogenic lipoproteins can vary widely among patients, but each always contains one ApoB protein. Measured ApoB thus provides an accurate assessment of atherogenic particle number, whereas LDL cholesterol (LDL-C) does not.2

Although LDL-C, non-HDL-C, and ApoB are highly correlated, "discordance analyses" have demonstrated that ASCVD risk tracks with ApoB, not the cholesterol measures, when levels differ.² The most consequential clinical scenario is when ApoB is elevated more than LDL-C levels would indicate, such as encountered frequently in hypertriglyceridemic patients with obesity, metabolic syndrome, or diabetes.²⁻⁴ Such patients may be undertreated if their elevated atherogenic particle burden remains unrecognized.

Current dyslipidemia management guidelines recommend the measurement of ApoB for two purposes. The first is in primary prevention, with high ApoB \geq 130 mg/dL in intermediate-risk patients without diabetes constituting a "risk-enhancing factor" that favors initiation of statin therapy.⁵ The second is to refine LDL-lowering therapeutic decision-making by identifying statin-treated patients with residual ASCVD risk who could benefit from additional therapy despite having achieved low target levels of LDL-C or non-HDL-C.6-8

Evidence that risk reduction is more strongly associated with ApoB decreases, rather than decreases in LDL-C or non-HDL-C, has come from a large meta-analysis of statin trials9 and two Mendelian randomization studies.^{10,11} These findings provide clinical support for the suggestion that add-on ezetimibe or PCSK9 inhibitor therapy

might benefit patients who have met cholesterol goals but not the corresponding ApoB goals² – either those recommended in guidelines⁶⁻⁸ or the lower targets based on percentile equivalence to LDL-C goals.3,12

In most guidelines, the ApoB particle targets for very high-risk and high-risk patients that correspond to LDL-C <70 and <100 mg/dL are ApoB <80 and <90 mg/dL, respectively.⁶⁻⁸ Based on percentile equivalence to these LDL-C targets, ApoB targets are lower: <60 and <80 mg/dL for very high-risk and high-risk patients, respectively.^{3,12} One guideline recognizes an "extreme risk" category of patients and recommends goals of LDL-C <55 mg/dL and ApoB <70 mg/dL.6

LabCorp offers the following to assist clinicians with cardiovascular risk management decision-making:

Test Name				Test Number
Apolipoprotein B				167015
Desirable < 90	Interval (mg/dL): Borderline High 90 - 99	High 100 - 130	Very High > 130	
Pharmacotherapy Guide: ASCVD Risk Category Very High Risk High Risk Moderate Risk		Therapeutic Target (mg/dL) < 80 (extreme risk < 70) < 90 < 90		
Lipid Cascade With Reflex to Apolipoprotein B				363676

For the most current information regarding test options, including specimen requirements and CPT codes, please consult the online Test Menu at www.LabCorp.com.

References

1. Ference BA, Ginsburg HN, Graham I, et al. Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. a consensus statement from the European Atherosclerosis Society Consensus Panel. Eur Heart J. 2017 Aug;38(32):2459-2472. 2. Cantey EP, Wilkins JT. Discordance between lipoprotein particle number and cholesterol content: an update. Curr Opin Endocrinol Diabetes Obes. 2018 Apr;25(2):130-136.

A sathipskimar V, Park J, Quispe R, et al. Impact of Novel Low-Density Lipoprotein-Cholesterol Assessment on the Utility of Secondary Non-High-Density Lipoprotein-C and Apolipoprotein B Targets in Selected Worldwide Dyslipidemia Guidelines. *Circulation.* 2018 Jul 17;138(3):244-254. 4. Kathiresan S, Otvos JD, Sullivan LM, et al. Increased small low-density lipoprotein particle number: a prominent feature of the metabolic syndrome in the Framingham Heart Study.

Circulation. 2006 Jan 3;113(1):20-29.

5. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2019 Jun 18;139(25):e1082-e1143 6. Jellinger PS, Handelsman Y, Kosenblit PD, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Guidelines for Management of Dyslipidemia

and Prevention of Cardiovascular Disease. Endocr Pract. 2017 Apr;23(Suppl 2):1-87. 7. Jacobson TA, Ito MK, Maki KC, et al. National Lipid Association Recommendations for patient-centered management of dyslipidemia: part 1 – full report. J Clin Lipidol. 2015 Mar-

Anderson TJ, Grégoire J, Pearson GJ, et al. 2016 Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult. Can J Cardiol. 2016 Nov;32(11):1263-1282.

9. Thanassoulis G, Williams K, Ye K, et al. Relations of change in plasma levels of LDL-C, Non-HDL-C, and apoB with risk reduction from statin therapy: a meta-analysis of randomized trials. J Am Heart Assoc. 2014 Apr 14;3(2):e000759.

10. Ference BA, Kasdtelein JJP, Ginsberg HN, et al. Association of Genetic Variants Related to CETP Inhibitors and Statins With Lipoprotein Levels and Cardiovascular Risk. JAMA. 2017 Sep 12:318(10):947-956

11. Ference BA, Kastelein JJP, Ray KK, et al. Association of Triglyceride-Lowering LPL Variants and LDL-C-Lowering LDLR Variants With Risk of Coronary Heart Disease. JAMA. 2019 Jan 29;321(4):364-373.

12. Wong ND, Chuang J, Zhao Y, Rosenblit PD. Residual dyslipidemia according to low-density lipoprotein cholesterol, non-high-density lipoprotein cholesterol, and apolipoprotein B among statin-treated US adults: National Health and Nutrition Examination Survey 2009-2010. J Clin Lipidol. 2015 Jul-Aug;9(4):525-532.



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Apr;9(2):129-169.