Flexibilization of Fasting for Laboratory Determination of the Lipid Profile in Brazil: Science or Convenience?

Caio Maurício Mendes de Cordova and Caroline Galgowski
Fundação Universidade Regional de Blumenau (FURB), Blumenau, SC – Brazil

A statement endorsed by medical specialty associations has been published in our country recommending the flexibilization of fasting before blood drawing for the laboratory determination of the lipid profile encompassing total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), triglycerides (TG) content and the corresponding calculation of non-HDL-cholesterol (TC – HDL-c).[1] It was considered that non-fasting results do not clinically differ from fasting ones, and prospective studies and meta-analyses have consistently demonstrated that non-HDL-C at a non-fasting state would be at least as good as LDL-c in the prediction of CVD. It was also recommended that when TG > 4.52 mmol/L the formula proposed by Martin et al.[2] should be used for LDL-c estimation.

The statement was based on the European Consensus on the matter published by Nordestgaard et al.[3] However, the automatic application of this approach in Brazil deserves deeper consideration, considering the impact that it may cause on patient care. Furthermore, it is far from a consensus among clinical laboratory scientists and professionals in the country, as it became evident during the 44th Brazilian Congress of Clinical Analysis held last June 11-14th, 2017, and the 51st Brazilian Congress of Clinical Pathology and Laboratory Medicine, held last September 26-29th, 2017.

Indeed, a non-fasting non-HDL-c result would be at least equivalent to LDL-c for goal setting.[4] However, a non-fasting LDL-cholesterol, as well as non-fasting non-HDL-c, could be less sensitive for CVD prediction,[5] especially in women.[6] This possible issue ought to be evaluated judiciously and independently in our specific population.

Secondly, it should be noted that the treatment target for non-HDL-c is simply 0.8 mmol/L (30 mg/dL) higher than the respective target for LDL-c.[7] This was set in an empirical manner, considering an average value of 0.8 mmol/L for VLDL-c. Obviously, this is not consistent with reality, especially in a post-prandial state. On the other hand, the treatment target levels for LDL-c are well established, based on large prospective studies for decades of sound scientific work.

Keywords

Fasting; Cholesterol; Lipids; Triglycerides; Cholesterol, LDL; Cholesterol, HDL.

Mailing Address: Caio Maurício Mendes de Cordova •
Rua São Paulo, 2171, Campus 3, FURB. Postal Code 89030-001, Itoupava Seca, Blumenau, SC – Brazil
E-mail: cmcordova@furb.br, profcaiocordova@gmail.com
Manuscript received November 29, 2017, revised manuscript April 11, 2018, accepted April 11, 2018

Third, the main motives for a non-fasting blood draw as suggested by the European consensus[3] and the Brazilian statement[1] seem to be more commercially driven than scientifically. The rationale included an alleged "inconvenience by having to return on a separate visit for a fasting lipid profile…, a laboratory burden due to a large volume of patients coming for tests in the morning…, a burden for clinicians to review and make decisions based on the findings of the lipid profile at a later date…", and a hypothesized improved "patient compliance with lipid testing".

Only the last motivation may have some scientific background but it yet remains to be proved. It also should be noted that blood sample drawing procedures in Brazil are quite different from those practiced in Western Europe and in the USA. In those countries, biological samples are often drawn right after the consultation with the clinician, at the clinic or hospital; the samples are collected at scheduled times by the laboratory logistics and the result is directly reported to the physician. The patients do not even know what a clinical laboratory is; they just know that their blood samples go somewhere to be analyzed by people who they have no idea what their skills and background are. In Brazil, by law, the laboratory results belong to the patients, and non-hospitalized patients often come to the laboratory collection facility, unless a home visit is scheduled, for blood drawing or other biological sample collection days after the first consultation, where they receive adequate instructions regarding the pre-analytical requirements for each requested test. The realities are completely different.

Fourth, precisely derived from the point above, the impact of these recommendations have not yet been evaluated on the patient's behavior regarding the required fasting for *other* laboratory tests. And even worse, we have already observed movements by some corporations indicating that fasting for *any* laboratory test would be no longer necessary. From the technical and scientific point of view, non-fasting blood samples are not suitable for measurement of several analytes that are influenced by meals, such as blood cell counts, hemoglobin, albumin, bilirubin, phosphate, calcium, magnesium, potassium,[8] insulin, growth hormone, glucagon, chloride, urine pH, and also those affected by diurnal variation, such as ACTH, catecholamines, TSH, PTH, renin, aldosterone, ALT, AST, alkaline phosphatase, blood urea nitrogen and iron,[9] to name a few. As it has been said,[10] in clinical laboratory medicine, no sample would be preferred to a bad sample, if one wishes to attain rigorous standards when providing clinicians with reliable laboratory information. The overall impact of the proposed non-fasting blood sample draw on the eventual rejection of the patient's samples has yet to be determined, due to the presence of other requested laboratory tests that need fasting and/or morning draw.

DOI: 10.5935/abc.20180174

And fifth, finally, the suggested Martin's formula still uses TG in its calculations, a parameter that has been demonstrated by many authors not to be correlated with LDL-c or TC. Martin et al.[2] have made a huge mathematical effort to achieve a satisfactory result to include TG in the calculation. And most importantly, this equation has to be validated or at least evaluated, in other populations before being universally recommended. For instance, the proposed Martin's formula, as well as ours, was evaluated in comparison to newly proposed formulas for LDL-c estimation in Iran, and the former was demonstrated to not add value to the estimations in a small cohort.[11]

Anyway, LDL-c remains a frequent parameter requested at clinical laboratories in medical routine, and will likely continue to be so, hence precise methods for its estimation are needed when its direct measurement is not available. A simple and accurate equation developed and evaluated in the Brazilian population has already been developed.[12] It should be noted that this equation performs equally well, for instance, in populations from Germany and United Kingdom,[13] but not as well in others, such as in South Africa,[14] Spain,[15] and Thailand.[16] It seems that the debate on which method to use for LDL-c determination, in each particular population of the globe, is more open than defined.[17]

Sadly, history is full of examples demonstrating that when corporate interests meet with poor science, the only losers are science itself, and patient care. It is apparent and worthy of concern that the Brazilian 'consensus' has recommended the use of an equation for LDL-c estimation that was not validated in the local population and was moved by reasons that are driven more by convenience than by rigorous and unbiased science.

Author contributions

Conception and design of the research: Cordova CMM; Acquisition of data, Analysis and interpretation of the data and Critical revision of the manuscript for intellectual content: Cordova CMM, Galgowski C; Writing of the manuscript: Galgowski C.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any thesis or dissertation work.

References

1. Sociedade Brasileira de Patologia Clínica – Medicina Laboratorial. SBPC-ML Necessidade de jejum para coleta de sangue para a realização de exams laboratoriais. [Citado em 2016 dez 10. Disponível em: http://www.sbpc.org.br/upload/conteudo/consenso_jejum_dez2016_final.pdf
2. Martin SS, Blaha MJ, Elshazly MB, Toth PP, Kwiterovich PO, Blumenthal RS, et al. Comparison of a novel method vs the Friedewald equation for estimating low-density lipoprotein cholesterol levels from the standard lipid profile. JAMA. 2013;310(19):2061-8.
3. Nordestgaard BG, Langsted A, Mora S, Kolovou G, Baum H, Bruckert E, et al; European Atherosclerosis Society (EAS) and the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) joint consensus initiative. Fasting is not routinely required for determination of a lipid profile: clinical and laboratory implications including flagging at desirable concentration cut-points-a joint consensus statement from the European Atherosclerosis Society and European Federation of Clinical Chemistry and Laboratory Medicine. Eur Heart J. 2016;37(25):1944-58.
4. Boekholdt SM, Arsenault BJ, Mora S, Pedersen TR, LaRosa JC, Nestel PJ, et al. Association of LDL cholesterol, non-HDL cholesterol, and apolipoprotein B levels with risk of cardiovascular events among patients treated with statins. JAMA. 2012;307(12):1302-9. Erratum in: JAMA. 2012;307(18):1915.
5. Mora S, Rifai N, Buring JE, Ridker PM. Fasting compared with nonfasting lipids and apolipoproteins for predicting incident cardiovascular events. Circulation. 2008;118(10):993-1001.
6. Mora S, Rifai N, Buring JE, Ridker PM. Comparison of LDL cholesterol concentrations by Friedewald calculation and direct measurement in relation to cardiovascular events in 27,331 women. Clin Chem. 2009;55(5):888-94.
7. Catapano AL, Reiner Z, De Backer G, Graham I, Taskinen MR, Wiklund O, et al; European Society of Cardiology (ESC); European Atherosclerosis Society (EAS). ESC/EAS Guidelines for the management of dyslipidaemias The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS). Atherosclerosis. 2011;217(1):3-46.
8. Guidi GC, Simundic AM, Salvagno GL, Aquino JL, Lima-Oliveira G. To avoid fasting time, more risk than benefits. Clin Chem Lab Med. 2015;53(10):e261-4.
9. Young DS, Bermes EW Jr. Preanalytical variables and biological variation. In: Burtis CA, Ashwood ER, Bruns DE. (editors). Tietz textbook of clinical chemistry and molecular diagnostics. 4th ed. St Louis: Elsevier; 2006. p. 449-84.
10. Simundic AM, Cornes M, Grankvist K, Lippi G, Nybo M. Standardization of collection requirements for fasting samples: for the Working Group on Preanalytical Phase (WG-PA) of the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM). Clin Chim Acta. 2014 May 15;432:33-7.
11. Rasouli M, Mokhtari H. Calculation of LDL-cholesterol vs direct homogenous assay. J Clin Lab Anal. 2017;31(3):e22057.
12. de Cordova CM, de Cordova MM. A new accurate, simple formula for LDL cholesterol estimation based on directly measured blood lipids from a large cohort. Ann Clin Biochem. 2013;50(Pt 1):13-9.
13. Sathyapalan T, Atkin SL, Kilpatrick ES. LDL cholesterol variability in patients with Type 2 diabetes taking atorvastatin and simvastatin: a comparison of two formulae for LDL-C estimation. Ann Clin Biochem. 2015;52(Pt 1):180-2.

14. Nigam PK. Calculated low density lipoprotein-cholesterol: Friedewald's formula versus other modified formulas. Int J Life Sci Med Res. 2014;4:25-31.

15. Laserna-Mendieta EJ, Timón-Zapata J. Comparison of the performance of the Brazilian equation for LDL-c estimation with other proposed formulae in a Spanish population. Ann Clin Biochem. 2013;50(Pt 5):501-2.

16. Dansethakul P, Thapanathamchai L, Saichanma S, Worachartcheewan A, Pidetcha P. Determining a new formula for calculating low-density lipoprotein cholesterol: data mining approach. EXCLI J. 2015 Mar 26;14:478-483.

17. Mendes de Cordova CM, de Santa Helena ET, Galgowski C, Figueira VH, Setter GB, Markus MR, et al. Evaluation of a new equation for LDL-c estimation and prediction of death by cardiovascular related events in a German population-based study cohort. Scand J Clin Lab Invest. 2018;78(3):187-96.