

ARTERIOSCLEROSIS

SOUTH STATE OF THE PROPERTY OF

www.elsevier.es/arterio

EDITORIAL

A step forward in the consensus on lipid profile characteristics for cardiovascular prevention



Un paso adelante en el consenso sobre las características del perfil lipídico para la prevención cardiovascular

Xavier Pintó^{a,*}, Juan Pedro-Botet^b

Atherothrombotic vascular disease (AVD) occurs silently for decades until the onset of ischaemic complications, which are often fatal or leave irreversible sequelae. Early action during this silent phase, by detecting and controlling the lipid and non-lipid risk factors that cause the disease, could prevent most ischaemic events, 1,2 and control the worldwide AVD epidemic. Lipid profiling is essential to detect lipid risk factors and to implement therapeutic strategies tailored to the individual's degree of AVD risk. Therefore, clinical biochemistry laboratories must provide accurate measurements of the different lipid levels and their reports must contain sufficient information to guide decisions on the diagnosis and treatment of dyslipidaemias in the prevention of AVD.^{3,4} This issue of Clínica e Investigación en Arteriosclerosis publishes the "Consensus document for lipid profile testing and reporting in Spanish clinical laboratories. What parameters should a basic lipid profile include?".5 This document identifies the need to test lipid profiles to assess the degree of vascular risk in the apparently healthy population and in those at higher risk, and in those affected by pathologies associated with secondary dyslipidaemias,

and to monitor lipid-lowering treatments to assess efficacy as well as therapeutic adherence. The document has been endorsed by many scientific societies working with AVD and is clearly necessary, given the great heterogeneity in the lipid profile reports provided by the different healthcare centres' biochemistry laboratories. These differences apply both to the values in these reports and the benchmark values. The document addresses both aspects and is based on the recent recommendations of the European Society of Cardiology, endorsed by the Spanish Interdisciplinary Vascular Prevention Committee.⁶ Thus, the document provides a consensus proposal on how the basic lipid profile tests for cardiovascular prevention should be performed and the criteria for lipid control targets to be included in laboratory reports. A key criterion in drafting the document was that benchmark lipid profile values should be based on the patient's vascular risk and not on percentiles derived from the distribution of lipid profile values in the general population. This can help us avoid considering excessive LDL-C values as "normal" in a patient at high cardiovascular risk, which can encourage therapeutic inertia and undertreatment and under-control of the risk of AVD. However, it is important to note that sometimes the differences in benchmark values between different laboratories are conditioned by the clinical practice guidelines of the health

E-mail address: xpinto@bellvitgehospital.cat (X. Pintó).

^a Unidad de Lípidos y Riesgo Vascular, Hospital Universitario de Bellvitge-Idibell-UB-Fipec-CiberObn

^b Unidad de Lípidos y Riesgo Vascular, Universidad Autónoma de Barcelona, Hospital del Mar

^{*} Corresponding author.

administrations and criteria that do not coincide with the recommendations of the main scientific societies involved in this field. ^{1,2,6,7} Because of their importance in the prevention of AVD, standardising the criteria used by health administrations, professionals, and scientific societies when setting benchmark values for lipid parameters can be considered a public health priority.

The document also includes factors that influence preanalytical variations and recommendations to avoid them, with special emphasis on the influence of acute conditions and fasting. With reference to the latter, it emphasises that lipid profile testing can be performed both with and without prior fasting and that measurements in both situations should be considered complementary. However, it stresses that in situations of overt hypertriglyceridaemia, patients who are to start treatment with drugs that can cause severe hypertriglyceridaemia and genetically predisposed individuals, or those with a history of lipidaemic pancreatitis, should undergo fasting lipid profile testing. It also indicates that, if lipid profile testing is accompanied by the measurement of other variables that may be altered in the absence of fasting, such as glucose, fasting is also preferable. Therefore, it seems obvious that most tests are and will continue to be performed after fasting from the night before. Another interesting aspect of the document is its mention of the frequency of analytical controls, a subject that has been little studied and on which there are fewer recommendations, based mainly on the criteria of experts in the area of AVD. It also highlights the importance of reporting the laboratory methods used and possible modifications to the units of measurement. Special attention is given to the equations used in the calculation of LDL-C and the different options for measuring it in situations of hypertriglyceridaemia, including alternative equations, the replacement of LDL-C by non-HDL-C or apoB, and also the possibility of direct measurement of LDL-C. Both direct measurement of LDL-C and apoB have an additional cost, whereas non-HDL-C, which can be obtained by simply subtracting HDL-C from total cholesterol, is costless and is a superior predictor of AVD risk than LDL-C, and can be performed in patients with hypertriglyceridaemia >400 mg/dL, some authors have postulated that direct measurement of LDL-C would not be necessary.⁸ Direct measurement of LDL-C may instead help to estimate triglyceride-rich lipoprotein remnant particles, i.e., remnant cholesterol, more accurately than the calculated LDL-C. In turn, apoB, despite having an additional cost, has higher predictive power than LDL-C and non-HDL-C, and when elevated it informs us of a potential residual risk despite LDL-C and non-HDL-C being on target, and therefore it is very likely that the measurement of apoB levels will increase in the near future.9

With reference to the quantities that should be included in the basic lipid profile, in addition to total cholesterol, HDL-C, triglycerides, non-HDL-C, and calculated LDL-C, the need to measure lipoprotein(a) concentrations at least once in a lifetime is emphasised, and it is pointed out that there are situations that may modify them and make repeated measurements necessary, highlighting the already good availability of drugs to treat hyperlipoproteinaemia(a). ¹⁰ The document also mentions the problem regarding the differences between methods and units of measurement, due

to the great variability in the structure and composition of lipoprotein(a) particles. ¹¹

Finally, this document includes two useful sections. One describes the alerts that the laboratory report should include when extreme levels of some lipids are observed and that may enable detection of severe dyslipidaemia or dyslipidaemia associated with a high risk of AVD and influence implementation of the necessary diagnostic and therapeutic measures. The other section refers to the clinical data required for telematic consultation or e-consultation, a form of consultation that has grown exponentially in recent years. The document is therefore very useful for professionals involved in the diagnosis and treatment of lipid metabolism disorders. It would be unfair not to mention here that these documents are of great scientific interest and are partly the mission of the scientific societies; but "anything and everything can be said on paper". Movement has been shown to be underway, therefore, and this is the responsibility of all health actors, especially the professionals involved in cardiovascular prevention.

References

- Visseren FLJ, Mach F, Smulders YM, Carballo D, Koskinas KC, Bäck M, et al. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice: developed by the Task Force for cardiovascular disease prevention in clinical practice with representatives of the European Society of Cardiology and 12 medical societies with the special contribution of the European Association of Preventive Cardiology (EAPC). Eur Heart J. 2021;42:3227-337, http://dx.doi.org/10.1093/eurheartj/ehab484.
- Mostaza JM, Pintó X, Armario P, Masana L, Real JT, Valdivielso P, et al. SEA 2022 standards for global control of cardiovascular risk. Clin Investig Arterioscler. 2022;34:130–79, http://dx.doi.org/10.1016/j.arteri.2021.11.003.
- Pedro-Botet J, Rodríguez-Padial L, Brotons C, Esteban-Salán M, García-Lerín A, Pintó X, et al. The ideal lipid report: a need for consensus. Rev Esp Cardiol (Engl Ed). 2018;71:512-4, http://dx.doi.org/10.1016/j.rec.2018.04.003.
- 4. Nordestgaard BG, Langlois MR, Langsted A, Chapman MJ, Aakre KM, Baum H, et al. European Atherosclerosis Society (EAS) and the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) Joint Consensus Initiative. Quantifying atherogenic lipoproteins for lipid-lowering strategies: consensus-based recommendations from EAS and EFLM. Atherosclerosis. 2020;294:46–61, http://dx.doi.org/10.1016/j.atherosclerosis.2019.12.005.
- 5. Arrobas-Velilla T, Guijarro C, Campuzano Ruiz R, Rodríguez Piñero M, Valderrama Marcos JF, Botana López AM, et al. Documento de consenso para la determinación e informe del perfil lipídico en laboratorios clínicos españoles ¿Qué parámetros debe incluir un perfil lipídico básico? Clin Invest Arterioscler. 2023.
- Armario P, Brotons C, Elosua R, Alonso de Lecinana M, Castro A, Clarà A, et al. Statement of the Spanish Interdisciplinary Vascular Prevention Committee on the updated European cardiovascular prevention guidelines. Clin Investig Arterioscler. 2021;33:85–107, http://dx.doi.org/10.1016/j.arteri.2020.11.004.
- Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, Badimon L, et al. ESC Scientific Document Group. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. Eur Heart J. 2020;41(January

- (1)):111–88, http://dx.doi.org/10.1093/eurheartj/ehz455. Erratum in: Eur Heart J. 2020 Nov 21;41(44):4255.
- 8. Langlois MR, Nordestgaard BG. Which lipids should be analyzed for diagnostic workup and follow-up of patients with hyperlipidemias? Curr Cardiol Rep. 2018;20:88, http://dx.doi.org/10.1007/s11886-018-1036-1.
- Pintó X, Fanlo M, Esteve V, Millán J, en representación del Grupo de Trabajo Dislipemia Aterogénica, Sociedad Española de Arteriosclerosis (SEA). Remnant cholesterol, vascular risk, and prevention of atherosclerosis. Clin Investig Arterioscler.
- 2023, http://dx.doi.org/10.1016/j.arteri.2023.02.001. S0214-9168(23)00008-6.
- Tsimikas S, Moriarty PM, Stroes ES. Emerging RNA therapeutics to lower blood levels of Lp(a): JACC focus seminar 2/4. J Am Coll Cardiol. 2021;77:1576–89, http://dx.doi.org/10.1016/j.jacc.2021.01.051.
- 11. Tsimikas S, Stroes ESG. The dedicated "Lp(a) clinic": a concept whose time has arrived? Atherosclerosis. 2020;300(May):1-9, http://dx.doi.org/10.1016/j.atherosclerosis.2020.03.003.