Lp(a) measurement bias

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Lp(a) is a LDL-like particle, with a single apolipoprotein B100 (apoB), covalently linked by a disulphide bond to a single apolipoprotein (a) (apo(a). The molecular mass of apo(a) can vary between 275 and 800 kDa [20,21] due to the inheritance of>40 different allelic *LPA* variants encoding different numbers of kringle IV type 2 repeat sequences in this polypeptide. Immunoassays, which recognize Kringle IV type 2 motifs have the potential to overestimate high molecular weight forms and underestimate low molecular weight forms. Because higher concentrations of Lp(a) are correlated with increased amounts of low molecular forms assay bias leads to underestimation of high concentrations and overestimation of low concentrations of Lp(a). This has led to the underestimation of the strength of the relation between Lp(a) in studies and persists in meta-analysis. The association between genetic polymorphisms causing increased Lp(a) and increased cardiovascular risk has rescued Lp(a) from controversy. Harmonisation of assays based on traceability of calibrants has proved impossible without elimination of isoform bias. HEART UK supports only the use of isoform insensitive assays with IFFC traceable calibrants. The size heterogeneity of Lp(a) also presents an insurmountable difficulty in preparing accurate calibrants in mass units and HEART UK only supports the use of molar units. There is international agreement on this approach. Harmonisation is essential for supporting agreed decision levels as has been achieved for cholesterol. Commercial assays should be critically assessed against these requirements.

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