The relative importance of particle count, type, and size of ApoB-containing lipoproteins in risk of myocardial infarction

J. Morze[1], G.E. Melloni[2], A. Rynkiewicz[1], M. Gruchala[3], M. Guasch-Ferre[4], C.T. Ruff[2], F.B. Hu[4], M.S. Sabatine[2], N.A. Marston[2]

[1]University of Warmia and Mazury in Olsztyn, Department of Cardiology and Internal Medicine, Olsztyn, Poland; [2]Harvard Medical School, Brigham and Women's Hospital, Thrombolysis in Myocardial Infarction (TIMI) Study Group, Boston, United States of America; [3]Medical University of Gdansk, 1st Department of Cardiology, Gdansk, Poland; [4]Harvard T. H. Chan School of Public Health, Department of Nutrition, Boston, United States of America

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Background: An accumulating body of evidence suggests that the number of apolipoprotein B-containing particles (ApoB-P) is more predictive of cardiovascular risk than their lipid content. However, it is unclear if this association is consistent across different lipoprotein types and sizes.

Purpose: We aimed to evaluate if particle type and size are associated with incident myocardial infarction (MI) beyond ApoB-P count. Moreover, we aimed to determine if the risk associated with lipoprotein(a) is additive to that of ApoB-P.

Methods: This prospective cohort study included 96,126 participants without prior history of stroke, coronary or peripheral artery disease or use of lipid-lowering medication from the UK Biobank. Count and size of VLDL, IDL, LDL, and HDL, as well as ApoB level and total ApoB-P count were measured in non-fasting plasma samples by nuclear magnetic resonance platform. Lipoprotein(a) was measured by immunoturbidimetric assay. We explored associations between these lipoprotein markers and incident MI using Cox proportional hazard models adjusted sequentially for clinical covariates, HDL count and size, and ApoB-P.

Results: Over a median follow-up of 12.1 years, 1702 participants had incident MI. In unadjusted models, 1-SD increases in ApoB-P count, ratio of VLDL to (LDL+IDL) particle counts, VLDL size and lipoprotein(a) were associated with a higher risk of MI, while LDL size was associated with a lower risk of MI (Table 1). When adjusting for clinical covariates and lipid parameters, only ApoB-P and lipoprotein(a) remained significantly associated with a higher risk of MI (HR: 1.40 [1.32; 1.48] and 1.20 [1.14; 1.27], respectively). Adjusted restricted cubic splines confirmed findings from linear trend Cox models (Figure 1). ApoB-P count was highly correlated with ApoB level (r=0.99), and replication of analyses replacing one for another revealed no change in results.

Conclusion: The risk of MI is independently associated with the total particle count of all ApoB-P, and not the size or type of these lipoproteins. ApoB level can be used as a very accurate surrogate of ApoB-P count in the clinical setting. Lipoprotein(a) is associated with MI risk independently of total particle count, and therefore, the combination of ApoB and lipoprotein(a) may provide the optimal clinical evaluation of lipid-mediated MI risk.

Table 1. Associations between 1-SD increase in baseline lipoprotein markers and incident myocardial infarction.

Lipoprotein marker	Model 1: Unadjusted		Model 2: Model 1 + Clinical covariates + HDL count and size		Model 3: Model 2 + ApoB-P	
	HR	95% CI	HR	95% CI	HR	95% CI
ApoB-P count	1.44	1.37, 1.52	1.40	1.32, 1.48	1.40	1.32, 1.48
VLDL/(LDL+IDL) counts ratio	1.38	1.31, 1.44	1.09	1.03, 1.16	1.04	0.98, 1.11
Average LDL size	0.90	0.86, 0.94	1.11	1.05, 1.17	1.04	0.99, 1.10
Average VLDL size	1.40	1.34, 1.47	1.02	0.95, 1.09	0.96	0.90, 1.04
Lipoprotein(a)	1.18	1.12, 1.24	1.21	1.14, 1.27	1.20	1.14, 1.27

ApoB-P = Apolipoprotein B-containing particles, HR = Hazard Ratio, CI = Confidence Interval,
Clinical covariates include age, sex, race, BMI, eGFR, history of hypertension, history of diabetes mellitus and fasting time.

Figure 1. Restricted cubic splines showing association between lipoprotein markers and incident myocardial infarction in adjusted model.