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

Jakub Morze, MD, Giorgio E. Melloni, PhD, Andrzej Rynkiewicz, MD, PhD, Marcin Gruchala, MD, PhD, Marta Guasch-Ferre, PhD, Christian T. Ruff, MD, Frank B. Hu, MD, PhD, Marc S. Sabatine MD, MPH, Nicholas A. Marston, MD, MPH

Jakub Morze, MD
Department of Cardiology and Internal Medicine
University of Warmia and Mazury in Olsztyn
Poland

27th August 2022
Introduction

• Traditionally, targets for lipid-lowering therapy with statins and other drugs have focused on LDL-C levels.

• Accumulating evidence suggests that apoB level is more predictive than TC, LDL-c, and TG levels for CHD risk.

• However, results from previous studies were based on conventional lipid panels, and not nuclear magnetic resonance (NMR) spectroscopy, which allows for a direct quantification of lipoprotein count and size.

• Our main aim was to evaluate if lipoprotein particle type and size (by NMR) are associated with incident myocardial infarction (MI) beyond apoB-containing lipoprotein particle count.
Materials & methods

UK Biobank (n=502 422)
NMR metabolomics substudy
(n = 118 082)

Excluded
Prevalent CAD, PAD, stroke,
lipid-lowering drugs users,
missing data (n=21 961)

Primary prevention subsample
(n=96 121)

Nightingale NMR Platform,
Immunoturbidimetric Lp(a) assay

Biomarkers included in Cox regression models and restricted cubic splines:
1. ApoB-containing particle count (ApoB-P)
2. Average VLDL size
3. Average LDL size
4. VLDL/(LDL+IDL) counts ratio
5. Lipoprotein(a)

Myocardial infarction ascertainment:
ICD10: I21, I22
ICD9: 410

Incident MI (n=1702)
Median follow-up:
12.1 years

Approved project: 75001
PI: Jakub Morze

Created with BioRender.com
# Participants’ Baseline Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Median (IQR) or %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>56 (49-62)</td>
</tr>
<tr>
<td>Male, %</td>
<td>42%</td>
</tr>
<tr>
<td>White, %</td>
<td>94%</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>26.3 (23.8-29.4)</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>42%</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>1.4%</td>
</tr>
<tr>
<td>ApoB-P, µmol/L</td>
<td>1.6 (1.4-1.9)</td>
</tr>
<tr>
<td>VLDL/(LDL+IDL) counts ratio</td>
<td>11.8 (10.6-13.1)</td>
</tr>
<tr>
<td>Average VLDL size, nm</td>
<td>38.5 (37.7-39.4)</td>
</tr>
<tr>
<td>Average LDL size, nm</td>
<td>23.9 (23.8-24.0)</td>
</tr>
<tr>
<td>Lipoprotein(a), nmol/L</td>
<td>20 (10-61)</td>
</tr>
</tbody>
</table>

**Pearson correlation heatmap**

- **ApoB-P**
  - VLDL count: 0.87
  - LDL count: 0.90
  - IDL count: 0.90
  - VLDL/LDL+IDL: 0.31
  - VLDL size: 0.38
  - LDL size: 0.07
- **VLDL count**
  - LDL count: 1.00
  - IDL count: 0.72
  - VLDL/LDL+IDL: 0.73
  - VLDL size: 0.68
  - LDL size: -0.18
- **IDL count**
  - LDL count: 0.89
  - VLDL/LDL+IDL: 0.12
  - VLDL size: 0.14
  - LDL size: 0.11
- **VLDL/LDL+IDL**
  - LDL count: 0.86
  - VLDL size: 0.28
  - LDL size: 0.08
- **VLDL size**
  - LDL size: 1.00
- **LDL size**
  - ApoB-P: -0.10
  - VLDL count: -0.46
  - IDL count: -0.46
  - VLDL/LDL+IDL: -0.46
  - VLDL size: -0.13
  - LDL size: 0.11
- **Lp(a)**
  - ApoB-P: 0.03
  - VLDL count: -0.02
  - IDL count: 0.07
  - LDL count: 0.03
  - VLDL/LDL+IDL: -0.10
  - VLDL size: -0.13
  - LDL size: 0.11
  - Lp(a): 1.00
Associations between baseline lipoprotein measures and incident myocardial infarction in UK Biobank

**Model 2:** Adjusted further for ApoB-containing particle count, fasting time, HDL count and size

<table>
<thead>
<tr>
<th>Measure</th>
<th>HR per 1-SD increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>ApoB-containing particle count</td>
<td>1.2</td>
</tr>
<tr>
<td>VLDL/(LDL+IDL) counts ratio</td>
<td>1.4</td>
</tr>
<tr>
<td>Average VLDL size</td>
<td>1.6</td>
</tr>
<tr>
<td>Average LDL size</td>
<td>1.6</td>
</tr>
<tr>
<td>Lipoprotein(a)</td>
<td>1.6</td>
</tr>
</tbody>
</table>
Associations between average lipoprotein particle count and incident myocardial infarction in UK Biobank

ApoB particle count

Lp(a) particle count

Unadjusted

Adjusted for clinical covariates
Associations between baseline lipoprotein type/size and incident myocardial infarction in UK Biobank

**Particle type**

- Unadjusted
- Adjusted for clinical covariates

**VLDL particle size**

- Hazard ratio vs. Average VLDL size (nm)

**LDL particle size**

- Hazard ratio vs. Average LDL size (nm)
Summary & Conclusions

• The risk of myocardial infarction is independently associated with the total particle count of all apoB-containing lipoproteins, and not the size or type of these lipoproteins.

• 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.