Association of the Serum Myeloperoxidase/High-Density Lipoprotein Particle Ratio and Incident Cardiovascular Events in a Multi-Ethnic Population: Observations From the Dallas Heart Study

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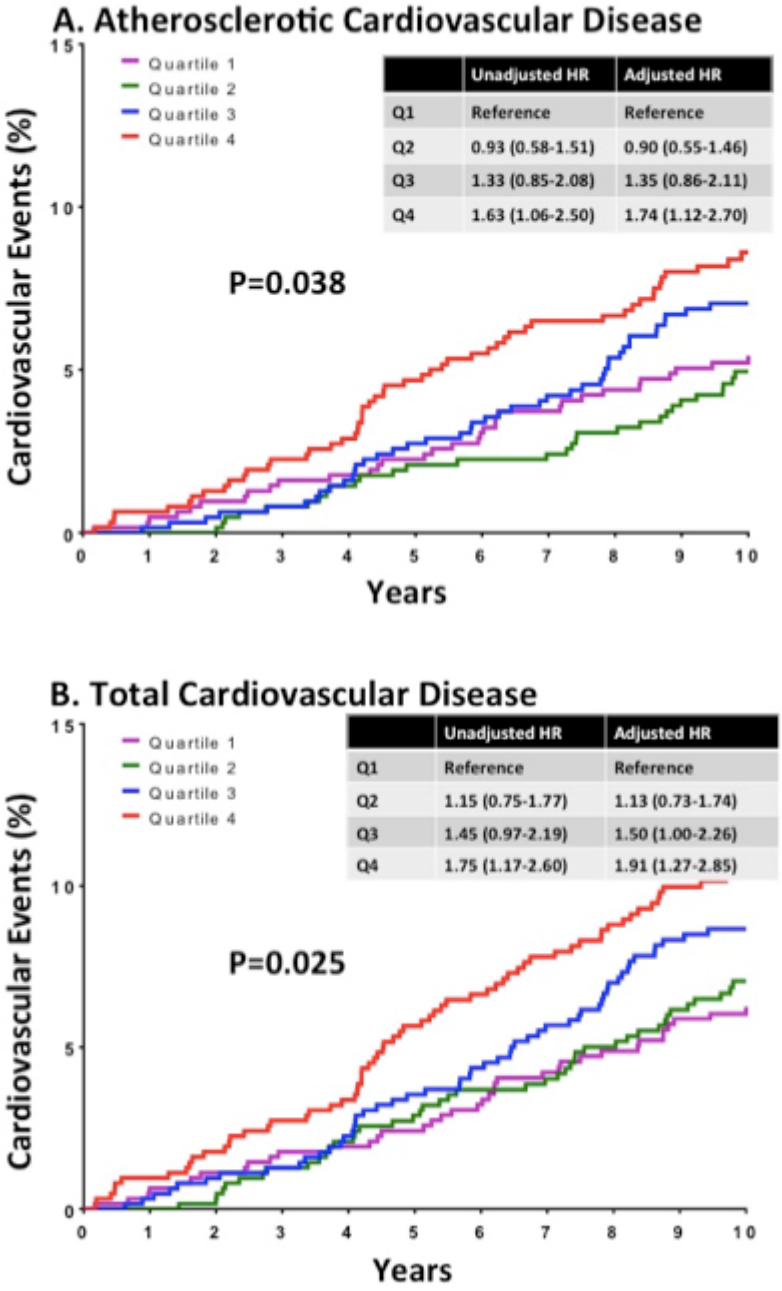
Introduction: Myeloperoxidase (MPO) promotes oxidation of lipoproteins whereas high-density lipoprotein (HDL) exerts anti-oxidative effects in part via paraoxonase-1 (PON1). MPO can induce dysfunctional HDL particles; however, the interaction of circulating levels of these measures in cardiovascular disease (CVD) has not been studied in humans. We hypothesized that increased serum levels of MPO indexed to HDL particle concentration would be associated with an adverse phenotype with increased CVD risk and tested this hypothesis in a large multiethnic population free of CVD at baseline.
Methods: Levels of MPO, HDL-C, and HDL particle concentration (HDLp) by NMR were measured at baseline in 2924 adults free of CVD (57% women, 49% black). The associations of the MPO/HDLp ratio with incident ASCVD (first nonfatal myocardial infarction, nonfatal stroke, coronary revascularization, or CVD death) and total CVD were assessed in Cox proportional-hazards models adjusted for traditional risk factors (age, sex, race, hypertension, smoking, total cholesterol, and statin use). The median follow-up period was 9.4 years.
Results: MPO/HDLp was associated directly with total cholesterol, C-reactive protein, interleukin 18, and body mass index, and inversely with PON1 arylesterase activity, HDL-C, and HDL size. In adjusted models, the highest versus lowest quartile of MPO/HDLp was associated with a 74% increase in incident ASCVD (aHR, 1.74, 95% CI 1.12-2.70) and a 91% increase in total CVD (aHR, 1.91, 95% CI 1.27-2.85).
Conclusion: Increasing MPO indexed to HDL particle concentration at baseline is associated with increased risk of incident CVD events in a population initially free of CVD, reflecting increased inflammation and decreased PON1 arylesterase activity. This is the first report of the MPO/HDLp ratio in a large human cohort. Further studies are warranted investigating MPO/HDLp as a biomarker of HDL metabolism and CVD risk.

Figure 1. Kaplan–Meier Curves and Hazard Ratios for Cardiovascular Events, According to Quartile of MPO/HDLp Ratio



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