Normal LDL-C and Atherosclerosis Without Risk Factors

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Summary By:	**Elizabeth A. Jackson, MD, FACC**

Study Questions:

What are predictors of subclinical atherosclerosis in individuals who are free of cardiovascular risk factors?

Methods:

Data from the PESA (Progression of Early Subclinical Atherosclerosis) study were used for the present study. Participants were included in this study if they were without conventional cardiovascular risk factors (no current smoking, untreated blood pressure <140/90 mm Hg, fasting glucose <126 mg/dl, total cholesterol <240 mg/dl, low-density lipoprotein cholesterol [LDL-C] <160 mg/dl, and high-density lipoprotein cholesterol ≥40 mg/dl). A subgroup with optimal cardiovascular risk factors was also defined as having blood pressure <120/80 mm Hg, fasting glucose <100 mg/dl, hemoglobin A1c <5.7%, and total cholesterol <200 mg/dl. Carotid, iliofemoral, and abdominal aortic plaques were evaluated through ultrasound. Coronary artery calcification (CAC), serum biomarkers, and lifestyle factors were also collected.

Results:

Of the 4,184 participants from the PESA study, 1,779 participants were included in the current study (mean age 45 ± 4.1 years, 50.5% female). A total of 740 participants were included in a subgroup with optimal cardiovascular risk factors. Subclinical atherosclerosis (plaque or CAC) was present in 49.7% of cardiovascular risk factor-free participants. Together with male sex and age, LDL-C was independently associated with atherosclerosis presence and extent, in both the cardiovascular risk factor-free and cardiovascular risk factor-optimal groups [odds

ratio (x10 mg/dl) 1.14-1.18, $p < 0.01$ for all]. Atherosclerosis presence and extent was also associated in the cardiovascular risk factor-free group with hemoglobin A1c levels.

Conclusions:

The authors concluded that many conventional cardiovascular risk factor-free middle-aged individuals have atherosclerosis. LDL-C, even at levels currently considered normal, is independently associated with the presence and extent of early systemic atherosclerosis in the absence of major conventional cardiovascular risk factors. These findings support more effective LDL-C lowering for primordial prevention, even in individuals conventionally considered at optimal risk.

Perspective:

These data suggest that subclinical atherosclerosis is not uncommon among middle-aged US patients, even those without evident cardiovascular risk factors. If maintaining a low LDL-C level throughout life could reduce plaque development, this would have widespread implications for when and who would benefit from pharmacotherapy to lower LDL-C.

Clinical Topics: **Diabetes and Cardiometabolic Disease, Dyslipidemia, Noninvasive Imaging, Prevention, Lipid Metabolism, Nonstatins, Echocardiography/Ultrasound, Diet**

Keywords: *Atherosclerosis, Aorta, Abdominal, Biological Markers, Blood Pressure, Cholesterol, LDL, Dyslipidemias, Fasting, Glucose, Hemoglobin A, Glycosylated, Life Style, Plaque, Atherosclerotic, Primary Prevention, Risk Factors, Ultrasonography*