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Vitamin D is associated with atheroprotective high-density lipoprotein profile in postmenopausal women

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BACKGROUND: Low vitamin D has been associated with low levels of high-density lipoprotein (HDL) cholesterol, a marker of coronary risk. Whether atheroprotective HDL particle composition accounts for this association and whether fat affects this association is not known.

OBJECTIVE: To explore the association between HDL particle composition and 25-hydroxy vitamin D (25[OH]D) in post-menopausal women.

METHODS: Vitamin D levels and lipoprotein composition were assessed in fasting blood samples of apparently healthy women from a diverse Chicago community. Visceral (VAT) and subcutaneous (SAT) abdominal fat area were assessed using computed tomography. Total body fat mass was measured by dual-energy X-ray absorptiometry.

RESULTS: We enrolled 78 women (50% black; 50% white), age 48 to 64 years, all of whom were participants in a longitudinal study of fat patterning. They had a mean 25[OH]D of 31 ± 15 μg/L, HDL cholesterol 57±11 mg/dL, and large HDL particle subclass 8.6±3.4 μmol/L. In a multivariable-adjusted regression model, each 5 μg/L higher 25[OH]D predicted 0.57 μmol/L (95%CI 0.20–0.95) higher large HDL particles, independent of race, season, and total HDL particle concentration. This association was only partially confounded by total body fat mass (0.49, 95%CI 0.10–0.89), SAT (0.50, 95%CI 0.11–0.90), or VAT (0.37, 95%CI 0.01–0.74). Age did not significantly influence the strength of associations.

CONCLUSIONS: Higher 25[OH]D levels are associated with large HDL particles. This association is stronger than that of HDL cholesterol and only partially confounded by body fat. Theoretically, vitamin D may protect against cardiovascular risk by promoting formation of large HDL particles, affecting reverse cholesterol transport.

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Higher levels of vitamin D,[1] assessed by serum 25-hydroxyvitamin D concentration (25[OH]D), and high-density lipoprotein (HDL) cholesterol[2] are both related to lower risk of coronary artery disease (CAD). Although several studies[3–5] suggested an association between 25[OH]D and HDL cholesterol, there are no published reports exploring whether this relationship can be better explained by HDL particle composition pattern (particularly, large HDL particle subclass, or particle number and size). Because HDL particle composition may be instrumental in understanding the link between HDL cholesterol and

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CAD risk,[6] determining the association between 25[OH]D and HDL particle composition can help elucidate any links between 25[OH]D and CAD risk.

It is particularly meaningful to investigate the association between 25[OH]D and HDL particle composition in postmenopausal women because this period is a critical one of increasing cardiovascular risk.[7] Adipose tissue may confound any relationship between vitamin D and HDL particle subclasses (Fig. 1). Because of fat-soluble 25[OH]D sequestration,[8] vitamin D levels are lower in people with more total adipose tissue,[9] subcutaneous adipose tissue (SAT),[9,10] and visceral adipose tissue (VAT).[10] VAT is related to HDL cholesterol and HDL particle composition[11,12] and is associated with increased cardiovascular risk during menopause.[13] Our focus was to explore whether (1) vitamin D is associated with atheroprotective HDL particle subclasses in women of postmenopausal age; and (2) these associations are independent of adipose tissue.

Methods

Subjects

Women included in this analysis were participants in a study of the impact of menopause on fat patterning.[13] Women were randomly selected from a population census with excellent representativeness and were approximately equivalent within both races on indices of socioeconomic status. For this report, we randomly selected from the ongoing study 80 postmenopausal women, ages 48 to 64 years. Selected participants had no history or symptoms of CAD and no known chronic debilitating health conditions, no estrogen replacement, and no diabetes or impaired fasting glucose. Two women did not have measurements required for the current analysis. Thus, our final sample consisted of 78 women (39 white; 39 black). The study was approved by the institutional review board at the Rush University Medical Center, and all women provided a written informed consent.

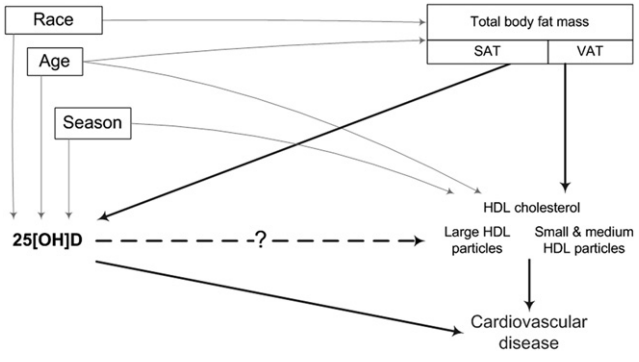

Figure 1 The diagram of association between vitamin D and HDL variables. The square around box around the nodes represents conditioning for variable in multivariable analysis.

Measurements

The blood pressure was taken with the use of standard techniques.[14] High blood pressure was defined according to the National Cholesterol Education Program Adult Treatment Panel III guidelines as a blood pressure greater than 130/85 mm Hg or taking antihypertensive medications. All 78 women underwent a fasting blood collection. Cardiovascular risk factors were measured using standard self-report questionnaires.

High-density lipoprotein composition

Lipoprotein subclasses were determined by nuclear magnetic resonance (NMR) spectroscopy (LipoScience Inc, Raleigh, NC), as previously described.[15] In brief, lipoprotein particles were quantified by their proton NMR signals, which differ according to particle diameter. The total plasma signal was deconvoluted into derived signal amplitudes for each lipoprotein subclass by the use of data from previously modeled reference subclasses. The quantity of each subclass is proportional to its signal amplitude, which is multiplied by a standard lipid amount to provide the cholesterol content carried in HDL particles (HDL cholesterol), or triglyceride content carried in very low-density lipoprotein (VLDL) and chylomicrones.

The NMR-derived measures for HDL cholesterol and triglycerides (but not for total and low-density lipoprotein cholesterol) correlate closely to the chemically measured values. The lipoprotein subclasses were categorized as large (60 to 200 nm), medium (35 to 60 nm), and small (27 to 35 nm) VLDL; large (21.3 to 23.0 nm), medium (19.8 to 21.2 nm), and small (18.3 to 19.7 nm) low-density lipoprotein (LDL); and large (8.2 to 13 nm) and small-to-medium (7.3 to 8.2 nm) HDL particles. Mean particle size was calculated for each lipid particle subclass (HDL, LDL, and VLDL) by weighting the concentration of each subclass by its standard reference diameter. The total HDL particle concentration was defined as the number of HDL particles per plasma volume, expressed in μmol/L.

Vitamin D

Serum vitamin D testing was performed by PPD Global Central Labs (Highland Heights, KY) with the use of a Chromosystems high-performance liquid chromatography kit for 25-OH vitamin D_2 and 25-OH vtamin D_3 and a Waters isocratic high-performance liquid chromatography pump system with UV detector (Milford, MA). Each assay detection limit was 5 μg/L; intraassay variability varied from 0.8% at 57.9 μg/L to 3.0% at 24.9 μg/L, and the interassay variation varied from 1.9% at 84.5 μg/L to 4.6% at 23.2 μg/L. We used total 25-OH vitamin D (25-OH vitamin D_2 + 25-OH vitamin D_3) concentration in the statistical analyses. Calcidiol (25-OH vitamin D_3) is the predominant source of vitamin D in humans and reflects endogenous vitamin D production, whereas ergocalciferol (vitamin D_2) is derived

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