ASSOCIATION OF PHYSICAL ACTIVITY WITH BIOACTIVE LIPIDS, BMI, AND RISK OF FUTURE CARDIOVASCULAR EVENTS
MEDICATION ANALYSIS FROM THE VITAMIN D AND OMEGA-3 TRIAL (VITAL) AND JUPITER STUDIES
Preventive Medicine, Brigham and Women’s Hospital/Harvard Med School, Boston, MA; Cardiovascular Medicine, Brigham and Women’s Hospital/Harvard Med School, Boston, MA; Biomedical Sciences, UCSF, La Jolla, CA; *contributed equally; fco-senior: rhoshii@bwh.harvard.edu

BACKGROUND

The biology of regular physical activity (PA) from a bioactive lipidome standpoint has the potential to enhance the mechanistic knowledge about benefits of exercising on cardiometabolic health.

Bioactive lipids are small molecules produced by lipid metabolism fundamental in immune regulation, modulation of inflammation, and internal body control of organic processes.

OBJECTIVES

1) To examine the association of plasma bioactive lipids (BAL) related to PA with incident cardiovascular disease (CVD);
2) To evaluate the extent to which body mass index (BMI) might mediate this association.

METHODS

➢ Study population
  • 2 sub-cohorts from VITAL1 (NCT01169259): 1032 participants who had individual clinical evaluations (VITAL) and 770 CVD case-control pairs (VITAL-CVD);
  • 2 sub-cohorts from JUPITER2 (NCT00239681): 589 non-cases (JUPITER) and 415 CVD case-control pairs (JUPITER-CVD);
➢ Study design: Two-stage analysis:
  1. Association with PA
  2. Association with incident CVD/VITAL-CVD
  ➢ Biomarker profiling: bioactive lipids using a high-throughput non-targeted LC-MS.
  ➢ Physical activity
    • Self reported leisure-time activity during past year;
    • Continuous variable in VITAL (MET-hr/wk);
    • Ordinal variable in JUPITER (rarely/never, <1d/wk, 1d/wk, 2-3 d/wk, 4-6 d/wk, daily)
➢ CVD: Composite variable of confirmed myocardial infarction, stroke, coronary revascularization, cardiovascular death (VITAL-CaCo) or all-cause death (JUPITER-CaCo).
➢ Statistical analysis:
  • Linear regression for associations with PA;
  • Conditional logistic regression for incident CVD;
  • Mediation analysis through BMI;
  • Adjustments for age, sex, race, smoking, LDL, and total cholesterol (no sex in conditional logistic regressions as a case-control matching variable);
  • False Discovery Rate (FDR) adjustment at 10% at all stages.

RESULTS AND CONCLUSION

145 BALs were significantly associated with PA after validation (FDR-1)

Medication analysis through BMI revealed 89 BAL-mediated and 56 non-mediated PA associations

Each set was carried over to examine the associations with CVD

Most of CVD-BAL associations (32) showed mediation through BMI and a few (4) indicated no mediation

• 15 CVD-BAL associations validated from BMI-mediated PA-BAL associations;
• No relationship with CVD from PA-BAL associations not mediated by BMI

Higher levels of 13 BALs associated with lower levels of PA. This seems reasonable as the same BALs showed increased risk for CVD.

Higher levels of 2 BALs associated with higher levels of PA. This seems reasonable as the same BALs showed reduced risk for CVD.

PA and BMI can influence each other, resulting in different products of metabolism. A relationship between BMI and CVD also exists, and we found that BMI-mediated associations with BALs were predominant. However, non-mediated effects were as well detected, implying that more than one pathway may play a role in the PA-BAL-CVD relationship.

Future steps include finding identifications and/or more clinical-related aspects for these yet unknown molecules.

References:

Disclosure: Hoshii RA: supported by the Lemann Foundation Cardiovascular Research Postdoctoral Fellowship. Demlert O: received support from Iowa, not related to the current work. Messa S: In-kind institutional support for performing laboratory assays in the VITAL trial; Quest Diagnostics, Research Grant; Abbvie Diagnostics and Pfizer. This project was supported in part by the National Institutes of Health grants: 5R01HL113142 and BMH Lever Research Award (Dentrix, O; R01AM051446 (Okereke, O; R01HL138811, 1R14AM134618, 1R01HL144227, 2K06HL168852, and R01DK112940 (Messa S). AbbVie funded the parent JUPITER trial.