MCNER Webinar Series

Don’t Take My Breath Away: Nutrition and Lung Health

Wednesday, May 15, 2024

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Don’t Take My Breath Away: Nutrition and Lung Health

Corri Hanson, PhD, RD, LMNT, FAND
Director, Medical Nutrition Program
Professor of Nutrition
University of Nebraska Medical Center
Don’t Take My Breath Away

The role of diet in the development and progression of lung disease

Corrine Hanson, PhD, RD, LMNT, FAND
Professor and Director, Medical Nutrition Education
University of Nebraska Medical Center
Dietary Intake is Associated with Lung Function in the Eclipse Cohort

Corinne Hanson, PhD, RD; Harlan Sayles, MS, PhD; Erica Ruben, PhD; Emelie Wodas, MD; William MacNee, MD, PhD; Peter Calverley, MD, PhD; Jane Meza, PhD; Stephen Freemantle, MD

University of Nebraska Medical Center, School of Allied Health Professions, Medical Nutrition Education; University of Nebraska Medical Center, College of Public Health Program Developmental Centre, Centre of Expertise for Chronic Obstructive Lung Disease, University of Edinburgh, Department of Pulmonary Medicine, University of Edinburgh, Department of Medicine, Clinical Sciences Centre, University of Edinburgh, Department of Pulmonary Medicine, University of Edinburgh, Department of Pulmonary Medicine, University of Edinburgh, Department of Pulmonary Medicine, University of Edinburgh, Department of Pulmonary Medicine

Background: Diet is a potentially modifiable risk factor in the development and progression of many diseases, including COPD.

Objective: The objective of this study is to evaluate the relationship between dietary intake and clinical characteristics of COPD in a large, well-characterized population of COPD patients and controls that were part of the Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints study (ECLIPSE).

Methods: Limited diet records were available for 2,167 subjects who provided dietary intake information at eight time points over a 5-year period.

- Subjects reported the amount they had consumed over the last 24 hours for four food categories which included grapefruit, fish, fish, bananas, and cheese.
- Intake of each food group was handled as a dichotomous variable (yes/no) 24 hours after the eighth follow-up visit at the third study visit. The two groups were then compared using clinical outcome measures at the last available follow-up.

Multivariate models for each food group and each outcome measure were run to adjust for confounding factors of age, sex, BMI, smoking (SGRQ and 6-min walk), and BMI (SGRQ and 6-min walk were also adjusted for BMI).

Results: Associations between intake of foods and outcome variables are given in the following table. Color legend: Green = The association had a positive impact on lung health; Red = The association had a negative impact on lung health. No color = no significant association.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Grapefruit p-value</th>
<th>Fish p-value</th>
<th>Bananas p-value</th>
<th>Cheese p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1 Post-Dose</td>
<td>0.08</td>
<td>0.02</td>
<td>0.07</td>
<td>0.04</td>
</tr>
<tr>
<td>FEV1 % Pred Post-Dose</td>
<td>2.1</td>
<td>0.17</td>
<td>1.3</td>
<td>0.23</td>
</tr>
<tr>
<td>FVC Post-Dose</td>
<td>0.14</td>
<td>0.05</td>
<td>0.09</td>
<td>0.06</td>
</tr>
<tr>
<td>FEV1 Post-Dose (annual rate of change in mL)</td>
<td>6.84</td>
<td>0.01</td>
<td>-1.5</td>
<td>0.41</td>
</tr>
<tr>
<td>Emphysema: % voxels &gt; 960HU</td>
<td>-0.63</td>
<td>0.45</td>
<td>-1.5</td>
<td>0.009</td>
</tr>
<tr>
<td>Emphysema: % voxels &lt; 960HU (change over 3 years)</td>
<td>-0.68</td>
<td>0.03</td>
<td>-0.41</td>
<td>0.07</td>
</tr>
<tr>
<td>6-Minute Walk</td>
<td>15.1</td>
<td>0.09</td>
<td>25.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SGRO score</td>
<td>-1.9</td>
<td>0.08</td>
<td>-1.9</td>
<td>0.02</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>0.74</td>
<td>0.90</td>
<td>-2.88</td>
<td>0.60</td>
</tr>
<tr>
<td>Clinical laboratory protein</td>
<td>-0.38</td>
<td>0.19</td>
<td>-0.13</td>
<td>0.32</td>
</tr>
<tr>
<td>C-reactive protein</td>
<td>-1.9</td>
<td>0.05</td>
<td>0.08</td>
<td>0.60</td>
</tr>
<tr>
<td>Total neutrophils</td>
<td>0.10</td>
<td>0.37</td>
<td>-0.18</td>
<td>0.02</td>
</tr>
<tr>
<td>Surfactant protein D</td>
<td>-1.68</td>
<td>0.06</td>
<td>-2.82</td>
<td>0.37</td>
</tr>
<tr>
<td>White Blood Cells</td>
<td>0.03</td>
<td>0.90</td>
<td>-0.21</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Conclusion: Subjects who demonstrated recent consumption of diets associated with a healthy diet, including fruits, and dairy products, had improved markers of lung function, less emphysema, improved 6-min walk and SGRO scores, and a decrease in certain inflammatory markers. The role of diet as a possible modifiable risk factor in COPD continues to warrant investigation.
Dietary Fiber Intake and Lung Function
Methods

We evaluated 1,929 adults in the NHANES cycle 2009-2010 who had spirometry measurements and information on daily fiber intake available.

The primary outcomes were lung function measurements (FEV₁, FVC, percent predicted FEV₁ and FVC).

We also conducted a categorical analysis of fiber intake and airflow restriction and obstruction based on GOLD and Spirometry Grade (SG) classifications.

Multivariate regression models were used to look at the association of lung function measurements and COPD with dietary fiber intake.
<table>
<thead>
<tr>
<th>Characteristic:</th>
<th>Fiber Intake Quartile</th>
<th>Mean (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤10.75 grams/day (n=360)</td>
<td>10.75-&lt;13.46 grams/day (n=461)</td>
</tr>
<tr>
<td>Continuous variables</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Age, yr</td>
<td>52.9 (0.5)</td>
<td>53.1 (0.5)</td>
</tr>
<tr>
<td>FEV₁ (L)</td>
<td>2.6 (0.04)</td>
<td>3.0 (0.04)</td>
</tr>
<tr>
<td>FEV₁, %pred</td>
<td>80.9 (0.8)</td>
<td>86.6 (0.8)</td>
</tr>
<tr>
<td>FVC (L)</td>
<td>3.3 (0.04)</td>
<td>3.9 (0.05)</td>
</tr>
<tr>
<td>FVC, %pred</td>
<td>82.3 (0.7)</td>
<td>87.2 (0.8)</td>
</tr>
<tr>
<td>FEV₁/FVC ratio</td>
<td>0.76 (0.005)</td>
<td>0.77 (0.005)</td>
</tr>
<tr>
<td>Socioeconomic Status (income:poverty status ratio)</td>
<td>2.96</td>
<td>3.55</td>
</tr>
<tr>
<td>C-Reactive protein (mg/dL)</td>
<td>0.47 (0.5)</td>
<td>0.41 (0.06)</td>
</tr>
<tr>
<td>Energy intake (kcals/day)</td>
<td>1868.4 (48.8)</td>
<td>2076.7 (46.6)</td>
</tr>
<tr>
<td>BMI</td>
<td>29.8 (0.5)</td>
<td>29.8 (0.4)</td>
</tr>
<tr>
<td>Discrete variables</td>
<td>N (%)</td>
<td>N (%)</td>
</tr>
<tr>
<td>Gender</td>
<td>N (%)</td>
<td>N (%)</td>
</tr>
<tr>
<td>Male</td>
<td>79 (18.4)</td>
<td>215 (45.2)</td>
</tr>
<tr>
<td>Female</td>
<td>283 (81.6)</td>
<td>246 (54.8)</td>
</tr>
<tr>
<td>Smoking</td>
<td>N (%)</td>
<td>N (%)</td>
</tr>
<tr>
<td>Never</td>
<td>162 (45.6)</td>
<td>239 (55.7)</td>
</tr>
<tr>
<td>Former</td>
<td>97 (27.6)</td>
<td>125 (29.7)</td>
</tr>
<tr>
<td>Current</td>
<td>103 (26.8)</td>
<td>97 (14.6)</td>
</tr>
<tr>
<td>Spirometry Grade Classifications:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal airflow</td>
<td>183 (50.1)</td>
<td>269 (50.1)</td>
</tr>
<tr>
<td>Airflow restriction</td>
<td>122 (29.8)</td>
<td>125 (29.7)</td>
</tr>
<tr>
<td>Airway obstruction</td>
<td>55 (20.1)</td>
<td>67 (16.9)</td>
</tr>
<tr>
<td>GOLD:</td>
<td>N (%)</td>
<td>N (%)</td>
</tr>
<tr>
<td>Normal</td>
<td>305 (80.0)</td>
<td>394 (85.9)</td>
</tr>
<tr>
<td>Airflow obstruction</td>
<td>55 (20.1)</td>
<td>67 (14.1)</td>
</tr>
</tbody>
</table>
Subjects in the highest quartile intake of fiber had:

Mean FEV\textsubscript{1} and FVC measurements that were 82 mL and 129 mL higher that the lowest quartile of intake (p=0.04 and 0.01)
Mean percent predicted FEV\textsubscript{1} and FVC values that were 2.4 and 2.8 percentage points higher (p=0.07 and 0.02).

In the categorical analysis, higher fiber intake was associated with:
A higher percentage of those with normal lung function (p=0.001)
A significant decline in the proportion of participants with airflow restriction (p=0.001).
Table 3. Low fiber is associated with higher odds of respiratory morbidity (NHANES)

<table>
<thead>
<tr>
<th></th>
<th>Q1 (low)</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4 (high)</th>
<th>Q1 vs. Q4 p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>gm/day</td>
<td>gm/day</td>
<td>gm/day</td>
<td>gm/day</td>
<td></td>
</tr>
<tr>
<td>Asthma, n = 13095</td>
<td>1.3 (1.0-1.8)</td>
<td>0.9 (0.7-1.2)</td>
<td>0.9 (0.7-1.1)</td>
<td>1</td>
<td>0.043</td>
</tr>
<tr>
<td>Wheeze, n = 13137</td>
<td>1.2 (1.0-1.5)</td>
<td>1.1 (0.9-1.4)</td>
<td>1.0 (0.9-1.2)</td>
<td>1</td>
<td>0.024</td>
</tr>
<tr>
<td>Cough, n = 8407</td>
<td>1.8 (1.3-2.5)</td>
<td>1.6 (1.2-2.1)</td>
<td>1.4 (1.0-1.8)</td>
<td>1</td>
<td>0.0005</td>
</tr>
<tr>
<td>Phlegm, n = 8410</td>
<td>1.6 (1.1-2.2)</td>
<td>1.4 (1.0-1.9)</td>
<td>1.3 (0.9-1.9)</td>
<td>1</td>
<td>0.008</td>
</tr>
</tbody>
</table>

Odds ratios (95% confidence intervals), adjusted for covariates
6. SCFA production by fermentation of dietary fiber

5. Promotion of fat storage

4. Promotion of intestinal angiogenesis

1. Protection against pathogens

2. Synthesis of vitamins

3. Immune system development

7. Modulation of central nervous system
Figures 3 & 4. Worse % predicted FEV₁ and dyspnea is associated with lower Firmicutes:Bacteroidetes ratio in CURE COPD (former smokers, cross sectional analysis at baseline, 3 months and 6 months, n = 18.)
Saturated Fat
Among subjects with spirometry-defined COPD: Subjects in the lowest quartile intake of saturated fat intake had:

- Mean $\text{FEV}_1$ and FVC measurements that were 126 mL and 166 mL lower that the highest quartile of intake ($p=0.04$ and 0.01)

- Mean percent predicted FVC values that were 3.3 percentage points lower ($p=0.03$).
• We evaluated intakes of individual fatty acids to attempt to determine if specific fatty acids were driving the observed association between saturated fat intake and lung function parameters in individuals with COPD.

• The relationships appear to be driven by butanoic, hexanoic, decanoic, dodecanoic and tetradecanoic acid.

  • **Butanoic**: C4  
  • **Hexanoic**: C6  
  • **Decanoic**: C10  
  • **Dodecanoic (lauric)**: C12  

• These would be classified as SCFA (C4) and medium chain fatty acids (C6-12)
Associations of Prenatal Dietary Inflammatory Potential with Wheeze Trajectory in Project Viva

Corrine Hanson, Sheryl Rifas-Shiman, N. Shivappa, M.D. Wirth, J. R. Hebert, Diane Gold, Carlos Camargo, M.W. Gillman, S. Sen, J. Sordillo, E. Oken, A. Litonjua
Our Goal:

• Determine the extent to which diets with a higher inflammatory potential during the first and second trimester of pregnancy (as measured by the DII) is independently associated with respiratory/allergy outcomes (asthma, wheeze, lung function) in the offspring in early and mid-childhood.
Overall DII score

• More negative scores represent anti-inflammatory diet potential while more positive scores represent pro-inflammatory diet
• Approximate range is -10 to 10
• The DII is not a dietary pattern in itself, but a way to assess the pro- or anti-inflammatory potential of any diet.
  • Thus, it differs from other dietary patterns studied in relation to respiratory outcomes.
A Study of Health for The Next Generation

Project Viva is a groundbreaking longitudinal research study of women and children. The goal of Project Viva is to find ways to improve the health of mothers and their children by looking at the effects of mother's diet as well as other factors during pregnancy and after birth.
Pregnancy

4102 pregnant women approached for participation

2670 (64%) women recruited at <22 weeks gestation

329 became ineligible
- 115 moved out of study area
- 19 multiple gestation
- 195 stillbirths or miscarriages

2341 women remained eligible
- 11 lost to follow-up
- 195 withdrew
- 7 other reason, not specified

2128 live births

After delivery

Infancy (4.9 to 10.6 months)

2035 pairs eligible for infancy visit

338 no data at infancy visit
- 2 unable to trace
- 336 declined

1497 completed an annual mailed questionnaire ages 1-2 years

• 1697 pairs with any data at infancy visit
  o 1124 in-person data
  o 573 questionnaire only

Early childhood (2.8 to 6.3 years)

1579 pairs eligible for early childhood visit

130 no data at early childhood visit
- 18 unable to trace
- 112 declined

1338 completed an annual mailed questionnaire ages 4-6 years

• 1449 pairs with any data at early childhood visit
  o 1204 in-person data
    - 815 child bloods
    - 294 dust samples
  o 155 questionnaire only

Mid-childhood (6.6 to 10.9 years)

1708 pairs eligible for mid-childhood visit

429 no data at mid-childhood visit
- 55 unable to trace
- 374 declined

1279 pairs with any data at mid-childhood visit
  o 1116 in-person data
    - 701 child bloods
  o 163 questionnaire only

* Cumulative number disenrolled from birth to visit
† Ineligible at early childhood visit because the mother provided no information on diet in pregnancy
Methods

Project Viva mothers who completed 1st or 2nd trimester dietary questionnaires whose children have been seen at least once in follow-up.

Dietary inflammatory index during pregnancy, calculated from FFQs administered during the first and second trimester of pregnancy.
Outcomes

- Confounders include maternal age, education, household income, race/ethnicity, parity, smoking history, pre-pregnancy BMI,

- Effect modifiers include sex of child, maternal BMI and maternal smoking status

Diagnosis of ever asthma (measured at early childhood and mid-childhood)

Wheezing (measured at early childhood and mid-childhood)

Wheeze Trajector

Lung function (FEV₁, FVC, FEV₁/FVC ratio, FEF₂₅-₇₅, % predicted FEV₁ and FVC measured at mid-childhood)
Results

• For wheeze trajectory, in the unadjusted analysis, 1st trimester DII scores and average (1st and 2nd semester) DII scores were significantly associated with early wheeze when compared to never wheeze (OR=1.83; 95% CI: 1.10, 3.04; and OR=1.66; 95% CI: 1.04, 2.65 for 1st trimester and average DII scores, respectively).

• This relationship remained significant after adjustment for confounders, with the odds of the child having early wheeze compared to never wheeze for mothers in the first vs. fourth quartile (i.e., more pro-inflammatory) of DII increasing by 1.84 (95% CI: 1.08, 3.14).

• A similar relationship was seen for average 1st and 2nd trimester DII scores for early wheeze vs. never wheeze (OR=1.87, 95% CI: 1.12, 3.11).
Results

After adjustment for confounders, those in quartile 4 had FEF_{25-75} values that were 136 ml lower when compared to those in quartile 1 (95% CI: -256, -15.8).

Similar results were seen for the average of the 1\textsuperscript{st} and 2\textsuperscript{nd} semester DII (β = -133, 95% CI: -251, -15.8 for the fourth DII quartile compared to the first).
Association Between A Plant Centered Diet, Incident Emphysema, and Lung Function Trajectory Among Smokers: Findings from the CARDIA Lung Study

COPD causes major morbidity and mortality

- 6.4% of US adults report a diagnosis of COPD
- Third overall disease related cause of death
- Among the chronic respiratory diseases, accounts for the majority of DALYs (Disability Adjusted Life Years)
Emphysema predicts disease progression

- Ever smokers, w/ emphysema & normal spirometry (GOLD 0)
- At baseline:
  - Lower baseline PFTs
  - Greater dyspnea
  - Worse QOL
- At 5 years:
  - Increased airflow obstruction
  - Greater progression of emphysema

In a GOLD stage 0 participant, A, baseline inspiratory CT showed trace emphysema and, B, 5-year follow-up CT showed moderate emphysema. FEV$_1$ decreased by 780 mL between visits.
Can earlier interventions alter lung function trajectory?

Liu et al., Chest 2021
Study Objectives

Among **Young Adults** who are **Ever Smokers**, we evaluated the association between a healthy plant-based diet and:

a. development of *radiographic emphysema*

b. longitudinal *lung function decline*

c. *spirometric obstruction*
Coronary Artery Risk Development in Young Adults (CARDIA)

- Enrolled 5115 young adult (18-30) black and white men and women
- Followed prospectively for 30 years
- Variables: dietary intake, repeat measures of spirometry, lung CT (many more)
Utilized the A Priori Diet Quality Score (APDQS) to determine adherence to a plant centered diet
  ○ higher score = better adherence
Multivariable-adjusted ORs (95% CIs) of incident emphysema (Year 25) according to quintiles of the APDQS among ever smokers, N=1351

<table>
<thead>
<tr>
<th></th>
<th>APDQS</th>
<th>Per 1 SD higher APDQS</th>
<th>P for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Quintile 1</td>
<td>Quintile 2</td>
<td>Quintile 3</td>
</tr>
<tr>
<td>APDQS median</td>
<td>53.3</td>
<td>60.5</td>
<td>66.7</td>
</tr>
<tr>
<td>Unadjusted cumulative incidence % (n/N)</td>
<td>25.5 (63/247)</td>
<td>18.4 (51/278)</td>
<td>11.6 (31/268)</td>
</tr>
<tr>
<td>Unadjusted OR</td>
<td>1 (ref)</td>
<td>0.66 (0.43–1.00)</td>
<td>0.38 (0.24–0.61)</td>
</tr>
<tr>
<td>MV model OR</td>
<td>1 (ref)</td>
<td>0.61 (0.37–1.01)</td>
<td>0.61 (0.34–1.09)</td>
</tr>
</tbody>
</table>
APDQS and lung disease

Percent of cohort with emphysema

APDQS Quintiles

1: 25.5%
2: 18.4%
3: 11.6%
4: 6.4%
5: 4.3%
Relative distribution of APDQS quintiles among different lung function trajectories (FEV₁ % predicted). Only participants with year 30 data and at least one other timepoint (n=3097) were included to ensure that trajectories reflected lung function changes into middle age. Quintile 5 APDQS was more represented in participants with preserved ideal and preserved good lung health, whereas participants with persistently poor lung health were more likely to have scores in quintile 1. The median APDQS scores were 52, 59.7, 66, 72.5, and 82 for quintiles 1, 2, 3, 4, and 5 respectively.
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Q&A

Moderator:
Lisa Diewald, MS, RDN, LDN
mcner@villanova.edu

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