Higher Intakes of Vegetables and Vegetable-Related Nutrients Are Associated with Lower Endometrial Cancer Risks

Michael Yeh, Kirsten B. Moysich, Vijayvel Jayaprakash, Kerry J. Rodabaugh, Saxon Graham, John R. Brasure, and Susan E. McCann

Abstract

A limited number of studies have investigated diet in association with endometrial cancer (EC). We examined the association between intakes of selected food groups and nutrients with EC risk among 541 women with histologically confirmed EC and 541 women with an intact uterus and noncancer diagnoses seen at Roswell Park Cancer Institute between 1982 and 1998. Self-reported dietary and other epidemiologic data were collected by questionnaire. Unconditional logistic regression was used to estimate odds ratios (OR) and 95% CI, adjusting for age, BMI, hormone replacement therapy use, cigarette smoking, lifetime duration of menstruation, and total energy intake. We observed significant inverse associations for women in the highest vs. lowest quartiles of intake of total vegetables (OR, 0.51; 95% CI, 0.34–0.75), vitamin E (OR, 0.44; 95% CI, 0.27–0.70), dietary fiber (OR, 0.60; 95% CI, 0.39–0.94), β-carotene (OR, 0.55; 95% CI, 0.37–0.82), lutein (OR, 0.52; 95% CI, 0.34–0.78), and folate (OR, 0.57; 95% CI, 0.36–0.91). Our results support that vegetables and related nutrients are associated with decreased risk of EC.

Introduction

Endometrial cancer (EC) is the 7th most common malignancy among women worldwide, with the highest incidence in the United States and Northern Europe (1,2). Known risk factors for EC include increased body mass, history of diabetes mellitus or hypertension, late age at menopause, early menarche, use of exogenous hormone replacement therapy, and nulliparity. Cigarette smoking and use of oral contraceptives also have been associated with decreased risk (2,3).

Prolonged exposure to estrogens is a common link among several known risk factors for EC. Estrogen exposure increases proliferation of endometrial cells, potentially leading to hyperplasia and carcinogenesis. BMI, reproductive factors, diabetes, and hypertension are all risk factors associated with EC that are also associated with circulating estrogen concentrations. Overweight and obesity may elevate concentrations of circulating estrogens because of the increased peripheral aromatization of plasma androstenedione in adipose tissue. Higher BMI is also associated with lower concentrations of plasma sex hormone-binding globulin (SHBG), which may increase free estradiol in the systemic circulation. Early menarche and late menopause may be markers of a prolonged period of estrogen exposure unopposed by progesterone, whereas parity may be protective due to high concentrations of progesterone during pregnancy. Diabetes is hypothesized to elevate androgens and lower SHBG concentrations in the blood, thereby increasing risk. Smoking may upregulate liver enzymes that lead to reduced estrogen concentrations, which may explain the apparent protective associations observed in epidemiologic studies (2). Low levels of physical activity are associated with greater risk, independent of obesity (4).

The relationship between diet and EC risk is not well characterized, although there are plausible mechanisms of action other than those mediated through obesity and diabetes. Many foods contain antioxidant nutrients and anticarcinogenic compounds. Phytoestrogenic compounds such as isoflavones and lignans in fruits and vegetables may also alter sex hormone metabolism (4–7). Dietary fiber affects intestinal microflora that can affect enterohepatic cycling of estrogen conjugates. Some observational studies have shown that vegetarians have higher concentrations of SHBG, lower free plasma estradiol, lower urinary estrogen excretion, and higher fecal estrogen excretion (1,6,8–10).

Previous studies have reported increased EC risks with high total dietary, saturated, and monounsaturated fat intakes (11–14). In general, consumption of foods of animal origin are positively associated with EC in most studies to date (3,15,16), although 1 study suggests that consumption of fatty fish may be inversely associated (17). Some investigators have reported...
Inconsistent results, with 1 large cohort study reporting a strong association with only BMI but not with most dietary factors and even a slight decrease in risk associated with saturated fat and animal fat (18). Another study found no association between EC and protein and fats but an inverse association with lactose, dairy foods, and calcium (19). Calcium supplements were associated with decreased risk, whereas iron supplements were associated with higher risk in 1 study (20). Glycemic index and load have also been reported as potential risk factors (21,22).

Diet high in plant-based foods (3,15,20,23,24), especially dark green or yellow vegetables, fresh legumes, alliums (3,23), whole grains (25), pulses, nuts, and seeds (26), appear to be protective, but the magnitude of these associations differs across studies and some have reported no effect (16). Several inquiries have shown an inverse association with EC risk for carotenoids (11,12,14,24,27), but these results are not consistent (16). Given the limited literature and sometimes inconsistent findings, we investigated the association between dietary intake and EC among patients seen at Roswell Park Cancer Institute (RPCI) between 1982 and 1998.

Participants and Methods

This study utilized data obtained from women who received medical care for cancer or a suspicion of cancer at RPCI between 1982 and 1998. Data were available for 541 women, aged 27–96 y, with incident, histologically confirmed endometrial carcinoma. Controls were selected from a pool of 4614 eligible women with an intact uterus seen at RPCI with a suspicion of cancer but without a cancer diagnosis. One control was randomly selected for each case, matched by 5-y age strata, resulting in 541 participants with no history of cancer or hysterectomy.

All participants completed the self-administered Patient Epidemiology Data System (PEDS) questionnaire, a 16-page instrument that assessed family history of cancer; reproductive, health, and medical histories; environmental and occupational exposures; medication and dietary supplements; tobacco use; alcohol consumption; and other potential risk factors. The protocol for the PEDS study was approved by the RPCI Institutional Review Board and all subjects provided informed consent.

As part of PEDS, diet was queried using a 44-item FFQ that assessed usual intake within the several years prior to diagnosis in cases or questionnaire completion in controls. For each food or beverage, a commonly used unit or portion size was specified and participants were asked how often they had consumed that amount of the food. For foods, there were 5 possible responses ranging from never to 5–7 times/wk. For beverages, there were 9 possible responses that ranged from never to >6 drinks/d.

The FFQ was designed to provide an assessment of intakes of fruits and vegetables, cruciferous vegetables, and foods providing good sources of vitamins A, C, and E, and fat and fiber. Because of the brevity of the FFQ, regression weights were used to calculate nutrient intakes. The methods for the derivation of regression weights have been described in detail previously (28,29). Briefly, multiple linear regression was used to identify foods explaining maximal variability in intake of vitamins A, C, and E, and fat and fiber from detailed diet interviews of 293 healthy participants in the Western New York Diet Study (1975–86). Gender- and nutrient-specific regression weights were then derived using dietary data from 1475 male and 780 female control participants of the Western New York Diet Study through multiple linear regression models, with the nutrient as the dependent variable and the foods identified previously as independent variables. The resulting regression coefficients for each food and nutrient were then multiplied by the frequency of use reported on the PEDS FFQ summed across foods to obtain an index of each nutrient (28,30). Nutrient data for the regression weights utilized food composition data primarily from the USDA (31).

Statistical analyses were conducted using SPSS for Windows version 11.0. All tests were 2-sided and were considered significant at $P < 0.05$. Descriptive characteristics of cases and controls were compared using the Student’s t test for continuous variables (values are means ± SD) and chi-square for categorical variables [values are n (%)]. To estimate the association between dietary intake and EC, mean daily intakes of total energy, food groups, and individual nutrients were divided into quartiles using the distributions of the controls. Analyses by food group were limited to total vegetables, cruciferous vegetables, and total fruits due to the brevity of the FFQ. We used unconditional logistic regression to compute odds ratios (OR) and 95% CI for each quartile of intake relative to the lowest quartile, which served as the referent group. Multivariate models were evaluated using the Hosmer-Lemeshow goodness of fit test (32).

In the logistic regression analyses, risks associated with food groups and individual nutrients were calculated adjusting for age, BMI, cigarette smoking, exogenous estrogen use, total menstrual months, and total energy intake, except when calculating risk associated with macronutrients. Because fat, carbohydrates, and protein are major contributors to total energy, we used the remaining 2 macronutrients as adjusting factors for each macronutrient logistic regression model. Tests for trend were performed from the 2-tailed P-value of the logistic regression for each continuous nutrient or food group variable.

<table>
<thead>
<tr>
<th>TABLE 1 Descriptive characteristics of EC cases and controls</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20–29</td>
<td>66 (12.6)</td>
<td>101 (18.7)</td>
</tr>
<tr>
<td>30–39</td>
<td>473 (87.4)</td>
<td>440 (81.3)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>78.6 ± 21.5</td>
<td>67.4 ± 14.4</td>
</tr>
<tr>
<td>Parity</td>
<td>2.3 ± 1.8</td>
<td>2.7 ± 2.1</td>
</tr>
<tr>
<td>Age at first pregnancy, y</td>
<td>19.6 ± 10.3</td>
<td>20.8 ± 9.9</td>
</tr>
<tr>
<td>Age at first birth, y</td>
<td>48.2 ± 15.6</td>
<td>42.1 ± 19.4</td>
</tr>
<tr>
<td>Total menstrual months, mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral contraceptive use, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>68 (12.6)</td>
<td>101 (18.7)</td>
</tr>
<tr>
<td>No</td>
<td>473 (87.4)</td>
<td>440 (81.3)</td>
</tr>
<tr>
<td>Ever pregnant, n (%)</td>
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<td></td>
</tr>
<tr>
<td>Yes</td>
<td>439 (81.1)</td>
<td>457 (84.5)</td>
</tr>
<tr>
<td>No</td>
<td>102 (18.9)</td>
<td>84 (15.5)</td>
</tr>
<tr>
<td>IUU use, n (%)</td>
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<td></td>
</tr>
<tr>
<td>Yes</td>
<td>27 (5.0)</td>
<td>33 (6.1)</td>
</tr>
<tr>
<td>No</td>
<td>514 (95.0)</td>
<td>508 (93.9)</td>
</tr>
<tr>
<td>Estrogen or DES, n (%)</td>
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<td></td>
</tr>
<tr>
<td>Yes</td>
<td>116 (21.4)</td>
<td>106 (19.6)</td>
</tr>
<tr>
<td>No</td>
<td>425 (78.6)</td>
<td>435 (80.4)</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>47 (8.7)</td>
<td>78 (14.4)</td>
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<tr>
<td>Never</td>
<td>333 (61.7)</td>
<td>296 (54.8)</td>
</tr>
<tr>
<td>Former</td>
<td>160 (29.6)</td>
<td>166 (30.7)</td>
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<tr>
<td>Education, n (%)</td>
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<td></td>
</tr>
<tr>
<td>&lt;8th grade</td>
<td>26 (5.2)</td>
<td>23 (4.3)</td>
</tr>
<tr>
<td>8th grade</td>
<td>43 (8.0)</td>
<td>33 (6.1)</td>
</tr>
<tr>
<td>Some high school</td>
<td>82 (15.2)</td>
<td>66 (12.2)</td>
</tr>
<tr>
<td>High school graduate</td>
<td>200 (37.1)</td>
<td>180 (33.3)</td>
</tr>
<tr>
<td>Some college</td>
<td>106 (19.7)</td>
<td>112 (20.7)</td>
</tr>
<tr>
<td>College graduate</td>
<td>80 (14.8)</td>
<td>126 (23.3)</td>
</tr>
<tr>
<td>Family income, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;$25,000</td>
<td>403 (73.6)</td>
<td>372 (70.3)</td>
</tr>
<tr>
<td>≥$25,000</td>
<td>116 (22.4)</td>
<td>157 (29.7)</td>
</tr>
</tbody>
</table>

1 Values are means ± SD.
2 $P < 0.05$.
3 Values are n (%); $x^2$ for differences in categorical variables between cases and controls.
Results
We compared descriptive statistics of the study participants using standard statistical methods (Table 1). Compared with controls, cases tended to have higher body weight, increased BMI, and later age at menopause. Controls were more likely than cases to have >12 y of education, higher family income, used oral contraceptives, and smoked cigarettes.

We also examined the association of EC with nondietary risk factors, adjusted for age (data not shown). Consistent with previous literature, EC was positively associated with BMI (OR, 2.46; 95% CI, 1.91–3.16; BMI, ≥25 vs. <25) and inversely associated with years of education (OR, 0.74; 95% CI, 0.56–0.97; ≥12 y vs. <12), cigarette smoking (OR, 0.75; 95% CI, 0.59–0.96; ever vs. never smoking), and oral contraceptive use (OR, 0.62; 95% CI, 0.44–0.86; ever vs. never). Weak, but not significant, inverse associations were observed with later age at menarche (OR, 0.62; 95% CI, 0.44–0.86; ever vs. never). Weak, but not significant, inverse associations were observed with later age at menarche (OR, 0.62; 95% CI, 0.44–0.86; ever vs. never smoking), and oral contraceptive use (OR, 0.62; 95% CI, 0.44–0.86; ever vs. never). Weak, but not significant, inverse associations were observed with later age at menarche (OR, 0.62; 95% CI, 0.44–0.86; ever vs. never) and pregnancy history (OR, 0.73; 95% CI, 0.53–1.02; ever vs. never pregnant; P < 0.10).

In our investigations of plant food groups and EC, we found a significantly reduced risk of EC in the highest quartile of total vegetable intake (OR, 0.51; 95% CI, 0.34–0.75) with a strong inverse dose-response trend (P-trend = 0.001). However, there were no consistent associations with intakes of either cruciferous vegetables and fruit examined separately (Table 2).

EC risk was not associated with the highest compared with lowest quartiles of any of the macronutrients examined (Table 3). However, significant inverse linear trends were observed with polyunsaturated fat intake and a borderline significant positive trend with saturated fat intakes.

Consistent with the findings for total vegetable intakes, significant inverse associations were observed in the highest intake quartiles of vitamin E (OR, 0.44; 95% CI, 0.27–0.70; P-trend < 0.001), dietary fiber (OR, 0.60; 95% CI, 0.39–0.94; P-trend = 0.02), β-carotene (OR, 0.55; 95% CI, 0.37–0.82; P-trend = 0.002), lutein (OR, 0.52; 95% CI, 0.34–0.78; P-trend = 0.001), and folate (OR, 0.57; 95% CI, 0.36–0.91) (Table 4). Although the quartile-specific estimates were not significant, there were inverse trends with vitamin C and α-carotene. Unexpectedly, vitamin D intake was significantly associated with increased risk in the highest quartile of intake.

Discussion
Studies on dietary patterns and risk of EC to date have found positive associations with higher intakes of total fat, saturated fat, polyunsaturated fat, protein from animal sources, and many foods of animal origin (11–15). Despite these findings, the evidence for specific dietary components as potential risk factors remains limited, as several investigators have reported inconsistent results from large observational studies (16,18,19,33).
TABLE 4 | OR and 95% CI for the association of EC with daily micronutrient intake

<table>
<thead>
<tr>
<th>Vitamin C, mg/d</th>
<th>Cases</th>
<th>Controls</th>
<th>OR (95%CI)</th>
<th>P-trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1 (≤116)</td>
<td>149</td>
<td>135</td>
<td>1.0</td>
<td>0.02</td>
</tr>
<tr>
<td>Q2 (117–179)</td>
<td>143</td>
<td>135</td>
<td>0.99 (0.73–1.41)</td>
<td>0.47</td>
</tr>
<tr>
<td>Q3 (180–250)</td>
<td>122</td>
<td>135</td>
<td>0.78 (0.54–1.23)</td>
<td>0.49</td>
</tr>
<tr>
<td>Q4 (≥251)</td>
<td>127</td>
<td>135</td>
<td>0.73 (0.48–1.10)</td>
<td>0.53</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vitamin D, IU/d</th>
<th>Cases</th>
<th>Controls</th>
<th>OR (95%CI)</th>
<th>P-trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1 (≤107)</td>
<td>105</td>
<td>135</td>
<td>1.0</td>
<td>0.06</td>
</tr>
<tr>
<td>Q2 (108–233)</td>
<td>137</td>
<td>135</td>
<td>1.25 (0.85–1.62)</td>
<td>0.17</td>
</tr>
<tr>
<td>Q3 (234–390)</td>
<td>119</td>
<td>135</td>
<td>1.16 (0.78–1.72)</td>
<td>0.56</td>
</tr>
<tr>
<td>Q4 (≥391)</td>
<td>180</td>
<td>135</td>
<td>1.78 (1.44–2.19)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vitamin E (total), mg/d</th>
<th>Cases</th>
<th>Controls</th>
<th>OR (95%CI)</th>
<th>P-trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1 (≤5.2)</td>
<td>158</td>
<td>134</td>
<td>1.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Q2 (5.3–6.7)</td>
<td>110</td>
<td>135</td>
<td>0.57 (0.39–0.83)</td>
<td>0.07</td>
</tr>
<tr>
<td>Q3 (6.8–9.7)</td>
<td>160</td>
<td>137</td>
<td>0.71 (0.48–1.04)</td>
<td>0.07</td>
</tr>
<tr>
<td>Q4 (≥9.8)</td>
<td>149</td>
<td>135</td>
<td>0.44 (0.27–0.70)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dietary fiber, g/d</th>
<th>Cases</th>
<th>Controls</th>
<th>OR (95%CI)</th>
<th>P-trend</th>
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<tbody>
<tr>
<td>Q1 (≤16)</td>
<td>136</td>
<td>135</td>
<td>1.0</td>
<td>0.02</td>
</tr>
<tr>
<td>Q2 (17–23)</td>
<td>152</td>
<td>134</td>
<td>1.06 (0.74–1.51)</td>
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<tr>
<td>Q3 (24–32)</td>
<td>138</td>
<td>136</td>
<td>0.80 (0.55–1.17)</td>
<td>0.03</td>
</tr>
<tr>
<td>Q4 (≥33)</td>
<td>115</td>
<td>136</td>
<td>0.60 (0.38–0.94)</td>
<td>0.02</td>
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</table>

<table>
<thead>
<tr>
<th>Retinol, µg/d</th>
<th>Cases</th>
<th>Controls</th>
<th>OR (95%CI)</th>
<th>P-trend</th>
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<tbody>
<tr>
<td>Q1 (≤409)</td>
<td>141</td>
<td>135</td>
<td>1.0</td>
<td>0.02</td>
</tr>
<tr>
<td>Q2 (410–935)</td>
<td>161</td>
<td>135</td>
<td>1.10 (0.77–1.56)</td>
<td>0.52</td>
</tr>
<tr>
<td>Q3 (936–1776)</td>
<td>137</td>
<td>136</td>
<td>0.88 (0.61–1.27)</td>
<td>0.2</td>
</tr>
<tr>
<td>Q4 (≥1777)</td>
<td>102</td>
<td>135</td>
<td>0.69 (0.47–1.02)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>α-Carotene, µg/d</th>
<th>Cases</th>
<th>Controls</th>
<th>OR (95%CI)</th>
<th>P-trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1 (≤489)</td>
<td>141</td>
<td>135</td>
<td>1.0</td>
<td>0.02</td>
</tr>
<tr>
<td>Q2 (490–935)</td>
<td>161</td>
<td>135</td>
<td>1.10 (0.77–1.56)</td>
<td>0.52</td>
</tr>
<tr>
<td>Q3 (936–1776)</td>
<td>137</td>
<td>136</td>
<td>0.88 (0.61–1.27)</td>
<td>0.2</td>
</tr>
<tr>
<td>Q4 (≥1777)</td>
<td>102</td>
<td>135</td>
<td>0.69 (0.47–1.02)</td>
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</table>

<table>
<thead>
<tr>
<th>β-Carotene, µg/d</th>
<th>Cases</th>
<th>Controls</th>
<th>OR (95%CI)</th>
<th>P-trend</th>
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<tbody>
<tr>
<td>Q1 (≤3439)</td>
<td>165</td>
<td>135</td>
<td>1.0</td>
<td>0.002</td>
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<td>Q2 (3440–5698)</td>
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<td>135</td>
<td>0.72 (0.51–1.03)</td>
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<tr>
<td>Q3 (5699–6681)</td>
<td>141</td>
<td>136</td>
<td>0.71 (0.50–1.02)</td>
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<tr>
<td>Q4 (≥6682)</td>
<td>108</td>
<td>135</td>
<td>0.55 (0.37–0.82)</td>
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</table>

<table>
<thead>
<tr>
<th>Cryptoxanthin, µg/d</th>
<th>Cases</th>
<th>Controls</th>
<th>OR (95%CI)</th>
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<tbody>
<tr>
<td>Q1 (≤4)</td>
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<td>135</td>
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<td>Q2 (5–61)</td>
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<tr>
<td>Q3 (62–250)</td>
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<td>136</td>
<td>1.36 (0.95–1.96)</td>
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<tr>
<td>Q4 (≥251)</td>
<td>163</td>
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<td>1.42 (0.98–2.04)</td>
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<table>
<thead>
<tr>
<th>Lycopene, µg/d</th>
<th>Cases</th>
<th>Controls</th>
<th>OR (95%CI)</th>
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<td>Q1 (≤2601)</td>
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<td>135</td>
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<tr>
<td>Q2 (2602–4279)</td>
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<td>135</td>
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<td>Q3 (4280–6620)</td>
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<td>136</td>
<td>0.80 (0.56–1.16)</td>
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<tr>
<td>Q4 (≥6621)</td>
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<td>135</td>
<td>1.01 (0.68–1.46)</td>
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<table>
<thead>
<tr>
<th>Lutein, µg/d</th>
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<th>Controls</th>
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<th>P-trend</th>
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<td>0.01</td>
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<td>132</td>
<td>135</td>
<td>0.61 (0.43–0.88)</td>
<td>0.01</td>
</tr>
<tr>
<td>Q3 (4280–6620)</td>
<td>131</td>
<td>136</td>
<td>0.69 (0.48–0.99)</td>
<td>0.01</td>
</tr>
<tr>
<td>Q4 (≥6621)</td>
<td>129</td>
<td>135</td>
<td>0.52 (0.34–0.78)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Folate, µg/d</th>
<th>Cases</th>
<th>Controls</th>
<th>OR (95%CI)</th>
<th>P-trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1 (≤288)</td>
<td>149</td>
<td>135</td>
<td>1.0</td>
<td>0.01</td>
</tr>
<tr>
<td>Q2 (289–371)</td>
<td>132</td>
<td>135</td>
<td>0.74 (0.51–1.07)</td>
<td>0.01</td>
</tr>
<tr>
<td>Q3 (372–473)</td>
<td>131</td>
<td>136</td>
<td>0.69 (0.46–1.01)</td>
<td>0.01</td>
</tr>
<tr>
<td>Q4 (≥474)</td>
<td>129</td>
<td>135</td>
<td>0.57 (0.36–0.91)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

**TABLE 4 Continued**

<table>
<thead>
<tr>
<th>Calcium, mg/d</th>
<th>Cases</th>
<th>Controls</th>
<th>OR (95%CI)</th>
<th>P-trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1 (≤570)</td>
<td>125</td>
<td>135</td>
<td>1.0</td>
<td>0.19</td>
</tr>
<tr>
<td>Q2 (571–927)</td>
<td>134</td>
<td>135</td>
<td>0.95 (0.65–1.39)</td>
<td>0.19</td>
</tr>
<tr>
<td>Q3 (928–1380)</td>
<td>102</td>
<td>136</td>
<td>0.86 (0.58–1.29)</td>
<td>0.19</td>
</tr>
<tr>
<td>Q4 (≥1381)</td>
<td>180</td>
<td>135</td>
<td>1.44 (0.90–2.30)</td>
<td>0.19</td>
</tr>
</tbody>
</table>

1 Values are OR and 95% CI, adjusted for age, BMI, HRT, smoking, total menstrual months, and total energy.
2 1 IU = 0.025 µg.
vitamin D concentrations and dietary intake of calcium and dairy foods have been found to be inversely associated with insulin resistance in several observational studies. Women with Type 2 diabetes are more likely to be deficient in vitamin D compared with controls with no history of diabetes. Other studies have found inverse associations between adiposity, body weight, and dietary calcium intake (45). Thus, the role of calcium and vitamin D in EC risk is unclear, because both are involved in many cellular processes, including estrogen biosynthesis, glucose metabolism, fatty acid metabolism, and regulation of body weight.

Strengths of this study include the relatively large sample size and available information on important covariates such as exogenous hormone use and reproductive factors. However, there are several limitations of our study that should be noted. As with any hospital-based, case-control study, selection bias may be present due to the possibility that individuals seeking medical care may have characteristics and exposures that are not comparable to the general population. Our hospital-based controls sought care at RPCI for nonneoplastic conditions and may have modified their diets as a result of various medical problems. Although we were able to control for several important covariates, there was no reliable data on hypertension and diabetes besides a binary (yes/no) variable on the self-reported PEDS questionnaire. Due to the large amount of missing data for these variables, as well as the problem of self-reporting for disease processes that may be present in the absence of clinical symptoms, we excluded these potential covariates from the analysis. Diseases such as diabetes can also affect dietary patterns when patients attempt to heed medical advice to modify their intake. On the other hand, many of these factors could also affect intake in the hospital-based controls, which would attenuate the true associations between dietary components and EC. In fact, our findings were consistent with much of the previous literature, suggesting that selection bias was not an important issue in this study.

Measurement error on the FFQ is a concern common to observational studies of diet. This can be attributed to limited recall of consumption or serving size, omission of certain foods, and changes in participants’ dietary patterns over time. Such random measurement error in dietary assessment can lead to nondifferential misclassification, which would also tend to underestimate any true associations. Also, we used a 44-item FFQ and intake of nutrients not directly measured from the food list were calculated using regression weights. Compared with the Harvard Semi-quantitative FFQ and the National Cancer Institute Health Habits and History FFQ, the 44-item questionnaire yielded somewhat different estimates of total energy and fat, whereas vitamins A and C, dietary fiber, and carotenoid estimates were comparable to the longer instruments (29,30). Although it is likely that some measurement error occurred in the estimation of dietary intake, it is unlikely that the dietary assessment of the cases differed systematically from that of the controls.

Because diet is a modifiable risk factor, a more detailed understanding of dietary components and patterns may be useful in developing population-based preventive strategies for EC. Our study provides additional evidence that diet may play an important role in the etiology of EC and that a vegetable-rich diet may have a protective effect. In summary, the findings of this investigation are consistent with most observational studies on diet and EC to date. Further studies will help identify specific dietary components, intake patterns, and biological mechanisms that contribute to risk.

Literature Cited


