The Role of Diet in the Etiology and Treatment of Breast Cancer

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Outline

- Introduction
- Diet and Breast Cancer
- Roles for the Nutrition Professional
- Future Research
- Take Home Messages
Learning Objectives

- Describe basics of breast cancer types, screening and diagnosis, and statistics.
- Outline the influence of BRCA1 and BRCA2 genes on breast cancer risk.
- Identify modifiable and non-modifiable risk factors for breast cancer and relate them to nutrition practice.
- Critically analyze the research outlining associations between diet and breast cancer risk including: dietary pattern, vitamins and supplements, and fat intake.
- Discuss the association between weight and breast cancer risk.
- Recognize cancer “fad diets” and how to address them in counseling.
Introduction

BREAST ANATOMY
SCREENING & DIAGNOSIS
TYPES OF BREAST CANCER & STAGING
STATISTICS
RISK FACTORS
BRCA1 AND BRCA2
ESTROGEN
Activity

- Breast Cancer – Myth or Fact?
WHAT BREAST CANCER CAN LOOK LIKE

- indentation
- skin erosion
- redness or heat
- new fluid
- hardening
- dimpling
- bump
- invisible lump
- growing vein
- nipple retraction
- new asymmetry
- orange peel skin

If you find new changes like this that stay around, show your doctor.

Fight breast cancer starting with you! Visit worldwidebreastcancer.com to learn, make a screening plan and share awareness with others through social media and printed materials. twitter: @mayorgirl
Screening & Diagnosis

Screening
- Mammograms (age 40+)
  - Find cancer before symptoms appear
  - XR to examine breast density
- Clinical Breast Exam & Breast Self-Exam (age 20+)
  - Palpate lumps
- MRI
  - High risk populations

Diagnosis
- Imaging (XR, US, MRI)
- Biopsy
- Hormone labs
Types of Breast Cancer

- **DCIS** – ductal carcinoma in situ (stage 0)
  - Non-invasive, pre-cancer
  - Nearly all can be cured

- **IDC** – invasive ductal carcinoma
  - Most common
  - Can metastasize

- **ILC** – invasive lobular carcinoma
  - Less common
  - Can metastasize
  - Difficult to detect via mammogram
Invasive Ductal Carcinoma – Excised
Stage 0 – Carcinoma in Situ
Stage IIA Breast Cancer

- Cancer in 1 to 3 lymph nodes in the axilla or near the breastbone.
- Tumor is 2 cm or smaller.
- Tumor is larger than 2 cm but not larger than 5 cm.

http://www.cancer.gov/cancertopics/pdq/treatment/breast/Patient/page2
Stage IIB Breast Cancer

- Tumor is larger than 2 cm but not larger than 5 cm
- Clusters of cancer cells in lymph nodes
- Cancer in 1 to 3 lymph nodes in the axilla or near the breastbone
Stage IIIA Breast Cancer

- No tumor or tumor is any size
- Cancer in 4 to 9 lymph nodes in the axilla or near the breastbone
- Tumor is larger than 5 cm
- Cancer in 1 to 3 lymph nodes in the axilla or near the breastbone

http://www.cancer.gov/cancertopics/pdq/treatment/breast/Patient/page2
Stage IIIB Breast Cancer

http://www.cancer.gov/cancertopics/pdq/treatment/breast/Patient/page2
Stage IIIc Breast Cancer

- Cancer in 10 or more lymph nodes in the axilla
- Cancer in lymph nodes above or below the collarbone
- Cancer in lymph nodes in the axilla and near the breastbone

No tumor or tumor is any size

http://www.cancer.gov/cancertopics/pdq/treatment/breast/Patient/page2
Stage IV Breast Cancer

Breast cancer has spread to other parts of the body:

- Brain
- Lungs
- Liver
- Bone

Cancer can spread through the blood to other parts of the body.

Lymph nodes

To other parts of the body

http://www.cancer.gov/cancertopics/pdq/treatment/breast/Patient/page2
Statistics & Risk Factors
Statistics

- 1 in 8 women in the US will have invasive breast cancer during their lifetime

- 2nd leading cause of death from cancer in women
  - But death rates from BC have been declining. Why?
    - Earlier detection, increased awareness, improved treatment.

- Incidence dropped 7% between 2002 and 2003
  - Why?
    - ↓ hormone replacement therapy (HRT) for menopause, published by Women’s Health Initiative in 2002
BRCA1 & BRCA2

- 5–10% cases attributed to genetics
  - Younger women
  - Eastern European Jewish descent
- Mutated BRCA1
  - 5–6x the risk on average
- Mutated BRCA2
  - 4–5x the risk
- Angelina Jolie underwent preventative double mastectomy (BRCA1)

The American Cancer Society, www.cancer.org
## Risk Factors (+)

### Modifiable
- **Parity, etc.**
  - No children or first child after age 30
  - Not breastfeeding
- **Hormones**
  - Oral contraceptives
  - HRT
- **Lifestyle**
  - EtOH use
  - Overweight/obese
  - Sedentary
  - ??? Diet
  - ??? Vitamins
  - ??? Tobacco
  - ??? Shift work

### Non-Modifiable
- **Female**
- **Age 55+**
- Mutated BRCA1 or BRCA2 genes
- Family history
- PMH of breast cancer
- Caucasian, African–American
- Early menstruation/late menopause
- XRT
- **Diethylstilbestrol (DES)**
  - 1940s–1960s to ↓ miscarriages

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The American Cancer Society, [www.cancer.org](http://www.cancer.org), Borugian et al 2013
Estrogen
Estrogen-Induced Proliferation of Existing Mutant Cells

Estrogen stimulation

Mutant breast cells (caused by error, inheritance, and/or environmental factors)

Artwork by Jeanne Kelly © 2010.
Estrogens – Good & Bad

- Estrogen = hormone family
- Estrone & Estradiol metabolized by liver into estrogen
  - Good estrogen (2-hydroxyestrone)
  - Bad estrogen (16-alpha-hydroxyestrone)
- So what?
- \(\rightarrow\) Bad estrogen
  - Cell initiation & promotion (proliferation)
Estrogen Metabolite Ratio

- **Low ratio = increased BC risk**
  - Sedentary lifestyle, heritage, obesity, high fat diet, HPV, tobacco smoke exposure, omega-6 fatty acids

- **High ratio = decreased BC risk**
  - Exercise, more LBM, low BMI, cruciferous vegetables, omega-3 fatty acids

- May be falling out of use; current literature does not support significant associations versus original theory in 1980s
Estrogen & Breast Cancer

- **Hormone Receptor Positive BC**
  - Tumor has receptors for the hormone; grows in response (proliferation)
  - 75% estrogen receptor (ER) positive
  - 60% likely to respond to hormone therapy
    - Can prevent recurrence by blocking hormone effect
  - Some trends in research showing different dietary response to ER+ versus ER− breast cancer
Critical Thinking

- How is breast cancer detected?
  - Mammography, clinical breast exams…
  - In general, access to healthcare.

- How would this affect incidence and mortality rates?
  - ↓ early detection in lower SES groups d/t limited access to healthcare
  - ↑ mortality related to breast cancer in these populations

- How does this link to possible risk factors such as obesity?
  - Lower SES groups tend to have poorer diets, are overweight/obese, and lead more sedentary lifestyles
Diet and Breast Cancer

DIETARY PATTERN
NUTRIENTS
WEIGHT
Diet and Breast Cancer Risk

Overall diet quality versus specific nutrient intake

Diet

Breast Cancer

Fat

Calories

Weight

Meat

Vitamins

Fruits & Veg

???
Dietary Patterns
Adapted Mediterranean dietary pattern associated with ↓ risk of breast cancer in European women. (p = 0.048)
Women’s Healthy Eating and Living (WHEL)

- **Rationale**: Lack of evidence that a dietary pattern high in vegetables, fruit and low in fat can influence breast cancer recurrence or survival

- **Design**: randomized controlled multicenter trial

- **Population**: 3088 women previously treated for early stage breast cancer
  - Enrollment 1995 through 2000
  - Follow up through June 2006

Pierce et al 2007
WHEL Study

Randomized

3,008 women previously treated for breast cancer

Treatment
Telephone counseling
Cooking classes
Newsletters promoting:
5 servings vegetables
+ 16 oz veg. juice
3 fruit servings
15-20% energy from fat
30 g fiber

Control
Print materials for “5-A-Day”
dietary guidelines

Pierce et al 2007
WHEL Results

• No significant changes in body weight
• Over 4 years, intervention group maintained significant differences in veg and fruit servings, fiber and fat intake
  o Validated F&V consumption by blood carotenoid levels
  o Recurrence: 16.7% vs 16.9% control
  o Death: 10.1% vs 10.3% control

Conclusion
No significant reduction in additional breast cancer events or mortality with this dietary pattern

Pierce et al 2007
Nutrients
MVI + Antioxidants

- Multivitamins
  - Contrasting evidence based on sample population
    - Previous BC diagnosis – lower mortality risk & recurrence
    - Epidemiological incidence – no effect
      - Confounding factors?

- Antioxidants
  - 18% lower mortality risk, 22% lower recurrence

Concern for negative interaction of vitamins and minerals, esp. antioxidants, with radiation and chemotherapy

Nechuta 2011, Neuhouser 2009
Women’s Health Initiative Dietary Modification Trial

48,835 healthy postmenopausal women, no prior history of breast cancer

Treatment
Reduced dietary fat

Reduced fat intake*
Modest weight loss
Fewer incidences of breast cancer

8 years

Control
No dietary intervention

Randomized

Prentice et al 2006
Women’s Intervention Nutrition Study (WINS)

- **Design:** randomized, prospective multicenter clinical trial

- **Population:** (n=2437) Women with early stage breast cancer, s/p resection & conventional therapy

- **Intervention:** dietary reduction in fat intake vs no dietary intervention (control)
  - Followed from 1994 to 2001

Chlebowksi et al 2006
WINS Results

- Intervention group: > 6 lb lower avg BW vs control group
- 9.85% relapse vs 12.4% in control group

Dietary effect on hormonal receptor status?
- Estrogen positive vs. estrogen negative BC

Chlebowski et al 2006

- ER+ influenced by estrogen
- ER- mediated by non-estrogen factors
  - factors that may be influenced by weight, diet
WINS Results

Conclusion

“A lifestyle intervention of reducing dietary fat intake with modest influence on body weight may improve relapse-free survival of breast cancer patients receiving conventional cancer management.”

Chlebowski et al 2006
Weight/BMI vs. dietary?

<table>
<thead>
<tr>
<th>Variable</th>
<th>Relapse events/total N</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dietary intervention</td>
</tr>
<tr>
<td>BMI†</td>
<td></td>
</tr>
<tr>
<td>&lt;25</td>
<td>8.9%</td>
</tr>
<tr>
<td>25–30</td>
<td>10%</td>
</tr>
<tr>
<td>&gt;30</td>
<td>11%</td>
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</tbody>
</table>

Study did not discuss effect of BMI on % relapse by intervention group  
(2006)
2013 Commentary from WINS PI

- Addressed the difficulty of separating dietary effects from the influence of body weight

- Lifestyle factor most strongly & consistently associated with ↓ risk is **physical activity**
  - Where risk = incidence and recurrence in early stage breast cancer
Vitamin D

- ↑ vit D intake/serum levels assoc. with ↓ BC incidence and recurrence

- Confounding variables?
  - Lower BW and higher physical activity levels associated with ↓ BC risk and ↑ vit D levels

- Women’s Health Initiative – RCT
  - Vitamin D + Calcium vs. placebo
    - Similar incidence of BC
    - No association when controlled for weight and activity levels

- Insufficient evidence to recommend vit D supplementation to ↓ BC risk

Weight
Weight & Breast Cancer Risk

- Obesity affects survival of women diagnosed with breast cancer
- Physical activity after diagnosis associated with decreased all-cause and cancer related mortality

Protani et al 2010
Mechanism

- No evidence for causal mechanism of weight gain/obesity & increased breast cancer risk
  - No evidence that weight loss in those who are OW/OB after diagnosis improves survival (vs. weight loss after remission)

- Modifying factors:
  - Diabetes
  - Chemotherapy
  - Underdosing medication d/t weight
  > Do they change the obesity effect?

Protani et al 2010
Weight & Breast Cancer

Breast Cancer Diagnosis

Obese woman

Remission

Recurrence

Exercise

Lose weight
Samantha is 65 years old and just diagnosed with breast cancer. Her treatment plan includes intensive chemotherapy.

She is 5’6” and weighs 200 pounds.

- What is her BMI?
  - BMI: 32
- Would you encourage her to lose weight? Why or why not?
  - Additional burden, lack of evidence.
Mechanism

- Insulin, insulin growth factor binding protein 1 (IGFBP1), sex steroids
  - Associated with adiposity
  - Influence tumor initiation and progression?

- IGFBP1 binds insulin growth factor 1 (IGF1)
  - IGF1 potentiates anabolic effects (important for growth in childhood) and can regulate cell growth and development and DNA synthesis
  - Levels affected by BMI, estrogen status, nutrition and exercise status, age
  - Increased IGF1 -> ? increased growth of existing cancers

Insulin resistance and hyperinsulinemia associated with ↑ breast cancer risk

- Concern over data evidence because many researchers have not controlled adequately for adiposity
  - BMI, waist–hip ratio, % body fat

- Borugian et al 2013 found inverse association between fasting insulin levels and breast density, direct association between IGFBP1 and breast density
  - Lost significance after adjusted for adiposity

Borugian et al 2013
Roles for the Nutrition Professional

- ‘CURE-ALL DIETS”
- SUPPLEMENTS
- JOBS
“Cure-All” Diets
“Cure–All” Diets

- Alternative diets that claim to cure cancer
- Similar to fad diets
  - Limited food choices
  - Special supplements/injections
  - Fasting
  - Enemas

Which Would You Prefer?
“Cure–All Diets” for BC

Gerson Therapy
Low-salt, low-fat, vegetarian diet, juice from ~20# fresh produce per day, coffee enemas

Kelly & Gonzalez Tx
150 daily supplements, laxatives or coffee enemas, fasting, exercising, chiropractic adjustments

Livingston-Wheeler Therapy
Vaccines, abx, digestive enzymes, MVI+M, enemas, vegetarian

Nutrition Implications?
• Dehydration
• Malnutrition
• Trauma to anus and rectum
Betty comes to see you at your nutrition counseling center. Last week, she was diagnosed with breast cancer. She is excited as she tells you she has bought some new supplements to take when she begins XRT and chemotherapy next month. This is what she shows you –>

What do you say?
Roles for Nutrition Professionals

- Research
  - Nutritional genomics
- Clinical practice
- Counseling practice
Future Research

- Weight and breast cancer risk
  - ? Mechanism
Take Home Messages

- There are a number of confounding factors that influence the relationship between diet, weight, and breast cancer.
- Large randomized control trials have yet to demonstrate significant reductions in breast cancer risk related to dietary pattern and intake of fat.
- Excessive supplement use by breast cancer patients may negatively interact with conventional treatments.
- Nutrition professionals have the opportunity to work with breast cancer patients regarding supplement use and fad diets.
References


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Thank you!