Obesity and Cancer Survivorship

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Objectives

• Describe the relationship between obesity, weight gain and cancer risk and survival
• Better understand the biological and psychosocial influences contributing to obesity
• Efforts for multidisciplinary cancer survivorship care to reduce the burden of obesity in cancer survivors
Obesity Trends* Among U.S. Adults
BRFSS, 1990, 2000, 2010
(*BMI ≥30, or about 30 lbs. overweight for 5’4” person)
Obesity Among Adults, by Black/White Race or Hispanic Ethnicity and Sex, United States, 2006–2008

Percentage

23.7%  25.4%  35.7%  39.2%  28.7%  27.8%  29.4%

White, non-Hispanic  Black, non-Hispanic  Hispanic

Both Sexes  Men  Women
Factors Associated with Obesity

• Independent of prior cancer diagnosis:
  • Age
  • Race/ethnicity
  • SES
  • Food and activity environment
  • Stress and eating response*
Stress and Obesity

Stress

CRH

ACTH

GH

IGF-1

Cortisol

VISCERAL OBESITY

INSULIN RESISTANCE
DYSPLIPIDEMIA
ATHEROSCLEROSIS
HYPERTENSION

CRP
FIBRINOGEN

IL-6
TNF-α

LH/FSH
SEX STEROIDS
# Obesity Defined: Is BMI Enough?

<table>
<thead>
<tr>
<th>Height (inches)</th>
<th>Weight (pounds)</th>
</tr>
</thead>
<tbody>
<tr>
<td>60</td>
<td>23 25 27 29 31 33 35</td>
</tr>
<tr>
<td>62</td>
<td>22 24 26 27 29 31 33 35</td>
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<td>64</td>
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<td>76</td>
<td>15 16 17 18 20 21 22 23</td>
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![Image of BMI chart]
Metabolic State and Body Shape

**Metabolically Healthy Obese (Pear)**
- High BMI
- Low Visceral Fat
- No Ectopic Fat
- Leptin Sensitivity
- Insulin Sensitivity
- Normal (Low) FFAs
- Normal Glucose Tolerance
- High HDL/LDL Ratio
- Low Triglycerides
- High Adiponectin Secretion
- Normal Adipokine Secretion
- No Inflammation

**“At Risk” Obese (Apple)**
- High BMI
- High Visceral Fat
- Significant Ectopic Fat
- Leptin Resistance
- Insulin Resistance
- Elevated FFAs
- Glucose Intolerance
- Low HDL/LDL Ratio
- High Triglycerides
- Low Adiponectin Secretion
- High Adipokine Secretion
- Significant Inflammation
Body Fat and Insulin Resistance
Adipocyte stromal cells have high angiogenic potential and as such may contribute to cancer progression
### Obesity-Associated Biomarkers of Cancer Risk and Recurrence

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Role</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin</td>
<td>Growth-promotion/ cell division, anti-apoptotic</td>
</tr>
<tr>
<td>IGF-1 and IGF-BP-1</td>
<td>Increased cell migration, prolonged elevated insulin, potentiates growth factors</td>
</tr>
<tr>
<td>C-reactive protein (CRP)</td>
<td>Inflammation, may correlate with estradiol</td>
</tr>
<tr>
<td>Interleukin 6</td>
<td>Inflammation, growth and differentiation of malignant cells</td>
</tr>
<tr>
<td>Tumor necrosis factor alpha</td>
<td>Inflammation, associated with insulin resistance</td>
</tr>
<tr>
<td>Serum amyloid A (SAA)</td>
<td>Low-grade chronic inflammation; associated with reduced survival in breast cancer</td>
</tr>
</tbody>
</table>
Medical Complications of Obesity

- Pulmonary disease
  - abnormal function
  - obstructive sleep apnea
  - hypoventilation syndrome

- Nonalcoholic fatty liver disease
  - steatosis
  - steatohepatitis
  - cirrhosis

- Gallbladder disease

- Gynecologic abnormalities
  - abnormal menses
  - infertility
  - polycystic ovarian syndrome

- Osteoarthritis

- Diabetics
- Dyslipidemia
- Hypertension
- Severe pancreatitis

- Cancer
  - breast, uterus, cervix
  - colon, esophagus, pancreas
  - kidney, prostate

- Phlebitis
  - venous stasis

Slide source: www.obesityonline.org
Psychological Effects of Obesity

- Eating dysregulation: Craving cycle
- Increase in stress
  - Body image
  - Mobility
- Depression
- Fatigue
- Overall effects on quality of life
Obesity is associated with risk for several cancers:

- Post-menopausal breast
- Endometrial/uterine
- Pancreatic
- Colorectal
- Ovarian
- Gallbladder
- Esophageal
Obesity and Cancer Survival

• In the survival setting associations are less consistent
  • Treatment efficacy; treatments employed; Recalcitrant disease
• Most studies in breast cancer
• Weight gain during therapy in those with normal BMI – greater risk?
• Metabolic co-morbidities are highly relevant

Parekh, Chandran and Bandera, 2012
Survival Varies by Race and Obesity
Combined influence of race and obesity on cancer survivorship.


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Cancer Therapies:
Surgery, Radiation, Chemotherapy, Hormone suppression

- Loss of lean mass
- Increased adiposity
- Inflammatory and/or abnormal metabolic response
- Fatigue, and/or reduced mobility

Interventions
- Diet
- Physical activity
- Sleep hygiene
- Anti-inflammatory drugs
- Weight control
Evidence?

- Limited intervention studies; most in breast cancer survivors
- Survivors report change in diet; trials suggest that behaviors can be modified after diagnosis
- Few assessed cancer endpoints; most evaluate intermediate biomarkers of disease risk
Low CHO versus Low Fat Weight Loss Diets

- 50 overweight breast cancer survivors on tamoxifen or aromatase inhibitors
- Randomized, 2-arm trial
- Face-to-face counseling with a dietitian weekly x 4 weeks, then monthly for 5 months
- Baseline, 3 and 6 month measures of:
  - Anthropometrics, body composition
  - Metabolic indices
  - Inflammation (CRP, IL-6)

Percent of Breast Cancer Survivors with Metabolic Syndrome Before and After Weight Loss

Metabolic Syndrome Diagnosis by NCEP ATPIII Criteria (w/ glucose >100mg/dl)

- Baseline: 52%
- 24 weeks: 28%

Thomson CA, J Women’s Health, 2009
Obesity-associated Co-Morbidities may Influence Cancer Survival

- **Women’s Healthy Eating and Living Study**
  - 3055 women treated for breast cancer
- **Diabetes** was associated with a 2-fold greater risk for breast cancer event and 2.5-fold higher risk for mortality
- **Combined co-morbidities:** CVD, HTN, DM increased mortality risk 2-fold
- **Recent analysis** in 636 ovarian cancer survivors showed DM increased mortality 84%
Weight Control Studies in the Survivor Population

African American Women’s study improved QOL

- Primary outcomes:
  - Chronic and late effects
  - Weight change
  - Improved function
  - Quality of Life
  - Reduced metabolic abnormalities

Lombardi study in African American Women: Sheppard and Adams-Campbell

http://www.youtube.com/watch?v=_I9xoqAUE-I&feature=player_embedded
ENERGY Trial

• Weight loss in breast cancer survivors (N=693)
• Daily activity, eating behaviors
• Outcome: breast cancer recurrence and disease-free survival
• Pilot data: 220 women demonstrated ≥5% weight loss decreased leptin, insulin, estrone, estradiol

ENERGY Trial

Summary: Interventions for Weight Control Post-Diagnosis

• No evidence of survival benefit demonstrated to date
  • Trials underway: ENERGY, LEAN, etc
• Weight loss diets will “correct” metabolic and inflammatory abnormalities
  • Trials with: RD counseling, Weight Watchers, Curves, etc
  • May reduce risk co-morbidities associated with poorer prognosis
• Diet-induced weight loss reduces lean mass and bone;
  • Physical activity, including strength training, should be considered in weight loss plans
  • Must address whole person
Where are we on Advice?

- ACS Guidelines, 2011
  - Promote weight control
  - Plant-rich diet
  - Physical activity > 30 minutes daily
  - Limit alcohol
  - Avoid energy-dense foods; sweetened beverages
- Lifestyle modification counseling and support
- Tailored to individual patient, prognosis and time-course of disease

Robien, Demark-Wahnefried and Rock, JAND, 2011
The Anti-inflammatory Mediterranean Diet

- **Healthy Sweets**: (such as plain dark chocolate) Sparingly
- **Red Wine**: (optional) No more than 1-2 glasses a day
- **Supplements**: Daily
- **Tea**: (white, green, oolong) 2-4 cups a day
- **Healthy Herbs & Spices**: (such as garlic, ginger, turmeric, cinnamon) Unlimited amounts

**Other Sources of Protein**: (high quality natural cheeses and yogurt, omega-3 enriched eggs, skinless poultry, lean meats) 1-2 a week

- **Whole Soy Foods**: (edamame, soy nuts, soymilk, tofu, tempeh) 1-2 a day
- **Fish & Seafood**: (wild Alaskan salmon, Alaskan black cod, sardinos) 2-6 a week
- **Healthy Fats**: (extra virgin olive oil, expeller-pressed canola oil, nuts - especially walnuts, avocados, seeds - including hemp seeds and freshly ground flaxseeds) 5-7 a day

- **Whole & Cracked Grains**: 3-5 a day
- **Pasta (al dente)**: 2-3 a week
- **Beans & Legumes**: 1-2 a day

- **Vegetables**: (both raw and cooked, from all parts of the color spectrum, organic when possible) 4-5 a day minimum
- **Fruits**: (fresh in season or frozen, organic when possible) 3-4 a day
Limited Evidence, but Biological Support Low Glycemic Diet

**Low Glycemic Index**
- Lentils
- Black beans
- Cashews
- Sweet potato
- Macaroni

**Moderate Glycemic Index**
- Brown rice
- Quick oats
- Bran muffin
- Pineapple
- Raisins
- Apricots

**High Glycemic Index**
- White Bread
- Baked potato
- Corn Flakes
- Watermelon
Exercise and Movement

- Yoga
- Tai Chi
- Walking
Mind-body Stress Reduction

- Mindfulness
- Meditation
- Breathing
Restorative Sleep
Lifestyle Behavioral Change
Resources:
Diet, Obesity and Cancer

- Academy of Nutrition and Dietetics – Oncology Dietetics Practice group: [www.oncologynutrition.org](http://www.oncologynutrition.org)

- American Cancer Society Guide: [www.cancer.org](http://www.cancer.org)

- American Institute for Cancer research: [www.AICR.org](http://www.AICR.org)


- Marian M and Roberts S. Clinical Nutrition for Oncology Patients, Jones & Bartlett, 2010

- The University of Arizona College of Nursing’s Community Cancer Connections Projects @ [www.linkin.nursing.arizona.edu](http://www.linkin.nursing.arizona.edu)
Questions???????????