Obesity and Cancer

Jessica Folek, MD
Disclosure:

I have no actual or potential conflict of interest related to this program/presentation.
Objectives

- Examine increased incidence of cancers in the obese
- Discuss molecular mechanisms implicated in increased cancer risk of obese patients
- Discuss American Cancer Society Guidelines on nutrition and physical activity for cancer prevention
- Examine if decreasing BMI can decrease cancer risk.
Obesity Epidemic

- One out of every three adults and one in 6 children are obese.
- Obesity contributes to increased costs, ~150 billion dollars per year - approaching 10% national medical budget
- Disease has reached epidemic proportions and is a major cause of morbidity
- Greater percentage of all surgical patients, not solely bariatric, are obese
Well known finding:

Higher BMI $\rightarrow$ Higher Cancer Risk
Increased body fat associated w/increased cancer risk for:

- Colon
- Esophageal
- Postmenopausal Breast
- Endometrial
- Kidney
- Possibly Gallbladder

BMI and Cancer risk Association

- ~282,000 incident cases examined from 221 data sets (141 articles)
- 5 kg/m2 increase in BMI associated with increase in following cancers:

In men: strongly associated with:
  - Esophageal adenoca (RR 1.52, p<0.0001)
  - Thyroid (1.33, p=0.02),
  - Colon (1.24, p<0.0001), and
  - Renal (1.24, p <0.0001) cancers.
BMI and Cancer risk Association

In women, strong associations between a 5 kg/m^2 increase in BMI and:

- Endometrial (1·59, p<0.0001),
- Gallbladder (1·59, p=0.04),
- Esophageal adenocarcinoma (1·51, p<0·0001),
- Renal (1·34, p<0.0001) cancers.

Primary mechanisms:

- Growth factors
- Inflammation
- Adipocytes
- Energy metabolism
Growth Factors

- Insulin, IGF-1
- Steroids
- Adipokines - leptin
- Inflammatory cytokines
Mechanism Growth factor

- Hyperinsulinemia – secondary to insulin resistance
- Hyperinsulinemia -- increased IGF production
- Estrogen- Increased production in secondary to aromatase expression in fatty tissue
Inflammation:

- TNF alpha, IL-6
- C reactive protein
- Adipokines, leptin
Obesity Cancer mechanism-hypothesis:

- Anabolic state & chronic inflammation increase carcinogenesis.
American Cancer Society Guidelines : Nutrition and physical activity for Cancer prevention

“About 2 out of 3 Americans are overweight or obese. Many Americans are also less physically active than they should be. Obesity increases the risk of many types of cancers......

...While it is not clear exactly how excess body fat, consuming too many calories, and lack of physical activity raise cancer risk, there is no question that they are linked to an increased risk of many types of cancer and that they are a serious and growing health problem.”

Achieve and maintain a healthy weight throughout life

- Be as lean as possible throughout life without being underweight.

- Avoid excess weight gain at all ages. For those who are overweight or obese, losing even a small amount of weight has health benefits and is a good place to start.

- Get regular physical activity and limit intake of high-calorie foods and drinks as keys to help maintain a healthy weight.
Be Physically Active

- Adults should get 150 min of moderate intensity or 75 min of vigorous intensity activity each week (or a combination), preferably spread throughout the week.

- Children and teens should get at least 1 hour of moderate or vigorous intensity activity each day, with vigorous activity on at least 3 days each week.
Be Physically Active

- Limit sedentary behavior such as sitting, lying down, watching TV, and other forms of screen-based entertainment.

- Doing some physical activity above usual activities, no matter what one’s level of activity, can have many health benefits.
Does decreasing BMI decrease cancer risk?

Patients participating in bariatric surgery have significant and sustained weight loss- representing a unique group to explore long-term voluntary weight loss on cancer.

National Institutes of Health (NHLBI). Obesity Research 1998;6:51S: 151
Studies looking at Bariatric Surgery and Cancer

- **Sjostrom L, et al Lancet Oncol 2009:**
  - Prospective controlled intervention study
  - Compare weight loss to cancer incidence

- 2010 bariatric surgery pts; 2037 matched obese controls

- First-time Ca: 117 surgery group, 169 control (p=.0009)

- Women: 79 surgery; 138 control (p= .0001)

- Men: 38 surgery; 39 control (p=.90)
Adams, T et al. *Obesity* 2009; 17:796-802

- Utah Cancer registry: 6956 pts s/p gastric bypass (1984-2002);
- 9,442 morbidly obese persons who applied for Utah driver’s license
- Outcomes- incidence, mortality of cancer by site and stage at dx of RYGB pts vs controls (mean f/u 12.5y)
- Total cancer incidence significantly lower in surgery group vs control (p=.0006)
- Cancer mortality 46% lower in surgery group vs control (p=.001)
Non-surgical interventions

Increasing physical activity results in 40-60% increased survival in breast and prostate cancer


<table>
<thead>
<tr>
<th>Type of study/Author (ref)</th>
<th>Cancer site</th>
<th>Population studied</th>
<th>Body weight loss</th>
<th>Cancer risk reduction (%)</th>
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</thead>
<tbody>
<tr>
<td><strong>Cohort studies</strong></td>
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<tr>
<td>Parker [4]</td>
<td>All sites</td>
<td>Post-menopausal Iowa women</td>
<td>≥16.4%*</td>
<td>11</td>
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<tr>
<td>Harvie [6]</td>
<td>Breast</td>
<td>Post-menopausal Iowa women</td>
<td>≥5%</td>
<td>64§</td>
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<td><strong>Bariatric surgery studies</strong></td>
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<tr>
<td>Sjöström [7]</td>
<td>All sites</td>
<td>Women</td>
<td>31.9%</td>
<td>42</td>
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<tr>
<td></td>
<td></td>
<td>Men</td>
<td>19.3%</td>
<td>3</td>
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<tr>
<td>Adams [8]</td>
<td>All sites</td>
<td>Women</td>
<td>31.1%</td>
<td>24</td>
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<td>Men</td>
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<td>2</td>
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<tr>
<td>Christou [9]</td>
<td>All sites</td>
<td>Men and women</td>
<td>31.9%§</td>
<td>78</td>
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<tr>
<td><strong>Dietary RCTs</strong></td>
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<tr>
<td>Pierce [10]</td>
<td>Breast†‖</td>
<td>Women</td>
<td>0.5% group difference</td>
<td>4</td>
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<tr>
<td>Chlebowski [12]</td>
<td>Breast†‖</td>
<td>Women</td>
<td>3.7% group difference</td>
<td>24</td>
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</table>

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<thead>
<tr>
<th>Hormonal Biomarker</th>
<th>Author (ref)</th>
<th>Study design</th>
<th>Population studied</th>
<th>N</th>
<th>% body weight loss</th>
<th>% change in biomarker</th>
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<tbody>
<tr>
<td>Oestradiol</td>
<td>Tchernof [15]</td>
<td>Pre–post</td>
<td>Post-menopausal women</td>
<td>61</td>
<td>15.6%</td>
<td>30% reduction</td>
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<td></td>
<td>Kaaks [16]</td>
<td>RCT of diet</td>
<td>Post-menopausal women</td>
<td>50</td>
<td>6.0%</td>
<td>18.3% reduction</td>
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<td></td>
<td>49</td>
<td>0.8%</td>
<td>6.4% reduction</td>
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<tr>
<td>Sex Hormone Binding Globulin</td>
<td>Kopp [17]</td>
<td>Pre–post</td>
<td>Premenopausal women</td>
<td>43</td>
<td>33.0%</td>
<td>312% increase</td>
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<td>Mingrone [18]</td>
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<td>RCT of diet or biliopancreatic diversion (BPD)</td>
<td>Women^</td>
<td>31</td>
<td>BPD: 28.0%</td>
<td>144% increase</td>
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<td></td>
<td>21</td>
<td>Diet: 5.9%</td>
<td>24.9% increase</td>
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<td>Harvie [19]</td>
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<td>RCT of Intermittent energy restriction (IER)</td>
<td>Premenopausal women</td>
<td>53</td>
<td>IED: 7.0%</td>
<td>13.9% increase</td>
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<td>versus Continuous energy restriction (CER)</td>
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<td>54</td>
<td>CER: 5.3%</td>
<td>6.2% increase</td>
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<td>Atkin [20]</td>
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<td>Pre–post</td>
<td>Premenopausal women</td>
<td>64</td>
<td>7.0%</td>
<td>16.7% increase</td>
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<tr>
<td>Kaaks [16]</td>
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<td>RCT of diet</td>
<td>Post-menopausal women</td>
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<td>25.2% increase</td>
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Conclusion

- Clear established link between obesity and several common cancers
- Insulin and IGF-1 axis, sex steroids, and adipokines, insulin resistance important mechanism but only part of the story.
- National guidelines recommending weight loss for cancer prevention supported by the literature but more studies are needed.
References


Thank you!