Obesity, the Obesity Paradox and Cancer Disparities

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Disclosers: No conflict

- Research support/grants:
  - Spatz medical
  - The Ohio State University Comprehensive Cancer Center

- Stock/Equity: None
- Consulting: None
Today's agenda:

A. Colorectal cancer (CRC): A bird eye view
B. The risk of CRC, Obesity and racial disparity
C. CRC outcomes: The obesity paradox and disparity

A. Colorectal cancer (CRC): A bird eye view
Colorectal cancer: The history


2017: U.S. cancer estimates

<table>
<thead>
<tr>
<th>Estimated New Cases</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>162,360</td>
<td>30%</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>136,690</td>
<td>14%</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>71,120</td>
<td>8%</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>60,490</td>
<td>7%</td>
</tr>
<tr>
<td>Melanoma of the skin</td>
<td>52,170</td>
<td>6%</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>46,650</td>
<td>5%</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>40,080</td>
<td>5%</td>
</tr>
<tr>
<td>Leukemia</td>
<td>36,290</td>
<td>4%</td>
</tr>
<tr>
<td>Oral cavity &amp; pharynx</td>
<td>33,720</td>
<td>4%</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>25,200</td>
<td>3%</td>
</tr>
<tr>
<td>All sites</td>
<td>836,150</td>
<td>100%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Estimated New Cases</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>252,720</td>
<td>30%</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>105,510</td>
<td>12%</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>64,200</td>
<td>3%</td>
</tr>
<tr>
<td>Urinary corpus</td>
<td>61,580</td>
<td>4%</td>
</tr>
<tr>
<td>Thyroid</td>
<td>42,470</td>
<td>5%</td>
</tr>
<tr>
<td>Melanoma of the skin</td>
<td>34,940</td>
<td>4%</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>32,160</td>
<td>4%</td>
</tr>
<tr>
<td>Leukemia</td>
<td>25,840</td>
<td>3%</td>
</tr>
<tr>
<td>Pancreas</td>
<td>23,700</td>
<td>3%</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>23,300</td>
<td>3%</td>
</tr>
<tr>
<td>All sites</td>
<td>852,630</td>
<td>100%</td>
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</table>

American cancer society 2017
U.S. CRC incidence trends by race/ethnicity: Females

CDC, accessed on 2/28/18

U.S. CRC incidence trends by race/ethnicity: Males

CDC, accessed on 2/28/18
Global CRC estimates


The U.S.: CRC incidence trends among young adults, 1992 to 2005

Predicted recto-sigmoid CRC incidence rate in 2030 by age compared to in 2010

Summary: Colorectal cancer risk

- Higher in 2017 compared to the distant past
- Higher risk in industrialized countries and NHB
- Increasing in patients < 50 y/o
Risk factors for colorectal cancer

- Alcohol, Tobacco
- Red and processed meet
- High fat diet
- Obesity

Can obesity explain the increased CRC risk and the racial disparity?
Obesity, CRC risk, and racial disparity

Global prevalence of obesity 2016
The U.S: Increasing prevalence of Obesity

Obesity is one of the strongest risk factors for CRC especially in men

5 units increase in BMI is associated with:
+ 20% increase in risk of colorectal adenomas
+ Increased CRC risk: 30% men, 12% women

Mechanism:
1. Increased Insulin resistance and IGF-1
2. Low grade inflammation
3. Increased Leptin: Adiponectin ratio

Ben, O; Gastroenterology. 2012 Apr;142(4):762-72
Obesity and CRC: Review of mechanisms

Zappia et al. Advances in nutrition and cancer 2014

The incidence of obesity-related cancer: 2005-2014 is increasing

CRC risk factors trend in young adults, 1999 to 2008


Obesity is higher in NHB and Hispanics

The metabolic influence of obesity is similar regardless of race/ethnicity

BMI is associated with IGF1 levels similarly in all race/ethnicity
Non-hispanic black have higher IGF-1 levels compared to white women
The higher CRC risk in NHB no significant after adjustment for IGF-1

Jung SY. Menopause. 2017 Mar;24(3):288-298
Fowke JH. Endocr Relat Cancer. 2010 Jan 29;17(1):51-60

Racial disparity and risk of CRC: Relation to diet of obese individuals

Obese non-hispanic black report eating less fruits/vegetables and more fast food
Western diet x 2 weeks to Native Africans: Increases in colonic biomarkers and microbiome associated with CRC
BMI and Health behaviors combined account for 43.9% of the association of education 36.2% of the association of neighborhood SES with risk of CRC.

Summary: Obesity

- Strongest risk factor for CRC
- Rising in the U.S. and worldwide, especially north America
- Rising in patients less than 50 years of age
- Higher in Hispanic and NHB
- Potentially responsible for the rising risk of CRC in industrialized countries and patients less than 50
- Partly responsible for the racial disparity in CRC

CRC outcomes: The obesity paradox and disparity
CRC peri-operative mortality and obesity

- Morbid obesity is higher in NHB compared to Hispanic and NHW.
- After adjustment for race/other confounders MO is associated with 80% higher CRC mortality risk
- Trend towards improved CRC mortality in mild-moderate obesity
- Improved CRC mortality after bariatric surgery irrespective of race


CRC long term mortality and obesity

- Pre- CRC diagnosis BMI > 30 is associated with 50% increased risk of mortality.
- Post-CRC diagnosis obesity was not associated with increased mortality
- CRC survivors have improved insulin resistance, likely due to significant weight loss in the peri-CRC period

Obi, Hussan et al. Current Problems in Cancer
Campbell PT, J Clin Oncol. 2012 Jan 1;30(1):42-52
CRC outcomes and the obesity paradox

- Association between BMI and CRC survival is U- or J-shaped
- Most favorable outcomes in overweight or class I obesity
- Possible relationship to fat distribution: Subcutaneous vs. visceral fat

Campbell PT, J Clin Oncol. 2012 Jan 1;30(1):42-52

Summary: CRC outcomes

- Increased CRC mortality in morbidly obese patients
- Mortality is not increased in mild obesity or in patients with obesity after diagnosis
- Obesity can partially explain racial disparity when it comes to mortality
THANK YOU!

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