Body Weight and Cancer: Prevention, Treatment and Survivorship

Lawrence Wagman, M.D.
Changing Paradigm

• Sixty is the new forty
• Sitting is the new smoking
• Excess Calories are the new tobacco
Types of Prevention

• Primary
• Secondary
• Tertiary
• Surveillance (monitoring for cancer recurrence)
Primary Prevention

• True prevention-disease never occurs
• Pre-pathogenesis of tissue change
• Reduce risk factors
• Prophylactic mastectomy
• Lifestyle
Secondary Prevention

• No symptoms
• Tissue changes show pathogenesis
• Pre-clinical stage
• Improve clinical outcomes with early diagnosis
Tertiary Prevention

• Limit disability
• Delay/prevent further progression of disease
• Tissue changes show resolution or sequelae of disease
Etiology of Cancer in the US: 1.5 million

- Tobacco: 30%
- Alcohol
- Overweight
- Physical Inactivity
- Diet
- Environment
- Medication
- Infection
- Sun & radiation
- Reproductive factors
- Family history

975,000 could have been avoided!
How do we measure obesity?

Body mass index (BMI)

• Formula of weight and height

• $\frac{W}{H^2}$: kg/m$^2$
**Body mass index (BMI)**

- Formula of weight and height
- \( \left( \frac{W}{H^2}; \text{kg/m}^2 \right) \)

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<th>Weight Categories</th>
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# Categorizing Body Weight

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Obesity Trends* Among U.S. Adults
BRFSS, 1990, 2000, 2010

*BMI ≥30, or about 30 lbs. overweight for 5'4" person

www.cdc.gov/obesity/data/adult.html#History
Obesity related cancers

• Prostate
• Liver (1.24 increase for every 5 kg/m2)
• Thyroid (1.33 per BMI increase by 1)
• Breast
• Endometrial
• Ovarian
• Esophagus (1.52)
• Colon (1.24)
• Acute lymphocytic leukemia
How does Obesity Increase Cancer Occurrence and outcome?

• Changes body’s hormonal environment
• Causes direct damage
• Dampens immunologic surveillance
• Interacts with treatment directly and via co-morbidities
Breast Cancer
Breast Cancer Model

- Excess body weight (obesity)
- Type II diabetes mellitus

Insulin resistance

Metabolic syndrome
- Increased adiposity
- Glucose intolerance
- Hypertension
- Dyslipidemia

Insulin-sex hormone axis
- Peripheral aromatase activity
- Estrogen bio-availability
- SHBG production
- Ovarian androgen

Insulin-IGF Axis

Hyperinsulinemia
- Adiponectin
- IGFBP-1
- IGFBP-2
- Bio-availability of IGF-1
- Free IGF-1

Target cell
- Cell proliferation
- Apoptosis

•(IGF, insulin-like growth factor; IGFBP, insulin-like growth factor–binding protein; SHBG, sex hormone–binding globulin.)
Breast Cancer and Obesity: Interaction with Treatment

• Physical
  – Harder to find the veins to give the chemotherapy
  – Radiation effects on the skin are exaggerated
Breast Cancer and Obesity: Interaction with Treatment

- Physiologic
  - Many drugs are calculated on “lean body mass” or “body surface area”
  - Drug distribution: large adipose area for the “fat soluable” agents
Breast Cancer and Obesity: Interaction with Treatment

• Co-morbidity
  – Heart disease that limits the amount of drugs that can be delivered:
    • chemotherapy(adriamycin)
    • targeted agent(trastuzumab)
  – Anti-hormones(SERMS and aromatase inhibitors)
    • hot flashes
    • venous thromboembolic disease
    • joint pains
  – Diabetes
    • Wound infection
Recurrence of Breast Cancer and BMI

- Locoregional alone
- Distant metastases
- BMI < 25
- BMI 25-29
- BMI ≥ 30
- BMI unknown

Healthy
Overweight
Obese

5%
Death from Breast Cancer and Obesity

[Graph showing the incidence of breast cancer-related death and other causes across different BMI categories, with a note indicating a 13% increase for Obese BMI categories.]
Liver Cancer
Progression from steatosis to Liver Cancer

• Fat infiltrates liver: minor changes in hepatocyte enzymes

• Inflammation results from fat: progress to the non-alcoholic steatohepatitis

• Scarring begins to develop: fibrosis similar to cirrhosis

• Cancer develops
Childhood Obesity in 2008
6-11 yo 19%
12-19 yo 18%

Double Normal Weight

Obesity induced Steatosis and Steatohepatitis
FATTY LIVER!
Steatotic “Fatty” Liver
Diffuse Hepatic Steatosis
Macrovesicular Steatois
BARIATRIC SURGERY LIVER EVALUATION QUALITY
PROJECT ALGORITHM

Patient being evaluated for bariatric surgery

Test LFT's: Alk Phosphatase, AST, ALT, TB
Consider USG

INTRA OPERATIVE LIVER BIOPSY
Large core needle or wedge

PATHOLOGIC EVALUATION

STEATOSIS
Routine F/U
LFT'S/USG

STEATOHEPATITIS
1. LFT's F/U
2. Imaging if not already performed
3. Consider referral to hepatologist

FIBROSIS 0 • 1 • 2
Referral to hepatologist

FIBROSIS 3 • 4
HCC screening:
1. Alphafetoprotein
2. Imaging
3. Referral to liver specialist
## NASH and Bariatric Surgery

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<td>1 year post op</td>
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In percent
# Fibrosis Scores

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Liver Cancer and BMI: Dose-dependent curve

Wang et al, The Oncologist, 2012
Screening Gaps

• Obese women are at higher risk of endometrial and breast cancer
  – AND these cancers develop at a younger age
  – BUT they undergo less screening

• Only about half of the bariatric surgeons required up-to-date breast cancer (mammogram) and gynecologic cancer (PAP) screening before bariatric surgery

• Primary care responsibility

Papers in the Journal of the American College of Surgeons—American Society for Metabolic and Bariatric Surgery Meeting
A Radical Approach?

• Surgical weight reduction
  – Esophageal banding
  – Gastric sleeve resection
  – Roux-en-Y gastric bypass
Obesity and Cancer

• In patients who have undergone gastric bypass surgery, long-term mortality from any cause in a surgery group decreased by 40%, compared with that of a control group.

• Cause-specific mortality in the surgery group decreased by 56% for coronary artery disease, by 92% for diabetes, and by 60% for cancer.

General Suggestions

• Maintain a healthy weight
• Food choice is the most effective method to manage sugar intake and potentially weight
• Balance caloric intake with physical activity
• Avoid excessive weight gain throughout the life cycle
• Achieve and maintain a healthy weight if currently overweight or obese
Exercise for Cancer Survivors

PRESCRIBE EXERCISE
Suggest moderate-intensity exercise:

30 MIN

5 DAYS/WK

ADULTS AGES 18-65
Exercise for Cancer Survivors

START SLOWLY

Patients with significant fatigue should start slowly and increase exercise in a gradual way.
Exercise for Cancer Survivors

BUILD INCREMENTALLY
Exercise can be broken down into shorter increments throughout the day while working toward a goal of 30 minutes per day.⁷

10 MIN  +  10 MIN  +  10 MIN  =  30 MIN/DAY
Exercise for Cancer Survivors

PERSONALIZE RECOMMENDATIONS

Use caution when recommending exercise to certain patients. For example, survivors with significant peripheral neuropathies or ataxia may experience weakness or loss of balance. Suggest a stationary reclining bicycle rather than a treadmill for these patients.\textsuperscript{15}
Wellness Program

• Named program in the Center for Cancer Prevention and Treatment
• Navigator
• Dietician
• Physical Therapy--Trainer
• Physiatrist
• Advisory Board
Closing Comments

• Prediction
• Prevention
• Early intervention
• Aggressive approaches
THANK YOU

Moonrise Machu Picchu, 2010

Acknowledgements: Drs Sami Hamamji, Justin Braverman and Brock D. Foster