Breast Cancer a comprehensive approach

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Magnitude of the problem

- 210,000 new cases in 2010
- 40,000 will die of breast cancer
- Second most common cause of death in women
- Main cause of death 40-59 old
- 10% associated with family history
- Lifetime risk 1 in 6 overall and 1 in 8 for invasive disease
Global variation

- Highest in North America and Northern Europe
- Lowest in Asia and Africa
- It is connected with cultural and environmental changes
- Higher incidence in second, third and fourth generation of migrants
Mortality

- Black women have the highest mortality
  - nature of tumors
  - stage presentation
  - access to care
- Decline was noted in women younger than 50
- Mortality declined in patients with ER, PR positive tumors.
- Mortality changed minimally in women older than 70.
Breast Cancer Mortality
Risk factors

- Age and gender
- Race and Ethnicity
- Benign breast disease
- Lifestyle and diet
- Reproduction and hormonal factors
- Family history and genetic factors
- Environmental factors
Age and Gender

- It occurs 100 times more frequently in women
- Incidence rises sharply at age 45-50
- At age 75-80 the curve flattens.
Age and Gender
Race and Ethnicity

- Whites 124/100,000
- Blacks 113/100,000
- Asians/Pacific Islanders 83/100,000
- Hispanic and Latina 90/100,000
- Black women have an earlier peak
- Black women have higher mortality
Benign breast disease

- Single benign lesion does not increase the risk
- Multiple non proliferative lesions increase the risk by 1.8
- Proliferative lesions without atypia increase the risk by 2
- Proliferative lesions with atypia increase the risk by 10
- More than one lesion with atypia increases even more
Lifestyle and Diet

- Higher socioeconomic status increases risk two fold.
- Connected with reproductive patterns such as age at first pregnancy
- Connected with utilization of screening mammogram
Body weight

- BMI has opposite effect on the risk in postmenopausal women as compared with premenopausal ones.
- Postmenopausal weight gain increases the risk
- Pooled data: >80 kg risk was 25% higher than <60 kg
- BMI >33 has 27% in the risk for breast cancer
- Due to higher levels of estrogen
Family History

• Important factor but accounts only for 10-15% of cases
• It is taken into consideration in Gail Model
• One first degree relative increases the risk by 1.8
• Two first degree relatives increases by 2.8
• Genetic mutations BRCA1&2 only 5-6% of all breast cancers
Genetic Testing Risk Assessment

• **Comb risk assess crit BRCA test**

• **Non-Jewish families High risk* breast-ovarian; Any of the following:**
  - One case of breast cancer ≤40 years old in a first or second-degree relative
  - One first or second-degree relative with both breast and ovarian cancer at any age
  - Two cases of breast cancer in first or second-degree relatives if one is diagnosed at ≤50 years of age or is bilateral
  - One first or second-degree relative with breast cancer diagnosed at ≤50 years old or bilateral and one first or second-degree relative with ovarian cancer
  - Three cases of breast and ovarian cancer (at least one case of ovarian cancer) in first or second-degree relatives
  - Two cases of ovarian cancer in first or second-degree relatives
  - One case of male breast cancer in a first or second-degree relative if another first or second degree relative has (male or female) breast or ovarian cancer

• **Moderate risk* breast; Any of the following:**
  - Two first-degree relatives if both diagnosed between 51 and 60 years of age
  - One first degree and one second-degree relative (mother or sister and maternal aunt or maternal grandmother), if the sum of their ages is ≤118 years old

• **Moderate risk ovarian:**
  - One first-degree relative with ovarian cancer

• **Jewish families High risk* breast-ovarian; Any of the following:**
  - One case of breast cancer ≤50 years old in a first or second-degree relative
  - One case of ovarian cancer at any age in a first or second-degree relative
  - A first or second-degree relative with ovarian cancer.
Premenopausal

- BMI $> 31$, 46% less likely to develop breast cancer
- Due to prolonged anovulatory cycles.
- Data quite conflicting and mechanism not completely understood.
- Height: increased height is associated with higher risk
Physical activity

- Regular activity provides modest protection in premenopausal women.
- Postmenopausal women benefit from regular exercise.
- Most likely explained by tight weight control and lower adipose tissue.
Diet

- Alcohol increases the risk and it is additive with HRT
- 322,000 women, every 10 grams of alcohol intake increases the risk by 9%
- Mechanism: increases the circulating estrogens
- It increases the mammary gland susceptibility
- It increases the risk for ER positive tumors
Fat intake

- Correlation much weaker
- 300,000 women pooled analysis did not prove any increased risk.
- Women Health Initiative by decreasing fat intake did not decrease the risk for breast CA.
- Women with much higher intake may develop invasive cancers
- Young women with higher fat intake have slightly higher risk
Diet

- Red meat > 5 servings per week increases risk for ER positive tumors.
- Calcium and Vitamin D: inverse relation between the calcium and vitamin D in premenopausal women
- Postmenopausal women in large pooled analysis did not show benefit
- VITAL would try to address the question
Phytoestrogens

- Found in soy and other legumes
- Isoflavones are weak estrogens compared with estradiol.
- High soy intake in Asians and low incidence of breast CA suggests protective effect.
- Proposed mechanism: binding to ER receptors and acting as an antiestrogen.
Soy and Breast Cancer

- Meta analysis: modest reduction in Westerners and no reduction in Asians.
- Meta analysis in both Westerners and Asians on much higher doses showed 29% risk reduction. No risk reduction in Westerners although consumed dose was much lower.
- Better protective effect if consumed in adolescence
Soy and Breast Cancer cont.

- NIH consensus: no definitive conclusion can be made.
- Considered to be safe to be consumed in doses required by Asian diet.
- Unclear about the protective effect at smaller doses and shorter period of time.
Antioxidants

- No evidence for Vitamin E, C or beta carotene. None have been associated with protective effect.
- Data on Vitamin A is quite conflicting
- Selenium in low doses increases the risk.
- Selenium high doses do not protect
Others

- Caffeine: no proven association
- Smoking: association biased by concomitant consumption of alcohol
  - modest increase in the risk
  - multiple studies with inconclusive results
  - second hand smoking, study was not corrected for other factors
Reproductive and Hormonal Factors

- Prolonged endogenous exposure to estrogen increases the risk,
- Age at menarche and menopause
  - every 2 years delay in menarche decreases the risk by 10%
  - for every year delay in menopause 1.3% increase in the risk
- Bilateral oophorectomy decreases the risk by 50%
Menstrual patterns

- Number of ovulatory cycles is correlated with total exposure to estrogen.
- Infertility data is inconsistent.
- Parity: nulliparous has RR of 1.7. Protective effect is not seen until 10 years after delivery.
- Age at first birth: earlier pregnancy would allow the full differentiation of the mammary gland earlier and much less susceptible to carcinogens.
Breast Feeding

- Multiple studies confirmed
- Correlated with parity and duration.
- 47 studies 50,302 women risk reduction by 4% for every 12 months
- 7% in addition for each birth
- It may delay ovulatory cycles.
Endogenous hormonal level

- Serum estrogen level correlated with risk
- MORE trial with $>12$ pmol had 2 fold higher risk.
- Higher estradiol level, bigger benefit from Raloxifene.
- NASBP P1 study no correlation with response to Tamoxifen
- Nurses study higher risk reduction seen in ER positive tumors
Premenopausal women

- Endogenous estradiol level role is less understood.
- Nested analysis in Nurses Study: higher level of estradiol in follicular phase, higher the risk is.
- Prolactin, androgens and IGF role is unclear
Breast Density

- It is an inherited trait
- Hormones increase it, Tamoxifen decrease it
- Independent risk factor
- >75% density risk is 4-5 times higher
- Guidelines recommend breast density needs to be reported
- Little consensus exist on how to quantify it.
Quantifying the risk for breast cancer

- If hereditary predisposition exists Gail Model
- Modified Gail Model exist for African American Ancestry
- Gail Model does not incorporate all the risk factors
- It is the most widely used
- New models are available
Other Risk Factors

- Nocturnal light exposure
  - 3 studies support increased risk by night exposure RR of 1.48.
  - exposure suppresses melatonin secretion and it directly correlates with risk.
  - shift work is now recognized by WHO as a carcinogen.
Prevention and Early Detection

- Mammography:
  - consensus to recommend 50-69.
  - debate over women 40-49 or over 70.
  - several studies found little difference between digital and traditional mammo.
  - DMIST found benefit for peri and premenopausal.
Frequency

- Limited data available in terms of frequency.
- Unclear if once a year or every other year is indicated.
- One study compared the two, no benefit in older women
- Reasonable to recommend yearly for young women and every other year for older ones.
MRI

- Requires contrast
- Based on angiogenesis and vascularity of the tumor.
- It assesses the uptake velocity and wash out kinetics
- American College of Radiology Standards:
  - b/l MRI, uses 1.5 Tesla magnet, dedicated coil, reports should be done using Bi-Rad system.
Indications for MRI

- Assessment of silicone implants
- Detection of occult breast cancers
- Extent of disease
- Response to neoadjuvant chemotherapy
- Diagnosis of recurrence
- Screening for high risk
Indications cont.

- Best tool to evaluate axillary LN presentation.
- Best tool to detect intra or extra capsular rupture.
- Preop evaluation remains controversial due to additional biopsies and delays.
- Response to neo adjuvant chemo but it may over or under estimate residual disease.
- ACRIN 6657 is on the way.
Breast MRI cont.

- Helps differentiate scar tissue from reoccurrence.
- Surgical scars do not enhance
- May be helpful in women with bilateral mastectomy and implants for chest wall reoccurrence detection
Screening high risk women

- Recommended in women > 20% lifetime risk
- No evidence if that translates in decreased mortality
- NCCN guidelines recommend it in BRCA1&2 carriers and >20%.
- Frequency and incorporating mammogram is unclear
New imaging techniques

- High field strength with 3 OR 7 Tesla
- Magnetic Resonance spectroscopy: may enhance specificity
- Breast specific gamma imaging: has better specificity and equal sensitivity
- PEM positron emission mammo: modified PET with 2 mm resolution
- It has 86-91 sensitivity and 91% specificity
- It does not detect low grade malignancies
- Can’t be used in screening
PET

- Can not detect lesions smaller than 1 cm
- May be beneficial in axillary staging
- May be beneficial in detecting distant disease but controversial.
- May lead in treatment delays.
- Routine PET is not recommended to monitor for reoccurrence.
Treatment

- Revolving door rapidly changing.
- Local and systemic:
  - Surgery
  - radiation therapy
  - Chemotherapy
  - endocrine therapy
Surgery

- BCT equivalent with mastectomy
- Breast reconstruction has increased in popularity
- Reconstruction can be done with implants or autologous tissue by TRAM flap or DIP
- Requires expertise from trained plastic surgeons
Radiation Therapy

- Whole breast radiation vs PBI
- Boost vs no boost still controversial although EORTC study that suggested benefit for boost
- Unclear of the impact on mortality
Systemic Therapy

- Chemotherapy and/or targeted therapy
- Use of OncotypeDx in quantifying the individual risk for systemic recurrence
- Currently used in ER positive patients, lymph node negative.
- Studies on the way for 1-3 positive lymph nodes as well neoadjuvant settings
Breast Cancer Survivorship

- Who do we follow
- How long we maintain them for surveillance
- What tests should we order
## Summary of 2006 ASCO guideline recommendations for surveillance after breast cancer treatment

<table>
<thead>
<tr>
<th>Mode of surveillance</th>
<th>Summary of recommendations</th>
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</thead>
<tbody>
<tr>
<td><strong>Recommended breast cancer surveillance</strong></td>
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<tr>
<td>History/physical examination</td>
<td>Every 3 to 6 months for the first three years after primary therapy; every 6 to 12 months for years 4 and 5; then annually</td>
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<tr>
<td>Patient education regarding symptoms of recurrence</td>
<td>Physicians should counsel patients about the symptoms of recurrence including new lumps, bone pain, chest pain, abdominal pain, dyspnea or persistent headaches; helpful websites for patient education include <a href="http://www.uptodate.com/patients">www.uptodate.com/patients</a> and <a href="http://www.cancer.net/portal/site/patient">www.cancer.net/portal/site/patient</a></td>
</tr>
<tr>
<td>Referral for genetic counseling/testing</td>
<td>Criteria include: Ashkenazi Jewish heritage; history of ovarian cancer at any age in the patient or any first- or second-degree relatives; any first-degree relative with a history of breast cancer diagnosed before the age of 50 years; two or more first- or second-degree relatives diagnosed with breast cancer at any age; patient or relative with diagnosis of bilateral breast cancers; or history of breast cancer in a male relative</td>
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<td>Breast self-examination</td>
<td>All women should be counseled to perform monthly breast self-examination</td>
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<tr>
<td>Mammography</td>
<td>First post-treatment mammogram 1 year after the initial mammogram that leads to diagnosis but no earlier than 6 months after definitive radiation therapy; subsequent mammograms should be obtained as indicated for surveillance of abnormalities</td>
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<tr>
<td>Coordination of care</td>
<td>Continuity of care for breast cancer patients is encouraged and should be performed by a physician experienced in the surveillance of cancer patients and in breast examination, including the examination of irradiated breasts; if follow-up is transferred to a PCP, the PCP and the patient should be informed of the long-term options regarding adjuvant hormonal therapy for the particular patient; this may necessitate referral for oncology assessment at an interval consistent with guidelines for adjuvant hormonal therapy</td>
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<tr>
<td>Pelvic examination</td>
<td>Regular gynecologic follow-up is recommended for all women; patients who receive tamoxifen should be advised to report any vaginal bleeding to their physicians</td>
</tr>
<tr>
<td><strong>Breast cancer surveillance testing; not recommended</strong></td>
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<tr>
<td>Routine blood tests</td>
<td>CBCs and liver function tests are not recommended</td>
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<tr>
<td>Imaging studies</td>
<td>Chest x-ray, bone scans, liver ultrasound, computed tomography scans, and FDG-PET scans are not recommended</td>
</tr>
<tr>
<td>Tumor markers</td>
<td>CA 15-3, CA 27.29, and carcinoembryonic antigen are not recommended</td>
</tr>
<tr>
<td>FDG-PET</td>
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Special cases

- BRCA1&2 carriers have similar in breast reoccurrence as general population.
- Higher rate of de novo breast cancers in the same breast or contralateral breast.
- Screening should be continued with diligence.
Long Term Effects

- Psyco-social associated with cancer stygmata
- Increased risk for Acute Leukemia
- Increased risk for osteoporosis due to prolonged estrogen suppression
- Vaginal dryness
- Infertility
Breast Cancer

- Complex disease very heavily emotionally loaded.
- Requires a multi-disciplinary approach:
  - imaging
  - breast surgeon
  - plastic surgeon
  - medical oncology
  - radiation oncology
  - genetic counselor
  - fertility specialist
  - Nutritionist
  - social worker
Thank you