Objectives

To review risk factors and screening for breast cancer

To discuss principles of breast cancer management
Breast Cancer Statistics

Over 192,000 invasive breast cancers diagnosed in 2010

Approximately 1% diagnosed in men

Over 40,000 breast cancer deaths each year

Recent decline in death rate by about 2%/yr

Lifetime risk for U.S. women is 12% (one in eight)

Overall 5 year survival 89%

Prevalence is approximately 2,500,000
Review Question:
Which of the following is most highly associated with an increased risk of developing breast cancer?

A. Late menarche
B. Early parity
C. Increased breast density
D. Cigarette smoking
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Risk Factors

Female gender

Menstrual/pregnancy history
  early menarche, late menopause, nulliparity
  or late parity

Exogenous hormones

Ionizing radiation exposure

LCIS, atypical hyperplasia

Mammographic breast density

Family history

Age
Screening mammography every other year starting at age 50

Individualize screening for those under age 50

No teaching of breast self examination

Insufficient evidence to recommend for or against clinical breast examination or mammography screening beyond age 70
Screening Recommendations: ACS

Discuss pros and cons of breast self examination from early 20’s

Clinical breast examination every three years from age 20 to 39, then annually as part of regular health exam

Annual mammography beginning at age 40

Earlier mammography in the setting of significant family history or other risk factors

MRI for selected high-risk groups
Breast Cancer Screening

Reduction in breast cancer mortality most strongly suggested for screening mammography in women age 50-69 (25-30% risk reduction)

Different from *diagnostic* evaluation which applies to an individual with symptoms or clinical findings
## Screening vs Diagnostic Imaging

<table>
<thead>
<tr>
<th>SCREENING</th>
<th>DIAGNOSTIC</th>
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<tbody>
<tr>
<td><strong>Asymtomatic population at risk</strong></td>
<td><strong>Signs or symptoms under evaluation</strong></td>
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<tr>
<td>Risk increases with age</td>
<td>Mass</td>
</tr>
<tr>
<td>Other risk factors considered</td>
<td>Abnormal screening</td>
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<tr>
<td>Two standard mammogram images of each breast</td>
<td>May include standard mammogram images, magnification views, ultrasound, etc.</td>
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<tr>
<td>Test should have high sensitivity, lower specificity is acceptable</td>
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Hereditary Breast Cancer

Suggestive Family History for BRCA1/BRCA2
- Multiple cases/bilateral
- Onset before the age of 45
- History of ovarian cancer
- Autosomal dominant inheritance pattern

Mutations in genes on chromosomes 17 and 13

Lifetime risk of breast cancer up to 85%; risk for ovarian and other cancers increased

Aggressive screening and/or preventive surgery discussion

Prognosis of breast cancer similar to age- and stage-matched, non hereditary breast ca.
Stage 0: DCIS (LCIS)

Stage I: Up to 2cm, node negative

Stage II: 2 or more cm and node negative (excluding T4) or up to 5cm and 1-3 nodes positive

Stage III: Tumor size >5cm with any LN+, or skin involvement (T4), or ≥4 axillary lymph nodes, or supraclavicular or IM lymph nodes

Stage IV: Distant metastases
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Treatment By Stage

Operable: Stage 0, I, II, III

- Surgery +/- radiation therapy
  - Mastectomy/lumpectomy
  - Axillary dissection/sentinel lymph node procedure
- Adjuvant systemic therapy
- Neoadjuvant systemic therapy

Inoperable: Stage III, IV

- Primary systemic therapy
- Neoadjuvant, Palliative
Prognosis in Operable BC

- Tumor size
- Histologic grade
- Hormone receptors
- Her2/neu overexpression
- Patient age
- Lymph node involvement
- Stage
Review Question

For a 55 y.o. woman with a 1.5 cm ER/PR+ lymph node-negative infiltrating ductal carcinoma which of the following will have the greatest impact on 10 year survival:

A. Endocrine treatment vs. no endocrine treatment
B. Mastectomy vs. Breast conservation
C. Chemotherapy vs. no chemotherapy
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Adjuvant Hormonal Therapy

Tamoxifen

In patients with ER+ tumors, 5 yrs of therapy reduces annual recurrence risk by approximately 50%

Benefit present in both pre- and post-menopausal ER+ or PR+ tumor

Benefit in both invasive and noninvasive cancer

Other Adjuvant Hormonal Rx:

Ovarian Ablation
Aromatase Inhibition
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Aromatase Inhibitors in EBC

Prevents conversion of adrenally produced androgens into estrogens but does not effectively prevent ovarian estrogen production

Modest advantage over tamoxifen alone in postmenopausal women

- As initial therapy instead of tamoxifen
- Following tamoxifen

Different Side Effect Profile

- Less risk of endometrial cancer and thromboembolism
- Higher risk of osteoporosis, fracture and musculoskeletal symptoms
**Adjuvant Chemotherapy**

CMF, CAF, CEF, AC, TC, AC>T, TAC

For operable *invasive* cancer, reduces recurrence risk by approximately one third

Benefit decreases with increasing age

Benefit greatest in node positive, hormone receptor negative, premenopausal patients

Adjuvant trastuzumab reduces recurrence risk in HER2neu overexpressing breast cancer (AC>TH, TCH)
Metastatic Breast Cancer

Spread of disease to organs outside of the breast and regional lymph nodes

Treatment directed at reducing symptoms and prolonging life

Life expectancy often measured in years

Modalities include hormonal therapy, chemotherapy, radiation therapy, biologic agents
A 56 y.o. post-menopausal treated for stage II breast cancer 8 years ago with MRM and CMF chemotherapy. On evaluation of back and rib pain she is found to have metastatic disease involving multiple bones. She has no neurologic symptoms and CT scans of chest, abdomen and pelvis reveal no other sites of disease. A bone biopsy demonstrates ER+ adenocarcinoma. Which do you recommend?

A. Initiate a selective aromatase inhibitor and IV bisphosphonates

B. Initiate combination chemotherapy with an anthracycline-containing regimen

C. Initiate trastuzumab in combination with taxane-based chemotherapy
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Predictors of Response to HT

- ER and/or PR positive
- Long disease free interval
- Disease limited to bone, pleura and soft tissues
- Prior response to hormonal therapy
Hormonal Therapy

Antiestrogens

- Tamoxifen, toremifene, fulvestrant

Ovarian ablation

- Premenopausal women

Aromatase inhibitors

- Inhibit peripheral conversion of adrenally produced androgens into estrogens in postmenopausal women

Other agents

- Progestins, androgens, high dose estrogens
Other Therapy for Metastatic Disease

Chemotherapy

Patients not eligible for or not responsive to hormonal therapy

Biologic Agents

- Trastuzumab in Her2neu + disease
- Lapatinib (inhibits Her2 and EGFR)
- Bevacizumab (anti-VEGF)

Pamidronate, Zolendronate, denosumab

Reduces skeletal events in lytic bone metastases

Radiation therapy

Experimental agents
In the setting of breast cancer prevention, tamoxifen 20 mg/day results in all of the following except:

A. Reduction in non-invasive breast cancer
B. Reduction in invasive breast cancer
C. Increase in 5-year survival
D. Increase in endometrial cancer
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Randomized controlled trial of tamoxifen x 5 years versus placebo in 13,388 women

- Age 60 or more or
- Age 35 or more with
  - Gail risk at least 1.66 OR LCIS

49% reduction in breast cancer risk was observed with tamoxifen (no survival difference)

Toxicity includes hot flashes, vaginal discharge, increased rates of cataracts, endometrial cancer and thromboembolic events
In postmenopausal women at risk for breast cancer, raloxifene use was nearly as good as tamoxifen in reducing breast cancer incidence.

Raloxifene was associated with a lower incidence of uterine cancer and thromboembolism compared to tamoxifen.

Raloxifene is an option for prevention but is not an acceptable substitute for tamoxifen in breast cancer treatment.