Evaluation and Management of Breast Cancer

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EPIDEMIOLOGY
Epidemiology

- Most frequent cancer among American women (if skin cancers excluded)
- The U.S has the highest incidence of breast cancer in the world
Top 10 Cancer Sites: 2005, Female, United States—All Races

- Breast: 117.7
- Lung & Bronchus: 55.2
- Colon & Rectum: 41.9
- Corpus & Uterus, NOS: 23.4
- Non-Hodgkin Lymphoma: 15.9
- Melanomas of the Skin: 15.1
- Thyroid: 14.9
- Ovary: 12.4
- Kidney & Renal Pelvis: 10.4
- Pancreas: 10.0

Rates per 100,000+
Female Breast Cancer Death Rates* by Race and Ethnicity, United States, 1975 to 2002

From Smigal, C. et al.

*Excludes non-Hispanic Other racial/ethnic groups and non-Hispanic Asian and Pacific Islander.
RISK FACTORS
Risk Factors

- Gender
- Age
<table>
<thead>
<tr>
<th>If current age is:</th>
<th>The probability of developing breast cancer in the next 10 years is:†</th>
<th>or 1 in:</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>0.05%</td>
<td>1,985</td>
</tr>
<tr>
<td>30</td>
<td>0.44%</td>
<td>229</td>
</tr>
<tr>
<td>40</td>
<td>1.46%</td>
<td>68</td>
</tr>
<tr>
<td>50</td>
<td>2.73%</td>
<td>37</td>
</tr>
<tr>
<td>60</td>
<td>3.82%</td>
<td>26</td>
</tr>
<tr>
<td>70</td>
<td>4.14%</td>
<td>24</td>
</tr>
<tr>
<td><strong>Lifetime risk</strong></td>
<td><strong>13.22%</strong></td>
<td><strong>8</strong></td>
</tr>
</tbody>
</table>

*Among those free of cancer at beginning of age interval. Based on cases diagnosed 2000-2002. Percentages and “1 in” numbers may not be numerically equivalent due to rounding.


American Cancer Society, Surveillance Research, 2005
Risk Factors

- Gender
- Age
- Family History of breast cancer
## Family History as Risk Factor for Breast Cancer

<table>
<thead>
<tr>
<th>Relative Type</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>First-degree relative</td>
<td>1.8</td>
</tr>
<tr>
<td>Pre-men. relative, unilateral breast cancer</td>
<td>3.0</td>
</tr>
<tr>
<td>Post-men. relative, unilateral breast cancer</td>
<td>1.5</td>
</tr>
<tr>
<td>Pre-men. relative, bilateral breast cancer</td>
<td>9.0</td>
</tr>
<tr>
<td>Post-men. relative, bilateral breast cancer</td>
<td>4.0-5.4</td>
</tr>
</tbody>
</table>

Risk Factors

- Gender
- Age
- Family History of breast cancer
- Hormonal factors
<table>
<thead>
<tr>
<th>Menstrual history</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Menarche before age 12 years</td>
<td>1.7-3.4</td>
</tr>
<tr>
<td>Menarche before age 17 years</td>
<td>0.3</td>
</tr>
<tr>
<td>Menopause before age 45 years</td>
<td>0.5-0.7</td>
</tr>
<tr>
<td>Menopause at age 45-54</td>
<td>1.0</td>
</tr>
<tr>
<td>Menopause at or after 55 years</td>
<td>1.5</td>
</tr>
<tr>
<td>Menopause at or after age 55 years with more than 40</td>
<td>2.0-4.0</td>
</tr>
<tr>
<td>Oopherectomy before age 35 years</td>
<td>0.4</td>
</tr>
<tr>
<td>Anovulatary menstrual cycles</td>
<td>2.0-4.0</td>
</tr>
</tbody>
</table>

### Hormonal Factors as Risk Factor for Breast Cancer

<table>
<thead>
<tr>
<th>Pregnancy history</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Term pregnancy before age 20 years</td>
<td>0.4</td>
</tr>
<tr>
<td>First term pregnancy at 20-34 years</td>
<td>1.0</td>
</tr>
<tr>
<td>First term pregnancy at or after 35 years</td>
<td>1.5-4.0</td>
</tr>
<tr>
<td>Nulliparous</td>
<td>1.3-4.0</td>
</tr>
</tbody>
</table>

Hormonal Factors as Risk Factor for Breast Cancer

- Exogenous hormone use
  - The data for both oral contraceptives and more hormone replacement therapy are mixed
Risk Factors

- Gender
- Age
- Family History of breast cancer
- Hormonal factors
- Proliferative Breast Disease
# Proliferative Breast Lesions and Risk of Breast Cancer

<table>
<thead>
<tr>
<th>No Increased Risk</th>
<th>1.5-2.0 X increased risk</th>
<th>5 X increased risk</th>
<th>10 X increased risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenosis</td>
<td>Hyperplasia (moderate/florid/papillary)</td>
<td>Atypical hyperplasia</td>
<td>LCIS</td>
</tr>
<tr>
<td>Apocrine metaplasia</td>
<td>Papillomatosis</td>
<td></td>
<td>Atypical hyperplasia with FH</td>
</tr>
<tr>
<td>Cysts</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duct ectasia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibroadenoma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibrosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperplasia (mild)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mastitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Squamous metaplasia</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Risk Factors

- Gender
- Age
- Family History of breast cancer
- Hormonal factors
- Proliferative Breast Disease
- Irradiation of Breast at child
- Personal history of cancer
- Lifestyle factors
Risk Assessment Tools

- Gail model
  - Women greater than 35 yo with no personal history of breast cancer
  - Estimates 5 year and lifetime risks of breast cancer
  - www.cancer.gov/bcrisktool
Risk Calculator

(Click a question number for a brief explanation, or read all explanations.)

1. Does the woman have a medical history of any breast cancer or of ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS)?

2. What is the woman’s age?
   *This tool only calculates risk for women 35 years of age or older.*

3. What was the woman's age at the time of her first menstrual period?

4. What was the woman's age at the time of her first live birth of a child?

5. How many of the woman's first-degree relatives - mother, sisters, daughters - have had breast cancer?

6. Has the woman ever had a breast biopsy?

   6a. How many breast biopsies (positive or negative) has the woman had?

   6b. Has the woman had at least one breast biopsy with atypical hyperplasia?

7. What is the woman's race/ethnicity?

   Calculate Risk >
Gail Risk Calculator


- Limitations:
  - Can not have personal history of breast cancer
  - Does not account for first degree relatives with breast cancer
  - Genetic mutations are not considered
SCREENING
Screening for Average Risk

- Average risk has not first degree relative with breast cancer, no personal history of breast cancer, no history of mantle cell radiation
- 20-39yo
  - Clinical breast exam every 1-3 years
- 40yo and older
  - Annual clinical breast exam
  - Annual screening mammogram

NCCN Breast Cancer Screening Guidelines
Screening for above average risk

- First-degree relative with breast cancer
- Evidence of genetic predisposition
- Personal history of atypical hyperplasia or breast cancer
- History of mantle cell radiation
- Gail score of > 1.7%
Screening with strong family history or genetic predisposition

- Under age 25yo
  - Annual clinical breast examination
  - Self examinations
- 25yo or older
  - Annual mammogram 5-10 years prior to youngest reported case or at 25yo for genetic predispositions
  - Possible breast MRI
  - Self examinations
  - Risk reduction strategies considered
  - Annual or biannual clinical breast examination
Screening with personal history of atypical hyperplasia or LCIS

- Annual mammogram
- Annual or biannual clinical breast examination
Screening with personal history of breast cancer

- Annual mammogram
- Clinical breast examination every 4-6 months for 5 years and then annually
Screening with history of mantle cell radiation

- Less than 25yo
  - Annual clinical breast examination
  - Self-examination

- 25yo or older
  - Annual mammogram beginning at 40yo or 8-10 years after radiation
  - Annual clinical breast examination
  - Self-examination
Screening with elevated Gail risk

- Annual mammogram
- Annual or biannual clinical breast examination
- Consider risk reduction strategies
STAGES OF BREAST CANCER
Ductal Carcinoma In Situ

- Non-invasive breast cancer of ductal origin
- Incidence has increased by 587% from 1973 to 1992
- Usually presents as calcifications in the breast (rarely as palpable mass)
- Risk factors for DCIS same as for invasive cancer
- Considered Tis
Ductal Carcinoma In Situ (DCIS)
Invasive Carcinoma
TNM Staging: Primary Tumor (T)

- TX: Primary tumor cannot be assessed.
- T0: No evidence of primary tumor.
- Tis: Carcinoma in situ (DCIS, LCIS, or Paget disease of the nipple with no associated tumor mass)
- T1: Tumor is 2 cm (3/4 of an inch) or less across.
- T2: Tumor is more than 2 cm but not more than 5 cm (2 inches) across.
- T3: Tumor is more than 5 cm across.
- T4: Tumor of any size growing into the chest wall or skin. This includes inflammatory breast cancer.
TNM Staging: Nodal  (N)

- **NX**: Nearby lymph nodes cannot be assessed (for example, removed previously).
- **N0**: Cancer has not spread to nearby lymph nodes.
- **N1**: Cancer has spread to 1 to 3 axillary (underarm) lymph node(s), and/or tiny amounts of cancer are found in internal mammary lymph nodes (those near the breast bone) on sentinel lymph node biopsy.
- **N2**: Cancer has spread to 4 to 9 axillary lymph nodes under the arm, or cancer has enlarged the internal mammary lymph nodes.
TNM Staging: Nodal (N)

- N3: One of the following applies:
  - Cancer has spread to 10 or more axillary lymph nodes.
  - Cancer has spread to the lymph nodes under the clavicle (collar bone).
  - Cancer has spread to the lymph nodes above the clavicle.
  - Cancer involves axillary lymph nodes and has enlarged the internal mammary lymph nodes.
  - Cancer involves 4 or more axillary lymph nodes, and tiny amounts of cancer are found in internal mammary lymph nodes on sentinel lymph node biopsy.
TNM Staging: Distant Metastases (M)

- **MX:** Presence of distant spread (metastasis) cannot be assessed.
- **M0:** No distant spread.
- **M1:** Spread to distant organs is present. (The most common sites are bone, lung, brain, and liver.)
## Breast Cancer Staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Tis</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>I</td>
<td>T1*</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IIA</td>
<td>T0</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1*</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IIB</td>
<td>T2</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IIIA</td>
<td>T0</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1*</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>N2</td>
<td>M0</td>
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<tr>
<td></td>
<td>T3</td>
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</tr>
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<td>N1</td>
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<td></td>
<td>T4</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td>IIIC</td>
<td>Any T</td>
<td>N3</td>
<td>M0</td>
</tr>
<tr>
<td>IV</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>

*T1 includes T1mic
Stage Specific Survival

CA Cancer J Clin 2006; 56:37-47
PRESENTATION
Mammographic Abnormality with normal breast exam

- Most common presentation of DCIS; also common presentation of invasive cancer
- BIRADS classification:
  - 1- normal
  - 2- benign finding
  - 3- probably benign, close follow-up
  - 4- concerning, suggest further evaluation
  - 5- highly suspicious of malignancy
Dominant Mass

- Common presentation of invasive cancers
- Benign lesions may also present as masses, especially in younger women (fibroadenomas, cysts)
Nipple discharge

- Concerning if spontaneous, unilateral, from one duct, serous, serosanguinous, or sanguinous
- Bilateral, non-spontaneous discharge typically has benign etiologies
Skin Changes

- Erythema and skin thickening (peau d’orange): concern about inflammatory breast cancer
- Nipple excoriation, scaling, eczema: consider Paget’s disease
DIAGNOSTIC TOOLS
Mammography

- Screening mammography has reduced breast cancer deaths by 29-45%
- Involves two views of the breast (Craniocaudal and Mediolateral oblique)
- 10% of individuals require further imaging (diagnostic mammogram)
- Diagnostic mammogram involves additional views tailored to area of interest
Normal Mammogram

Magee-Women’s Hospital of UPMC
Benign calcification

Malignant calcification
Ultrasonography

- Used as an adjunct to mammography
- Can distinguish cysts from solid masses and also note features of solid masses that suggest that they are benign (ex. Fibroadenomas)
- May find additional masses
- Initially focused sonography but whole breast more common
- Useful for loco-regional staging (axilla and IM)
MRI

- Use as general screening is controversial
- Common roles for MRI:
  - Screening of high risk individuals (BRCA1 and BRCA2)
  - Evaluate for rupture of breast implants
  - Evaluate extent of malignancy
Tissue is the Issue

- Historically, excisional biopsy
- Fine needle aspiration
  - Multiple passes with 22- to 25- gauge needle
  - Similar results to core needle biopsy for solid lesions
  - Used to evaluate concerning lymph nodes
- Core needle biopsy
  - Multiple passes with usually 14- to 18- gauge needle
  - Main method used to biopsy primary tumros
Types of Biopsy

- Ultrasound guided
- Stereotactic
- MRI guided
FINALLY, SURGERY
Excisional Biopsy

- Historically, common method to determine diagnosis of mammographic anomalies and palpable masses
- Still has role for lesions that can not be biopsied (location) or indeterminant diagnosis on core or concern of sampling error
Breast Conserving Surgery

- Removing a portion of the breast
- Often used for limited DCIS and invasive carcinoma
- Aim to limit surgical intervention on normal breast tissue
- Orientation of specimen is critical
- Clips placed to identify site of surgery
- Usually outpatient surgery
Total mastectomy

- Removal of all obvious breast tissue
- Currently, common to perform skin sparing mastectomy
- Newer approach is NAC (nipple areolar complex) sparing mastectomy
Axillary Staging

- Reason:
  - Assist in determining prognosis
  - Treatment planning
- Traditional technique: complete axillary dissection of levels I & II
Sentinel lymph node surgery

- Sentinel lymph nodes: first nodes to receive lymphatic drainage from an area
- SLN’s are most likely to contain metastases
- Technetium labeled sulfur colloid and lymphazurin
- Axillary dissecton reserved for those who have positive sentinel lymph nodes (intraoperatively or postoperatively)
Lymphoscintigraphy
Evaluation for Distant Disease

- Stage I - Liver function tests, Chest X-ray
- Stage II+ - CT (abdomen), bone scan
- If concern about neurologic symptoms, MRI (brain)
Common Surgeries

- Segmental mastectomy only - limited DCIS
- Segmental mastectomy with sentinel lymph node biopsy - amenable invasive cancers
- Total mastectomy with sentinel lymph node biopsy - multifocal DCIS, invasive cancers
- Segmental mastectomy with axillary dissection - amenable invasive cancer with LN involvement
- Modified radical mastectomy - invasive cancer with lymph node involvement
Who needs radiation?

- All segmental mastectomies for DCIS and invasive cancer
- 6 weeks, 5 days a week, total of 60 gray (10 gray boost to surgical site)
- Patients with T3 or N2 invasive cancer need chest wall radiation
- Partial breast irradiation - awaiting results of studies
Chemotherapy

- Consider in larger T1 lesions, especially if ER negative
- Used to decrease recurrence rates
- Generally 12-24 weeks, though consideration of shorter regimens
- Oncotype Dx
- Neoadjuvant chemotherapy
Hormonal Therapy

- For ER positive breast cancer patients
  - Premenopausal- Tamoxifen for 5 years
  - Postmenopausal- Aromatase Inhibitor for 5 years
Reconstruction

- Tissue arrangement for segmental mastectomy
- Mastectomy
  - Implant based
  - Autologous tissue
    - TRAM
    - LD
Case #1

- 49 yo female with a mammographic abnormality on screening mamogram

- What is our next step?
Case #1

- Diagnostic mammogram with possible biopsy
- 1.5cm Invasive ductal carcinoma

What are our next steps?
Case #1

- Ultrasound
- Chest X-ray
- Consider MRI
- Liver function tests
- Surgical oncology consult
- Genetic counseling?
Case #2

- 65yo female with large area concerning for DCIS on screening mammogram

- What is our next step?
Case #2

- Diagnostic mammogram with possible biopsy
- Multifocal DCIS, moderate grade
Case #2

- Surgical oncology consult
Case #3

- 65yo female with a concerning palpable mass in her left breast

- What are our next steps?
Case #3

- Diagnostic mammogram
- Ultrasound with possible biopsy

- 3.3cm invasive ductal carcinoma

- What are our next steps?
Case #3

- Chest X-ray
- LFT’s
- CT (abdomen)
- Bone scan
- Surgical oncology consult
- Medical oncology consult