Breast Cancer: The Benefits of Early Screening

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We are making steady progress in improving breast cancer survival…

- Death rate decreasing about 2-3% per year
- But still 268,600 new cases and 41,760 deaths in the US in 2019
- Second leading cause of cancer death in women in the US

### FDA Drug Approvals

<table>
<thead>
<tr>
<th>Year</th>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>2019</td>
<td>Atezolizumab</td>
</tr>
<tr>
<td></td>
<td>Alpelisib</td>
</tr>
<tr>
<td>2018</td>
<td>Olaparib</td>
</tr>
<tr>
<td></td>
<td>Talazoparib</td>
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<tr>
<td>2017</td>
<td>Abemaciclib</td>
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<tr>
<td></td>
<td>Pertuzumab</td>
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<tr>
<td>2015</td>
<td>Neratinib</td>
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<td>Ribociclib</td>
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<td>Palbociclib</td>
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</tbody>
</table>
### Established Risk Factors for Breast Cancer: Modifiable Factors

<table>
<thead>
<tr>
<th>Factor</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exogenous hormones</td>
<td></td>
</tr>
<tr>
<td>Oral contraceptive pills</td>
<td>0.9–1.0</td>
</tr>
<tr>
<td>Estrogen replacement (&gt; 10 years)</td>
<td>1.1</td>
</tr>
<tr>
<td>Estrogen and progesterone</td>
<td>1.4–3.0</td>
</tr>
<tr>
<td>Postmenopausal obesity (BMI &gt; 30)</td>
<td>2.5</td>
</tr>
<tr>
<td>Exercise (&gt; 3 hours/week)</td>
<td>0.6</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>1.1–2.2</td>
</tr>
<tr>
<td>Diet</td>
<td>1.0</td>
</tr>
<tr>
<td>Extremely dense mammographic tissue</td>
<td>4.0–6.0</td>
</tr>
</tbody>
</table>

Abbreviation: BMI, body mass index.

### Established Risk Factors for Breast Cancer: Fixed Factors

<table>
<thead>
<tr>
<th>Factor</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (female vs. male)</td>
<td>100</td>
</tr>
<tr>
<td>Age (≤ 50 vs. &gt; 50)</td>
<td>6.7</td>
</tr>
<tr>
<td>Endocrine factors</td>
<td></td>
</tr>
<tr>
<td>Age at menarche (&lt; 10)</td>
<td>1.4–1.9</td>
</tr>
<tr>
<td>Age at first birth (&gt; 35)</td>
<td>1.7</td>
</tr>
<tr>
<td>Nulliparity</td>
<td>1.4</td>
</tr>
<tr>
<td>Age at menopause (&gt; 55)</td>
<td>1.3</td>
</tr>
<tr>
<td>Benign breast disease</td>
<td></td>
</tr>
<tr>
<td>ADH, LCIS</td>
<td>4.0–5.0</td>
</tr>
<tr>
<td>Family history</td>
<td></td>
</tr>
<tr>
<td>First-degree relatives</td>
<td>2.0–7.0</td>
</tr>
<tr>
<td><em>BRCA1</em> or <em>BRCA2</em> mutation</td>
<td>10–30</td>
</tr>
<tr>
<td><em>PALB2</em> mutation</td>
<td>5.0–9.0</td>
</tr>
<tr>
<td><em>p53</em> (Li–Fraumeni)</td>
<td>1.5–6.0</td>
</tr>
<tr>
<td>Cowden syndrome</td>
<td>2.0–4.0</td>
</tr>
<tr>
<td>Ashkenazi Jewish ethnicity</td>
<td>1.4</td>
</tr>
<tr>
<td>Therapeutic radiation</td>
<td>35</td>
</tr>
</tbody>
</table>

Abbreviations: ADH, atypical ductal hyperplasia; LCIS, lobular carcinoma in situ.
Firefighters and Breast Cancer

- Women are not included in most studies of firefighters’ health
- Only 2 reported studies (to date) evaluated women firefighters’ cancer risk—numbers small
- Overall cancer incidence appears elevated
  - Cervical, thyroid, bladder significantly elevated
  - Breast appears elevated but not yet statistically significant

San Francisco Fire Dept reported 15% of female firefighters between 40 and 50 have been diagnosed with breast cancer (6X national average)

Why screen? Early detection saves lives
• 42 year old female firefighter with no family history of breast cancer
• When should she have her first screening mammogram?
When to start screening mammography and how often to screen?
**Guidelines**

**SBI, ACR, ASBrS, NCCN**
- Start at 40
- Yearly
- Cease when life expectancy is <10 years

**American Cancer Society**
- Informed decision making with health care provider from 40-44
- Yearly from 45-54
- Every 1-2 years from age 55 on, while in good health

**U.S. Preventative Services and Task Force**
- Informed decision making with health care provider from 40-49
- Every 2 years from 50-74
Facts

- Risk of breast cancer increases steadily with age
- Age of 50 originally chosen as surrogate for menopause, but no data to show any effect of menopause on cancer screening
- 1 in 6 breast cancers occur in women aged 40-49
- Annual screening beginning at age 40 saves more lives than delaying screening until age 50 or less frequent screening (biennial vs yearly)
- More than 40 percent of the years of life lost to breast cancer are among women diagnosed in their 40s.
Harms of screening mammograms

- Anxiety of callbacks
- False positives/unnecessary biopsies
  - For every 1000 women screened, ~100 are recalled. 19 undergo a minimally invasive needle biopsy, and at least 5 of them have breast cancer
- Overdiagnosis
- Radiation exposure
  - Risk remains theoretical. Single screening mammo: 0.4 mSv (compared to 3 mSv/yr background)
Additional Screening Tools

- Ultrasound
- Tomosynthesis
- Breast MRI
Screening breast ultrasound

- Screening ultrasound identified an additional 4.3 cancers / 1000 over mammography
- BUT these were high risk patients (dense breast tissue plus other risk factors)
- Markedly increased rate of follow-up imaging and biopsy recs, AND decreased positive predictive value of biopsy
- Additional 5% of women screened went to bx (2% from mammo), and very poor positive predictive value, even with incidence screening

Invasive lobular cancer
Digital Breast Tomosynthesis: 3-D Mammography

- Improves cancer detection and reduces false positives
- Two prospective, population-based screening:
  - Oslo trial (interim analysis) – n=12,631, cancer detection rate improved from 6.1 to 8.1 per 1000 exams (p<0.001) and false-positive rate decreased by 15% (p<0.001)
  - Italian (STORM) trial – n=7,292, cancer detection rate improved from 5.3 to 8.1 per 1000 exams (p<0.0001) and false-positive rate decreased by 17%.

Sources: Skaane 2013, Ciatto 2013
DBT reveals occult invasive lobular carcinoma

2D FFDM

Tomosynthesis Slice

Cyst

Lobular Carcinoma
Screening breast MRI

- Not recommended as a routine screening tool for all women
- Recommended for women at high risk for breast cancer due to strong family history and/or genetic mutation
- High false positive rate

Subtraction MRI showing breast cancer missed by follow-up ultrasound and mammogram
Half of women having mammograms have dense breasts
that the patient’s mammogram shows dense breast tissue;

- the degree of density apparent and an explanation of that degree of density;

- that dense breast tissue is common and not abnormal, but that dense breast tissue may increase the risk of breast cancer;

- that dense breast tissue can make it more difficult to find cancer on a mammogram and that additional testing may be needed for reliable breast cancer screening;

- that additional screening may be advisable and that the patient should discuss the results of the mammogram with the patient’s referring physician or primary care physician;
Current Effort for Women Firefighters and Cancer

• Women Firefighters Biomonitoring Collaborative
  – San Francisco Bay Area
  – UC Berkeley, UCSF, Silent Spring Institute
  – Examining exposure to chemicals by collecting blood samples from >80 female firefighters
Conclusions

- Despite progress, breast cancer remains second leading cause of cancer death among women
- Early detection saves lives!
- Screening guidelines are confusing
- Breast cancer risk among female firefighters is unknown
- For otherwise average risk female firefighters, speak to your doctor but reasonable to start annual mammograms at age 40
  - Tomosynthesis preferred
- For higher-risk female firefighters due to family history, talk to your doctor about breast MRI screening