Natural History and Epidemiology of Breast Cancer

2019 Dialogue I Prevent Cancer Foundation

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Objectives

• Ø Epidemiology of breast cancer
• Ø Risk factors for breast cancer
• Ø Controversies in screening
## Estimated New Cancer Cases* in the US in 2017

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>19%</td>
<td>30%</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>14%</td>
<td>12%</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>9%</td>
<td>8%</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>7%</td>
<td>7%</td>
</tr>
<tr>
<td>Melanoma of skin</td>
<td>6%</td>
<td>4%</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>5%</td>
<td>4%</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>5%</td>
<td>3%</td>
</tr>
<tr>
<td>Leukemia</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Oral cavity &amp; pharynx</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>All other sites</td>
<td>23%</td>
<td>22%</td>
</tr>
</tbody>
</table>

*Excludes basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder.
Breast specific data

• Breast cancer is the most commonly diagnosed cancer in U.S. women (1/8)
  • Every 3 minutes a female in U.S. diagnosed

• In 2018, ~268,600 new cases of invasive breast cancer are expected to be diagnosed in women in the U.S., along with
  • 62,930 new cases of non-invasive (in situ) breast cancer
Male breast cancer

• 1% of breast cancers are in men
• About 2,670 new cases of invasive breast cancer are expected to be diagnosed in men in 2019
• A man’s lifetime risk of breast cancer is about 1 in 1,000
Mortality

- ACS - 2nd leading cause of cancer death
  - 41,760 breast cancer deaths est. 2019
Breast cancer development
Anatomy of the Breast
Lymphatics

- Sappey’s plexus
  - >75% of lymphatic flow from breast into axillary lymph nodes
Breast cancer

95% of breast cancers originate in the epithelium of the ductal-lobular system.
Breast cancer subtypes

A population-based study of the tumor status of women diagnosed with breast cancer in the Atlanta, Georgia, metropolitan area yielded these incidence rates by broad subtype. ER indicates estrogen receptor; HER2, human epidermal growth factor receptor 2; PR, progesterone receptor; TNBC, triple-negative breast cancer.

Risk factors
BREAST CANCER RISK

- **Sporadic**: 70%
- **Familial**: 20%
- **Hereditary**: 10%
General risk factors

- Being female
- Older age
- Having a mutation in the BRCA1 or BRCA2 breast cancer genes
- Having a previous biopsy showing hyperplasia
- Lobular carcinoma in situ (LCIS)
- A family history of breast cancer
- Having high breast density on a mammogram
- Radiation exposure (woman with hx. HD)
- A personal history of breast or ovarian cancer starting menopause after age 55
- Never having children
- Having your first child after age 35
- High bone density
- Early menarche (age less than 12)
- Alcohol intake
- Obesity
Hereditary breast cancer

• BRCA-1 and -2
• Tumor suppressor genes
• Estimated lifetime risk for breast cancer is up to 85%
• BRCA 1 55-85% risk
  • Ovarian cancer (15-45%), colon cancer, prostate cancer
• BRCA 2 37-85%
  • Ovarian cancer (20-30%), pancreatic and laryngeal cancer, prostate cancer
• Increased risk of local recurrence as well as contralateral breast cancer
• Genetic counseling and testing
Next generation sequencing

- The first evidence for the existence of a gene encoding for a DNA repair enzyme involved in breast cancer susceptibility was provided by Mary-Claire King's laboratory at UC Berkeley in 1990.

Table 1. DNA-repair genes that increase breast cancer risk and are included in the BROCA capture oligo set.

<table>
<thead>
<tr>
<th>Gene</th>
<th>Syndrome</th>
<th>Biological pathway</th>
<th>Breast cancer risk</th>
<th>% of FBC**</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATM</td>
<td>Ataxia-telangiectasia</td>
<td>Base excision repair</td>
<td>2-5x</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>BARD1</td>
<td>Tumor suppressor with BRCA1</td>
<td>2-5x</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>BRCA1</td>
<td>BrOv syndrome</td>
<td>ds break &amp; nucl. excision repair</td>
<td>&gt;5x</td>
<td>20%</td>
</tr>
<tr>
<td>BRCA2</td>
<td>BrOv &amp; Fanconi anemia</td>
<td>ds break repair</td>
<td>&gt;5x</td>
<td>10%</td>
</tr>
<tr>
<td>BRIP1 (FANCJ)</td>
<td>Fanconi anemia</td>
<td>ds break repair</td>
<td>&gt;5x</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>CHEK2</td>
<td>Li-fraumeni</td>
<td>Nucleotide excision repair</td>
<td>2-5x</td>
<td>3%</td>
</tr>
<tr>
<td>MRE11</td>
<td>Nijmegen breakage synd.</td>
<td>MRN complex ds break repair</td>
<td>2-5x</td>
<td>2%</td>
</tr>
<tr>
<td>NBS1</td>
<td>Nijmegen breakage synd.</td>
<td>MRN complex ds break repair</td>
<td>2-5x</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>PALB2 (FANCN)</td>
<td>Fanconi anemia</td>
<td>DNA crosslink repair</td>
<td>2-5x</td>
<td>3%</td>
</tr>
<tr>
<td>PTEN</td>
<td>Cowden syndrome</td>
<td>Tumor suppressor of Rad51</td>
<td>&gt;5x</td>
<td>1%</td>
</tr>
<tr>
<td>RAD50</td>
<td>Nijmegen breakage synd.</td>
<td>MRN complex ds break repair</td>
<td>2-5x</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>RAD51</td>
<td>Fanconi anemia</td>
<td>ds break repair</td>
<td>&gt;5x</td>
<td>1%</td>
</tr>
<tr>
<td>STK11</td>
<td>Peutz-Jegher syndrome</td>
<td>Tumor suppressor</td>
<td>&gt;5x</td>
<td>1%</td>
</tr>
<tr>
<td>TP53</td>
<td>Li-Fraumeni syndrome</td>
<td>Nucleotide excision repair</td>
<td>&gt;5x</td>
<td>1%</td>
</tr>
</tbody>
</table>

**FBC = familial breast cancer

Total 50%
Breast density
mammographic density

- The main tissue types in breasts are adipose tissue and stromal tissue, which contains collagen.

- The ratio of fat to collagen determines density of the breast.
Mammographic density

Categories of percentage mammographic density estimated by radiologists

A=0. B=10%. C=25%. D=50%. E=75%. F=75%.

Breast density as a link?

- Women with greater than or equal to 75% breast density are at a four to six-fold greater risk of breast cancer compared to those with fatty breasts.


Legislation on breast density reporting

http://areyoudenseadvocacy.org/
Lifestyle factors
Alcohol, tobacco and breast cancer – collaborative reanalysis of individual data from 53 epidemiological studies, including 58 515 women with breast cancer and 95 067 women without the Disease

British Journal of Cancer (2002) 87, 1234 – 1245
Limit Alcohol

1 alcoholic beverage per day

Shufelt C, et al "Red versus white wine as a nutritional Aromatase inhibitor in premenopausal women"

*J Womens Health* 2011; DOI:10.1089/jwh.2011.3001
Obesity and breast cancer

- Increased body fat increases risk in that fat produces more estrogen.

**Relationship between obesity and breast cancer.** Principal mechanisms through which the obesity condition may promote breast cancer development and progression.

Adiposity and breast cancer risk in postmenopausal women: Results from the UK Biobank prospective cohort

Guo, et al. *Int J Cancer.* 2018

- 162,691 postmenopausal women in UK Biobank followed from 2006-2014
- The magnitude of risk greater in women who had been postmenopausal for 12 or more years
Prevention with screening
Secondary prevention in the form of mammographic screening is recognized as an important strategy for reducing mortality from breast cancer.

Mammography has been shown to reduce breast cancer mortality in women aged 50-69 years by as much as 30%.

Younger women, ages 40-49, have also been shown to benefit from mammography with reduced breast cancer mortality.

Loberg et al. Benefits and harms of mammography screening Breast Cancer Res. 2015; 17(1): 63
Survival rates from early detection

Breast cancer screening

• Tests can find breast cancer early, when it's most treatable
  • Clinical breast exam
  • Mammography screening
Recent Changes

NEW BREAST CANCER SCREENING GUIDELINES
AMERICAN CANCER SOCIETY

- Old:
  Begin annual mammograms at 40
- New:
  Begin annual mammograms at 45
  After 55, may choose every other year

New Breast Cancer Screening Guideline
for women with average risk

AGE 40
Talk with your doctor about when to begin screening.
Women should have the opportunity to begin screening if they choose.

AGE 45
Begin yearly mammograms by age 45.

AGE 55
Transition to mammograms every other year at age 55 or continue with annual mammography, depending on your preferences.

AGE 55+
Continue to have regular mammograms for as long as you're in good health.

Oeffinger KC et al, JAMA 2015
## Seeking Consensus on Mammograms

Some doctors are trying to reconcile various groups’ recommendations for what age women should start getting mammograms and how often.

<table>
<thead>
<tr>
<th></th>
<th>USPSTF*</th>
<th>ACOG**</th>
<th>American Cancer Society</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>40s</strong></td>
<td>No specific</td>
<td>Every year</td>
<td>45+ every year</td>
</tr>
<tr>
<td></td>
<td>recommendation</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>50-74</strong></td>
<td>Every two years</td>
<td>Every year</td>
<td>Every other year starting at 55</td>
</tr>
<tr>
<td><strong>75+</strong></td>
<td>No specific</td>
<td>No upper age limit</td>
<td>Every other year while life expectancy</td>
</tr>
<tr>
<td></td>
<td>recommendation</td>
<td>for screening</td>
<td>is 10 years or more</td>
</tr>
</tbody>
</table>

*U.S. Preventive Services Task Force
**American College of Obstetricians and Gynecologists
Controversies on screening

• Frequency
• Adopting advanced technology (i.e. 3D)
• Supplemental imaging
New technology

- Tomosynthesis (3D mammography)
- 4.1 cancers for every 1,000 patients vs. 2.9 cancers for every 1,000 patients with digital mammography alone. That’s a more than 35 percent improvement in detection!

Supplemental imaging?

- Ultrasound
Supplemental imaging?

- MRI
Current screening statistics
Percent of women aged 50-74 years who had mammography within the past 2 years. All Races, 1987-2015

Healthy People 2020 Target (81.1)

Stable
1998-2015
APC = -0.29

Rising
1987-1998
APC = 6.79*

Recent Trend
2010-2015
Stable
AAPC = -0.29

HP 2020 Target C-17: 81.1%
Source: Centers for Disease Control and Prevention, National Center for Health Statistics, National Health Interview Survey.
Data are age-adjusted to the 2000 US standard population using age groups: 50-64, 65-74. Weighted regression lines are calculated using the Joinpoint Regression Program, Version 4.3.1.0 April 2016, National Cancer Institute.
The AAPC is the Average Annual Percent Change and is based on the APCs calculated by Joinpoint.
* The Annual Percent Change (APC)/Average Annual Percent Change (AAPC) is statistically significant.
• A recent systematic review and meta-analysis of racial disparities in screening mammography shows that disparities in utilization of screening mammography are still evident in black and Hispanic populations in the U.S.

Barriers to mammography

- Poverty, lower education, worse health status, no insurance or absence of private insurance, not having a regular source of care, and fewer physician visits

- In addition, lack of knowledge of breast cancer and breast cancer screening, cultural beliefs/fatalism, bad experience from prior mammograms, and lack of social support

Komenka IK, JNCI 2010
Stanley S, J Public Health 2012
Conclusion

• To improve breast cancer outcomes in women we need to:
  • Stress prevention:
    • Follow screening guidelines
    • Healthy lifestyle
    • Increase awareness and education, with focus on black and Hispanic women who continue to have lower screening rates
Acknowledgements

• My mentor Dr. Lucile Adams Campbell- Director of Minority Health and Health Disparities

• Capital Breast Care Center