Controversies in breast cancer screening

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April 19, 2017
Objectives

• Ø Epidemiology of breast cancer
• Ø Genetics and breast cancer
• Ø Risk factors for breast cancer
• Ø Breast cancer screening as part of breast health
• Ø Screening options and the issue of dense breasts
<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Males 836,150</th>
<th>Females 852,630</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>19%</td>
<td></td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>14%</td>
<td>30%</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>9%</td>
<td>12%</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>7%</td>
<td></td>
</tr>
<tr>
<td>Melanoma of skin</td>
<td>6%</td>
<td>8%</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>5%</td>
<td>7%</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>Leukemia</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Oral cavity &amp; pharynx</td>
<td>4%</td>
<td>4%</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.
Statistics

• Breast cancer most common form of cancer for females
• Estimated that 178,480 females diagnosed
• 40,460 women will die in 2007
• 1 in 8 women diagnosed in their lifetime
• Every three minutes a female in U.S. diagnosed
Breast specific data

• Breast cancer is the most commonly diagnosed cancer in U.S. women (1/8)

• 2nd leading cause of cancer death

• In 2016, est. 246,660 new cases of invasive breast cancer are expected
  • 61,000 new cases of non-invasive (in situ)
  • 40,450 breast cancer deaths

• 1% of breast cancers are in men
Female Breast Cancer Incidence Rates* by State, 2009†
Breast cancer development
Anatomy of the Breast
Lymphatics

- Sappey’s plexus
- >75% of lymphatic flow from breast into axillary lymph nodes
95% of breast cancers originate in the epithelium of the ductal-lobular system.
Risk factors
BREAST CANCER RISK

- **Sporadic**: 70%
- **Familial**: 20%
- **Hereditary**: 10%
BRCA Genes

• 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></td>
<td>2-5x</td>
<td>3%</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-Jehner 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%
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)
- Obesity
Prevention with screening
Breast cancer screening

- Tests can find breast cancer early, when it's most treatable
  - Clinical breast exam
  - Mammography 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
• A Healthy People 2010 goal set by the U.S. Departments of Health and Human Services was at least 70% of women 40 and over to have received a mammogram within the last two years.

• Healthypeople.gov
The figure above is a line chart showing the percentage of adults up-to-date with screening for breast, cervical, and colorectal cancers by test, sex, and year, in the United States during 2000-2013.

Sabatino et al. MMWR / May8,2015 / Vol.64 / No.17
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

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

AGE 40
Talk with your doctor about
when to begin screening.

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.

LEARN MORE ABOUT BREAST CANCER SCREENING
# 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 recommendation</td>
<td>Every year</td>
<td>45+ every year</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 recommendation</td>
<td>No upper age limit for screening</td>
<td>Every other year while life expectancy is 10 years or more</td>
</tr>
</tbody>
</table>

*U.S. Preventive Services Task Force

**American College of Obstetricians and Gynecologists
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.
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
Mammographic density

Categories of percentage mammographic density estimated by radiologists
A=0. B=10%. C=25%. D=50%. E=75%. F=75%.
Legislation on breast density reporting

http://areyoudenseadvocacy.org/
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)

Rising 1987-1998
APC = 6.79*

Stable 1999-2007
APC = -0.29

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

- Emphasis should now be on addressing unacceptably low mammography utilization in certain subgroups within the black community

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