Breast cancer risk and prevention: the facts, the myths, and the gray areas in between

Emily Bellavance, MD MS

2017 New cases 252,710
1/8 chance
Lifetime risk 12.5%

2017 Deaths 40,610
From 1989 to 2015
Deaths decreased by 39%
322,600 averted deaths

Breast
Lung & bronchus
Colorectum
Urinary bladder
Metastatic melanoma of skin
Kidney & renal pelvis
Non-Hodgkin
lymphoma
Leukemia
One cavity & pharynx
Liver & intrahepatic bile duct
All other sites

2016 New cases 262,520

2016 Deaths 40,000
From 1989 to 2015
Deaths decreased by 36%
262,500 averted deaths

Breast
Lung & bronchus
Colorectum
Liver & intrahepatic bile duct
Leukemia
Non-Hodgkin lymphoma
Brain & other nervous system
All other sites

Five-year relative survival rates (%), 1975-2012

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>All sites</td>
<td>46</td>
<td>55</td>
<td>69</td>
</tr>
<tr>
<td>Breast (female)</td>
<td>72</td>
<td>84</td>
<td>91</td>
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<tr>
<td>Colorectum</td>
<td>50</td>
<td>59</td>
<td>66</td>
</tr>
<tr>
<td>Leukemia</td>
<td>34</td>
<td>43</td>
<td>63</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>12</td>
<td>13</td>
<td>19</td>
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<tr>
<td>Melanoma of the skin</td>
<td>50</td>
<td>88</td>
<td>93</td>
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<tr>
<td>Non-Hodgkin lymphoma</td>
<td>47</td>
<td>51</td>
<td>73</td>
</tr>
<tr>
<td>Ovary</td>
<td>36</td>
<td>38</td>
<td>46</td>
</tr>
<tr>
<td>Pancreas</td>
<td>3</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>Prostate</td>
<td>69</td>
<td>83</td>
<td>90</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>72</td>
<td>79</td>
<td>79</td>
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</tbody>
</table>
Breast Cancer Myths

• The most common cause of breast cancer is family history or a genetic mutation - MYTH

Risk Factors for Sporadic Breast Cancer

• Modifiable risk factors
  - Diet/obesity
  - Smoking
  - Alcohol
  - Activity level
  - Hormone replacement therapy

• Non-modifiable risk factors
  - Parity
  - Age
  - Gender
  - Age of menarche
  - Age of menopause
  - Breast density
  - Atypical or “high risk lesions”

Reproductive cycle and breast cancer

• Lifetime exposure to estrogen
  - Early menarche
  - Late menopause

• Timing of exposure to estrogen
  - Early menarche has a greater effect than late menopause
  - Late menopause effect is more pronounced in early menarche patients

• Age-dependent effects of estrogen on the mammary glands
  - Increased level of estrogen in pregnancy is beneficial at a young age and detrimental at older ages


58 studies
58,515 women with breast cancer
95,067 controls
↑ 5% for every year younger
≥ 13 years

≥ 13 years

Up to 18% RR ≥ 13 years
Reproductive cycle and breast cancer - menarche

- **WECARE STUDY**: Relative risk of breast cancer increases by 5% for each year younger at menarche
- Average age of menarche is 12 years (Historically older 16.5 yrs)
- 2-3 month decline in age of menarche per decade from 18th to 20th century in Europe and the US
- Factors influencing age of menarche
  - Gestational exposure - smoking, DES (diethylstilbestrol), pre-pregnancy diabetes, and pregnancy related hypertensive disorder.
  - Diet - ↑ energy intake, meats, polyunsaturated fats
  - BMI – genetic and environmental factors

Reproductive cycle and breast cancer - menopause

- Large-scale case control studies and meta-analysis consistently show that younger age at menopause decreases ER + breast cancer risk
- Each year older at menopause increases the risk by 3-4%
- Nurse's Health Studies
  - Prospective cohort studies of registered nurses in the US
  - 121,000 ages 30-55 years in 1976
  - 116,430 ages 25-52 years in 1989
  - Age at menopause associated with Luminal A and Luminal B cancers (4% per year increase) but not associated with basal-like tumors.

Reproductive cycle and breast cancer - pregnancy

- First birth < 35 years can decrease the risk of breast cancer by 50%
  - Does not apply to ER negative breast cancers
  - Evidence that early age of parity is associated with ER negative cancers
- Age of first birth > 35 years increases lifetime breast cancer risk above that of nulliparous women
- Reason is unclear
  - Number of menstrual cycles
  - Change in the hormonal profile of parous women
  - Mammary gland changes
- What about pregnancies that do not come to term?

Reproductive cycle and breast cancer – the myths

- Protective effect of parity is associated with term pregnancies
  - Spontaneous or induced abortions DO NOT increase a woman's risk of breast cancer
  - Studies previously reporting an increased risk with termination were retrospective after breast cancer diagnosis – women with breast cancer more likely to report terminations that counterparts
  - More recent studies with prospectively collected data consistently show not association between induced termination and elevated breast cancer risk
- But induced terminations ALSO do not have the protective effect of a full term pregnancy
Reproductive cycle and breast cancer

- Birth Control
- Data is inconsistent
- Collaborative Group on Hormonal Factors in Breast Cancer
  - Current OCP and recent use (not long term use) is associated with a small increased risk (RR = 1.24) and disappears within 10 years of stopping
  - RR increased when started < 20 years
  - Attributable breast cancer cases in USA and Europe per 10,000 women within 10 years of stopping OCP is 0.5
  - Associated with better prognosis
- Nurses Health Group – no increased risk for whole population/ > 10 year use/ women < 45 years

Breast cancer risk – contraception

- Data on OCP’s and breast cancer risk is conflicting
- High dose oral contraception may mildly increase risk of breast cancer if started at a young age
- Modern oral contraception is unlikely to increase risk
- In patients with a BRCA mutation, there may be a mildly increased relative risk of breast cancer
- However, the decreased risk of ovarian cancer risk with OCP’s far outweighs the possible increase breast cancer risk

Exposure to exogenous estrogen – HRT

- Randomized controlled trial comparing post menopausal hormone replacement with combined estrogen/progesterone with placebo (50-79 years)
- Do the benefits outweigh the risks?
- Planned duration 8.5 years
- Stopped at 5.2 years
Exposure to exogenous estrogen - HRT

- CHD: 1.29 (1.02-1.63) with 286 cases
- Breast cancer: 1.26 (1.00-1.59) with 290 cases
- Stroke: 1.41 (1.07-1.85) with 212 cases
- Pulmonary embolism: 2.13 (1.39-3.25) with 101 cases
- Colorectal cancer: 0.63 (0.43-0.92) with 112 cases
- Endometrial cancer: 0.83 (0.47-1.47) with 47 cases
- Hip fracture: 0.66 (0.45-0.98) with 106 cases

8 year follow up

Similar histology and grade

More likely to be node-positive 34% vs 16%

Chebowski et al. JAMA 2010

Exposure to exogenous estrogen - HRT

- All cause mortality in P+E group with 18 year follow up was the same (26 and 26.4%)
- With 18 year follow up breast cancer specific morality for P + E group was not significantly increased but higher (HR 1.44)
- WHI Estrogen alone for 7.2 years – no increased breast cancer risk
- Early menopause HRT?

Manson et al. JAMA 2017

Exposure to exogenous estrogen – HRT

- HRT is effective treatment for the vasomotor symptoms and genitourinary symptoms of menopause
- Estrogen + Progesterone hormone replacement therapy increases breast cancer risk
- With long term follow up breast cancer specific mortality is not increased
- Estrogen alone has no effect on breast cancer risk
- Conversation about HRT usually prioritizes effects on specific diseases rather than long term risks and benefits as a whole
- Recommendations need to be individualized based on the benefit risk ratio of each patient and patient’s values

Breast Cancer Risk – The VICES
Breast cancer risk – the Vices

• Smoking

Relative risk of breast cancer incidence in function of the duration of ever actively smoking (in years) among 12 studies with prospective designs.

Breast cancer risk – smoking

• Smoking has both carcinogenic and anti-estrogenic properties
• Associations were stronger when smoking started early
  • Danish nurse cohort study 21,831 women
  • 18% higher in ever smokers 27% higher in current smokers
  • Dose response relationship (> 20 pack years RR 1.32)
  • Highest in heavy smokers prior to 1st birth (RR 1.58)
  • Risk not modified by menopausal status, obesity, E2OH or HRT
  • Evidence of increased risk with passive smoke exposure (less robust)

Breast cancer Risk – The Vices

• 58,515 women with breast cancer
• 95,067 controls
• 58 studies
• Estimated cumulative incidence of breast cancer per 100 women in developed countries, according to the number of alcoholic drinks consumed each day
  • 7 Light alcohol intake (<1 drink/day)

Breast cancer – Obesity

• Obesity
  • Body mass index = weight (kg)/height(m²)
  • Overweight = 25-29.9
  • Obesity = > 30
  • Premenopausal obesity is associated with a modest decrease in breast cancer risk
  • Obesity is a risk factor for post-menopausal cancer
    • ↑ with time from menopause
    • Associate with upper body obesity
    • Nurses Health Study higher waist to hip ratio increased breast cancer risk (no HRT)
  • > 20kg in adult life doubles postmenopausal breast cancer risk

Estrogen and Adipose Tissue

Breast cancer - obesity

• Reversal of weight gain can reduce the breast cancer risk
  • Iowa Women’s Health Study based on 34 000 women
    • Maintaining ≥5% weight loss reduced post-menopausal breast cancer risk by approximately 20%
  • Nurse’s Health Cohort Study
    • Weight loss after menopause decreases breast cancer risk in no HRT
    • > 10 kg weight loss since menopause RR 0.43
  • Increase in physical activity can decrease breast cancer risk 25-30%
  • Normal and overweight BMI

Collaborative Group in Hormonal Factors in Breast Cancer British J of Med 2002

Rose and Davis Maturitas 2010

Howell et al. Cancer Epidemiol Biomarkers Prev 2005

Eliassen et al. JAMA 2006.
High risk lesions

- Atypical ductal hyperplasia
  - Epithelial proliferative lesion of the duct
  - Risk of "upgraded" pathology on excision is 15-30%

- Atypical lobular hyperplasia
  - ALH is a proliferation of atypical epithelial cells of terminal lobules that appear as small round cells that lack cohesion due to the loss of E-cadherin and cause distention of the acinar spaces (Hartmann 2015).
  - ALH and LCIS are distinguished by the degree of lobular involvement, with distortion of <50% of involved lobular acinar spaces categorized as ALH and >50% as LCIS.
  - Published upgrade rates for excision of ALH varied widely, from 0-43%

- Lobular carcinoma in situ
  - Epithelial proliferative lesion in the Lobular unit
  - Increased risk of developing a breast Cancer (invasive lobular, DCIS, or invasive ductal in either breast 0.7 % per year)
  - Risk of upgraded pathology is 4-20%
  - Surgical excision is controversial

Breast cancer risk “high risk breast lesions”

- Confer an increased risk of developing breast cancer
- Also associated with atypia/DCIS/invasive cancer on excisional biopsy
  - Atypical ductal hyperplasia
  - Atypical lobular hyperplasia
  - Lobular carcinoma in situ
  - Flat epithelial atypia
  - Intraductal papilloma (multiple ATYPICAL papillomas ↑ risk of developing breast cancer)
  - Complex sclerosing lesion/Radial scar

Tamoxifen can reduce risk of breast cancer by 86%

- ATYPICAL LOBULAR HYPERPLASIA

  - ALH is a proliferation of atypical epithelial cells of terminal lobules that appear as small round cells that lack cohesion due to the loss of E-cadherin and cause distention of the acinar spaces (Hartmann 2015).
  - ALH and LCIS are distinguished by the degree of lobular involvement, with distortion of <50% of involved lobular acinar spaces categorized as ALH and >50% as LCIS.
  - Published upgrade rates for excision of ALH varied widely, from 0-43%

Tamoxifen can reduce risk of breast cancer by 50%

Pleomorphic LCIS re-evaluated and found to have invasive lobular carcinoma
High risk lesions

<table>
<thead>
<tr>
<th>Histologic Finding</th>
<th>Relative Risk</th>
<th>Absolute Risk</th>
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<tbody>
<tr>
<td>Normal (age 30 years)</td>
<td>1</td>
<td>1% by age 90y of age</td>
</tr>
<tr>
<td>FTA</td>
<td>1.5 (age increased)</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Phyllodes tumors</td>
<td>&lt;2</td>
<td>&lt;12% at 29y</td>
</tr>
<tr>
<td>Phyllodes tumor</td>
<td>&lt;2</td>
<td>&lt;12% at 29y</td>
</tr>
<tr>
<td>AH or ALH</td>
<td>&lt;6</td>
<td>&lt;1% per y</td>
</tr>
<tr>
<td>LID</td>
<td>&lt;10</td>
<td>&gt;20%-25% at 29y</td>
</tr>
</tbody>
</table>

Degirmen Surg Clin N America 2013

High risk histology

800 women with benign breast disease 40 years follow up

AH = atypical lobular hyperplasia
ALH = atypical ductal hyperplasia

Hartmann et al. NEJM 2003

Risk Reduction

- The use of hormonal therapy has been shown to reduce the incidence of breast cancer in women with increased risk.
- Selective Estrogen Receptor Modulators (SERM)
- Aromatase Inhibitors

Selective Estrogen Receptor Modulators (SERM)

- **Agents**
  - Tamoxifen
  - Raloxifene

- **Mechanism of action**
  - Competitive inhibitor of estrogen receptors on breast tissue

- **Indications**
  - Premenopausal women at increased risk of breast cancer (tamoxifen only)
  - Post menopausal women at increased risk of breast cancer

- **Side effects**
  - Vasomotor symptoms
  - Venous thromboembolic (VTE) events
  - Increased bone density
  - Tamoxifen (not raloxifene) increases the risk of endometrial cancer

Breast Cancer Prevention Trial

**NSABP – P1**

- 13,388 women > 35 years
  - Estimated 5 year risk of developing breast cancer ≥ 1.66%
- 20 mg Tamoxifen versus placebo
- Stopped after average of 4 years
- Median follow up 55 months
- 50% Reduction in invasive and non-invasive cancer

Fisher JNCI 1998

SERM TRIALS

<table>
<thead>
<tr>
<th>Trial</th>
<th>Agent</th>
<th>FU</th>
<th>HR</th>
<th>CI</th>
<th>ER</th>
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<tr>
<td>Royal Marsden</td>
<td>TAM</td>
<td>20y</td>
<td>0.48</td>
<td>0.29-0.79</td>
<td>ER+</td>
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<tr>
<td>IBIS-1</td>
<td>TAM</td>
<td>36y</td>
<td>0.71</td>
<td>0.60-0.83</td>
<td>0.66 (HR+)</td>
</tr>
<tr>
<td>IBIS-P-21</td>
<td>TAM</td>
<td>5y</td>
<td>1.02</td>
<td>0.82-1.28</td>
<td></td>
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<tr>
<td>MORE</td>
<td>RAL</td>
<td>3y</td>
<td>0.24</td>
<td>0.13-0.44</td>
<td></td>
</tr>
<tr>
<td>Italian</td>
<td>TAM</td>
<td>5y</td>
<td>0.34</td>
<td>0.19-0.58</td>
<td></td>
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</table>
Breast cancer risk – breast density

- Density is associated with other risk factors
  - Pregnancy decreases breast density
  - Larger number of live births associated with decreased density
  - Inversely associated with body weight
  - Decreases with increasing age
  - Estrogen with progestin therapy increases breast density
  - Estrogen alone does not increase density

Breast cancer risk – breast density

- Breast density – mammographic finding of connective and epithelial tissues in the breast (white)
- Percentage of breast area comprised of these tissues = breast density
- Breast density has been shown to be associated with breast cancer risk
  - Association is stronger in asymptomatic versus symptomatic women
  - Stronger in incident versus prevalent cancer populations
  - Did not differ by age, menopausal status, or ethnicity
  - Can not be explained by the “masking” of cancers by dense tissue

Breast cancer risk – breast density

- Breast Density Awareness Bill 2013

  **This notice contains the results of your recent mammograms, including information about breast density.**

  If your mammogram shows that your breast tissue is dense, you should know that dense breast tissue is a common finding and is not abnormal, with about half of women having dense or highly dense breasts. However, dense breast tissue can make it harder to detect cancer on a mammogram and may also be associated with an increased risk of cancer. This information is given to raise your awareness and to inform your conversation with your physician. Together, you can decide which screening options are right for you based on your mammogram results, individual risk factors, or physical examination.

  A report of your results was sent to your physician.
Digital Breast Tomosynthesis

**Increase Cancer Detection**
- > 40-53% increase in cancer detection
- > 115% increase in positive predictive value

**Decrease Recall**
- 15-37% decrease in recall
- Decrease patient anxiety

**Cost Benefits**
- Better monetary benefit for screening 3D versus 2D mammograms
- Cost savings related to decrease recalls and biopsies

**Same Radiation Dose**
- Similar radiation dose with synthesized 2D images

**HB 675 – Health Insurance Coverage for Digital Tomosynthesis**

Establishing that a specified coverage requirement that applies to specified insurers, nonprofit health service plans, and health maintenance organizations includes coverage for digital tomosynthesis, a radiologic breast cancer screening procedure, under specified circumstances; prohibiting a copayment or coinsurance requirement that is greater than for other breast cancer screenings.

**Family History and Genetic mutations**

**Features of Hereditary Breast & Ovarian Cancer (HBOC)**
- Early age at diagnosis
- Multiple cases of breast cancer in the same genetic lineage, particularly at a young age
- Presence of breast and ovarian cancer on the same side of the family
- Male breast cancer
- Bilateral breast cancer
- Ashkenazi Jewish heritage
BRCA1 and BRCA2

- BR east Cancer-1 / BR east Cancer-2
- Autosomal Dominant
  - 50% chance of inheritance to first degree relatives (sisters, offspring)
  - Incomplete penetrance
- Tumor Suppressor Genes
  - 2-hit hypothesis
  - Role in DNA repair

Low Risk Category
- Non-Jewish family
- BRCApro estimate = 2.5%

Moderate Risk Category
- Non-Jewish family
- BRCApro estimate = 22%

High Risk Category
- Non-Jewish family
- BRCApro estimate = 85%

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>BRCA1</th>
<th>BRCA2</th>
<th>General Population</th>
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<tbody>
<tr>
<td>Breast</td>
<td>55-85%</td>
<td>55-85%</td>
<td>10-13%</td>
</tr>
<tr>
<td>Contralateral</td>
<td>Up to 60%</td>
<td>Up to 50%</td>
<td></td>
</tr>
<tr>
<td>Ovarian</td>
<td>25-40%</td>
<td>Up to 27%</td>
<td>1.5%</td>
</tr>
<tr>
<td>Prostate</td>
<td>20-30%</td>
<td>20-30%</td>
<td>15%</td>
</tr>
<tr>
<td>Male Breast</td>
<td>Increased</td>
<td>Increased</td>
<td>0.10%</td>
</tr>
<tr>
<td>Colon</td>
<td>Possible Inc. Risk</td>
<td>Possible Inc. Risk</td>
<td>6%</td>
</tr>
<tr>
<td>Pancreatic</td>
<td>2-5%</td>
<td>2-5%</td>
<td>1.3%</td>
</tr>
<tr>
<td>Others</td>
<td>Uterine, Cervical</td>
<td>Gallbladder, Stomach, Melanoma</td>
<td></td>
</tr>
</tbody>
</table>

Other High Risk Breast Cancer Genes

<table>
<thead>
<tr>
<th>Gene</th>
<th>Prevalence</th>
<th>Breast Cancer Risk</th>
<th>Other cancers</th>
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</thead>
<tbody>
<tr>
<td>BRCA1</td>
<td>1/5000-20,000</td>
<td>30%</td>
<td>Sarcoma, brain, leukemia, colon, childhood</td>
</tr>
<tr>
<td>BRCA2</td>
<td>1/200,000</td>
<td>40-50%</td>
<td>Uterine, thyroid, colon</td>
</tr>
<tr>
<td>PTEN</td>
<td>1/60,000-300,000</td>
<td>50%</td>
<td>Colon, ovarian</td>
</tr>
<tr>
<td>STK11</td>
<td>1/100,000-300,000</td>
<td>30-40%</td>
<td>Gastric (60-80%)</td>
</tr>
<tr>
<td>ATM</td>
<td>1/60,000</td>
<td>15-20%</td>
<td>Lymphoid cancers</td>
</tr>
<tr>
<td>CHK2</td>
<td>&lt; 1/100</td>
<td>20-45%</td>
<td>Thyroid, colon</td>
</tr>
<tr>
<td>PALB2</td>
<td>1/1000</td>
<td>30-60%</td>
<td>Pancreatic, Male breast (?)</td>
</tr>
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</table>
Genetic Testing Considerations

**Benefits**
- Clarify future cancer risks
- Provide information for at-risk family members
- Provide sense of relief / understanding
- Consideration of risk-reducing management options
- Assist with decision making for the newly diagnosed

**Risks / Disadvantages**
- Limitations of negative test result
- May cause anxiety, depression, anger, guilt...
- Stress to family dynamics
- Survivor guilt
- Efficacy of screening and risk-reduction options unclear
- Insurance Concerns

Legislative Update

- HIPAA (1996)
  - Health Insurance Portability & Accountability Act
- GINA (2008)
  - Genetic Information Nondiscrimination Act

Why is genetic counseling essential?

- Provides accurate risk assessment
- In-depth meeting to discuss pros and cons of testing and management options
- Help patient decide if testing is right for her/him
- Assist patient in talking to family members about important health topics
- Ensures most up to date testing

Genetic Counseling

- Review of cancer genetic risk assessment studies showed overall:
  - Reduction in distress
  - Improved accuracy of perceived risk
  - Improved knowledge of cancer genetics
  - In person and telemedicine counseling options available

Breast Cancer Screening for genetic carriers and very high risk patients (> 20%)

- Monthly self breast exam
- Clinical breast exam, 2-4x/year, beginning ~25-35
- Annual mammography, beginning 30 yrs.
- Annual Breast MRI beginning at 25 years


- "Strongly recommends that genetic testing be done only in the setting of pre and post test counseling, which should include discussion of possible risks and benefits of cancer early detection and prevention modalities"
- Responsibility of the clinical oncologist to identify individuals and families who may have a hereditary risk for cancer


Burke et al. JAMA 1997, 277:997
Saslow et al. CA Cancer J Clin 2007; 57:75-89
Recommendations for Breast MRI Screening

- BRCA1/BRCA2 mutation/high risk mutation
- First degree relative of BRCA/high risk gene carrier, but untested
- Lifetime breast cancer risk of 20-25% or greater, based upon appropriate risk assessment model (BRCApro, Claus)

Breast Cancer Risk-Reduction Options

- Chemoprevention
  - Limited data regarding tamoxifen and primary prevention
  - NSABP P-1 re-examined patients with known BRCA mutation
  - 62% reduction in BRCA-2 patients
  - No reduction in BRCA-1 patients

- Prophylactic Bilateral Mastectomy
  - Retrospective and prospective data shows risk reduction over 90%

Bilateral prophylactic mastectomy

- Simple mastectomy – breast and overlying skin
- Skin sparing mastectomy – breast tissue/nipple/areola
- Nipple sparing mastectomy – breast tissue

Nipple Sparing Mastectomy

- Nipple sparing mastectomy first reported by Freeman and colleagues in 1962 for treatment of benign breast lesions

Prophylactic Nipple Sparing Mastectomy

- Hartmann et al. NEJM 1999
  - Retrospective study of all women with a FH of breast ca undergoing bilateral prophylactic mastectomy (1980-1991)
  - High risk and moderate risk groups
  - Control study of sisters of high-risk probands and the Gail model used to predict the number of expected breast cancers
  - 639 women
    - 214 high risk
    - 425 moderate risk
    - Median length of follow up 14 years
    - 90% patients underwent subcutaneous mastectomies
    - >90% risk reduction for the development of breast cancer
    - Of the 7 patients BC, 1 in NAC complex (0.2%)
Nipple Sparing Mastectomy

Risk reduction with prophylactic surgery – the data

- The PROSE Study Group
  - All women with disease-associated BRCA 1 or 2 mutations studied for the occurrence of breast cancer
  - Carriers who underwent bilateral prophylactic mastectomy vs. carriers with no history of BPM matched to gene, center, age
  - Previous or concurrent breast cancer patients excluded

- Risk reduction:
  - 90% risk reduction with intact ovaries
  - 95% risk reduction prior to or concurrent with PBSO

- Reoperation: 1 recurrence in axilla
- 1 in “substantial residual breast tissue”

Nipple Sparing Mastectomy in BRCA

- Risk reduction in BRCA1 and BRCA2 patients
  - Of the 176/214 high-risk women
    - 26 women with BRCA1 or BRCA2
    - 8 deleterious
    - 8 uncertain significance
    - None developed breast cancer after a median of 13.4 years
  - 3/214 known to develop breast cancer
    - 2 known BRCA1/2 negative
    - 1 blood sample not available
    - 1/3 in nipple
Bilateral Mastectomy

- Important considerations
  - Psychosocial effects
    - Majority of women satisfied with decision
  - Loss of sensation
  - Rarely can result in chronic pain
  - "Phantom breast" sensation
  - Not an urgent procedure
    - Encourage patients to speak with others who have undergone procedure
    - Review pictures of reconstruction (all pictures)

Male breast cancer

- Overall 1:100,000
- BRCA +
  - 7% lifetime risk
  - Screening mammogram
- Possible PALB-2
- Klinefelter’s syndrome (47XXY)
- Estrogen exposure
- Transgender 4:100,000

Conclusions

- Estrogen exposure is related to breast cancer risk – the relationship is complex and is likely related to multiple factors including the timing of exposure and age-dependent effects of estrogen on the mammary glands.
- Contraception does not appear to increase risk of breast cancer
- Spontaneous and induced abortions do not increase risk of breast cancer
- Decisions regarding hormone replacement and breast cancer risk need to be made on an individual basis
- More research on preventing triple negative breast cancers and cancers in women with high risk genetic mutations with non-surgical options.

Conclusions

- Know your family history
- See a genetics counselor/Breast specialist

Estimated Cancer Deaths in the US in 2017

- Don’t smoke
- Drink in moderation
- Try not to gain weight
- Stay active

Males 318,420 Females 282,500

- Lung & bronchus 27%
- Lung & bronchus 25%
- Breast 14%
- Colon & rectum 8%
- Pancreas 7%
- Ovary 5%
- Uterine corpus 4%
- Leukemia 4%
- Liver & intrahepatic bile duct 3%
- Non-Hodgkin lymphoma 3%
- Brain & other nervous 3%
- Brain & other nervous 3%
Conclusions