Male Breast Cancer Surgery

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Disclosure

- There are no conflicts of interest or relevant financial interests in making this presentation and indicated that my presentation does not include discussion of an unlabeled use of a commercial product, or an investigational use not yet approved for any purpose.

Objectives

- Describe risk factors for male breast cancer
- Understand the genetic implications for male breast cancer
- Discuss surgical treatment options for male breast cancer

Male breast cancer

- 1% of all breast cancers occur in men
- Incidence of invasive breast cancer 1.1 : 100,000 (female 126 :100,000)
- Somewhat higher rates in African-American men
- Median age at initial diagnosis is 68 y/o (female 62 y/o)
- In both male and female, age-adjusted rate of BC increases by 5th decade of life.
- Plateaus in woman by 6th decade but continues to rise in men through 7th decade of life.

Gucalp et al. 2019.
Howlader et al. 2017.

Characteristics of male breast cancer (BC)

- Male BC diagnosed at later stage. More likely node positive and/or metastatic disease (50 %). In contrast 2/3 of woman present with localized disease at presentation.
- 90% of male BC is invasive ductal (rare to have invasive lobular or triple negative)
- Male BC express estrogen receptors (80-100%), progesterone receptor and androgen receptor (AR)
- Nipple retraction and palpable mass is a common physical exam finding.

SEER Explorer 2018.

Genetic alteration in male breast cancer

- Family history of BC increases the risk of male BC
- 20% of men with BC have a 1st degree relative with BC. Risk of male BC increases 5 fold when the number of relatives increases.
- 4%-40% of male BC have inherited germline mutations
- BRCA 2 gene mutation most common (5-10% risk of developing BC), 1-5% risk for BRCA 1 gene mutation carriers.
- Mutations in CHEK2 and PALB2 are also associated with male BC

Cardoso et al 2018

Risk factors for male breast cancer

- Age
- Radiation exposure, occupation, alcohol consumption
- Klinefelter's syndrome (genetic condition with extra X Chromosome/altered balance of androgens and estrogens and gonadotrophins) increases male BC risk 50-fold.
- Use of exogenous estrogens
  - Estrogen treatment of prostate cancer
  - Hormone therapy for male-to-female transexuals

Cardoso et al 2018

Risk factors for male breast cancer

- Other causes of hyperestrogenization linked to increased BC risk in men include:
  - Obesity
  - Cirrhosis
  - Mumps orchitis
  - Undescended testes or testicular injury

Table 1. Risk factors for breast cancer in men

Age [80, 127, 135, 220–222]
Genetic factors
Well-established
Family history [8–14]
BRCA2 >> BRCA1 [15–33]
Possible
PALB2 [36, 39, 42, 44]
Androgen receptor [40, 43]
CYP17 [41]
CHEK2 [35, 37, 38]
Conditions associated with an abnormal estrogen-to-androgen ratio
Klinefelter's syndrome [48, 49]
Exogenous estrogen or testosterone use [50, 56]
Obesity [9, 10, 49, 51–53]
Orchitis/epididymitis [49]
Finasteride [54, 55]
Lifestyle
Lack of exercise [8]
Exposures
Well-established
Radiation [223, 224]
Possible
Electromagnetic fields [64, 65]
Heat [66]
Volatile organic compounds (e.g. tetrachloroethylene, perchloroethylene, trichloroethylene, dichloroethylene, and benzene) chemicals [67–69]
Miscellaneous possible risk factors
Birth order (possible higher risk in first borns) [225]
Bone fracture after age 45 [8]

Ruddy et al. 2013.

Surgical treatment of male breast cancer

- General approach similar to that of women based on TMN staging
  - Mastectomy + sentinel lymph node biopsy
  - Lumpectomy + sentinel lymph node biopsy + radiation
  - Same considerations for neoadjuvant systemic therapy
- Male patients who had cancer in a sentinel node were more likely to have additional cancer containing axillary lymph nodes than female patients with cancer in a sentinel node (63% vs 21%).

Boughey et al. Comparative Analysis of sentinel lymph node operation in male and female breast cancer patients. J Am Coll Surg 2006;203(4):475-480.

Surgical treatment of male breast cancer

- More often mastectomy, although all surgical approaches are possible. Approximately 10-15 % treated with breast conserving surgery per SEER database.
  - Special considerations:
    - Size of tumor relative to breast size/male anatomy
    - A SEER database study found that only 9% of male breast cancer is DCIS
    - Skin/nipple involvement. Majority of male BC develops centrally and involves the nipple
- There is similar cancer-specific survival and overall survival in men treated with lumpectomy/radiation or with mastectomy.

Anderson et al. 2005.
Cloyd et al. 2013.


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Surgical treatment of male breast cancer

- Reconstruction
  - Usually used to achieve skin closure after mastectomy
  - TRAM flaps not only replace skin and fat but also provides hair bearing cover similar to the normal male breast skin
  - Latissimus dorsi flap
    - The reduction in shoulder function may be unacceptable
- Contralateral mastectomy or reduction mammoplasty for those men with gynecomastia is an option

Table 1 Morbidity after surgery for MBC (Fogh et al. [37])

Procedure	Lymphoedema	Shoulder restriction
MRM ($n=30$)	7 (23%)	8 (27%)
TM ($n=4$)	0	2 (50%)
BCS ($n=8$)	0	0

Fentiman 2018.

Survivorship issues

- Failure to follow through with adjuvant Radiation Therapy
  - Data from the International Male Breast Cancer Program
    - Radiation Therapy was not delivered to 45% treated with BCS (regardless of node status)
    - Radiation Therapy was not delivered to 30.7 % with node positive tumors treated with mastectomy
- Men often experience bothersome symptoms from endocrine therapy and most men discontinue it early due to hot flashes or sexual dysfunction.
  - Xu et al reported a cohort of 116 male BC patients with ER+ disease. After 1 year only 65% were still taking Tamoxifen, 46% after 2 years, 29% at 3 years, 26 % at 4 years and only 18% in the final year.
  - The 10 year disease-free survival of the compliant patients was 96% compared with 42% of the non-compliers.

Xu et al. 2012.

Survivorship issues

- Optimal surveillance strategies are uncertain in male breast cancer survivors.
  - Risk of a new second primary breast cancer is just under 2 % in a male breast cancer survivor. No screening mammogram for surveillance. Some may consider annual mammography of remaining breast tissue (surveillance for local recurrence).
  - Men with a history of breast cancer are at elevated risk for developing a different non-breast cancer—that risk elevated for new primary cancer of the prostate (26.7%), colorectal (11.6%), lung (10.7%), and non-melanoma skin cancer (8.9%).

Hemminki et al. 2005.
Cardoso et al. 2017.

Poorer Overall Survival

- Present with later stage disease
  - No screening
  - Lack of suspicion
- Greater comorbidity
  - Prostate cancer
  - Metabolic syndrome
  - Older (median age 68)
- Somewhat more aggressive biologically
  - SEER database (2010-2013)- of 1388 men with ER+/HER 2- BC, 25% had GHI RS reported. 21% had high risk RS compared with 14% of women.

Altman AM et al. Ann Surg Oncol 2018: 25: 2296-2302.

Conclusion

- Surgical treatment of male breast cancer managed in a similar way to BC in woman based on TNM staging
- Reconstruction is an option
- All men with BC should have genetic counseling and germline testing
- Follow up after treatment for breast cancer in men: Screening mammography not required in these men by 2020 NCCN guidelines. ? consideration for ipsilateral annual mammogram for men with breast conserving surgery and contralateral annual mammogram if history of BC and germline mutation.

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