



# Breast cancer and its impact in male transsexuals

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## Abstract

**Introduction** Lesbian, gay, and bisexuals have unique healthcare needs. Breast cancer is leading cancer in women, worldwide, accounting for 25% of all cases. Annual incidence rates increased significantly in all countries and age groups. The occurrence of breast cancer is rare in transgender population. As they have very limited access to medical care, it is much less likely to pursue breast cancer screening than in other individuals not identified as transgender.

**Review of the cases from literature** Up to date, only 13 cases of the breast cancer transsexuals (female to male) have been reported in six published papers worldwide. Histological examination of the breast tumor in female-to-male transgender showed progesterone/estrogen-positive invasive ductal carcinoma.

**Discussion** Gender identity describes a person's inherent sense of being a woman, man, or of neither gender, whereas sexual orientation refers to how people identify their physical and emotional attraction to others. Gender reassignment surgery, a series of complex surgical genital and non-genital procedures, is recognized as the most effective treatment for patients with gender dysphoria. The two main principles of hormone therapy for transgender patients are to reduce endogenous hormone levels and their associated sex characteristics and replace them with hormones of the preferred sex. Breast cancer infrequently occurs in transgender patients. Even breast core biopsies can be difficult for interpreting after changes in breast tissue in female-to-male transsexuals following gender reassignment.

**Conclusion** Reviewing the literature, so many different data concerning probability of breast cancer in sexual minority can be found. Breast cancer screening program should be offered to all transgender individuals according to national guidelines. Very important is to take into consideration a transgender person's natal and surgical anatomy, unique clinical concerns for depression and anxiety, risk of suicide together with risk factors including experiences of harassment or physical or sexual violence, low education level, and unemployment. Understanding the need for mammography in these often marginalized groups is very important in addressing breast cancer disparities despite differences in insurance coverage in some countries and greater concern for the cancer of the breast in residual breast tissue. The best screening rule, ever, for breast cancer in male transsexuals and other similar population should be, besides surgical history and hormonal status, "Screen Now, Screen Regularly and Screen What You Have."

**Keywords** Breast cancer · Transsexualism · Screening · Mammography

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## Introduction

Lesbian, gay, bisexual population—approximately 9 million people in the United States, and transgender—700,000 adults, (LGBT) people have unique healthcare needs [1]. Breast cancer is leading cancer in women, accounting for 25% of all cases worldwide. It resulted in 1.68 million of new cases and 522,000 deaths [2]. It is more common in developed countries [3] and more than 100 times common in women than in men [4, 5]. Annual incidence rates increased significantly in all countries and age groups. Mortality rates

decreased significantly in all age groups in most countries, but increased up to 5% annually above the age of 55 in Ukraine, Serbia, Moldova, and Cyprus [6]. The incidence of breast carcinoma after prophylactic mastectomy is probably less than 2% [3, 7]. Breast cancer can be found in residual mammary tissue after breast ablation [8], and therefore skin sparing mastectomy should be avoided in patients during sex reassignment surgery [9].

The occurrence of the breast cancer is rare in transgender population. Mastectomy and sex reassignment surgery allow female-to-male (FtM) transsexuals to live as their desired sex. If they are testosterone treated, the future prospect of breast cancer without breast tissue seems to be with a very small chance to get the breast cancer [10]. There are no formal recommendations for surgery selection in this population [11] in spite of the studies which estimated that this cohort includes more than 0.5% of the population and is rapidly growing [12, 13]. Transgender (TG) veterans do not display an increase in breast cancer incidence greater than in general population [14]. As they have very limited access to medical care, it is much less likely to pursue breast cancer screening than in other individuals who are not identified as transgender [15].

## Review of the cases from the literature

Up to date, only 13 worldwide cases with breast cancer in FtM transsexuals have been reported in six published paper [3, 10, 14, 16–18].

In paper published by Burcombe, in 2003, FtM transsexual aged 33 developed breast cancer 10 years after bilateral prophylactic mastectomy [16]. Tumor was invasive ductal carcinoma 11 mm, grade I, 0/13 lymph nodes, ER positive, and PR positive, infiltrating the underlying pectoralis muscle.

Shao in 2011 described two cases of patients with breast cancer who did not go through the whole process of transgender surgery including bilateral prophylactic mastectomy. Both patients underwent bilateral mastectomy with sentinel lymph node biopsy. In one case, just after breast cancer was revealed and SLNB was positive, axillary dissection was done [17]. Patient, 48 years old, was diagnosed with invasive ductal carcinoma 9 mm, grade II, negative SLN. ER was 90% positive, PR was negative, and HER 2 was 3+ positive. His test was negative for BRCA mutations. Family history was positive. After surgery and post adjuvant therapy he was free of recurrence for 2 years. The second patient was 27 years old with invasive ductal carcinoma 25 mm, grade III, 1 positive of 14 lymph nodes after left axillary lymph node dissection. ER was positive 90%, PR was 10% positive, and HER 2 was 3+. Staging positron emission tomography

showed no evidence of metastatic disease. His test was negative for BRCA mutations.

Gooren notes that out of 795 FtM patients, only one case of breast cancer was confirmed. Routine histological examination of the left breast showed an ER+/PR+ tubular adenocarcinoma, grade 1, with a diameter of 9 mm. The follow-up was event-free [18].

Nine-year follow-up study of 473 patients with one-stage gender reassignment surgery (GRS) in female-to-male transsexuals (FtM) in Serbia showed only one case with breast carcinoma in the postoperative period [3, 19]. Nikolic et al., in 2012, showed the importance of precise preoperative and postoperative diagnostics and hormonal monitoring, besides gender reassignment surgery (total abdominal hysterectomy with bilateral salpingo-oophorectomy, colpocleisis, metoidioplasty, phalloplasty, urethroplasty with scrotoplasty and perineoplasty) with prophylactic bilateral mastectomy in revealing breast cancer of the possible residual glandular breast tissue due to hormonal impact with testosterone therapy [3]. Patient was 42 years old, with invasive ductal carcinoma, 63 × 54 × 50 mm, grade IV, 12+/13 lymph nodes, PR negative, and ER negative; HER 2 was 3+.

Brown and Jones in 2015 paper wrote about seven cases of confirmed PR/ER positive (out of two unknown hormonal status) breast cancer in FtM out of 5135 TG veterans in USA for the period of 17 years [14].

Katayama et al. described breast cancer in a 41-year-old FtM transsexual, who underwent GRS and continuously received testosterone for 15 years. Hypoechoic nodular lesion, approximately 20 mm in size, was in left breast with no obvious metastasis seen on positron emission tomography. Core needle biopsy of tumor showed invasive ductal carcinoma. Later on, breast specimen was defined as neuroendocrine cancer of the breast: PR positive, ER positive, HER negative, Ki-67 20%. Sentinel lymph node was negative [10].

In all papers published up to date, which have pathology report described, histological examination of the breast tumor in FtM TG showed invasive ductal carcinoma of the breast tissue, PR/ER positive [3, 16, 17].

## Discussion

Gender identity describes a person's inherent sense of being a woman, man, or of neither gender, whereas sexual orientation refers to how people identify their physical and emotional attraction to others [20, 21]. Gender reassignment surgery, as series of complex surgical genital and non-genital procedures, is recognized as the most effective treatment for patients with gender dysphoria [22]. The two main principles of hormone therapy for transgender patients are to reduce endogenous hormone levels and their associated sex characteristics and replace

with hormones of the preferred sex [23]. Transgender persons (TG) usually receive cross-sex hormone treatments as a part of treatment strategy before, during, and after surgery without great knowledge about their incidence of breast cancer, especially in female-to-male (FtM) TG. Incidence of male breast cancer is less than 1%. Incidence of male-to-female (MtF) transsexuals is still unknown. However, the risk of long-term use of hormonal treatment following transgender surgery [24] found breast cancer incidence equivalent to rates among natal males [18]. It is necessary to know that only absolute contraindications to hormone therapy are estrogen-responsive or testosterone-responsive tumors. There are still controversies about the incidence of BC in TG population. Burcombe stated that higher percentage of BC in transsexual population is due to the fact that many FtM use testosterone replacement for the alleviation of symptoms on by-surgical menopause than on other population [16], though Gooren [18] said that combination of mastectomy and testosterone treatment in FtM subjects can greatly reduce risk. Katayama wrote about two possible pathways of exogenously supplied testosterone that stimulates the activity of hormone receptors in residual breast tissue. Aromatase converts testosterone to estradiol (E2), which stimulates breast cell proliferation by activating ERs. In this pathway, testosterone indirectly stimulates ERs [25, 26]. In the second, 5 $\alpha$ -reductase converts testosterone to dihydro-testosterone, which directly affects ARs in AR-positive breast cancer patients [26]. The precise causative role of androgens in breast cancer etiology is unclear. High circulating androgens in post-menopausal women may increase estrogens via peripheral aromatization of dihydro-epiandrosterone (DHEA) to oestradiol (E2) and oestrone in breast and adipose tissue. Metabolites of DHEA compete with E2 to stimulate estrogen receptors (Ers). Prolonged and unopposed estrogen and androgen stimulation increases breast cancer risk [23, 25–29]. Due to that, it is obvious rule for all TG to have estradiol and testosterone levels measured quarterly during the first year of treatment, and then every 6–12 months thereafter once goal levels are achieved. In all FtM patients who developed breast cancer, testosterone administration was stopped due to the fact that high levels of circulating androgens increase the risk of developing breast cancer [30, 31], whereas other studies showed opposite results [32, 33]. Brown showed that in spite of this complex process, these patients do not show greater incidence of breast cancer (BC) than the general population [6]. Breast cancer infrequently occurs in TG patients. Even breast core biopsies can be difficult for interpreting after changes in breast tissue in female-to-male transsexuals following gender reassignment (GRA) [34].

Good to know are data from the large retrospective studies from Mayo Clinic that breast cancer occurred in all

high-risk women who underwent subcutaneous mastectomy [35].

From two biggest studies, first in Europe, Dutch study [8] Gooren noted that for 795 FtM patients only one case with BC was confirmed. The second biggest study in the USA in a group of 293 female-to-male gender dysphoric patients reported that breast cancer was proven in seven patients.

## Conclusion

Reviewing the literature, so many different data concerning probability of BC in sexual minority can be found.

Although Meads stated the fact that woman who report partnering with women or identified as lesbian or bisexual may experience elevated breast cancer risk [36], Brown revealed reverse data [14].

Breast cancer screening program should be offered to all TG individuals according to national guidelines. It is very important to take into consideration a transgender person's natal and surgical anatomy, unique clinical concerns for depression and anxiety, risk of suicide together with risk factors including experiences of harassment or physical or sexual violence, low education level, and unemployment [1]. It is necessary to know that besides higher risk for breast cancer, including overweight, obesity, and excessive alcohol intake in transgender people, everyday experiences of higher discrimination than in heterosexual people were reported. Approximately 42% are attributed to the bisexual orientation [37].

One of the big issues can be the reality of obtaining screening mammography less often than in other women, so consensus group recommend that female-to-male transmen without bilateral mastectomy follow screening guidelines for cisgender women [38–40] as they remain at risk for breast cancer. Transgender men who did not have mastectomy should think about the risks and benefits of breast cancer screening and consider mammography as recommended by the American Cancer Society [23]. Even in patients with bilateral prophylactic mastectomy, they are not completely abolished from cancer risk. The inability of subcutaneous mastectomy to remove all glandular tissue is a major limitation, particularly in high-risk individuals in whom any residual breast tissue has significant neoplastic potential [41–45]. Understanding the need for mammography in these often marginalized groups is very important in addressing breast cancer disparities [46] despite differences in insurance coverage in some countries and greater concern for the cancer of the breast in residual breast tissue [8]. The best screening rule, ever, for breast cancer in male transsexuals and other LBGT population should be, besides surgical history and hormonal status, “Screen Now, Screen Regularly and Screen What You Have.”

## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** For this type of study formal consent is not required.

**Informed consent** Informed consent was obtained from all individual participants included in the study.

## References

- McNamara M, et NG H (2016) Best practices in LGBT care: A guide for primary care physicians. *Clev Clin J Med* 83(7):533–540
- "World Cancer Report" (2014) World Health Organization. 2014. pp. Chapter 1.1. ISBN 92-832-0429-8
- Nikolic DV, Djordjevic ML, Granic M, Nikolic AT, Stanimirovic VV, Zdravkovic D, Jelic S (2012) Importance of revealing a rare case of breast cancer in a female to male transsexual after bilateral mastectomy. *World J Surg Oncol* 10:280
- World Cancer Report (2008) International Agency for Research on Cancer
- Male Breast Cancer Treatment (2014) National Cancer Institute
- Dimitrova N, Znaor A, Agius D, Eser S, Sekerija M, Ryzhov A, Primic-Žakelj M, Coebergh JW, SEE + Working Group (2017) Breast cancer in South-Eastern European countries since 2000. Rising incidence and decreasing mortality at young and middle ages. *Eur J Cancer* 83:43–55
- Willemsen HW, Kaas R, Peterse JH, Rutgers EJ (1998) Breast carcinoma in residual breast tissue after prophylactic bilateral subcutaneous mastectomy. *Eur J Surg Oncol* 24(4):331–332
- Gooren LJ (2014) Management of female-to-male transgender persons: medical and surgical management, life expectancy. *Curr Opin Endocrinol Diabetes Obes* 21(3):233–238
- Ramos Boyero M (2008) Skin-sparing mastectomy: an alternative to conventional mastectomy in breast cancer. *Cir Esp* 84(4):181–187
- Katayama Y, Motoki T, Watanabe S, et al (2015) A very rare case of breast cancer in a female-to-male transsexual. *Breast Cancer*. <https://doi.org/10.1007/s12282-015-0661-4>
- Pivo S, Montes J, Schwartz S, Chun J, Kiely D, Hazen A, Schnabel F (2017) Breast cancer risk assessment and screening in transgender patients. *Clin Breast Cancer* 17(5): e225–e227
- Burcombe RJ, Makris A, Pirtam M et al (2003) Breast cancer after bilateral subcutaneous mastectomy in female to male case. *Breast* 12:290–293
- Bevers TB (2010) Breast cancer prevention. an update of the STAR trial. *Curr Treat Options Oncol* 11:66–69
- Brown GR, Jones KT. Incidence of breast cancer in a cohort of 5,135 transgender veterans. *Breast Cancer Res Treat* 149(1):191–198
- Bazzi AR, Whorms DS, King DS et al (2015) Adherence to mammography screening guidelines among transgender persons and sexual minority women. *Am J Public Health* 105:2356–2358
- Burcombe RJ, Makris A, Pittam M, Finer N (2003) Breast cancer after bilateral subcutaneous mastectomy in a female to male transsexual. *Breast* 12(4):290–293
- Shao T, Grossbard LM, Klein P (2011) Breast cancer in Female to male transsexuals: two cases with a review of physiology and management. *Clin Breast Cancer* 11(6):417–419
- Gooren LJ, van Trotsenburg MA, van Diest GiltayEJ (2013) PJ.: Breast cancer development in transsexual subjects receiving cross-sex hormone treatment. *J Sex Med* 10(12):3129–3134
- Kotsopoulos J, Steve A (2017) Androgens and breast cancer. *J Sex Med* 14(5):741–746
- Spack NP (2013) Management of transgenderism. *JAMA* 309:474–484
- National LGBT Health Education Center (2016) Achieving health equity for lesbian, gay, bisexual, and transgender (LGBT) people, Module 1. <http://www.lgbthealtheducation.org/wp-content/uploads/Achieving-Health-Equity-for-LGBT-People-1.pdf>. Accessed May 19, 2016
- Selvaggi G, Bellringer J (2011) Gender reassignment surgery: an overview. *Nat Rev Urol* 8(5):274–282
- Hembree WC, Cohen-Kettenis P, Delemarre-van de Waal HA et al (2009) Endocrine treatment of transsexual persons: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 94:3132–3133
- Teoh ZT, Archampong D, Gate T (2015) Breast cancer in male to female (MtF) transgender patients: is formonereceptor negativity a feature? *BMJ Case Rep*. <https://doi.org/10.1136/bcr-2015-209396>
- Yager JD, Davidson NE (2006) Estrogen carcinogenesis in breast cancer. *New Engl J Med* 354:270–282
- Secreto G, Zumoff B (2012) Role of androgen excess in the development of estrogen receptor-positive and estrogen receptor-negative breast cancer. *Anticancer Res* 32:3223–3228
- Hankinson SE et al (1998) Plasma sex steroid hormone levels and risk of breast cancer in postmenopausal women. *J Natl Cancer Inst* 90(17):1292–1299
- Veronesi U, Pizzocaro G (1968) Breast cancer in women subsequent to cystic disease of the breast. *Surg Gynecol Obstet* 126(3):529–532
- Secreto G et al (1984) Increased androgenic activity and breast cancer risk in premenopausal women. *Cancer Res* 44(12 Pt 1):5902–5905
- James RE, Lukanova A, Dossus L, Becker S, Rinaldi S, Tjonneland A et al (2011) Postmenopausal serum sex steroids and risk of hormone receptor-positive and -negative breast cancer: a nested case-control study. *Cancer Prev Res* 4:1626–1635
- Diaz-Chico N, German Rodriguez B, Gonazalez F, Ramirez A, Bilbao R, Cabrera de Lekon C, et al (2007) Androgens and androgen receptors in breast cancer. *J Steroid Biochem Mol Biol* 105:1–15
- Adly L, Hill D, Sherman ME, Sturgeon SR, Fears T, Mies C et al (2006) Serum concentrations of estrogens, sex hormone-binding globulin, and androgens and risk of breast cancer in postmenopausal women. *Int J Cancer* 119:2702–2707
- Danforth KN, Eliassen AH, Tworoger SS, Missmer SA, Barbieri PL, Rosner BA et al (2010) The association of plasma androgen levels with breast, ovarian and endometrial cancer risk among postmenopausal women. *Int J Cancer* 126:199–207
- Mathwe H, Hamid B (2013) Context is everything: an unusual breast core biopsy case. *Int J Surg Pathol* 21(5):502–503
- Hartmann LC et al (1999) Efficacy of bilateral prophylactic mastectomy in women with a family history of breast cancer. *New Engl J Med* 340(2):77–84
- Meads C, Moore D (2013) Breast cancer in lesbians and bisexual women: systematic review of incidence, prevalence and risk studies. *BMC Public health* 13:1127
- Mays VM, Cochran SD (2001) Mental health correlates of perceived discrimination among lesbian, gay, and bisexual adults in the United States. *Am J Public Health* 91:1869–1875
- Center of Excellence for Transgender Health (2011) Primary care protocol for transgender patient care. Department of Family and Community Medicine, University of California, San Francisco
- Hembree WC, Cohen-Kettenis P, Delemarre-van de Waal HA et al (2009) Endocrine treatment of transsexual persons: an Endocrine

- Society clinical practice guideline. *J Clin Endocrinol Metab* 94(9):3132–3154
40. Sherbourne Health Center (2009) Guidelines and protocols for comprehensive primary care for trans clients. Sherbourne Health Center, Toronto
  41. Eldar S, Meguid MM, Beatty JD (1984) Cancer of the breast after prophylactic subcutaneous mastectomy. *Am J Surg* 148(5):692–693
  42. Goodnight JE, Quagliana JM, Morton DL (1984) Failure of subcutaneous mastectomy to prevent the development of breast cancer. *J SurgOncol* 26(3):198–201
  43. Ziegler LD, Kroll SS (1991) Primary breast cancer after prophylactic mastectomy [clinical conference]. *Am J Clin Oncol* 14(5):451–454
  44. Bowers DG, Radlauer CB (1969) Breast cancer after prophylactic subcutaneous mastectomies and reconstruction with silastic prostheses. *Plast Reconstr Surg* 44(6):541–544
  45. Holleb AI, Montgomery R, Farrow JH (1965) The hazard of incomplete simple mastectomy. *SurgGynecol Obstet* 121(4):819–822
  46. Robertson Bazzi A, Whorms SD, King SD, Potter J (2015) Adherence to mamography screening guidelines among transgender persons and sexual minorities. *Am J Public Health* 105(11):2356–2358