

# A Systematic Review of Breast Cancer Risk in Transgender Patients After Top Surgery

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## Background

Approximately 0.5-1.5% of the population identifies as transgender, with an estimated 25 million transgender individuals worldwide. Transgender males are born anatomically female but psychologically identify as male. Many individuals opt to undergo gender reassignment in the form of hormone replacement therapy (HRT) and/or gender reassignment surgery.

Top surgery is the most common gender reassignment surgery undergone by transgender males. The goal of top surgery is to achieve a masculine chest via removal of breast tissue and excess skin, repositioning and reducing the nipple, removing the inferior mammary fold, and creating proper chest contouring.

The risk of breast cancer remains post-top surgery. The transgender population is less likely to seek screening and medical care due to lack of inclusivity and discrimination by healthcare staff.

## Methods

Using the PRISMA guidelines, a systematic review identified peer-reviewed articles in PubMed evaluating breast cancer risk in the transgender population after androgen therapy and top surgery. The reported data included:

Tumor histopathology, hormone status, use of androgens +/- top surgery for gender reassignment, and treatment of oncologic diagnosis (Table 1).

We also compared the incidence of breast cancer in the transgender population to the incidence in cis-gender males and females. Finally, we reviewed current transgender health guidelines.

Article	Age (dx)	Cancer	ER+	PR+	HER2+	Hormone gender reassignment therapy	Family Hx	BRCA	Treatment	Hormone Modulators	Top surgery
Burcombe 2003	33	Invasive Ductal Carcinoma	yes	yes	NR	testosterone	no	NR	Mastectomy with ALND + level 2 + radiation	Tamoxifen	yes
Shao 2011	53	Invasive Ductal Carcinoma	yes	no	yes	testosterone	yes (breast + ovarian)	(-)	B/I mastectomy w/ SLNB + chemotherapy	Tamoxifen + Trastuzumab	no
	27	Invasive Ductal Carcinoma	yes	no	yes	testosterone	yes (breast)	(-)	B/I mastectomy w/ ALND + chemotherapy	Tamoxifen	no
Nikolic 2012	42	Metastatic Invasive Ductal Carcinoma	no	no	yes	testosterone	no	NR	NAC + radical mastectomy w/ ALND + chemotherapy	Trastuzumab	yes
Gooren 2013	27	Tubular Carcinoma	yes	yes	NR	testosterone	NR	NR	Tumor found during top surgery, no additional tx	NR	yes
	57	Ductal Carcinoma	yes	no	no	conjugated estrogens	NR	NR	Unknown	NR	no
Gooren 2015	48	Invasive Ductal Carcinoma	no	no	no	testosterone	NR	NR	Lumpectomy + chemotherapy	NR	yes
	41	Invasive Ductal Carcinoma	yes	yes	no	none	NR	(-)	Chemotherapy + ALND + radiation	Tamoxifen	no
	41	Tubular Carcinoma	yes	yes	no	testosterone	NR	NR	Mastectomy + SLNB	NR	yes
Brown 2015	74	Metastatic Infiltrative Ductal Carcinoma	yes	no	yes	testosterone	NR	NR	Lumpectomy + chemotherapy	NR	no
	47	Breast cancer	yes	yes	NR	none	None	NR	Mastectomy	None	No
	48	Breast cancer	yes	yes	NR	testosterone	NR	NR	Mastectomy	NR	No
	42	Breast cancer	NR	NR	NR	testosterone	yes (lung)	NR	B/I mastectomy with reconstruction	NR	No
	57	Breast cancer	NR	NR	NR	conjugated estrogens + medroxyprogesterone	no	NR	Lumpectomy + radiation	NR	No
	42	Breast cancer	Yes	Yes	NR	estrogen OCP + testosterone	Yes (breast)	NR	Lumpectomy + B/L NSM	NR	No
	64	Breast cancer	yes	yes	NR	conjugated estrogens	NR	NR	Lumpectomy + chemotherapy	Tamoxifen	No
Katayama 2016	41	Neuroendocrine Carcinoma	yes	yes	no	testosterone	no	NR	Lumpectomy + SLNB + radiation	Aromatase Inhibitor	yes

Table 1. NR: Not Reported. ALND: Axillary Lymph Node Dissection. SLNB: Sentinel Lymph Node Biopsy. NAC: Neoadjuvant Chemotherapy. OCP: Oral Contraceptive Pills. NSM: Nipple Sparing Mastectomy.

## Results

Our literature search yielded 131 articles, 7 of which met the inclusion criteria. A total of 16 cases of breast cancer in transgender male patients with a mean age of 45 were observed (Table 1). Invasive ductal carcinoma was the most common reported tumor histology (50% of cases), followed by tubular adenocarcinoma (12.5%). In our review, the tumor histopathology was reported only as 'breast cancer' in 37.5% of cases. The majority of cases were ER-positive disease (68.8%), with PR-positive in 56.25% and Her-2 positive in 25% of cases. The majority of patients (68.8%) were using testosterone replacement for gender reassignment therapy, and 37.5% underwent top surgery. Two diagnoses of breast cancer were identified after pathologic examination of the top surgery specimen. The mean follow up was 8.39 years, reported in 11 of 16 cases identified.

## Discussion

The estimated incidence of breast cancer is 5.9 per 100,000 person-years for transgender males, while the incidence for cis-gender females and males is 154.7 per 100,000 person-years and 1.1 per 100,000 person-years, respectively.

The most common surgical procedure chosen by transitioning patients is top surgery. It is important to note that top surgery is not an oncologic mastectomy and therefore, patients who choose top surgery, continue to require breast cancer screening. In addition to top surgery, female to male transgender patients commonly employ androgen therapy to elicit masculine effects. It is well documented that estrogen exposure increases one's risk for breast cancer, however, the oncologic consequences of prolonged testosterone supplementation for gender reassignment remain unclear.

## Conclusion

Breast cancer risk persists in transgender patients, regardless of their chosen method for achieving gender reassignment. Given our observations, in addition to education in transgender health care, performing oncologic mastectomy for top surgery may prove to be an important augmentation to an existing aesthetic procedure.

One surgical consideration is that oncologic resections post-top surgery have the potential to be more technically challenging. These patients may present with later stage disease and anatomic distortion.

Knowledge of transgender healthcare is lacking amongst healthcare providers. We recommend gender inclusive intake forms and trans-health education by all providers, including breast surgeons.

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