Breast Cancer in Transgender Patients Following Medical and Surgical Intervention

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Introduction

Current breast cancer (BCa) screening guidelines do not adequately address transgender populations, despite known differences in hormone exposure and post-operative anatomy between transgender and cisgender patients of the same gender. The effects of gender-affirming hormone therapy (HT) and surgical intervention (SX) on BCa risk in transgender individuals remain poorly understood.

Methods

Using TriNetX (TriNetX, Inc., Cambridge, MA, United States), a de-identified health research network, we identified adults with a diagnosis of Gender Identity Disorder (GID) (ICD-10: F64.x) from 2003–2023. Patients were divided by sex assigned at birth and categorized into cohorts based on gender-affirming intervention: no intervention (NI), HT alone (≥1 year), and HT with SX. SX was limited to top surgeries, such as breast contouring and mastectomies. Patients with a past history of BCa, bottom surgery, or inconsistent medical timelines were excluded. The primary outcome was a diagnosis of malignant neoplasm of the breast (ICD-10: C50.x), recorded in at least two instances. Logistic regression was used to identify predictors of BCa risk.

Key Findings

- Hormone therapy alone does *not* increase breast cancer risk in either transgender women or transgender men.
- Transgender men who received *both* hormone therapy and top surgery had significantly higher breast cancer prevalence compared to those receiving hormone therapy alone (0.25% vs. 0.07%) and had 3.6× higher odds of breast cancer.
- Black race and older age at gender identity disorder diagnosis were consistent independent predictors of breast cancer risk across transgender men and women.

Results

Table 2: Transgender Female Cohort Logistic Regression Analysis Demonstrating Relationship of Baseline Characteristics and Development of Breast Cancer

Factors	Odds ratio	95% CI	*p*-value
Hormone Therapy Only	0.628	0.03, 6.992	0.727
Hormone + Surgical Therapy	0.728	0.052, 6.025	0.788
Age at Gender Identity Disorder Diagnosis	**1.07**	**1.051, 1.089**	**<0.001**
Race			
Black	**2.705**	**1.133, 5.764**	**0.015**
Other	0.997	0.151, 3.577	0.997
Interaction effects			
Intervention*Age			
(Hormone Therapy only)*Age	0.996	0.931, 1.054	0.905
(Hormone + Surgical Therapy)*Age	**1.042**	**1.003, 1.088**	**0.043**

Table 4: Transgender Male Cohort Logistic Regression Analysis Demonstrating Relationship of Baseline Characteristics and Development of Breast Cancer

Factors	Odds ratio	95% CI	*p*-value
Hormone Therapy Only	0.502	0.079, 1.769	0.36
Hormone + Surgical Therapy	**3.623**	**1.021, 10.135**	**0.024**
Age at Gender Identity Disorder Diagnosis	**1.071**	**1.051, 1.091**	**<0.001**
Race		,	
Black	**3.352**	**1.202, 8.145**	**0.012**
Other	1.929	0.303, 6.835	0.384
Ethnicity (Not Hispanic)	1.675	0.267, 5.748	0.487

Results

Among 33,775 transgender women (assigned male at birth), 12 (0.036%) were diagnosed with BCa. Of these, 83.3% had no intervention, 16.7% received HT, and none received both HT and SX. HT alone was not associated with increased risk of developing BCa. Independent predictors of BCa included age at GID diagnosis (OR =d 1.07 per year, 95% CI: 1.05–1.09, p < 0.001) and Black race (OR = 2.71, 95% CI: 1.13–5.76, p = 0.015). Among 44,117 transgender men (assigned female at birth), 37 (0.084%) were diagnosed with BCa. Most cases occurred in those with no intervention (72.9%), followed by HT+SX (21.6%), and HT alone (5.4%). Hormone therapy alone was not associated with increased risk. Individuals who received both HT and SX had significantly higher BCa prevalence compared to those with HT alone (0.25% vs. 0.07%, p = 0.01). Multivariate analysis showed increased odds of BCa with combined HT and SX (OR = 3.62, 95% CI: 1.02–10.14, p = 0.024), Black race (OR = 3.35, 95% CI: 1.20–8.15, p = 0.012), and age at GID diagnosis (OR = 1.07 per year, 95% CI: 1.05–1.09, p < 0.001).

Discussion

This is the largest cohort study to date assessing BCa risk among transgender patients, and the first study to stratify risk by level of gender-affirming intervention. HT alone does not appear to increase BCa risk in transgender individuals. However, among transgender men, the combination of HT and SX was associated with significantly elevated risk. These findings may reflect differences in tissue preservation during mastectomy, lower screening rates, or increased pathological surveillance post-surgery. Black race and age at GID diagnosis were also associated with greater risk among both trans men and women. Our findings underscore the need for revised BCa screening guidelines that reflect the unique risk profiles of transgender populations and address intersectional disparities in care.