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REVIEW ARTICLE – BREAST ONCOLOGY

Breast Cancer Risk and Screening in Transgender Persons: A Call for Inclusive Care

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ABSTRACT The Society of Surgical Oncology is committed to reducing health disparities adversely affecting sexual and gender minorities. Transgender persons represent a socially disadvantaged group who frequently experience discrimination and receive disparate care, resulting in suboptimal cancer outcomes. The rate of breast cancer development in transgender individuals differs from rates observed in their cisgender counterparts, however there is little evidence to quantify these differences and guide evidence-based screening and prevention. There is no consensus for breast cancer screening guidelines in transgender patients. In this review, we discuss barriers to equitable breast cancer care, risk factors for breast cancer development, and existing data to support breast cancer screening in transgender men and women.

Approximately 4% of US adults identify as sexual and gender minorities (SGMs), including individuals who are lesbian, gay, bisexual, transgender, and intersex (LGBTI).[1] Several studies have demonstrated disparities in cancer-specific outcomes among SGM populations due to a combination of increased cancer risk, late-stage at presentation, decreased access to care, discrimination, stigmatization, and poor patient–provider communication that often result in diminished quality of care.[2–5] A paucity of data regarding the etiology of these factors at both the individual and population levels results in a persistent knowledge gap in how to effectively improve cancer outcomes for this at-risk patient population.

Over 1.4 million Americans identify as transgender. The term transgender refers to individuals whose gender identity or expression defers from their sex assigned at birth. Transgender patients are at particular risk for cancer disparities. They face additional barriers to care, including lack of physician compliance or understanding of patient gender identity, stigmatization, psychosocial trauma when undergoing procedures related to sex assigned at birth that contradict gender identity, possible increased cancer risk related to endocrine therapies often prescribed during gender-affirming care (GAC), and lack of insurance coverage for necessary tests or procedures based only on sex assigned at birth.

Current literature regarding the development of breast cancers in transgender individuals is largely limited to small retrospective studies and case reports. Burns et al. recently published a retrospective case-series of transgender patients with cancer.[6] The article highlighted areas for improvement in oncologic care and identified the need for prospective studies with larger cohorts to better characterize this patient demographic.[6] The authors reported two transgender patients who developed breast cancer. These cases raise interesting questions regarding practical and ethical decisions in hormonal therapy, breast cancer screening and surveillance in transgender breast cancer patients. Systematic reviews have established small case cohorts for further discussion; however, a lack of prospective data hinders efforts to accurately assess breast

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cancer risk in transgender individuals and best practices for screening.[7–9] In this review, we outline general considerations for creating an inclusive practice and breast cancer screening for transgender patients.

DEVELOPING AN INCLUSIVE AND WELCOMING PRACTICE FOR SEXUAL AND GENDER MINORITIES

Despite increasing social acceptance and support for transgender rights in the US, the transgender patient population remains underrepresented in cancer research and cancer care standards. Additionally, acceptance of transgender rights does not automatically translate to competence in administering equitable patient care. In one study of surveyed healthcare providers, only 35% felt comfortable and 29% felt equipped to routine provide gynecological care to transgender female and transgender males, respectively.[10] In the same study, 59% of providers were unaware of breast cancer screening recommendations for transgender females.[10] Furthermore, transgender patients frequently report significant distrust of the healthcare system related to experienced discrimination and marginalization. Specifically, up to 68% of transgender patients reported mistreatment or discrimination while seeking care from health professionals.[11–13] The burden of discrimination is shared by both institutions and individual providers and must be eliminated by both in order to provide equitable care for transgender persons. Common failures reported by transgender patients include provider use of sex assigned at birth and lack of acknowledgment of gender identity, inconsistent use of their chosen name and preferred pronoun, failure of institutions to consistently collect gender identity as a part of the medical record, failure of institutions to provide gender-affirming spaces, including appropriate restroom facilities, and lack of appropriate patient education materials.[14] These persistent negative experiences often deter transgender patients from seeking appropriate and timely health care.[12,13]

To provide inclusive care, health systems must help patients feel safe and comfortable disclosing SGM identities. Physicians must familiarize themselves with appropriate terminology to establish trust when addressing transgender patients. A glossary of commonly used terms in the care of transgender individuals is provided in Table 1. We encourage all providers to ask non-presumptive questions about gender, identity, and patient partners. Once a patient's gender identity is declared, all appropriate documentation, including the electronic medical record and verbal acknowledgments, should reflect the patients preferred pronoun and chosen name. Mistakes will occur despite the best intentions; when they do, providers should be encouraged to acknowledge, apologize promptly, and ease unintended consequences. When in doubt of the appropriate terminology or pronoun to use, it is best to ask the patient what they prefer. Providers should also be cognizant of imagery and advertisements in and around care spaces to ensure inclusive language and photos.

Transgender patients should have access to referrals for support and advocacy networks as needed as they progress through their cancer care. The American Society of Clinical Oncology recommends all SGM patients have access to additional resources, including care navigators, and partnering programs linking SGM patients with cancer and their caregivers with cancer survivors and advocates.[15] Educational materials should be tailored to the needs of transgender patients, with special emphasis on relevant treatment effects, appropriate follow-up care, and available psychological or other support services of patient and caregivers. Every effort to incorporate GAC providers in oncologic treatment planning should be made in order to minimize the negative psychosocial impact and distress that may result if there is an imbalance in patient gender identity and physical characteristics. For example, cessation of feminizing hormone therapy may be medically necessary in some cases; however, the impact of subsequent physical changes may be ameliorated with other treatment options. Building an SGM-inclusive practice demands intention. To ensure the practice environment is truly culturally competent, providers should consider partnering with patient transgender advocacy groups or existing SGM-centered group practices to perform a thorough needs assessment and subsequent implementation of targeted and effective programs.

BREAST CANCER RISK AND SCREENING IN TRANSGENDER WOMEN (MALE TO FEMALE)

Transgender women often receive gender-affirming hormones (sex steroids) to reduce psychological distress and to induce desired physical changes, such as change in voice pitch and a feminized body composition. Feminizing cross-sex hormonal (CSH) therapies typically include the use of exogenous estrogens and antiandrogens. Several case reports and small cohort studies have suggested that prolonged estrogen exposure due to CSH therapies may increase the risk of developing breast cancer in transgender females when compared with rates observed in cisgender males.[7,16–18] de Blok et al. investigated the incidence of breast cancer in a Dutch cohort of transgender persons.[19] In that study, transgender women had a 46-fold higher incidence of breast cancer when compared with cisgender men, but a much lower incidence (0.3 odds ratio) when compared with cisgender women.[19] Other studies have shown a

TABLE 1 Glossary of transgender terminology

Terminology	Definition
Cisgender	A person whose gender identity and gender expression is consistent with their sex assigned at birth
Gender-affirming hormones	The use of sex steroids to reduce or induce desired physical changes in line with gender identity. Also referred to as cross-sex hormonal therapies
Gender-affirming surgery	Surgeries to modify a person's body to be more aligned with that person's gender identity. Types of gender-affirming surgery include chest and genital surgeries, facial feminization, body sculpting, and hair removal
Gender identity	A person's inner sense of being a girl/woman/female, boy/man/male, something else, or having no gender
Preferred pronouns	The pronouns by which someone would like to be referred. Examples of pronouns are she/her/hers, he/him/his, and they/them/theirs. The appropriate phrasing is "What are your pronouns?" when seeking this information
Transgender	Describes a person whose gender identity and sex assigned at birth do not correspond based on traditional expectations
Transgender female	A transgender person whose gender identity is girl/woman/female but whose sex assigned at birth was male
Transgender male	A transgender person whose gender identity is boy/man/male but whose sex assigned at birth was female
Sex assigned at birth	The sex (male or female) assigned to an infant, most often based on the infant's anatomical and other biological characteristics
Sexual and gender minorities	A broad umbrella term individuals who identify as lesbian, gay, bisexual, asexual, transgender, two-spirit, queer, and/or intersex, as well as those who do not self-identify with one of these terms, but whose sexual orientation, gender identity, or reproductive development varies from traditional, societal, cultural, or physiological norms

similar trend, with a fourfold increased risk of breast cancer development in transgender females undergoing CSH therapy when compared with cisgender males; however, these data did not reach statistical significance.[20]

These data have prompted several organizations to develop guidelines for breast cancer screening in transgender women (Table 2). Based on these guiding principles, the authors recommend breast cancer screening for transgender females with no family history of breast cancer begin at age 50 years and with at least 5 years of feminizing hormone use. Screening mammography is the primary recommended modality and should be performed every 2 years. In transgender female patients with a family history of breast cancer or a known pathogenic genetic mutation, we recommend an individualized approach with consideration for earlier screening based on available

TABLE 2 Summary of current breast cancer screening guidelines for transgender persons

	Transgender female	Transgender male without top surgery	Transgender male who has undergone top surgery
University of California San Francisco[29]	Age ≥50 years AND at least 5 years of hormone therapy: screening mammography every 2 years	Screening similar to that for cisgender women	Dialog with patients about risks
Fenway Health[30]	Age ≥50 years AND at least 5 years of hormone therapy: screening mammography annually	Screening similar to that for cisgender women	Consider yearly chest examinations
University Hospitals Cleveland Medical Center[31]	Age ≥50 years AND at least 5 years of hormone therapy: screening mammography every 2 years	Screening similar to that for cisgender women	–
Susan G. Komen Puget Sound[32]	Age ≥50 years AND at least 5 years of hormone therapy: screening mammography annually	Annual screening mammography beginning at age 50 years	Annual chest and axillary examinations If breast tissue remaining, annual screening mammography beginning at age 50 years
Canadian Cancer Society[33]	Age 50–69 years AND at least 5 years of hormone therapy: screening mammography every 2 years	Screening mammography every 2 years between age 50 and 69 years	Screening mammography every 2 years between age 50 and 69 years
Endocrine Society Clinical Practice Guidelines[34]	Screening similar to that for cisgender women, no prescribed length of hormone exposure	Screening similar to that for cisgender women	–

family cancer history data. It is important to note that transgender women may find breast examinations to be gender-affirming.

BREAST CANCER RISK AND SCREENING IN TRANSGENDER MEN (FEMALE TO MALE)

Transgender men often receive gender-affirming androgen-based CSH therapy to induce more masculine characteristics. Exogenous testosterone administration usually results in significant reduction in breast glandular tissue but an increase in fibrous connective tissue.[20] Transgender males may opt to undergo sex reassignment surgery to achieve a more masculine physique. Chest masculinization surgery, also referred to as 'top surgery', is a common cosmetic procedure pursued by transgender men. The procedure involves the removal of some, but often not all, breast tissue as well as repositioning and reshaping of the nipple areolar complex to create a more masculine chest contour. Masculinizing chest surgery should not be considered an oncologic or preventative breast cancer surgery as breast tissue is left behind. Several cases of breast cancer development in transgender males after gender-affirming chest masculinization surgery have been reported.[21–24]

It is not clear whether exogenous testosterone therapy impacts the rate of breast cancer development in transgender men. Testosterone can be aromatized into estrogens with peripheral tissues and may have a stimulatory effect on breast tissues and breast cancers.[17,25]. A recent systematic review identified 23 transgender males who developed breast cancer while undergoing androgen-based CSH therapy.[9] Median age at diagnosis was 42 years, with a median of 4.5 years (IQR 2.5–11.2) of exogenous testosterone use. The majority of patients presented with a palpable breast mass, however in 9 of 23 cases (39%), breast cancers were found incidentally at the time of chest masculinization surgery.[9] Eight of the remaining 14 patients had undergone prior bilateral mastectomies during gender-affirming chest masculinization surgery. This and other studies have suggested a higher rate of breast cancer in transgender males when compared with cisgender males, but about a 0.3-fold decrease in risk when compared with cisgender women.[19,26]

While more evidence is needed to refine breast cancer screening in transgender males, we recommend transgender men who have not undergone chest masculinization surgery follow the same breast cancer screening guidelines established for cisgender females. There are no formal recommendations for breast cancer screen in transgender men status post gender-affirming mastectomies. Abnormalities, such as palpable breast mass or concerning findings on screening mammography, should be evaluated promptly with standard breast diagnostic imaging.[27] Mammography for the evaluation of palpable lesions after mastectomy may not always be technically feasible, therefore diagnostic alternatives such as ultrasound and/or magnetic resonance imaging may be necessary to guide treatment.

Breast cancer screening in transgender male patients is often at odds with the patient's gender identity. As such, an additional barrier to breast cancer screening in this patient population may include psychological distress that may hinder willingness to seek examination. A recent study demonstrated that transgender patients are less likely to receive recommended cancer screening compared with the cisgender population.[28] Specifically, rates for breast cancer screening were significantly lower in transgender individuals at 33% versus 65% in cisgender patients ($p < 0.001$).[28] These data highlight the need for cancer-focused SGM patient and community education outreach programs, as well as targeted physician education, to close the gaps in care for these patients.

CONCLUSION

In summary, transgender individuals face significant barriers to equitable breast cancer screening and high-quality cancer care, leaving them as high-risk for suboptimal oncologic outcomes. Prolonged exposure to CSH therapies may increase the risk of breast cancer development in this patient population. More prospective data are needed to better characterize these risks and refine existing guidelines for breast cancer screening in transgender patient populations. Institutions and providers must strive to address barriers to optimal transgender healthcare, with a focus on educating the healthcare workforce, creating safe and equitable treatment facilities, eliminating patient discrimination, stigmatization and marginalization, and enhancing patient experience and educational materials.

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