

Screening for breast cancer in transgender individuals undergoing gender-affirming hormone therapy: institutional protocol at a university hospital

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ABSTRACT

This study describes the development and implementation of an institutional breast cancer screening protocol for transgender individuals, based on a scoping review and clinical experience at a university hospital. Gender-affirming hormone therapy is widely used among transgender individuals to induce secondary sexual characteristics aligned with gender identity, and in transfeminine individuals, breast development typically occurs within the first months of estrogen exposure, reaching maximal maturation after approximately two years. Despite biological plausibility of oncologic risk associated with prolonged exogenous hormone exposure, evidence regarding breast cancer incidence in this population remains limited and heterogeneous. A scoping review was conducted in the LILACS, PubMed, SciELO, and MEDLINE databases, including publications from 2012 to 2022. In parallel, an institutional protocol was implemented at the Trans Mastology Outpatient Clinic of the Federal University of São Paulo, integrating available evidence with clinical practice. Screening strategies were defined according to risk stratification, duration of hormone exposure, presence of breast tissue, and international radiologic recommendations. All patients received structured counseling regarding current evidence and existing uncertainties. The resulting protocol recommends annual mammography for transfeminine individuals aged 40 years or older with at least five years of continuous estrogen exposure. Transmasculine individuals with preserved breast tissue follow the same screening strategy. For individuals who underwent mastectomy, clinical follow-up is recommended, with imaging reserved for symptomatic cases or those at increased risk. The protocol incorporates international radiologic guidance and Brazilian screening standards within a shared decision-making framework. In conclusion, this institutional protocol provides a structured and risk-adapted approach to breast cancer screening in transgender individuals, integrating biological plausibility, observational data, and clinical guidelines in the context of limited high-level evidence.

KEYWORDS: transgender health; breast cancer screening; mammography; gender-affirming hormone therapy; transfeminine; transmasculine.

INTRODUCTION

Gender-affirming hormone therapy constitutes a central component of medical transition for many transgender individuals¹. The concept of gender, consolidated in academic discourse during the 1970s, distinguishes the sociocultural dimension of identity from biological sex and genetic determinants². Gender identity refers to an individual's internal experience of gender, which may or may not correspond to the sex assigned at birth³. Contemporary recognition of gender

diversity encompasses transgender men, transgender women, non-binary individuals, and genderqueer identities⁴.

In Brazil, public health policy formally recognizes the need for comprehensive healthcare for LGBTQIA+ individuals through national frameworks aimed at reducing disparities⁵. Epidemiological studies estimate that approximately 2% of Brazil's adult population identifies as transgender or non-binary⁶. Despite increasing visibility, structural barriers persist

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in preventive healthcare access. Lower rates of cancer screening among transgender individuals have been documented, frequently associated with institutional discrimination, discomfort during clinical encounters, and insufficient professional training⁷.

In transfeminine individuals, feminizing therapy typically combines estrogen with antiandrogen agents, inducing ductal proliferation and stromal development in mammary tissue^{8,9}. Breast maturation generally occurs within the first two years of therapy. Breast tissue develops in a more lateral and caudal position on the chest compared to cisgender women, reflecting the broader anatomical configuration of the male thoracic wall¹⁰. Radiological findings in this population may include benign calcifications, implant-related complications, inflammatory lymphadenopathy secondary to cosmetic procedures, and silicone-related granulomatous changes¹¹.

In cisgender postmenopausal women, prolonged combined estrogen-progestin therapy has been associated with increased breast cancer incidence, as demonstrated in randomized trials such as the Women's Health Initiative¹². However, extrapolation to transgender populations is limited by differences in endocrine baseline, age at hormone initiation, formulation, and cumulative exposure. Estrogen influences cellular proliferation, promotes mitotic activity, and may contribute to genomic instability under sustained exposure.

Observational data remain heterogeneous. Early case series suggested incidence comparable to cisgender men¹³, whereas nationwide cohort data from the Netherlands demonstrated higher incidence in transgender women compared to cisgender men, though still lower than cisgender women¹⁴. Median hormone exposure in that cohort exceeded 15 years, suggesting cumulative duration as a potential determinant. Among transmasculine individuals, incidence appears low, although residual glandular tissue following chest masculinization surgery may preserve baseline oncologic risk^{15,16}. Histological studies indicate reduction — but not elimination — of glandular elements after prolonged testosterone exposure¹⁵.

Mammography remains the gold standard for breast cancer screening due to its demonstrated mortality reduction in population-based programs¹⁷. Ultrasound functions as a complementary diagnostic modality, particularly in individuals with dense breast tissue or focal symptoms, but is not recommended as a primary screening modality in average-risk populations¹⁸. Magnetic resonance imaging (MRI) offers superior sensitivity and plays a key role in high-risk populations, particularly in individuals with known genetic mutations such as BRCA1 or BRCA2¹⁹.

The absence of standardized screening protocols for transgender populations reflects limited prospective data and lack of randomized trials²⁰. International recommendations vary, with some advocating extrapolation from cisgender guidelines^{21,22}, while others support individualized risk-based approaches²³.

In Brazil, the Ministry of Health recommends biennial mammographic screening for women aged 50 to 69 years within the public health system, as established in the 2015 national

guidelines^{24,25}. Professional societies have previously advocated earlier initiation at age 40 with annual intervals²⁶. These recommendations are structured according to biological sex and do not specifically address transgender populations.

The American College of Radiology (ACR) Appropriateness Criteria[®] state that screening mammography “may be appropriate” for transfeminine individuals aged ≥40 years with at least five years of estrogen exposure²⁷. This designation reflects limited high-level evidence and emphasizes individualized clinical assessment rather than universal recommendation. The National Comprehensive Cancer Network (NCCN, United States) endorses these criteria and recommends that transgender individuals consult with their primary care physician to determine when screening would be appropriate²⁸.

Given this context of evolving evidence and regulatory gaps, the Mastology Discipline at the Federal University of São Paulo developed an institutional screening protocol tailored for transgender individuals under specialized follow-up. This article describes the theoretical basis and practical implementation of this protocol.

METHODS

Study design

This study combines a scoping review with structured clinical implementation in a university outpatient setting. The objective was to synthesize available evidence regarding breast cancer risk and screening in transgender individuals undergoing gender-affirming hormone therapy and to operationalize this synthesis into an institutional screening protocol.

No interventional procedures were performed for research purposes. The protocol implemented in the outpatient setting was derived from previously published guidelines and observational evidence. Clinical decisions were made within routine care, based on existing international radiologic criteria and national screening recommendations.

Scoping review

Electronic searches were performed in the LILACS, PubMed, SciELO, and MEDLINE databases, covering publications between 2012 and 2022. The temporal delimitation reflects the contemporary phase of structured gender-affirming endocrine care and the emergence of imaging-specific literature addressing transgender populations.

The search strategy included combinations of descriptors related to transgender health, gender-affirming hormone therapy, breast cancer incidence, breast imaging, and cancer screening.

Inclusion criteria comprised

- Original research articles, cohort studies, systematic reviews, and imaging-focused publications;
- Publications in English, Portuguese, and Spanish;

- Availability of full text; and
- Relevance to breast cancer risk or screening in transgender populations.

The search retrieved 4 articles from LILACS, 97 from PubMed, 1 from SciELO, and 85 from MEDLINE. Titles and abstracts were screened, followed by full-text evaluation. Data extraction focused on breast cancer incidence, hormone exposure duration, imaging findings, and screening recommendations.

Clinical implementation

The screening protocol was implemented at the Trans Mastology Outpatient Clinic at Unifesp. All decisions were made within a shared decision-making framework.

Patients were informed about

- Current epidemiological evidence;
- Biological plausibility of hormone-mediated risk;
- Limitations of available data; and
- Differences between Brazilian public health guidance and international radiologic criteria.

All imaging studies were interpreted and reported according to the ACR Breast Imaging Reporting and Data System (BI-RADS).

RESULTS

Development of the institutional screening protocol

The primary outcome of this study was the development of a structured institutional breast cancer screening algorithm for transgender individuals without known hereditary predisposition, derived from an integrative literature synthesis and clinical implementation experience (Figure 1).

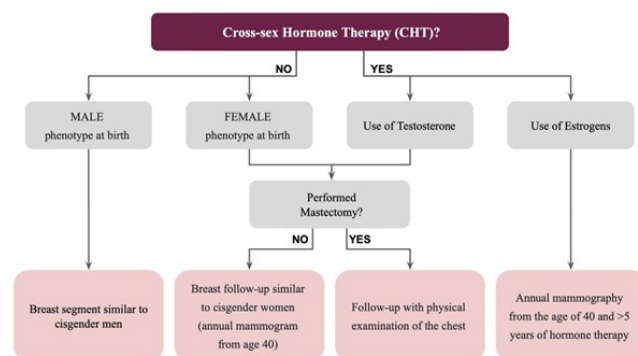


Figure 1. Flowchart for breast cancer screening in transgender individuals. Trans Mastology Outpatient Clinic, Federal University of São Paulo (Unifesp), 2021.

Initial risk stratification

All patients undergo a standardized clinical assessment including:

- Age;
- Hormone therapy duration and type;
- Surgical history (mastectomy, implants);
- Personal history of breast or ovarian cancer;
- Family history of breast and ovarian cancer;
- Known BRCA mutations;
- Reproductive history in individuals retaining the uterus and ovaries (age at menarche, parity, breastfeeding history).

Transfeminine individuals

Screening mammography is recommended when both criteria are met:

- Age ≥ 40 years;
- Continuous estrogen exposure ≥ 5 years.

Screening interval:

- Annual.

Rationale:

- Cumulative estrogen exposure as a biologically plausible proliferative factor;
- Alignment with the ACR Appropriateness Criteria, which classify screening at this threshold as “may be appropriate”²⁷;
- Shared decision-making framework acknowledging limited high-level evidence.

Transmasculine individuals

Post-mastectomy:

- Routine clinical examination. Imaging reserved for symptomatic cases or individuals at high genetic risk.

Retained breast tissue:

- Annual mammography beginning at age 40.

High-risk individuals

Patients with BRCA mutations or strong family history undergo:

- Genetic counseling;
- High-risk imaging pathways;
- Consideration of annual contrast-enhanced breast MRI^{19,28}.

Complementary imaging

A subset of participants underwent additional imaging examinations depending on clinical presentation and surgical history:

- Breast ultrasound for dense breast tissue or focal symptoms;
- Contrast-enhanced breast MRI for high-risk individuals.

Imaging systems used in the institutional setting included digital mammography, high-resolution ultrasound equipment, and dedicated breast MRI protocols using gadolinium-based intravenous contrast.

DISCUSSION

Breast cancer screening in transgender individuals occupies a clinically complex and methodologically limited domain. Current observational evidence suggests intermediate incidence patterns in transfeminine individuals — higher than cisgender men but lower than cisgender women¹⁴. This positioning challenges binary screening paradigms structured exclusively around sex assigned at birth.

Brazilian normative screening (50–69 years, biennial) does not incorporate exogenous hormone duration or surgical heterogeneity^{24,25}. In contrast, the ACR criteria recognize potential appropriateness of earlier screening in transfeminine individuals with sustained estrogen exposure²⁷.

The institutional protocol developed at Unifesp recommends screening initiation at age 40 rather than 50 years for transfeminine individuals with ≥5 years of estrogen exposure. This earlier threshold reflects alignment with the ACR guidance, which classifies screening at this age as “may be appropriate.” The choice prioritizes cumulative endocrine exposure rather than relying exclusively on population-based mortality modeling derived from cisgender cohorts. Importantly, this decision is implemented within a shared decision-making framework, explicitly acknowledging that evidence remains limited and that individual risk factors — including family history, obesity, and duration of hormone exposure — should guide clinical decisions.

In transmasculine individuals, oncologic risk is primarily determined by retained glandular tissue. Post-mastectomy patients are managed with clinical surveillance, whereas individuals retaining breast tissue follow structured imaging protocols. This approach aligns with current recommendations that emphasize residual tissue as the primary determinant of screening necessity^{21,22,27}.

All screening decisions are made under shared decision-making with explicit acknowledgment of evidentiary limitations. Patients are informed about the absence of randomized screening trials in transgender populations, the observational nature of incidence data, and the regulatory gap in national guidelines.

Limitations

The principal limitations of this protocol include:

- Absence of randomized controlled trials in transgender populations;
- Limited long-term follow-up in existing cohort studies;
- Heterogeneity in hormone regimens across studies;
- Variability in surgical techniques for chest masculinization;
- Literature review limited to 2012–2022, potentially excluding more recent publications;
- Protocol based on extrapolation from cisgender population data;

- Need for prospective validation of screening efficacy in this population.

Risk estimates are therefore derived from observational cohorts and indirect extrapolation from cisgender populations. Given these limitations, screening strategies must balance biological plausibility, available epidemiological evidence, radiologic expertise, and regulatory frameworks.

Educational context

The Trans Mastology Outpatient Clinic at Unifesp also functions as an academic and training environment for residents and medical students. The clinic provides structured exposure to the healthcare needs of the LGBTQIA+ population, integrating oncologic vigilance with inclusive care principles.

CONCLUSION

Breast cancer screening in transgender individuals remains an evolving field characterized by limited prospective evidence and absence of unified national directives.

The institutional protocol developed at the Federal University of São Paulo integrates:

- Literature synthesis;
- International radiologic criteria (ACR);
- Brazilian normative screening guidance;
- Individualized risk stratification;
- Shared decision-making.

This structured framework provides a pragmatic and ethically grounded approach to inclusive oncologic vigilance while recognizing persistent knowledge gaps.

Longitudinal studies with extended follow-up are necessary to refine incidence estimates and optimize screening intervals tailored to transgender populations.

AUTHORS' CONTRIBUTION

MPRS: Conceptualization, Data curation, Formal analysis, Investigation, Writing – original draft, Writing – review & editing. NMC: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – review & editing. MDS: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – review & editing. MRDS: Formal analysis, Supervision, Validation; Writing – review & editing. SE: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Supervision, Validation, Writing – review & editing.

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