Rethinking prostate cancer screening in transgender women: Bridging the gap in inclusive healthcare

Asmaa Ismail[1], Ruba Abdul Hadi[2], Husain Alaradi[2], Krishna Jani[2], Hazem Elmansy[2], Ahmed Zakaria[2], Ahmed Kotb[1]
[1]Grande Prairie Regional Hospital, Grande Prairie, AB, Canada; [2]Thunder Bay Regional Health Science Centre, Thunder, Bay, ON, Canada

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Corresponding author: Dr. Ahmed Kotb, Grande Prairie Regional Hospital, Grande Prairie, AB, Canada; drahmedfali@gmail.com

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ABSTRACT

Introduction: Over the years, the number of people openly identifying as transgender has steadily increased, leading to a greater need for transgender-specific healthcare information. Among transgender women (TW), there remains a risk of prostate cancer since the prostate is not removed during gender-affirming hormone therapy (GAHT) or surgery; however, there is limited knowledge about prostate cancer screening in the transgender population. Although there are few reported cases of prostate cancer screening or prostate-specific antigen (PSA) testing in TW, the impact of hormone therapies on PSA levels is well-documented. Notably, GAHT for TW and hormone therapy for treating prostate cancer share similarities. Drawing on these similarities, we aimed to develop guidelines for baseline PSA levels and prostate cancer screening in TW.
Methods: Through a systematic review, we examined the existing PubMed publications on PSA levels and prostate cancer screening in TW, as well as expected PSA levels in patients with prostate cancer undergoing hormone therapies. We also investigated other aspects considered for the diagnosis of prostate cancer. Given the limited research on TW, we also included relevant case studies. These publications and case reports were reviewed and analyzed to create a comprehensive overview of expected baseline PSA levels and prostate cancer screening guidelines for TW.
Results: Currently, there are no established guidelines for PSA or prostate cancer screening in TW; however, these case studies indicated a range of PSA values from 3.3 to <100 ng/ml. Existing literature on expected PSA levels in prostate cancer patients undergoing hormone

therapy shows a reduction in PSA of over 50% post-therapy. This evidence suggests that PSA values in TW presenting with prostate cancer may be lower than those observed in cisgender males with the disease.

Conclusions: While TW exhibit lower prostate cancer incidence compared to cisgender men, the impact of hormone therapy on PSA levels presents significant challenges for screening and diagnosis. The parallels between PSA level reductions in TG women and cisgender men undergoing estrogen therapy highlight the need for revised screening protocols. Addressing these challenges through targeted research and personalized care approaches will be vital for improving prostate cancer management in transgender individuals.

INTRODUCTION

An estimated 0.4-1.3% of the global population identifies as transgender [(1)]. In Canada, approximately 1 in every 300 people identifies as transgender or non-binary [(2)]. This growing visibility highlights the need for inclusive medical research and practices. For transgender women (TW), the risk of prostate cancer remains a significant concern because the prostate gland is retained after gender-affirming hormone therapy (GAHT) and surgery [(1, 3)].

Transgender individuals experience a gender identity that differs from their sex assigned at birth. TW are those assigned male at birth but who identify as female. Gender-affirming treatments, including hormone therapy and surgery, play a critical role in their transition process. Hormone therapy, typically involving estrogen and anti-androgens, alters prostate-specific antigen (PSA) levels, a key marker used in prostate cancer screening. PSA is a protein produced by both normal and malignant prostate cells, and elevated levels can indicate the presence of prostate cancer. Standard PSA thresholds for prostate cancer risk, such as values greater than 4 ng/mL being considered abnormal, may not be directly applicable to TW because of hormone therapy [(1, 4)].

This review aims to establish guidelines for prostate cancer screening in TW by conducting a systematic review to identify baseline PSA values indicative of cancer risk and to evaluate optimal biopsy methods based on prior gender-affirming procedures.

METHODS

We conducted a systematic review of the literature to identify studies examining prostate cancer in transgender women, with a focus on PSA levels, screening practices, and biopsy methods. We included peer-reviewed articles, case reports, and cohort studies published to the current time, which provided data on PSA values and cancer diagnoses in TW. Data sources included PubMed, Google Scholar, and academic databases relevant to oncology and transgender health. MeSH terms and keywords used: “transgender women.” “Prostate cancer,” “prostate-specific antigen,” “hormone therapy,” “gender-affirming surgery,” “PSA level in transgender women.”

The inclusion criteria were:

1. Studies involving transgender women diagnosed with prostate cancer.
2. Data on PSA levels at diagnosis and during follow-up.
3. Details on hormone therapy and surgical history.
4. Studies providing information on biopsy methods and cancer management.

We extracted data on the following variables: age at diagnosis, PSA levels at diagnosis, duration and type of GAHT, and biopsy methods. Data were synthesized to establish a baseline PSA value for TW and to assess the efficacy of different biopsy approaches.
Exclusion criteria included studies that did not report PSA levels or prostate cancer diagnosis in transgender women, or that were irrelevant to prostate cancer screening.

RESULTS

Our initial research identified 300 articles across the databases. After screening titles and abstracts, 240 articles were excluded due to irrelevance to prostate cancer in transgender women. A full-text review was then performed for 60 articles, of which 9 articles included data on PSA values and information on hormonal therapy for prostate cancer in transgender women.

In transgender women with diagnosed prostate cancer, PSA levels at the time of diagnosis varied significantly, ranging from 3.3 ng/mL to 1710 ng/ml. These patients had been on GAHT for 10 to 41 years. The GAHT regimens included injectable estrogen, estrogen tablets, bilateral orchiectomy, and intranasal gonadotropin-releasing hormone (GnRH). The patient's case reported by van Haarst et al. (1998) showed an exceptionally high PSA level of 1710 ng/mL after 10 years of GAHT. Cases that had bilateral orchiectomy did not always result in deficient PSA levels, as seen in Dorff et al. (2007) and Turo et al. (2013), who had PSA levels of 20.6 ng/mL and 13.5 ng/mL, respectively. Data are summarized in table (1).

The results of hormone therapy in cisgender men with prostate cancer demonstrated a consistent PSA decline of over 50% following different hormone treatments. For instance, studies such as Fleshner et al. [(14)] reported a PSA decline from 42.9 ng/mL to 2.9 ng/mL over six months of finasteride and flutamide treatment. Other therapies, including diethylstilbestrol (DES), abiraterone acetate, and conjugated estrogens, also led to significant reductions in PSA levels of >50% [(15- 19)].

DISCUSSION

Our analysis reveals that while prostate cancer in transgender women is less common compared to cisgender men, the complexity of their medical histories necessitates a special approach to screening and management.

Transgender women, who typically undergo hormone therapy as part of their gender-affirming treatment, have a lower incidence of prostate cancer compared to cisgender men. However, the presence of residual prostate tissue and the potential impacts of long-term hormone therapy complicate the landscape of prostate cancer risk and management in this population. The review identifies a substantial gap in large-scale studies and comprehensive data specifically addressing prostate cancer in transgender women.

The lower incidence of prostate cancer in transgender women is likely attributed to the effects of estrogen therapy, which is thought to suppress prostate tissue growth. However, there is limited consensus on the degree of risk reduction or the impact of various hormone regimens. Loria et al [(20)] did a study using data from the TriNetX database and found that TG women have 2.56 folds lower risk of prostate cancer compared to cis-gender men, and for men aged 50- 64, the risk was only 2.06 fold less. Moreover, diagnostic challenges persist due to the lack of standardized protocols tailored to transgender women, leading to potential delays in detection and treatment.

Research on hypogonadal men revealed that the incidence of prostate cancer was twice as high in those with PSA levels below 4 ng/ml compared to eugonadal men with similar low PSA levels [(21)]. Men with low serum testosterone have been shown to have more aggressive prostate cancer at presentation [(22)]. This should raise a question about whether prostate cancer in TG women is rare or under-diagnosed.

The median age at diagnosis of prostate cancer in TG women was 64 years, which is comparable to that of cisgender men. However, transgender women often present with additional variables, such as the effect of long-term hormone therapy and advanced or metastatic disease at diagnosis. We hypothesize that TG women may develop prostate cancer at a younger age than cisgender men due to the influence of hormone manipulation. Furthermore, it is plausible that long-term hormone therapy and testosterone depletion could activate alternative pathways for prostate cancer growth, potentially accelerating the progression to castration-resistant metastatic prostate cancer, which is more challenging to manage. These hypotheses, however, require further clinical investigation for validation.

The examination of transgender women for prostate cancer is a developing area within transgender healthcare, with limited attention in the literature. Digital rectal exam (DRE) remains applicable and is the preferred method for transgender women [(23)]. In TG women who have undergone vaginoplasty, there is a potential for transvaginal examination of the prostate [(24)].

Prostate biopsy presents unique considerations, largely because the existing literature on this topic is limited and primarily extrapolated from practices involving cisgender men. Transrectal ultrasound (TRUS) guided biopsy remains applicable for transgender women [(23)]. Transvaginal biopsy was also reported as a possible successful alternative [(13)]. Another approach is the transperineal (TP) biopsy which may be preferred for those who experience discomfort with the transrectal/ transvaginal methods or have anatomical variations due to prior surgeries. We could only identify a case report describing a successful TP biopsy in a 35-year-old TG woman [(25)]. The choice of biopsy method should be guided not only by technical considerations but also by patient comfort and preferences.

Beyond the biological and clinical aspects, the mental health and psychosocial well-being of transgender women undergoing screening for prostate cancer are critical considerations. Many transgender women experience significant levels of stigma, discrimination, and healthcare disparities, which can lead to reluctance in seeking care, particularly for conditions associated

with male anatomy, such as prostate cancer. In counselling for prostate cancer screening, healthcare providers must adopt a sensitive, affirming approach that acknowledges these psychosocial stressors. Ensuring privacy, using appropriate language that aligns with the patient's gender identity, and providing emotional support during the process can help reduce distress.

Artificial intelligence (AI) is becoming an integrated part of our current world, ranging from the simple daily use of cell phones to data analysis and personalized medicine. AI was found to improve the diagnosis and treatment planning for patients with prostate cancer [(26)]. Theoretically; AI can enhance screening protocols for TG women by analyzing their medical history, including hormone therapy and other risk factors, leading to more effective and personalized screening recommendations.

Limitations

Most of the studies are small-scale, with limited longitudinal data, which restricts the generalizability of findings. The variability in hormone regimens and the heterogeneity in study designs further complicate the interpretation of results. There is also a significant lack of research on the long-term outcomes of prostate cancer in transgender women, which is critical for developing effective management strategies.

While AI was suggested to have an added value to personalize the screening, data limitation and quality can be a significant barrier.

CONCLUSIONS

While transgender women exhibit lower prostate cancer incidence compared to cisgender men, the impact of hormone therapy on PSA levels presents significant challenges for screening and diagnosis. The parallels between PSA level reductions in TG women and cisgender men undergoing estrogen therapy highlight the need for revised screening protocols. Addressing these challenges through targeted research and personalized care approaches will be vital for improving prostate cancer management in transgender individuals.

PSA values of >2 ng/ml may be considered high to trigger a prostate biopsy. Prostate examination and biopsy methods should consider the patient's preference and comfort.

The development and implementation of AI tools tailored to the needs of transgender individuals could improve diagnostic accuracy and personalized care, but this requires further research and attention to data inclusivity and ethical considerations.

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FIGURES AND TABLES

Table 1. PSA values for transgender women with diagnosed prostate cancer

Reference	Age at diagnosis (years)	PSA at diagnosis (ng/mL)	Length of GAHT (years)	Types of GAHT
Deebal et al (2017)[5]	65	7.5	20	Injectable estrogen therapy
Thurston et al (1994)[6]	64	27.0	12	Unknown
van Haarst et al (1998)[7]	53	1710.0	10	Unknown
Miksad et al (2006)[8]	64	240.0	41	Estrogen tablets, bilateral orchiectomy
Dorff et al (2007)[9]	78	20.6	23	Estrogen therapy, bilateral orchiectomy
Turo et al (2013)[10]	75	13.5	30	Estrogen tablets, bilateral orchiectomy
Ellent et al (2016)[11]	65	19.0	35	Estrogen therapy
Sharif et al (2017)[12]	56	5.0	20	Estrogen therapy
Ingham et al (2018)[13]	60	3.3	20	Intranasal GnRH

GAHT: gender-affirming hormone therapy; GnRH: gonadotropin-releasing hormone; PSA: prostate-specific antigen.