Rethinking prostate cancer screening in transgender women

Bridging the gap in inclusive healthcare

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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 TW 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 one 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 >4 ng/mL being considered abnormal, may not be directly applicable to TW because of hormone therapy.[1,4]

We aimed 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 TW, with a focus on PSA levels, screening practices, and biopsy methods. We included peer-reviewed articles, case reports, and cohort studies published until 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 included: "transgender women," "prostate cancer," "prostate-specific antigen," "hormone therapy," "gender-affirming surgery," and "PSA level in transgender women."

The inclusion criteria were:

1. Studies involving TW diagnosed with prostate cancer.
2. Data on PSA levels at diagnosis and during followup.
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 TW, or that were irrelevant to prostate cancer screening.

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)[22]	65	7.5	20	Injectable estrogen therapy
Thurston et al (1994)[23]	64	27.0	12	Unknown
van Haarst et al (1998)[5]	53	1710.0	10	Unknown
Miksad et al (2006)[24]	64	240.0	41	Estrogen tablets, bilateral orchiectomy
Dorff et al (2007)[6]	78	20.6	23	Estrogen therapy, bilateral orchiectomy
Turo et al (2013)[7]	75	13.5	30	Estrogen tablets, bilateral orchiectomy
Ellent et al (2016)[25]	65	19.0	35	Estrogen therapy
Sharif et al (2017)[26]	56	5.0	20	Estrogen therapy
Ingham et al (2018)[19]	60	3.3	20	Intranasal GnRH

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

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 TW. A full-text review was then performed for 60 articles, of which nine articles included data on PSA values and information on hormonal therapy for prostate cancer in TW.

In TW with diagnosed prostate cancer, PSA levels at the time of diagnosis varied significantly, ranging from 3.3–1710 ng/ml. These patients had been on GAHT for 10–41 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 showed an exceptionally high PSA level of 1710 ng/mL after 10 years of GAHT.[5] Cases that had bilateral orchiectomy did not always result in deficient PSA levels, as seen in Dorff et al[6] and Turo et al,[7] 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 reported a PSA decline from 42.9 ng/mL to 2.9 ng/mL over six months of finasteride and flutamide treatment.[8] Other therapies, including diethylstilbestrol (DES), abiraterone acetate, and conjugated estrogens, also led to significant reductions in PSA levels of >50%.[9-13]

DISCUSSION

Our analysis reveals that while prostate cancer in TW 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. This review identifies a substantial gap in large-scale studies and comprehensive data specifically addressing prostate cancer in TW.

The lower incidence of prostate cancer in TW 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 did a study using data from the TriNetX database and found that TG women have 2.56-fold lower risk of prostate cancer compared to cisgender men, and for men aged 50–64, the risk was only 2.06-fold less.[14] Moreover, diagnostic challenges persist due to the lack of standardized protocols tailored to TW, 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 <4 ng/ml compared to eugonadal men with similar low PSA levels.[15] Men with low serum testosterone have been shown to have more aggressive prostate cancer at presentation.[16] This should raise a question about whether prostate cancer in TW women is rare or underdiagnosed.

The median age at diagnosis of prostate cancer in TW was 64 years, which is comparable to that of cisgender men; however, TW often present with additional variables, such as the effect of long-term hormone therapy and advanced or metastatic disease at diagnosis. We hypothesize that TW 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 TW 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 TW.[17] In TW who have undergone vaginoplasty, there is a potential for transvaginal examination of the prostate.[18]

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 TW.[17] Transvaginal biopsy was also reported as a possible successful alternative.[19] 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 TW.[20] The choice of biopsy method should be guided not only by technical considerations but also by patient comfort and preferences.

> “ Parallels between PSA level reductions in transgender women and cisgender men on estrogen therapy highlight the need for revised screening protocols. ”

Beyond the biological and clinical aspects, the mental health and psychosocial well-being of TW undergoing screening for prostate cancer are critical considerations. Many TW 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 counseling 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.[21] Theoretically, AI can enhance screening protocols for TW 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 TW, 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 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 TW 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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REFERENCES

1. Winter S, Diamond M, Green J, et al. Transgender people: Health at the margins of society. *Lancet* 2016;388:390-400. https://doi.org/10.1016/S0140-6736(16)00683-8
2. Statistics Canada. Daily: Canada's changing demographics. https://www150.statcan.gc.ca/n1/daily-quotidien/220427/dq220427b-eng.htm. Accessed September 4, 2024.
3. Bertoncelli Tanaka M, Sahota K, Burn J, et al. Prostate cancer in transgender women: What does a urologist need to know? *BJU Int* 2022;129:113-22. https://doi.org/10.1111/bju.15521
4. Nik-Ahd F, Jarjour A, Figueiredo J, et al. Prostate-specific antigen screening in transgender patients. *Eur Urol* 2023;83:48-54. https://doi.org/10.1016/j.eururo.2022.09.007
5. van Haarst EP, Newling DW, Gooren LJ, et al. Metastatic prostatic carcinoma in a male-to-female transsexual. *Br J Urol* 1998;81:776. https://doi.org/10.1046/j.1464-410x.1998.00582.x
6. Dorff TB, Shazer RL, Nepomuceno EM, et al. Successful treatment of metastatic androgen-independent prostate carcinoma in a transsexual patient. *Clin Genitourin Cancer* 2007;5:344-6. https://doi.org/10.3816/CGC.2007.n.016
7. Turo R, Jallad S, Prescott S, et al. Metastatic prostate cancer in transsexual diagnosed after three decades of estrogen therapy. *Can Urol Assoc J* 2013;7:E544-6. https://doi.org/10.5489/cuaj.175
8. Fleshner NE, Trachtenberg J. Combination finasteride and flutamide in advanced carcinoma of the prostate: Effective therapy with minimal side effects. *J Urol* 1995;154:1642-6.
9. Shamash J, Stebbing J, Sweeney C, et al. A validated prognostic index predicting response to dexamethasone and diethylstilbestrol in castrate-resistant prostate cancer. Cancer 2010;116:3595-602. https://doi.org/10.1002/cncr.25194
10. Mendonça Macedo A, Gameiro Marques R, Cunha André M, et al. Prostate-specific antigen response after abiraterone treatment in mCRPC: PSA as a predictor of overall survival. *Arch Ital Urol Androl* 2023;95:11052. https://doi.org/10.4081/aiua.2023.11052
11. Condappa A, Gossell-Williams M, Aiken W. Favourable response of serum prostate-specific antigen to conjugated oestrogen in castrate-resistant prostate cancer in Jamaica. *Ecancermedicalscience* 2018;12:829. https://doi.org/10.3332/ecancer.2018.829
12. Hellerstedt B, Pienta KJ, Redman BG, et al. Phase II trial of oral cyclophosphamide, prednisone, and diethylstilbestrol for androgen-independent prostate carcinoma. *Cancer* 2003;98:1603-10. https://doi.org/10.1002/cncr.11686
13. Omlin A, Pezaro CJ, Zaidi S, et al. Antitumour activity of abiraterone and diethylstilboestrol when administered sequentially to men with castration-resistant prostate cancer. *Br J Cancer* 2013;109:1079-84. https://doi.org/10.1038/bjc.2013.446
14. Loria M, Gilbert D, Tabernacki T, et al. Incidence of prostate cancer in transgender women in the US: A large database analysis. *Prostate Cancer Prostatic Dis* 2024 Feb 7; Epub ahead pf print. https://doi.org/10.1038/s41391-024-00804-4
15. Ramasamy R, Fisher ES, Schlegel PN. Testosterone replacement and prostate cancer. *Indian J Urol* 2012;28:123-8. https://doi.org/10.4103/0970-1591.98449
16. Morgentaler A, Rhoden EL. Prevalence of prostate cancer among hypogonadal men with prostate-specific antigen levels of 4.0 ng/mL or less. *Urology* 2006;68:1263-7. https://doi.org/10.1016/j.urology.2006.08.1058
17. Crowley F, Mihalopoulos M, Gaglani S, et al. Prostate cancer in transgender women: Considerations for screening, diagnosis and management. *Br J Cancer* 2023;128:177-89. https://doi.org/10.1038/s41416-022-01989-y
18. Weyers S, De Sutter P, Hoebeke S, et al. Gynaecological aspects of the treatment and follow-up of transsexual men and women. *Facts Views Vis Obgyn* 2010;2:35-54
19. Ingham MD, Lee RJ, MacDermed D, et al. Prostate cancer in transgender women. *Urol Oncol* 2018;36:518-25. https://doi.org/10.1016/j.urolonc.2018.09.011
20. Coleman-Belin J, Amakiri UO, Deng FM, et al. Hematospermia in a transgender woman with evidence for endometrial tissue in the prostate. *AACE Clin Case Rep* 2024;10:80-3. https://doi.org/10.1016/j.aace.2024.01.006
21. Azadi Moghadam P, Bashashati A, Goldenberg SL. Artificial intelligence and pathomics: Prostate cancer. *Urol Clin North Am* 2024;51:15-26. https://doi.org/10.1016/j.ucl.2023.06.001
22. Deebel NA, Morin JP, Autorino R, et al. Prostate cancer in transgender women: Incidence, etiopathogenesis, and management challenges. *Urology* 2017;110:166-71. https://doi.org/10.1016/j.urology.2017.08.032
23. Thurston AV. Carcinoma of the prostate in a transsexual. *Br J Urol* 1994;73:217. https://doi.org/10.1111/j.1464-410x.1994.tb07503.x
24. Miksad RA, Bubley G, Church P, et al. Prostate cancer in a transgender woman 41 years after initiation of feminization. *JAMA* 2006;296:2316-7. https://doi.org/10.1001/jama.296.19.2316
25. Ellent E, Matrana MR. Metastatic prostate cancer 35 years after sex reassignment surgery. *Clin Genitourin Cancer* 2016;14:e207-9. https://doi.org/10.1016/j.clgc.2015.11.007
26. Sharif A, Malhotra NR, Acosta AM, et al. The development of prostate adenocarcinoma in a transgender male-to-female patient: Could estrogen therapy have played a role? *Prostate* 2017;77:824-8. https://doi.org/10.1002/pros.23322

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