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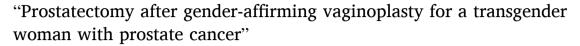
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ABSTRACT

We present the case of a 75 year old transgender woman 18 months post gender-affirming vaginoplasty found to have unfavorable, intermediate risk prostate cancer. She elected a robotic radical prostatectomy with bilateral pelvic lymph node dissection. Postoperatively, the patient resumed neovaginal dilation without difficulty, and had improvements on International Prostate Symptom Score when compared to post-vaginoplasty, pre-prostatectomy. Incontinence measured by Revised Urinary Incontinence Scale remained mild. Robotic prostatectomy can, under appropriate circumstances, allow preservation of the neovaginal vault, but requires considerable experience and multidisciplinary intraoperative collaboration.

1. Introduction

The incidence of prostate cancer in transgender women on genderaffirming hormone therapy or following gender-affirming surgery has been estimated to be 2.5 to 5-fold lower than age-matched cisgender men. The incidence may actually be higher, since cancer registries and other datasets relying on electronic health records may underestimate incidence among transgender populations.² Despite this, there is currently no consensus on values or frequency for prostate-specific antigen (PSA) level screening in transgender women.³ Transgender patients are significantly less likely to undergo PSA level screening and less likely to have ever had a PSA level recorded relative to cisgender men. 1 Case reports and population-based datasets have detailed development of prostate cancer following estrogen-based hormonal therapy. 4-6 To our knowledge, only 6 cases of prostate cancer following gender-affirming vaginoplasty have been described, which were treated with radiation and/or chemotherapy alone,^{7–11} brachytherapy,¹² or laparoscopic prostatectomy with neovaginal canal foreshortening. 13

2. Case presentation

A 75-year-old transgender woman with a past medical history of cardiovascular disease presented with bothersome lower urinary tract

At the time of her vaginoplasty, she was on tamsulosin and reported a longstanding history of obstructive voiding symptoms. Following her vaginoplasty, she developed chronic dysuria managed with prophylactic Cefalexin without symptom resolution. Due to a waxing and waning elevated PSA level, with values as high as 2.8 ng/ml prior to vaginoplasty and 3.6 ng/ml 5 months after vaginoplasty, the patient was counseled regarding further screening for prostate cancer. Additional risk factors included a family history of prostate cancer (brother) and her 40 pack-year smoking history.

At age 75, a SelectMDx prostate cancer biomarker test was performed following digital prostate exam via the neovaginal canal to

symptoms following gender-affirming vaginoplasty. She reported that she was born with one undescended testicle, and had been continually taking 50 mg of testosterone cypionate weekly by intramuscular injection for 30 years to treat hypogonadism. She began her medical transition at age 67 and trialed oral estradiol 1 mg BID for one month before discontinuing due to nausea. A multidisciplinary gender-affirming surgery team determined that she was appropriate for surgical treatment despite her lack of one year of hormone therapy due to contraindication to estrogen, in accordance with the contemporaneous World Professional Association for Transgender Health Standards of Care version 7.
She underwent orchiectomy at age 67 and had gender-affirming penile inversion vaginoplasty at age 73.

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produce the non-invasive urine test. ¹⁵ This predictor of prostate biopsy returned a 47 % likelihood of prostate cancer on biopsy and a 20 % likelihood of Gleason Score \geq 7 (3 + 4). A multi-parametric prostate MRI was performed, revealing a 1 cm, PIRADS Score 4 lesion in the left posterior medial peripheral zone at mid gland level (Fig. 1) and neovagina in contact with the prostatic apex (Fig. 2). A transperineal MRI-ultrasound fusion prostate biopsy was performed. Eight out of 16 total cores obtained were positive for intermediate-risk prostate cancer, all from the left lobe of the prostate, including 4/4 from the targeted lesion. Seven of these positive cores were Gleason Score 7 (3 + 4) prostate cancer; 1 random core from the left posterior base showed Gleason Score 7 (4 + 3) prostate cancer. The patient was advised to discontinue testosterone therapy.

The patient was counseled on the risks and benefits of active surveillance, radiation, and surgical therapy. Through shared decision making, and after discussing her care with her vaginoplasty surgeon, she elected to undergo robot-assisted laparoscopic radical prostatectomy with bilateral pelvic lymph node dissection using the DaVinci Xi platform (Intuitive Surgical Inc.). During her previous penile inversion vaginoplasty, the neovaginal vault was constructed using inverted penile skin and scrotal skin graft applied directly on the posterior prostate capsule. The patient was therefore counseled that a significant breach of the neovaginal vault during prostatectomy would necessitate a partial or total neovaginectomy to prevent the development of a urethroneovaginal fistula. She consented to a gracilis or alternate flap transfer to obliterate the neovaginal vault if the defect was sufficiently large. Additionally, given the potential disruption of the pelvic floor during creation of the neovaginal canal, the patient was counseled that prostatectomy may result in persistent urinary incontinence.

Her pre-biopsy prostate MRI was used to aid in surgical planning. The patient was positioned in lithotomy to allow access to the neovagina during the case. The plastic surgeon confirmed that a speculum exam could be performed while the robot remained docked. A posterior-approach prostatectomy was performed, dissecting the seminal vesicles and vasa free first, developing the potential space between the posterior layers of Denonveillier's fascia, and transecting the prostatic pedicles with sealing electrocautery. Dense scarring was encountered along the left prostatic pedicle, bilateral neurovascular bundles, and broadly along the posterior apex necessitating a partial neurovascular bundle sacrifice on this side. The dorsal venous complex was transected

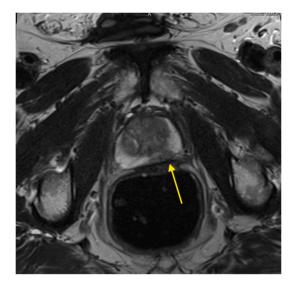


Fig. 1. Pre-Surgical Lesion on Imaging **Fig. 1** Legend. T2 Axial view of the prostate depicts a PRADS-4 lesion in the left

posterior medial peripheral zone at mid gland level (yellow arrow). (For

interpretation of the references to colour in this figure legend, the reader is

referred to the Web version of this article.)

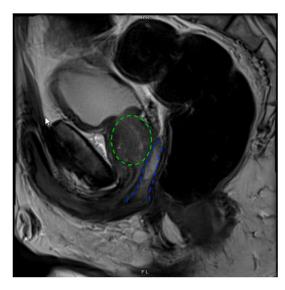


Fig. 2. Pre-Surgical Relation of the Neovagina to Prostate **Fig. 2** Legend. T2 Sagittal view of the prostate (outlined in green) abutting the neovagina (outlined in blue). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

sharply and oversewn. The prostate apex was swept back from the urethra to maximize urethral length, and the urethra was sharply transected. All of the apical dissection was completed sharply given the dense adhesions of the neovagina to the posterior prostate apex. During the final release of the apical prostate from the neovaginal graft, a 2 mm full-thickness defect in the anterior wall of the neovagina was noted (Fig. 3).

Following completion of prostatic capsule release and removal, the plastic surgeon performed a speculum exam. Given the small size of the defect and the availability of local tissue for repair, the decision was made that a primary repair should be undertaken. The anterior neovaginal wall defect was closed robotically in 2 layers. A regional 3 cm \times 2 cm tissue flap based upon the distal left neurovascular bundle vasculature was mobilized and rotated over the neovaginal defect to reinforce this repair. The flap was then secured in place to the neovaginal posterior wall with interrupted suture. On repeat neovaginal exam, the defect was well-approximated without air leak from abdominal insufflation. The bladder neck required tailoring to approximate an anatomical size of the urethra. To avoid having a suture line in contact with the neovagina repair posteriorly, an anterior, running, midline bladder neck repair was performed. A Rocco posterior anastomotic support stitch was then completed using an anchoring suture for posterior reconstruction of

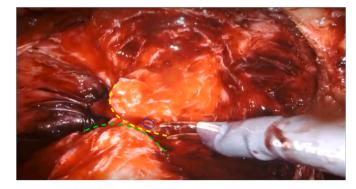


Fig. 3. Neovaginal Vault Defect During Apical Prostatic Dissection
Fig. 3 Legend. Defect in neovaginal vault (within blue circle), created during
release of the apical prostate (outlined in green) from the anterior wall of the
neovagina (outlined in yellow). (For interpretation of the references to colour in
this figure legend, the reader is referred to the Web version of this article.)

the rhabdomyosphincter to provide posterior support for the urethra and urethro-sphincteric complex in an effort to improve continence. ¹⁶ A running vesico-urethral anastomosis was completed, and an anterior U-stitch was placed to approximate the anterior bladder neck and the dorsal venous complex tissue in an effort to alleviate tension on the urethral anastomosis.

The patient tolerated the 278 minute procedure well and was discharged on postoperative day 2. Final pathology showed a correlating 1.3 cm dominant tumor nodule at the left mid/base of the transitional zone; Gleason scoring could not be performed due to post-hormonal treatment changes. Examined margins were negative and seminal vesicles and lymph nodes were uninvolved.

Following surgery, no urethro-neovaginal fistula occurred and the patient was able to resume neovaginal dilation. She reported stress urinary incontinence at the 6-week postoperative visits, as described by clinically standardized patient-reported outcomes including the International Prostate Symptom Score (IPSS) and Revised Urinary Incontinence Scale (RUIS-5) in Table 1. She initially required 5 incontinence briefs per day. This was down to 1 brief per day 4 months after surgery. She no longer required undergarments for incontinence 6 months after surgery. At her most recent follow up 14 months after initial surgery, her most bothersome urinary symptom was nocturia 4 times nightly.

The patient was followed by gynecology for ongoing gender-affirming care. Risks of further hormone treatment were discussed with the multidisciplinary team. Her urologic oncologist advised against continuing testosterone replacement therapy in the immediate post-operative period. She began estradiol 0.05 mg/24 hour weekly patch 3 months postoperatively. Her post-operative PSA level has been undetectable with routine surveillance, and the patient was advised she can resume exogenous testosterone if this remains the case 2 years post-prostatectomy.

3. Discussion

The lower incidence of prostate cancer in transgender women has largely been attributed to the protective effects of androgen deprivation, through orchiectomy or anti-androgen medication, though lack of appropriate prostate cancer screening may also contribute. In our patient's case, she had no significant history of estrogen-based hormone therapy, and her risk profile was likely equivalent to cisgender men her age with a family history of prostate cancer.

3.1. Prostate screening

Patients need to be aware that they can still develop prostate cancer after vaginoplasty. In a 2022 study of Thai transgender women who underwent vaginoplasty, only 15 of 100 patients knew about the presence of their remaining prostate gland, with limited prostate cancer risk awareness linked to lower levels of education, time from operation >10 years, and lack of surgeon counseling. 17 In this patient, PSA levels prior to surgery were no higher than 2.9 ng/ml; however, further prostate cancer assessments prior to vaginoplasty given this patient's age, family history, and obstructive voiding symptoms would have been warranted. Opportunities exist prior to gender-affirming vaginoplasty to consider a patient's prostate cancer risks and discuss prostate cancer screening via

Table 1Patient reported outcomes.

Patient- Reported Outcome Measure	Post-Vaginoplasty, Pre-Prostatectomy	Post-Prostatectomy (4 months post- operative)	Long Term (14 months post- operative)
IPSS IPSS QOL	28 (severe) 3 (mixed)	18 (moderate) 5 (unhappy)	8 (moderate) 4 (mostly
RUIS-5	1 (none/mild)	8 (mild)	dissatisfied) 7 (mild)

a shared decision-making process.

For all gender-affirming vaginoplasty patients, we advocate for lifelong, yearly follow-up with clinicians who are equipped perform neovaginal exams when indicated. ¹⁸ As this patient had significant personal risk factors and symptoms, she continued to receive PSA level screenings following vaginoplasty. In this way, the patient benefited from receiving care at an academic medical center with long experience in managing patients after gender-affirming vaginoplasty.

3.2. Perioperative care

The consent process for prostatectomy following vaginoplasty must be tailored to the patient-specific anatomy. Without intervening tissue between the neovaginal lining and the prostate capsule, there is a risk of compromise of the integrity of the neovagina during prostatectomy. Any significant defect in the anterior neovaginal wall would result in a risk of urethro-neovaginal fistula. Patients need to be informed of this risk and accept that a partial or total neovaginectomy with the addition of a flap closure may be required. A preoperative prostate MRI is crucial for prostate cancer diagnosis and surgical planning in this patient group. Sharp dissection was used primarily for the apical dissection to avoid thermal injury to the neovaginal vault. A small rent in the neovaginal vault was repaired without sequelae of urethro-neovaginal fistula or of neovaginal stenosis. In the only previously reported prostatectomy after vaginoplasty, a partial neovaginal colpocleisis was performed after a portion of the anterior neovaginal wall was removed with the prostate. ¹³

Due to potential alterations to the urethral sphincter complex during penile inversion vaginoplasty, our patient was counseled regarding the likely increased risk for longer-term urinary incontinence after prostatectomy when compared to the standard post-prostatectomy course for a cisgender patient. While patient-reported urinary outcomes in transgender patients after vaginoplasty have not been robustly evaluated, de novo incontinence after gender-affirming vaginoplasty has been observed (4%–16 % prevalence), ¹⁹ likely related to division of the pelvic floor musculature to create the neovaginal introitus. For this reason, our patient was counseled regarding increased risk for urinary incontinence following prostatectomy surgery. In the only previously reported prostatectomy after vaginoplasty, the patient had severe sphincteric incontinence refractory to urethral bulking agents. In our case, the patient's urinary incontinence measured by the RUIS-5 increased but remained mild at 14-month postoperative follow-up, and she was able to stop using incontinence undergarments by 6 months after prostatectomy. Her IPSS score decreased overall from severe to moderate following prostatectomy, with an increase in bothersome nocturia.

After her prostatectomy, she has been collaboratively managed by a urologic oncologist, a plastic surgeon, and a gynecologist who have all contributed to her hormone and post-surgical care. Her ongoing surveillance plan is continued PSA level screening following standard protocol. Given barriers to care faced by transgender patients, ²⁰ urologic oncologists add a crucial skillset, providing ongoing comprehensive care in a sensitive and culturally competent manner.

4. Conclusion

Gender identity, hormonal exposure, family history, and past surgical procedures are important factors to consider when screening and treating prostate cancer in transgender patients. Optimal care for prostate cancer after vaginoplasty is delivered in a multidisciplinary setting by surgeons familiar with post-vaginoplasty anatomy.

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CRediT authorship contribution statement

Gaines Blasdel: Conceptualization, Investigation, Methodology, Visualization, Writing – original draft, Writing – review & editing. Luca Borah: Conceptualization, Data curation, Investigation, Writing – original draft, Writing – review & editing. Roberto Navarrete: Conceptualization, Investigation, Methodology, Visualization, Writing – original draft, Writing – review & editing. Rebecca Howland: Data curation, Investigation, Writing – original draft, Writing – review & editing. William M. Kuzon: Conceptualization, Investigation, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing. Jeffrey S. Montgomery: Conceptualization, Investigation, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing.

References

- Ma SJ, Oladeru OT, Wang K, et al. Prostate cancer screening patterns among sexual and gender minority individuals. *Eur Urol*. 2021;79(5):588–592. https://doi.org/ 10.1016/j.eururo.2020.11.009.
- Borah L, Lane M, Nathan H. Missing, inconsistent, and other—a call to improve transgender representation in oncology research. *JAMA Oncol*. 2023;9(7):891–894. https://doi.org/10.1001/jamaoncol.2023.1344.
- Nik-Ahd F, Jarjour A, Figueiredo J, et al. Prostate-specific antigen screening in transgender patients. Eur Urol. 2023;83(1):48–54. https://doi.org/10.1016/j. eururo 2022 09 007
- Ingham MD, Lee RJ, MacDermed D, Olumi AF. Prostate cancer in transgender women. *Urol Oncol*. 2018;36(12):518–525. https://doi.org/10.1016/j. urolong/2018/09/011
- Baraban E, Ding CC, White M, et al. Prostate cancer in male-to-female transgender individuals: histopathologic findings and association with gender-affirming hormonal therapy. Am J Surg Pathol. 2022;46(12):1650–1658. https://doi.org/ 10.1097/pas.000000000001964.
- Nik-Ahd F, De Hoedt A, Butler C, et al. Prostate cancer in transgender women in the veterans affairs health system, 2000-2022. *JAMA*. 2023;329(21):1877–1879. https://doi.org/10.1001/jama.2023.6028.
- Dorff TB, Shazer RL, Nepomuceno EM, Tucker SJ. Successful treatment of metastatic androgen-independent prostate carcinoma in a transsexual patient. Clin Genitourin

- Cancer. 2007/06/01/2007;5(5):344–346. https://doi.org/10.3816/CGC.2007.
- van Haarst EP, Newling DW, Gooren LJ, Asscheman H, Prenger DM. Metastatic prostatic carcinoma in a male-to-female transsexual. Br J Urol. 1998;81(5):776. https://doi.org/10.1046/j.1464-410x.1998.00582.x.
- Turo R, Jallad S, Prescott S, Cross WR. Metastatic prostate cancer in transsexual diagnosed after three decades of estrogen therapy. Can Urol Assoc J. 2013;7(7-8): E544–E546. https://doi.org/10.5489/cuaj.175.
- Miksad RA, Bubley G, Church P, et al. Prostate cancer in a transgender woman 41 years after initiation of feminization. *JAMA*. 2006;296(19):2316–2317. https://doi. org/10.1001/jama.296.19.2316.
- Mansur A, Kempf AM, Bitterman D, et al. Clinical outcomes of radiation therapy for transgender and genderexpansive people with cancer. Front Oncol. 13:1135400.
- Chandran K, Grochot R, de Los Dolores Fenor De La Maza M, et al. A transgender patient with prostate cancer: lessons learnt. Eur Urol. 2023/04/01/2023;83(4): 379–380. https://doi.org/10.1016/j.eururo.2022.12.027.
- Kumar S, Tyldesley S, Poon CI, Saunders JT, Hoag CC. Case–Laparoscopic radical prostatectomy in a transgender woman after gender-affirming vaginoplasty. Canadian Urological Association Journal. 2024;18(3).
- Coleman E, Bockting W, Botzer M, et al. Standards of care for the health of transsexual, transgender, and gender-nonconforming people, version 7. Int J Transgenderism. 2012;13(4):165–232.
- Haese A, Trooskens G, Steyaert S, et al. Multicenter optimization and validation of a 2-gene mRNA urine test for detection of clinically significant prostate cancer before initial prostate biopsy. J Urol. 2019;202(2):256–263. https://doi.org/10.1097/ in.00000000000000233
- Rocco B, Cozzi G, Spinelli MG, et al. Posterior musculofascial reconstruction after radical prostatectomy: a systematic review of the literature. *Eur Urol.* 2012;62(5): 779–790. https://doi.org/10.1016/j.eururo.2012.05.041.
- Pitak-Arnnop P, Messer-Peti R, Tangmanee C, Neff A, Meningaud JP. Prostate cancer awareness among transgender women after gender-affirming surgery. *Prostate*. 2022;82(10):1060–1067. https://doi.org/10.1002/pros.24355.
- Bruce LK, Morris MP, Swanson M, Kuzon WM, Morrison SD. Post penile inversion vaginoplasty clinical examination: considerations and techniques. *Plast Reconstr Surg Glob Open*. 2022;10(5), e4338. https://doi.org/10.1097/gox.0000000000000004338.
- Blasdel G, Dy GW, Nikolavsky D, Ferrando CA, Bluebond-Langner R, Zhao LC. Urinary reconstruction in genital gender-affirming surgery: checking our surgical complication blind spots. *Plast Reconstr Surg.* 2023;153(4):792e–803e. https://doi. org/10.1097/PRS.000000000010813.
- Chung PH, Spigner S, Swaminathan V, Teplitsky S, Frasso R. Perspectives and experiences of transgender and non-binary individuals on seeking urological care. *Urology*. 2021;148:47–52. https://doi.org/10.1016/j.urology.2020.10.026.