Specific aims:

Primary aims:

- Stage 1: To understand postoperative urologic, sexual, and pelvic floor experiences of transgender women
- Stage 2: To validate a questionnaire measuring the frequency and severity of postoperative urogynecologic symptoms in transgender women

Secondary aims:

- To understand the types of urologic, sexual and pelvic floor complaints and their degree of bother
- To evaluate the relationship between procedure technique and symptomatology
- To understand the temporal impact on symptomatology after surgery
- To assess the impact of hormonal therapy or other gender confirming treatments on urologic and pelvic floor symptoms.

Background/significance:

It has been estimated that approximately 1 in 60000 individuals globally suffer from gender dysphoria with male-to-female (MTF) gender dysphoria being 4 times more common than female-to-male (FTM) (1). Oftentimes, these individuals are subjected to social stigmatization, abuse, and a general lack of support, leading to depression and higher than average rates of suicide (2). Partially for these reasons, currently only about 13% of transgender patients undergo genital surgery for cosmetic purposes with or without gonadectomy, known as gender confirmation or reassignment surgery (GCS) (3). While some patients elect to forgo gender confirmation surgery voluntarily, others who do desire it are hindered due to cost, availability of trained providers, or the challenges in meeting the WPATH (World Professional Association for Transgender Health) guidelines for transitioning. Patient satisfaction following surgery is high, particularly regarding sexual and cosmetic outcomes; however, unexpected negative functional outcomes such as bowel and bladder dysfunction and sexual impairment can impact overall patient satisfaction (4,5).

Male-to-female genital surgery typically includes bilateral orchiectomy, penectomy, urethroplasty, labioplasty, and creation of a neovagina and neoclitoris. This can be done in one or two stages with the potential for additional reconstructive procedures in the future. Of the various vaginoplasty techniques available, the type most commonly performed involves vaginoplasty using penile skin inversion and clitoroplasty utilizing the glans penis and preserved neurovascular bundle. Other vaginoplasty techniques involve use of bowel, skin, or cheek mucosal graft. The penile portion of the urethra is amputated, followed by excision of posterior corpus spongiosum and marsupialization of the distal urothelium to the anterior skin flap (1). Bleeding and stenosis of the urethral meatus are complications associated with this approach to urethroplasty (6–9). Subsequent follow-up of patients has shown an increased risk for voiding dysfunction, abnormal urinary stream, incontinence,

and overactive bladder during both the immediate and long-term postoperative period (6,7,9–11). Thus far, postoperative urologic evaluations of MTF patients are based on retrospective analysis, single-provider samples, and simple urologic questionnaires that have no validation within this population. A recent systematic review noted that the majority of literature on outcomes was low to intermediate quality with poor comparability due to differences in data collection and surgical technique (12). The available information suggests that 16-33% of patients experience incontinence postoperatively, with stress predominance, 32-47% experience abnormal voiding, and 24-66% experience overactive bladder symptoms (10,13,14).

Outside of the typically assessed voiding symptoms, unique complaints of MTF postoperative patients include obstructive voiding symptoms due to urethral stenosis, persistent perimeatal erectile tissue, and prostatic hypertrophy (6,8,11). Unfortunately, these conditions cannot accurately be evaluated using standard urogynecologic tools, and they have not been thoroughly characterized in prior studies regarding their severity, effect on voiding, and optimal treatment strategies.

Other unique aspects of MTF patients with urologic complaints include the high dose hormonal treatments and unique neovaginal flora. The male urethra and bladder contains both alpha and beta estrogen receptors (15). Given the continuous systemic exogenous estrogen exposure, one can theorize that these receptors become activated promoting a cascade of change. This, in conjunction with an altered microbiome due to exposure to different flora after surgery, can lead to an alteration in the histology and physiology of the bladder and urethra. Anatomically, the creation of a neovagina in a previously non-occupied space below the urethra and bladder can trigger bladder irritation by mass effect, theoretically leading to the overactive bladder symptoms and voiding changes reported by some. Depending on the tissue source, the unique flora of the neovagina can seed the lower urinary tract structures, thus potentiating a reactive, potentially irritative, process.

Additionally, it has been estimated that about 8% of patients will have symptomatic neovaginal prolapse, and many will require corrective surgery (13). This is likely an underestimation as the follow-up rates for patients tends to be very low, and the lack of adequate support mechanisms for the neovagina preclude it to descend more easily than a natural vagina.

We suggest that further clarification regarding MTF postoperative urologic and pelvic floor complaints can be achieved via a mixed methods approach. By using focus group interviews to create specific evaluative questions for this unique population, we can then prospectively assess patients undergoing surgery and be more proactive in addressing their needs. A unique patient-reported outcome (PRO) questionnaire will additionally allow this patient group to feel supported and involved in their own care. In all, this will enhance the quality of our care, patient satisfaction, and success of their gender confirmatory process.

Hypotheses:
Stage 1 Unit of Analysis: To understand the urologic and pelvic floor symptoms transgender women experience following genital surgery
Stage 2 Null Hypothesis: Male-to-female gender confirmation surgery has no impact on urologic and pelvic floor symptoms including overactive bladder symptoms, incontinence, voiding dysfunction, sexual dysfunction, and prolapse.

Methodology:

Research design:
This will be a mixed methods study in an exploratory sequential design structure involving qualitative analysis via focus groups comprised of postoperative transgender women (Stage 1), followed by the distribution and testing of a questionnaire packet to male-to-female patients planning to undergoing GCS at academic transgender care centers in the United States (Stage 2). The intent of the Stage 1 focus group questions will be to clarify the presentation and severity of urogynecologic symptoms in this patient group. Moderators will also ask the participants about the type and timing of their gender confirmation surgery, additional procedures, use of hormonal therapies, and neovaginal care. Please review attached Moderator Guide for the concepts to be addressed. The themes and categories generated from the focus groups will be used to create a unique screening questionnaire for this patient population that will be tested for reliability and validity in the Stage 2 component. We estimate that about 3 to 4 focus groups will be required to reach data saturation; however, additional groups may be necessary.

Stage 2 will be conducted in coordination with participating academic medical centers with affiliated gender surgeons or internal transgender care centers with surgical providers. After patient recruitment, postoperative questionnaires will be distributed which will be comprised of the Pelvic Floor Distress Inventory-20 (PFDI-20), Pelvic Floor Impact Questionnaire-7 (PFIQ-7), WHO Quality of Life BREF (WHOQOL-BREF), and the new questionnaire created from the Stage 1. We estimate about 10 minutes will be required to compete the entire questionnaire packet. A test-retest reliability challenge will be performed two weeks later with the new questionnaire only. Patient data and questionnaire answers will be entered into a universal RedCap database. All data will be analyzed at Weill Cornell Medicine. Operative information for Stage 2 participants as well as postoperative exams and treatments will be reviewed at the time of data collection and entered for analysis.

Patient recruitment for Stage 1 will be facilitated by provider referrals through transgender clinics and LGBTQ centers as well as flyer distribution to local support groups and networks (Appendix 1). A website URL (Appendix 2) will be included on the flyer for additional participation information for both Stage 1 and Stage 2.

During the focus group sessions, patients will be consented and reminded of confidentiality rules. In the advent that any disclosed information requires

immediate medical or supportive care, the participant will be placed in direct contact with their primary provider for further assistance. This will be explicitly written in the consent form and verbally announced prior to the start of the focus group. Focus group participants will be provided with a light meal and round trip Metrocard® for travel reimbursement.

There will a separate informed written consent for Stage 2 participants. These will need to be reviewed and authorized by each participating institution prior to distribution.

Participants:
Male-to-female transgender patients who have either undergone or plan to undergo gender confirmative genital surgery.

Stage 1: In-person focus groups comprised of MTF postoperative patients who participate in support groups in various New York City LGBTQ centers. Participants will be selected using homogeneous sampling methods. We will also reach out to online support communities to set up virtual focus groups or phone interviews if feasible. We plan to embed snowballing sampling to permit recommended individuals to participate.

Stage 2: Patients scheduled to undergo gender confirmative genital surgery or recently completed surgery within academic transgender medicine centers in the United States. They will be recruited on a rolling basis.

Sample size/power:

- Stage 1: Three to four in-person/online focus groups, comprising 10-12 participants with possible one-on-one phone interviews until data saturation reached
- Stage 2: Estimated 100-150 patients (approx 10 patients per question)

Inclusion criteria:

- Stage 1 -- Male-to-female transgender women who are at least 4 weeks postoperative following genital surgery for gender confirmation
- Stage 2 -- Male-to-female transgender women who are scheduled to undergo surgery or are within 4 weeks postoperative
- Both stages -- Minimum age 18 years old
- Both stages -- English fluency
- Both stages -- Reliable contact information and/or permanent residence

Exclusion criteria:

- Preexisting pelvic pathology, including abnormal anatomy or baseline voiding dysfunction
- Urinary or intestinal problems prior to surgery lasting greater than 6 weeks

Primary outcomes:

- Stage 1: Characterization of genital, urologic, bowel, and sexual symptoms following male-to-female gender confirmation surgery
- Stage 2: Validity and reliability testing of new questionnaire

Secondary outcomes:

- Frequency and severity of symptoms
- Relationship between surgical technique and symptoms
- Effect of hormonal therapy usage and symptoms
- Length of time since surgery and development of symptoms

Confounding factors:
Patient age, race/ethnicity, weight, procedure technique, presence of non-iatrogenic causes of symptoms, co-morbidity, mobility restrictions, medication interactions, diet, infection, type and duration of hormonal therapy, prostate size, sexual activity

Research setting:
Focus groups will take place at the Lesbian, Gay, Bisexual and Transgender Community Center on 208 W 13 St New York, NY 10011.
Stage 2 will be conducted at various academic centers within the United States. Committed programs include Boston Medical Center and Weill Cornell Medicine. Study team members will reach out to additional programs at national conferences and through established networks.
All data will be collected and analyzed within Weill Cornell Medicine

Study instruments:
ATLAS.ti qualitative data analysis software (Berlin, Germany)
PFDI-20 (Pelvic Floor Distress Inventory-20)
PFIQ-7 (Pelvic Floor Impact Questionnaire-7)
WHOQOL-BREF (permission for use granted)

Data collection parameters:
DEMOGRAPHICS/ PRE-TREATMENT DETAILS

- Age
- Race/ethnicity
- Height
- Weight
- BMI (body mass index)
- Smoking status
- Sexual activity
- Medications
- Date of surgery
- Type and extent of hormonal therapy usage
- Additional genital surgical procedures

- History of preoperative urologic complaints
- History of prostatic hypertrophy or prostate cancer

POST-TREATMENT DETAILS

- Operative technique
- Complications
- Postoperative care
- Resumption of hormonal therapy
- Urinary tract infections
- Sexual activity
- Medications

Qualitative data analysis:

- Stage 1: transcript coding with thematic analysis
- Stage 2: Continuous variables will be calculated using student's t- test
    - Categorical data and outcomes will be calculated using chi-square analysis
    - Multiple regression analysis will be performed to assess for a correlation between symptomatology and operative technique, hormonal therapy, or demographics
    - The new questionnaire reliability will be challenged with internal consistency testing and 2-week test-retest
    - Construct validity will be challenged with face validity and convergent validity using the other questionnaires

Ethical issues:

- Patient consent for enrollment will be obtained prior to onset of focus groups or questionnaire completion
- All patient information at the time of enrollment will be de-identified and recorded in a password-protected secured electronic database.
- No additional treatments or provider appointments will be required of the participants above the standard of care.

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