

Postoperative Complications following Primary Penile Inversion Vaginoplasty among 330 Male-to-Female Transgender Patients



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Abbreviations and Acronyms

BMI = body mass index

DVT = deep vein thromboembolism

GAS = gender affirming surgery

HRT = hormone replacement therapy

MTF = male-to-female

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Purpose: Studies of surgical complications of penile inversion vaginoplasty are limited due to small sample sizes. We describe postoperative complications after penile inversion vaginoplasty and evaluated age, body mass index and years on hormone replacement therapy as risk factors for complications.

Materials and Methods: We retrospectively reviewed the records of male-to-female patients who presented for primary penile inversion vaginoplasty to a high volume surgeon (MLB) from 2011 to 2015. Complications included granulation tissue, vaginal pain, wound separation, labial asymmetry, vaginal stenosis, fistula formation, urinary symptoms including spraying stream or dribbling, infection, vaginal fissure or vaginal bleeding. We classified complications by Clavien-Dindo grade. Multivariable logistic regression was performed to determine the independent effects of age, body mass index and hormone replacement therapy on postoperative surgical complications.

Results: A total of 330 patients presented for primary penile inversion vaginoplasty. Median age at surgery was 35 years (range 18 to 76). Median followup in all patients was 3 months (range 3 to 73). Of the patients 95 (28.7%) presented with a postoperative complication. Median time to a complication was 4.4 months (IQR 1–11.5). Rectovaginal fistulas developed in 3 patients (0.9%). A total of 30 patients (9.0%) required a second operation. There were no complications greater than Clavien-Dindo grade IIIB. Age, body mass index and hormone replacement therapy were not associated with complications.

Conclusions: Penile inversion vaginoplasty is a relatively safe procedure. Most complications due to this surgery develop within the first 4 months postoperatively. Age, body mass index and hormone replacement therapy are not associated with complications and, thus, they should not dictate the timing of surgery.

Key Words: penis, transgender persons, sex reassignment procedures, hormone replacement therapy, postoperative complications

An estimated 1.4 million people in the United States, or about 0.6% of the adult population, identify as transgender.¹ A similar prevalence was

reported in European nations.² The medical and surgical needs of this population are becoming more recognized.³ Sex confirmation procedures,

including genital reconstruction, have become medically necessary treatments which are now covered by many insurance companies.⁴ Many European universal health care plans also cover sex confirmation procedures.⁵

The benefits of genital reconstruction for gender dysphoria have been previously described, including improvements in sexuality and overall psychosocial well-being,^{6–9} and yet the rate of complications is high.⁶ Genital reconstruction is a technically demanding surgery that must produce satisfactory functional and subjectively pleasing cosmetic outcomes. Genital reconstruction complications are known, such as lower urinary tract symptoms, sexual dysfunction, wound necrosis and fistula, among others.^{10,11} However, complication data are limited by small sample sizes. To our knowledge patient risk factors for complications following GAS are currently unknown.

WPATH (World Professional Association for Transgender Health) guidelines for MTF GAS state that patients must live at least 12 months in a gender role that is congruent with the patient gender identity and be of legal consenting age in the country of origin.¹² Because GAS has recently become more widely accepted, to our knowledge the age at which patients should undergo GAS is unknown. Whether increased age places one at risk for postoperative complications after GAS merits future research.

During the period before surgery it is also recommended that patients use feminizing hormones such as estrogen and progesterone, although many patients have received HRT for years prior to GAS.¹² Genitourinary changes due to HRT include decreased spontaneous erections, male sexual dysfunction, decreased testicular volume and decreased sperm production.¹² Penile skin is also susceptible to changes from HRT, including penile atrophy.¹³ In penile inversion vaginoplasty long-term systemic HRT may make the penile skin more challenging to use during surgery and predispose patients to surgical complications.

We describe complications following primary penile inversion vaginoplasty in a large cohort of MTF patients. We evaluated the effects of age and long-term (greater than 1 year) systemic HRT on the development of complications. Because HRT may lead to an increase in body fat,¹⁴ we also evaluated BMI as an independent risk factor for postoperative complications. We hypothesized that all 3 factors would put patients at risk for complications after GAS.

MATERIAL AND METHODS

Study Design

We retrospectively reviewed the records of all MTF patients who presented for primary GAS to 1 high volume

surgeon (MLB) from 2011 to 2015. Preoperative clinic visit notes were reviewed for demographic and medical data. In particular we collected age at surgery, years on HRT before surgery, smoking status, BMI in kg/m², systolic blood pressure, HIV status and medical comorbidities, including hypertension, diabetes mellitus, coronary artery disease, chronic obstructive pulmonary disease, depression, anxiety and benign prostatic hyperplasia. Surgical histories were also collected including prior orchiectomy, breast augmentation, tracheal shaving and/or vasectomy.

All patients included in study met WPATH standards for GAS.¹² Only patients who presented for initial GAS surgery were included and those undergoing revision GAS were excluded from analysis. The surgical technique of penile inversion vaginoplasty was previously described.¹⁵

All patients were receiving estradiol with or without progesterone and spironolactone. In all patients HRT was tapered to 2 mg estradiol at least 2 weeks before surgery while progesterone and spironolactone were stopped completely 2 weeks before surgery. All patients were seen at our clinic 7 days after surgery for postoperative evaluation and followed with 6 and 12-week telephone calls. Secondary followup clinic visits were offered on an as needed basis. We collected followup data on all reported complications along with median time from surgery to the presentation of the complication.

Surgical characteristics included whether a concurrent procedure was completed at GAS, such as tracheal shaving and/or breast augmentation. In addition, estimated blood loss, intraoperative vaginal depth measurement in cm and intraoperative surgical complications (ie rectal enterotomy) were recorded. Recorded postoperative characteristics included the number of days from surgery to postoperative visits and postoperative vaginal depth in cm. Vaginal depth was measured using dilators with known dimensions. We collected surgical as well as cosmetic complications (ie cosmesis not satisfactory to the patient) that required a secondary followup visit. Time to reoperation and the nature of reoperation were also captured. All complications were classified with the Clavien-Dindo surgical complications grading scale.¹⁶ Cosmetic complications were excluded from this classification.

Variables

Predictor. We assessed age and BMI at surgery and the number of years that the patient had received HRT before GAS as risk factors for complications.

Outcome. We recorded surgical complications, including granulation tissue in and around the neovagina, vaginal pain, wound separation, labial asymmetry (cosmetic), vaginal stenosis, fistula (rectoneovaginal or vesicovaginal), a deflecting urinary stream or dribbling, infection, vaginal fissure, vaginal bleeding, difficulty dilating, DVT or pulmonary embolism.

Statistical Methods

Data analysis was performed with STATA®, version 13.0. Summary statistics were used to describe the population, surgical characteristics, complications, time to complication and reoperations. We performed multivariable

logistic regression to determine the independent effects of age, BMI and HRT on our outcomes of interests, which were fistula formation, wound separation/granulation tissue formation and vaginal stenosis. Patient age, BMI and years on HRT were determined a priori. We used the most common complications, including wound separation/granulation tissue formation and vaginal stenosis, as the outcome of multivariable modeling to have a sufficient number of outcomes. Rectoneovaginal or vesicovaginal fistula was also included in multivariable modeling as this is the most severe complication. All models were controlled for patient distance from the clinic using the ZIP Code®. Statistical significance was considered at $p < 0.05$. The internal review board at the primary surgeon institution approved the study.

RESULTS

A total of 330 patients presented for primary GAS from 2011 to 2015. Median age at surgery was 35 years (range 18–76). Table 1 lists patient demographic characteristics, and medical and surgical histories. The median number of years on HRT before GAS was 3 (range 1 to 42, IQR 2–6). All patients in our sample were on HRT for at least 1 year. Median BMI was 24.5 kg/m² (IQR 22–29).

Table 1. Patient and surgery characteristics of those who presented for and underwent MTF GAS from 2011 to 2015

No. pts	330	
Median age (range)	35	(18–76)
Median HRT yrs (IQR)	3	(2–6)
No. smoking status (%):		
Never	273	(82.7)
Former	28	(8.5)
Current	18	(5.5)
Marijuana	11	(3.3)
Median kg/m ² BMI (IQR)	24.5	(22–29)
Median systolic blood pressure (IQR)	120	(115–128)
No. HIV pos (%)	9	(2.7)
No. medical comorbidity (%):		
Hypertension	32	(9.7)
Type 2 diabetes	20	(6.1)
Coronary artery disease	11	(3.3)
Chronic obstructive pulmonary disease	3	(0.9)
Depression	99	(30.0)
Anxiety	39	(11.8)
Benign prostatic hyperplasia	6	(1.8)
Congenital genitourinary anomaly	10	(3.0)
No past medical history	135	(40.9)
No. surgical history (%):		
Orchiectomy	32	(9.7)
Breast augmentation	66	(20.0)
Tracheal shave	20	(6.1)
Vasectomy	17	(5.2)
No past surgical history	71	(21.5)
No. concurrent additional procedure (%):		
None	303	(91.8)
Tracheal shave	15	(4.6)
Breast augmentation	5	(1.5)
Median ml estimated blood loss (IQR)	200	(200–350)
Median inches vaginal depth at surgery (IQR)	6	(5.5–6.5)
No. intraop complications (%):		
None	320	(98.5)
Rectal enterotomy	5	(1.5)
Median inches postop vaginal depth (IQR)	6.25	(6–6.5)

Table 1 also lists all surgery characteristics. An additional procedure was performed in 20 patients (6.0%), of which the most common was a tracheal shave in 15 (4.6%). Median estimated blood loss was 200 ml (IQR 200–350). Rectal enterotomy was rare, occurring in 5 patients (1.5%). All cases were managed by primary closure.

The supplementary table (<http://jurology.com/>) shows all complications and reoperations. Median followup in all patients was 3 months (range 3 to 73) and 29 patients (8.8%) had more than 1 year of followup. A total of 95 patients (28.7%) presented with a complication attributable to GAS. Median time to a postoperative complication was 4.4 months (IQR 1–11.5). The most common complication was the formation of granulation tissue, which was noted in 24 cases (7.3%). The most common complication within a month postoperatively was wound separation, which was observed in 17 patients (5.2%). Rectoneovaginal fistulas developed in 3 patients (0.9%), including 2 in whom an intraoperative rectal enterotomy was identified and repaired. All patients with a fistula were referred to colorectal surgery for definitive repair. Vesicovaginal fistulas developed in 3 patients (0.9%) without intraoperative complications.

No patient experienced deep vein thrombosis or pulmonary embolism perioperatively. All complications were Clavien-Dindo grade I–IIIb. A total of 30 patients (9.0%) required a second operation. Median time from initial surgery to reoperation was 10.9 months (IQR 6.2–19.6). Of patients with a second operation the most common procedure was revision labioplasty, which was done in 90%. Of all patients who underwent labioplasty it was performed in 10 (52.6%) due to cosmetic reasons. Granulation tissue was the most common complication, noted in 24 cases. However, this was removed in the operating room in only 3 of these patients (12.5%) while the remaining patients were treated in an outpatient setting. Urethral reconstruction was required in 5 patients (21%) due to a deflecting urinary stream. None of these patients had a urethral stricture. One patient was returned to the operating room 7 days after GAS due to severe vaginal bleeding.

Table 2 shows the results of multivariable logistic regression. Age, BMI and HRT were not independent risk factors for wound complications, fistula formation or vaginal stenosis. The adjusted OR for patient distance from the clinic and wound complications was significant at 0.93 (95% CI 0.88–0.97). This suggests that patients with a wound complication were more likely to be followed at our clinic instead of one not participating in the study.

Table 2. Age, BMI, and years on HRT as potential risk factors for complications

	Multivariable OR (95% CI)		
	Fistula	Wound Separation or Granulation Tissue	Vaginal Stenosis
Age	1.02 (0.94–1.10)	0.97 (0.94–1.01)	0.99 (0.92–1.05)
BMI	1.05 (0.82–1.34)	1.07 (0.98–1.16)	0.98 (0.82–1.17)
HRT	0.65 (0.28–1.50)	1.02 (0.95–1.09)	1.04 (0.92–1.16)
Clinic distance*	0.95 (0.84–1.08)	0.93 (0.88–0.97)†	0.98 (0.90–1.06)

* Adjusted for more than 100 miles.

† Significant at $p < 0.05$.

DISCUSSION

We determined risk factors for complications in penile inversion vaginoplasty in what is to our knowledge the largest published cohort of MTF patients treated with GAS. Overall surgical complications developed within the first 4 months postoperatively. About a quarter of the patients who presented due to complications required a second operation. MTF GAS is a relatively safe operation with no reported grade IV or grade V complications. All patients continued small doses of HRT until the time of surgery, which is contrary to most other reports,⁶ and we noted no thromboembolic events during or after surgery. No baseline factor (age, BMI or HRT) predicted wound complications, fistula formation or vaginal stenosis.

Overall the prevalence of complications in our study mirrors that in other small scale studies.^{6,11,17} The most dreaded complication, which is rectoneovaginal fistula, was reported to develop in about 0.8% to 17% of all penile inversion vaginoplasty cases.⁶ The prevalence of rectoneovaginal fistula in our cohort was 0.9%. Rectoneovaginal fistula most commonly develops due to rectal enterotomy, which occurred in two-thirds of our patients with rectal enterotomy during surgery. Goddard et al suggested carefully checking for enterotomy after prostate and bladder mobilization by digital rectal examination.¹⁸ Careful dissection that closely follows the urethra along its track from the central tendon of the perineum up through the lower pole of the prostate is critical. After Denonvilliers' fascia is exposed only blunt dissection is encouraged. Colonic injury should be closed intraoperatively.

In the current series no patient required colostomy, although fistulas formed in 2 patients in our series. Age, BMI and years on HRT were not associated with fistula formation. Importantly patients with a vesiconeovaginal fistula are referred to a reconstructive urologist for definitive repair, usually in the home region.

Urinary symptoms can develop after penile inversion vaginoplasty. Symptoms include a weak or deflecting stream, which can be due to urethral

stenosis, asymmetrical labia or an adhesion band. Revision surgery may be required, which often involves labioplasty with lysis of adhesions. Longer study is needed of complications due to the reconstructed urethra.

Poor cosmetic appearance of the vulva is common. In the series by Amend et al in 24 patients the most common reason for reoperation was cosmetic correction in the form of mons pubis plasty and mucosa reduction in 50% of patients.¹¹ Goddard et al reported repeat labioplasty in only 2.5% of patients.¹⁸ We try to minimize scarring using a 1-stage surgical approach and the lateralization of surgical scars to the groin. The inner labial lining attains a realistic vulvar appearance with the use of the divided male urethra. This also provides minor secretory and erectile/erotic function. Despite these techniques 5.6% of the patients required labial revision.

Regardless, cosmetic issues pertaining to GAS outcomes are often patient driven. Preoperative patient education is necessary to counsel patients on the range of cosmesis. We counsel patients that they must wait a minimum of 3 months before the cosmetic outcome can be assessed. Factors that determine patient satisfaction in regard to cosmesis require future study.

Most surgeons suggest that patients stop all HRT 6 weeks before MTF GAS.^{6,18} This has traditionally been thought to prevent DVT during the perioperative period but to our knowledge no study has confirmed this. The rate of DVT after MTF GAS was reported to be less than 1%.^{8,18} We have patients taper HRT to 2 mg estradiol at least 2 weeks before surgery and we have not diagnosed postoperative DVT or pulmonary embolism. Beyond the potential drawbacks of HRT at surgery the benefits of HRT in general have been reported.^{19,20} Gender affirming HRT has been associated with decreased stigmatization and decreased risky sexual behavior.²⁰ A more recent study showed that feminizing hormones decrease blood pressure in transgender women.¹⁹ In our experience continuing low dose estradiol contributes to patient well-being and avoids depressed mood and other symptoms of hormone withdrawal.²¹ Additionally, cisgender women who receive oral contraceptives commonly continue this medication before surgical procedures despite using doses much higher than transgender women.²²

However, we suggest that patients with previous DVT discontinue HRT completely 2 weeks before surgery. Routine DVT prophylaxis, such as early postoperative ambulation, sequential compression stockings and prophylactic anticoagulation, may be sufficient in most patients.

If a patient presented with a complication elsewhere, this was not recorded in our database.

Therefore, we probably underestimated complications, especially minor complications such as wound separation or the formation of granulation tissue. Because this is a surgical population, results may not be generalizable to all MTF transgender individuals. Despite these limitations, to our knowledge this is the largest cohort of MTF patients who underwent GAS and it provides a framework for future research.

CONCLUSIONS

Penile inversion vaginoplasty is a relatively safe procedure but 1 of 10 patients requires a second operation. Most complications due to MTF GAS develop within the first 4 months after surgery. Stopping HRT 6 weeks before MTF GAS may be unnecessary. Age, BMI and HRT are not associated with complications and, thus, they should not dictate the timing of surgery.

REFERENCES

- Flores A, Herman J, Gates G et al: How Many Adults Identify as Transgender in the United States? Los Angeles: The Williams Institute 2016.
- De Cuypere G, Van Hemelrijck M, Michel A et al: Prevalence and demography of transsexualism in Belgium. *Eur Psychiatry* 2007; **22**: 137.
- Stroumsa D: The state of transgender health care: policy, law, and medical frameworks. *Am J Public Health* 2014; **104**: e31.
- WPATH Clarification on Medical Necessity of Treatment, Sex Reassignment and Insurance Coverage in the USA. Minneapolis: World Professional Association for Transgender Health 2008.
- Kreukels B, Haraldsen I, De Cuypere G et al: A European network for the investigation of gender incongruence: the ENIGI initiative. *Eur Psychiatry* 2012; **27**: 445.
- Horbach SE, Bouman MB, Smit JM et al: Outcome of vaginoplasty in male-to-female transgenders: a systematic review of surgical techniques. *J Sex Med* 2015; **12**: 1499.
- De Cuypere G, T'Sjoen G, Beerten R et al: Sexual and physical health after sex reassignment surgery. *Arch Sex Behav* 2005; **34**: 679.
- Lawrence AA: Patient-reported complications and functional outcomes of male-to-female sex reassignment surgery. *Arch Sex Behav* 2006; **35**: 717.
- Lawrence AA: Factors associated with satisfaction or regret following male-to-female sex reassignment surgery. *Arch Sex Behav* 2003; **32**: 299.
- Hoebek P, Selvaggi G, Ceulemans P et al: Impact of sex reassignment surgery on lower urinary tract function. *Eur Urol* 2005; **47**: 398.
- Amend B, Seibold J, Toomey P et al: Surgical reconstruction for male-to-female sex reassignment. *Eur Urol* 2013; **64**: 141.
- 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 Transgend* 2012; **13**: 165.
- Reed HM, Yanes RE, Delto JC et al: Non-grafted vaginal depth augmentation for transgender atresia, our experience and survey of related procedures. *Aesthetic Plast Surg* 2015; **39**: 733.
- Fuss J, Hellweg R, Van Caenegem E et al: Cross-sex hormone treatment in male-to-female transsexual persons reduces serum brain-derived neurotrophic factor (BDNF). *Eur Neuropsychopharmacol* 2015; **25**: 95.
- Bowers M: Aesthetic male-to-female transsexual surgery. *Female Genital Plastic Cosmet Surg* 2016; **120**.
- Dindo D, Demartines N and Clavien PA: Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004; **240**: 205.
- Sigurjonsson H, Rinder J, Möllermark C et al: Male to female gender reassignment surgery: Surgical outcomes of consecutive patients during 14 years. *JPRAS Open* 2015; **6**: 69.
- Goddard JC, Vickery RM, Qureshi A et al: Feminizing genitoplasty in adult transsexuals: early and long-term surgical results. *BJU Int* 2007; **100**: 607.
- Deutsch MB, Bhakri V and Kubicek K: Effects of cross-sex hormone treatment on transgender women and men. *Obstet Gynecol* 2015; **125**: 605.
- Sevelius JM: Gender affirmation: a framework for conceptualizing risk behavior among transgender women of color. *Sex Roles* 2013; **68**: 675.
- Johnson R, Hemington-Gorse S and Dhital S: Do cosmetic surgeons consider estrogen-containing drugs to be of significant risk in the development of thromboembolism? *Aesthetic Plast Surg* 2008; **32**: 743.
- Oakes J, Hahn PM, Lillcrap D et al: A survey of recommendations by gynecologists in Canada regarding oral contraceptive use in the perioperative period. *Am J Obstet Gynecol* 2002; **187**: 1539.

EDITORIAL COMMENT

This retrospective review of MTF transgender patients who underwent primary penile inversion vaginoplasty has the conclusion that age, BMI and HRT are not associated with complications.

The followup protocol consisted of a 1-week postoperative visit and scheduled telephone calls at 6 and 12 weeks. It would be interesting to see whether results would be affected with longer followup via patient visits. Also, complications such as dyspareunia, urinary retention and incontinence were not included (reference 6 in article).

An interesting finding is that BMI was not associated with complications, in contrast to the outcomes of other soft tissue surgery. Further studies are encouraged to determine whether vaginoplasty is uniquely free of obesity related complications.¹

The authors report that surgery was performed with the patient on HRT. The absence of thromboembolic events should provide a guide toward the safety of this practice. We caution the reader about applying this finding as estrogen has been

associated with increased deep venous thrombosis in multiple studies.²

The authors should be commended on the scope of this project. The development of a standardized followup protocol and validated questionnaire is important to allow for effective comparison of outcomes across institutions.

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REFERENCES

1. Gust MJ, Smetona JT, Persing JS et al: The impact of body mass index on reduction mammoplasty: a multicenter analysis of 2492 patients. *Aesthet Surg J* 2013; **33**: 1140.
2. Practice Committee of the American Society for Reproductive Medicine: Combined hormonal contraception and the risk of venous thromboembolism: a guideline. *Fertil Steril* 2017; **107**: 43.