THE JOURNAL OF
SEXUAL MEDICINE

ORIGINAL RESEARCH & REVIEWS

Estrogen Continuation and Venous Thromboembolism in Penile Inversion Vaginoplasty

Ian T. Nolan, BM,[1] Caleb Haley, BS,[2] Shane D. Morrison, MD, MS,[3] Christopher J. Pannucci, MD MS,[4] and Thomas Satterwhite, MD[5]

ABSTRACT

Background: Estrogen therapy and penile inversion vaginoplasty (PIV) are necessary, life-saving interventions for many transfeminine patients. Patients undergoing PIV are generally at low baseline risk for venous thromboembolism (VTE) based on Caprini Score. Estrogen therapy may increase VTE risk in surgical patients, but its cessation may be psychiatrically dysphoric for transfeminine patients.

Aim: This study examines whether perioperative estrogen cessation impacts VTE risk in patients undergoing PIV.

Methods: This was a pre-post study of patients undergoing PIV. From 2014 through 2018, all patients stopped estrogen therapy for 2 weeks before surgery and resumed 1 week postoperatively (group 1). Starting in 2019, all patients continued estrogen therapy perioperatively, with dose reductions for those whose dose was >6 mg/day (group 2).

Outcomes: The primary outcome was 90-day VTE rate.

Results: 178 patients were included in the study, with 117 in group 1 and 61 in group 2. Median Caprini Score was 4 in group 1 (interquartile range: 3–6) and 3 in group 2 (interquartile range: 3–4) ($P = .011$). Complications per patient were higher in group 1 (2.2 vs 0.9, $P < .001$), with a longer follow-up (14.1 vs 10.2 months, $P < .001$). Rates of 90-day VTE were not different between groups (0.0% vs 1.6%, $P = .166$).

Clinical Implications: Patients undergoing PIV are generally at low risk for VTE, based on 2005 Caprini Scores. This study provides preliminary evidence that perioperative estrogen therapy continuation does not appear to substantially increase VTE risk in transfeminine patients undergoing PIV with low Caprini Scores, although more investigation is needed to establish true safety.

Strengths & Limitations: Strengths include the pre-post design and single-surgeon experience, high proportion of patients with 90-day follow-up, and relatively large series to understand baseline VTE risk by Caprini Score in a PIV population. The main weakness of this study is its limited power to measure true differences in VTE risk based on estrogen continuation.

Conclusions: This study suggests that perioperative estrogen continuation may be safe for patients undergoing PIV, the overwhelming majority of whom are at low baseline VTE risk. However, clinicians should weigh the magnitude of the risks and benefits of estrogen cessation on a case-by-case basis. **Nolan IT, Haley C, Morrison SD, et al. Estrogen Continuation and Venous Thromboembolism in Penile Inversion Vaginoplasty. J Sex Med 2020;XX:XXX–XXX.**

Copyright © 2020, International Society for Sexual Medicine. Published by Elsevier Inc. All rights reserved.

Key Words: Penile Inversion Vaginoplasty; Estrogens; Transgender Persons; Gender Affirmation Surgery; Venous Thromboembolism

Received July 14, 2020. Accepted October 24, 2020.

[1]Hansjörg Wyss Department of Plastic Surgery, Grossman School of Medicine, New York University, New York City, NY, USA;

[2]University of Michigan Medical School, Ann Arbor, MI, USA;

[3]Division of Plastic Surgery, Department of Surgery, University of Washington School of Medicine, Seattle, WA, USA;

[4]Plastic Surgery Northwest, Spokane, WA, USA;

[5]Align Surgical Associates Incorporated, San Francisco, CA, USA

Copyright © 2020, International Society for Sexual Medicine. Published by Elsevier Inc. All rights reserved.

https://doi.org/10.1016/j.jsxm.2020.10.018

INTRODUCTION

Treatment of gender dysphoria in transgender people includes hormonal and surgical modalities.[1] For transfeminine people (including transgender women and nonbinary people assigned male at birth), options include estrogen therapy and a variety of surgical interventions, including penile inversion vaginoplasty (PIV). Genital surgeries frequently take place after initiation of hormone therapy in accordance with current World Professional Association for Transgender Health Standards of Care.[1]

Frequently, health-care professionals are faced with an important consideration when delivering feminizing gender affirmation: the possibility of venous thromboembolism (VTE) from estrogen therapy in patients undergoing PIV. The prothrombotic effects of estrogen therapy, independent of surgical intervention, are well-documented in both cisgender and transgender women.[2–5] Elevated risk of VTE is more strongly associated with oral vs transdermal formulations,[2,5–9] and the risk appears to be dose-dependent.[9]

Surgery is an acknowledged risk factor for VTE development, and VTE risk increases linearly with time spent under general anesthesia.[10] PIV surgeries typically take at least 4 hours and have the possibility of lasting up to 8 hours.

Estrogen and surgery may have a synergistic effect on thrombotic risk, and thus, many surgeons currently recommend discontinuation of hormone therapy preoperatively.[4,11–13] However, data supporting the discontinuation of estrogen therapy, either in cisgender or transgender people, are limited.[14] Existing data for VTE risk in patients undergoing pelvic surgery are derived from people with abdominal and pelvic cancer, which is clearly a high-risk group.[15,16] Unique data for transfeminine people are required as patients undergoing PIV are generally younger and physically healthier than patients undergoing other major pelvic surgeries (eg, gynecologic or urologic tumor resection and subsequent reconstruction) and thus generally expected to be at lower risk for VTE as quantified by the 2005 Caprini Score.

The 2005 Caprini Score Thrombosis Risk Factor Assessment is an instrument to stratify the risk of VTE in surgical patients based on numerous patient-specific risk factors (Figure 1).[17] Using the Caprini Score, a 14-fold variation in VTE risk has been identified among surgical patients, with lower scores correlating with lower rates of VTE.[18] Patients undergoing plastic surgery with Caprini Scores less than 8 have been shown to have significantly decreased rate of VTE compared with patients with Caprini Scores greater than 8.[19] In addition, the risk of VTE among patients undergoing plastic surgery with Caprini Scores less than 5 has been calculated at 0.61%.[19] Although estrogen is well established as a risk factor for VTE,[20] most patients undergoing PIV are otherwise assumed to be at low risk for VTE as calculated by the Caprini Score. A recent retrospective review of 706 patients undergoing gender-affirmation surgeries reported a mean Caprini Score of 3, although this study included both transfeminine and transmasculine patients undergoing a variety of surgeries.[21] Given that estrogen use contributes only one point to the Caprini Score,[17] for patients at low-moderate baseline risk with Caprini Scores less than 7, estrogen cessation would decrease VTE risk by a fraction of one percent per the study by Pannucci et al.[19] This is also supported by a recent systematic review that estimates baseline VTE risk among transfeminine people prescribed estrogen to be 2.3 per 1,000 person-years, with the acknowledgment that their findings may be unreliable because of high heterogeneity of their study population.[22] Using this logic, Haveles et al[23] have recommended surgeons engage transfeminine people in a careful discussion of both the risks of estrogen continuation and estrogen cessation.

Of special consideration to transfeminine people regarding perioperative estrogen cessation is the potential gender dysphoria caused by abrupt cessation of exogenous estrogen and also endogenous testosterone (from orchiectomy during PIV), which may lead to menopause-like symptoms and gender dysphoria exacerbations.[9,24] Although this has not been robustly studied, as PIV and other gender-affirming surgery procedures aim to alleviate gender dysphoria, avoidance of gender dysphoria exacerbations resulting from perioperative estrogen cessation would be preferable, if proven safe. The relatively high prevalence of other psychiatric comorbidities in transgender and nonbinary people, which largely result from long-term systemic discrimination and transphobia, further emphasizes the importance of avoidance of gender dysphoria exacerbation.[25]

A recent systematic review stated the current evidence does not support the need to routinely discontinue all hormonal therapy preoperatively in transfeminine people.[9] This was based on the inconsistent risk data regarding the impact of exogenous estrogen in the perioperative period for cisgender women, as well as the lack of research directly examining the safety of hormonal therapies in the perioperative period for transfeminine people. It was recommended that estrogen continuation decisions should be made on a patient-specific basis, and the need for further research was acknowledged.

When considering surgery, providers are forced to balance 2 sets of risks regarding estrogen for patients undergoing PIV: the potential to increase VTE risk with estrogen continuation vs the potential to exacerbate gender dysphoria with estrogen cessation. Although the true incidence and magnitude of gender dysphoria exacerbations caused by estrogen cessation has not been robustly studied, any avoidance of gender dysphoria in transfeminine people is desirable. To contribute to knowledge of this growing topic of concern, we conducted a retrospective pre-post study comparing the incidence of 90-day postoperative VTE in transfeminine people undergoing PIV with or without perioperative estrogen cessation.

MATERIALS AND METHODS

Study Design and Patient Selection

A retrospective pre-post study was performed of a single surgeon's (T.S.) experience with PIV for transfeminine people from 2014 to 2019. Outcomes of a portion of this cohort have been

reported previously.[26,27] All patients gave consent for all aspects of the study. Institutional Review Board approval was obtained (Advarra [Columbia, Md.] Institutional Review Board protocol number Pro00031075). Data were collected on patient characteristics, details of perioperative hormone therapy regimens, operative outcomes, and complications including 90-day rates of VTE. All data necessary for completion of Caprini Score were collected.[17] The 2005 Caprini Score was used, as it has been validated for plastic surgery inpatients and is formally recommended by the American Society of Plastic Surgeons, the American Association of Plastic Surgeons, and the American College of Chest Physicians.[19,28–30]

Statistical Analysis Plan

Descriptive and comparative statistics were performed using Excel (Microsoft, Redmond, WA) and SPSS (IBM, Armonk, NY). Continuous variables were compared using means and

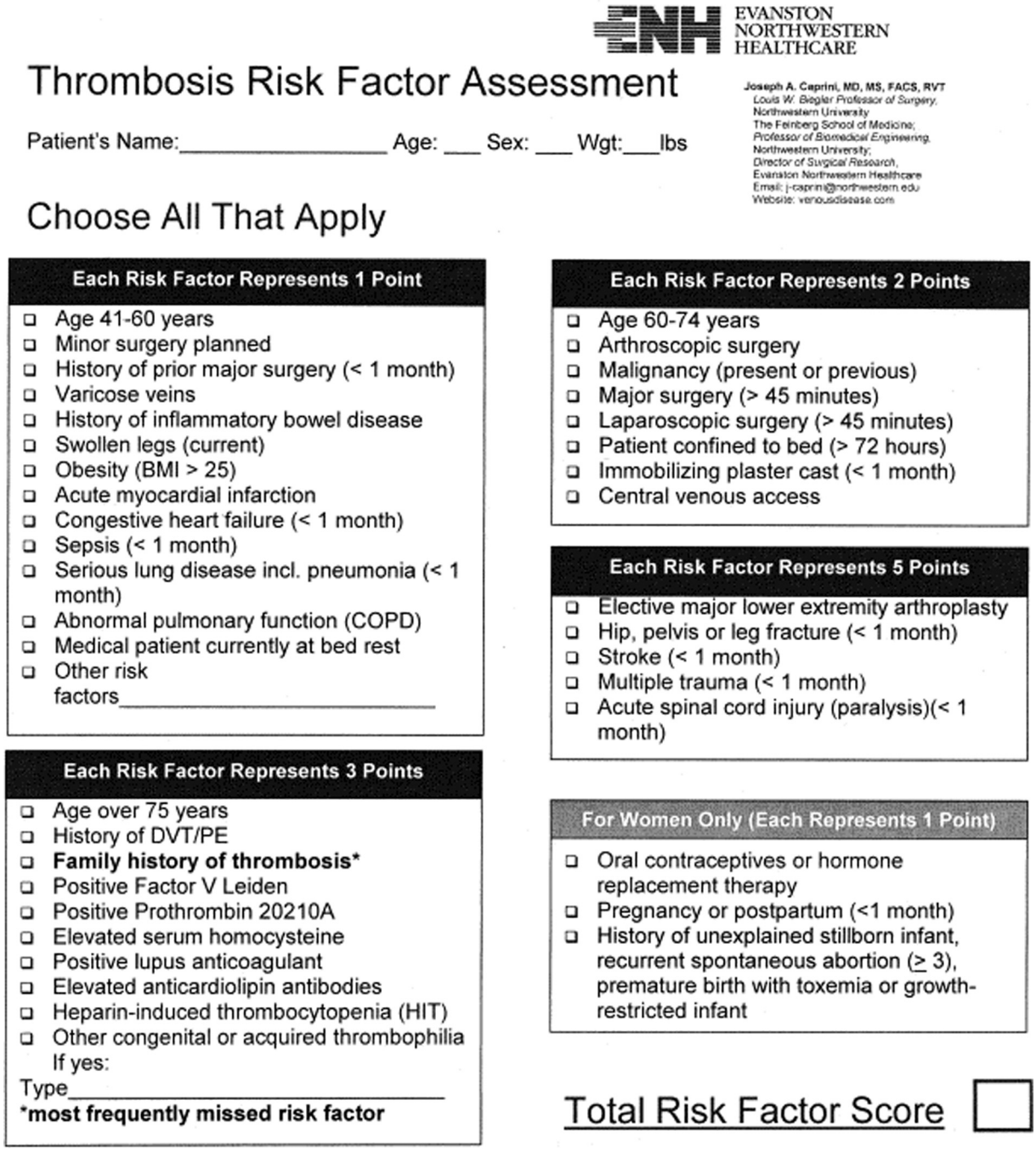

Figure 1. Caprini score thrombosis risk factor assessment. Thrombosis Risk Factor Assessment as presented by Joseph A. Caprini, MD in "Thrombosis risk assessment as a guide to quality patient care" in *Disease-A-Month*, published in March 2005.

standard deviations with Student's *t*-tests. Dichotomous variables were compared using proportions and Chi-squared tests. Ordinal variables were compared using medians with interquartile ranges and nonparametric tests, as appropriate. Statistical significance was set at $P < .05$.

Surgical Technique and Perioperative Care

Surgical technique was PIV for all patients. Details of this technique as performed by T.S. have been described previously.[26] A pre-post study design was adopted to compare outcomes and complications before and after a change in practice was made to have patients continue estrogen therapy perioperatively. This decision was made based on the lack of high-quality evidence or consensus between surgeons suggesting the necessity of estrogen cessation in addition to the author's experience with estrogen cessation causing mood swings, depression, anxiety, and psychosis in patients postoperatively, although the true incidence or magnitude of these effects has not been robustly examined in the literature. From 2014 through the end of 2018, patients were instructed to discontinue all hormonal therapy for 2 weeks before surgery, with resumption of hormone therapy on postoperative day 7 (group 1). From 2019, patients were instructed to continue estrogen therapy through the perioperative period (group 2). However, if estrogen dose was >6 mg preoperatively, patients were instructed to halve their dosage for 2 weeks before surgery. Since the half-life of oral and transdermal estrogens is approximately 13–20 hours and 37 hours, respectively, a significant decrease in overall estrogen availability was likely seen by the time of surgery.[31,32]

All patients were instructed to stop all tobacco and nicotine products 1 month preoperatively. Cotinine testing was only performed if there was suspicion of noncompliance. Patients' travel history was not a factor in their VTE prophylaxis planning. Progesterone therapy was discontinued 2 weeks before surgery for all patients and resumed at postoperative day 7. Sequential compression devices (SCDs) were placed intraoperatively and continued postoperatively until ambulating on postoperative day 1. No perioperative chemoprophylaxis was given for VTE prevention because of concern for postoperative bleeding. In addition, most patients were assumed to be at low risk for VTE based on the Caprini Score.[19]

Patients were maintained on bedrest for 24 hours after surgery. Per protocol, patients were instructed to ambulate with assistance on postoperative day 1 and were discharged on postoperative day 3. Outpatient clinic follow-up was conducted at postoperative days 7, 14, and 21, then subsequently every 3 months for the first year.

Outcomes of Interest

Primary outcome was 90-day VTE rate. The 90-day period was used to ensure that all patients had equal follow-up for this outcome, with the assumption that VTE development within 90 days of PIV is likely related to surgical intervention, and VTE development after 90 days is unrelated to surgical intervention. Patients were screened for deep venous thrombosis (DVT) and pulmonary embolism (PE) at postoperative visits using history and clinical examination. Patients with concerning signs or symptoms were sent for venous duplex ultrasound or PE-protocol CT scan as appropriate. In line with existing data from national plastic surgery organizations and the American College of Chest Physicians, no patient was screened for VTE (eg, screening duplex ultrasound) in the absence of symptoms.[30] Secondary outcomes include wound healing complications and psychiatric admissions after PIV.

RESULTS

Patient Characteristics

A total of 178 patients were included in the study, with 117 in the estrogen cessation cohort (group 1) and 61 in the estrogen continuation cohort (group 2). Group 1 was older than group 2 (mean 38.4 vs 32.0 years, $P = .001$), with higher rates of hypertension (12.0% vs 1.6%, $P = .024$) and diabetes (6.8% vs 0%, $P = .041$) (Table 1). BMI and rates of other comorbidities

Table 1. Patient characteristics of estrogen cessation (group 1) and estrogen continuation (group 2) cohorts

Parameter	Group 1 (N = 117)	Group 2 (N = 61)	*P* value
Age, mean years (SD)	38.4 (13.0)	32.0 (10.5)	.001
BMI, mean years (SD)	25.5 (5.0)	24.6 (4.4)	.294
Duration of hormone therapy, mean years (SD)	5.7 (6.4)	5.4 (5.0)	.782
Hypertension, % (n)	**12.0 (14)**	**1.6 (1)**	**.024**
Diabetes, % (n)	**6.8 (8)**	**0.0 (0)**	**.041**
Tobacco History, % (n)	15.4 (18)	8.2 (5)	.205
Hyperlipidemia, % (n)	6.0 (7)	8.2 (5)	.589
HIV, % (n)	6.8 (8)	1.6 (1)	.143
Liver disease/Hepatitis, % (n)	6.0 (7)	0.0 (0)	.056
Caprini Score, median (IQR)	**4 (3–6)**	**3 (3–4)**	**.011**

Bolded rows reflect statistically significant findings.
BMI = body mass index; IQR = interquartile range.

ARTICLE IN PRESS

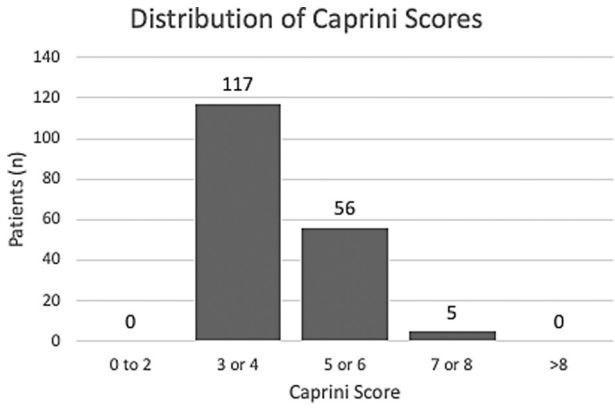

Figure 2. Distribution of Caprini Scores within the penile inversion vaginoplasty cohort. Caprini Score calculations of VTE risk are shown for the entire cohort of 178 penile inversion vaginoplasty patients. The 2005 Caprini Score Calculator was used.

were not different between groups. Patients had a history of estrogen therapy for a mean duration of 5.7 (group 1) and 5.4 (group 2) years. Overall, the patients were at low risk of VTE based on Caprini Score (Figure 2). Median Caprini Score was significantly higher in group 1 (median 4, IQR 3–6) than that in group 2 (median 3, IQR 3–4) ($P = .011$) (Table 1).

Outcomes and Complications

The overall complication rate was not statistically significant between the 2 cohorts of patients with 70.1% in group 1 and 54.1% in group 2 ($P = .208$) (Table 2). The mean complication rate per patient was statistically significant with 2.2 (SD 2.3) complications per patient in group 1 and 0.9 (SD 1.1) in group 2 ($P < .001$). Mean follow-up was longer in group 1 than that in group 2 (14.1 vs 10.2 months, $P < .001$).

The 2005 Caprini Score in PIV Patients

Patients' individual VTE risk was quantified using the 2005 Caprini Score.[17] No patient in group 1 or group 2 received perioperative anticoagulation, but SCDs were used perioperatively until ambulation on postoperative day 1. Baseline VTE risk was stratified at established cutpoints, specifically Caprini Scores of 0–2, 3–4, 5–6, 7–8, and >8; these cutpoints have been shown to identify stepwise increases in VTE risk.[19] Of this study's PIV population, 97.2% have Caprini Scores of ≤6, placing them in the low-to-moderate group for VTE risk (Figure 2). Only 2.8% had Caprini Scores of ≥7, the cutpoint at which postoperative chemical prophylaxis has been shown to decrease VTE risk.[29]

Primary Outcomes: 90-Day VTE

Rates of 90-day VTE were not different between groups 1 and 2 (0.0% vs 1.6%, $P = .166$), and there were no PE in either group (Table 2). A singular DVT was detected in a patient with a Caprini Score of 3 from the estrogen continuation group (group 2) during routine clinical examination screening on postoperative week 3 and was treated with therapeutic oral anticoagulation with complete resolution. Given that no VTEs occurred in group 1, it was not possible to calculate odds or risk ratios.

Secondary Outcomes

Rates of wound-healing complications, including hematoma, infection, wound breakdown, skin graft loss, and granulation tissue, were not different between cohorts (Table 2). Postoperative inpatient psychiatric care within 90 days of surgery was required by 2.6% (n = 3) of group 1 and 3.3% (n = 2) of group 2 patients, and these patients had an average of 4.6 complications each.

Table 2. Outcomes and complications of estrogen cessation and continuation cohorts

Complication	Group 1 (N = 117)	Group 2 (N = 61)	*P* value
Complications rate, % (n)	70.1 (82)	54.1 (33)	.208
Complications per patient, mean (SD)	**2.2 (2.3)**	**0.9 (1.1)**	**<.001**
Follow-up, mean months (SD)	**14.1 (5.6)**	**10.2 (3.1)**	**<.001**
Primary outcomes			
90-day DVT, % (n)	0.0 (0)	1.6 (1)	.166
90-day PE, % (n)	0.0 (0)	0.0 (0)	-
Secondary outcomes			
Hematoma, % (n)	11.1 (13)	3.3 (2)	.088
Surgical site infection, % (n)	2.6 (3)	1.6 (1)	.696
Wound breakdown, % (n)	17.1 (20)	16.4 (10)	.914
Skin graft loss, % (n)	0.9 (1)	0.0 (0)	.470
Granulation tissue, % (n)	25.6 (30)	14.8 (9)	.141
90-day Inpatient psychiatric care, % (n)	2.6 (3)	3.3 (2)	.787

Bolded rows reflect statistically significant findings.
DVT = deep venous thrombosis; PE = pulmonary embolism.
Outcomes and complications are listed, and rates are compared between group 1 (estrogen cessation cohort) and group 2 (estrogen continuation cohort).

DISCUSSION

Patients undergoing PIV in this study were generally at low risk for VTE, with median Caprini Scores of 4 and 3 for groups 1 and 2, respectively (Figure 2). In addition, to help mitigate the risk of VTE, most patients in this study were ambulating on postoperative day 1, and SCDs were used perioperatively until ambulation occurred. Among this low-risk study population, rates of 90-day symptomatic VTE were not impacted by perioperative estrogen cessation. To our knowledge, this is the first objective study of transgender people undergoing PIV that compares outcomes between those who continued perioperative estrogen to those who discontinued estrogen. This study responds to calls for further investigation into the effects of perioperative estrogen on VTE risk in transgender people.[9] Previous studies have either reported patient-reported VTE or have only reported outcomes of either estrogen cessation or continuation, not both.[24]

Only one patient was found to have a DVT (Caprini Score of 3), which was noted on clinical examination, confirmed with ultrasound, and successfully managed with oral anticoagulation. This study's low rate VTE is consistent with existing evidence regarding thromboembolic risk in patients undergoing PIV.[24] This study also confirms what is known from other subgroups of patients undergoing plastic surgery: Observed rates of VTE in patients undergoing plastic surgery with low Caprini Scores are low.[19] For patients with low baseline risk, further risk modification of estrogen cessation would decrease VTE risk by a fraction of one percent at the potential harm of gender dysphoria exacerbation, although the true incidence or magnitude of this harm has not been clearly demonstrated. Thus, active discussion between the patient and surgeon about the risks and benefits of estrogen cessation would be appropriate.

Lower rates of overall complications in group 2 (estrogen continuation cohort) are likely a factor of decreased follow-up period and also increased surgical experience on the part of the senior author (T.S.), as these patients were operated on more recently than group 1 (ie, since 2019). Rates of short-term wound healing complications including hematoma, surgical site infection, wound breakdown, skin graft loss, and granulation tissue were not different between groups, suggesting estrogen continuation or cessation has little role in wound healing. Relatively high overall complication rates are likely a result of our choice to report all complications, to better reflect lived patient experience with these procedures.

A significant complication in our cohort was the need for inpatient psychiatric treatment in the 90-day postoperative period (2.6% in group 1 and 3.3% in group 2, $P = .787$). Although these data demonstrate that there was no increased rate of severe psychiatric complications in the estrogen cessation group (group 1), this is likely an insensitive measure of gender dysphoria exacerbations and thus not truly identifying its incidence.

Our finding of no difference in rates of psychiatric hospitalization between cohorts does not negate our suspicion that discontinuation of perioperative estrogen therapy may reduce psychological stress on patients undergoing PIV, which may be significant perioperatively and postoperatively. Estrogen cessation, especially when concurrent with loss of endogenous testosterone from orchiectomy during PIV, is a known psychological stressor for transgender people.[33] In the senior author's anecdotal experience, postoperative experience has generally been improved by continuing estrogen therapy. However, this has not been robustly demonstrated in the literature, and our measure of 90-day rates of psychiatric hospitalization is not a sensitive measure to identify these psychiatric symptoms which can usually be managed without hospitalization. Allowing for estrogen continuation will likely prove beneficial to many patients. However, further study, ideally a prospective, subjective survey study, will be necessary to elucidate this issue which cannot be fully addressed by examining hospitalization rates.

Postoperative psychiatric health is also likely to be affected by high complication rates—our patients with psychiatric admission had an average of 4.6 complications per patient, higher than the 2.2 in group 1 or 0.9 in group 2 overall. Therefore, any attempts to improve postoperative psychiatric health must not do so at the risk for increased complications.

The authors strongly suggest that decisions regarding perioperative estrogen be made with shared decision-making between the patient and physician taking into consideration the magnitude of the benefits and risks of estrogen continuation as morbidity or mortality from an untreated or missed VTE can be devastating.

Strengths of this study include its pre-post design and single-surgeon experience, which controls for confounders related to surgical technique, high proportion of patients with 90-day follow-up, and relatively large series to understand baseline VTE risk by Caprini Score in a PIV population.

The main weakness of this study is its limited power to measure true differences in VTE risk based on estrogen continuation. However, such a study using pre-post design and single-surgeon experience is impossible to conduct because of unreasonably large sample sizes. Our cohort had an overall 90-day VTE rate of 0.56% (1 in 178). A well-designed clinical trial to examine an intervention that doubled risk to 1.12% would require 4,781 patients per group (9,562 patients in total) to achieve 90% power. Future studies with a greater number of patients are needed to achieve greater power. This would allow future authors to determine the true safety of estrogen continuation in the perioperative period for transfeminine people undergoing PIV.

This study also has potential confounding factors, including tobacco use, as less patients in group 2 had a tobacco history than those in group 1, although this difference was not statistically significant (Table 1). Furthermore, cotinine testing was not

ARTICLE IN PRESS

performed on all patients preoperatively which would be necessary to assess true adherence. Another potential confounder includes other hormonal therapies used by our patients, including progesterone or antiandrogen medications. Unfortunately, we did not have access to these data. In addition, a recent systematic review found inconclusive evidence regarding the thrombotic risk associated with these medications, and therefore, these medications were not examined in our study.[9]

Areas for future study include the effect of perioperative estrogen continuation on length of stay after PIV, the effect of various estrogen preparations (oral vs transdermal) on VTE risk in transfeminine people, the true incidence and magnitude of gender dysphoria exacerbations or menopause-like symptoms caused by estrogen cessation in the transfeminine population, and the relative risk of VTE for patients undergoing PIV with higher BMI than that represented in our cohort.

CONCLUSIONS

Estrogen continuation is likely an important consideration to improve the operative experience for transfeminine people undergoing gender-affirming surgery, without apparent increased risk for thrombotic complications. Our comparative study of gender-affirming PIV patients demonstrate that this population is generally at low risk for VTE, based on 2005 Caprini Scores. The study also supports that perioperative estrogen therapy continuation in low-risk patients may not substantially increase VTE risk. As estrogen cessation may promote gender dysphoria exacerbation, surgeons should engage patients in an active preoperative discussion regarding the magnitude of the benefits and risks of estrogen discontinuation.

Corresponding Author: Ian T. Nolan, BM, Hansjörg Wyss Department of Plastic Surgery, Grossman School of Medicine, New York University, 550 1st Avenue, New York, NY 10016, USA. Tel: (518) 932-5680; Fax: (646) 502-6826.; E-mail: Ian.Nolan@nyulangone.org

Conflict of Interest: Within the past 24 months, Dr Pannucci has received direct research support for an unrelated study examining enoxaparin metabolism in thoracic surgery patients from the CHEST Foundation. None of the other authors have any relevant financial disclosures.

Funding: None.

STATEMENT OF AUTHORSHIP

Ian T. Nolan: Conceptualization, data curation, formal analysis, investigation, methodology, writing the original draft, and reviewing and editing the article. Caleb Haley: Writing the original draft and reviewing and editing the same. Shane D. Morrison: Conceptualization, methodology, and reviewing and editing the article. Christopher J. Pannucci: Conceptualization, project administration, methodology, reviewing and editing the article, and supervision. Thomas Satterwhite: Conceptualization, resources, project administration, reviewing and editing the article, and supervision.

REFERENCES

1. 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;13:165-232.**
2. de Bastos M, Stegeman BH, Rosendaal FR, et al. Combined oral contraceptives: venous thrombosis. **Cochrane Database Syst Rev 2014:CD010813.**
3. Gomes MP, Deitcher SR. Risk of venous thromboembolic disease associated with hormonal contraceptives and hormone replacement therapy: a clinical review. **Arch Intern Med 2004;164:1965-1976.**
4. Asscheman H, T'Sjoen G, Lemaire A, et al. Venous thromboembolism as a complication of cross-sex hormone treatment of male-to-female transsexual subjects: a review. **Andrologia 2014;46:791-795.**
5. Shatzel JJ, Connelly KJ, DeLoughery TG. Thrombotic issues in transgender medicine: a review. **Am J Hematol 2017;92:204-208.**
6. Olie V, Canonico M, Scarabin PY. Risk of venous thrombosis with oral versus transdermal estrogen therapy among postmenopausal women. **Curr Opin Hematol 2010;17:457-463.**
7. Canonico M, Plu-Bureau G, Lowe GD, et al. Hormone replacement therapy and risk of venous thromboembolism in postmenopausal women: systematic review and meta-analysis. **BMJ 2008;336:1227-1231.**
8. Goldstein Z, Khan M, Reisman T, et al. Managing the risk of venous thromboembolism in transgender adults undergoing hormone therapy. **J Blood Med 2019;10:209-216.**
9. Boskey ER, Taghinia AH, Ganor O. Association of surgical risk with exogenous hormone use in transgender patients: a systematic review. **JAMA Surg 2019;154:159-169.**
10. Kim JY, Khavanin N, Rambachan A, et al. Surgical duration and risk of venous thromboembolism. **JAMA Surg 2015;150:110-117.**
11. Wierckx K, Mueller S, Weyers S, et al. Long-term evaluation of cross-sex hormone treatment in transsexual persons. **J Sex Med 2012;9:2641-2651.**
12. Meriggiola MC, Jannini EA, Lenzi A, et al. Endocrine treatment of transsexual persons: an Endocrine Society clinical practice guideline: commentary from a European perspective. **Eur J Endocrinol 2010;162:831-833.**
13. Tollinche LE, Walters CB, Radix A, et al. The perioperative care of the transgender patient. **Anesth Analg 2018;127:359-366.**
14. Seim LA, Irizarry-Alvarado JM. Perioperative management of female hormone medications. **Curr Clin Pharmacol 2017;12:188-193.**
15. Bergqvist D, Agnelli G, Cohen AT, et al. Duration of prophylaxis against venous thromboembolism with enoxaparin after surgery for cancer. **N Engl J Med 2002;346:975-980.**
16. Broyles JM, Khavanin N, Walia GS, et al. Increased incidence of symptomatic venous thromboembolism following pedicled

ARTICLE IN PRESS

lower extremity flap harvest for abdominal and perineal reconstruction in patients receiving mechanical prophylaxis and chemoprophylaxis: a case for heightened awareness. **Plast Reconstr Surg 2019;143:840e-847e.**

17. Caprini JA. Thrombosis risk assessment as a guide to quality patient care. **Dis Mon 2005;51:70-78.**
18. Pannucci CJ, Swistun L, MacDonald JK, et al. Individualized venous thromboembolism risk stratification using the 2005 caprini score to identify the benefits and harms of chemoprophylaxis in surgical patients: a meta-analysis. **Ann Surg 2017;265:1094-1103.**
19. Pannucci CJ, Bailey SH, Dreszer G, et al. Validation of the caprini risk assessment model in plastic and reconstructive surgery patients. **J Am Coll Surg 2011;212:105-112.**
20. Valente DS, Carvalho LA, Zanella RK, et al. Venous thromboembolism following elective aesthetic plastic surgery: a longitudinal prospective study in 1254 patients. **Plast Surg Int 2014;2014:565793.**
21. Kozato A, Henry Pang J, Fox C, et al. Venothromboembolism risk and hormone therapy in the elective surgery patient. **Plast Reconstr Surg Glob Open 2019;7(8 Suppl).**
22. Khan J, Schmidt RL, Spittal MJ, et al. Venous thrombotic risk in transgender women undergoing estrogen therapy: a systematic review and metaanalysis. **Clin Chem 2019;65:57-66.**
23. Haveles CS, Wang MM, Arjun A, et al. Effect of cross-sex hormone therapy on venous thromboembolism risk in male-to-female gender-affirming surgery. **Ann Plast Surg 2020. https://doi.org/10.1097/SAP.0000000000002300.**
24. Lawrence AA. Patient-reported complications and functional outcomes of male-to-female sex reassignment surgery. **Arch Sex Behav 2006;35:717-727.**
25. James SE, Herman JL, Rankin S, et al. The report of the 2015 U.S. transgender survey. Washington, DC: National Center for Transgender Equality; 2016.
26. Massie JP, Morrison SD, Van Maasdam J, et al. Predictors of patient satisfaction and postoperative complications in penile inversion vaginoplasty. **Plast Reconstr Surg 2018;141:911e-921e.**
27. Boas SR, Ascha M, Morrison SD, et al. Outcomes and predictors of revision labiaplasty and clitoroplasty after gender-affirming genital surgery. **Plast Reconstr Surg 2019;144:1451-1461.**
28. Murphy RX Jr, Alderman A, Gutowski K, et al. Evidence-based practices for thromboembolism prevention: summary of the ASPS venous thromboembolism task force report. **Plast Reconstr Surg 2012;130:168e-175e.**
29. Pannucci CJ, MacDonald JK, Ariyan S, et al. Benefits and risks of prophylaxis for deep venous thrombosis and pulmonary embolus in plastic surgery: a systematic review and meta-analysis of controlled trials and consensus conference. **Plast Reconstr Surg 2016;137:709-730.**
30. Gould MK, Garcia DA, Wren SM, et al. Prevention of VTE in nonorthopedic surgical patients: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. **Chest 2012;141(2 Suppl):e227S-e277S.**
31. Stanczyk FZ, Archer DF, Bhavnani BR. Ethinyl estradiol and 17β-estradiol in combined oral contraceptives: pharmacokinetics, pharmacodynamics and risk assessment. **Contraception 2013;87:706-727.**
32. Naunton M, Al Hadithy AF, Brouwers JR, et al. Estradiol gel: review of the pharmacology, pharmacokinetics, efficacy, and safety in menopausal women. **Menopause 2006;13:517-527.**
33. White Hughto JM, Reisner SL. A systematic review of the effects of hormone therapy on psychological functioning and quality of life in transgender individuals. **Transgend Health 2016;1:21-31.**