GYNECOLOGY

Uterine pathology in transmasculine persons on testosterone: a retrospective multicenter case series

Frances W. Grimstad, MD; Kylie G. Fowler, MD, MS; Erika P. New, MD, MPH; Cecile A. Ferrando, MD, MPH; Robert R. Pollard, MD; Graham Chapman, MD; Veronica Gomez-Lobo, MD; Meredith Gray, MD

BACKGROUND: As part of transition, transmasculine persons often use testosterone gender-affirming hormone therapy; however, there is limited data on its long-term effects. The impact of exogenous testosterone on uterine pathology remains unclear. While testosterone achieves amenorrhea in the majority of this population, persistence of abnormal uterine bleeding can be difficult to manage. Excess androgens in cisgender females are associated with pathologic uterine processes such as polycystic ovary syndrome, endometrial hyperplasia, or cancer. There are no guidelines for management of abnormal uterine bleeding or endometrial surveillance in this population.

OBJECTIVE: The aim of this study was to describe the characteristics of uterine pathology after the initiation of testosterone in transmasculine persons.

MATERIALS AND METHODS: A retrospective, multicenter case series was performed. Uterine pathology reports of transmasculine persons who received testosterone and subsequently underwent hysterectomy were reviewed. The endometrial phase and endometrial thickness were recorded.

RESULTS: A total of 94 subjects met search criteria. The mean age of participants was 30 ± 8.6 years, and the mean interval from initiation of testosterone to hysterectomy was 36.7 ± 36.6 months. Active endometrium was found in the majority of patients (n = 65; 69.1%). One patient had complex hyperplasia without atypia. There were no cases of endometrial cancer.

CONCLUSION: Despite amenorrhea in the majority of transmasculine persons on testosterone, endometrial activity persists with predominantly proliferative endometrium on histopathology. Individualized counseling for abnormal uterine bleeding is encouraged in this patient population.

Key Words: endometrium, testosterone, transmale, transmasculine person, uterine pathology

As transgender equality advances, more transmasculine persons are seeking gender-affirming hormone therapy (Table 1). Despite the widespread use of testosterone in transmasculine persons, there are limited data on its long-term effects and safety. As this population seeks care, it becomes the unique responsibility of gynecologists to lead research and management recommendations for transmasculine persons experiencing gynecologic symptoms or to identify those at risk for gynecologic malignancies. In regard to the testosterone effect on the uterine endometrium, existing literature is conflicting.[1–4] Excess androgens in cisgender women are associated with pathologic processes such as polycystic ovary syndrome and endometrial cancer.[5–6] However, in vitro studies suggest that androgens suppress endometrial activity and induce atrophy of endometrial cells.[7]

The objective of this study is to describe the characteristics of endometrial pathology after the initiation of testosterone in transmasculine persons.

Materials and Methods

This study is a retrospective, multicenter, descriptive case series approved by the Institutional Review Boards at the University of Kansas School of Medicine (Kansas City, KS), the University of South Florida (Tampa, FL), MedStar Washington Hospital Center (Washington, DC), The Cleveland Clinic (Cleveland, OH), and MetroHealth Medical Center (Cleveland, OH). Inclusion criteria were all transmasculine patients age 18 years and older who underwent hysterectomy with or without oophorectomy following administration of exogenous testosterone from 2015 to 2017. There was no minimum duration of testosterone use prior to surgery. Demographic information collected included age and race. Complete medical, surgical, obstetric and gynecologic history was obtained by chart review including body mass index (BMI), medical comorbidities, previous surgeries, parity with obstetric outcomes, menstrual history including presence or absence of complete amenorrhea, history of abnormal uterine bleeding (AUB) prior to testosterone use, previous or current estrogen and/or progesterone use, length, dose, and route of testosterone therapy, tobacco use, and current medications at the time of hysterectomy. Laboratory data collected included the most recent total testosterone and estradiol levels prior to surgery, and pre- and postoperative hemoglobin and hematocrit. From surgical pathology, uterine weight and measurements, endometrial thickness, endometrial classification, cervical description, use of histopathologic stains or markers, and any listed diagnoses were recorded. When available, preoperative transvaginal ultrasound reports were reviewed for measurement of radiologic endometrial thickness. Operative data collected included intraoperative

Cite this article as: Grimstad FW, Fowler KG, New EP, et al. Uterine pathology in transmasculine persons on testosterone: a retrospective multicenter case series. Am J Obstet Gynecol 2019;220:257.e1-7.

0002-9378/$36.00

https://doi.org/10.1016/j.ajog.2018.12.021

Click Supplemental Materials under article title in Contents at ajog.org

AJOG at a Glance:

Why was this study conducted?

There are no current guidelines for the management of abnormal uterine bleeding or endometrial surveillance in transmasculine persons on testosterone.

Key findings

Our study describes the characteristics of uterine pathology after the initiation of testosterone in transmasculine persons in a retrospective multicenter case series of transmasculine patients undergoing hysterectomy, finding that despite the majority having amenorrhea, endometrial activity persisted, with predominantly proliferative endometrium on histopathology.

What does this add to what is known?

Based on our data and current literature, individualized assessments of a transmasculine person's etiology for abnormal uterine bleeding continue to be necessary, as the risk for concerning pathology is still present.

estimated blood loss, any listed complications, and declared pre- and postoperative diagnoses. The retrospective nature of data collection resulted in incomplete records; however, all patients had documented endometrial histopathology and length of testosterone administration.

All data collected via retrospective chart review was deidentified. Study data were collected and managed using REDCap electronic data capture hosted at the University of Kansas Medical Center and MedStar Washington Hospital Center.[8]

Statistical analysis consisted of descriptive statistics to tabulate means, ranges, standard deviations, and 95% confidence intervals. Using IBM SPSS software, Mann−Whitney *U* tests were used to assess for differences between groups; spearman's rho was used to assess for correlations between continuous and ordinal variables; and χ^2 analysis was run for associations between groups. In cases of significance, multivariate analysis was used to control for confounders. In the case of χ^2 associations, select continuous variables were grouped. The groupings and rationale are described in Table 2.

Results

Multicenter retrospective data collection resulted in a total of 94 subjects (Table 3). The average age of participants was 30.0 ± 8.6 years at the time of hysterectomy (range, 18−53 years; 95% CI, 27.8−31.3). Average BMI was 29.6 ± 7.3 kg/m^2 (range, 16.1−59.4 kg/m^2; 95% CI, 28.1−31.1).

The majority of patients were nulliparous (80.9%, n = 76). One-fourth (25.5%, n = 24) had a documented history of menstrual irregularities including polycystic ovary syndrome or AUB prior to initiation of testosterone. Only 1 subject used puberty suppression (Table 1) prior to testosterone. Comorbidities of subjects included mental health conditions (n = 29, 30.9%), tobacco use (n = 13, 13.9%), hypothyroidism (n = 11, 11.7%) endometriosis (n = 8, 8.5%), hypertension (n = 6, 6.4%), hyperlipidemia (n = 6, 6.4%), asthma (n = 6, 6.4%), and diabetes (n = 5, 5.3%).

Of the subjects, 52 had complete documentation of gynecologic symptomatology. Of these 52, 12 (23.1%) had documented persistence of bleeding on testosterone, and 30 (57.7%) endorsed some form of intermittent pelvic pain, usually noted as "cramps," while on testosterone. Thirteen subjects used estrogen and/or progesterone therapy while on testosterone (13.8%). Of these 13 individuals, 7 used combined oral contraceptives, 4 used depomedroxyprogesterone, and 3 used a 52-mg levonorgestrel intrauterine device (1 subject used 2 methods sequentially).

The mean interval from initiation of hormone therapy to hysterectomy was 36.7 ± 36.6 months (range, <1 to 228 months; 95% CI, 29.2−44.2). The majority of subjects used intramuscular testosterone cypionate (n = 74, 78.7%). The second most common route of administration was subcutaneous testosterone cypionate (n = 15, 16.0%). One subject used a combination intramuscular testosterone preparation (Sustanon 250, containing a 250-mg/mL combination of 30 mg testosterone propionate, 60 mg testosterone phenylpropionate, 60 mg testosterone isocaproate, and 100 mg testosterone decanoate), and 3 subjects used a transdermal testosterone preparation. In all, 54 subjects had documented testosterone levels within the year prior to surgery. The mean level was 548.6 ng/dL ± 325.8 (95% CI, 460.8−638.6). A total of 34 subjects had documented estradiol levels within the year prior. The mean level was 44.1 pg/mL ± 28.6 (95% CI, 34.1−54.1).

Of the subjects, 23 had documented ultrasounds prior to hysterectomy. The mean endometrial thickness measurement was 4.9 mm ± 2.1 (95% CI, 4.0−5.9). Ultrasound endometrial thickness measurement was not associated with testosterone duration.

Of the 94 uterine pathology specimens, histology was documented as atrophic in 23 subjects (24.5%), secretory in 4 (4.3%), and proliferative in 61 (64.9%). Documented uterine and endometrial pathology included endometrial polyps or fibroids in 9 subjects (9.6%), adenomyosis in 7 (7.4%), complex hyperplasia without atypia in 1 (1.1%), and other benign pathology in 4 (4.3%). Estrogen and/or progesterone therapies are known to independently affect the endometrium. As such, a subanalysis was done excluding the 13 patients on estrogen and/or progesterone. The histologic distributions were noted to be similar to the primary analysis (atrophic in 22 subjects, 27.2%; secretory in 2, 2.5% proliferative in 54, 66.7%; complex hyperplasia without atypia in 1, 1.2%; and other benign pathology in 2, 2.5%) (χ^2 = 0.645, P = .886).

Endometrial thickness on histopathology was documented in 82 specimens. Mean thickness was 2.0 mm ± 1.3 (95% CI, 1.7−2.3). A total of 35 subjects

TABLE 1
Transgender and gender-based care definitions

Word/terminology	Definition
Transgender	A person whose gender identity differs from the sex that was assigned at birth. May be abbreviated to trans.
Cisgender	A person whose gender identity is congruent with their sex assigned at birth.
Transmasculine	A transmasculine person is someone assigned female at birth, who identifies along a masculine spectrum gender identity. Transmasculine persons are inclusive of gender nonconforming or nonbinary persons and transgender men.
Gender-affirming hormone therapy	Gender -affirming hormone therapy is the use of hormones allowing for development of secondary sex characteristics congruent with an individual's gender identity. In the case of transmasculine persons, this is achieved with testosterone.
Puberty suppression	Use of gonadotropin-releasing hormone (GnRH) analogues to delay, or to avoid altogether, the development of undesired secondary sex characteristics resulting from an unwanted endogenous pubertal process.

Grimstad et al. Uterine pathology in transmasculine persons on testosterone. Am J Obstet Gynecol 2019.

(42.7%) measured 1 mm, 27 (32.9%) measured 2 mm, 10 (12.2%) measured 3 mm, 8 (9.8%) measured 4 mm, and 2 (2.4%) measured 7 mm. Uterine weight was documented in 51 cases with a mean weight of 77.2 g (95% CI, 53.7−100.6). There was no correlation between uterine weight and endometrial thickness. Although ultrasounds were available in only 23 of 94 patients, no association was seen between active endometrial histology and thickness of endometrium on ultrasound. There was also no correlation between endometrial thickness on pathology and testosterone duration. Further analysis was performed, and no association was noted between endometrial thickness on pathology and testosterone duration when testosterone and endometrial thickness were grouped (as in Table 2), and no association between endometrial histology and testosterone duration. These findings remained true when the 13 patients with estrogen and/or progesterone therapy were excluded from analysis. Similarly, we found no association between BMI (as grouped in Table 2) and endometrial histology or thickness. Because we found no statistically significant relationships, multivariate analysis was not performed.

Analysis of the 52 individuals with complete documented gynecologic history revealed only 12 subjects with persistent bleeding while on testosterone. Acknowledging these small numbers, use of estrogen and/or progesterone was not associated with presence or absence of amenorrhea. Persistent bleeding was also not associated with obesity or active endometrium (histology distribution was atrophic in 2 subjects (16.7%), secretory in 2 (16.7%), proliferative in 6 (50%), complex hyperplasia without atypia in 1 (8.3%), and other benign pathology in 1 (8.3%).

In all, 37 patients with complete gynecologic history also had documentation of recent testosterone levels. There was no difference in the testosterone levels of patients who had persistent bleeding compared to those with amenorrhea. There was no difference between the age or BMI of subjects with persistent bleeding compared to those with amenorrhea (Table 4).

TABLE 2
Variable groupings for statistical analysis

Variable	Groupings	Rationale
Endometrial thickness (ultrasound and pathology)	<4 mm	An endometrial thickness <4 mm in postmenopausal cisgender women has greater than 99% negative predictive value for ruling out endometrial cancer[30] (however, it is known that this cannot be directly applied to premenopausal patients, and no available data exist on premenopausal endometrial thickness on testosterone)
	≥4 mm	
Testosterone duration	0−1 year	Most patients achieve amenorrhea within 1 year of testosterone gender-affirming hormone therapy.[31] Virilization effects of testosterone can take 2−5 years to reach maximum effect.[32]
	>1−2 years	
	>2−4 years	
	>4 years	
BMI	<30	Obesity is a known risk factor for endometrial hyperplasia.[15]
	≥30	

Grimstad et al. Uterine pathology in transmasculine persons on testosterone. Am J Obstet Gynecol 2019.

TABLE 3
Results in study participants

Variable	n (%)
Age (mean ± SD)	30.0 ± 8.6
Race	
Hispanic	0 (0)
Non-Hispanic white	45 (86.5)
Non-Hispanic black	5 (9.6)
Asian Pacific Islander	1 (1.9)
American Indian	1 (1.9)
Other	0 (0)
Missing	42
BMI (kg/m^2)	
<18.5	2 (2.1)
18.5–25.0	27 (28.7)
25.1–30.0	22 (23.4)
30.1–40.0	35 (37.2)
>40.0	8 (8.5)
Comorbidities	
Mental health diagnosis	29 (30.9)
Hypothyroid	11 (11.7)
Endometriosis	8 (8.5)
Hypertension	6 (6.4)
Hyperlipidemia	6 (6.4)
Asthma	6 (6.4)
Type 2 diabetes	5 (5.3)
Endometrial classification	
Atrophy	22(23.4)
Secretory	4 (4.3)
Proliferative	61 (64.9)
Complex hyperplasia without atypia	1 (1.1)
Polyps/fibroids	9 (9.6)
Adenomyosis	7 (7.4)
Duration of testosterone use	
0–1 year	22 (23.4)
>1–2 years	30 (31.9)
>2–4 years	19 (20.2)
>4 years	23 (24.5)
Type of testosterone used	
IM cypionate	74 (78.7)
SubQ cypionate	15 (16.0)
IM sustanon	1 (1.1)
Transdermal	3 (3.2)

Grimstad et al. Uterine pathology in transmasculine persons on testosterone. Am J Obstet Gynecol 2019. (continued)

Of the 82 subjects with documented endometrial thickness on pathology report, 54 had recent testosterone values. There was no correlation between testosterone value and endometrial thickness on pathology.

Comment

Although research on the effects of exogenous testosterone in transmasculine persons is early, our results are consistent with an emerging pattern of evidence. This pattern suggests the persistence of endometrial activity in many transmasculine persons on testosterone with a predominance of proliferative endometrium on histopathology.

A comprehensive literature review was performed to understand our results in the context of already published data. When we take into account our data and the 4 studies that have already been published on this subject matter, a total of 269 patients have been studied, with half (50.1%) of patients having active endometrium on pathology. These studies have also found that transmasculine persons on testosterone continue to have typical uterine and endometrial pathology such as polyps, leiomyomata, and adenomyosis. Importantly, hyperplasia without atypia was reported in 9 of the 269 subjects and there was 1 reported case of endometrial adenocarcinoma.[1–4] In addition, we determined that pre–testosterone-use rates of AUB in our patient population (25.5%) were similar to that of the general cis female population (14–25%).[9]

The incidence of endometrial cancer in the United States is 1 in 342 under age 49 years and 1 in 166 between the ages of 50 and 59. It is the fourth leading cause of cancer in the United States among cisgender women.[10] In our review of currently available data, including the original data presented in this article, there was 1 reported case of endometrial cancer in 269 subjects ranging in age from 18 to 53 years.[2] There were 9 patients with simple hyperplasia, which carries a 3% risk of progression to complex hyperplasia.[11] Although we cannot determine the risk of endometrial carcinoma in transmasculine

TABLE 3
Results in study participants *(continued)*

Variable	n (%)
Persistent bleeding on testosterone	
Yes	12 (23.1)
No	40 (76.9)
Missing	42
Concomitant hormonal use	
Combined oral contraceptives	7 (50.0)
Depo-medroxyprogesterone	4 (28.6)
Levonorgestrel 52 mg intrauterine device	3 (21.4)
Missing	81

IM, intramuscular; *SD*, standard deviation; *SubQ*, subcutaneous.
Grimstad et al. Uterine pathology in transmasculine persons on testosterone. Am J Obstet Gynecol 2019.

persons on testosterone relative to their cisgender counterparts, it appears to be on par with baseline population risk despite the majority of patients reporting amenorrhea.

Proliferative endometrium, found in the majority of our subjects, occurs during the follicular phase of the menstrual cycle when the predominant reproductive hormone is estrogen.[12] The predominance of proliferative endometrium in our data suggests that the endometrial lining is being exposed to estrogen, likely secondary to peripheral conversion of testosterone to estrogen by aromatase.[13] Estrogen exposure unopposed by progesterone is a well-established risk factor for endometrial cancer.[11] In addition to the risk presented by unopposed estrogen, transmasculine persons also have increased rates of obesity (a limitation of our study is the inability to control for this), nulliparity, and alcohol use, further increasing their lifetime endometrial cancer risk.[14,15] Exogenous androgens may also be associated with an increased risk for type 2 diabetes and insulin resistance, further exacerbating the endometrial cancer risk in transmasculine persons.[16]

A case report of stage IIIC, grade 2 endometrial adenocarcinoma in a previously amenorrheic transgender male was published in 2011, along with a review of other reported gynecologic malignancies in transmasculine persons.[17] In this paper, the authors suggest routine screening for cervical cancer based on established guidelines, as well as cervical and endometrial evaluation prior to hysterectomy.[16] The Endocrine Society and the World Professional Association for Transgender Health (WPATH) do not have specific guidelines for endometrial cancer surveillance in transmasculine persons; however, they do recommend consideration of gynecologic malignancies in evaluation of abdominopelvic complaints or abnormal bleeding.[18,19] Our subject with complex hyperplasia without atypia would support this evaluation, as that individual had persistent bleeding on testosterone.

In the setting of a negative workup, there is no consensus on management of persistent uterine bleeding while on testosterone therapy.[20] Progestin-based treatments and aromatase inhibitors are most commonly used.[21] Progestin-based treatment acts directly on the progesterone receptors in the endometrium to arrest glandular proliferation and to decrease glandular cellularity by inducing apoptosis.[22,23] In addition, the etonorgestrel implant or levonorgestrel intrauterine device provides excellent contraception for transmasculine persons, as spontaneous ovulation and pregnancy can occur.[24,25] Aromatase inhibitors block conversion of testosterone to estradiol, thereby decreasing plasma estrogen levels. Although the endometrium does not have aromatase, aromatase inhibitors do target the proposed mechanism of ongoing proliferative endometrium in transmasculine persons.[26]

A randomized, open-label trial comparing testosterone undecanoate, testosterone undecanoate plus letrozole, and testosterone undecanoate plus dutasteride was published in 2011. This study was underpowered, with only 5 patients in each arm; however, the investigators found a statistically significant decrease ($P < .008$) in bone density in the group receiving letrozole.[27] Most data on long term letrozole use and bone health are in women with breast cancer, with well documented detrimental bone effects with letrozole use in this population.[28,29] The extent to which this evidence can be applied to transmasculine persons with persistent uterine bleeding is unknown. However, the authors of this article prefer to use progestin-based therapy to treat persistent or

TABLE 4
Comparison of persistent bleeding vs amenorrhea in transmasculine persons on testosterone

Variable	Persistent bleeding on testosterone (mean ± SD)	Amenorrhea on testosterone (mean ± SD)	*P* value
Age	30.3 ± 11.5	26.3 ± 5.9	.557
BMI	28.9 ± 7.0	28.4 ± 6.2	.983
Duration on testosterone	53.8 ± 61.1	40.1 ± 35.2	.519

BMI, body mass index; *SD*, standard deviation.
Grimstad et al. Uterine pathology in transmasculine persons on testosterone. Am J Obstet Gynecol 2019.

abnormal bleeding in transmasculine patients due to the concern for bone health with use of aromatase inhibitors as well as the predominance of proliferative endometrium in this population. Other benefits of progestin include its use as a contraceptive, and ability to reduce risk of endometrial cancer.[11,24]

Strengths of this study include the multisite nature, which allows for diversity in patient population and treatment patterns. This is the first study of its kind to look at large numbers within the population of the United States, as current data on the subject is from mostly European and other international groups.

However, this study has significant limitations. Distinguishing the immediate and long-term effects of exogenous testosterone are difficult to determine with retrospective observational data alone. Dose adjustments of testosterone are frequent, and therefore documented dosing and route of administration may not be accurate. Compliance cannot be assessed through review of chart data. In addition, the retrospective nature of the study and different practice patterns contributed to a lot of incomplete data, as some sites do not universally document the same demographics (ie, 1 major contributing site did not consistently accurately document race, and therefore it was not included in the study), and not all providers use laboratory or imaging evaluation prior to hysterectomy when gender dysphoria is the sole indication. There is also no current standard for pre-testosterone assessment of the endometrium, so we cannot guarantee that pathology was not present prior to initiation of testosterone. The population is also heterogeneous, providing difficulty in controlling for confounders.

Based on present data, individualized assessments of a transmasculine person's etiology for AUB continue to be necessary, as the risk for abnormal pathology is still present. It is imperative that the field of gynecology continue to evaluate gynecologic concerns of the growing transmasculine population. This will allow us to establish guidelines and to provide the best management for our patients, in addition to providing them affirming and inclusive medical practices. ■

Acknowledgments

The authors would like to acknowledge Dr. Monica Gaddis for assistance with statistical analysis, as well as Dr. Lauri Hochberg for her guidance and ultrasound expertise.

References

1. Perrone AM, Cerpolini S, Maria Salfi NC, et al. Effect of long term testosterone administration on the endometrium of female-to-male (FtM) transsexuals. J Sex Med 2009;6:3193–200.
2. Grynberg M, Fanchin R, Dubost G, et al. Histology of the genital tract and breast tissue after long-term testosterone administration in a female-to-male transsexual population. Repro Biomed Online 2010;20:553–8.
3. Loverro G, Resta L, Dellino M, et al. Uterine and ovarian changes during testosterone administration in young female-to-male transsexuals. Taiwan J Obstet Gynecol 2016;55:686–91.
4. Khalifa MA, Toyama A, Klein ME, Santiago V. Histologic features of hysterectomy specimens from female-male transgender individuals. Int J Gynecol Pathol 2018 [Epub ahead of print].
5. Fearnley EJ, Marquart L, Spurdle AB, Weinstein P, Webb PM. Australian Ovarian Cancer Study Group and Australian National Endometrial Cancer Study. Polycystic ovary syndrome increases the risk of endometrial cancer in women aged less than 50 years: an Australian case-control study. Cancer Causes Control 2010;21:2303–8.
6. Allen NE, Key TJ, Dossus L, et al. Endogenous sex hormones and endometrial cancer risk in the European Investigation into Cancer and Nutrition (EPIC). Endocr Relat Cancer 2008;15:485–97.
7. Tuckerman EM, Okon MA, Laird SM. Do androgens have a direct effect on endometrial function? An in vitro study. Fertil Steril 2000;74:771–9.
8. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap): a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009;42:377–81.
9. Whitaker L, Critchley HO. Abnormal uterine bleeding. Best Pract Res Clin Obstet Gynaecol 2016;34:54–65.
10. Siegel RL, Miller KD, Jemal A. Cancer statistics 2018. Ca Cancer J Clin 2018;68:7–30.
11. Chandra V, Kim JJ, Benbrook DM, Dwivedi A, Rai R. Therapeutic options for management of endometrial hyperplasia. J Gynecol Oncol 2016;27:e8.
12. Jurgensen A, Mettler L, Volkov NI, Parwaresch R. Proliferative activity of the endometrium throughout the menstrual cycle in infertile women with and without endometriosis. Fertil Steril 1996;66:369–75.
13. Enriori CL, Reforzo-Membrives J. Peripheral aromatization as a risk factor for breast and endometrial cancer in postmenopausal women: a review. Gynecol Oncol 1984;17:1–21.
14. Institute of Medicine. The health of lesbian, gay, bisexual, and transgender people: building a foundation for better understanding. Washington, DC: National Academies Press; 2011.
15. Cote ML, Alhajj T, Ruterbusch JJ, Bernstein L, Brinton LA, Blot WJ. Risk factors for endometrial cancer risk in black and white women: a pooled analysis from the epidemiology of endometrial cancer consortium. Cancer Causes Control 2015;26:287–96.
16. Elbers JM, Giltay EJ, Teerlink T, et al. Effects of sex steroids on components of the insulin resistance syndrome in transsexual subjects. Clin Endocrinol 2003;58:562–71.
17. Urban R, Teng NNH, Kapp DS. Gynecologic malignancies in female-to-male transgender patients: the need of original gender surveillance. Am J Obstet Gynecol 2011;204:e9–12.
18. World Professional Association for Transgender Health (WPATH). Standards of care for the health of transsexual, transgender, and gender nonconforming people, 7th Version. WPATH 2012. Available at: http://www.wpath.org/site_page.cfm?pk_association_webpage_menu=1351. Accessed March 6, 2018.
19. Hembree WC, Cohen-Kettenis P, Gooren L, et al. Endocrine treatment of gender dysphoric/gender-incongruent persons: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2017;102:1–35.
20. American College of Obstetrics and Gynecology. Diagnosis of abnormal uterine bleeding in reproductive-aged women. ACOG Practice Bulletin No. 128. Obstet Gynecol 2012;120:197–206.
21. Carswell JM, Roberts SA. Induction and maintenance of amenorrhea in transmasculine and nonbinary adolescents. Transgender Health 2017;2:195–201.
22. Deligdisch L. Hormonal pathology of the endometrium. Mod Pathol 2000;13:285–94.
23. Amezcua CA, Lu JJ, Felix JC, Stanczyk FZ, Zheng W. Apoptosis may be an early event of progestin therapy for endometrial hyperplasia. Gynecol Oncol 2000;79:169–76.
24. American College of Obstetrics and Gynecology. Long-acting reversible contraception: implants and intrauterine devices. ACOG Practice Bulletin No. 186. Obstet Gynecol 2017;130:e251–69.
25. Light AD, Obedin-Maliver J, Sevelius JM, Kerns JL. Transgender men who experienced pregnancy after female-to-male gender transitioning. Obstet Gynecol 2014;124:1120–7.
26. Pavone ME, Bulun SE. The use of aromatase inhibitors for ovulation induction and superovulation. J Clin Endocrinol Met 2013;98:1838–44.
27. Meriggiola MC, Armillotta F, Costantino A, et al. Effects of testosterone undecanoate administered alone or in combination with letrozole or dutasteride in female to male transsexuals. J Sex Med 2008;5:2442–53.

28. DeCensi A, Sun Z, Guerrieri-Gonzaga A, et al. Bone mineral density and circulating biomarkers in the BIG 1-98 trial comparing adjuvant letrozole, tamoxifen, and their sequences. Breast Cancer Res Treat 2014;144:321–9.

29. Coleman RE, Body JJ, Gralow JR, Lipton A. Bone loss in patients with breast cancer receiving aromatase inhibitors and associated treatment strategies. Cancer Treat Rev 2008;34:S31–42.

30. American College of Obstetrics and Gynecology. The role of transvaginal ultrasonography in evaluating the endometrium of women with postmenopausal bleeding. ACOG Committee Opinion Number 734. May 2018. Obstet Gynecol 2018;131:e124–9.

31. Pelusi C, Costantino A, Martelli V. Effects of three different testosterone formulations in female-to-male transsexual persons. J Sex Med 2014;11:3002–11.

32. 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;13:165–232.

Author and article information

From the Department of Obstetrics and Gynecology (Drs Grimstad and Gray), University of Kansas Medical Center, Kansas City, KS; Department of Pediatric and Adolescent Gynecology (Drs Fowler and Gomez Lobo), Children's Hospitals and Clinics of Minnesota, Minneapolis, MN; Department of Obstetrics and Gynecology (Dr New), University of South Florida Morsani College of Medicine, Tampa, FL; Center for Urogynecology and Pelvic Reconstructive Surgery (Dr Ferrando), Center for LGBT Care, Cleveland Clinic, Cleveland, OH; and University Hospitals Cleveland Medical Center/MetroHealth Medical Center (Drs Pollard and Chapman), Cleveland, OH.

Received Sept. 6, 2018; revised Nov. 29, 2018; accepted Dec. 12, 2018.

The authors report no conflict of interest.

Presented in part at the following: 32nd Annual National Association for Pediatric and Adolescent Gynecology Clinical Meeting, April 12—14, West Palm Beach, FL; 2017 University of California, San Francisco National Transgender Health Summit, Nov. 11—12, Oakland, CA; 35th Annual Conference on Lesbian, Gay, Bisexual, and Transgender Health by the Gay and Lesbian Medical Association, Sept. 13—16, Philadelphia, PA; 2017 Philadelphia Trans Health Conference, Sept. 7—9, Philadelphia, PA; and 2nd Annual University of Kansas Department of Obstetrics and Gynecology Research Forum, May 15, 2017, Kansas City, KS.

Reprints: Frances Grimstad, MD, Department of Pediatric Surgery, Children's Mercy Hospital, 2401 Gillham Road, Kansas City, MO, 64108. fgrimstad@gmail.com