

UCSF

UC San Francisco Previously Published Works

Title

Ovarian stimulation for fertility preservation or family building in a cohort of transgender men.

Permalink

<https://escholarship.org/uc/item/8ps705hq>

Journal

Journal of assisted reproduction and genetics, 36(10)

ISSN

1058-0468

Authors

Adeleye, Amanda J
Cedars, Marcelle I
Smith, James
[et al.](#)

Publication Date

2019-10-01

DOI

10.1007/s10815-019-01558-y

Peer reviewed



Ovarian stimulation for fertility preservation or family building in a cohort of transgender men

Amanda J. Adeleye¹ · Marcelle I. Cedars¹ · James Smith² · Evelyn Mok-Lin¹

Received: 21 April 2019 / Accepted: 6 August 2019 / Published online: 21 August 2019
© Springer Science+Business Media, LLC, part of Springer Nature 2019

Abstract

Purpose The purpose of this study was to compare ovarian stimulation and pregnancy outcomes between transgender men (1) with and without a history of testosterone use (HRT) and (2) to cisgender women.

Methods Retrospective chart review between January 1st 2015 and March 1st, 2019 of transgender men and cisgender women seeking ovarian stimulation (OS) matched by BMI and age. Outcomes were compared using Fisher's exact or Wilcoxon's rank sum tests.

Results Thirteen transgender men presented for OS, 7 who used HRT. When comparing transgender men with and without a history of HRT, there were no differences in the baseline follicle count, cycle length, or FSH and hmG used ($p = 0.193, 0.306, 0.200, \text{ and } 0.197$, respectively). Transgender men who used HRT had lower peak estradiol and oocytes retrieved compared to transgender men with no HRT use; peak estradiol levels of 1175 pg/mL IQR [559.5–2684] vs 2713.5 pg/mL IQR [2335–3105]; oocytes retrieved 12 IQR [4–26] vs. 25.5 [18–28] ($p = 0.046, \text{ and } 0.038$, respectively). There were no differences in the estradiol level per oocyte, meiosis II oocyte yield, or maturity rate (MII/oocytes) between the two groups ($p = 1.000, 0.148, \text{ and } 0.147$, respectively). Peak estradiol levels were lower among transgender men compared to cisgender women ($p = 0.016$), but the remaining cycle characteristics were similar between the two groups. Three successful pregnancies were conceived using the oocytes of transgender men who used HRT.

Conclusion HRT use may not negatively impact ovarian stimulation outcomes. Clinical pregnancies are possible from the oocytes of transgender men with a history of HRT.

Keywords Transgender · Fertility preservation · Transgender men

Introduction

Several studies have shown that transgender people have a desire to have genetically related children like many cisgender individuals. However, medical interventions such as gender affirming hormonal medications or certain surgical treatments may impact the gonads and potentially the gametic pool. [1, 2]

For this reason, the general consensus is that transgender people with an interest in genetically related children should be counseled about the possibility of fertility preservation prior to the commencement of gender affirming treatments. [3–5] Understanding the outcomes of fertility preservation procedures or pregnancy outcomes from assisted reproductive technologies in this population is critically important to aid in counseling patients about reproductive considerations during gender affirmation.

For transmasculine individuals, data regarding ovarian stimulation are limited. In an anonymous survey of 41 transgender men who experienced pregnancy, 12% used reproductive technologies. Given the nature of the survey, data regarding the reason for intervention, the medical approach, and ART outcomes were not described. [6] Maxwell et al. described their experience with three transgender men who underwent ovarian stimulation for fertility preservation; however, these patients had not yet initiated testosterone. [7] A

✉ Amanda J. Adeleye
Amanda.Adeleye@ucsf.edu

¹ Division of Reproductive Endocrinology and Infertility, Department of Obstetrics, Gynecology and Reproductive Sciences, University of California San Francisco, 550 16th St, 7th floor, San Francisco, CA 94107, USA

² Department of Urology, University of California San Francisco, 400 Parnassus Ave, San Francisco, CA 94117, USA

Swedish study reviewed the experiences of 15 transgender men who underwent fertility preservation. Among this group of transgender men, seven used testosterone prior to fertility preservation. This descriptive study focused on the journey to fertility preservation and their reactions to the experience. The authors described the ovarian stimulation protocol used and the number of oocytes collected. [8] Although discussions about fertility preservation are encouraged between providers and patients prior to the commencement of gender affirming hormones, outcomes of this process are limited to small case series. Without such data, it can be difficult to counsel patients effectively about fertility preservation, particularly among transgender men with a history of testosterone use. Finally, there are no detailed cases of successful pregnancies resulting from in vitro fertilization (IVF) among transgender men utilizing testosterone.

The objective of this study was to compare the outcomes of ovarian stimulation among transgender men, with and without prior testosterone exposure. A secondary aim was to describe any differences in ovarian stimulation outcomes between transgender men and matched cisgender women. Finally, this study sought to describe a series of successful clinical pregnancies conceived with oocytes from transgender men with prior testosterone use.

Material and methods

Study population

A chart review was performed for all transgender men presenting to an academic fertility clinic for ovarian stimulation for fertility preservation or in vitro fertilization (IVF) between January 1st 2015 and March 1st, 2019. All transgender men self-identified at the time of the initial consultation. Patients who pursued ovarian stimulation were included in the study. Demographics, testosterone usage, and stimulation outcomes were reviewed. Among patients seeking to build a family, IVF and pregnancy outcomes were assessed. Transgender men were matched 1:1 to a cohort of cisgender women undergoing ovarian stimulation by body mass index (BMI) and age. Cisgender women sought ovarian stimulation for either male infertility, social oocyte cryopreservation, or in the case of the pediatric patients, fertility preservation due to a cancer diagnosis. All patients were treated with an antagonist-based protocol. The majority of cycles were initiated with menses or started randomly in the luteal phase. This study was approved by the University of California IRB 10-04868.

Primary outcomes included oocyte yield, peak serum estradiol, estradiol per oocyte retrieved, MII oocytes, and the maturity rate (MII oocytes/total oocytes collected). The occurrence of a clinical pregnancy or live birth among transgender men who utilized IVF was a secondary outcome.

Statistics

Demographic parameters were compared using a Fisher's exact test or Wilcoxon's rank sum test as appropriate. When comparing ovarian stimulation outcomes between transgender men with or without a history of testosterone use, a Wilcoxon's rank sum test was used. When comparing transgender men matched to cisgender women, a Wilcoxon's sign rank test was used to compare paired samples. Statistical significance was determined at $p < 0.05$. All statistics were conducted with Stata 14.2.

Results

Twenty-three transgender men presented for a fertility consultation, 13 proceeded with ovarian stimulation. Of the transgender men seeking ovarian stimulation, six subjects presented prior to initiating testosterone and seven presented after discontinuing testosterone. Three of the patients underwent ovarian stimulation for IVF. The median age of the cohort was 22.4 years [range 14.6 to 37.1 years]. There were no differences in age, race, initial antral follicle count, or follicle count at the initiation of the cycle between transgender men with or without a history of testosterone use. All participants utilized an antagonist-based protocol. There was no difference in luteal phase preparation prior to an ovarian stimulation cycle between the two groups ($p = 0.56$). Demographics are detailed in Table 1. Among subjects with a history of testosterone use, the median length of testosterone exposure was 46 months. The median time of discontinuation of testosterone prior to stimulation was 6 months [range 1–13 months].

Ovarian stimulation

A total of ten cycles were initiated without a period of down-regulation. Six cycles were initiated on cycle day 2 and four started randomly. The remaining patients were suppressed with oral contraceptives ($n = 2$) or estradiol 1 mg PO daily ($n = 1$) prior to gonadotropin stimulation (Table 1). The median number of stimulation days was 10 [range 8–14 days]. When comparing transgender men with a history of testosterone use to those without a history of testosterone use, there were no differences in the number of follicles at cycle start, the number of stimulation days, or the amount of follicle-stimulating hormone (FSH) or human menopausal gonadotropin (hMG) used ($p = 0.193, 0.306, 0.200, \text{ and } 0.197$, respectively). There was a difference in the peak estradiol level achieved between the two groups ($p = 0.046$). The median peak estradiol achieved among transgender men without a history of testosterone was 2713.5 pg/mL [IQR 2335–3105] compared to 1175 pg/mL [IQR 559.5–2684] among transgender men with prior testosterone use. There was also a

Table 1 Demographics

	All subjects (<i>n</i> = 13)		No testosterone (<i>n</i> = 6)		Testosterone (<i>n</i> = 7)		<i>P</i> value
Age	22.4	[19.4–32.5]	20.3	[15.2–25.5]	26.9	[20.9–36.5]	0.09
Race							0.874
Caucasian	30.8%	(<i>n</i> = 4)	16.7%	(<i>n</i> = 1)	42.9%	(<i>n</i> = 3)	
Black	30.8%	(<i>n</i> = 4)	33.3%	(<i>n</i> = 2)	28.6%	(<i>n</i> = 2)	
Asian	30.8%	(<i>n</i> = 4)	33.3%	(<i>n</i> = 2)	28.6%	(<i>n</i> = 2)	
Pacific Islander	7.6%	(<i>n</i> = 1)	16.7	(<i>n</i> = 1)	0%		
Initial AFC	18	[8–25]	22	[21–23]	11.5	[8–30]	0.29
Baseline AFC	20.5	[11.5–22.5]	22	[20–23]	13	[6–22]	0.19
Amenorrhea at cycle start							0.46
No	92.3%	(<i>n</i> = 12)	83.3%	(<i>n</i> = 5)	100%	(<i>n</i> = 7)	
Yes	7.7%	(<i>n</i> = 1)	16.7%	(<i>n</i> = 1)	0%	(<i>n</i> = 0)	
Luteal phase priming							0.66
None	46.2%	(<i>n</i> = 6)	33.3%	(<i>n</i> = 2)	57.1%	(<i>n</i> = 4)	
Estradiol	7.7%	(<i>n</i> = 1)	0%	(<i>n</i> = 0)	14.3%	(<i>n</i> = 1)	
OCP	15.4%	(<i>n</i> = 2)	16.7%	(<i>n</i> = 1)	14.3%	(<i>n</i> = 1)	
Random	30.8%	(<i>n</i> = 4)	50%	(<i>n</i> = 3)	14.3%	(<i>n</i> = 1)	

Values reported as median [interquartile range] or percentage (number). Luteal phase priming: none = initiation of cycle without pretreatment medication, estradiol priming: estrace 1 mg daily, OCP = oral contraceptive pill, random = random start of gonadotropins. Note some percentiles do not sum to 100% due to rounding

difference in the number of oocytes retrieved between the two groups; transgender men without testosterone use had a median of 25.5 [IQR 18–28] oocytes collected compared to 12 [IQR 4–26] oocytes among transgender men with a history of testosterone use *p* = 0.038 (Table 2). However, the proportion of oocytes collected dependent upon the baseline AFC was not different between the two groups *p* =

0.167 (Table 2). There were two outliers among the transgender men; these men had diminished ovarian reserve with initial AFCs less than 5. Repeating the analysis without these two outliers resulted in no difference in any of the ovarian stimulation parameters including peak estradiol level and the number of oocytes retrieved *p* = 0.144 and 0.119, respectively.

Table 2 Comparison of ovarian stimulation outcomes reported as median [25–75%] between cisgender women and transgender men and transgender men with and without a history of testosterone use. Baseline

follicle count—number of follicles seen at initiation of cycle (*n* = 9 per group); four pediatric patients in cisgender group had a random start cycles without a baseline follicle count collected

	Cisgender women (<i>n</i> = 13)		Transgender men				<i>P</i> value			
			All transgender men (<i>n</i> = 13)		Transgender men with no testosterone (<i>n</i> = 6)		Transgender men with testosterone history (<i>n</i> = 7)		Cis vs. Trans ^a	T vs no T ^b
Follicles at cycle start	15	[13–20]	20.5	[11.5–22.5]	22	[20–23]	15	[6–22]	0.953	0.193
Cycle length (days)	10.5	[9.5–12]	10	[9–11]	10.5	[10, 11]	10	[8–11]	0.811	0.306
Total FSH (IU)	2025	[1500–2250]	1425	[1200–2100]	1275	[1200–1950]	1950	[1350–2400]	0.311	0.20
Total LH (IU)	1350	[825–1575]	1200	[1050–1500]	1425	[1200–1500]	1050	[1050–1350]	0.459	0.197
Peak estradiol (pg/mL)	2753	[2268–4508]	2335	[1175–2800]	2713.5	[2335–3105]	1175	[559.5–2684]	0.016	0.046
Peak estradiol per oocyte (pg/mL)	161.7	[141.3–185.3]	129.4	[99.4–145.9]	130.5	[100.0–145.9]	117.6	[97.9–178.9]	0.100	1.000
Oocytes retrieved	20	[18–27]	18	[12–27]	25.5	[18–28]	12	[4–26]	0.294	0.038
Number of M2s	16	[11–25]	13	[9–22]	14.5	[13–23]	9	[4–21]	0.396	0.148
Oocytes/baseline follicle count	1.2	[0.8–1.6]	1.0	[0.6–1.3]	1.3	[0.9–1.1]	0.9	[0.4–1.3]	0.314	0.167
Maturity rate (%)	83.3	[78.2–88.9]	84.4	[73.6–96.2]	77.2	[59.3–86.7]	91.2	[77.8–100]	0.823	0.147

^a Cisgender women and transgender men with and without a history of testosterone use

^b Transgender men with and without a history of testosterone use

Testosterone exposure did not have a significant impact on markers of follicular function or oocyte maturity. The peak estradiol per oocyte retrieved was 130.5 pg/mL [IQR 100.0–145.9] among transgender men without a history of testosterone use and 117.6 pg/mL [IQR 97.9–178.9] among transgender men who used testosterone $p = 1.000$. Transgender men without testosterone exposure had a median of 14.5 [IQR 13–23] mature oocytes retrieved and a maturity rate of 77.2% [IQR 59.3–86.7]. Transgender men with a history of testosterone use had a median of nine mature oocytes retrieved [IQR 4–21] and a maturity rate of 91.2% [IQR 77.8–100]. There were no differences in the number of mature oocytes collected or the maturity rate between the two groups $p = 0.148$ and 0.147 , respectively (Table 2).

When comparing transgender men matched by age and BMI to cisgender women, there were no differences in the number of follicles at cycle start, cycle length, or the total amount of gonadotropins used (FSH and hMG), between the two groups ($p = 0.953$, 0.811 , 0.311 , and 0.459 , respectively). Transgender men, including those who had never been exposed to testosterone, had lower peak estradiol levels 2335 pg/mL [IQR 1175–2800] compared to cisgender women 2753 pg/mL [IQR 2268–4508] $p = 0.016$. Granulosa cell function and oocyte maturity were not different between cisgender women and transgender men. The peak estradiol per oocyte retrieved was 161.7 pg/mL [IQR 141.3–185.3] among cisgender women and 129.4 pg/mL [99.4–145.9] among transgender men $p = 0.100$. Cisgender women had a median of 20 oocytes retrieved [IQR 18–27], 16 [IQR 11–25] mature oocytes, and a maturity rate of 83.3% [IQR 78.2–88.9]. Transgender men had a median of 18 oocytes retrieved [IQR 12–27], 13 [IQR 9–22] mature oocytes, and a maturity rate of 84.4% [IQR 73.6–96.2]. The proportion of oocytes collected dependent upon the baseline follicle count was no different between the two groups $p = 0.314$. There were no differences in the number of oocytes collected, mature oocytes collected, or the maturity rate between the two groups $p = 0.294$, 0.396 , and 0.823 , respectively (Table 2.)

Fertility outcomes

Three transgender men presented with their partners for family building care. All three men had a history of testosterone use and discontinued prior to ovarian stimulation. A summary of their treatment and outcomes can be found in Table 3.

Patient 1, a 37-year-old transgender man, presented with his cisgender male partner. The patient's cisgender male partner had virtual azoospermia. At an outside fertility clinic, the partner had a testicular sperm extraction, cryopreservation, and the couple underwent IVF. Their first IVF cycle resulted in 5 eggs retrieved, 4 fertilized and none that survived to day 3. The couple then presented to our clinic for continued fertility care. At the time of presentation, patient 1 had been on

testosterone for 3 years and discontinued 11 months prior to treatment. At the initiation of his cycle, he had 15 antral follicles. His cycle lasted 9 days during which he received FSH 2400 IU and hMG 1200 IU. On the day of trigger, 11 follicles were identified and he attained a peak serum estradiol of 967.3 pg/mL. His cycle resulted in 10 oocytes retrieved of which nine were mature and fertilized by ICSI. Fertilization resulted in 6 2PNs that developed to six good quality day 3 embryos. Two embryos were transferred and the remainder were frozen on day 3. His fresh transfer resulted in a spontaneous abortion at 7 weeks. In a subsequent medicated frozen embryo transfer cycle, he tolerated supplemental estradiol well and achieved a peak endometrial thickness of 11.7 mm but did not conceive with this cycle. He and his partner transferred remaining embryos to a clinic in their home country.

Patient 2, a 32-year-old transgender man, presented with his cisgender female partner. The indication for treatment was for reciprocal IVF as he wanted genetically related offspring but did not want to carry the pregnancy. He had been on testosterone cypionate 150 mg IM for 9 years prior to seeking fertility care and discontinued testosterone for 6 months prior to ovarian stimulation. At the initiation of his cycle, he had an antral follicle count of 27. His ovarian stimulation cycle lasted 14 days during which he utilized a total of FSH 1425 IU and hMG 1050 IU. On the day of trigger, 20 follicles were identified and he reached a peak estradiol of 1175 pg/mL. This cycle resulted in 12 oocytes retrieved that were conventionally inseminated, eight 2PNs, and ultimately one good quality blastocyst that was transferred fresh to his partner. This cycle resulted in a successful pregnancy with an uncomplicated delivery at 40 weeks.

Patient 3, a 34-year-old transgender man, presented for care with his cisgender female partner also with an indication of reciprocal IVF. He had been on testosterone 200 mg IM weekly for 2 years and had discontinued for 2 months, prior to ovarian stimulation. Immediately prior to stimulation, he had an AFC of 21. His cycle lasted 8 days during which he received FSH 1050 IU and hMG 1050 IU. On the day of trigger, 26 follicles were identified and he reached a peak estradiol of 2684 pg/mL. Twenty-seven oocytes were retrieved of which 21 were MIIs. These 21 MIIs were fertilized via ICSI with donor sperm resulting in 19 2PNs from which 8 good quality blasts resulted. His partner underwent two frozen embryo transfers. The first medicated frozen single embryo transfer did not result in pregnancy. The second medicated single embryo transfer resulted in a successful ongoing intrauterine pregnancy.

Discussion

This study contributes to the literature on fertility preservation and family building for transgender men. Further, this is the

Table 3 Pregnancy outcomes after ovarian stimulation for three transgender men. Good quality embryos—number of embryos transferred or frozen; AFC—antral follicle count at start of cycle

Patient	Testosterone use			Ovarian stimulation				IVF outcomes				
	Dose (mg/week)	Time on (months)	Time off (months)	AFC	Length of cycle (days)	Total FSH (IU)	Total LH (IU)	Peak estradiol (pg/mL)	Oocytes retrieved	2PN	Good quality embryos	Pregnancy outcome
1 ^a	160	46	11	15	9	2400	1200	967.3	10	6	6	Spontaneous abortion—patient
2 ^b	150	108	6	27	14	1425	1050	1175	12	8	1	Live birth—partner
3 ^c	200	26	2	21	8	1050	1050	2684	27	19	8	Ongoing pregnancy—partner

^a ICSI fertilization, fresh transfer of day 3 embryo

^b Conventional insemination, fresh transfer to partner

^c ICSI fertilization, frozen transfer to partner

first detailed report of successful pregnancies from assisted reproductive technology using oocytes from transgender men with a history of testosterone use. Importantly, our data show that an antagonist-based protocol is feasible means of ovarian stimulation in this population. Although the oocyte yield and peak estradiol were lower in transgender men with a history of testosterone use, the peak estradiol per retrieved oocyte and the maturity rate were no different between testosterone exposed and unexposed cycles. This may suggest that the follicular development and potentially oocyte quality may not be significantly impacted by prior testosterone exposure; however, the sample size was small, and aside from peak estradiol levels, this study was not powered to detect such differences. Our findings may not be surprising in light of data that suggests that in spite of testosterone exposure, the pool of primary oocytes that can be normally in vitro matured is relatively preserved among transgender men. [9] Further, when testosterone-exposed oocytes are in vitro matured immediately, or after thawing from cryopreservation, the spindle structure is generally preserved. [10] However, our data do not support a minimum period of testosterone discontinuation that would result in a normalized follicular pool with follicles identifiable at the secondary stage and beyond.

Interestingly, our cohort of transgender men on testosterone experienced a lower number of oocytes retrieved and consequently, a lower peak estradiol level compared to transgender men who had not ever used testosterone. Two patients in this cohort had diminished ovarian reserve with one patient having four oocytes retrieved and another having only one oocyte retrieved; both had a history of prior testosterone use. Given the small size of our cohort, these possible “outliers” may have impacted the oocyte yield comparison. When this analysis was repeated excluding the two outliers, there was no difference in estradiol levels between the two groups. A related study from Leung et al. described a cohort of 22 transgender men. Their 25 ovarian stimulation cycles were compared to 75 control cycles among cisgender women. The mean number of oocytes collected in the transgender group was significantly higher than the control group. Peak estradiol levels were similar between the two groups although peak estradiol per oocyte was not reported. [11] When our cohort of 13 transgender men was compared to matched cisgender controls, outcomes from ovarian stimulation were essentially the same between the two groups. Peak estradiol levels remained lower among transgender men. Importantly, the estradiol level per oocyte was no different between the two groups suggesting that aspects of granulosa cell function are maintained. Lower total estradiol levels may be attributable to lower follicle counts which did not reach significance between cisgender women and transgender men who used testosterone. It is possible that testosterone may subtly suppress the follicular pool. Caanen et al. demonstrated a significant decrease in anti-mullerian hormone levels among 22 transgender men after

16 weeks of testosterone exposure. [12] It is also conceivable that long-term testosterone use may impact the follicle count via the hypothalamic pituitary ovarian axis. Testosterone may be converted to estrogen at the hypothalamus, inducing negative feedback via a reduction in FSH which would decrease the number of secondary FSH sensitive follicles available for recruitment during ovarian stimulation. Such a decrease in the follicular pool might influence the timing of stimulation and expectations of oocyte yield; however, our data and other supporting recent studies do not suggest impaired function of the recruited follicles.

Multiple histologic studies have demonstrated that testosterone exposure may induce a polycystic appearance to the ovary. Features may include collagenization of the stroma, cystic appearing follicles, follicular atresia, and stromal leutenization. [2, 13] However, some have argued that transgender men have a higher incidence of PCOS even before testosterone exposure. [2] It is also possible that transgender men may be predisposed to higher circulating levels of sex steroids. When Bentz et al. compared 49 transgender men to 102 transgender women and over 1000 cisgender control patients, transgender men had a higher incidence of a functional SNP in the CYP17 enzyme which results in higher levels of estradiol, progesterone, and testosterone. [14] Transgender men who have not had testosterone exposure may be the most appropriate comparator to transgender men using testosterone, as was done in our study, given the possibility that there may be differences in sex steroid hormone metabolism among transgender men compared to cisgender women. Regardless of possible endogenous differences between cisgender women and transgender men, comparing these cohorts may help clinicians to set expectations around how transgender men may respond to ovarian stimulation.

Although we do not currently have experiential data on how our patients felt about the process of ovarian stimulation, it should be noted that at our clinical center, we have intake forms that specifically query a patient's chosen name and pronouns. Additional alerts have been added to the electronic medical records of transgender patient charts to help ensure staff and practitioners are cognizant of addressing patients properly. Furthermore, we query about the preferred name for body parts to be used in subsequent discussions and physical evaluations. Finally, we offer all patients ultrasound monitoring transrectally or transabdominally if they are uncomfortable with a transvaginal approach. These strategies have been developed in concert with patient feedback over the years and recent data on the transgender male experience with ovarian stimulation as described by Armaund et al. [8]

A strength of this study is that it begins to address the question of what transgender men and their ART providers may expect in terms of ovarian stimulation outcomes. Prior studies on the experiences of transgender men undergoing ovarian stimulation have been descriptive in nature. Additionally, while

there have been studies reviewing ovarian stimulation for transgender men previously, only Armaund et al. included transgender men who had used testosterone previously. [7, 8] While it is ideal that transgender people present for fertility preservation prior to the commencement of gender affirming treatment, the reality is that patients will seek assistance at varying points of gender affirmation. This study serves as one of the first studies to examine ART outcomes among transgender men.

The question of whether or not testosterone-exposed transgender men can carry pregnancies has been established. There have been prior studies reporting pregnancies among transgender men who were able to conceive spontaneously after discontinuing testosterone treatment or at times had unplanned pregnancies while on testosterone treatment. [6, 15] However, our cohort contributes to the limited data on conception with ART for testosterone-exposed men who desire to carry the pregnancy themselves or who desire to have their partner carry the pregnancy. Notably, all three transgender men that sought to conceive with their own oocytes after testosterone exposure were able to do so. In our cohort, one transgender man chose to carry his pregnancy but experienced a spontaneous abortion. Though no conclusions can be made from this singular instance, it is important to note that testosterone may have short- and long-term impacts on the endometrium. Grynberg et al. described the histology of the genital tracts of a cohort of transgender men. [13] They noted two different histological patterns, either atrophic endometrium or proliferative endometrium. Additionally, Perrone et al. evaluated the endometrium of 30 transgender men and noted a predominance of atrophic endometrium. [16] Future studies may consider examining whether or not endometrial receptivity is impacted by a history of HRT use.

Limitations of this study include the small sample size which discourages any definitive statements about differences in ovarian stimulation outcomes between testosterone-exposed and -unexposed transgender men. Furthermore, the sample size limits the ability to make any conclusive statements about the length of time transgender men should discontinue testosterone prior to ovarian stimulation if at all. Future studies should seek to critically define the ideal period of testosterone discontinuation prior to the commencement of ovarian stimulation. The degree of suppression follicular suppression, if any, should be characterized and ideally the rate of recovery of the mature follicular pool.

Given the well-described social and financial hurdles that transgender patients face in accessing care, the number of patients seeking fertility preservation at a given institution may be small. [17] In the future, it would be prudent for transgender care providers to collaborate on a national or international level to pool all reported cases of transgender people pursuing fertility preservation to determine best practices and pregnancy outcomes.

Conclusion

~~Ovarian stimulation is feasible for transgender men with an antagonist protocol. In our cohort, a history of testosterone use did not negatively impact the peak estradiol level per follicle, which may be a proxy for granulosa cell function or the maturity rate of oocytes retrieved. Finally, clinical pregnancies are possible from the oocytes of transgender men with a history of testosterone use.~~

Financial support None.

Compliance with ethical standards

Disclosures Amanda Adeleye is a shareholder of Carrot. The remaining authors have nothing to disclose.

References

- Schneider F, Kliesch S, Schlatt S, Neuhaus N. Andrology of male-to-female transsexuals: influence of cross-sex hormone therapy on testicular function. *Andrology*. 2017;5(5):873–80.
- Ikeda K, Baba T, Noguchi H, Nagasawa K, Endo T, Kiya T, et al. Excessive androgen exposure in female-to-male transsexual persons of reproductive age induces hyperplasia of the ovarian cortex and stroma but not polycystic ovary morphology. *Hum Reprod*. 2013;28(2):453–61.
- Hembree WC, Cohen-Kettenis P, Delemarre-van de Waal HA, Gooren LJ, Meyer WJ III, Spack NP, et al. Endocrine treatment of transsexual persons: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2009;94(9):3132–54.
- Coleman E, Bockting W, Botzer M, Cohen-Kettenis P, DeCuypere G, Feldman J, et al. Standards of Care for the Health of transsexual, transgender, and gender-nonconforming people, version 7. *Int J Transgenderism*. 2012;13(4):165–232.
- Martinez F, International Society for Fertility Preservation–ESHRE–ASRM Expert Working Group. Update on fertility preservation from the Barcelona International Society for Fertility Preservation–ESHRE–ASRM 2015 expert meeting: indications, results and future perspectives. *Fertil Steril*. 2017;108(3):407–415.e11.
- Light AD, Obedin-Maliver J, Sevelius JM, Kerns JL. Transgender men who experienced pregnancy after female-to-male gender transitioning. *Obstet Gynecol*. 2014;124(6):1120–7.
- Maxwell S, Noyes N, Keefe D, Berkeley AS, Goldman KN. Pregnancy outcomes after fertility preservation in transgender men. *Obstet Gynecol*. 2017;129(6):1031–4.
- Armuan G, Dhejne C, Olofsson JI, Rodriguez-Wallberg KA. Transgender men's experiences of fertility preservation: a qualitative study. *Hum Reprod*. 2017;32(2):383–90.
- De Roo C, et al. Ovarian tissue cryopreservation in female-to-male transgender people: insights into ovarian histology and physiology after prolonged androgen treatment. *Reprod BioMed Online*. 2017;34(6):557–66.
- Lierman S, Tilleman K, Braeckmans K, Peynshaert K, Weyers S, T'Sjoen G, et al. Fertility preservation for trans men: frozen-thawed in vitro matured oocytes collected at the time of ovarian tissue processing exhibit normal meiotic spindles. *J Assist Reprod Genet*. 2017;34(11):1449–56.
- Leung A, Sakkas D, Pang S, Thornton K, Resetskova N. Female to male transgender patients have good egg yields with controlled ovarian hyperstimulation. *Fertil Steril*. 2018;110(4):e21–2.
- Caanen MR, Soleman RS, Kuijper EAM, Kreukels BPC, de Roo C, Tilleman K, et al. Antimüllerian hormone levels decrease in female-to-male transsexuals using testosterone as cross-sex therapy. *Fertil Steril*. 2015;103(5):1340–5.
- Grynberg M, Fanchin R, Dubost G, Colau JC, Brémont-Weil C, Frydman R, et al. Histology of genital tract and breast tissue after long-term testosterone administration in a female-to-male transsexual population. *Reprod BioMed Online*. 2010;20(4):553–8.
- Bentz E-K, Hefler LA, Kaufmann U, Huber JC, Kolbus A, Tempfer CB. A polymorphism of the CYP17 gene related to sex steroid metabolism is associated with female-to-male but not male-to-female transsexualism. *Fertil Steril*. Jul. 2008;90(1):56–9.
- Light A, Wang L-F, Zeymo A, Gomez-Lobo V. Family planning and contraception use in transgender men. *Contraception*. 2018;98(4):266–9.
- Perrone AM, Armillotta F, Formelli G, Casadio P, Salfi NCM, Badiali de Giorgi L, et al. T04-O-05 high dose testosterone (T) treatment has no adverse effects on the endometrium of female to male transsexuals (FtM). *Sexologies*. 2008;17:S78–9.
- Grant J, Mottet L, Tanis J, Herman J, Harrison J, Keisling M. National Transgender Discrimination SURvey report on health and health care. National Center for Transgender Equality; 2010.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.