

Testosterone therapy at the time of vasectomy reversal: Impact on intraoperative decision-making and interpretation of postoperative outcomesEthan D. Grober¹, Udi Blankstein²¹Division of Urology, Department of Surgery, Women's College Hospital & Sinai Health System, University of Toronto, Toronto, ON, Canada; ²Division of Urology, Department of Surgery, McMaster University, Hamilton, ON, Canada**Cite as:** Grober ED, Blankstein U. Testosterone therapy at the time of vasectomy reversal: Impact on intraoperative decision-making and interpretation of postoperative outcomes. *Can Urol Assoc J* 2024 June 17; Epub ahead of print. <http://dx.doi.org/10.5489/cuaj.8725>

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ABSTRACT

Introduction: During vasectomy reversal (VR), accurate intraoperative microscopic assessment of the vasal fluid for sperm presence and quality is essential in determining the indication for a vasovasostomy (VV) or vasoepididymostomy (VE). The use of testosterone therapy (TT), known to suppress spermatogenesis, can potentially interfere with this determination. This initiative evaluated the impact of TT on vasal and epididymal fluid sperm characteristics and intraoperative decision-making among men on TT at the time of VR.

Methods: Of 2622 consecutive VRs performed from 2007–2023, patients actively using TT at the time of VR were identified. Details as to the type, dose, and duration of TT were documented. All patients were counselled regarding the impact of TT on spermatogenesis and encouraged to discontinue TT if possible. During VR, vasal and epididymal fluid (as indicated) was sampled and each aspirate underwent microscopic evaluation for sperm presence and

KEY MESSAGES

- Use of TT at the time of VR does not appear to impact microscopic identification of sperm within the reproductive fluid or the indication for VV/VE.
- Postoperative patency rates and total motile sperm counts may be lowered by use of TT and TT discontinuation if possible is generally advised for optimal reproductive outcomes following VR.
- The determination to the etiology azoospermia postoperatively (production vs. obstruction) may be clouded using TT during VR. In such circumstances, cessation of TT may be informative.

quality, and categorized as: motile sperm/intact-non-motile sperm/sperm parts/no sperm. Rates of sperm presence/absence in the vasal/epididymal fluid, frequency of VV/VE, postoperative patency (presence of motile sperm), and semen parameters were compared among patients on TT vs. clinically matched patients not using TT at the time of VR.

Results: Among the 2622 VRs reviewed, 54 men (2%) reported using TT at the time of their VR. Despite its impact on spermatogenesis, intraoperative microscopic analysis of the reproductive fluid (vasal or epididymal) identified the presence of sperm in 95% (51/54) of patients. Testis biopsy confirmed sperm production among three patients with absence of sperm within the vasal or epididymal fluid. Rates of VV or VE did not significantly differ among men using TT at the time of VR compared to nonusers. Postoperative patency rates (TT: 78 % vs. no TT: 93%) and mean total motile sperm counts (TMC) were lower among patients using TT at the time of VR (7.9 vs. 28.3, $p=0.02$).

Conclusions: Use of TT at the time of VR does not appear to impact rates of intraoperative microscopic identification of sperm within the reproductive fluid or the indication for VV/VE. Postoperative patency rates and total motile sperm counts may be lowered by use of TT. Moreover, the determination to the etiology azoospermia postoperatively (production vs. obstruction) may be clouded by the use of TT during VR.

INTRODUCTION

Testosterone therapy (TT) is known to have a contraceptive effect on sperm production.¹⁻³ Exogenous testosterone administration initiates negative feedback on the pituitary gland, dampening both follicle stimulation hormone (FSH) and luteinizing hormone (LH) release from the anterior pituitary. Consequently, signaling of endogenous testosterone production and testicular spermatogenesis is diminished, often resulting in severe oligospermia or azoospermia within the ejaculate.^{1,2} Among men who have undergone vasectomy, using the ejaculate as an indicator as to the specific impact of testosterone therapy on spermatogenesis is challenging as the occlusive nature of the vasectomy in and of itself is expected to result in azoospermia.⁴

During vasectomy reversal (VR), accurate intra-operative microscopic assessment of the vasal fluid for sperm presence and quality is essential in determining the indication for a vasovasostomy (VV) or vasoepididymostomy (VE).^{5,6} Contemporary guidelines (American Society Reproductive Medicine - ASRM)⁷, generally recommend that a VV be performed if the presence of sperm or sperm parts are identified within the aspirate of fluid expressed from the testicular end vas. Whereas a VE is indicated if no sperm are identified within the vasal fluid.⁷ A noted exception, favoring VV, being the absence of sperm within clear and copious vasal fluid. The suppressive impact TT on testicular sperm production can potentially interfere with this determination and theoretically lead to erroneous intra-operative decision making.¹ For example,

in a patient on TT at the time of VR, the absence of sperm within an intra-operative fluid aspirate from the testicular end vas could be indicative of either epididymal obstruction or diminished spermatogenesis consequent to TT in the absence of epididymal obstruction. Consequently, a clear indication for VV or VE would be uncertain.

The current initiative evaluates the impact TT on vasal and epididymal fluid sperm characteristics and intra-operative decision-making among men on testosterone therapy at the time of VR.

METHODS

This study received research ethics board approval for infertility research at the Sinai Health System at the University of Toronto. A retrospective evaluation of a prospectively maintained patient data series of vasectomy reversal surgeries performed by a single surgeon (EG) between 2007 to 2023 was analyzed.

Patients

Of 2622 consecutive VRs, patients actively using TT at the time of VR were identified. Details as to the type, dose and duration of TT were documented. Prior to reversal surgery, all patients were counselled by an experienced testosterone specialist regarding the potential suppressive impact of TT on spermatogenesis and encouraged to discontinue TT if possible and alternative treatments were discussed. Patients using human chorionic gonadotrophin (HCG) or a selective estrogen receptor modulator (SERM) concurrent with or as a transition from TT were excluded from this analysis. Testosterone levels were not specifically measured by the VR surgeon as part of the study protocol prior to surgery.

During VR, vasal fluid was manually expressed and sampled from the freshly transected testicular-end vas and the *vasal fluid quality* was characterized (thick-paste/opaque/translucent/clear).⁵ The *vasal fluid volume* was documented as copious/minimal.⁵ Immediately following vasal fluid aspiration, each sample underwent intra-operative bench microscopic evaluation at 200 power to determine *sperm presence* (yes/no) and *vasal sperm quality* - categorized as motile sperm/intact non-motile sperm/sperm parts (sperm heads or tails)/no sperm (American Society for Reproductive Medicine-ASRM guidelines).⁷ As indicated, fluid from the epididymal tubules was similarly analyzed and categorized. Testis tissue biopsy was performed only among patients demonstrating an absence of sperm within both the vasal and epididymal fluid samples.

Rates of sperm presence/absence in the vasal/epididymal fluid, frequency of VV/VE, post-operative patency (presence of motile sperm in the ejaculate) and semen parameters were compared among patients on TT vs. clinically-matched (age and vasal occlusion interval) patients not using TT at the time of VR. Post-operative semen analyses were performed beginning 3-months following surgery. All patients using TT at the time of their VR remained on TT for post-operative semen testing. SPSS software was used to support the statistical analysis as part of this study.

RESULTS

Among the 2622 VRs performed during the study time frame, 54 men (2%) reported using TT at the time of their VR. Mean patient age was 43 years and mean vasal occlusion interval (time from vasectomy to VR) was 6.7 years. Prior to VR, the average time on testosterone therapy was 39 months with topical gels used by 62% of patients (25-100mg/day), injectables by 26% (cypionate or enanthate 100-200mg biweekly), intra-nasal administration by 6% (11-33mg/day), axillary by 4% (60mg/day) and oral agents by 2% (120mg/day). Dosing was within manufacturers' guidelines for all testosterone products used. All patients reported biological fatherhood prior to both their VR and initiation of TT.

In spite of the known impact of testosterone therapy on spermatogenesis, intra-operative microscopic analysis of the reproductive fluid (vasal or epididymal) identified the presence of sperm in 95% (51/54) of all patient subjects. Among these patients, 86% (44/51) has sperm identified within the vasal fluid and had a VV performed, while the remaining 14% (7/51) of men had evidence of sperm within the epididymal fluid aspirate and underwent VE. Testis biopsy confirmed sperm production among the 3 (5%) patients with an absence of sperm within both the vasal or epididymal fluid. Among these patients, all had a VV completed. Collectively, 100% of men on TT demonstrated evidence of spermatogenesis at the time of VR.

Compared to clinically matched nonusers of TT, rates of VV or VE, did not significantly differ among men using TT at the time of VR. Post-operative patency rates (TT:78 % vs. No TT:93%) and mean total motile sperm counts (TMC) were lower among patients using TT at the time of VR (TT: 7.9 vs. No TT 28.3, $p=0.02$). Clinical, operative and post-operative characteristic of the testosterone and non-testosterone VR cohorts is summarized in Table 1.

DISCUSSION

The current study sought to evaluate the impact TT use at the time of VR on vasal and epididymal fluid sperm characteristics and the potential influence of such use on intra-operative decision-making and surgical outcomes. Despite the known suppressive influence of TT on spermatogenesis, overall, we found that sperm production was preserved (although likely diminished), with sperm identifiable in the reproductive tract in all patients at the time of VR. Consequently, the established evidence-based intra-operative algorithms for determining the indication for VV or VE during VR remain informative.^{6,7} As such, rates of VV or VE should be relatively uninfluenced by TT use at the time of VR as demonstrated in the current study.

With respect to post-operative outcomes, our analysis does highlight the suppressive nature of TT use (vs. non users) on total motile sperm counts and patency rates.¹ Accordingly, patients should be counselled that optimization of fertilization potential and conception is best achieved through discontinuation of TT. The route of testosterone administration or product type did not impact the primary outcomes of this study.

Appreciating that TT in and of itself can lead to the absence of sperm within the ejaculate, determining the etiology of post VR azoospermia presents a diagnostic challenge to the clinician tasked with differentiating a deficit in sperm production from persistent reproductive

tract obstruction. Under these circumstances, cessation of TT and allowing time for the reproductive hormonal axis to recover may be informative. Recovery of spermatogenesis following TT discontinuation would be consistent with hormonal suppression of sperm production as a consequence TT, while persistent azoospermia would suggest anastomotic failure.

The current investigation represents that largest analysis of the impact of TT on VR outcomes published to date. Consistent with the findings of the current study, a retrospective case series of 14 men by Bash et al. (2022)⁸ reported high rates of VV (96%) and sustained patency rates among patients using TT prior to VR. Moreover, Coward et al (2014)⁹ reported an overall patency rate of 83% with spontaneous pregnancy rates of 50% among 6 men with prior TT, suggesting that VR after TT can have outcomes comparable to those in the general population.

With respect to study limitations, the authors acknowledge that measurement of serum testosterone levels and reproductive gonadotropins (Luteinizing hormone - LH, follicle stimulating hormone - FSH) may have offered a more comprehensive understanding as to the nature and degree of testosterone absorption and suppression of hypothalamic-pituitary-gonadal hormonal axis in this patient population. Such information may allow for individualized counselling and prognostication with respect to TT use and impact on sperm production. Moreover, testis biopsy specimens were only evaluated for the presence or absence of sperm in order to guide real-time, intra-operative decision making related to the indication for VV or VE and not for comprehensive histological staging of spermatogenesis. Finally, our methodology may have resulted in unnecessary epididymal violation in limited number of patients. Learning from the study data, a reasonable forward-thinking approach would be only to sample epididymal fluid among patients demonstrating an absence of sperm within the vasal fluid, but sperm presence on testis biopsy. In this case a VE would be indicated.

CONCLUSIONS

Use of TT at the time of VR does not appear to impact rates of intra-operative microscopic identification of sperm within the reproductive fluid or the indication for VV/VE. Post-operative patency rates and total motile sperm counts may be lowered by use of TT and TT discontinuation if possible is generally advised for optimal reproductive outcomes following VR. Finally, the determination to the etiology azoospermia post-operatively (production vs. obstruction) may be clouded by the use of TT during VR. In such circumstances, cessation of TT may be informative.

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FIGURES AND TABLES

Table 1. Clinical and operative characteristic of testosterone and no testosterone VR cohorts						
	Mean age	Mean vasal occlusion interval	VV/VE	% sperm identified in vasal or epididymal fluid	% patent	Total motile sperm count
Testosterone	43 years	6.7 years	87%/13%	95% *5% had sperm identified in testis tissue	78% overall VV: 81% VE: 57%	7.9
No testosterone	42 years	7 years	85%/15%	100%	93% overall VV: 97% VE: 62%	28.3 (p=0.02)

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