Post-vasectomy semen analysis compliance with use of a home-based test

James Trussler, MD, Brendan Browne, MD, Manuel Merino, MD, Daneil Kuftinec, MD, Andrew McCullough, MD
Lahey Hospital and Medical Center, Institute of Urology, Burlington, Massachusetts, USA

TRUSSLER J, BROWNE B, MERINO M, KUFTINEC D, MCCULLOUGH A. Post-vasectomy semen analysis compliance with use of a home-based test. *Can J Urol* 2020;27(5):10388-10393.

Introduction: *Although the importance of post-vasectomy semen analysis (PVSA) is well known, compliance with this test has historically been low. We sought to compare compliance with PVSA when using a home-based testing kit with traditional office based microscopy, and to estimate the impact of compliance differences on the risk of undetected vasectomy failure.*
Materials and methods: *A retrospective review of vasectomies performed by three providers was performed. Patients were prescribed either traditional office-based PVSA testing (Group 1) or home-based PVSA testing (Group 2). Compliance with PVSA testing was defined as completion of at least one PVSA test. Decision analysis methodology was applied to estimate the risk of undetected vasectomy failure in each group.*
Results: *A total of 226 vasectomies were reviewed, 141 in Group 1 and 85 in Group 2. The compliance rate was 65.96% in Group 1 compared to 76.47% in Group 2 ($p = .095$). When utilizing a single home-based test, the estimated risk of undetected vasectomy failure was 3.65% in Group 1 compared to 4.09% in Group 2. When utilizing two serial home-based tests, the estimated risk in Group 2 decreased to 2.87%.*
Conclusion: *As home-based PVSA tests become more widely available, it is important to understand their impact. The availability of such tests may lead to improved compliance with PVSA testing. In turn, increased compliance may offer increased detection of vasectomy failure. Further study is needed with regard to the impact of home-based tests.*

Key Words: vasectomy, post-vasectomy semen analysis, compliance

Introduction

Vasectomy is a very common urologic procedure for elective sterilization, with some estimates indicating over 500,000 procedures performed annually.[1] Procedural success is defined as azoospermia or < 100,000 non-motile sperm/mL (NMS), equivalent to < 1 sperm per high power field on microscopy,[2] and is classically evaluated 8 to 16 weeks post-procedure utilizing a laboratory-based post-vasectomy semen analysis (PVSA).[2,3] This test requires a patient to provide a fresh semen sample to the office or laboratory where the uncentrifuged specimen is microscopically examined for sperm count and motility. A negative PVSA is essential to confirm postoperative sterility, but published PVSA compliance rates remain surprisingly low.[3,4]

In 2008, the FDA approved SpermCheck Vasectomy (DNA Diagnostics, Fairfield, OH, USA) as the first home-based test to detect the presence of sperm in semen samples following vasectomy. SpermCheck Vasectomy is an immunoassay that provides qualitative detection of sperm counts above 250,000 sperm/mL

Accepted for publication July 2020

Address correspondence to Dr. James Trussler, Lahey Hospital and Medical Center, Institute of Urology, 41 Mall Road, Burlington, MA 01805 USA

with a negative predictive value of 98%.[5] Home testing would ideally remove the obstacles of inconvenience and embarrassment that prevent the majority of non-compliant patients from providing PVSA specimens.[6,7] The procedure for use of this kit is relatively simple, wherein a semen sample is left to liquefy in a collection container for 20 minutes, subsequently introduced to solution and placed in a sample well on the device. After 7 minutes a positive or negative result is produced and available for interpretation.

Home-based PVSA testing is still relatively new and it has not been widely accepted by the urologic community, however it is gaining more attention.[8] The AUA guideline panel found insufficient data to provide any recommendation for or against its use.[2] To better understand the role home-based sperm testing in post-vasectomy patients, this study was designed to evaluate the compliance rate of SpermCheck Vasectomy compared with traditional laboratory testing to confirm azoospermia.

Materials and methods

We conducted a retrospective chart review of patients who underwent vasectomy by one of three surgeons between May 2017 and November 2018. Patients were excluded if they had undergone prior vasectomy or vasectomy reversal, or if they were planned to undergo concomitant procedures. All vasectomies were performed in accordance with AUA 2015 guideline statements 1-10[2] and were performed in a similar fashion. Following vasectomy, two surgeons prescribed laboratory-based PVSA testing (Group 1) while the third surgeon prescribed a home-based sperm antigen test, SpermCheck Vasectomy (Group 2). Patients prescribed a home-based sperm antigen test were instructed to communicate their results directly to the office. If no results were communicated within 12 weeks of the procedure, the patient was sent a letter as a reminder, with a second letter sent if there were still no results communicated. All patients in Group 2 were offered a choice of laboratory-based or home-based PVSA testing, but all patients opted for home-based testing.

Compliance was primarily assessed by completion of at least one PVSA in accordance with AUA guideline statement 12.[2] For patients in Group 1, vasectomy failure was defined in two ways. A true failure was defined as the presence of > 100,000 NMS without a follow up PVSA demonstrating < 100,000 NMS. This represents the proportion of men who may require either further PVSA testing or repeat vasectomy. Additionally, the proportion of patients failing to achieve azoospermia in any number of tests represented the positive test rate, or failure by strict criteria. For Group 2 failure was defined as any positive test without a subsequent negative test. Absolute risk of undetected vasectomy failure was calculated post-hoc by decision analysis methodology.

Results

A total of 226 vasectomies were identified at our institution during the specified time period. Group 1 included 141 procedures while Group 2 included 85. The two groups were similar with respect to age (39.45 years versus 40.01 years, p = .520), prior paternity (95.7% versus 92.9%, p = .374), and number of children fathered (2.30 versus 2.39, p = .565).

A total of 158 patients (69.9%) completed at least one PVSA. Ninety-three patients in Group 1 were compliant compared to 65 in Group 2 (65.96% versus 76.47%, p = 0.095). Patients in Group 1 who had an initial positive PVSA demonstrated a 73.53% compliance with repeat PVSA testing, similar to those in Group 2 who completed a second home-based test (78.46%, p = 0.581). In Group 2, all patients received an initial letter regarding performance of the home-based test. Reminder letters were sent to 28 patients in Group 2, however only 1 non-compliant patient (1.18%) became compliant after receiving a reminder letter. Thirty-three patients in Group 1 had a follow up visit with their surgeon after vasectomy, and compliance among these patients was similar to those who did not have a follow up visit (69.70% versus 64.81%, p = 0.604), suggesting that a follow up appointment does not materially affect compliance. There were 55.5% of PVSA tests among both groups performed within the AUA recommended 8-16 week period. In Group 1, 8.4% were performed prior to 8 weeks while 32.5% were performed later than 16 weeks. In Group 2, 11.3% had tests performed only prior to 8 weeks, while 2.1% had tests performed only after 16 weeks. The proportion of tests performed prior to 8 weeks was similar between groups (p = .622).

The proportion vasectomy failures was similar between Group 1 and Group 2 (7.09% versus 4.71%, p = .577). However the rate of positive tests was higher in Group 1 compared to Group 2 (14.18% versus 4.71%, p = .026). The pooled failure rate was 6.19% while the pooled positive test rate was 10.62%. The number of sperm present in each positive PVSA test and serial tests is shown in Figure 1.

The estimated risk of undetected vasectomy failure is shown in Tables 1 and 2. We utilized the following assumptions in our calculations: light microscopy

TABLE 1. **Parameters used for estimating the risk of undetected vasectomy failure. The compliance rates used for calculations were extracted from our dataset. The positive test rate represents any man failing to achieve azoospermia in Group 1 or any positive test in Group 2. The false negative risk for Group 1 is based on the estimate for late recanalization of 1/2000 procedures. The false negative risk for Group 2 is based on the SpermCheck Vasectomy data submitted to the FDA.**

	Compliance rate		Positive test rate		Risk of undetected failure	
Group 1		65.96%		14.18%		
	Single test	18.16%	< 100,000 NMS	7.09%	Single test	0.05%
	Serial tests	47.80%	> 100,000 NMS	7.09%	Serial tests	0.000025%
Group 2		76.47%		4.71%		
	Single test	16.47%	< 100,000 NMS	**	Single test	2.08%
	Serial tests	60.00%	> 100,000 NMS	**	Serial tests	0.09%
Pooled risk				10.62%		
			< 100,000 NMS	n/a		
			> 100,000 NMS	6.19%		

**not able to be measured for this group; NMS = non motile sperm

based PVSA is the gold standard test; the risk of late recanalization is approximately 0.05%; the false negative rate of the SpermCheck Vasectomy test is 2.08%. Various failure risk parameters were used to estimate the absolute risk of vasectomy failure in each group, as detailed in Tables 1 and 2. A schematic example of the method for calculation in shown in Figure 2.

TABLE 2. **Risk estimation for Group 1 and Group 2 under various circumstances and parameters. A schematic for a sample calculation of Absolute Risk Estimation is seen in Figure 2. The observed risk column represents what was observed in our study population. The pooled risk of any positive test represents those patients who may require further testing, but not necessarily those who require further procedures. The relative risk reduction compares estimated risk in Group 2 compared to Group 1. NNT = number needed to treat**

	Measured risk	Pooled risk excluding special criteria	Pooled chance of any positive test	Lowest measured failure rate
Group 1				
Failure rate	7.09%	6.19%	10.62%	4.71%
Single test	2.45%	2.14%	3.65%	1.64%
Serial tests	2.42%	2.12%	3.62%	1.61%
Group 2				
Failure rate	4.71%	6.19%	10.62%	4.71%
Single test	2.70%	3.05%	4.09%	2.70%
Serial tests	1.51%	1.86%	2.90%	1.51%
Absolute risk reduction				
Single test	-0.25%	-0.91%	-0.44%	-1.06%
Serial tests	0.92%	0.26%	0.73%	0.11%
NNT				
Single test	-396	-111	-227	-95
Serial tests	110	384	138	953
Relative risk reduction				
Single test	-10.34%	-42.38%	-12.09%	-64.98%
Serial tests	37.80%	12.33%	20.06%	6.52%

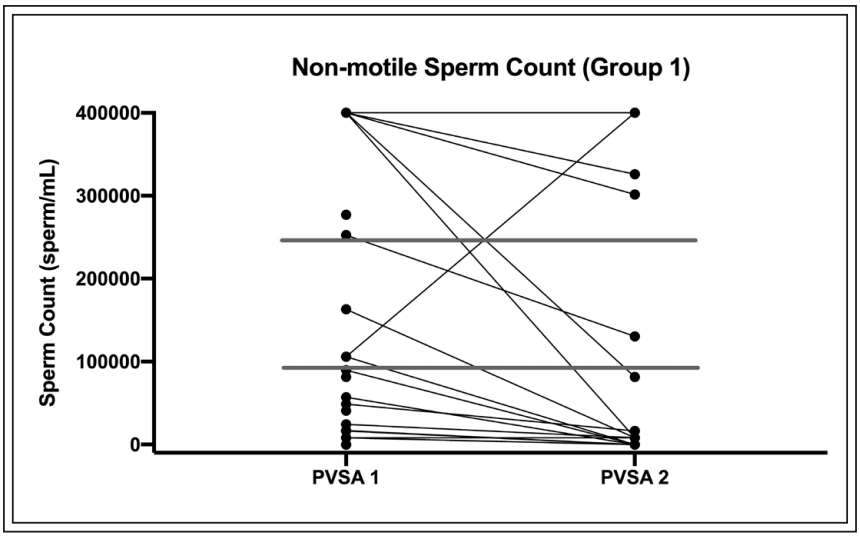

Figure 1. Quantitative measure of non-motile sperm present in each PVSA sample among compliant patients in Group 1. The upper bound represents a sperm count of 250,000 sperm/mL, the cut off of detection for the home-based test. The lower bound represents a sperm count of 100,000 sperm/mL, the suggested limit for special clearance among men who do not achieve azoospermia after vasectomy. PVSA = post vasectomy semen analysis.

When utilizing a single home-based test for PVSA clearance, the absolute risk of vasectomy failure favors Group 1. Given that the home-based test kit provides a second test, when utilizing two serial home-based tests, the risk of undetected vasectomy failure favors Group 2 across all measured risk parameters, as demonstrated in Table 1. The maximal risk reduction favoring serial home-based PVSA testing occurred in the case of a higher measured failure rate in Group 1, which was likely driven primarily by the lower sensitivity of the home-based test. However, when evaluating the estimated risk using the lowest measured failure rate of 4.71% applied to both groups, serial testing continued to favor Group 2, driven primarily by the higher rate of compliance. Using the compliance rates measured in our study, the point of equivalent risk between each group occurs at a failure rate of approximately 3.7%.

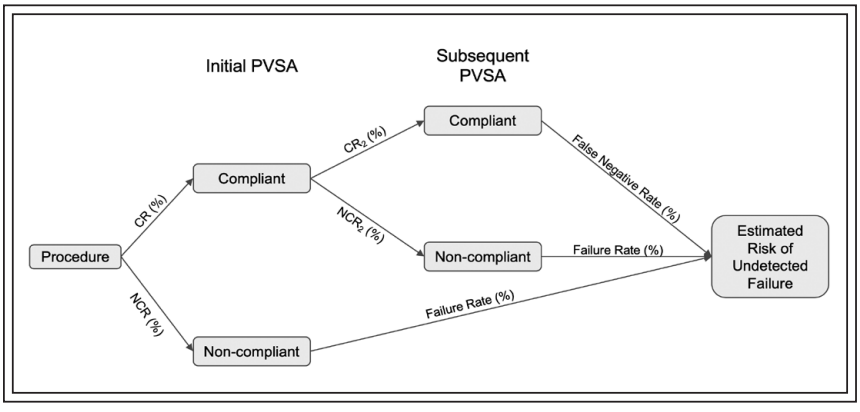

Figure 2. Sample schematic representation of the estimated risk calculation. CR = compliance rate; NCR = non-compliance rate; PVSA = post vasectomy semen analysis. Subscript 2 indicates rates with respect to subsequent testing.

Discussion

Vasectomy is a highly reliable option for long term contraception, but rare procedural failures do occur, underscoring the importance of PVSA. Despite this fact, compliance with traditional laboratory-based PVSA is remarkably low, prompting the development of home-based semen analysis assays. This study is the first comparison of PVSA compliance between lab-based and home-based options.

Our observed compliance rate for the office-based PVSA group is similar to prior publications,[3,4] and although statistically similar, our home-based testing group showed greater than 10% increased compliance. There are several explanations for this reduction in impediment including increased convenience and reduced stigma.[6,7] This is supported by recent findings suggesting the time commitment necessary to complete laboratory based PVSA testing are a major factor towards non-complicance.[8] Other factors which may negatively influence compliance with home-based testing include the cost of purchase, which is variable between available tests. For the SpermCheck Vasectomy kit used in this study, the out of pocket cost is typically between $40-$60 for two tests. Furthermore, increased compliance and the use of serial home-based tests improved the risk profile of undetected failures after vasectomy, theoretically reducing this risk by between 6% and 38% compared to traditional testing. Confounding factors that limit the applicability of

this finding include differences in follow up contact regimens between the two groups, the inability to control for PVSA testing occurring outside of our system, and the fundamental differences in testing parameters between the SpermCheck Vasectomy assay and traditional light microscopy. Furthermore, it must be noted that risk estimations are made by extrapolation from retrospective data. Although the conclusion holds true across a variety of risk and failure parameters, it must be verified prospectively in the future. Lastly, the assigned risk values utilized in our estimations reflect a variety of conditions including true failures requiring reoperation, patients who would meet special clearance parameters, and patient who may require further testing. In spite of these differences, the home-based PVSA regimen shows promise in potentially reducing undetected vasectomy failures.

Improving PVSA compliance is a notable goal, but the ultimate goal for PVSA testing is to avoid unintentional pregnancy. A notable shortcoming of the SpermCheck Vasectomy assay is the inability to detect motile sperm, and motility has proven to be a major factor with regards to fertility. Furthermore, while surrogate data from studies of fertility and contraception have shown very low rates of fertility with sperm counts between 100,000 and 1,000,000 sperm/mL, the test limit of detection (250,000 sperm/mL) is above the recommended threshold of sterility in the current AUA Guidelines.[9] Not all risk accrued by a positive test is attributable to fertility and may not necessarily result in an unintended pregnancy. Although the risk of retained fertility may be higher in the home testing group due to the elevated limit of detection, a portion of that risk attributable to the detection gap would actually not result in unintended pregnancy. As the market for home-based testing grows, comparison of fertility rates at different PVSA thresholds will be important to confirm that improving compliance goes hand-in-hand with decreasing undesired pregnancy.

A primary limitation of this study is the retrospective nature and therefore lack of ability to randomize patients between testing groups. Results in such a setting must be interpreted through that lens. An additional limitation is the possibility that different follow-up protocols between surgeons could influence compliance rates. Patients completing home-based testing received reminder letters to complete a PVSA if they had not reported results within 12 weeks. Our findings showed that only one patient in our dataset completed a PVSA test after receiving a reminder letter, suggesting this may not be a major influence. Written materials given to patients after their procedure logically would influence compliance, but no studies to date have shown an impact of late postoperative contact on compliance. Furthermore, 23% of patients in Group 1 had follow up contact with their providers, and among those patients compliance was similar to those who did not have follow up contact. Nevertheless, differences in the follow up regimen between our two groups could be a confounding factor. The small sample size is another limitation that could prevent us from finding statistical significance between the two groups.

Home-based assays have not been widely accepted in part due to higher false negative rates. The SpermCheck Vasectomy test reports a negative predictive value of 98% compared with the 99.95% rate for laboratory testing. Serial tests theoretically improve the negative predictive value, but this also comes with another opportunity for lack of compliance as well as increased costs. In spite of this, our data demonstrates that utilization of two serial home-based tests reduces the theoretical risk of an undetected vasectomy failure.

There is still considerable research to be done before the role for home-based kits is established, whether for PVSA, infertility, or other assessments of sperm quality and quantity. Another home-based assay is the YO sperm test kit, which employs a smartphone camera platform. The device was FDA approved in 2016 for qualitative assessment of sperm motility, reporting motile sperm above and below a 6M/mL threshold. Again, this home-test lacks the precision of laboratory testing, but it demonstrates that motility can be assessed and future products may achieve the same accuracy achieved with traditional microscopes. Broader validation with larger patient cohorts and multi-institutional collaboration would help verify our results and we should continue to assess and validate the role for new home-based semen analysis technologies as they develop.

This is the first study to our knowledge comparing laboratory-based and home-based tests to assess the PVSA compliance rates. In our retrospective review, although not statistically significant, we did observe an increase in compliance with PVSA testing when patients were offered the opportunity to perform the testing at home. Despite a lower sensitivity and specificity compared to traditional PVSA testing, industry will likely continue efforts to improve these parameters to bring them more in line with what is a clinically acceptable testing methodology. As more and better tests become available, the urology community may have the opportunity to improve patients' convenience, experience, and compliance with this important test.

Conclusion

PVSA testing is key to confirming the success of vasectomy and reducing the risk of unintended pregnancy. Utilization of a home-based PVSA test may reduce the risk of undetected vasectomy failure by improving compliance. In the future, development of home-based tests with improved sensitivity and specificity profiles may lead to a more prominent role of home-based PVSA testing. Further prospective study will be required to better elucidate and define any difference in compliance rates between home and laboratory based testing assays. □

References

1. Eisenberg ML, Lipshultz LI. Estimating the number of vasectomies performed annually in the United States: data from the National Survey of Family Growth. *J Urol* 2010;184(5): 2068-2072.
2. Sharlip ID, Belker AM, Honig S et al. Vasectomy: AUA guideline. *J Urol* 2012;188(6 Suppl):2482-2491.
3. Bieniek JM, Fleming TB, Clark JY. Reduced postvasectomy semen analysis testing with the implementation of special clearance parameters. *Urology* 2015;86(3):445-449.
4. Duplisea J, Whelan T. Compliance with semen analysis. *J Urol* 2013;189(6):2248-2251.
5. Klotz KL, Coppola MA, Labrecque M et al. Clinical and consumer trial performance of a sensitive immunodiagnostic home test that qualitatively detects low concentrations of sperm following vasectomy. *J Urol* 2008;180(6):2569-2576.
6. Smucker DR, Mayhew HE, Nordlund DJ, Hahn WK, Palmer KE. Postvasectomy semen analysis: why patients don't follow-up. *J Am Board Fam Pract* 1991;4(1):5-9.
7. Lopategui DM, Antoniassi MP, Ibrahim E, Ramasamy R, Brackett NL. How long does it take a man to collect his semen specimen in a busy infertility clinic? *Transl Androl Urol* 2019;8(Suppl 1):S1-S5.
8. Bradshaw A, Ballon-landa E, Owusu R, Hsieh TC. Poor compliance with postvasectomy semen testing: analysis of factors and barriers. *Urology* 2020;136:146-151.
9. Turner L, Conway AJ, Jimenez M et al. Contraceptive efficacy of a depot progestin and androgen combination in men. *J Clin Endocrinol Metab* 2003;88(10):4659-4667.