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Vasectomy has No Impact on Future Lower Urinary Tract Symptoms Diagnoses: A Retrospective Cohort Claims Database Analysis

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Purpose: The aim of this study was to assess whether there is an association between vasectomy and benign prostatic hyperplasia with associated lower urinary tract symptoms (BPH/LUTS) due to inflammatory etiology.

Materials and Methods: We assessed the incidence of BPH/LUTS in men who had undergone vasectomy in a matched cohort analysis using the TriNetX Research Network. We identified men aged 30 to 60 years who underwent vasectomy and had a follow-up visit within 6 months to 5 years after vasectomy from January 2010 through December 2022 and compared them with matched controls. Outcomes recorded include diagnoses of BPH (N40, N40.1), BPH-related medication prescriptions, and BPH-related procedures. We accounted for confounding variables through propensity score-matching for age; race; and history of comorbid medical conditions: hyperlipidemia (International Classification of Disease-10: E78), metabolic syndrome (E88.81), overweight or obesity (E66), testicular hypofunction (E29.1), hypertension (I10-I16), nicotine dependence (F17), and obstructive sleep apnea (G47.33).

Results: There was no significant difference in BPH diagnosis between postvasectomy men vs controls (0.84% vs 0.80%, RR: 0.95, 95% CI 0.86-1.05) or BPH/LUTS diagnosis (0.48% vs 0.44%, RR: 0.92, 95% CI 0.81-1.05) within 6 months to 5 years after vasectomy, respectively. No differences in BPH medication prescription (0.94% vs 0.84%) or rate of BPH procedures (0.022% vs 0.017%) were detected between the 2 groups.

Conclusions: This study suggests that vasectomy does not increase the risk of BPH development and/or LUTS worsening compared with the general population, providing assurance to both patients and health care providers who may consider vasectomy as a safe family planning option.

Key Words: vasectomy; prostate; BPH; LUTS

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INTRODUCTION

Vasectomies are elective sterilization procedures that obstruct or remove portions of the vas deferens to prevent sperms from reaching the ejaculatory ducts.[1] The procedure is as effective as tubal ligation, but has a lower surgical risk and failure rate in comparison.[2] Although the frequency of vasectomies seems to have declined in the past decade,[3] it remains an effective, reversible, and economical outpatient sterilization procedure used by approximately 500,000 men in the United States yearly.[4,5]

Although vasectomy is a relatively safe and effective form of contraception, concerns have been raised about

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potential long-term complications, including the potential risk of prostate cancer (PCa), which remains controversial in current literature.[6] In a recent meta-analysis by Baboudjian et al, vasectomy was found to be associated with low-grade, localized PCa, similar to other previous studies.[7-9] However, Nutt et al showed in a recent study that there is lack of sufficient evidence to indicate a causal relationship between the 2, citing that many studies that do report a link may have the potential for selection bias and confounding, which may explain positive associations that were found.[6] While the exact biological mechanisms behind a potential association between vasectomy and PCa have yet to be well-established, recent studies have shown that the onset of PCa may be mediated through inflammation-induced cellular stress.[10-13] Interestingly, a recent study by Suarez Arbelaez et al found that vasectomy may alter the seminal microbiome, potentially causing dysbiosis.[14] These microbial changes may lead to systemic inflammation and cellular stress, potentially caused by changes in seminal pH, viscosity, and prostaglandin levels after vasectomy.[14-16] Moreover, inflammation has been established as a risk factor of benign prostate hyperplasia (BPH), as inflammation can lead to activation of interleukin-triggered growth pathways in the prostate.[17,18] Because there is common inflammatory pathophysiology in both PCa and BPH, vasectomy-induced inflammation from seminal microbiome alterations may be involved in the onset of BPH and associated lower urinary tract symptoms (LUTS).[14,19,20] There is currently a paucity of literature directly investigating this relationship; therefore, the aim of our study was to investigate the association between vasectomy and BPH using a large US claims database.

MATERIALS AND METHODS

Data Source and Study Design

The data used in this study were collected and analyzed in January 2023 from the TriNetX, LLC Diamond Network (Cambridge, MA), which provided access to electronic medical records (diagnoses, procedures, medications, laboratory values, genomic information), as well as medical insurance and pharmaceutical claims for approximately 212 million patients from 92 health care organizations. Data from TriNetX included information on patient demographics, diagnoses, procedures, prescriptions, and laboratory values, regardless of commercial insurance plan changes. Diagnoses were recorded using International Classification of Disease (ICD) codes, and procedures were recorded using Current Procedural Terminology (CPT) codes. Information on medications was obtained from prescriptions, orders, inpatient medication reconciliations, and charted medications and were identified in the database using the Veterans Affairs (VA) Drug classification system. The data used in this study covered the period from January 2010 through December 2022.

The process by which the data were deidentified is attested to through a formal determination by a qualified expert as defined in Section §164.514(b)(1) of the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule. Because studies using TriNetX deidentified patient records do not involve the collection, use, or transmittal of individually identifiable data, the qualified expert has determined that these studies are exempted from the need of institutional review board approval. As a result, patient counts fewer than 10 are obfuscated to secure patient anonymity. In addition, only aggregate patient counts and statistical summaries are provided to protect all patient health information and ensure deidentification.

Cohorts

To evaluate whether there is an association between vasectomy and LUTS, we constructed a cohort of adult men aged 30 to 60 years who underwent vasectomy (CPT: 55250) and had a follow-up or office visit within 5 years of vasectomy (CPT: 1013626). A control cohort (age-matched) was also created of adult men aged 30 to 60 years who did not have a recorded history of vasectomy with an index follow-up or a primary office visit with an additional office visit within 5 years of inclusion. The outcomes of interests were diagnoses of benign prostatic hypertrophy (ICD-10: N40); diagnoses of benign prostatic hypertrophy (N40.1); prescribing on BPH-related medications: finasteride (VA Class 25025), dutasteride (228790), tamsulosin (77492), terazosin (37798), doxazosin (49276), alfuzosin (17300), silodosin (720825), or 5 mg daily tadalafil (358263); or BPH-related procedures: transurethral resection of the prostate (CPT 52601), laser vaporization of the prostate (52648), laser enucleation of the prostate (52649), cystourethroscopy with insertion of prostatic lift (52441), or transurethral destruction of prostate tissue by radiofrequency-generated water vapor thermotherapy (53854). We assessed the incidence of the above outcomes 6 months to 5 years after vasectomy or inclusion for both cohorts (Figure 1).

Statistical Analysis

Data were reported as mean and SD. Baseline characteristics before propensity score-matching were compared using the t test and chi-square test. We then used propensity score-matching—a statistical technique that uses logistic regression to build cohorts of equal sizes based on covariates of interest. We used 1:1 greedy nearest-neighbor propensity score-matching to control for confounding variables through the TriNetX platform. In this analysis, we controlled for age at index, current age, race/ethnicity, hyperlipidemia (ICD-10: E78), metabolic syndrome (E88.81), overweight or obesity (E66), testicular hypofunction (E29.1), hypertension (I10-I16), nicotine dependence (F17), and obstructive sleep apnea (G47.33). Statistical analysis was performed using Python and R software built into the TriNetX platform. We determined that the 2 groups had minimal differences after balancing because the standardized differences between propensity scores were less than 0.1.

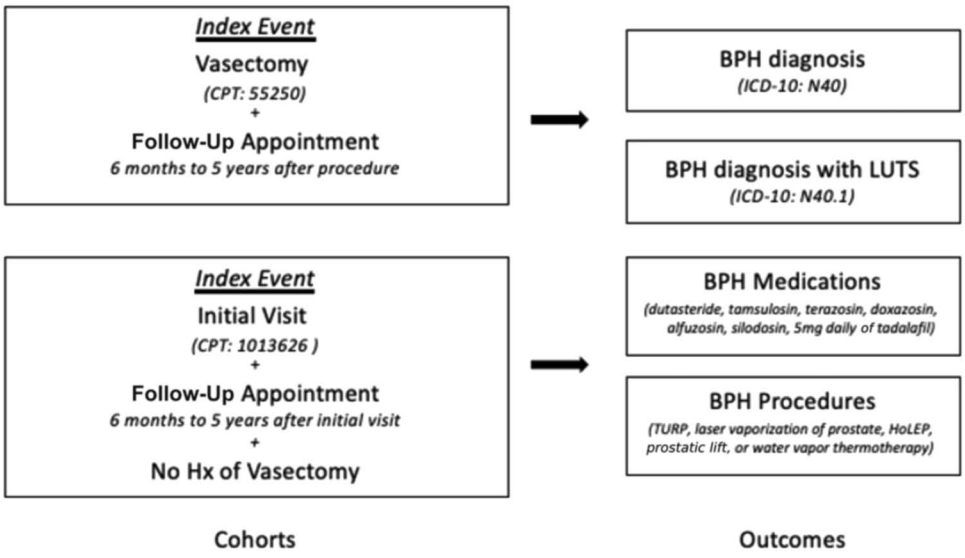

Figure 1. Sample criteria and outcomes.

RESULTS

Before matching, we identified a total of 162,153 men who underwent vasectomy and had follow-up 1 to 5 years after and 6,094,147 control men. After matching, we identified 101,186 men in each group with an average age of 45.6 ± 6.1 (SD) years in men undergoing vasectomy and 44.8 ± 6.5 years in controls (Table 1).

When comparing the rate of BPH with that of unspecified LUTS, 0.84% men undergoing vasectomy had a BPH diagnosis between 6 months and 5 years after vasectomy while 0.80% of controls who never had a vasectomy received a diagnosis in 6 months to 5 years of follow-up (Relative risk (RR): 0.95, 95% CI 0.86-1.05). When assessing diagnoses of BPH with LUTS, 0.48% of men undergoing vasectomy received this diagnosis in follow-up compared with 0.44% of control men (RR: 0.92, 95% CI 0.81-1.05). There was no difference in the prescribing of BPH medications, with 0.94% of postvasectomy men receiving a prescription compared with 0.84% of control men within 5 years. Finally, there was no difference in the rate of BPH procedures with 0.022% of men with a history of vasectomy undergoing a surgical procedure compared with 0.017% of men who never underwent a vasectomy in 6 months to 5 years of follow-up.

DISCUSSION

Vasectomies are simple, outpatient surgeries undergone by approximately 10% of couples in the United States who use contraception.[21] Currently, there are no fully substantiated risks associated with undergoing a vasectomy; however, increased risk of PCa after vasectomy has been a topic of controversy in current literature.[7-9] In a recent meta-analysis, Cheng et al[9] showed that vasectomy

Table 1. *Baseline and Post-matching Cohort Characteristics*

	Before matching			After matching		
	Men with Hx of vasectomy	Men w/o vasectomy	*P*-value	Men with Hx of vasectomy	Men w/o vasectomy	*P*-value
Current age	46.3 ± 6.1	47.6 ± 8.9	<0.0001	45.6 ± 6.1	44.8 ± 6.5	<0.0001
Age at index	40.2 ± 5.9	42.8 ± 8.8	<0.0001	40.6 ± 6.0	39.9 ± 6.6	<0.0001
Race/ethnicity						
Unknown race	72.71%	76.41%	<0.0001	72.54%	69.81%	<0.0001
White	25.44%	20.27%	<0.0001	25.41%	28.17%	<0.0001
Black or African American	1.53%	2.81%	<0.0001	1.71%	1.54%	0.002
Unknown Ethnicity	70.07%	74.16%	<0.0001	69.61%	66.22%	<0.0001
Not Hispanic or Latino	27.63%	23.07%	<0.0001	28.02%	31.16%	<0.0001
Comorbidities						
Hyperlipidemia	23.70%	38.64%	<0.0001	26.61%	23.38%	<0.0001
Hypertension	18.75%	37.80%	<0.0001	22.63%	18.58%	<0.0001
Overweight and obesity	13.71%	23.31%	<0.0001	17.18%	16.83%	0.04
Sleep disorders	15.05%	22.73%	<0.0001	17.85%	16.34%	<0.0001
Nicotine dependence	9.90%	20.48%	<0.0001	11.99%	10.10%	<0.0001
Testicular hypofunction	5.68%	6.72%	<0.0001	6.12%	6.71%	<0.0001
Metabolic syndrome	0.46%	0.89%	<0.0001	0.56%	0.62%	0.05

is associated with a 9% higher risk of PCa. However, another study by Bhindi et al showed that although vasectomy may be associated with a slightly higher risk of overall PCa, there was no association with increased risk of high-grade, advanced, or fatal PCa, similar to the results of the aforementioned study by Baboudjian et al.[7,22] While there are mixed results in the literature, the overall clinical impression is that any potential correlation between vasectomy and PCa is weak and without established biological explanation and that vasectomy is considered a safe contraceptive option.[22-24] Contradictions about PCa as a potential risk of vasectomy may be because of detection bias because men who undergo vasectomies are more likely to have a urologist who screens for prostate cancer. This same selection bias can apply to the diagnosis of BPH after vasectomy. While vasectomies are still commonplace and safe procedures that allow for effective family planning, relative uncertainty about PCa association highlights the need for further research.

The premise for the present study stems from a recent pilot study by Suarez Arbelaez et al,[14] in which a decreasing trend for α-diversity and changes in the relative abundance of bacterial flora was observed in the semen microbiome after vasectomy, potentially leading to dysbiosis and subsequent systemic inflammation. Inflammation has been discussed to play a role in prostate carcinogenesis through genome damage and consequent cell proliferation.[10-13] Similarly, dysbiosis-induced inflammation after vasectomy may also be a risk factor of BPH/LUTS, as prior studies have indicated the role of seminal dysbiosis in increasing BPH/LUTS in older men, who exhibit a decreased total number of bacteria in the distal urethra with age.[25-28] Because inflammatory processes are common to the etiology of both PCa and BPH, the question of whether vasectomy is directly associated with an increased risk of BPH/LUTS was raised. The relationship between vasectomy and risk of BPH/LUTS, to our best knowledge, has not been directly explored before.

In this article, we have investigated the association between vasectomies and BPH/LUTS using TriNetX. This study looked at a cohort of 101,186 men who underwent vasectomy along with a matched control group of those with no recorded history of vasectomy. The results show that there is no significant difference after 6 months to 5 years of follow-up in the diagnosis of BPH, of BPH/LUTS, of BPH medication prescriptions, or of BPH procedures. These time points were chosen to avoid effects of immediate postoperative complications of vasectomy and to assess long-term follow-up while limiting the effect of age as an additional risk factor of BPH/LUTS. Taken together, these results imply there is no increased risk of BPH/LUTS after vasectomy, despite a potential biological hypothesis based on inflammation caused by an altered seminal microbiome.

While this article shows a lack of association between vasectomies and BPH/LUTS, there exists controversy in existing literature about the association between vasectomies and other complications that act to increase the complexity behind a patient's decision to pursue this sterilization procedure. The choice to pursue a vasectomy involves thorough patient-provider decision making weighing the benefits and potential risks.[29] Our findings add to the ongoing conversation surrounding potential complications of undergoing vasectomy. With the data from this study, health care providers can confidently inform their male patients that vasectomy is not associated with an increased risk of BPH/LUTS during discussion of family planning options. This knowledge can provide peace of mind about quality of life after the procedure because BPH/LUTS has been shown to be associated with increased anxiety and depression.[30]

One of the major strengths of our study is the number of patients we were able to compare. This is the first study to our knowledge that compares the incidence of BPH/LUTS after vasectomy. With over 200,000 men in our analysis, we were able to have adequate power for our primary outcome. One of the major limitations of our study is that because of using an anonymized database, we lost the ability to investigate individual patient factors in the analysis and do not have symptom scores to pair with diagnoses. Without this individual patient data, we are unable to perform regression analysis and treat symptom scores as a continuous variable. Instead, we relied on the incidence of diagnoses, prescriptions, and procedures. Future directions include long-term follow-up studies, including collecting patient symptom scores, to uncover any relationships between vasectomies and other urological complications. In addition, further research is needed to explore the potential link between vasectomy and inflammation-inducing changes in the seminal microbiome and its possible clinical implications.

CONCLUSIONS

Vasectomies are a commonplace and highly effective method of reversible surgical sterilization for men. Vasectomies are not associated with an increased risk of BPH/LUTS after 5 years of follow-up, as determined by this retrospective cohort claims database analysis. The results of this study provide

assurance to patients and health care providers who may consider vasectomy as a family planning option.

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DISCLOSURES
None.

DECLARATIONS OF INTEREST
None.

ATTESTATION STATEMENT
Data regarding any of the subjects in the study has not been previously published.

Available data will be made available to the editors of the journal for review or query on request.

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