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Vasectomy and prostate cancer risk: a pooled of cohort studies and Mendelian randomization analysis

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Abstract

Background The relationship between vasectomy and the risk of prostate cancer (PCa) remains unclear, with observational studies reporting inconsistent results. To clarify this ambiguity, we embarked on a comprehensive investigation comprising both a meta-analysis and a Mendelian randomization (MR) study. This dual approach aimed to thoroughly examine not only the association but also the causality between undergoing a vasectomy and the subsequent risk of PCa.

Methods Our systematic review meticulously examined cohort studies published until January 2024, employing a random effects model for the computation of relative risks (RR) and their 95% confidence intervals (CI). For MR Analysis, we leveraged aggregated data from the IEU Open GWAS database, investigating the correlation between genetic predisposition to vasectomy and PCa. We chose single nucleotide polymorphisms (SNPs) of European descent as instrumental variables (IVs) for this analysis. The primary method for calculating the odds ratios (ORs) and their 95% CIs was inverse variance weighting (IVW). Through sensitivity analysis, we confirmed the robustness of our findings.

Results Our investigation synthesized data from 19 cohort studies, encompassing over four million participants. The combined analysis revealed a statistically significant link between vasectomy and an elevated risk of PCa across any grade (RR = 1.09; 95%CI: 1.05–1.14; $P = 0.001$; $I^2 = 83.3\%$). This association was observed for both localized PCa (RR = 1.08; 95% CI: 1.04–1.13; $P < 0.001$; $I^2 = 48.8\%$) and advanced PCa (RR = 1.07; 95% CI: 1.01–1.13; $P = 0.016$; $I^2 = 0\%$). Nonetheless, the discovery cohort MR Analysis indicated no genetic causal link between vasectomy and PCa (OR = 0.067; 95%CI = 0.002–1.535; $P = 0.09$). A validation set in the Finnish population confirmed the robustness of the results. This conclusion remained consistent even after controlling for variables such as prostate-specific antigen (PSA) testing and body mass index (BMI), suggesting that while a statistical association exists, the genetic evidence does not support a causal relationship.

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Conclusion The cumulative analysis indicates a possible elevated risk of PCa in patients who have had a vasectomy. However, MR Analysis has not confirmed a direct causal link between vasectomy and PCa. This suggests that the association observed may not stem from direct causation, allowing for the continued consideration of vasectomy as a viable long-term contraceptive choice. Further research is imperative to uncover any factors that could potentially link vasectomy to an increased risk of prostate cancer, aiming to provide a more comprehensive understanding of the implications.

Keywords Vasectomy, Prostate cancer, Mendelian randomization, Risk, Cohort

Introduction

Vasectomy is a widely used and efficient long-term contraceptive method, often performed as an outpatient procedure under local anesthesia in developed countries. Compared to tubal ligation (a similar sterilization procedure for women), it is less expensive and associated with fewer complications [1]. It is estimated that approximately 33 million men globally rely on vasectomy for contraception [2]. Vasectomy has been debated for its potential long-term biochemical and physiological effects on the male reproductive system. While its efficacy in contraception is well-established, emerging studies highlight divergent findings regarding its impact on prostate health, fertility parameters, and hormonal regulation. Specifically, biochemical markers such as prostate-specific antigen (PSA), sperm characteristics, and testosterone levels have been proposed as critical indicators to evaluate the systemic consequences of vasectomy. Existing research on PSA levels post-vasectomy remains controversial. Some studies suggest elevated PSA in vasectomized men, potentially linked to prostate inflammation or altered fluid dynamics, while others report no significant difference compared to non-vasectomized controls [3, 4]. Similarly, sperm characteristics—such as reduced motility, abnormal morphology, or residual sperm granulomas—may reflect adaptive changes in spermatogenesis after vas deferens obstruction, though long-term equilibrium between sperm production and degradation has been observed [4, 5]. Furthermore, the hormonal axis, particularly testosterone secretion, is a focal point of debate. Although vasectomy theoretically disrupts sperm transport, current evidence suggests no substantial alteration in testosterone levels, implying preserved Leydig cell function despite potential testicular pressure changes [3, 4].

Prostate cancer (PCa), the second most common malignant tumor among men, ranks as the fifth leading cause of cancer death worldwide. In 2020, nearly 1.4 million new cases of PCa were diagnosed globally, accounting for 7.3% of all cancer cases and resulting in about 375,000 deaths [6]. Male reproductive factors are thought to influence the risk of PCa in later life, as cohort studies have shown significant statistical associations between lower ejaculation frequency, sperm quality, and fewer offspring with an increased risk of subsequent PCa [7–9]. However, epidemiological studies investigating the relationship between vasectomy and PCa risk present conflicting viewpoints [10–12]. These discrepancies are mainly due to the lack of clear causal evidence and more frequent follow-up for prostate-specific antigen (PSA) screening among patients who undergo vasectomy. Screening behavior could introduce significant confounding factors, as men who regularly undergo screenings tend to adopt a range of healthier behaviors. While screening is closely associated with an increased likelihood of PCa diagnosis, over time, it may also reduce the risk of fatal disease.

Given the inherent biases, confounding factors, and reverse causality challenges inevitable in traditional epidemiological studies, investigating the causal relationship between vasectomy and PCa over their relatively long development duration through randomized controlled trials (RCTs) would be logical. Mendelian randomization (MR), a novel epidemiological approach, offers a method akin to RCTs [13]. Furthermore, MR leverages Mendel's second law, using single-nucleotide polymorphisms (SNPs) as instrumental variables (IVs) to eliminate the effects of confounders. Considering the publication of numerous large-scale, high-quality cohort studies, incorporating these studies into the aforementioned meta-analyses would increase the sample size, enhance the accuracy of effect size estimates, and potentially influence outcomes. Cohort studies help mitigate selection bias and recall bias. Therefore, compared to the previous meta-analysis, we conducted a comprehensive systematic review and meta-analysis based on the most extensive and up-to-date evidence, ultimately assessing the potential causal link between vasectomy and PCa risk through MR analysis.

Methods

Meta-analysis

This study adheres to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines (Table S1) and has been registered with PROSPERO (CRD42024513423) [14].

Search strategy, inclusion, and exclusion criteria

We conducted a thorough literature review, sourcing publications from databases including MEDLINE (via

the Cochrane Library), PubMed, Web of Science, Scopus, and Google Scholar, covering literature up to January 1, 2024. This review was guided by the structured PICOS framework, focusing on: P (patients) - Men without a PCa diagnosis; I (intervention) - Vasectomy; C (comparator) - non-vasectomized men; O (outcomes) - Subsequent diagnosis of PCa; S (study type) - prospective and retrospective cohort studies. The search strategy involved a careful selection of terms, merging medical subject headings with key terms: (vasectomy OR deferentectomy OR vasoligation) AND (prostate cancer OR prostate carcinomas OR prostate neoplasm). Inclusion criteria required that studies report risk measures such as odds ratio (OR), relative risk (RR), hazard ratio (HR), or standardized incidence ratio (SIR), along with their 95% confidence intervals (CIs), and that the studies present original research published in English. Exclusion criteria eliminated single-arm studies, those devoid of meta-analysis data, and documents categorized as reviews, letters, case reports, or conference proceedings. When encountering overlapping study populations, priority was given to the most recent or comprehensive reports.

Data acquisition and quality evaluation

Researchers WL and SY employed EndNote X9 for the initial screening, efficiently eliminating duplicate records. They then rigorously reviewed titles and full texts for detailed evaluation. Essential data were systematically organized into an Excel spreadsheet, capturing critical information including the first author's name, publication year, study locale, follow-up duration, number of participants, and effect estimates with 95% CIs for the vasectomy-PCa link. Additional details encompassed PSA screening practices, PCa detection methods, tumor characteristics, and significant confounders. The study was primarily focused on the detection of any PCa cases, with a secondary emphasis on classifying these cases by disease stage. This classification included localized PCa, high-grade localized PCa, advanced PCa, and fatal PCa instances.

To evaluate the quality of the studies, the Newcastle-Ottawa Scale was applied to cohort studies, assigning scores ranging from 0 to 9 [15]. Studies were then classified based on their average quality score into low-medium quality (score < 7) and high quality (score ≥ 7) categories. The level of evidence (LOE) was assessed according to the Oxford Centre for Evidence-Based Medicine's guidelines [16]. Any discrepancies were settled through discussion.

Mendelian randomization

This study strictly followed the Strengthening the Reporting of Observational Studies in Epidemiology Mendelian Randomization (STROBE-MR) guidelines [17](Table S2). MR is predicated on three essential assumptions: IVs must be strongly associated with vasectomy, devoid of confounding variables, and should affect PCa exclusively through the examined exposure. Figure 1 delineates these core assumptions and outlines the MR study design. Given the study's reliance on publicly accessible aggregated data, it was exempt from the need for ethical approval.

Data source and SNP selection

The study utilized summary data from the IEU open GWAS project, with details provided in Table 1. To establish a stable causal link between exposure and outcome, we applied specific criteria for selecting IVs. To establish a threshold for genome-wide significance in vasectomy studies, a p-value of less than 5×10^{-6} is set. Additionally, cluster analysis is utilized to manage the linkage disequilibrium (LD) among IVs, applying criteria such as an r^2 value below 0.001 and a kb distance of 10,000. Only SNPs exhibiting a minor allele frequency (MAF) greater than

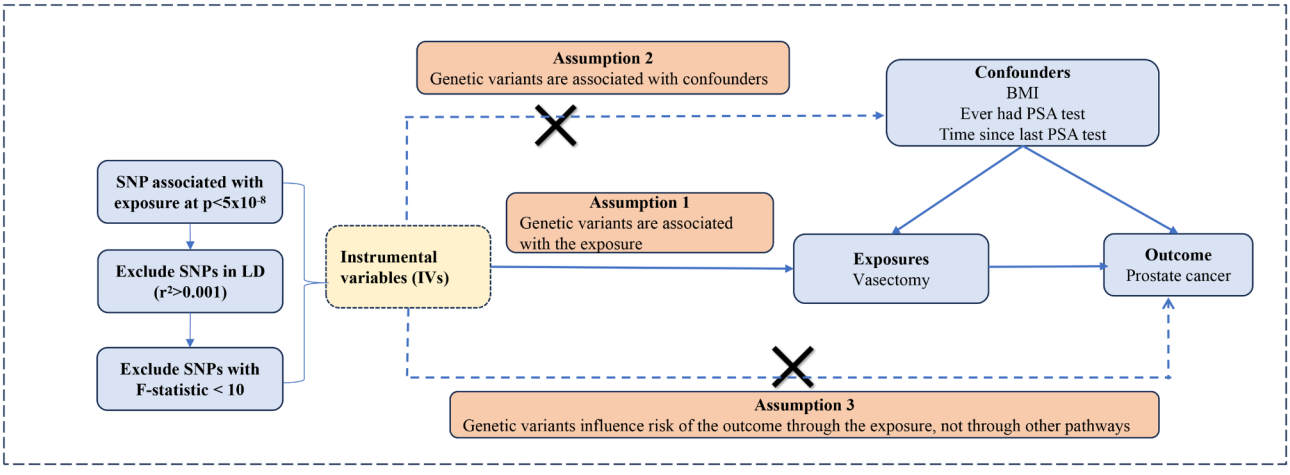

Fig. 1 The three main assumptions of Mendelian randomization

Table 1 Characteristics of the included GWAS summary studies in Mendelian randomization

Trait	Author	Consortium	Population	Sample size	Number of (cases/controls)	Year	GWAS ID/ Data address
Vasectomy	Ben Elsworth	MRC-IEU	European	462,993	11,330/ 451,603	2018	ukb-b-10,167
Prostate cancer	Schumacher	PRACTICAL	European	140,254	79,148/ 61,106	2018	ieu-b-85
Prostate cancer	NA	FinnGen	European	170,7039	6,311/ 88,902	2021	finn-b-C3_PROSTATE
BMI	Locke AE	GIANT	European	681,275	NA	2018	ieu-a-785
Ever had PSA test	Ben Elsworth	MRC-IEU	European	200,410	62,489/ 137,921	2018	ukb-b-15,695
Time since last PSA test	Ben Elsworth	MRC-IEU	European	46,104	NA	2018	ukb-b-6515

GWASs genome-wide association studies, *BMI* body mass index; *PSA* prostate specific antigen. *PRACTICAL* Prostate Cancer Association Group to Investigate Cancer Associated Alterations in the Genome, *GIANT* genetic investigation of anthropometric traits consortium, *MRC-IEU* MRC Integrative Epidemiology Unit, *NA* not available

0.01 are considered. Furthermore, the robustness of IVs is evaluated based on their F-value, calculated as the square of the beta coefficient (β^2) divided by the standard error (SE), with IVs presenting an F-value lower than 10 being excluded to mitigate the influence of weak instrumental variables [18]. In this context, β denotes the magnitude of the exposure effect, while SE refers to the standard error, enhancing the precision of the analysis. Additionally, The LDlink online tool was employed to identify potential confounders like body mass index (BMI) and PSA test.

Statistical analysis

Given the relatively low incidence of prostate cancer overall, the estimated relative risk (RR) figures across the four types of measurements displayed consistency. Our analysis synthesizes these findings with those from earlier meta-analyses, employing RR values for presentation [19, 20]. Acknowledging considerable variance among the studies ($P<0.05$, $I^2>50\%$), we opted for random effects models to compute pooled effect sizes. In contrast, where studies exhibited minimal variance ($P>0.05$, $I^2<50\%$), fixed-effects models were utilized. Publication bias was evaluated using Egger's test and funnel plots, ensuring comprehensive assessment. Sensitivity analyses were methodically performed by excluding studies one at a time, affirming the robustness of our results. Moreover, subgroup analyses were conducted with a focus on variables such as study location, risk of bias, duration of follow-up, and year of publication. All meta-analyses, executed using Stata 16.0, established significance at $p<0.05$.

While, in MR analysis, we utilized the inverse-variance weighted (IVW) method, acclaimed for its statistical rigor [18]. To ensure the validity of genetic variation as an IV, we incorporated additional validation methods, including the weighted median, MR-Egger regression, maximum likelihood estimation, and the simple mode [21, 22]. The initial step in our sensitivity analysis, crucial for detecting heterogeneity and potential biases in MR studies, was employing Cochran's Q test. This test assesses the weighted sum of squared discrepancies between individual estimates and the overall IVW estimate [23]. For outlier detection, the MR Pleiotropy Residual Sum and Outlier (MR-PRESSO) method was applied [24]. Additionally, MR-Egger regression was conducted to identify any horizontal pleiotropy, with a p-value of less than 0.05 deemed significant. A leave-one-out analysis was also performed to ensure the robustness of our results. Variability among specific causal estimates was examined for heterogeneity, utilizing scatter and funnel plots to identify outliers. The study then explored potential bidirectional effects between SNPs linked to vasectomy and PCa, using the MR Steiger Filtering test [25]. Furthermore, to assess the impact of confounding variables on PCa, multivariate MR (MVMR) analyses were conducted. MR analyses were conducted in R version 4.2.2, employing the "TwoSampleMR" and "MRPRESSO" packages. The MR analysis was quantified using ORs and 95% CIs, with a P-value of less than 0.05 indicating statistical significance.

Result

Meta-analysis results

Study characteristics and quality evaluation

The PRISMA flowchart delineates the search strategy, resulting in the selection of 19 articles [8, 11, 12, 26–41] for quantitative synthesis after a thorough final evaluation, as depicted in Fig. 2. The essential features of these studies are showcased in Table S3 and Figure S1, aggregating a total of 4,846,990 male participants. Spanning publications from 1991 to 2020, the research included subjects from various countries: the United States [8, 11, 26, 28, 29, 32, 35, 37, 38, 40], United Kingdom [27, 31, 39], Denmark [12, 30], Netherlands [33], Brazil [34], Canada [36], and Finland [41]. An evaluation of the risk of bias, summarized in Table S4, identified 8 studies as having a high risk of bias.

PCa risk among vasectomy patients

A pooled analysis of 19 cohort studies [8, 11, 12, 26–41] revealed a statistically significant correlation between vasectomy and an increased risk of PCa, with a RR of 1.09 and a 95%CI of 1.05–1.14 ($p<0.001$), despite substantial heterogeneity among the studies ($I^2=83.3\%$, $p=0.001$) (Fig. 3). Stratification based on PCa grades and stages indicated a notable association with both localized and

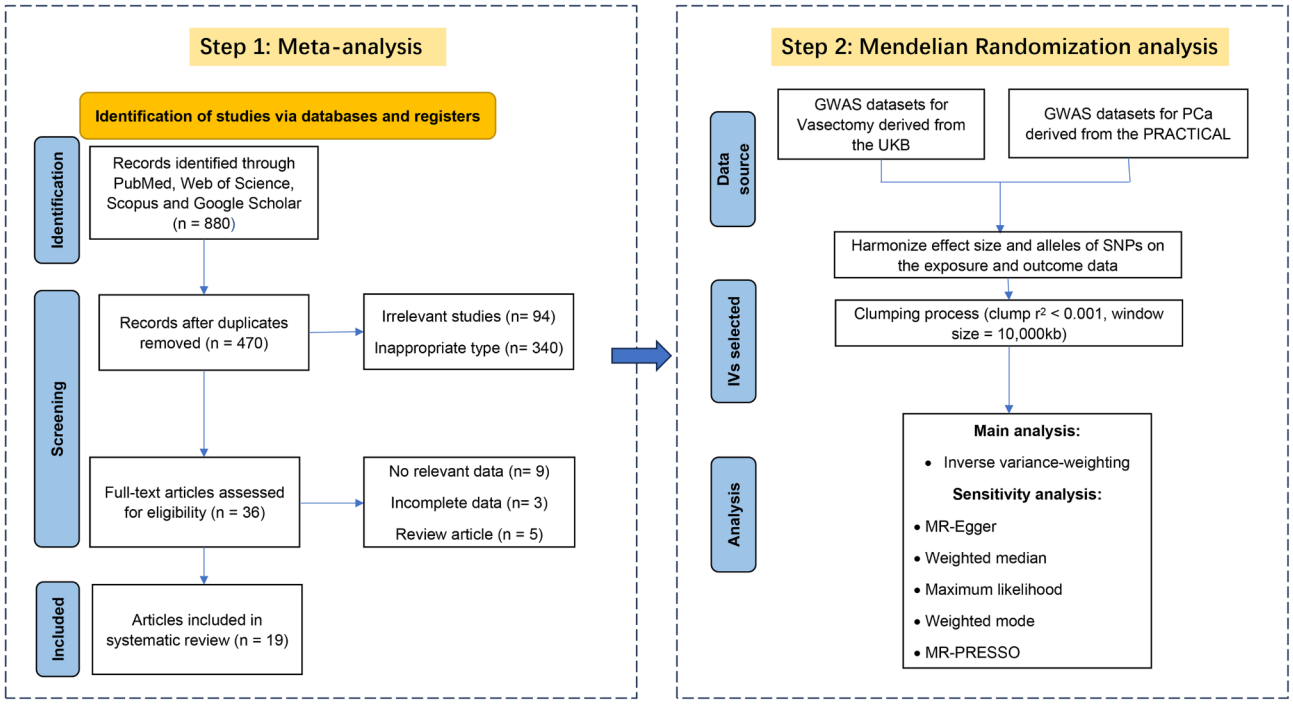

Fig. 2 Flow chart for meta-analysis and Mendelian randomization analysis

advanced forms of PCa, with RRs of 1.08 (95% CI, 1.04–1.13; $p < 0.001$) and 1.07 (95% CI, 1.01–1.13; $p = 0.016$), respectively (Fig. 4). Further detailed in Table 2, subgroup analyses highlighted an increased PCa risk related to vasectomy in studies with a follow-up duration exceeding 10 years (RR = 1.07, 95%CI: 1.03–1.12). Moreover, a decade-wise assessment of the literature suggested that more recent studies (2011–2020) tend to report a higher increase in PCa risk following vasectomy (RR = 1.19, 95% CI: 1.05–1.34), a trend observed across different geographical locations and irrespective of study bias risk levels. No significant interactions were observed for these factors in all analyses based on meta-regression models (Table 2, all P for interaction > 0.05).

Sensitivity analysis

The sensitivity analysis confirmed the robustness of our findings, showing that removing any single study from the analysis did not significantly alter the results; the RR fluctuated within a narrow range of 0.80 to 0.96, as illustrated in Figure S2. Additionally, evaluations for potential bias using funnel plots, Egger's test ($p = 0.887$), and Begg's test ($p = 0.726$) revealed no significant evidence of bias, further substantiating the reliability of our results (Figure S3).

Mendelian randomization results

Effect of Vasectomy on PCa

Under two-sample univariate in discovery cohort (PRACTICAL consortium), we identified a total of 12 SNPs that were strongly associated with vasectomy (F > 10) (Table S5). Searches within the LDlink online tool identified links between instrumental variables and traits associated with BMI (rs2815752) (Table S6). after a rigorous Steiger filtering process, there was no significant association between genetic susceptibility to vasectomy and the development of PCa under the IVW approach (OR = 0.063; 95% CI: 0.002–1.535; $P = 0.091$) (Fig. 5A, B; Table S7). Sensitivity analyses found no evidence of heterogeneity ($p = 0.967$) or horizontal pleiotropy ($p = 0.432$). The MR-PRESSO test showed no outliers (Global test $p = 0.965$), and leave-one-out analyses did not indicate that causal estimates were driven by specific SNPs (Fig. 5C, D; Table S7).

Consequently, BMI and Prostate-Specific Antigen (PSA) testing parameters, including whether an individual has ever undergone PSA testing and the duration since the last test, were incorporated as confounding factors in the MVMR analysis. The application of LASSO regression revealed no covariance among the four exposures, thereby justifying their collective inclusion in the MVMR framework. Under the IVW method, the heterogeneity index was recorded at 0.108. Despite adjustments for BMI and PSA test variables, the results demonstrated an absence of causal linkage between vasectomy and the risk of PCa (OR = 0.002, 95% CI: 1.77×10^{-7}- 36.185, $p = 0.221$) (Table 3). These results were confirmed in the validation cohort of the Finnish population (Table S8-S10).

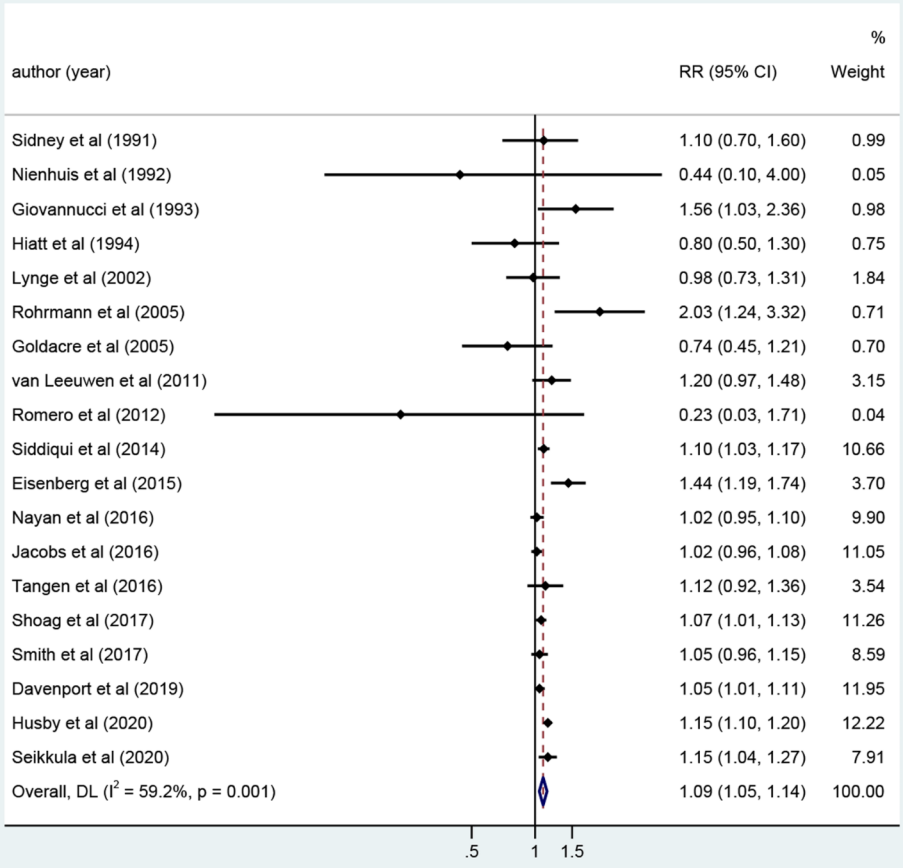

Fig. 3 Forest plot of cohort studies examining the association between vasectomy and prostate cancer

Discussion

In our study, meta-analysis found a positive association between vasectomy and PCa, while MR analysis found no causal association between the two. This difference may be due to the following reasons: The meta-analysis pooled the results of multiple observational studies that may have been influenced by confounding factors, such as PSA screening and lifestyle, which may have masked true cause-and-effect relationships. By using genetic variation as an instrumental variable, Mendelian randomization can eliminate the interference of confounding factors to a certain extent, so as to evaluate causality more accurately. Therefore, although the meta-analysis showed an association, the results of the MR Analysis suggest that this association may not be causal, but may be influenced by other confounding factors. Consequently, our findings underscore the need for more comprehensive research to clarify these associations.

Compared to previous results [42], we performed a meta-analysis, integrating previous cohort studies, which could improve statistical power and may find associations that were not detected by previous individual studies. then added validation sets, which may have enhanced the reliability and generalization of the results. In addition, the meta-analysis addressed some of the heterogeneity and confirmed the consistency of the results through subgroup analysis or sensitivity analysis.

Male fertility is often considered a marker of overall health, with male infertility being clearly associated with an increased risk of testicular cancer [43, 44]. Additionally, Walsh and colleagues reported [45] that male infertility is a risk factor for high-grade prostate cancer. Del Giudice and collaborators conducted a systematic review and meta-analysis, providing the most recent evidence regarding the impact of male infertility on the relative risks of testicular and prostate cancer [46]. The authors were able to determine that among men with reduced fertility or infertility, the risks for both cancers were significantly elevated, nearly doubling the risk. Importantly, while the relative risks are significant and relevant, the absolute risk of cancer remains low, with both cancers having a risk of less than 1%.

Sheth et al. [10]. first reported a protective effect of vasectomy against PCa in 1982, finding it to be a

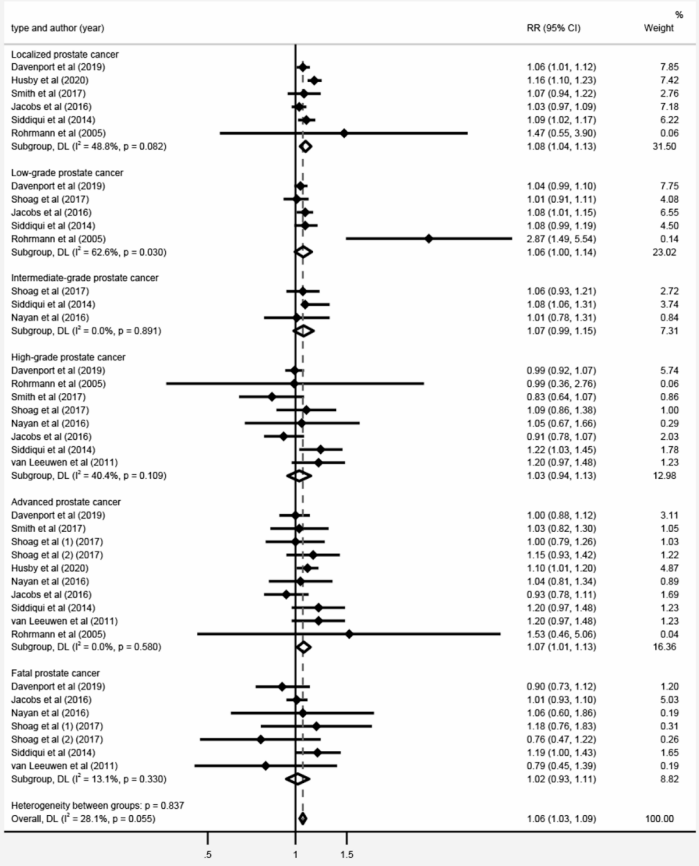

Fig. 4 Forest plots showing the relation between vasectomy and prostate cancer by disease stage

Table 2 Subgroup analysis of the association between vasectomy and prostate cancer

Analysis	Number of studies	Number of patients	RR (95% CI)	*P* for interaction	*P* value	I^2 (%)
Study location				0.081		
Europe	7	2,570,615	1.11 (1.05–1.18)		< 0.001	27.9
Non- Europe	12	2,276,375	1.09 (1.03–1.15)		0.003	60.9
Risk-of-Bias				0.408		
Low risk	11	284,257	1.07 (1.03–1.12)		0.001	50.7
Intermediate/High risk	8	4,562,733	1.18 (1.03–1.35)		0.016	59.2
Follow-up Duration				0.062		
> 10 years	11	3,811,204	1.07 (1.03–1.12)		0.008	45.1
≤ 10 years	7	162,301	1.11 (0.94–1.32)		0.091	58.2
Year of publication				0.839		
2011–2020	12	4,476,743	1.19 (1.05–1.13)		0.002	62.9
2001–2010	3	245,557	1.13 (0.67–1.89)		0.11	77.7
1991–2000	4	124,690	1.09 (0.76–1.56)		0.148	43.9

protective factor. In contrast, several high-quality cohort studies have shown a positive correlation between vasectomy and PCa, suggesting an increased risk [11, 39]. Meanwhile, a nationwide population-based case-control study in New Zealand found no association between PCa and vasectomy [47]. Meta-analyses attempting to clarify these results have been inconsistent. Three meta-analyses found no relation between vasectomy and PCa risk [47–50]. Interestingly, two other studies indicated an increased risk of PCa following vasectomy, although the association was relatively weak [51, 52].

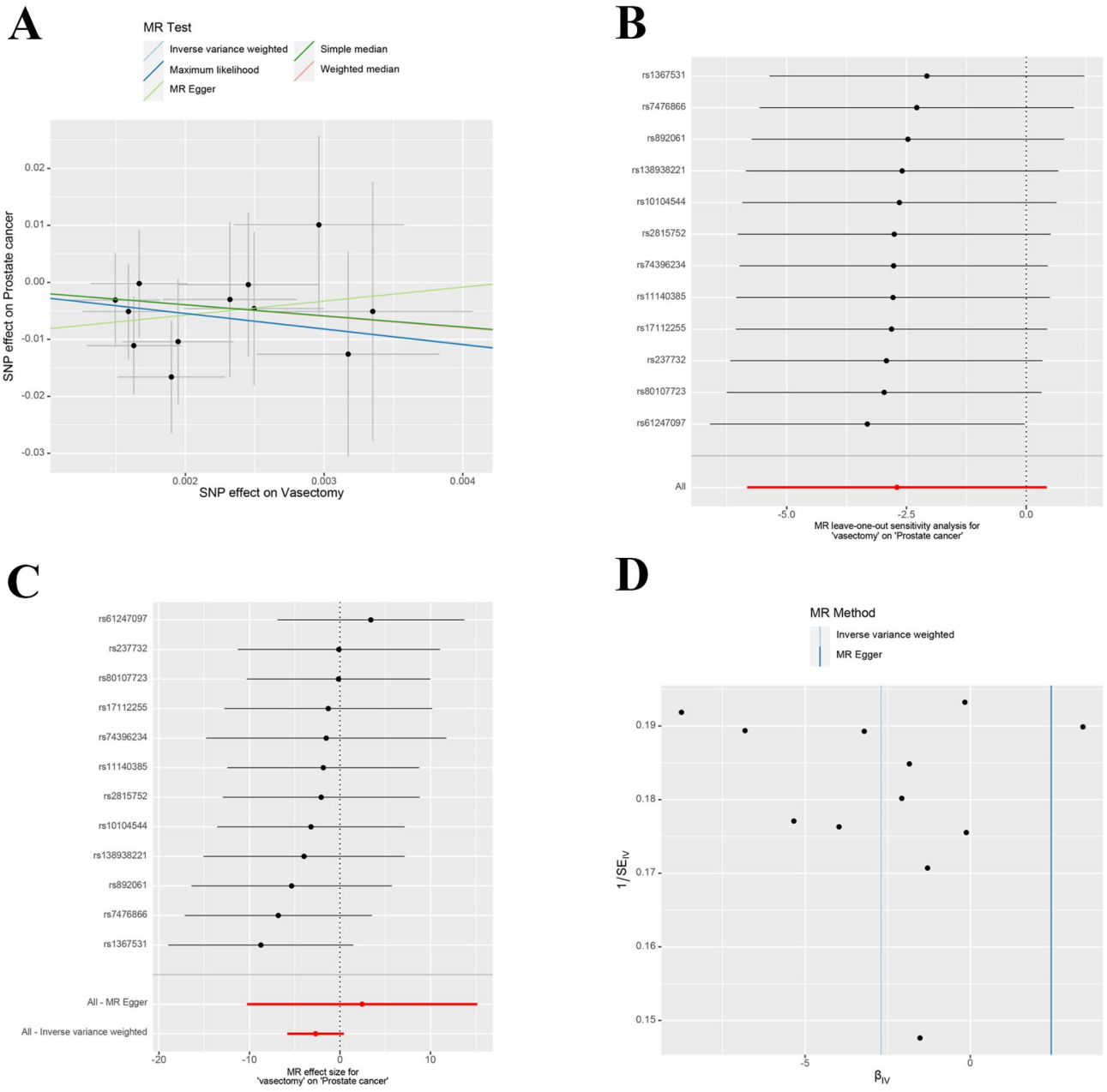

Fig. 5 Scatter plot (**A**), forest plot (**B**), leave-one-out plot (**C**), and funnel plot (**D**) of the causal effect of vasectomy on prostate cancer risk

Table 3 Effect estimates for MVMR in discovery cohort

Exposure	Outcome	No. of SNPs	Inverse-variance weighted			
			OR	Lower 95%CI	Upper 95%CI	*P*-value
Operation code: vasectomy	Prostate cancer	27	0.002	1.77E-07	36.185	0.221
Body mass index		27	0.796	0.704	0.901	0.0002
Ever had prostate specific antigen (PSA) test		27	2.648	0.357	19.599	0.340
Time since last prostate specific antigen (PSA) test		27	0.362	0.093	1.400	0.141

MVMR, multivariable Mendelian randomization; SNP, single nucleotide polymorphisms; OR, odds ratio; CI, confidence interval;

Several hypotheses have been proposed to elucidate the heightened susceptibility to PCa in individuals who have undergone vasectomy, including the diminution of prostatic secretion volume which may lead to extended carcinogen exposure, elevated levels of circulating androgens or enhanced affinity of androgen receptor proteins, the emergence of antisperm antibodies impacting immunological responses, and a decline in seminal plasma constituents like IGF-1 and IGFBP3, which play a role in the oncogenesis of the prostate [53, 54]. Nonetheless, these postulated molecular pathways connecting vasectomy to PCa are conjectural. Consequently, the existence of a direct causal relationship is uncertain, given the possibility of underlying confounding factors.

It is theorized that a variety of factors may skew the detection of PCa in those who undergo vasectomy. Men choosing vasectomy tend to engage in more frequent health check-ups, potentially leading to a heightened identification rate of localized PCa, while the likelihood of discovering advanced stages might not increase correspondingly [55, 56]. In the MVMR analysis, a causal link was not found by correcting for the PSA test. Therefore, the link between vasectomy and a higher incidence of advanced prostate cancer identified in this meta-analysis appears less attributable to detection bias.

Significant differences were more pronounced in studies with longer follow-up and newer publication times. Recent research suggests that reduced ejaculation frequency may correlate with a higher likelihood of developing prostate cancer later on [9, 57, 58]. From this viewpoint, vasectomy, which effectively reduces ejaculation frequency to none, could further corroborate the increased prostate cancer risk among vasectomized individuals. This relationship might be explained by the prostate stasis hypothesis, which posits that altered secretions, possibly associated with cancer development, accumulate in the prostate, thus increasing the chances of cancerous growths forming [59].

MR Analysis can mitigate the impact of confounding variables and reverse causation to a degree, offering a more reliable assessment of the causal link between vasectomy and PCa compared to meta-analytic outcomes. By limiting our meta-analysis to cohort studies, we aimed to minimize the effects of selection and recall biases. Integrating findings from both meta-analysis and MR Analysis could enhance our comprehension of the relationship between vasectomy and PCa. While our investigation boasts several merits, it is important to acknowledge its constraints. To begin with, the MR assessments were confined to confirming findings within European demographics, potentially narrowing the scope of associations observed. Moreover, the inherent design of MR might not adequately reflect the fluctuating dynamics of exposure over time, and the inherent diversity of data in meta-analyses often results in considerable variability and due to the lack of mediation analysis, the underlying biological speculation has not been fully confirmed. Lastly, the limited number of participants in our study could undermine the stability of effects observed in subgroups, highlighting the necessity for subsequent research endeavors to engage more extensive cohorts to bolster result fidelity.

Conclusion

Evidence gathered from cohort studies indicates a potential link between undergoing a vasectomy and a heightened risk of PCa. Nonetheless, such an association was not established through MR Analysis. The significant links reported in epidemiological research could be attributed to various biases, including but not limited to, unaccounted confounding factors, inconsistencies in the frequency of PSA testing, and the size of the studied populations where prostate cancer occurrences were noted. There is a pressing need for further epidemiological investigations employing stricter methodologies and larger participant groups to solidify these preliminary findings. Moreover, a cautious approach is imperative in the interpretation and depiction of causal relationships when utilizing MR Analysis for binary exposure variables. Progress in MR research, incorporating a more extensive spectrum of genetic markers, holds the promise of delivering more authoritative and conclusive proof regarding the causal connection between vasectomy and PCa.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12885-025-13750-8 .

Supplementary Material 1

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Author contributions
Conceptualization: WL, SY, XR. Search and evaluation: KP, WL, XR. Data Analysis: WL, SW. Writing—original draft and Visualization: WL, LY. Writing—Review and Revision: LY. Super-vision and Project Management: WL, SY, KP, LY.

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Data availability
All datasets in this study are available for download in the online dataset/supplementary file and further contact the corresponding author if necessary.

Declarations

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Conflict of interest
The authors declare that they have no competing interests.

Ethics approval
Not applicable.

Informed consent
Not applicable.

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