

# ASSOCIATION BETWEEN MALE INFERTILITY AND PROSTATE CANCER: A NARRATIVE REVIEW

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## Abstract

**Objective:** This review examines the emerging link between male infertility and prostate cancer (PCa), highlighting underlying biological mechanisms and relevant clinical considerations. **Methods:** A narrative review was conducted using PubMed, Scopus, and Google Scholar databases. The search included the terms “infertility,” “prostatic neoplasm,” and “sperm count,” targeting studies published between 2015 and 2024 in English, Spanish, and Portuguese. After screening, 15 articles were selected for inclusion based on relevance and quality. **Results:** Emerging evidence supports a biological connection between prostate function and male fertility, particularly through zinc-dependent pathways essential for maintaining seminal plasma composition. Disruptions in prostate health—such as malignancy—may adversely impact semen quality. Studies have reported elevated PSA levels and compromised sperm parameters in infertile men, particularly those under 40. Moreover, large cohort studies indicate that men undergoing assisted reproductive technologies (e.g., IVF or ICSI) may be at increased risk of developing prostate cancer at a younger age compared to their fertile counterparts. **Conclusion:** While the association between male infertility and prostate cancer remains inconclusive, it is biologically plausible. Additional longitudinal and mechanistic studies are necessary to better elucidate this relationship and support the development of future clinical guidelines.

**Keywords:** “Infertility,” “Prostatic neoplasm,” and “Sperm count”

## Introduction

Infertility affects over 180 million individuals globally, with male factors accounting for approximately 50% of cases.<sup>1</sup> Despite its prevalence, male infertility remains understudied, with nearly half of cases lacking a clear etiology based on conventional diagnostic methods.<sup>2</sup> Recent studies from the United States and Europe have proposed semen quality as a potential biomarker for overall male health, drawing parallels between infertility and chronic diseases or mortality.<sup>3</sup> Among malignancies, prostate cancer (PCa) and testicular cancer are the most extensively studied in relation to male infertility. However, no clinical guidelines currently address the seminal quality of individuals with prostate neoplasia.

Emerging evidence suggests that infertile men may face an elevated risk of developing PCa.<sup>4</sup> This association may be underpinned by genetic factors, such as Y chromosome microdeletions, which are implicated in both male infertility and PCa.<sup>5</sup> Additionally, epigenetic modifications and environmental factors may contribute to the shared pathophysiology of these conditions.<sup>6</sup>

The management of PCa, particularly through radical prostatectomy, often results in erectile dysfunction and diminished quality of life, underscoring the importance of discussing fertility preservation with patients prior to treatment. This review aims to synthesize current evidence on the association between male infertility and PCa, highlighting potential biological mechanisms and clinical implications.

## Methods

This narrative review is based on a comprehensive literature search conducted across PubMed, Scopus, and Google Scholar. The search utilized the keywords “infertility,” “prostatic neoplasm,” and “sperm count,” with a focus on studies published between 2015 and 2024 in Spanish, Portuguese, and English. A total of 15 articles were selected for inclusion and analysis.

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## Results and Discussion

### Pathophysiology of Prostate Cancer in Male Infertility

Male fertility is intricately linked to prostate function, particularly through a zinc-dependent metabolic pathway in the Krebs cycle within prostate epithelial cells.<sup>7</sup> Zinc (Zn) and citrate, regulated by androgens, play critical roles in maintaining prostate homeostasis and seminal fluid composition. Seminal plasma, comprising prostate fluid (rich in Zn, citrate, and kallikreins) and seminal vesicle secretions (rich in semenogelin), is essential for sperm motility and function.<sup>8</sup>

Disruptions in prostate health, such as inflammation or proliferative disorders, can impair Zn accumulation and citrate secretion, potentially compromising fertility.<sup>9</sup> While aging is associated with endocrine changes and proliferative prostate disorders (e.g., benign prostatic hyperplasia and PCa), the direct impact of these conditions on fertility remains poorly understood.<sup>10</sup>

### Infertility as a Predictor of Prostate Cancer

A meta-analysis revealed a 50-60% reduction in sperm counts associated with increased morbidity and mortality, though research on this topic remains limited.<sup>11</sup> Notably, a study published in *\*European Urology\** found that infertile men under 40 years of age exhibited elevated prostate-specific antigen (PSA) levels (>1 ng/ml) and reduced sperm concentration and motility compared to fertile counterparts.<sup>12</sup>

Further evidence from the Swedish Medical Birth Register indicated that men who underwent assisted reproductive technologies (ART), such as in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI), had a higher incidence of PCa at a younger age compared to those who conceived naturally.<sup>13</sup> However, methodological limitations, including inconsistent characterization of infertility and lack of seminal samples, complicate the interpretation of these findings.

### Association Between Male Infertility and Prostate Cancer

A meta-analysis of four studies suggested a slightly elevated risk of PCa in subfertile or infertile men, though the absolute risk remained below 1%.<sup>14</sup> Conversely, other studies, including a systematic review by Subfertility Health and Assisted Reproduction, found no significant association between subfertility and PCa risk.<sup>15</sup> The heterogeneity among studies and populations underscores the need for further research to clarify this relationship.

A Swedish cohort study compared PCa diagnoses among fathers who conceived through IVF, ICSI, and natural conception. The results indicated a slightly higher incidence of PCa in ART fathers (0.37% for IVF and 0.42% for ICSI) compared to naturally conceiving fathers (0.28%), with earlier onset in the ART groups.<sup>14</sup> These findings suggest a potential link between male infertility and PCa, though the clinical significance remains uncertain.

## Conclusion

The relationship between male infertility and prostate cancer remains complex and incompletely understood. Further research is needed to elucidate the biological mechanisms underlying this association and to develop evidence-based guidelines for managing fertility in men with PCa."

## References

1. Esteves SC, Zini A, Coward RM, Evenson DP, Gosálvez J, Lewis SEM, et al. Sperm DNA fragmentation testing: Summary evidence and clinical practice recommendations. *Andrologia*. 2021;53(2):e13874. <http://doi.org/10.1111/and.13874>. PMID:33108829.
2. Del Giudice F, Kasman AM, De Berardinis E, Busetto GM, Belladelli F, Eisenberg ML. Association between male infertility and male-specific malignancies: systematic review and meta-analysis of population-based retrospective cohort studies. *Fertil Steril*. 2020;114(5):984-96. <http://doi.org/10.1016/j.fertnstert.2020.04.042>. PMID:32709378.
3. Moss JLF, Keeter MK, Brannigan RE, Kim ED. Erectile dysfunction and infertility in male cancer patients: addressing unmet needs. *Future Oncol*. 2016;12(20):2293-6. <http://doi.org/10.2217/fo-2016-0335>. PMID:27581499.
4. Sharma A, Jayasena CN. Male infertility linked to risk of prostate cancer. *BMJ*. 2019;366:l5525. <http://doi.org/10.1136/bmj.l5525>. PMID:31554620.
5. Kabukçu C, Çil N, Çabuş Ü, Alataş E. Effect of ejaculatory abstinence period on sperm DNA fragmentation and pregnancy outcome of intrauterine insemination cycles: a prospective randomized study. *Arch Gynecol Obstet*. 2021;303(1):269-78. <http://doi.org/10.1007/s00404-020-05783-0>. PMID:32902676.
6. Marín de Jesús S, Viguera-Villaseñor RM, Cortés-Barberena E, Hernández-Rodríguez J, Montes S, Arrieta-Cruz I, et al. Zinc and its impact on the function of the testicle and epididymis. *Int J Mol Sci*. 2024;25(16):8991. <http://doi.org/10.3390/ijms25168991>. PMID:39201677.

7. Chen Y, Wang X, Zhou J, Wang G, Gao T, Wei H, et al. Association of seminal plasma zinc levels with human semen quality and its toxic effects on sperm motility. *Ecotoxicol Environ Saf*. 2024;284:116889. <http://doi.org/10.1016/j.ecoenv.2024.116889>. PMID:39186840.
8. Verze P, Cai T, Lorenzetti S. The role of the prostate in male fertility, health and disease. *Nat Rev Urol*. 2016;13(7):379-86. <http://doi.org/10.1038/nrurol.2016.89>. PMID:27245504.
9. Levine H, Jørgensen N, Martino-Andrade A, Mendiola J, Weksler-Derri D, Mindlis I, et al. Temporal trends in sperm count: a systematic review and meta-regression analysis. *Hum Reprod Update*. 2017;23(6):646-59. <http://doi.org/10.1093/humupd/dmx022>. PMID:28981654.
10. Boeri L, Capogrosso P, Cazzaniga W, Ventimiglia E, Pozzi E, Belladelli F, et al. Infertile men have higher prostate: specific antigen values than fertile individuals of comparable age. *Eur Urol*. 2021;79(2):234-40. <http://doi.org/10.1016/j.eururo.2020.08.001>. PMID:32814638.
11. Rubin R. Assessing whether infertile men have a higher risk of prostate cancer. *JAMA*. 2019;322(24):2371-2. <http://doi.org/10.1001/jama.2019.19203>. PMID:31799992.
12. Laukhtina E, Mori K, Pradere B, Shariat SF. Association between male infertility and prostate cancer: a systematic review and meta-analysis. *Curr Opin Urol*. 2021;31(4):346-53. <http://doi.org/10.1097/MOU.0000000000000886>. PMID:33965979.
13. Hanson BM, Eisenberg ML, Hotaling JM. Male infertility: a biomarker of individual and familial cancer risk. *Fertil Steril*. 2018;109(1):6-19. <http://doi.org/10.1016/j.fertnstert.2017.11.005>. PMID:29307404.
14. Al-Jebari Y, Elenkov A, Wirestrand E, Schütz I, Giwercman A, Lundberg Giwercman Y. Risk of prostate cancer for men fathering through assisted reproduction: nationwide population based register study. *BMJ*. 2019;366:l5214. <http://doi.org/10.1136/bmj.l5214>. PMID:31554611.
15. Tran S, Boissier R, Perrin J, Karsenty G, Lechevallier E. Review of the different treatments and management for prostate cancer and fertility. *Urology*. 2015;86(5):936-41. <http://doi.org/10.1016/j.urology.2015.07.010>. PMID:26368508.

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