Original Research Paper

Volume - 14 | Issue - 11 | November - 2024 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

General Surgery

A PROSPECTIVE STUDY OF THE EFFECT OF 5-ALPHA-REDUCTASE ON BENIGN PROSTATIC HYPERPLASIA AND PROSTATIC CARCINOMA

Saransh Dubey* PG Trainee, Department of General Surgery,.com GSVM Medical College Kanpur. *Corresponding Author

Vinay Kumar Singh Professor, Department of General Surgery, GSVM Medical College Kanpur.

Yogendra Narayan Verma Assistant Professor, Department of Pathology, GSVM Medical College Kanpur.

ABSTRACT **Introduction:** Prostate cancer is the second most common cancer among men globally, with significant regional variations in incidence and mortality. Despite lower rates in Asia, the incidence of prostate cancer is rising in countries like India. Five-alpha reductase inhibitors (5-ARIs), commonly used for benign prostatic hyperplasia (BPH), are being studied for their potential in reducing prostate cancer risk. This study aims to evaluate the therapeutic efficacy and prognostic impact of 5-ARIs in the management of BPH and prostatic carcinoma. **Material and Methods:** This prospective observational study was conducted at GSVM Medical College, Kanpur, from January 2022 to January 2024. Fifty male patients aged 50-75 years, diagnosed with BPH or prostatic carcinoma, were enrolled. Diagnoses were confirmed through imaging or histopathology, and statistical analyses were performed using Origin Pro software. **Results:** The study found a significant positive correlation between overall serum PSA levels (S.PSA OA) and AI-specific PSA levels (S.PSA AI) ($r = 0.46843$, $p < 0.001$). The mean RP/Gleason score was 3.9, with no significant correlation between age and RP/Gleason scores. The study did not observe significant differences in cancer detection rates between 5-ARI users and non-users. Non-normal distribution was noted in most study variables except for S.PSA AI. **Conclusion:** The findings support the use of PSA as a key biomarker in prostate cancer detection, with advanced imaging techniques like MRI playing a crucial role in diagnostics. However, the potential impact of 5-ARIs on imaging and diagnostic outcomes requires careful consideration. Further large-scale studies are needed to refine diagnostic strategies and improve patient outcomes in prostate cancer care.

KEYWORDS : Prostate cancer, benign prostatic hyperplasia, five-alpha reductase inhibitors, PSA, Gleason score, MRI, prostate cancer diagnostics.

INTRODUCTION

Prostate cancer is the second most common cancer affecting men globally, accounting for approximately 14.2% of all newly diagnosed cancer cases in males. The age-adjusted incidence rate of prostate cancer is 29.4 per 100,000 individuals. Regions such as North America, Europe, and Australia have notably higher prostate cancer incidence rates compared to the significantly lower rates observed in Asia and Africa. Specifically, Asia reports the lowest incidence and mortality rates, with an age-adjusted incidence of 12.6 and a mortality rate of 3.8 per 100,000 people as of 2022. Despite the overall lower rates in Asia, there has been a growing trend in the incidence of prostate cancer in many Asian countries, including India, over the past decade. This increase is attributed to a combination of factors, such as lifestyle changes, better access to healthcare, and enhanced screening efforts. According to recent projections, the incidence rate of prostate cancer stands at 173.7 cases per 100,000 person-years, reflecting a 41% rise since the early 1990s. Projections suggest that this figure will escalate to 233 cases per 100,000 person-years by 2035. Prostate cancer remains a significant contributor to cancer-related deaths in men, accounting for 13% of all male cancer deaths. Given its long latency period, early detection and preventive measures could significantly lower prostate cancer-related morbidity, mortality, and healthcare costs. One of the landmark studies in this area is the Prostate Cancer Prevention Trial (PCPT), which evaluated the effects of finasteride, a 5-ARI, on the risk of prostate cancer. The PCPT enrolled over 18,000 healthy men and followed them for seven years. The results showed that men treated with finasteride had a 25% lower relative risk of developing prostate cancer compared to those in the placebo group. This significant reduction in prostate cancer risk demonstrated the potential of 5-ARIs as a preventive therapy. Similarly, the REDUCE trial, which involved 6,729 men who were at high risk for prostate cancer, evaluated the effect of dutasteride, another 5-ARI, over four years. The study demonstrated a 23% reduction in the relative risk of prostate cancer for men treated with dutasteride compared to those who received a placebo. These findings further support the idea that 5-ARIs could serve as a viable option for prostate cancer chemoprevention.

Despite these concerns, the available evidence suggests that 5-ARIs offer considerable benefits for men at risk of prostate cancer, particularly those with BPH or other risk factors. By reducing the production of DHT, these inhibitors not only help manage the symptoms of BPH but may also reduce the likelihood of prostate cancer development. This dual benefit makes 5-ARIs a key area of focus for future prostate cancer prevention strategies.

MATERIAL AND METHODS

STUDY DESIGN

This study is a prospective observational study conducted over two years, from January 2022 to January 2024. The research was conducted in the Department of General Surgery at GSVM Medical College, Kanpur. The study was a collaborative effort, with involvement from the Department of Radiology and the Department of Pathology. A total of 50 patients were included in the study. After obtaining informed consent, male patients aged 50-75 were screened for BPH and prostatic carcinoma and prospectively enrolled from January 2022 to January 2024. Patient records were reviewed, and diagnoses were confirmed via imaging or histopathology.

INCLUSION AND EXCLUSION CRITERIA

The inclusion criteria for the study were male patients aged 45 to 85 years who had an established diagnosis of BPH confirmed by ultrasound or a diagnosis of prostatic carcinoma confirmed by histopathology. The study specifically included patients with Grade 3 and Grade 4 carcinoma. Patients were excluded if they declined participation, had active respiratory or cardiac disease, had a history of allergic reactions, had previous hormonal therapy, or existing hormonal disorders.

METHODOLOGY

The study's ultrasound findings in BPH patients showed increased prostate volume (over 30 mL), central gland enlargement, median lobe hypertrophy, intravesical mass effect, calcifications, elevated post-micturition residual volume, and bladder wall changes. In prostatic carcinoma, multi-parametric MRI (mpMRI) revealed low signal intensity on T2-weighted imaging, restricted diffusion, and early enhancement on contrast imaging. The Prostate Imaging-Reporting and Data System (PI-RADS) assessed the likelihood of significant prostate cancer (SPCA), ranging from PI-RADS 1 to 5.

Distribution of Participants by Age

This table summarizes the age distribution of the participants in the study. The mean age of the participants was 67.84 years with a standard deviation (SD) of 11.76 years, indicating that most participants were

clustered around this age with a moderate amount of variability. The median age, which is the middle value when the ages are ordered, was 66.5 years, suggesting that half of the participants were younger than this age and half were older. The interquartile range (IQR) for the median age was 64.49 to 71.82 years, indicating that the central 50% of participants were within this age range, demonstrating a relatively narrow spread around the median. The age of the participants ranged from 47 to 89 years, reflecting a wide span of ages included in the study, from middle-aged individuals to elderly participants. This distribution provides a comprehensive overview of the age demographic within the study, highlighting that the sample was primarily older adults, which is pertinent given the study's focus on conditions like benign prostatic hyperplasia (BPH) and prostatic carcinoma, which are more prevalent in older populations.

Table 1: Distribution of Participants by Age (Years)

Age (Years)	
Mean (SD)	67.84 (11.76)
Median (IQR)	66.5 (64.49 - 71.82)
Range	47 - 89

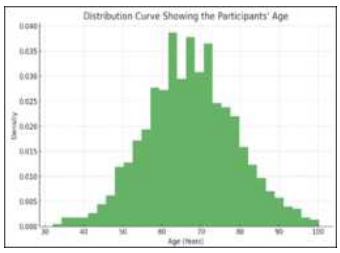
DESCRIPTIVE ANALYSIS OF THE PARTICIPANTS IN TERMS OF AGE

This table provides a detailed descriptive analysis of the age distribution among the 50 participants in the study. The mean age of the participants is 67.84 years, with a standard deviation of 11.76 years, indicating a moderate spread of ages around the mean. The 95% confidence interval (CI) for the mean age ranges from 64.49 to 71.18 years, suggesting that the true mean age of the population is likely to fall within this range. The ages of the participants span from a minimum of 47 years to a maximum of 89 years, with a median age of 66.5 years. This median value indicates that half of the participants are younger than 66.5 years and half are older, giving a sense of the central tendency in the age distribution. The data presented in this table is crucial for understanding the age-related characteristics of the study population, particularly in the context of conditions like BPH and prostatic carcinoma, which are more prevalent in older individuals.

Table 2: Descriptive Analysis of the Participants in Terms of Age (Years)

N total	Mean	Standard Deviation	Lower 95% CI of the Mean	Upper 95% CI of the Mean	Minimum	Median	Maximum
50	67.84	11.76	64.49	71.18	47	66.5	89

Figure 1: Distribution Curve Showing the Participants' Age



DISTRIBUTION OF THE PARTICIPANTS IN TERMS OF AGE GROUP

This table illustrates the distribution of participants based on their age groups. The study participants were categorized into three age groups: 40-60 years, 61-80 years, and those above 80 years. The majority of participants, 48% (N=24), fell into the 61-80 years age group, reflecting the study's focus on conditions like BPH and prostatic carcinoma, which are more common in older adults. The 40-60 years age group comprised 34% (N=17) of the participants, indicating that a significant portion of the study population was also in their early senior years. Finally, 18% (N=9) of the participants were over 80 years old, representing the oldest segment of the study population. Overall, this distribution highlights that nearly half of the participants were in the 61-80 years age range, which is likely to be highly relevant for understanding the prevalence and characteristics of the conditions under study.

Table 3: Distribution of the Participants in Terms of Age Group

Age Group (Years)	N	Percentage (%)
40-60 Years	17	34
61-80 Years	24	48
>80 Years	9	18
Total	50	100

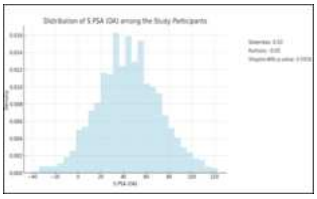


Figure 2: Distribution of S.PSA (OA) among study participants

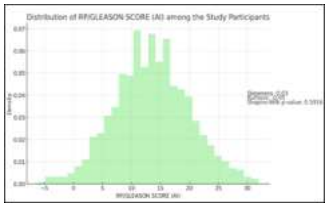


Figure 3: Distribution of RP/GLEASON SCORE (AI) among study participants

DESCRIPTIVE STATISTICAL ANALYSIS OF STUDY PARTICIPANTS

The table presents a descriptive statistical analysis of 50 study participants, detailing key variables such as age, serum PSA levels, and the RP/Gleason score. The participants had an average age of 67.84 years with a standard deviation of 11.76, ranging from 47 to 89 years. The serum PSA overall average (OA) was 45.552 ng/mL, with a standard deviation of 27.958, and values ranging from 7 to 98 ng/mL. For the AI-specific serum PSA (S.PSA), the mean was 13.84 ng/mL, with a standard deviation of 6.563, ranging from 3 to 27 ng/mL. The RP/Gleason score, which reflects the aggressiveness of prostate cancer, had a mean of 3.9 with a standard deviation of 1.092, with scores ranging from 3 to 6. This data provides a snapshot of the participants' demographic and clinical characteristics, useful for understanding the study population.

Table 3 : Descriptive Statistical Analysis of Study Participants

Variable	N	Mean	SD	Min	Max
AGE	50	67.84	11.76185	47	89
S.PSA (OA)	50	45.552	27.95823	7	98
S.PSA (AI)	50	13.84	6.56322	3	27
RP/GLEASON SCORE (AI)	50	3.9	1.09265	3	6

PEARSON'S CORRELATION ANALYSIS AMONG STUDY VARIABLES OF PARTICIPANTS

The Pearson's correlation analysis presented in Table 5 examines the relationships among key study variables, including age, serum PSA levels (both overall average [S.PSA (OA)] and AI-specific [S.PSA (AI)]), and the RP/Gleason score for the study participants. The results indicate that there is a significant positive correlation between S.PSA (OA) and S.PSA (AI) ($r = 0.46843$, $p < 0.001$), suggesting that higher overall PSA levels are associated with higher AI-specific PSA levels. However, the analysis shows no significant correlations between age and any of the other variables, with correlation coefficients and p-values as follows: age and S.PSA (OA) ($r = 0.02785$, $p = 0.84777$), age and S.PSA (AI) ($r = -0.10899$, $p = 0.45117$), and age and RP/Gleason score ($r = -0.05209$, $p = 0.71942$). Additionally, the RP/Gleason score does not show a significant correlation with either S.PSA (OA) ($r = 0.21188$, $p = 0.13963$) or S.PSA (AI) ($r = 0.06602$, $p = 0.64872$). These findings indicate that while there is a notable relationship between overall and AI-specific PSA levels, other variables, such as age and RP/Gleason score, do not exhibit significant correlations within this cohort. The analysis utilized a 2-tailed test of significance, with significant correlations marked at the 0.05 level.

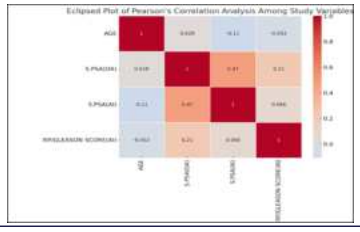


Figure 5: Eclipsed plot of Pearson's Correlation analysis among study variables

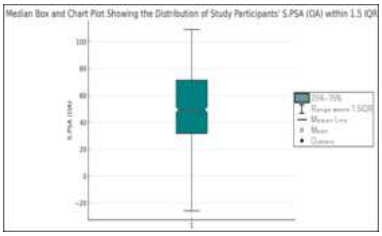


Figure 6: Median box and chart plot showing the distribution of study participants age within 1.5 interquartile range (IQR)

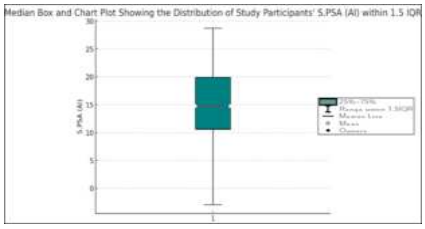


Figure 7: Median box and chart plot showing the distribution of study participants S.PSA (OA) within 1.5 interquartile range (IQR)

DISCUSSION

The results from our study, which involved 50 older adults with an average age of 67.84 years, provide valuable insights into the relationships between serum PSA levels, RP/Gleason scores, and imaging modalities in the context of prostate cancer diagnostics. Our findings align with existing literature, while also contributing to the ongoing discourse on the complexities of prostate cancer detection and management, particularly in the presence of 5-alpha reductase inhibitor (5ARI) use.

Serum PSA levels have long been established as a key biomarker for prostate cancer detection and monitoring. In our study, we identified a significant positive correlation between overall serum PSA (S.PSA OA) and AI-specific PSA (S.PSA AI) levels ($r = 0.46843$, $p < 0.001$), reinforcing the role of PSA as an indicator of prostate volume and potential malignancy. This finding is consistent with earlier studies by Catalona et al [10] and Carter et al [11] which demonstrated that elevated PSA levels are strongly associated with increased prostate volume and higher cancer stages. Building on this foundation, recent clinical trials such as PROMIS and PRECISION have further validated the importance of PSA in guiding the use of advanced imaging techniques, particularly multiparametric MRI (mpMRI). These trials demonstrated that mpMRI can detect more clinically significant cancers while reducing the detection of clinically insignificant ones, thereby enabling a significant percentage of men to avoid unnecessary biopsies. The correlation observed in our study between higher PSA levels and increased use of MRI and CT scans aligns with this evolving clinical practice, highlighting PSA's pivotal role in prompting further diagnostic evaluation.

The RP/Gleason score, which reflects the histological aggressiveness of prostate cancer, is a critical factor in determining the appropriate management strategy. Our study found a mean RP/Gleason score of 3.9, indicating a range of cancer severities among participants. However, we did not observe a significant correlation between age and RP/Gleason scores, which is in line with some studies suggesting that Gleason scores do not necessarily correlate with patient age. For instance, Moul et al [12] have noted that while Gleason scores are crucial for prognosis, they may not be strongly influenced by age.

The role of 5ARI use in prostate cancer detection adds a layer of complexity to this discussion. Medina et al. raised concerns about the potential for 5ARI use to be associated with MRI-invisible prostate cancer, although their study did not distinguish between clinically significant and insignificant cancers. In our cohort, we did not find significant differences in prostate cancer detection between 5ARI users and non-users, which aligns with Medina et al.'s findings [13]. This suggests that while PSA and Gleason scores remain important diagnostic tools, their interpretation in the context of 5ARI use requires careful consideration to avoid misdiagnosis or underestimation of cancer severity. Further complicating the picture, Kim et al [14] evaluated the effect of 5ARI treatment on prostate cancer detection using MRI-TRUS fusion biopsy and concluded that 5ARI use did not significantly impact cancer detection or mpMRI performance. This finding is particularly relevant to our study, where we similarly observed no significant difference in cancer detection rates between 5ARI users and non-users. However, the study by Giganti et al. suggested that 5ARI use might alter MRI readings, particularly the apparent diffusion coefficient (ADC), which could influence the detection of tumors in different prostate zones. These findings underscore the need for clinicians to consider the potential effects of 5ARI on MRI interpretation and to maintain a high index of suspicion when assessing patients with a history of 5ARI use [15].

In analyzing our data, we found that age, S.PSA OA, and RP/Gleason scores did not follow a normal distribution, while S.PSA AI did. This non-normal distribution is consistent with findings in other prostate cancer studies, where variables such as PSA levels and Gleason scores often exhibit skewed distributions due to the heterogeneity of the disease and patient demographics. For example, Roehrborn noted that PSA levels can be heavily skewed, reflecting the wide variability in prostate cancer presentation [16].The presence of non-normal distributions in our study highlights the importance of employing appropriate statistical methods when analyzing prostate cancer data. Non-parametric statistical approaches may be more suitable for handling skewed data, ensuring that the analyses accurately reflect the underlying patterns and relationships within the cohort. This consideration is crucial for deriving meaningful conclusions from studies involving prostate cancer biomarkers and clinical outcomes.

Our study revealed a significant association between the use of MRI and CT scans, reflecting the increasing reliance on these imaging modalities in prostate cancer diagnostics. This finding is supported by literature emphasizing the complementary roles of MRI and CT in providing a comprehensive assessment of prostate cancer, particularly in cases where PSA levels are elevated but inconclusive. Studies by Hoeks et al. and Turkbey et al. have demonstrated that multiparametric MRI, in particular, enhances the detection and staging of prostate cancer, making it a valuable tool in the diagnostic pathway [17,18].

The inclusion of MRI as an early evaluation tool for men with suspected prostate cancer, as recommended by international guidelines, further underscores its importance in modern clinical practice. Our study's findings align with these recommendations, as we observed a trend toward increased MRI and CT usage in patients with higher PSA levels. This association suggests that imaging modalities are being appropriately utilized to complement PSA testing, thereby improving the accuracy of prostate cancer diagnosis.

However, as noted earlier, the potential impact of 5ARI use on MRI interpretation remains a topic of ongoing research. While our study did not find significant differences in cancer detection between 5ARI users and non-users, the observations by Giganti et al. regarding changes in ADC values in 5ARI-treated patients highlight the need for further investigation. Understanding how 5ARI use influences imaging results will be crucial for optimizing diagnostic strategies and ensuring that clinically significant cancers are accurately identified and managed [15].

CONCLUSION

In conclusion, our study adds to the growing body of evidence that underscores the complexity of prostate cancer diagnostics. The significant correlation between overall PSA and AI-specific PSA levels supports the continued use of PSA as a key biomarker in prostate cancer detection. However, the observed non-normal distributions and the nuanced impact of 5ARI use on imaging and diagnostic outcomes highlight the challenges faced by clinicians in accurately diagnosing and managing prostate cancer. As the role of advanced imaging techniques, particularly MRI, continues to expand, it is essential for clinicians to remain vigilant about the potential influences of medications like 5ARIs on diagnostic outcomes. Larger, prospective studies are needed to further explore these relationships and to refine the integration of biomarkers, imaging, and clinical judgment in the diagnosis and treatment of prostate cancer. Through such research, we can continue to improve patient outcomes and advance the field of prostate cancer care.

REFERENCES

1. Ferlay J, Ervik M, Lam F, Laversanne M, Colombet M, Mery L Global Cancer Observatory:Cancer Today 2024 Lyon, France International Agency for Research on Cancer Available from: https://gco.iarc.who.int/today [Last accessed on 2024 Apr 01]
2. Stewart B, Wild C, Weiderpass E World Cancer Report:Cancer Research for Cancer Prevention Lyon IARC Press 2020.

3. Rastogi T, Devesa S, Mangtani P, Mathew A, Cooper N, Kao R, et al. Cancer incidence rates among South Asians in four geographic regions:India, Singapore, UK and US Int J Epidemiol 2008;37: 147–60.
4. Sathishkumar K, Chaturvedi M, Das P, Stephen S, Mathur P. Cancer incidence estimates for 2022 &projection for 2025:Result from national cancer registry programme, India Indian J Med Res 2022;156: 598–607.
5. Office for National Statistics: Cancer registration statistics, England: 2017. 2017.
6. Fitzpatrick JM, Schulman C, Zlotta AR, et al.: Prostate cancer: a serious disease suitable for prevention. BJU Int. 2009;103(7):864–70. 10.1111/j.1464-410X.2008.08206.x
7. Thomas LN, Douglas RC, Lazier CB, et al.: Type 1 and Type 2 5α-Reductase Expression in the Development and Progression of Prostate Cancer. Eur Urol. 2008;53(2):244–252. 10.1016/j.eururo.2007.10.052
8. Thompson IM, Goodman PJ, Tangen CM, et al.: The influence of finasteride on the development of prostate cancer. N Engl J Med. 2003;349(3):215–24. 10.1056/NEJMoa030660
9. Andriole GL, Bostwick DG, Brawley OW, et al.: Effect of dutasteride on the risk of prostate cancer. N Engl J Med. 2010;362(13):1192–202. 10.1056/NEJMoa0908127
10. Catalona WJ, Smith DS, Ratliff TL, Basler JW. Detection of organ-confined prostate cancer is increased through prostate-specific antigen-based screening. JAMA. 1993;270(8):948–54. doi:10.1001/jama.1993.03510080074036.
11. Carter HB, Pearson JD, Metter EJ, et al. Longitudinal evaluation of prostate-specific antigen levels in men with and without prostate disease. JAMA. 1992;267(16):2215–20. doi:10.1001/jama.1992.03480160069034.
12. Moul JW, Connelly RR, Lubeck DP, et al. Predicting risk of prostate cancer recurrence based on the Cancer of the Prostate Risk Assessment (CAPRA) score. Cancer. 2009;115(11):2507–15. doi:10.1002/cncr.24246.
13. Medina A, Rodríguez-Patrón R, Ruiz Hernández M, et al. Identifying risk factors for MRI-invisible prostate cancer in patients undergoing transperineal saturation biopsy. Res Rep Urol. 2021;13:723–31. doi:10.2147/RRU.S327938.
14. Kim JK, Lee HJ, Hwang SI, Choe G, Kim HJ, Hong SK. The effect of 5 alpha-reductase inhibitor therapy on prostate cancer detection in the era of multi-parametric magnetic resonance imaging. Sci Rep. 2019;9(1):17862. doi:10.1038/s41598-019-54054-3.
15. Giganti F, Gambarota G, Moore CM, et al. Prostate cancer detection using quantitative T(2) and T(2) -weighted imaging: the effects of 5-alpha-reductase inhibitors in men on active surveillance. J Magn Reson Imaging. 2018;47(6):1646–53. doi:10.1002/jmri.25913.
16. Roehrborn CG. Benign prostatic hyperplasia: an overview. Rev Urol. 2005;7(Suppl 9) –14.
17. Hoeks CM, Barentsz JO, Hambrock T, et al. Prostate cancer: multiparametric MR imaging for detection, localization, and staging. Radiology. 2011;261(1):46–66. doi:10.1148/radiol.11101913.
18. Turkbey B, Mani H, Shah V, et al. Multiparametric 3T prostate magnetic resonance imaging to detect cancer: histopathological correlation using prostatectomy specimens processed in customized magnetic resonance imaging based molds. J Urol. 2011;186(5):1818–24. doi:10.1016/j.juro.2011.07.013.