

# Impact of 5-alpha reductase inhibitors on pre-biopsy MRI interpretation: effects on PI-RADS assessment and local staging

Arianna Tumminello,<sup>1</sup> Giuseppe Reitano,<sup>1</sup> Elisa Tonet,<sup>1</sup> Giovanni Basso,<sup>1</sup> Felice Crocetto,<sup>2</sup> Iliana Bednarova,<sup>3</sup> Francesca Caumo,<sup>3</sup> Matteo Todisco,<sup>4</sup> Alberto Lauro,<sup>4</sup> Carmelo Lacognata,<sup>4</sup> Francesca Galuppini,<sup>5</sup> Giorgio De Conti,<sup>4</sup> Giovanni Betto,<sup>1</sup> Massimo Iafrate,<sup>1</sup> Giacomo Novara,<sup>1</sup> Fabrizio Dal Moro,<sup>1</sup> Fabio Zattoni<sup>1\*</sup> 

<sup>1</sup>Urology Clinic, Department of Surgery, Oncology and Gastroenterology (DISCOG), University of Padova, Padova, Italy

<sup>2</sup>Department of Neurosciences, Reproductive Sciences and Odontostomatology, University of Naples "Federico II", Naples, Italy

<sup>3</sup>Radiology Unit, Veneto Institute of Oncology IOV-IRCCS, Padua, Italy

<sup>4</sup>Radiology Unit, Department of Radiology, University Hospital of Padua, Padua, Italy

<sup>5</sup>Surgical Pathology & Cytopathology Unit, Department of Medicine (DIMED), University of Padova, Padova, Italy

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5-alpha reductase inhibitors (5-ARIs) are widely prescribed for the management of benign prostatic hyperplasia and are known to induce morphological and metabolic changes in prostatic tissue. This narrative review summarizes current evidence on the impact of 5-ARI therapy on multiparametric magnetic resonance imaging (mpMRI) findings and the potential clinical implications. While some studies report reduced discrimination on T2-weighted and

apparent diffusion coefficient (ADC) metrics after long-term exposure, others suggest improved lesion visibility due to a more homogeneous benign background. Most studies found no significant difference in the Prostate Imaging Reporting and Data System (PI-RADS) lesion distribution between 5-ARI users and non-users. However, conflicting evidence exists regarding mpMRI sensitivity and specificity in 5-ARI-treated patients. Limited data is available on the effect of 5-ARIs on local staging accuracy. Overall, the effect of 5-ARIs on prostate mpMRI interpretation appears complex, highlighting the need for prospective studies and treatment-adjusted risk assessment tools to support clinical decision-making.

**Key Words:** 5-alpha reductase inhibitors, multiparametric MRI, prostate cancer, PI-RADS, imaging interpretation

## Introduction

Multiparametric magnetic resonance imaging (mpMRI) of the prostate, standardized through the Prostate Imaging Reporting and Data System (PI-RADS), has become central to the detection, localization, and risk stratification of clinically significant prostate cancer (csPCa).<sup>1</sup> mpMRI offers a non-invasive method to support clinical decisions and improve diagnosis accuracy. Accordingly, mpMRI is now integrated into international

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\*Corresponding Author: Fabio Zattoni.

Email: [fabio.zattoni@unipd.it](mailto:fabio.zattoni@unipd.it)

guidelines for the evaluation of men with suspected prostate cancer (PCa) and in active surveillance protocols.<sup>2,3</sup>

Among men undergoing imaging, a substantial proportion are also treated for benign prostatic hyperplasia (BPH) with 5- $\alpha$  reductase inhibitors (5-ARIs), such as dutasteride and finasteride. These drugs inhibit the conversion of testosterone to dihydrotestosterone (DHT), leading to a reduction in prostate volume and changes in the histological architecture of the gland.<sup>4</sup> Specifically, 5-ARIs can increase the proportion of stromal and fibrotic tissue while reducing glandular components, potentially altering mpMRI characteristics.<sup>5–8</sup> Structural and metabolic changes in the prostate can influence the appearance of both benign and malignant tissues on mpMRI. These alterations may either obscure or enhance cancer detection, depending on sequence type, treatment duration, and tumor grade. Evidence is mixed, with some studies showing reduced discrimination (especially on T2-weighted and apparent diffusion coefficient (ADC) metrics after long-term exposure), while others suggest improved lesion visibility due to a more homogeneous benign background. In detail, tumor-associated choline levels remain stable, whereas in BPH, the levels of prostatic secretory metabolites decrease. This reduction may enhance the contrast of cancer-related metabolite signals.<sup>9,10</sup>

Following 5-ARI exposure, androgen-sensitive and BPH tissues undergo rapid atrophy. Iczkowski et al. reported that 5-ARI induces epithelial shrinkage and increases the stromal/epithelial ratio in prostate cancer.<sup>11</sup>

These pharmacologically induced changes may complicate image interpretation. Several studies suggest that long-term use of 5-ARIs (typically >6 months) is associated with significant imaging alterations, while short-term use appears to have a negligible impact.<sup>7,12</sup> Consequently, awareness of a patient's medication history is essential for radiologists and urologists to avoid underdiagnosis or misclassification of lesions.

This narrative review aims to synthesize the existing evidence on how 5-ARIs influence prostate mpMRI findings and the implications for clinical practice.

## Literature Search and Analysis

A narrative review was conducted to identify published studies from 2010 to 2025 concerning the role of 5-ARIs in the interpretation of mpMRI. The PubMed

database was searched using the following combination of keywords: ((*prostate MRI*) AND (*prostate cancer diagnosis*)) AND ((*finasteride*) OR (*dutasteride*)); (*prostate MRI*) AND (*5- $\alpha$  reductase inhibitors*). In this narrative analysis of the literature, articles were included if they directly addressed the subject of the review and demonstrated acceptable methodological quality, with a preference for observational studies, randomized trials, meta-analyses and those involving large populations. Exclusion criteria were a lack of MRI-based outcomes, absence of a 5-ARI-specific subgroup, case reports, editorials. Where reported by the authors, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy were directly extracted from the original publications. In studies in which these diagnostic performance metrics were not explicitly provided, they were recalculated using the raw data reported in the manuscripts (i.e., true positives, true negatives, false positives, and false negatives). Calculations were performed using standard diagnostic accuracy formulas implemented in a Microsoft Excel spreadsheet. No additional statistical modeling or meta-analytic pooling was conducted. In all included studies, prostate cancer detection was based on biopsy results rather than whole-gland pathology. The collected studies formed the basis for a narrative analysis of the literature.

## Mechanism of 5-ARI Influence on Prostatic Tissue and Imaging

**Table 1** summarizes the overall characteristics of the populations in the different studies and **Table 2** the main radiological findings.

Based on current biological understanding, 5-ARI therapy may reduce the contribution of glandular tissue on mpMRI, resulting in a more uniform background. In this scenario, cancerous tissues could become more visible.

Starobinets et al. suggested that glandular atrophy and tissue shrinkage may make PCa detection more challenging on T2-weighted images.<sup>10</sup> Similarly, Purysko et al. observed that long-term exposure to 5-ARIs—defined as at least 12-month-therapy—may affect the ability of ADC metrics to discriminate between MRI lesions (both suspected for csPCa and iPCa) and benign tissue.<sup>13</sup> These results contrast with the findings of Starobinets et al. The MAPPED trial,<sup>14</sup> a randomized, double-blind, placebo-controlled trial suggested that six-month exposure to dutasteride was associated with an important reduction in prostate cancer volumes (36%) compared to an

TABLE 1. Overall characteristics of the populations in the studies

| Study                                | Design of the study                     | Inclusion criteria                                                                                                                       | Patients (n, %)                           | MRI/biopsy before 5-ARI | Duration 5ARI                                               | Age (median (IQR) or mean ± SD) | PSA (median (IQR) or mean ± SD) | Prostate volume (median (IQR) or mean ± SD) | Suspicious DRE (n, %) | Pca family history (n, %) | AS (n, %) | Previous neg biopsies (n, %) |
|--------------------------------------|-----------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------|-------------------------|-------------------------------------------------------------|---------------------------------|---------------------------------|---------------------------------------------|-----------------------|---------------------------|-----------|------------------------------|
| Morote et al. (2024) <sup>5</sup>    | Case-control multicentric               | <ul style="list-style-type: none"><li>Suspicion of PCa (PSA &gt; 3 or DRE+)</li><li>mpMRI</li><li>biopsy</li></ul>                       | 5-ARI: 118 (50)<br>No 5-ARI: 118 (50)     | No                      | >12 mo.                                                     | 72 (68-76)                      | 8.0 (5.2-12.9)                  | 67 (49-95)                                  | 42 (35.6)             | 5 (4.2)                   | No        | 43 (36.4)                    |
| Falagario et al. (2023) <sup>6</sup> | Retrospective multicentric cohort study | <ul style="list-style-type: none"><li>Suspicion of PCa</li><li>mpMRI prior to biopsy</li></ul>                                           | 5-ARI: 705 (9.2)<br>No 5-ARI: 6913 (90.8) | No                      | ≥3 mo.                                                      | 69 (65-73)                      | 6.0 (4.0-9.0)                   | 53 (40-72)                                  | 179 (25.4)            | -                         | No        | 186 (26.4)                   |
| Kim et al. (2019) <sup>15</sup>      | Retrospective                           | <ul style="list-style-type: none"><li>Suspicion of PCa</li><li>mpMRI-fusion biopsy</li></ul>                                             | 5-ARI: 80<br>No 5-ARI: 626                | No                      | 1-3 yrs: 45 (56.3)<br>3-5 yrs: 35 (43.7)<br>>5 yrs: 20 (25) | 69 (63-73)                      | 5.56 (3.92-11.50)               | 41 (27-57)                                  | -                     | -                         | No        | -                            |
| Moore et al. (2017) <sup>14</sup>    | Randomized trial                        | <ul style="list-style-type: none"><li>LR/IR biopsy-proven PCa (GS ≤ 3 + 4, PSA ≤ 15)</li><li>mpMRI-T2w visible lesion ≥ 0.2 mL</li></ul> | 5-ARI: 21 (50)<br>No 5-ARI: 21 (50)       | Yes                     | 6 mo.                                                       | 63.9 ± 7.3                      | 6.94 ± 3.0 (4.91-11.05)         | 47.02 ± 20.7                                | -                     | -                         | 21 (100)  | 0                            |
| Savin et al. (2024) <sup>8</sup>     | Retrospective                           | <ul style="list-style-type: none"><li>PIRADS ≥ 3</li><li>mpMRI-US TP fusion biopsy</li></ul>                                             | 5-ARI: 52 (8.7)<br>No 5-ARI: 548 (91.3)   | No                      | ≥6 mo.                                                      | 72 (69-75)                      | 6.8 (4-8.4)                     | 60 (43-96)                                  | 14 (27)               | 4 (8)                     | 15 (29)   | 36 (69)                      |
| Aksu et al. (2024) <sup>16</sup>     | Retrospective                           | <ul style="list-style-type: none"><li>PIRADS ≥ 3</li><li>TRUS-guided cognitive biopsy</li></ul>                                          | 5-ARI: 70 (16.3)<br>No 5-ARI: 359 (83.7)  | No                      | ≥6 mo.                                                      | 68.66                           | 5.37                            | 59.9                                        | -                     | -                         | No        | -                            |
| Wang et al. (2023) <sup>17</sup>     | Retrospective                           | <ul style="list-style-type: none"><li>LUTS and PSA &gt; 4 or PIRADS ≥ 3 (regardless of execution of previous biopsies)</li></ul>         | 5-ARI: 54 (15.4)<br>No 5-ARI: 297 (84.6)  | No                      | <6 mo: 16 (29.6)<br>6-12 mo: 8 (14.8)<br>>12 mo: 27 (50)    | 67.6 ± 6.21                     | 11.0 ± 8.33                     | 64.9 ± 33.5                                 | 13 (24.1)             | -                         | 3 (5.56)  | 21 (38.9)                    |
|                                      |                                         |                                                                                                                                          |                                           |                         |                                                             | 65.6 ± 6.85                     | 9.41 ± 8.41                     | 48.1 ± 21.8                                 | 72 (24.2)             | -                         | 61 (20.5) | 77 (25.9)                    |

(Continued)

TABLE 1. (Continued)

| Study                                   | Design of the study             | Inclusion criteria                                                                                                                                                           | Patients (n, %)                     | MRI/biopsy before 5-ARI | Duration 5ARI | Age (median (IQR) or mean $\pm$ SD) | PSA (median (IQR) or mean $\pm$ SD)                                                                    | Prostate volume (median (IQR) or mean $\pm$ SD) | Suspicious DRE (n, %) | Pca family history (n, %) | AS (n, %)              | Previous neg biopsies (n, %) |
|-----------------------------------------|---------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|-------------------------|---------------|-------------------------------------|--------------------------------------------------------------------------------------------------------|-------------------------------------------------|-----------------------|---------------------------|------------------------|------------------------------|
| Starobinets et al. (2017) <sup>10</sup> | Retrospective                   | <ul style="list-style-type: none"><li>GS 3 + 3 biopsy-proven PCa</li><li>Previous mpMRI</li><li>Cohorts matched per prostate volume</li></ul>                                | 5-ARI: 10 (50)<br>No 5-ARI: 10 (50) | No                      | $\geq 12$ mo. | 70.8 $\pm$ 9.1                      | 5.84 $\pm$ 6.56                                                                                        | 47.03 $\pm$ 28.77                               | -                     | -                         | 10 (100)               | -                            |
| Giganti et al. (2017) <sup>12</sup>     | Randomized trial                | <ul style="list-style-type: none"><li>AS (GS 3 + 3 or 3 + 4 within 2yrs)</li><li>PSA &lt; 15</li><li>PIRADS <math>\geq 4</math></li></ul>                                    | 5-ARI: 18 (49)<br>No 5-ARI: 19 (51) | Yes                     | 6 mo.         | 65 (49–79)                          | Baseline: 7.14 $\pm$ 2.23<br>6mo: 4.14 $\pm$ 1.65<br>Baseline: 6.12 $\pm$ 2.20<br>6mo: 6.72 $\pm$ 2.39 | -                                               | -                     | -                         | 18 (100)               | -                            |
| Obinata et al. (2022) <sup>7</sup>      | Retrospective                   | <ul style="list-style-type: none"><li>Suspicion of PCa</li><li>mpMRI previous biopsy</li><li>systematic biopsy</li><li>propensity score match based on age and PSA</li></ul> | 5-ARI: 96 (50)<br>No 5-ARI: 96 (50) | No                      | -             | 73.40 $\pm$ 7.92                    | 12.76 $\pm$ 15.64<br>19.71 $\pm$ 44.32                                                                 | -                                               | -                     | -                         | No                     | 3 (3)<br>0 (0)               |
| Purysko et al. (2021) <sup>13</sup>     | Retrospective (matched cohorts) | <ul style="list-style-type: none"><li>mpMRI for initial detection or AS</li></ul>                                                                                            | 5-ARI: 59 (50)<br>No 5-ARI: 59 (50) | No                      | $\geq 12$ mo. | 69.8 $\pm$ 5.2                      | -                                                                                                      | -                                               | -                     | -                         | 33 (55.9)<br>33 (55.9) | 26 (44.1)<br>26 (44.1)       |

Note. 5-ARI (5-alpha reductase inhibitors), AS (Active Surveillance), DRE (Digital Rectal Examination), GS (Gleason Score), IQR (interquartile range), LR/IR PCa (low-risk/intermediate-risk prostate cancer), LUTS (Low Urinary Tract Symptoms), mo. (months), mpMRI (multiparametric Magnetic Resonance Imaging), PCa (Prostate Cancer), PIRADS (Prostate Imaging Reporting and Data System), PSA (Prostate Specific Antigen), SD (standard deviation), TRUS (trans-rectal ultrasound), US (ultrasound), yrs (years), The sign “–” is used when data are unavailable.

TABLE 2. Main radiological findings

| Study                                | Group    | Lesions                                                |      | PIRADS (n, %)                               |   |            |             |             | mpMRI sequences (T2<br>DWI, ADC) findings |       |                                                                                                     |  |
|--------------------------------------|----------|--------------------------------------------------------|------|---------------------------------------------|---|------------|-------------|-------------|-------------------------------------------|-------|-----------------------------------------------------------------------------------------------------|--|
|                                      |          | Number<br>(n, %)                                       | p    | Volume (cc) (mean ±<br>SD or median + IQR)  | p | < /= 2     | 3           | 4           |                                           | 5     | p                                                                                                   |  |
| Morote et al. (2024) <sup>5</sup>    | 5-ARI    | -                                                      | -    | -                                           | - | 15 (45.5)  | 20 (58.8)   | 56 (50)     | 27 (47.4)                                 | 0.685 | -                                                                                                   |  |
|                                      | No 5-ARI | -                                                      | -    | -                                           | - | 18 (54.5)  | 14 (41.2)   | 56 (50)     | 30 (52.6)                                 |       | -                                                                                                   |  |
| Falagario et al. (2023) <sup>6</sup> | 5-ARI    | -                                                      | -    | Index lesion<br>0.52 (0.27–1.29)            | - | 141 (20)   | 158 (22.4)  | 258 (36.6)  | 148 (21.0)                                | <0.01 | ADC: less efficiency in<br>distinction of<br>csPCa / non-csPCa                                      |  |
|                                      | No 5-ARI | -                                                      | -    | Index lesion<br>0.52 (0.27–1.37)            | - | 878 (12.7) | 1764 (25.5) | 2948 (42.6) | 1323 (19.1)                               |       | -                                                                                                   |  |
| Kim et al. (2019) <sup>15</sup>      | 5-ARI    | -                                                      | -    | -                                           | - | 22 (27.5)  | 30 (37.5)   | 28 (35.1)   |                                           | 0.543 | -                                                                                                   |  |
|                                      | No 5-ARI | -                                                      | -    | -                                           | - | 151 (24.2) | 216 (34.5)  | 259 (41.4)  |                                           |       | -                                                                                                   |  |
| Moore et al. (2017) <sup>14</sup>    | 5-ARI    | -                                                      | -    | T2w<br>0 mo: 0.55 ± 0.5<br>6mo: 0.38 ± 0.4  | - | -          | -           | -           | -                                         | -     | 3-mo. cancer volume<br>change (%)<br>T2: 34%                                                        |  |
|                                      |          | -                                                      | -    | DCE<br>0 mo: 0.58 ± 0.5<br>6 mo: 0.35 ± 0.3 | - | -          | -           | -           | -                                         | -     | 6-mo. cancer volume<br>change (%):<br>T2: −35.73 ± 25.7<br>DCE: −42.32 ± 25.6<br>DWI: −33.46 ± 21.8 |  |
|                                      |          | -                                                      | -    | DWI<br>0 mo: 0.48 ± 0.6<br>6mo: 0.30 ± 0.3  | - | -          | -           | -           | -                                         | -     | 3-mo. cancer volume<br>change (%)<br>T2 0.21%                                                       |  |
|                                      |          | -                                                      | -    | T2w<br>0 mo: 0.65 ± 0.8<br>6mo: 0.76 ± 0.9  | - | -          | -           | -           | -                                         | -     | 6-mo. cancer volume<br>change (%):<br>T2: 12.15 ± 37.2<br>DCE: −4.20 ± 38.5<br>DWI: −7.01 ± 35.9    |  |
|                                      |          | -                                                      | -    | DCE<br>0 mo: 0.67 ± 0.8<br>6 mo: 0.66 ± 0.8 | - | -          | -           | -           | -                                         | -     |                                                                                                     |  |
|                                      | No 5-ARI | -                                                      | -    | DWI<br>0 mo: 0.42 ± 0.3<br>6mo: 0.45 ± 0.4  | - | -          | -           | -           | -                                         | -     | -                                                                                                   |  |
|                                      |          | -                                                      | -    | -                                           | - | -          | -           | -           | -                                         | -     | -                                                                                                   |  |
|                                      |          | -                                                      | -    | -                                           | - | -          | -           | -           | -                                         | -     | -                                                                                                   |  |
|                                      |          | -                                                      | -    | -                                           | - | -          | -           | -           | -                                         | -     | -                                                                                                   |  |
|                                      |          | -                                                      | -    | -                                           | - | -          | -           | -           | -                                         | -     | -                                                                                                   |  |
| Savin et al. (2024) <sup>8</sup>     | 5-ARI    | 1: 26 (50)<br>2: 28 (38)<br>3: 6 (12)<br>4+: 0 (0)     | 0.71 | -                                           | - | -          | 15 (29%)    | 28 (54%)    | 9 (17%)                                   | 0.69  | -                                                                                                   |  |
|                                      | No 5-ARI | 1: 240 (44)<br>2: 209 (38)<br>3: 76 (14)<br>4+: 23 (4) |      | -                                           | - | -          | 130 (24%)   | 308 (56%)   | 110 (20%)                                 |       | -                                                                                                   |  |

(Continued)

TABLE 2. (Continued)

| Study                                   | Group    | Lesions                                                                                  |       | PIRADS (n, %)                           |   |         | mpMRI sequences (T2, DWI, ADC) findings                                                                                                                                                                                                                                                              |
|-----------------------------------------|----------|------------------------------------------------------------------------------------------|-------|-----------------------------------------|---|---------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                         |          | Number (n, %)                                                                            | p     | Volume (cc) (mean ± SD or median + IQR) | p | < /= 2  |                                                                                                                                                                                                                                                                                                      |
| Aksu et al. (2024) <sup>16</sup>        | 5-ARI    | -                                                                                        | -     | -                                       | - | -       | <ul style="list-style-type: none"><li>Decreased CE of lesions (worst DWI visibility)</li><li>PIRADS4: 53.90%</li><li>PIRADS5: 77.80%</li></ul>                                                                                                                                                       |
|                                         | No 5-ARI | -                                                                                        | -     | -                                       | - | -       |                                                                                                                                                                                                                                                                                                      |
| Wang et al. (2023) <sup>17</sup>        | 5-ARI    | Index lesion: 0: 3 (5.55) 1: 34 (63.0) 2: 12 (22.2%) 3: 3 (5.55) 4: 1 (1.85) 5: 1 (1.85) | 0.347 | -                                       | - | 3 (5.5) | 0.255                                                                                                                                                                                                                                                                                                |
|                                         | No 5-ARI | Index lesion: 0: 18 (6.06) 1: 186 (62.6) 2: 69 (23.2) 3: 19 (6.39) 4: 5 (1.68) 5: 0 (0)  | -     | -                                       | - | 27 (9)  |                                                                                                                                                                                                                                                                                                      |
| Starobinets et al. (2017) <sup>10</sup> | 5-ARI    | -                                                                                        | -     | ROI size 0.32 ± 0.26                    | - | -       | <ul style="list-style-type: none"><li>Lower PCa/BPH contrast in T2w</li><li>Higher LR PCa/BPH contrast in DCE and DWI</li><li>Lower variability in functional imaging measures</li><li>Potential misdiagnosis of GS 3 + 3 lesion as HG PCa due to higher conspicuity at functional imaging</li></ul> |
|                                         | No 5-ARI | -                                                                                        | -     | ROI size 0.40 ± 0.33                    | - | -       |                                                                                                                                                                                                                                                                                                      |

(Continued)

TABLE 2. (Continued)

increase (12%) in the placebo group on T2-weighted images, but also in the functional mpMRI sequences.

Starobinets et al. investigated whether 5-ARIs affect the ability to distinguish low-grade PCa from benign tissue on mpMRI. They found no statistically significant differences in the size of both benign and malignant ROIs between the untreated and 5-ARI-treated groups ( $p = 0.24$  and  $p = 0.58$ , respectively). However, they observed better separation between benign and cancerous tissues in the treated group on ADC and Diffusion-Weighted Imaging (DWI) sequences. The ROC AUC values for distinguishing benign from malignant tissues were consistently higher in the 5-ARI group, except for T2-weighted images. The increased uniformity of benign prostatic tissue in the 5-ARI group provides a more consistent background, potentially improving the detection of malignant lesions.<sup>10</sup>

The heterogeneity observed across studies likely reflects several sources of variability, including differences in treatment duration, variability in MRI protocol standardization, reader expertise, and differences in cancer grade distribution. In particular, studies focusing on GS 3 + 3 populations demonstrated different imaging behaviour than those including higher-grade cancers, which may partly explain conflicting ADC and T2-weighted results.

## Effect of 5-ARI on PI-RADS Distribution

Regarding PIRADS classification, the effect of 5-ARIs has been analyzed in recent studies (results are summarized in Table 2). Most of them report no significant difference in PI-RADS lesion distribution. Morote et al.,<sup>5</sup> in a retrospective case-control study, observed similar distributions of PI-RADS categories between untreated patients and 5-ARI users ( $p = 0.238$ ). Furthermore, they found no significant differences in the detection rates of csPCa and iPCa across PI-RADS categories. Similar findings were reported by Savin et al. in a retrospective study.<sup>8</sup> They found no significant difference in PIRADS distribution ( $p = 0.69$ ) or in targeted csPCa detection ( $p = 1$ ). Although a  $p$ -value of 1.00 is relatively uncommon, it may occur when outcome distributions between groups are virtually identical, particularly when exact statistical tests are applied.

In a multicentre cohort study, Falagario et al.<sup>6</sup> observed higher rates of high-grade PCa in the 5-ARI group, but most were identified as PIRADS 4 and 5 lesions. They concluded that exposure to 5-ARIs does not affect the association between PIRADS score and csPCa. However, in treated patients, ADC metrics

were less effective in distinguishing between benign and malignant lesions (both csPCa and non-csPCa).

Similarly, Giganti et al.,<sup>12</sup> in a randomized study involving men with a diagnosis of low-grade PCa, the effect of 6-month therapy with dutasteride. They observed that all lesions remained visible at six months, but with some differences in imaging sequences. While 5-ARI exposure did not significantly influence T2-weighted images, they found notable changes in conspicuity—defined as the mean ADC of the peripheral zone divided by the mean ADC of the tumor—as well as in DWI and ADC sequences. These included a decrease in mean tumor conspicuity ( $p = 0.013$ ), a decrease in signal intensity on DWI ( $p = 0.039$ ), and an increase in tumor ADC ( $p = 0.048$ ). It is important to note that peripheral zone tumors were overrepresented, which may explain the observed reduction in ADC.

In contrast, Aksu et al. reported that 5-ARI intake may affect lesion characteristics on mpMRI and PI-RADS distribution. They found a significantly higher number of patients with PIRADS 3 lesions in the 5-ARI group compared to controls (31.1% vs. 20.6%,  $p = 0.009$ ), as well as a higher detection rate in patients with PIRADS 4 lesions (53.9% vs. 32%,  $p = 0.031$ ).<sup>16</sup>

Likewise, Wang et al. found no difference in PIRADS lesion distributions between the two groups, but 5-ARI patients had a lower rate of PCa detection across all PIRADS categories (46.3% in the 5-ARI group vs. 68.0% in the control group— $p < 0.01$ ). This finding suggests that 5-ARI use may confound MRI findings.<sup>17</sup>

## Impact on mpMRI Sensitivity and Specificity

Tables 3 and 4 present a comparative analysis of several studies evaluating prostate cancer detection methods, specifically focusing on the performance of PI-RADS scores  $\geq 4$ .

In general, sensitivity tends to be higher than specificity in most studies. For instance, Morote et al. (2024) reported a sensitivity of 96% and specificity of 50% in the 5-ARI group, compared to 86.66% sensitivity and 97.70% specificity in the non-5-ARI group.<sup>5</sup>

The impact of 5-ARI on detection performance is inconsistent across studies. Some, like Kim et al. (2019), show improved performance with 5-ARI use (sensitivity 82.60%, specificity 84.21%, accuracy 83.75% for 5-ARI vs. 71.72%, 45.36%, and 51.76% respectively for non-5-ARI).<sup>15</sup> However, others like

| TABLE 3. csPCa detection                |       |                         |                        |                      |                      |                  |                                                                                                                                                                        |
|-----------------------------------------|-------|-------------------------|------------------------|----------------------|----------------------|------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Study                                   | Group | PCa detection N, %      |                        | ISUP GG N, %         |                      |                  | Association measures for csPCa (OR, IC95%)                                                                                                                             |
|                                         |       | csPCa                   | iPCa                   | 3                    | 4                    | 5                |                                                                                                                                                                        |
| Morote et al.<br>(2024) <sup>5</sup>    | 5-ARI | 50 (52.6)               | 15 (37.5)              | 10 (15.4)            | 15 (23.1)            | 12 (18.5)        | –                                                                                                                                                                      |
|                                         |       | • PIRADS3 2/20 (10)     | • PIRADS3 3/20 (15)    |                      |                      |                  |                                                                                                                                                                        |
|                                         |       | • PIRADS4 26/56 (46.4)  | • PIRADS4 10/56 (17.9) |                      |                      |                  |                                                                                                                                                                        |
|                                         |       | • PIRADS5 22/27 (81.5)  | • PIRADS5 1/27 (3.7)   |                      |                      |                  |                                                                                                                                                                        |
| No 5-ARI                                |       | 45 (47.4)               | 25 (62.5)              | 12 (17.1)            | 8 (11.4)             | 7 (10)           | –                                                                                                                                                                      |
|                                         |       | • PIRADS3 3/14 (21.4)   | • PIRADS3 1/14 (7.1)   |                      |                      |                  |                                                                                                                                                                        |
|                                         |       | • PIRADS4 16/56 (28.6)  | • PIRADS4 18/56 (32.1) |                      |                      |                  |                                                                                                                                                                        |
|                                         |       | • PIRADS5 23/30 (76.7)  | • PIRADS5 5/30 (16.7)  |                      |                      |                  |                                                                                                                                                                        |
| Falagario et al.<br>(2023) <sup>6</sup> | 5-ARI | 276 (39.1)              | 114 (16.2)             | 65 (9.2)             | 47 (6.7)             | 48 (6.8)         | Multivariable logistic regression<br>1.05 (0.6–1.84)                                                                                                                   |
|                                         |       | • PIRADS3 30 (19)       | • PIRADS3 32 (20.2)    |                      |                      |                  |                                                                                                                                                                        |
|                                         |       | • PIRADS4 114 (44.1)    | • PIRADS4 52 (20.2)    |                      |                      |                  |                                                                                                                                                                        |
|                                         |       | • PIRADS5 115 (77.7)    | • PIRADS5 18 (12.2)    |                      |                      |                  |                                                                                                                                                                        |
| No 5-ARI                                |       | 2718 (39.3)             | 1295 (18.7)            | 608 (8.8)            | 468 (6.8)            | 225 (3.3)        | • PIRADS5 1.06 (0.98–1.15)                                                                                                                                             |
|                                         |       | • PIRADS3 358 (20.3)    | • PIRADS3 383 (20.6)   |                      |                      |                  |                                                                                                                                                                        |
|                                         |       | • PIRADS4 1282 (43.5)   | • PIRADS4 630 (21.4)   |                      |                      |                  |                                                                                                                                                                        |
|                                         |       | • PIRADS5 971 (73.4)    | • PIRADS5 176 (13.3)   |                      |                      |                  |                                                                                                                                                                        |
| Kim et al.<br>(2019) <sup>15</sup>      | 5-ARI | 23 (28.8)               | 57 (713)               | Biopsy:<br>7 (24.1)  | Biopsy:<br>10 (34.5) |                  | Univariate logistic regression                                                                                                                                         |
|                                         |       | • PIRADS 3 2 (6.7)      |                        | RP: 9                | RP: 3                |                  |                                                                                                                                                                        |
|                                         |       | • PIRADS ≥ 4 19 (67.9)  |                        | (47.4)               | (15.8)               |                  |                                                                                                                                                                        |
|                                         |       |                         |                        |                      |                      |                  |                                                                                                                                                                        |
| No 5-ARI                                |       | 152 (24.3)              | 474 (75.7)             | Biopsy:<br>31 (13.6) | Biopsy:<br>49 (21.5) | RP: 14<br>(10.9) | • Age 1.062 (1.035–1.090)<br>• PSA 1.062 (1.034–1.095)<br>• Prostate volume 0.956 (0.943–0.970)<br>• PIRADS 3: 1.315 (0.666–2.593)<br>• PIRADS 4: 5.528 (3.017–10.130) |
|                                         |       | • PIRADS3 28 (13)       |                        |                      |                      |                  |                                                                                                                                                                        |
|                                         |       | • PIRADS ≥ 4 109 (42.1) |                        |                      |                      |                  |                                                                                                                                                                        |
|                                         |       |                         |                        |                      |                      |                  |                                                                                                                                                                        |

TABLE 3. (Continued)

| Study                            | Group    | PCa detection N, %          |          | ISUP GG N, % |   |   | Association measures for csPCa (OR, IC95%) |   |
|----------------------------------|----------|-----------------------------|----------|--------------|---|---|--------------------------------------------|---|
|                                  |          | csPCa                       | iPCa     | 3            | 4 | 5 |                                            |   |
| Savin et al. (2024) <sup>8</sup> | 5-ARI    | Overall 23 (44)             | 7 (13)   | -            | - | - |                                            | - |
|                                  |          | Targeted 16 (31)            |          |              |   |   |                                            |   |
|                                  |          | • PIRADS 3: 1 (6)           |          |              |   |   |                                            |   |
|                                  |          | • PIRADS 4: 7 (25)          |          |              |   |   |                                            |   |
|                                  |          | • PIRADS 5: 8 (89)          |          |              |   |   |                                            |   |
|                                  | No 5-ARI | Overall 188 (34)            | 165 (30) | -            | - | - |                                            | - |
|                                  |          | Targeted 166 (30)           |          |              |   |   |                                            |   |
|                                  |          | • PIRADS 3: 8 (6)           |          |              |   |   |                                            |   |
|                                  |          | • PIRADS 4: 87 (28)         |          |              |   |   |                                            |   |
|                                  |          | • PIRADS 5: 71 (65)         |          |              |   |   |                                            |   |
| Aksu et al. (2024) <sup>16</sup> | 5-ARI    | Malignancy detection rate   |          |              |   |   |                                            |   |
|                                  |          | 33 (47.1)                   |          |              |   |   |                                            |   |
|                                  |          | • PIRADS3: 19.30%           |          |              |   |   |                                            |   |
|                                  |          | • PIRADS4: 53.90%           |          |              |   |   |                                            |   |
|                                  |          | • PIRADS5: 77.80%           |          |              |   |   |                                            |   |
|                                  | No 5-ARI | Malignancy detection rate   |          |              |   |   |                                            |   |
|                                  |          | 174 (48.5)                  |          |              |   |   |                                            |   |
|                                  |          | • PIRADS3: 36.50%           |          |              |   |   |                                            |   |
|                                  |          | • PIRADS4: 32.00%           |          |              |   |   |                                            |   |
|                                  |          | • PIRADS5: 71.90%           |          |              |   |   |                                            |   |
| Wang et al. (2023) <sup>17</sup> | 5-ARI    | All PCa 46.3%               |          |              |   |   |                                            |   |
|                                  |          | <6 mo: 5 (31.3)             |          |              |   |   |                                            |   |
|                                  |          | 6–12 mo: 2 (25)             |          |              |   |   |                                            |   |
|                                  |          | >12 mo: 17 (63)             |          |              |   |   |                                            |   |
|                                  |          | csPCa 31.5%                 |          |              |   |   |                                            |   |
|                                  | No 5-ARI | • PIRADS3: 2 (8.7) (26)     |          |              |   |   |                                            |   |
|                                  |          | • PIRADS4: 10 (47.6) (9.5)  |          |              |   |   |                                            |   |
|                                  |          | • PIRADS5: 5 (71.5) (9.5)   |          |              |   |   |                                            |   |
|                                  |          | <6 mo: 2 (12.5)             |          |              |   |   |                                            |   |
|                                  |          | 6–12 mo: 0 (0)              |          |              |   |   |                                            |   |
|                                  | 5-ARI    | >12 mo: 14 (51.9)           |          |              |   |   |                                            |   |
|                                  |          | csPCa 31.5%                 |          |              |   |   |                                            |   |
|                                  |          | • PIRADS3: 2 (8.7) (26)     |          |              |   |   |                                            |   |
|                                  |          | • PIRADS4: 10 (47.6) (9.5)  |          |              |   |   |                                            |   |
|                                  |          | • PIRADS5: 5 (71.5) (9.5)   |          |              |   |   |                                            |   |
|                                  | No 5-ARI | <6 mo: 2 (12.5)             |          |              |   |   |                                            |   |
|                                  |          | 6–12 mo: 0 (0)              |          |              |   |   |                                            |   |
|                                  |          | >12 mo: 14 (51.9)           |          |              |   |   |                                            |   |
|                                  |          | csPCa 45.5%                 |          |              |   |   |                                            |   |
|                                  |          | • PIRADS3: 18 (20.4) (22.7) |          |              |   |   |                                            |   |
|                                  | 5-ARI    | • PIRADS4: 82 (56.6)        |          |              |   |   |                                            |   |
|                                  |          | • PIRADS5: 31 (83.8) (24.8) |          |              |   |   |                                            |   |
|                                  |          | All Pca 68%                 |          |              |   |   |                                            |   |
|                                  |          | • PIRADS3: 20 (22.7)        |          |              |   |   |                                            |   |
|                                  |          | • PIRADS4: 36 (24.8)        |          |              |   |   |                                            |   |
|                                  | No 5-ARI | PIRAD55: 5 (13.5)           |          |              |   |   |                                            |   |
|                                  |          | csPCa 45.5%                 |          |              |   |   |                                            |   |
|                                  |          | • PIRADS3: 18 (20.4) (22.7) |          |              |   |   |                                            |   |
|                                  |          | • PIRADS4: 82 (56.6)        |          |              |   |   |                                            |   |
|                                  |          | • PIRADS5: 31 (83.8) (24.8) |          |              |   |   |                                            |   |

| TABLE 3. (Continued)                                                                                                                                                                                                                                                                                                                                                                                                                  |          |                    |      |              |         |                                                                                                                                                                                                                                                                         |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|--------------------|------|--------------|---------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Study                                                                                                                                                                                                                                                                                                                                                                                                                                 | Group    | PCa detection N, % |      | ISUP GG N, % |         |                                                                                                                                                                                                                                                                         |
|                                                                                                                                                                                                                                                                                                                                                                                                                                       |          | csPCa              | iPCa | 3            | 4       | 5                                                                                                                                                                                                                                                                       |
| Obinata et al. (2022) <sup>7</sup>                                                                                                                                                                                                                                                                                                                                                                                                    | 5-ARI    | GS ≥ 832 (61.5)    |      | –            | –       | –                                                                                                                                                                                                                                                                       |
|                                                                                                                                                                                                                                                                                                                                                                                                                                       |          |                    |      |              |         | Univariate logistic regression<br>• Age 1.07 (1.040–1.187)<br>• PSA 1.05 (1.009–1.096)<br>• Prostate volume 6.75 (2.036–22.38)<br>Multivariable logistic regression<br>• Age 1.089 (1.012–1.171)<br>• PSA 1.026 (0.977–1.077)<br>• Prostate volume 5.681 (1.614–19.996) |
| Purysko et al. (2021) <sup>13</sup>                                                                                                                                                                                                                                                                                                                                                                                                   | No 5-ARI | GS ≥ 827 (42.1)    |      | –            | –       | –                                                                                                                                                                                                                                                                       |
|                                                                                                                                                                                                                                                                                                                                                                                                                                       | 5-ARI    |                    | –    | 7 (11.9)     | 1 (1.7) | 3 (5.1)                                                                                                                                                                                                                                                                 |
|                                                                                                                                                                                                                                                                                                                                                                                                                                       | No 5-ARI |                    | –    | 3 (5.1)      | 4 (6.8) | 0 (0.0)                                                                                                                                                                                                                                                                 |
|                                                                                                                                                                                                                                                                                                                                                                                                                                       |          |                    |      |              |         |                                                                                                                                                                                                                                                                         |
| Note. 5-ARI (5-alpha reductase inhibitors), CI (confidence interval), csPCa (clinically significant prostate cancer), GS (Gleason score), iPCa (indolent prostate cancer), ISUP GG (grade group of International Society of Urological Pathology), OR (odds ratio), PIRADS (Prostate Imaging Reporting and Data System), PSA (Prostate Specific Antigen), RP (radical prostatectomy). The sign “–” is used when data are unavailable. |          |                    |      |              |         |                                                                                                                                                                                                                                                                         |

TABLE 4. Sensibility, specificity and accuracy rates

| Study                                | Group           | Se (%) | Sp (%) | PPV (%) | NPV (%) | Accuracy (%) |
|--------------------------------------|-----------------|--------|--------|---------|---------|--------------|
| Morote et al. (2024) <sup>5</sup>    | 5-ARI           | 96     | 50     | 57.83   | 94.56   | 69.16        |
|                                      | PIRADS $\geq$ 4 |        |        |         |         |              |
|                                      | No 5-ARI        | 86.66  | 97.7   | 45.34   | 99.7    | 97.46        |
| Falagario et al. (2023) <sup>6</sup> | PIRADS $\geq$ 4 |        |        |         |         |              |
|                                      | 5-ARI           | 82.97  | 58.74  | 56.4    | 84.28   | 68.23        |
|                                      | PIRADS $\geq$ 4 |        |        |         |         |              |
|                                      | 5-ARI           | 93.84  | 28.9   | 45.92   | 87.94   | 54.33        |
|                                      | PIRADS $\geq$ 3 |        |        |         |         |              |
|                                      | No 5-ARI        | 82.89  | 51.9   | 52.75   | 82.4    | 64.08        |
| Kim et al. (2019) <sup>15</sup>      | PIRADS $\geq$ 4 |        |        |         |         |              |
|                                      | No 5-ARI        | 96.06  | 18.38  | 43.26   | 87.81   | 48.92        |
|                                      | PIRADS $\geq$ 4 |        |        |         |         |              |
|                                      | No 5-ARI        | 82.6   | 84.21  | 67.86   | 92.3    | 83.75        |
| Savin et al. (2024) <sup>8</sup>     | PIRADS $\geq$ 4 |        |        |         |         |              |
|                                      | No 5-ARI        | 71.72  | 45.36  | 29.62   | 83.33   | 51.76        |
|                                      | PIRADS $\geq$ 4 |        |        |         |         |              |
|                                      | No 5-ARI        | 65.21  | 24.13  | 40.54   | 46.66   | 42.30        |
| Aksu et al. (2024) <sup>16</sup>     | PIRADS $\geq$ 4 |        |        |         |         |              |
|                                      | No 5-ARI        | 84.04  | 27.78  | 37.79   | 76.92   | 47.08        |
|                                      | PIRADS $\geq$ 4 |        |        |         |         |              |
| Wang et al. (2023) <sup>17</sup>     | 5-ARI           | 84.9   | 56.8   | –       | –       | –            |
|                                      | No 5-ARI        | 56.4   | 79.7   | –       | –       | –            |
|                                      | 5-ARI           | 88.23  | 64.86  | 53.57   | 92.3    | 72.22        |
|                                      | PIRADS $\geq$ 4 |        |        |         |         |              |
| Purysko et al. (2021) <sup>13</sup>  | No 5-ARI        | 83.7   | 57.41  | 62.09   | 80.87   | 69.36        |
|                                      | PIRADS $\geq$ 4 |        |        |         |         |              |
|                                      | 5-ARI           | 88     | 43     | –       | –       | –            |
| Purysko et al. (2021) <sup>13</sup>  | No 5-ARI        | 96     | 26     | –       | –       | –            |
|                                      | PIRADS $\geq$ 4 |        |        |         |         |              |

Note. 5-ARI (5-alpha reductase inhibitors), PIRADS (Prostate Imaging Reporting and Data System), PPV (positive predictive value), NPV (negative predictive value), Se (sensitivity), Sp (specificity). The sign “–” is used when data are unavailable.

Savin et al. (2024) show lower performance in the 5-ARI group.<sup>8</sup>

Accuracy rates also vary widely, ranging from around 42% to 97% across different studies and patient groups. The highest accuracy reported was by Morote et al. (2024) in the non-5-ARI group at 97.46%, while the lowest was by Savin et al. (2024) in the 5-ARI group at 42.30%.

Overall, a consistent pattern emerges while sensitivity tends to increase modestly in 5-ARI users, specificity often decreases. This may reflect improved conspicuity of malignant tissue on diffusion-based sequences but increased homogeneity of benign tissue, which may lead to higher false-positive rates.

## Effect on Local Staging

There is currently no direct evidence that 5-ARIs alter the ability of mpMRI to detect extraprostatic extension (EPE) features. While the impact of 5-ARIs on overall MRI performance has been analyzed, no studies have specifically reported changes in the visibility of capsular bulging, irregular margins or other typical signs of extraprostatic extension. Similarly, there are no data suggesting that 5-ARI therapy impairs the detection of Seminal Vesicle Invasion (SVI). In conclusion, although 5-ARIs may reduce diffusion-weighted signal intensity—potentially complicating lesion classification—they do not appear to degrade anatomical definition. However, due to the influence of 5-ARI on prostatic tissue, especially prostate

TABLE 5. Summary of the main findings of the studies

| Aspect                               | Effect of 5-ARIs                                                                                                                                                 | Implications                                                                                                                 |
|--------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------|
| Prostatic tissue                     | <ul style="list-style-type: none"><li>• Glandular atrophy</li><li>• Increased stroma/epithelium ratio</li><li>• Reduction in prostate volume</li></ul>           | <ul style="list-style-type: none"><li>• Possible alteration of benign and malignant tissue appearance on MRI</li></ul>       |
| T2-weighted imaging                  | <ul style="list-style-type: none"><li>• Conflicting results</li><li>• Possible reduction in lesion visibility</li></ul>                                          | <ul style="list-style-type: none"><li>• Potential difficulty in distinguishing between benign and malignant tissue</li></ul> |
| Diffusion-weighted imaging (DWI)     | <ul style="list-style-type: none"><li>• Increased uniformity of benign tissue</li><li>• Possible improvement in cancer visibility</li></ul>                      | <ul style="list-style-type: none"><li>• Potential improvement in PCa detection</li></ul>                                     |
| Apparent Diffusion Coefficient (ADC) | <ul style="list-style-type: none"><li>• Possible reduction in the ability to discriminate between benign and malignant lesions</li></ul>                         | <ul style="list-style-type: none"><li>• Potential increase in false positives or negatives</li></ul>                         |
| PI-RADS distribution                 | <ul style="list-style-type: none"><li>• Most studies report no significant differences</li><li>• Some studies suggest an increase in PI-RADS 3 lesions</li></ul> | <ul style="list-style-type: none"><li>• Generally does not influence PI-RADS categorization</li></ul>                        |
| MRI sensitivity                      | <ul style="list-style-type: none"><li>• Conflicting results</li><li>• Some studies report an increase</li></ul>                                                  | <ul style="list-style-type: none"><li>• Potential improvement in PCa detection</li></ul>                                     |
| MRI specificity                      | <ul style="list-style-type: none"><li>• Conflicting results</li><li>• Some studies report a decrease</li></ul>                                                   | <ul style="list-style-type: none"><li>• Possible increase in false positives</li></ul>                                       |
| Local staging                        | <ul style="list-style-type: none"><li>• Limited data</li><li>• Possible underestimation of tumor extent due to prostate volume reduction</li></ul>               | <ul style="list-style-type: none"><li>• Need for caution in evaluating extraprostatic extension</li></ul>                    |
| Treatment duration                   | <ul style="list-style-type: none"><li>• More evident effects with long-term use (&gt;6 months)</li></ul>                                                         | <ul style="list-style-type: none"><li>• Importance of considering treatment duration in interpretation</li></ul>             |

Note. 5-ARI (5-alpha reductase inhibitors), MRI (magnetic resonance imaging), PCa (prostate cancer).

shrinkage, there is a risk of underestimating local tumor extent, particularly in cases of subtle EPE.

Discussion

The influence of 5-ARIs on prostate tissue and mpMRI imaging remains a complex and evolving area of study. Table 5 schematically summarizes the main results of the studies. Evidence suggests that 5-ARI therapy induces histological changes—such as glandular atrophy and epithelial shrinkage—which may alter the imaging characteristics of both benign and malignant prostatic tissues. These changes can enhance the uniformity of the benign background on MRI, potentially improving cancer conspicuity, particularly on DWI and ADC maps. However, the effect on T2-weighted sequences appears less consistent, with some studies reporting reduced lesion visibility. Discrepancies in the literature regarding the impact of 5-ARIs on PI-RADS distribution and detection rates of csPCa may be attributed to heterogeneous study populations, variations in exposure duration, and differences in imaging protocols. While

some studies suggest improved sensitivity in 5-ARI-treated patients, others report potential confounding effects or reduced specificity. Importantly, the impact of 5-ARI exposure on local staging features—such as capsular bulging or seminal vesicle invasion—has not been definitively characterized. Although no evidence currently suggests that 5-ARIs impair anatomical resolution on mpMRI, the risk of underestimating tumor extent due to prostate shrinkage remains a concern. Moreover, in several cohorts, patients presented with a suspicious Digital Rectal Examination (DRE). This clinical finding likely identifies a subgroup of men with a higher baseline probability of csPCa. Importantly, none of the available studies stratified results according to validated risk calculators, making it difficult to distinguish how much of the observed csPCa detection is attributable to mpMRI performance versus underlying clinical risk. Beyond imaging appearance, the influence of 5-ARI therapy extends to diagnostic performance metrics. A recurring pattern across studies suggests that sensitivity for csPCa detection may increase modestly in treated patients, whereas specificity

tends to decrease. This may reflect improved lesion conspicuity against a more homogeneous background, coupled with reduced diffusion contrast between benign and malignant tissues, leading to higher false-positive rates. However, the magnitude of these changes varies widely, and no consistent directional effect can be conclusively established.

Importantly, the clinical implications of these findings go beyond radiological interpretation and directly affect biopsy decision-making. In daily practice, the indication for prostate biopsy is frequently guided by multivariable risk calculators, most notably the Stichting Wetenschappelijk Onderzoek Prostaatkanker (SWOP) Prostate Cancer Risk Calculator, derived from the European Randomized Study of Screening for Prostate Cancer (ERSPC) cohorts. These tools integrate PSA, digital rectal examination, prostate volume, and—in updated versions—mpMRI findings. However, they do not incorporate 5-ARI exposure as an independent variable.<sup>18,19</sup>

This omission may represent a structural limitation. It is well established that 5-ARI therapy reduces serum PSA levels by approximately 50% after six months of treatment.<sup>4,20</sup> This effect has been confirmed in more recent studies, which highlight significant interindividual variability in PSA suppression and raise concerns about the reliability of empirical correction factors in clinical practice.<sup>21,22</sup> Although clinicians often compensate by doubling PSA values in treated patients, this empirical correction assumes a uniform biological response and does not account for interindividual variability. Moreover, prostate shrinkage induced by 5-ARIs may alter PSA density calculations, potentially influencing risk stratification. A reduction in gland volume without proportional tumor regression may artificially increase PSA density, whereas marked PSA suppression may lower calculated cancer probability. Consequently, the estimated risk of csPCa may reflect pharmacological modulation rather than intrinsic tumor biology.

When mpMRI findings are integrated into risk calculators, the potential for compounded bias arises. This issue becomes particularly relevant in the contemporary MRI-driven diagnostic pathway. Studies evaluating MRI-based diagnostic strategies have demonstrated that the integration of imaging findings into predictive models significantly alters biopsy decision-making.<sup>23–25</sup> In this context, any pharmacological factor affecting both PSA levels and MRI appearance—such as 5-ARI therapy—may introduce

a dual-layer bias that is currently not accounted for in available risk calculators. If 5-ARI therapy modifies both PSA dynamics and diffusion-based imaging parameters, then both biochemical and radiological components of prediction models may be simultaneously affected. Currently, no prospective recalibration of commonly used risk calculators has been performed specifically in populations stratified by 5-ARI exposure. Therefore, clinicians should interpret calculated probabilities cautiously in long-term 5-ARI users, particularly when imaging findings are equivocal.

Reduced prostate volume, which commonly occurs in men treated with 5-ARIs, may theoretically enhance targeted biopsy accuracy by decreasing sampling error and improving needle trajectory precision. This represents an additional methodological limitation and may contribute to the variability observed across studies.

Histological patterns should be considered: cribriform architecture, which is less conspicuous on mpMRI, may be underdetected in both treated and untreated patients.<sup>26</sup> Whether 5-ARI-induced tissue remodelling further influences the detection of such variants remains unclear and warrants further study.

Recent evidence also supports the potential role of Prostate-Specific Membrane Antigen (PSMA)-based imaging as a complementary tool in patients in whom mpMRI performance may be uncertain. Unlike diffusion and T2-weighted MRI signals, which may be variably affected by 5-ARI-induced stromal remodeling, PSMA uptake reflects a molecular phenotype that is not influenced by prostate shrinkage or epithelial atrophy. In this context, the prospective study by Pepe et al.<sup>27</sup> demonstrated that <sup>68</sup>Ga-PSMA PET/CT achieved higher diagnostic accuracy than mpMRI (83.3% vs. 70.2%) in men on active surveillance. Although the population did not specifically include 5-ARI users, these findings highlight the potential value of PET-PSMA as an adjunct modality when assessing the risk of csPCa in scenarios where mpMRI interpretation may be challenging.<sup>28–30</sup>

Despite the widespread use of 5-ARIs, current clinical guidelines and key studies do not address specific guidance on the interpretation of mpMRI findings in this patient population.

This study is not without limitations. The retrospective nature of this analysis may introduce a selection bias. Furthermore, the lack of a systematic methodology may reduce the comprehensiveness of the findings.

Further prospective studies are needed to better understand these findings and to support the development of an adjusted risk calculator that can more accurately guide clinical decision-making.

## Conclusions

Current evidence indicates that 5-ARIs induce histological and morphological alterations that can influence mpMRI interpretation. The variability in findings across studies highlights the need for caution in clinical decision-making, especially regarding PI-RADS distribution and staging accuracy.

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## Author Contributions

Arianna Tumminello contributed to project development, data collection, writing, and editing. Elisa Tonet and Giovanni Basso were involved in data collection and writing. Giuseppe Reitano, Felice Crocetto, Iliana Bednarova, Francesca Caumo, Matteo Todisco, Alberto Lauro, Carmelo Lacognata, Francesca Galupini, Giorgio De Conti, Giovanni Betto, Massimo Iafrate, Giacomo Novara, Fabrizio Dal Moro were involved in project development and supervision. Fabio Zattoni performed ideations, supervision, and editing. All authors reviewed and approved the final version of the manuscript.

## Availability of Data and Materials

Not applicable.

## Ethics Approval

Not applicable.

## Conflicts of Interest

The authors declare no conflicts of interest.

## References

1. Turkbey B, Rosenkrantz AB, Haider MA et al. Prostate imaging reporting and data system version 2.1: 2019 update of prostate imaging reporting and data system version 2. *Eur Urol* 2019;76(3):340–351. doi:10.1016/j.eururo.2019.02.033.
2. Ahmed HU, El-Shater Bosaily A, Brown LC et al. Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. *The Lancet* 2017;389:815–822. doi:10.1016/S0140-6736(16)32401-1.
3. EAU Guidelines. Edn. presented at the EAU annual congress London 2026. [cited 2026 Mar 25]. Available from: <https://uroweb.org/guidelines/prostate-cancer/chapter/citation-information>.
4. 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. doi:10.1056/nejmoa0908127.
5. Morote J, Picola N, Muñoz-Rodríguez J et al. Effect of 5-alpha reductase inhibitors on magnetic resonance imaging and prostate cancer detection. *Biomolecules* 2024;14(2):193. doi:10.3390/B10M14020193.
6. Falagario UG, Lantz A, Jambor I et al. Diagnosis of prostate cancer with magnetic resonance imaging in men treated with 5-alpha-reductase inhibitors. *World J Urol* 2023;41(11):2967–2974. doi:10.1007/S00345-023-04634-2.
7. Obinata D, Nakahara K, Yoshizawa T, Mochida J, Yamaguchi K, Takahashi S. Characteristics of prostate biopsy in patients under the dutasteride treatment. *Medicine* 2022;101(44):E31658. doi:10.1097/MD.00000000000031658.
8. Savin Z, Shem-Tov Dlugy A, Grinbaum M et al. Do 5-alpha reductase inhibitors influence the features of suspicious lesions on magnetic resonance imaging and targeted biopsy results for prostate cancer diagnosis?. *Diagnostics* 2024;14(22):2567. doi:10.3390/DIAGNOSTICS14222567.
9. Chung HT, Noworolski SM, Kurhanewicz J, Weinberg V, Roach M. A pilot study of endorectal magnetic resonance imaging and magnetic resonance spectroscopic imaging changes with dutasteride in patients with low risk prostate cancer. *BJU Int* 2011;108:4806. doi:10.1111/J.1464-410X.2010.10061.X.
10. Starobinets O, Kurhanewicz J, Noworolski SM. Improved multiparametric MRI discrimination between low-risk prostate cancer and benign tissues in a small cohort of 5 $\alpha$ -reductase inhibitor treated individuals as compared with an untreated cohort. *NMR Biomed* 2017;30(5):e3696. doi:10.1002/NBM.3696.
11. Iczkowski KA, Qiu J, Qian J et al. The dual 5-alpha-reductase inhibitor dutasteride induces atrophic changes and decreases relative cancer volume in human prostate. *Urology* 2005;65(1):76–82. doi:10.1016/j.urology.2004.08.042.
12. Giganti F, Moore CM, Robertson NL et al. MRI findings in men on active surveillance for prostate cancer: does dutasteride make MRI visible lesions less conspicuous? Results from a placebo-controlled, randomised clinical trial. *Eur Radiol* 2017;27(11):4767–4774. doi:10.1007/S00330-017-4858-0.
13. Puryrsko AS, Bullen J, Valdez R, Austhof E, D'ippolito G, Klein EA. Influence of 5-alpha reductase inhibitors on prostate cancer detection with magnetic resonance imaging: a matched

- cohort study. *J Urol* 2021;206(5):1139–1146. doi:10.1097/JU.0000000000001932.
14. Moore CM, Robertson NL, Jichi F et al. The effect of dutasteride on magnetic resonance imaging defined prostate cancer: MAPPED—a randomized, placebo controlled, double-blind clinical trial. *J Urol* 2017;197(4):1006–1013. doi:10.1016/J.JURO.2016.11.090.
  15. 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/S41598-019-54464-9.
  16. Aksu M, Oğuz U, Aslan S et al. The effect of 5-alpha reductase inhibitors on the detection of prostate cancer with multiparametric magnetic resonance imaging and prostate biopsy. *Croat Med J* 2024;65(5):417–423. doi:10.3325/CMJ.2024.65.417.
  17. Wang Z, Wang K, Ong HY, Tsang WC, Wu QH, Chiong E. 5-alpha reductase inhibitors and MRI prostates: actively reducing prostate sizes and ambiguity. *BMC Urol* 2023;23(1):61. doi:10.1186/S12894-023-01235-4.
  18. Roobol MJ, Van Vugt HA, Loebe S et al. Prediction of prostate cancer risk: the role of prostate volume and digital rectal examination in the ERSPC risk calculators. *Eur Urol* 2012;61(3):577–583. doi:10.1016/j.eururo.2011.11.012.
  19. Denijs FB, van Harten MJ, Meenderink JJL et al. Risk calculators for the detection of prostate cancer: a systematic review. *Prostate Cancer Prostatic Dis* 2024;27(3):544–557. doi:10.1038/s41391-024-00852-w.
  20. 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):215–224. doi:10.1056/nejmoa030660.
  21. Jirásko M, Viták R, Pecan L et al. Serum levels of prostate specific antigen, free PSA, [-2]proPSA, fPSA/tPSA ratio, Prostate Health Index, and glycosylation patterns of free PSA in patients with benign prostatic hyperplasia pharmacotherapy. *Prostate* 2025;85(1):65–72. doi:10.1002/pros.24801.
  22. Loloi J, Wei M, Babar M, Zhu D, Fram EB, Maria P. Rates of false-negative screening in prostate specific antigen secondary to 5-alpha reductase inhibitor usage: a quality-improvement initiative. *Int Braz J Urol* 2022;48(4):688–695. doi:10.1590/S1677-5538.IBJU.2022.0099.
  23. Hamm CA, Asbach P, Pöhlmann A et al. Oncological safety of MRI-informed biopsy decision-making in men with suspected prostate cancer. *JAMA Oncol* 2025;11(2):145–153. doi:10.1001/jamaoncol.2024.5497.
  24. Kamal O, Comerford J, Foster BR, Young DJ, Amling C, Coakley FV. Intermediate-term oncological outcomes after a negative endorectal coil multiparametric MRI of the prostate in patients without biopsy proven prostate cancer. *Clin Imaging* 2022;92(1):112–116. doi:10.1016/j.clinimag.2022.09.002.
  25. Moldovan PC, Van den Broeck T, Sylvester R et al. What is the negative predictive value of multiparametric magnetic resonance imaging in excluding prostate cancer at biopsy? A systematic review and meta-analysis from the european association of urology prostate cancer guidelines panel. *Eur Urol* 2017;72(2):250–266. doi:10.1016/j.eururo.2017.02.026.
  26. Carletti F, Maggi M, Fazekas T et al. Diagnostic accuracy of multiparametric MRI for detecting unconventional prostate cancer histology: a systematic review and meta-analysis. *Eur Radiol* 2026;36(1):17–29. doi:10.1007/s00330-025-11603-3.
  27. Pepe P, Pepe L, Tamburo M et al. <sup>68</sup>Ga-PSMA PET/CT evaluation in men enrolled in prostate cancer Active Surveillance. *Arch Ital Urol Androl* 2023;95:31–34. doi:10.4081/aiua.2023.11322.
  28. Uprimny C, Kroiss AS, Decristoforo C et al. <sup>68</sup>Ga-PSMA-11 PET/CT in primary staging of prostate cancer: PSA and Gleason score predict the intensity of tracer accumulation in the primary tumour. *Eur J Nucl Med Mol Imaging* 2017;44(6):941–949. doi:10.1007/s00259-017-3631-6.
  29. Privé BM, Israël B, Schilham MGM et al. Evaluating F-18-PSMA-1007-PET in primary prostate cancer and comparing it to multi-parametric MRI and histopathology. *Prostate Cancer Prostatic Dis* 2021;24(2):423–430. doi:10.1038/s41391-020-00292-2.
  30. Perera M, Papa N, Roberts M et al. Gallium-68 prostate-specific membrane antigen positron emission tomography in advanced prostate cancer—updated diagnostic utility, sensitivity, specificity, and distribution of prostate-specific membrane antigen-avid lesions: a systematic review and meta. *Eur Urol* 2020;77(4):403–417. doi:10.1016/j.eururo.2019.01.049.