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Research Article

Multiparametric magnetic resonance imaging and clinical variables: Which is the best combination to predict reclassification in active surveillance patients?

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ABSTRACT

Introduction & objectives: We tested the role of multiparametric magnetic resonance imaging (mpMRI) in disease reclassification and whether the combination of mpMRI and clinicopathological variables could represent the most accurate approach to predict the risk of reclassification during active surveillance.

Materials & methods: Three-hundred eighty-nine patients (pts) underwent mpMRI and subsequent confirmatory or follow-up biopsy according to the Prostate Cancer Research International Active Surveillance (PRIAS) protocol. Pts with negative (−) mpMRI underwent systematic random biopsy. Pts with positive (+) mpMRI [Prostate Imaging Reporting and Data System, version 2 (PI-RADS-V2) score ≥3] underwent targeted + systematic random biopsies. Multivariate analyses were used to create three models predicting the probability of reclassification [International Society of Urological Pathology ≥ Grade Group 2 (GG2)]: a basic model including only clinical variables (age, prostate-specific antigen density, and number of positive cores at baseline), an Magnetic resonance imaging (MRI) model including only the PI-RADS score, and a full model including both the previous ones. The predictive accuracy (PA) of each model was quantified using the area under the curve.

Results: mpMRI negative (−) was recorded in 127 (32.6%) pts; mpMRI positive (+) was recorded in 262 pts: 72 (18.5%) had PI-RADS 3, 150 (38.6%) PI-RADS 4, and 40 (10.3%) PI-RADS 5 lesions. At a median follow-up of 12 months, 125 pts (32%) were reclassified to GG2 prostate cancer. The rate of reclassification to GG2 prostate cancer was 17%, 35%, 38%, and 52% for mpMRI (−), PI-RADS 3, 4, and 5, respectively ($P < 0.001$). The PA was 69% and 64% in the basic and MRI models, respectively. The full model had the best PA of 74%: older age ($P = 0.023$; Odds ratio (OR) = 1.040), prostate-specific antigen density ($P = 0.037$; OR = 1.324), number of positive cores at baseline ($P = 0.001$; OR = 1.441), and PI-RADS 3, 4, and 5 (overall $P = 0.001$; OR = 2.458, 3.007, and 3.898, respectively) were independent predictors of reclassification.

Conclusions: Disease reclassification increased according to the PI-RADS score increase, at confirmatory or follow-up biopsy. However, a no-negligible rate of reclassification was found also in cases of mpMRI

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(−). The combination of mpMRI and clinicopathological variables still represents the most accurate approach to pts on active surveillance.

1. Introduction

Active surveillance (AS) is a therapeutic strategy based on close monitoring of cancer and its active treatment when it shows signs of progression. AS is nowadays considered a safe option for men with low-grade prostate cancer (PCa) and is becoming progressively the gold standard in International Society of Urological Pathology (ISUP) Grade Group 1 (GG1) patients (pts), as suggested by different international guidelines [1,2]. The identification of best candidates for AS is crucial. Indeed, an important limitation to AS is the significant proportion of GG1 pts harboring more aggressive disease, which is undetected by initial biopsies [3,4]. Therefore, the diagnostic strategy to identify low-risk diseases is pivotal to reduce overtreatment and taking care of those pts with progressive disease without losing the curability window.

For this reason, AS programs recommend strict follow-up with digital rectal examination, serial prostate-specific antigen (PSA) measurements, and surveillance biopsies to avoid tumor progression misdiagnosis [5]. However, repeated biopsies are burdened by the risk of complications such as infections or bleeding and thus may invalidate the follow-up compliance, that is, essential for the oncological safety of AS [6]. Less invasive methods are needed to detect disease progression for men in AS to reduce morbidity related to repeated biopsies. Although several biomarkers appear promising tools in the management of AS pts, studies have not provided results robust enough to enable their use in the common clinical practice [7].

In this context, multiparametric magnetic resonance imaging (mpMRI) is becoming a tool to increase identification of more aggressive cancer, improving disease reclassification and thus triggering an active treatment. mpMRI-targeted fusion biopsies (MRI-TBx) of suspicious Magnetic resonance imaging (MRI) lesions [Prostate Imaging Reporting and Data System (PI-RADS) 3−5] can detect aggressive pathological lesions, previously missed by systematic random biopsies (R-Bx) [8−9]. Moreover, the high negative predictive value (NPV) of mpMRI could have implications for a rebiopsy strategy in men with low-risk disease on AS, who might be able to avoid or defer repeat biopsy [10−11].

However, it has been demonstrated that several clinical or pathological variables, such as age [12−13], prostate-specific antigen density (PSAD) [14−15], or the number of positive cores at diagnostic biopsy, are predictors of the risk of reclassification during AS [12,16].

The aim of our study was to evaluate the role of mpMRI in predicting disease reclassification of pts on AS, who underwent confirmatory biopsy (after 12-month interval from initial diagnosis) or follow-up biopsy according to the protocol. We tested whether mpMRI could be considered as a stand-alone test for disease reclassification or if the combination of mpMRI and other clinical variables could represent the most accurate approach to pts on AS.

2. Materials and methods

2.1. Study population

The protocol for the research project was approved by our institutional Ethics Committee (registration number 134/18). We retrospectively evaluated 389 pts, undergoing the AS protocol, collected from 4 Italian centers from January 2016 to December 2018. Pts were selected for AS according to PRIAS criteria. Inclusion criteria were a clinical T1c or T2a disease, a PSA <10 ng/mL, PSAD < 0.2, and ISUP GG1 in ≤2 positive cores, or, in case of saturation biopsies, up to 15% of the total core number can be positive. None of the pts included in this study had mpMRI before inclusion in the AS protocol.

2.2. Biopsy strategy and follow-up

Pts underwent confirmatory or follow-up biopsies according to the PRIAS protocol. Confirmatory biopsy was performed within a 12-month time interval from the inclusion in PRIAS. Follow-up biopsies are indicated 48 and 84 months after the inclusion (per protocol biopsies). Additional biopsies, of the per protocol scheme, were performed in case of PSA >10 ng/mL, PSAD >0.2 ng/ml/cc, changes in digital rectal examination, or PSA doubling time <10 years. All pts underwent mpMRI before confirmatory or follow-up biopsy. mpMRI was standardized and performed on a 1.5 T, with an endorectal coil, or 3 T magnet, using triplanar T2-weighted imaging, axial diffusion-weighted imaging with apparent diffusion coefficient reconstruction, and dynamic contrast-enhanced sequences after injection of paramagnetic contrast agents, according to the PI-RADS, version 2 (V2), guidelines [17]. A dedicated radiologist was available at each center. Central review of mpMRi was not performed.

Pts with mpMRI negative (−) subsequently underwent systematic random biopsies, within at most 3-month time span. Pts with mpMRI positive (+) (defined as having PI-RADS-V2 score ≥3) underwent transrectal or transperineal targeted fusion prostate biopsies (3 cores) + systematic R-Bx (12-18 cores according to prostate volume).

Fusion biopsies were performed using a Hitachi 70 Arietta ecograph with a real-time virtual sonography fusion system (Hitachi Ltd, Tokyo, Japan) with a transperineal approach (Catania) or with a MyLabClassC ecograph with a virtual navigator fusion system (Esaote S.p.A., Genoa, Italy) equipped with an end-fire endorectal probe (Bergamo, Milan). At the Humanitas Research Hospital (Rozzano), a Biojet fusion system and software (D&K Technologies, Braum, Germany) with a transperineal or transrectal approach was used, according to PI-RADS lesion location (Rozzano): transrectal biopsies were performed in case of peripheral gland lesions, while transperineal biopsies were performed for anteriorly located lesions.

2.3. Pathologic evaluation

Each PCa-positive biopsy was evaluated according to ISUP consensus conference on PCa grade groups [18]. ISUP GG1 was defined as the presence of only individual discrete well-formed glands, whereas ISUP Grade Group 2 (GG2) as the presence of predominantly well-formed glands, with a lesser component of poorly formed, fused or cribriform glands. An experienced uropathologist was available at each center.

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2.4. Objectives

The primary objective of this study was to identify upgrading to ISUP GG2 or higher in men on AS with GG1 PCa, according to mpMRI findings (PI-RADS-V2 score). Furthermore, we tested and compared the accuracy of three models in predicting the risk of reclassification, defined as presence of PCa ISUP GG $\geq$ 2 at confirmatory or follow-up prostate biopsy.

2.5. Statistical analysis

Statistical analyses consisted in descriptive statistic to analyze frequencies and proportions of categorical variables or means and 95% confidence interval for continuous variables. Chi-square and Analysis of Variance (ANOVA) tests were used to examine the differences in categorical and continuous variables, respectively. Multivariate logistic regression analysis was used to create three models predicting the probability of disease reclassification: a basic model including only clinical variables (age, PSAD, and number of positive cores at baseline), an MRI model including only the PI-RADS score, and a full model including both the previous ones. The predictive accuracy (PA) of each model was quantified using the Area Under the Curve (AUC). The clinical net benefit deriving from the use of each model was assessed with the use of decision curve analysis.

3. Results

3.1. Patient characteristics are displayed in Table 1

The median patient age and PSA were 67 years (Interquartile range (IQR): 61-72) and 5.8 ng/ml (IQR: 4.1-8.0), respectively. The median PSAD was 0.11 ng/ml/cm^3 (IQR: 0.07-0.17). The median number of positive cores at initial biopsy was 1 (IQR:1,2). MpMRI (−) was recorded in 127 (32.6%) pts; mpMRI (+) was recorded in 262 pts: 72 (18.5%) pts had PI-RADS 3, 150 (38.6%) PI-RADS 4, and 40 (10.3%) PI-RADS 5 lesions. Confirmatory biopsies and follow-up biopsies were performed in 320 and 69 pts, respectively. The rate of reclassification was 34% and 23% in the confirmatory and follow-up groups, respectively. At a median follow-up of 12 months, 125 pts (32%) were reclassified to GG2 PCa and switched to active treatment (mainly open or robotic radical prostatectomy or external beam radiation therapy). In pts with mpMRI (−), the overall rate of reclassification was 17%. In mpMRI (+), the overall rate of reclassification to GG2 PCa, at MRI-TBx plus systemic R-Bx, was 35%, 38%, and 52% according to PI-RADS 3, 4, and 5, respectively ($P < 0.001$).

The participating centers collected 182 pts (Bergamo), 40 pts (Milan), 41 pts (Catania), and 126 pts (Rozzano). No difference in the rate of reclassification was found between the centers: 59 of 182 (32.4%), 14 of 40 (35.0%), 14 of 41 (34.3%), and 38 of 126 (30.1%) for Bergamo, Milan, Catania, and Rozzano, respectively ($P = 0.372$). Seventy-three of the 245 pts (31.1%) who underwent transrectal biopsies and 49 of the 144 pts (33.1%) who underwent transperineal biopsies were reclassified to GG2 ($P = 0.364$). Moreover, the rate of reclassification according to the type of mpMRI performed was similar: 95/317 (30%) vs 28/81 (34.6%) for 3 T mpMRI vs 1.5 T mpMRI, respectively ($P = 0.118$).

Three different models were analyzed. In the basic model, older age, PSAD, and the number of positive cores at baseline biopsy were independent predictors of risk of reclassification ($P = 0.025$; OR = 1.038, $P = 0.001$; OR = 1.54 per 0.1-unit increase, and $P = 0.001$; OR = 1.426, respectively), with a PA of 69% as reported in Table 2. In the MRI model, PI-RADS 3, 4, and 5 were predictors of reclassification (all $P \leq 0.006$; OR = 2.539, 2.925, and 5.275, respectively), and the PA was lower than that in the basic model (AUC 64%) as depicted in Table 3. The full model that includes clinical variables and MRI results had the best PA of 74% Table 4. Older age ($P = 0.023$; Odds ratio (OR) = 1.040), PSAD ($P = 0.037$; OR = 1.324 per 0.1-unit increase), the number of positive cores at baseline ($P = 0.001$; OR = 1.441), and PI-RADS 3, 4, and 5 (overall $P = 0.001$; OR = 2.458, 3.007, and 3.898, respectively) were independent predictors of reclassification. Fig. 1 depicts clinical net benefit deriving from the use of the three evaluated models. Fig. 2 depicts Receiver operating characteristic (ROC) curves with AUC for the 3 predictive models.

4. Discussion

We evaluated the role of mpMRI in predicting the risk of reclassification during confirmatory or follow-up biopsy. We further investigated whether the combination of clinicopatological variables and mpMRI findings may help to better stratify pts at higher risk of reclassification. Our data suggest that disease reclassification increases in case of positive mpMRI findings: the rate of reclassification was 35%, 38%, and 52% in case of PI-RADS 3, 4, and 5, respectively. However, a no-negligible rate of reclassification of 17% was found also in case of negative mpMRI findings (PI-RADS 1-2), suggesting that negative MRI is not accurate enough to omit systematic random biopsies during the AS follow-up. These findings are in agreement with the study by Schulman et al [19] that showed mpMRI may miss up to 15% of clinical significant cancer during the AS follow-up. Several studies have shown that the NPV for the detection of clinically significant PCa, in centers performing high-quality mpMRI, is very high [9–11]. However, Klotz et al [20]

Table 1
Patient characteristics

Variables	Total
Age (yrs),mean (95% CI)	66.7 (66.1 − 67.4)
PSA (ng/mL),mean (95% CI)	6.50 (6.10 − 6.89)
Prostate volume (mL), mean (95% CI)	53.9 (51.4 − 56.3)
PSAD (ng/ml/cc), mean (95% CI)	0.12 (0.09-0.16)
Positive cores at baseline # (%)	
1	226 (58.1)
2	114 (29.3)
>2	49 (12.6)
Biopsy, n (%)	
Confirmatory	320 (82.3)
Follow-up	69 (17.7)
PI-RADS, n (%)	
1-2 (negative)	127 (32.6)
3	72 (18.5)
4	150 (38.6)
5	40 (10.3)
Rebiopsy results, n (%)	
No upgrading	264 (67.9)
GG2	94 (24.2)
$\geq$ GG3	31 (7.9)

PSA: prostate-specific antigen; PSAD: prostate-specific antigen density; PI-RADS: Prostate Imaging Reporting and Data System; GG: Grade Group; CI: confindence interval.

Table 2
Basic Model: Multivariable logistic regression model predicting disease reclassification (presence of GG2 PCa); AUC: 0.69

Predictors	Multivariable analysis	
	OR (95% CI)	*P*-value
Age	1.038 (1.005 − 1.073)	0.025
PSAD (per 0.1-unit increase)	1.548 (1.160 − 1.751)	0.001
Number of positive cores at baseline	1.426 (1.206 − 1.988)	0.001

PSAD: prostate-specific antigen density; GG2: Grade Group 2; PCa: prostate cancer; CI: confindence interval; OR: odds ratio; AUC: area under the curve.

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Table 3
MRI Model: Multivariable logistic regression model predicting disease reclassification (presence of GG2 PCa); AUC: 0.64

Predictors	Multivariable analysis	
	OR (95% CI)	*P*-value
PI-RADS		
1-2	Ref	
3	2.539 (1.301 – 4.953)	0.006
4	2.925 (1.662 – 5.150)	<0.001
5	5.275 (2.437 – 11.418)	<0.001

PI-RADS: Prostate Imaging Reporting and Data System; GG2: Grade Group 2; PCa: prostate cancer; CI: confindence interval; OR: odds ratio; AUC: area under the curve.

Table 4
Full Model: Multivariable logistic regression model predicting disease reclassification (presence of GG2 PCa); AUC: 0.74

Predictors	Multivariable analysis	
	OR (95% CI)	*P*-value
Age	1.040 (1.005 – 1.076)	0.023
PSAD (per 0.1-unit increase)	1.324 (1.017 – 1.724)	0.037
Number of positive cores at baseline	1.441 (1.168 – 1.778)	0.001
PI-RADS		
1-2	Ref	
3	2.458 (1.213 – 4.979)	0.013
4	3.007 (1.643 – 5.505)	<0.001
5	3.898 (1.699 – 8.944)	0.001

PSAD: prostate-specific antigen density; PI-RADS: Prostate Imaging Reporting and Data System; GG2: Grade Group 2; PCa: prostate cancer; CI: confindence interval; OR: odds ratio; AUC: area under the curve.

recently demonstrated in a randomized multicenter prospective study (Active Surveillance Magnetic Resonance Imaging Study - ASIST) that the NPV of mpMRI in their cohort was 85%. Therefore, they confirm our findings, suggesting that systematic biopsy should be always performed, especially in pts with higher risk of clinically significant PCa, according to other clinicopathological parameters, even if mpMRI is negative. On the other hand, they suggested that, in pts with favorable parameters, such as low PSAD or limited PCa core volume, an mpMRI (–) may replace systematic biopsies with reasonable safety.

In the present study, we tested three different models predicting the risk of reclassification at confirmatory biopsy: the mpMRI model, including only the PI-RADS score value, had the lowest PA of 64%. The basic model including only clinical variables (age, PSAD, and number of positive cores at initial biopsy) showed 69% PA. The best result was obtained in the full model, combining mpMRI findings and clinical features, with a PA of 74%.

Older age is associated with higher risk of reclassification, with a 4% increasing risk per year, and the number of positive cores at diagnostic biopsy (per core OR = 1.44), after adjusting for PI-RADS score findings. These results are in agreement with those of Dai et al [12]: they observed that increasing age and more positive cores at diagnosis were associated with a higher risk of reclassification, independent of the PSA value, prostate volume, and type of reclassification biopsy (including MRI-targeted biopsies). Recently, Tosoian et al [16] reported the long-term results of the Johns Hopkins AS program. Older age and the number of positive cores were factors associated to grade reclassification, as well as performance of mpMRI and targeted biopsy at diagnostic or confirmatory biopsy.

Finally, our study supports the role of PSAD in stratifying pt risk of reclassification during confirmatory or follow-up biopsies.

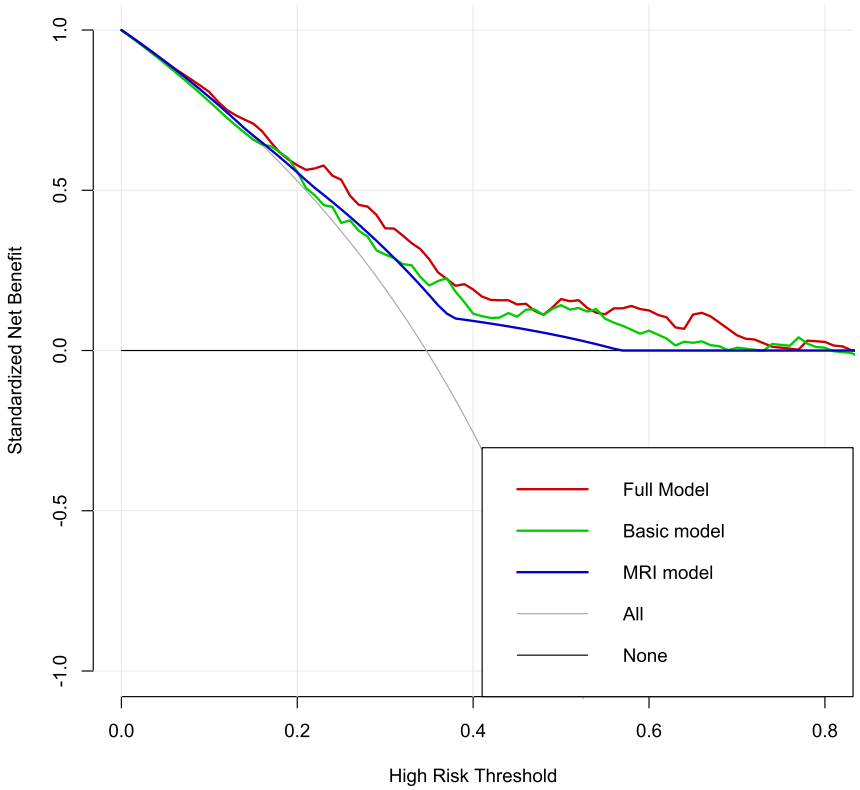

Fig. 1. Clinical net benefit deriving from the use of the three evaluated models.

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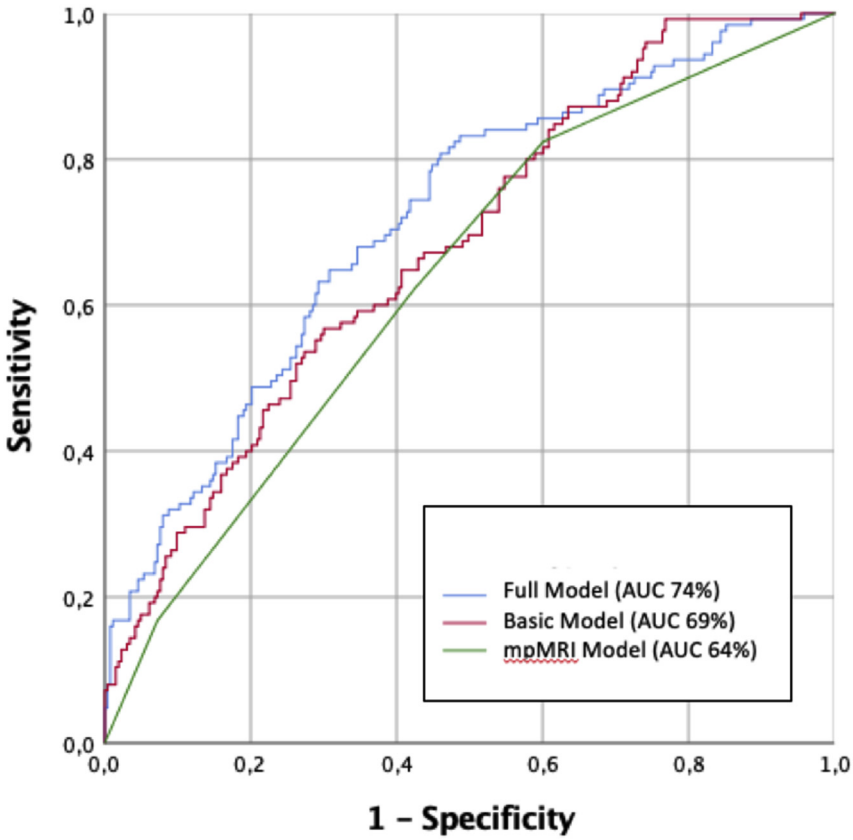

Fig. 2. ROC curves with AUC for the three predictive models. ROC, receiver operating characteristic; AUC, area under the curve.

Indeed, a higher PSAD is associated with higher risk of reclassification (OR = 1.35 per 0.1-unit increase), at any PI-RADS score findings. These results are in agreement with those of Tosoian et al [16] (OR = 1.32 per 0.1-unit increase) and those of Druskin et al [21] (OR = 1.25 per 0.1-unit increase, even though they evaluated the risk of GG3 or more reclassification). Furthermore, it has recently been demonstrated that, in case of PI-RADS 3 or lower and PSAD < 0.15 ng/mL^2, the risk of reclassification is very low, both at MRI-TBx and R-Bx at each time point of AS. Therefore, unnecessary follow-up biopsies in men on AS could be avoided, based on PI-RADS and PSAD risk stratification [14–15].

We are aware that mpMRI and targeted biopsies play a pivotal role in selecting more significant cancer. The recent 2-year follow-up update of the ASIST trial [22] observed a lower rate of upgrading and a 50% reduction in the rate of AS failure in pts submitted to mpMRI and targeted biopsy, compared with those who underwent systematic confirmatory biopsy only, thus highlighting the value of mpMRI in the management of AS pts. However, our results suggest that a combination of readily available clinicopathological parameters, together with the PI-RADS score findings at mpMRI, still allow the risk of reclassification at confirmatory or follow-up biopsy to be predicted with better accuracy.

Several limitations of our study deserve a comment. First, our database consists of a multi-institutional cohort, based on different mpMRI systems and protocols, as well as different fusion biopsy modalities. However, no difference was found in the rate of reclassification between centers performing 1.5 T or 3 T magnet mpMRI. Similarly, our study does not demonstrate differences in the rate of reclassification between centers, whatever biopsy technique, and fusion platform were used. Second, the assessment of targeted and random biopsy specimens was performed by uropathologists from different hospitals. No central review was available for mpMRI or pathologic specimens. However, this is reflective of daily clinical practice, and therefore, we believe that our results are widely applicable. Third, none of our pts had mpMRI at baseline but only before confirmatory or follow-up biopsy. The absence of a baseline imaging could have affected our population of very low– or low-risk PCa suitable for AS, giving a higher risk of reclassification during follow-up protocol biopsies. Moreover, we were not able to assess the role of sequential mpMRI. Indeed, the Prostate Cancer Radiological Estimation of Change in Sequential Evaluation (PRECISE) panel recently provided a consensus set of parameters to define and report radiographic progression on serial mpMRI in men on AS [23], and recent studies suggest that the PRECISE score might allow to monitor AS pts without rebiopsy and limit follow-up biopsy only in men with a PRECISE score of 3 or more on follow-up [24].

5. Conclusions

During the AS protocol, disease reclassification increased according to the PI-RADS score increase, at confirmatory or follow-up biopsy. However, a no-negligible rate of reclassification was found also in cases of mpMRI (–) findings, suggesting that mpMRI (–) is not accurate enough to omit systematic random biopsies during the AS follow-up. The combination of mpMRI and other clinical and pathological variables still represents the most accurate approach to pts on AS.

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Conflicts of interest

All authors have no conflict of interest to declare.

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References

[1]. Clinically Localized Prostate Cancer. AUA/ASTRO/SUO Guideline; 2019 http://www.auanet.org/guidelines/clinically-localized-prostate-cancer-new-(aua/astro/suo-guideline-2019.
[2]. Morash C, Tey R, Agbassi C, Klotz L, McGowan T, Srigley J, et al. Active surveillance for the management of localized prostate cancer: Guideline recommendations. Can Urol Assoc J 2015;9:171–8.
[3]. Suardi N, Briganti A, Gallina A, Salonia A, Karakiewicz PI, Capitanio U, et al. Testing the most stringent criteria for selection of candidates for active surveillance in patients with low-risk prostate cancerx. BJU Int 2010;105:1548–52.
[4]. Lee MC, Dong F, Stephenson AJ, Jones JS, Magi-Galluzzi C, Klein EA. The Epstein criteria predict for organ-confined but not insignificant disease and a high likelihood of cure at radical prostatectomy. Eur Urol 2010;58:90–5.
[5]. Bruinsma SM, Bangma CH, Carroll PR, Leapman MS, Rannikko A, Petrides N, et al. Movember GAP3 consortium. Active surveillance for prostate cancer: a narrative review of clinical guidelines. Nat Rev Urol 2016;13:151–67.
[6]. Loeb S, Vellekoop A, Ahmed HU, Catto J, Emberton M, Nam R, et al. Systematic review of complications of prostate biopsy. Eur Urol 2013;64:876–92.
[7]. Briganti A, Fossati N, Catto JWF, Cornford P, Montorsi F, Mottet N, et al. Active surveillance for low-risk prostate cancer: the European Association of Urology Position in 2018. Eur Urol 2018;74:357–68.
[8]. Recabal P, Assel M, Sjoberg DD, Lee D, Laudone VP, Touijer K, et al. The Efficacy of Multiparametric Magnetic Resonance Imaging and Magnetic Resonance Imaging Targeted Biopsy in Risk Classification for Patients with Prostate Cancer on Active Surveillance. J Urol 2016;196:374–81.
[9]. Schoots IG, Niebor D, Giganti F, Moore CM, Bangma CH, Roobol MJ. Is magnetic resonance imaging-targeted biopsy a useful addition to systematic confirmatory biopsy in men on active surveillance for low-risk prostate cancer? A systematic review and meta-analysis. BJU Int 2018;122:946–58.
[10]. Wysock JS, Mendhiratta N, Zattoni F, Meng X, Bjurlin M, Huang WC, et al. Predictive value of negative 3T multiparametric magnetic resonance imaging of the prostate on 12-core biopsy results. BJU Int 2016;118:515–20.
[11]. Itatani R, Namimoto T, Atsuji S, Katahira K, Morishita S, Kitani K, et al. Negative predictive value of multiparametric MRI for prostate cancer detection: outcome of 5-year follow-up in men with negative findings on initial MRI studies. Eur J Radiol 2014;83:1740–5.
[12]. Dai C, Ganesan V, Nyame YA, Almassi N, Greene DJ, Hettel D, et al. Older Age at Diagnosis and Initial Disease Volume Predict Grade Reclassification Risk on Confirmatory Biopsy in Patients Considered for Active Surveillance. Urology 2019;130:106–12.
[13]. Anderson CB, Sternberg IA, Karen-Paz G, Kim PH, Sjoberg D, Vargas HA, et al. Age is Associated with Upgrading at Confirmatory Biopsy among Men with Prostate Cancer Treated with Active Surveillance. J Urol 2015;194:1607–11.
[14]. Alberts AR, Roobol MJ, Drost FJH, van Leenders GJ, Bokhorst LP, Bangma CH, et al. Risk-stratification based on magnetic resonance imaging and prostate-specific antigen density may reduce unnecessary follow-up biopsy procedures in men on active surveillance for low-risk prostate cancer. BJU Int 2017;120:511–9.
[15]. Schoots IG, Osses DF, Drost FJH, Verbeek JFM, Remmers S, van Leenders GJ, et al. Reduction of MRI-targeted biopsies in men with low-risk prostate cancer on active surveillance by stratifying to PI-RADS and PSA-density, with different thresholds for significant disease. Transl Androl Urol 2018;7:132–44.
[16]. Tosoian JJ, Mamawala M, Epstein JI, Landis P, Macura KJ, Simopoulos Demetrios N, et al. Active Surveillance of Grade Group 1 Prostate Cancer: Long-term Outcomes from a Large Prospective Cohort. Eur Urol 2020;77:675–82.
[17]. Barentsz JO, Weinreb JC, Verma S, Thoeni HC, Tempany CM, Shtern F, et al. Synopsis of the PI-RADS v2 guidelines for multiparametric prostate magnetic resonance imaging and recommendations for use. Eur Urol 2016;69:41–9.
[18]. Epstein JI, Egevad L, Amin MB, Delahint B, Srigley JR, Humphrey PA, Grading Committee. The 2014 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma: Definition of Grading Patterns and Proposal for a New Grading System. Am J Surg Pathol 2016;40:244–52.
[19]. Schulman AA, Sze C, Tsivian E, Gupta RT, Moul JW, Polascik TJ. The contemporary role of multiparametric magnetic resonance imaging in active surveillance for prostate cancer. Curr Urol Rep 2017;18:52.
[20]. Klotz L, Loblaw A, Sugar L, Moussa M, Berman DM, Van der Kwast T, et al. Active Surveillance Magnetic Resonance Imaging Study (ASIST): Results of a Randomized Multicenter Prospective Trial. Eur Urol 2019;75:300–9.
[21]. Druskin SC, Mamawala M, Tosoian JJ, Epstein JI, Pavlovich CP, Ballentine Carter H, et al. Older Age Predicts Biopsy and Radical Prostatectomy Grade Reclassification to Aggressive Prostate Cancer in Men on Active Surveillance. J Urol 2019;201:98–105.
[22]. Klotz L, Pond G, Loblaw A, Sugar L, Moussa M, Berman D, et al. Randomized Study of Systematic Biopsy Versus Magnetic Resonance Imaging and Targeted and Systematic Biopsy in Men on Active Surveillance (ASIST): 2-year Post-biopsy Follow-up. Eur Urol 2019 Nov 7. https://doi.org/10.1016/j.eururo.2019.10.007. pii: S0302-2838(19)30773-0, [Epub ahead of print].
[23]. Moore CM, Giganti F, Albertsen P, Allen C, Bangma C, Briganti a, et al. Reporting magnetic resonance imaging in men on active surveillance for prostate cancer: the PRECISE Recommendations—a report of a European School of Oncology Task Force. Eur Urol 2017;71:648–55.
[24]. Panebianco V, Barchetti G, Simone G, Del Monte M, Ciardi A, Grompone MD, et al. Negative multipara-metric magnetic resonance imaging for prostate cancer: what's next? Eur Urol 2018;74:48–54.

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