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UROGENITAL

Preoperative multiparametric MRI of the prostate for the prediction of lymph node metastases in prostate cancer patients treated with extended pelvic lymph node dissection

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Abstract

Objectives To assess the role of preoperative multiparametric MRI (mpMRI) of the prostate in the prediction of nodal metastases in patients treated with radical prostatectomy (RP) and extended pelvic lymph node dissection (ePLND).

Methods We retrospectively analyzed 101 patients who underwent both preoperative mpMRI of the prostate and RP with ePLND at our institution. For each patient, complete preoperative clinical data and tumour characteristics at mpMRI were recorded. Final histopathologic stage was considered the standard of reference. Univariate and multivariate logistic regression analyses were performed.

Results Nodal metastases were found in 23/101 (22.8%) patients. At univariate analyses, all clinical and radiological parameters were significantly associated to nodal invasion (all $p<0.03$); tumour volume at MRI (mrV), tumour ADC and tumour T-stage at MRI (mrT) were the most accurate predictors (AUC = 0.93, 0.86 and 0.84, respectively). A multivariate model including PSA levels, primary Gleason grade, mrT and mrV showed high predictive accuracy (AUC = 0.956). Observed prevalence of nodal metastases was very low among tumours with mrT2 stage and mrV<1cc (1.8%).

Conclusion Preoperative mpMRI of the prostate can predict nodal metastases in prostate cancer patients, potentially allowing a better selection of candidates to ePLND.

Key points

- *Multiparametric-MRI of the prostate can predict nodal metastases in prostate cancer*
- *Tumour volume and stage at MRI are the most accurate predictors*
- *Prevalence of nodal metastases is low for T2-stage and < 1cc tumours*
- *Preoperative mpMRI may allow a better selection of candidates to lymphadenectomy*

Keywords Magnetic resonance imaging · Prostate cancer · Tumour volume · Lymph nodes · Lymph node dissection

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Abbreviations

PCa	Prostate Cancer
mpMRI	Multi-parametric MRI
RP	Radical Prostatectomy
ePLND	Extended Pelvic Lymph Node Dissection
LN	Lymph Node
N-staging	Lymph Node Staging
mrT-stage	T-stage at MRI
mrV	Tumour Volume at MRI

Introduction

In men treated with radical prostatectomy for localized prostate cancer (PCa), the presence of lymph node (LN)

metastases is a strong adverse prognostic factor associated with higher recurrence rates and with decreased long-term survival [1]. Thus, accurate nodal staging (N-staging) is essential for treatment planning and postsurgical follow-up.

CT, MRI and PET imaging techniques have been widely used for this purpose, but none of these methods proved to be accurate for N-staging prior to surgery [2]. Indeed, CT and MRI rely on dimensional and morphological criteria in the detection of pathologic LNs and are associated with low sensitivity, as metastatic foci may be present in normal-sized LNs [3, 4]. The additional use of functional imaging techniques such as DW-MRI may improve the detection of metastases in non-enlarged LNs, but its role has still to be determined [5, 6]. Interestingly, MRI lymphography with ultrasmall superparamagnetic iron oxide (USPIO) nanoparticles has achieved the best results in the detection of clinically occult nodal metastases, even if its use has been limited by commercial availability and side effects [7]. PET-CT using 11C/18F-labeled choline or targeted radiotracers such as Prostate-Specific Membrane Antigen (PSMA) is currently indicated for restaging of PCa at the time of recurrence, as it is associated with high sensitivity at a per-patient level [8]. Conversely, in the primary setting, its sensitivity remains sub-optimal and varies considerably according to PCa features and LN size [6, 8, 9].

To date, the gold standard for N-staging is still represented by extended pelvic lymph node dissection (ePLND). The decision to perform lymphadenectomy should be guided by the preoperative probability of LN metastases [2, 10], as this surgical procedure is associated with increased morbidity and higher complications rates [11]. The individual risk for nodal metastases can be estimated using preoperative nomograms [12–15]. All these tools, however, rely exclusively on clinical information (PSA, clinical stage, biopsy Gleason score and percentage of positive cores) and do not take in account any information derived from preoperative multiparametric MRI (mpMRI) of the prostate. Conversely, we hypothesized that LN metastases at final histopathology could be predicted by imaging parameters of the primary tumour derived from preoperative mpMRI.

Thus, the purpose of our study was to retrospectively assess the role of preoperative mpMRI of the prostate in the prediction of LN metastases, in a cohort of patients treated with anatomically defined ePLND at the time of radical prostatectomy (RP).

Materials and methods

This is a retrospective study approved by our Institutional Review Board; written informed consent was obtained from all patients.

Study population

The study cohort consisted of a series of 112 consecutive patients who underwent both preoperative mpMRI of the prostate and RP with ePLND at a single tertiary care referral centre, between January 2012 and December 2016 (Fig. 1). ePLND was performed in all patients for a predicted risk of nodal metastases >5%, according to a Briganti nomogram [2, 13]; with patients having a predicted risk ≤5% not undergoing ePLND, and, thus, were not included in our study. Of the patients suitable for the analyses, 11 were excluded for the following reasons: (1) absence of measurable lesion at mpMRI (n=5); (2) poor MRI image quality (n=1); and (3) neoadjuvant hormonal therapy (n=5). The final assessable population consisted of 101 patients. For each patient, the following clinical variables were evaluated: serum PSA level at the time of mpMRI, PSA density and biopsy Gleason grade. Moreover, complete data were available with regards to age at surgery, pathological stage and grade. Presence of nodal metastases at final histopathologic examination was considered the standard of reference.

MRI protocol

All patients underwent a 1.5-T mpMRI study (Achieva and Achieva dStream, Philips Medical Systems, Best, Netherlands) with both surface and endorectal coil (Prostate eCoil™, Medrad®, Indianola, PA, USA). Gastrointestinal peristalsis was suppressed by intramuscular administration of 20 mg of scopolamine-butylbromide (Buscopan, Boehringer Ingelheim) immediately before MR scanning. The imaging protocol fulfilled the requirements of the ESUR guidelines [16], and consisted of multiplanar turbo spin-echo T2-weighted images, echo-planar DWI with b values of 50, 800 and 1600 s/mm^2 (ADC maps were automatically elaborated on a pixel-by-pixel basis using b values of 50

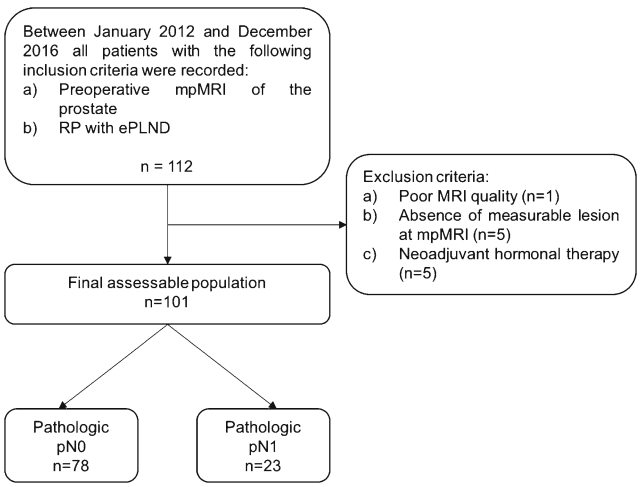

Fig. 1 Flow chart of the study population

and 800 s/mm^2), 3-D fast field-echo dynamic contrast-enhanced (DCE) MRI and delayed axial turbo spin echo T1-weighted images with fat suppression. For DCE-MRI, an IV bolus of 0.1 mmol/kg of gadobutrol (Gadovist, Bayer Schering Pharma, Germany) at a flow rate of 4 ml/s was injected. For patients who had previously undergone prostatic biopsies, mpMRI scans were performed at least after 4 weeks from biopsies, and pre-contrast T1-weighted images were performed to rule out post-biopsy haemorrhagic artefacts.

MRI Image analysis

Images were reviewed in consensus by two radiologists (F.D.C. and G.B. with 10 and 3 years of experience on prostate mpMRI interpretation, respectively) blinded to clinical information and to the final histopathological result. All mpMRI images and suspicious lesions were scored and reported according to the Prostate Imaging Reporting and Data System (PI-RADS) version 2 criteria [17]. For ADC values calculation, region of interests (ROI) were manually drawn on the ADC map including only the inner aspect of the lesion, to reduce partial volume artefacts; the ADC ratio was obtained dividing pathological ADC value by that of a correspondent prostatic area with clear absence of pathologic alterations on the ADC map. When multiple suspicious lesions were detected, only the index lesion was analysed. The index lesion was considered as the one with the highest PI-RADS score, or the one with the highest volume for lesions with the same PI-RADS score. For volume measurement, lesions were manually contoured on each axial slice, and volume was calculated by the dedicated PACS software; final contouring was performed on T2W sequences, although DW-MRI and DCE-MRI sequences were used in conjunction for correct identification and delineation of the lesion, when needed. Information regarding extraprostatic extension, namely extracapsular extension (ECE) and seminal vesicles invasion (SVI), were reported in conjunction as the MRI-stage (mrT-stage) of the index lesion. For the definition of pathologic LNs, a threshold of 10 mm in the short-axis for oval nodes and 8 mm for round nodes was used [18]. On DWI sequences, LNs were considered pathologic when hyperintense on high b-values (800-1600 s/mm^2). For each patient, the following radiological variables were recorded: tumour location, tumour ADC and ADC ratio, tumour volume, tumour stage at MRI, PI-RADS score of the suspicious lesions, presence of enlarged LNs and presence of LNs with restricted diffusion.

Surgery and histopathology

All RPs were performed applying the same anatomic template for ePLND. The ePLNDs consisted in the excision of fibrofatty tissue along the external iliac vein proximally including the bifurcation of the common iliac artery, with the genitofemoralis nerve as lateral limit and perivescical fat as the medial limit. LNs along medially and laterally to the internal iliac vessels were removed. All fibrofatty tissue within the obturator fossa was also removed. Dedicated uropathologists examined the ePLND specimens for the presence of nodal metastasis according to a previously described methodology [13].

Statistical analyses

In descriptive statistics, means, medians and interquartile ranges (IQR) were reported for continuous variables, while frequencies and proportions were reported for categorical variables. Univariate and multivariate logistic regression analyses were performed to test the association between the preoperative variables and nodal invasion. Receiver operating characteristics (ROC) curves were fitted by means of Gaussian kernel estimators with bandwidth selected by unbiased cross validation. To determine optimal cut offs for variables, we dichotomized continuous variables according to the "top-left" rule. To predict nodal invasion, the general linear model was fitted with variables selected by the best subset selection approach, optimizing the Akaike Information Criteria (AIC) [19, 20]. As a measure of the relationship between the variables and the outcome, the fitted logarithm of the Odds Ratios (logOR) was reported. To avoid any optimistic bias, the diagnostic performance of the multivariate model (sensitivity, specificity, negative and positive predictive values) was assessed by Leave One Out Cross Validation (LOOCV). Exact p-values were computed by means of permutation methods, to avoid any distributional assumptions or asymptotic approximation. All statistical tests were performed using R software v.3.0.2 (R Foundation, Vienna, Austria). All tests were two-sided with a significance level set at p value <0.05.

Results

Nodal metastases were found in 23/101 patients (22.8%), with a mean number of pathologic lymph nodes of 3.6 (range: 1-18). The two sub-populations of men with and without nodal invasion did not differ significantly in terms of mean age at MRI and PSA density values (all $p \geq 0.44$); conversely, they differed significantly in all the other clinical, pathological and radiological parameters considered in the study (all $p \leq 0.006$). Clinical, pathological and radiological characteristics of the study cohort are summarized in Tables 1 and 2.

Overall, 13/101 (12.9%) patients had pathologic LNs at MRI suggestive for PCa involvement: enlarged pelvic LNs were found in 6/101 patients (5.9%), LNs with restricted diffusion were found in 11/101 (10.9%) of which 7/11 (63.6%) were normal in size. In patients with nodal metastases, 8/23 (34.8%) had suspected pathologic lymph nodes at

Table 1. Demographic, clinical and histopathological characteristics of the study cohort

Parameter	Overall (n = 101)	pN0 (n = 78)	pN1 (n = 23)	P value
Age at MRI, y				0.44
Mean (median)	64.7 (64.2)	64.4 (64.3)	65.8 (64.3)	
IQR	59-71	58-71	60-71	
PSA level, ng/ml				0.002
Mean (median)	11.2 (7.1)	8.6 (7.0)	21.4 (12.0)	
IQR	5.3-10.8	5.0-10.1	6.4-32.4	
PSA density, ng/ml/cc				0.51
Mean (median)	0.25 (0.19)	0.22 (0.18)	0.35 (0.19)	
IQR	0.12-0.31	0.13-0.28	0.09-0.55	
Biopsy Gleason Score (%)				0.006
6	24 (23.8)	23 (29.5)	1 (4.3)	
7	48 (47.5)	38 (48.7)	10 (43.5)	
8-10	29 (28.7)	17 (21.8)	12 (52.2)	
Primary Gleason Grade (%)				0.001
≤ 3	60 (59.4)	53 (67.9)	7 (30.4)	
≥ 4	41 (40.6)	25 (32.1)	16 (69.6)	
Pathologic stage (%)				<0.001
pT2	52 (51.5)	51 (65.4)	1 (4.3)	
pT3a	31 (30.7)	23 (29.5)	8 (34.8)	
pT3b	18 (17.8)	4 (5.1)	14 (60.9)	
Pathologic Gleason Score (%)				<0.001
2-6	7 (6.9)	7 (9.0)	0 (0.0)	
7	61 (60.4)	55 (70.5)	6 (26.1)	
8-10	33 (32.7)	16 (20.5)	17 (73.9)	
No. of examined lymph nodes				<0.001
Mean (median)	19.8 (16.0)	17.9 (15.0)	26.6 (25.5)	
IQR	12-25	11-24	16-38	
No. of pathologic lymph nodes				-
Mean (median)	-	-	3.6 (2.0)	
IQR	-	-	1-6	

Percentages are referred to the total of patient of the correspondent population (overall, pN0 or pN1). *pN0* absence of nodal metastases at pathologic examination, *pN1* presence of nodal metastases at pathologic examination, *IQR* interquartile, *PSA* prostate specific antigen

preoperative MRI: 4/23 (17.4%) had enlarged nodes and the other 4/23 (17.4%) had normal-sized lymph nodes with restricted diffusion, all located in the same anatomic area of nodal metastases found at histopathologic examination.

Univariate logistic regression analyses and diagnostic performance characteristics of preoperative variables are listed in Table 3. At univariate analyses, all clinical and radiological variables were significantly associated with nodal metastases at final histopathology (all p <0.03). Overall, mpMRI parameters showed the highest accuracy in the prediction of nodal metastases. Among them, tumour volume at MRI (mrV) ≥1cc was the most accurate predictor (AUC = 0.93), followed by tumour ADC < 0.73 x 10^{-3} mm^2/s (AUC = 0.86), and MRI stage of T3 (AUC = 0.84). Seminal vesicles invasion at MRI (mrT3b stage) showed the highest specificity in detecting LN metastases (98.7%), with high positive predictive value (PPV = 92.3%). Conversely, the use of morpho-dimensional criteria and DWI-MR for the detection of nodal metastases showed very low sensitivity (17.3% and 30.4%, respectively), with low PPV (66.7% and 63.6%, respectively) and low accuracy (AUC = 0.57 and 0.63, respectively).

At multivariate analysis, the best estimated predictive model included the following variables: PSA value, primary Gleason grade, tumour stage and tumour volume at MRI (Table 4). Sensitivity, specificity, PPV and NPV of the model were respectively 82.6%, 96.2%, 86.4% and 94.9%, with an AUC value of 0.956. Of the variables included, mrV (p value: 0.001) and MRI stage of T3 (p value: T3a=0.023, T3b=0.003) were independent predictors of LN metastases. When patients were stratified according to tumour stage and tumour volume

Table 2. Radiological characteristics of the study cohort

Parameter	Overall (n=101)	pN0 (n=78)	pN1 (n=23)	P value
Location at MRI (%)				<0.001
PZ	80 (79.2)	63 (801)	17 (73.9)	
TZ	13 (12.9)	13 (16.7)	1 (4.4)	
PZ + TZ	8 (7.9)	2 (2.6)	5 (21.7)	
PI-RADS score				<0.001
3	10(9.9)	9(11.5)	1(4.35)	
4	47 (46.5)	46 (59.0)	1 (4.35)	
5	44 (43.6)	23 (29.5)	21 (91.30)	
Tumour ADC, $10^{-3}mm^2/s$				<0.001
Mean (median)	0.80 (0.79)	0.84 (0.83)	0.67 (0.66)	
IQR	0.69-0.89	0.75-0.92	0.62-0.70	
ADC ratio				<0.001
Mean (median)	0.46 (0.46)	0.48 (0.48)	0.38 (0.38)	
IQR	0.38-0.51	0.42-0.53	0.35-0.41	
Tumour Volume, cc				<0.001
Mean (median)	2.06 (0.50)	0.78 (0.34)	6.46 (3.18)	
IQR	0.22-1.46	0.17-0.76	1.76-6.37	
MRI T-stage (%)				<0.001
mrT2	66 (65.3)	63 (80.8)	3 (13.0)	
mrT3a	22 (21.8)	14 (17,9)	8 (34.8)	
mrT3b	13 (12.9)	1 (1.3)	12 (52.2)	
Pelvic lymph nodes (%)				
Enlarged	6 (5.9)	2 (2.6)	4 (17.4)	0.037
Restricted diffusion	11 (10.9)	4 (5.1)	7 (30.4)	0.003

Percentages are referred to the total or patient of the correspondent population (overall, pN0 or pN1). *pN0* absence of nodal metastases at pathologic examination, *pN1* presence of nodal metastases at pathologic examination, *IQR* interquartile range, *ADC* aparent diffusion coefficient

at MRI, the relative prevalence of nodal metastases was significantly higher in patients with mrT3 tumours, mrV>1 cc tumours, or both (Table 5). Based on these data, the adoption of a cut off of mrT3 and mrV≥1cc for performing PLND would have spared 56/101 (55.4%) PLNDs at the cost of missing 1/23 (4.3%) of patients with nodal metastases.

Table 3. Univariate logistic regression and diagnostic performance analyses

Parameter	Threshold	Sens %	Spec %	PPV %	NPV %	AUC	LogOR	P value
PSA, ng/ml	> 10.5	65.2	79.5	48.4	88.6	0.76	1.98	< 0.001
Biopsy Gleason Score	≥3+4	95.7	29.5	28.5	95.8	0.62	2.22	0.03
Primary Gleason Grade	> 3	69.6	67.9	88.3	68.3	0.69	1.57	0.002
Tumour ADC, $10^{-3}mm^2/s$	< 0.73	82.6	78.2	52.8	93.8	0.86	2.84	< 0.001
ADC ratio	< 0.41	78.2	79.5	52.9	92.5	0.81	2.64	< 0.001
Tumour Volume, cc	≥1	91.3	85.9	65.6	97.1	0.93	4.16	< 0.001
MRI stage								
	T3a	87.0	80.8	57.1	95.5	0.84	3.33	< 0.001
	T3b	52.1	98.7	92.3	87.5	0.75	4.43	< 0.001
PI-RADS score	>4	91.3	70.5	47.7	96.5	0.75	3.22	< 0.001
Enlarged LNs	+	17.3	97.4	66.7	80.0	0.57	2.08	0.02
Restricted diffusion LNs	+	30.4	94.9	63.6	82.2	0.63	2.09	0.002

Sens sensitivity, *Spec* specificity, *PPV* positive predictive value, *NPV* negative predictive value, *AUC* area under the receiver operating curve, *LogOR* logarithm of the Odds Ratio, *LN* lymph node

Table 4. Multivariate logistic regression analysis

Parameter	LogOR	SE	P value
PSA, ng/ml	1.54	0.93	0.096
Primary Gleason grade	1.7	0.94	0.070
Tumour Volume, cc	3.31	1.01	0.001
MRI stage			
T3a	2.21	0.97	0.023
T3b	4.35	1.47	0.003
Multivariable model AUC*		0.956	

*Sensitivity, speccificity, PPV and NPV of the model = 82.6%, 96.2%, 86.4%, and 94.9%

LogOR, logarithm of the Odds Ratio, *SE* Standard Error

Discussion

In men with prostate cancer, the use of CT and MRI for preoperative N-staging is not recommended because of their low sensitivity [2–4, 10].

According to guidelines, the decision to perform nodal dissection should be guided by the preoperative probability of LN metastases [2]. The individual risk can be estimated using preoperative nomograms, currently based on clinical parameters alone [12–15]. Preoperative mpMRI of the prostate, however, may provide additional information regarding several characteristics of the prostatic tumour that are associated with LN metastases.

In particular, prostate mpMRI is the preferred imaging technique for local staging prior to surgery, and improves the prediction of the pathological T-stage when combined with clinical data [2, 21]. This is of great importance in this setting, as higher tumour stage at histopathologic examination is associated with higher rates of nodal metastases [22]. Accordingly, in our study, MRI stage of T3 was an accurate predictor of LN metastases (AUC 0.84), and prevalence of nodal metastases was significantly higher in patients with mrT3 versus mrT2 tumours (57.1% vs. 4.5%; $p<0.001$); overall, mrT3 stage alone showed 95.5% of NPV for nodal invasion.

Table 5. Prevalence of LN metastases according to T-Stage and Tumour Volume at preoperative MRI

MRI T-stage (mrT)		p <0.001
MrT2	3/66 (4.5%)	
MrT3	20/35 (57.1%)	
MrT3a	8/22 (36.4%)	
MrT3b	12/13 (92.3%)	
Tumour Volume (mrV)		p <0.001
< 1cc	2/69 (2.9%)	
≥ 1cc	19/22 (86.4%)	
MRI T-Stage and Tumour Volume		p < 0.001
mrT2 and mrV < 1cc	1/56 (1.8)	
mrT3 and mrV ≥ 1cc	19/22 (86.4%)	

mrT T-stage at MRI, *mrV* tumour at MRI

To our knowledge, the potential role of tumour volume at MRI in the prediction of LN metastases has never been investigated. Tumour volume at histopathology has been correlated to malignant potential, adverse outcome and, more specifically, to the risk of positive nodes [23–25]. Interestingly, we were able to show that tumour volume measured at MRI was the best predictor of LN metastases (AUC 0.93), and the prevalence of nodal metastases was significantly higher in patients with tumour mrV ≥1cc versus mrV <1cc (65.6% vs. 2.9%; $p<0.001$); overall, mrV≥1 cc alone had 97.1% of NPV for nodal invasion. Before the widespread use of prostate MRI, several data derived from random prostate needle biopsy were linked to whole gland tumour volume at pathologic examination (e.g.: number of positive cores, percentage of positive cores and linear millimetres of total carcinoma) [26, 27]. In the study of Briganti et al. [13] the percentage of positive cores represented the most important predictor of LN invasion; similarly, in a novel model proposed to identify candidates for ePLND [15], the maximum percentage of single core involvement and tumour length in cores with the highest and lower grade diseases were predictors of nodal metastases. Direct measurement of the size of the tumour at MRI, however, allows a more accurate estimation of actual tumour volume with good interobserver variability, even if underestimation or overestimation can occur [28–30].

In the present study, the foremost importance of mrT-stage and mrV in the prediction of LN metastases was further supported by the fact that a multivariable model combining these parameters with clinical parameters (primary Gleason score at biopsy and preoperative PSA values), showed very high predictive accuracy (AUC: 0.956). Of note, the observed prevalence of nodal metastases in patients with mrT2 and mrV<1cc tumours was as low as 1/56 (1.8%). Despite all patients were already screened prior to surgery on the basis of a Briganti nomogram, the adoption of a cut off of mrT3 and mrV≥1cc lesions for performing lymphadenectomy would have allowed sparing 55% more PLNDs at the cost of missing only one patient (4.3%) with nodal metastases. Taken together, these data support the potential role of preoperative local tumour staging with mpMRI for the selection of patients that could safely avoid ePLND at the time of RP.

Our results are in line with those of previously published studies [31–33]. In the study of Wang et al. [31] the combination of MRI findings of T3 (ECE, SVI) and N1 disease (enlarged pelvic lymph nodes) with a Partin nomogram improved MR predictive value of nodal metastases. In another study by Park et al. [32] MRI stage yielded the highest accuracy (AUC: 0.954) in the prediction of metastases in normal sized LNs. However, both these studies are based mainly on limited or standard PLND, which can lead to significant underestimation

of nodal metastases [34]. Conversely, all patients included in the present cohort underwent an anatomically defined ePLND. Similar to our study, when ePLND was applied, tumours with PI-RADS scores less than 5 have been associated with very low risk of nodal metastases [33]; of note, the reported prevalence of ECE and SVI at final histopathology in PI-RADS 5 tumours was up to 86.7% and 36.1%, respectively.

In our multivariate model, however, we did not include a PI-RADS score for several reasons. First, PI-RADS 5 lesions are defined as suspicious lesions ≥ 1.5cm in greatest dimension and with definite extraprostatic extension [17]. In our analyses, dimensions and invasive behaviour of the lesions were evaluated by means of tumour volume and tumour stage at MRI: compared to PI-RADS score alone, these parameters provide additional information regarding clinically relevant tumour characteristics (e.g.: exact volume of the lesion at MRI, differentiation between T3a and T3b lesions). Accordingly, in univariate analyses, PI-RADS score proved to be less accurate than both staging at MRI and tumour volume in detecting nodal metastases (Table 3). Furthermore, since tumour volume and MRI stage are highly correlated to PI-RADS 5 score (Fisher's exact test p-value <0.001), the inclusion of all those parameters in regression analyses would lead to incorrect and biased coefficient estimation due to collinearity. Finally, considering tumour volume and stage instead of PI-RADS score enhances the reproducibility of the model, as that information can be reported also by authors adopting the Likert scoring system.

Despite several strengths, our study has limitations. Although we evaluated a high number of men with lymph node metastases, the total number of patients was relatively limited (n=101): further studies with larger and non-selected populations are thus needed to confirm our findings. Moreover, the observed prevalence of nodal metastases in our cohort (23/101, 22.8%) is higher than reported in other series [22], as most of the patients harboured predominantly intermediate or high risk disease. These factors may represent a possible limitation in terms of generalizability of our findings, potentially undermining the reproducibility of the results; for this reason, we did not propose a novel nomogram for individual risk estimation in the present study. On the other hand, it further emphasizes the ability of preoperative mpMRI in detecting a subset of patients with low prevalence of nodal metastases (mrT2 and mrV <1cc) in which ePLND could be potentially avoided, even in a relatively high risk population.

In conclusion, we provided evidence that imaging parameters of prostate cancer at preoperative mpMRI are able to predict nodal metastases at final histopathology. Among them, T-stage and tumour volume at MRI showed the highest predictive accuracy. Together with clinical data, they have the potential to improve the selection of patients that could avoid ePLND and associated morbidity, and should be considered in future updates of preoperative risk prediction models.

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Compliance with ethical standards

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Informed consent Written informed consent was obtained from all subjects (patients) in this study.

Ethical approval Institutional Review Board approval was obtained.

Methodology
- retrospective
- observational
- performed at one institution

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